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Chemical Reactions: Marijuana, Opioids, and Our Families

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Abstract
Chemical Reactions: Marijuana, Opioids, and Our Families is the seventh Massachusetts Family Impact Seminar. This seminar was designed to emphasize a family perspective in policymaking on issues related to the legalization of marijuana and managing the opioid abuse crisis in the Commonwealth. In general, Family Impact Seminars analyze the consequences an issue, policy, or program may have for families.

Keywords
Marijuana, Opioids, Families, Family Impact Seminars, Addication

CHEMICAL REACTIONS:
Marijuana, Opioids, and Our Families

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Chemical Reactions:
Marijuana, Opioids, and Our Families

2016 MASSACHUSETTS FAMILY IMPACT SEMINAR

BRIEFING REPORT

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Purpose and Presenters

In 2009, Clark University was accepted to represent Massachusetts in the Family Impact Institute at the University of Wisconsin — Madison (familyimpactseminars.org), an organization of universities nationwide that conduct Family Impact Seminars. In 2014, the Family Impact Institute moved its host site to Purdue University.

Family Impact Seminars are a series of annual seminars, briefing reports, and discussion sessions that provide up-to-date, solution-oriented research on current issues for state legislators and their aides. The seminars provide objective, nonpartisan research on current issues and do not lobby for particular policies. Seminar participants discuss policy options and identify common ground where it exists.

Chemical Reactions: Marijuana, Opioids, and Our Families is the seventh Massachusetts Family Impact Seminar. This seminar was designed to emphasize a family perspective in policymaking on issues related to the legalization of marijuana and managing the opioid abuse crisis in the Commonwealth. In general, Family Impact Seminars analyze the consequences an issue, policy, or program may have for families.

THIS SEMINAR FEATURED THE FOLLOWING SPEAKERS:

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Introduction

By Denise A. Hines, Ph.D.

Two major issues relating to drugs have been hitting the headlines recently, and Massachusetts legislators are working hard to address them. The first is the legalization of recreational marijuana use in the Commonwealth of Massachusetts.

Although medical marijuana use is currently legal, citizens of our state will be faced with a ballot question in the November 2016 elections regarding whether to legalize recreational use. Polls show that Massachusetts voters are closely divided on the issue, and if they vote for legalization this November, Massachusetts legislators will have the monumental task of figuring out how to implement it.

While we are considering legalizing one substance, another substance has caught legislators' and the public's attention because of its rising rates of abuse, overdoses, and deaths: opioids. As the opioid abuse crisis reaches epidemic levels, legislators are working hard to find ways to help addicts and their families avoid or recover from addiction.

After consultation with legislators, we decided that our 2016 Massachusetts Family Impact Seminar would focus on these two substance use and abuse issues. The title of our seminar in March of 2016 was "Chemical Reactions: Marijuana, Opioids, and Our Families," and we brought in four experts to speak to legislators, their staff, public health officials, and other interested parties.

This briefing report represents a summary of that seminar. It contains the transcripts and slides of the four talks from our seminar. It also contains four policy briefs written by each of our experts that were distributed at the seminar.

Our morning session featured two experts on the use and abuse of marijuana, and on policy options available to deal with it. Dr. Staci Gruber of McLean Hospital and Harvard Medical School spoke about marijuana's influence on the developing brain. Her take-away message was that marijuana is not harmless as it is often thought to be, particularly for adolescents, and therefore, any policies regulating its use needs to consider how to keep it out of the hands of young people. Dr. John Kelly of Massachusetts General Hospital then spoke about the public health and safety impact of potential recreational marijuana legalization. He compared and contrasted it to our history with alcohol legalization, and offered suggestions for how to minimize potential negative public health and safety impacts of recreational marijuana legalization.

Our afternoon session featured two experts on opioid abuse. Dr. Kathleen Palm Reed of Clark University focused on issues of relapse — what predicts relapse and what safeguards can be put in place to try to prevent relapse. Dr. Hilary Smith Connery of McLean Hospital and Harvard Medical School talked about dispelling many of the myths circulating about opioid abuse; she focused particularly on the use of medications to treat opioid addiction, and its co-occurrence with other mental health problems.

The Massachusetts Family Impact Seminars are a project supported by the Mosakowski Institute of Public Enterprise at Clark University. A core mission of the Mosakowski Institute is to improve the effectiveness of government and other institutions in addressing social concerns through the successful mobilization of use-inspired research.

The goal of this seminar series is to provide objective high-quality university-based research to state legislators and their staff, who are well-positioned to make decisions based upon that research. Over the past six years, we have received high marks for our objectivity and the quality of the work we present, and we hope to maintain this reputation in years to come.

The Family Impact Seminars are where research meets policy on family issues. We are part of a national network of universities that do Family Impact Seminars in their states, with one university per state designated as the Family Impact Seminar site for that state. Please consult the following webpage for more information regarding the FIS around the country: purdue.edu/hhs/hdfs/fii

Overall, these Family Impact Seminars have two goals. First, we try to promote greater use of objective, non-partisan university research in policy decisions, and we do this through the presentations themselves; through discussions among the experts, legislators, and other seminar attendees; and through this briefing report.

Second, we try to encourage policymakers to examine the family impact of policies and programs. One way we do this is by encouraging policymakers to ask three questions:

(1) How are families, rather than individuals, affected by the issue?

(2) In what ways, if any, do families contribute to the issue?

(3) Would involving families in the solution result in better policies?

For more information about the Massachusetts Family Impact Seminar, please go to the following webpage: http://wordpress.clarku.edu/dhines/familyimpactseminars/ and/or contact me at dhines@clarku.edu.

The Family Impact Guide for Policymakers

VIEWING POLICIES THROUGH THE FAMILY IMPACT LENS

- **Most policymakers would not think of passing a bill without asking, "What's the economic impact?"**
- **This guide encourages policymakers to ask, "What is the impact of this policy on families?" "Would involving families result in more effective and efficient policies?"**

When economic questions arise, economists are routinely consulted for economic data and forecasts. When family questions arise, policymakers can turn to family scientists for data and forecasts to make evidence-informed decisions. The Family Impact Seminars developed this guide to highlight the importance of family impact and to bring the family impact lens to policy decisions.

WHY FAMILY IMPACT IS IMPORTANT TO POLICYMAKERS

Families are the most humane and economical way known for raising the next generation. Families financially support their members and care for those who cannot always care for themselves — the elderly, frail, ill, and disabled. Yet families can be harmed by stressful conditions —the inability to find a job, afford health insurance, secure quality child care, and send their kids to good schools. Innovative policymakers use research evidence to invest in family policies and programs that work, and to cut those that don't. Keeping the family foundation strong today pays off tomorrow. Families are a cornerstone for raising responsible children who become caring, committed contributors in a strong democracy, and competent workers in a sound economy [1].

In polls, state legislative leaders endorsed families as a sure-fire vote winner [2]. Except for two weeks, family-oriented words appeared every week Congress was in session for over a decade; these mentions of family cut across gender and political party [3]. The symbol of family appeals to common values that hold the potential to rise above politics and to provide common ground. However, family considerations are not systematically addressed in the normal routines of policymaking.

HOW THE FAMILY IMPACT LENS HAS BENEFITED POLICY DECISIONS

- In one Midwestern state, using the family impact lens revealed differences in program eligibility depending upon marital status. For example, seniors were less apt to be eligible for the state's prescription drug program if they were married than if they were unmarried but living together.
- In a rigorous cost-benefit analysis of 571 criminal justice programs, those most cost-beneficial in reducing future crime were targeted at juveniles. Of these, the five most cost-beneficial rehabilitation programs and the single most cost-beneficial prevention program were family-focused approaches [4].
- For youth substance use prevention, programs that changed family dynamics were found to be, on average, more than nine times more effective than programs that focused only on youth [5].

QUESTIONS POLICYMAKERS CAN ASK TO BRING THE FAMILY IMPACT LENS TO POLICY DECISIONS:

- How are families affected by the issue?
- In what ways, if any, do families contribute to the issue?
- Would involving families result in more effective policies and programs?

HOW POLICYMAKERS CAN EXAMINE FAMILY IMPACTS OF POLICY DECISIONS

Nearly all policy decisions have some effect on family life. Some decisions affect families directly (e.g., child support or long-term care), and some indirectly (e.g., corrections or jobs). The family impact discussion starters below can help policymakers figure out what those impacts are and how family considerations can be taken into account, particularly as policies are being developed.

Family impact discussion starters

How will the policy, program, or practice:

- support rather than substitute for family members' responsibilities to one another?
- reinforce family members' commitments to each other and to the stability of the family unit?
- recognize the power and persistence of family ties, and promote healthy couple, marital, and parental relationships?
- acknowledge and respect the diversity of family life (e.g., different cultural, ethnic, racial, and religious backgrounds; various geographic locations and socio-economic statuses; families with members who have special needs; and families at different stages of the life cycle)?
- engage and work in partnership with families?

Ask for a full Family Impact Analysis

Some issues warrant a full family impact analysis to more deeply examine the intended and unintended consequences of policies on family well-being. To conduct an analysis, use the expertise of both family scientists, who understand families, and policy analysts, who understand the specifics of the issue.

- Family scientists in your state can be found at familyimpactseminars.org
- Policy analysts can be found on your staff, in the legislature's nonpartisan service agencies, at university policy schools, etc.

Apply the Results

Viewing issues through the family impact lens rarely results in overwhelming support for or opposition to a policy or program. Instead, it can identify how specific family types and particular family functions are affected. These results raise considerations that policymakers can use to make decisions that strengthen the many contributions families make for the benefit of their members and the good of society.

ADDITIONAL RESOURCES

Several family impact tools and procedures are available on the website of the Family Impact Institute (familyimpactseminars.org).

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We are especially grateful to Sen. Jason Lewis, Co-Chair of the Joint Committee on Public Health. He and his staff, particularly Dennis Burke, provided invaluable guidance to the marijuana portion of this seminar, and we were honored that Sen. Lewis provided opening remarks at our seminar.

We would also like to thank the House Co-Chair of the Joint Committee on Public Health, Rep. Kate Hogan, and the Co-Chairs on the Joint Committee on Mental Health and Substance Abuse, Sen. Jennifer Flanagan and Rep. Elizabeth Malia, who gave us their time and guidance on our presentations this year.

We would like to express our continued gratitude for the support of the Co-Chairs of the Joint Committee on Children, Families and Persons with Disabilities: Rep. Kay Khan and Sen. Jennifer Flanagan. They and their staff members, particularly Ernestina Mendes, provide continued guidance on the selection of our topics each year.

The Massachusetts Family Impact Seminars are a project of the Mosakowski Institute for Public Enterprise at Clark University. The support of the staff at the Mosakowski Institute has been essential for the execution of the Family Impact Seminars. Our thanks go to Lisa Coakley, Executive Assistant to the Director, Jana Kelnhofer '18, Mickayla Aboujaoude '17, Samantha Arsenault '15, '16, and Sarah Philbrick '15, '16.

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For more information about the Massachusetts Family Impact Seminars, please contact:

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Taking a Hit: Assessing the Impact of Early Onset Marijuana Use on the Brain

By Staci A. Gruber, Ph.D.

POLICY BRIEF

Marijuana is seemingly everywhere, from newspaper and television headlines, to online blogs and social media feeds, and it remains the most widely used illicit substance in the world.

RECREATIONAL MARIJUANA USE IN ADOLESCENCE

With the ongoing debates regarding legalization of recreational marijuana and approval of medical marijuana in more than 23 states, it is important to consider what children and adolescents are thinking. According to the most recent national Monitoring the Future Survey,[1] 16.5% of 8th graders, 14.8% of 10th graders, and 21.3% of 12th graders had used marijuana in the past month. Also, for the first time in the survey's 40-year history, daily marijuana use (6%) was reported to be higher than daily cigarette use (5.5%) in this age group.

Unfortunately, adolescence is a particularly vulnerable period for exposure to substances, including marijuana, because the brain not only continues to develop during this time, but critical reorganization of neural networks occurs. Through a process known as pruning, frequently used neuronal pathways are refined and strengthened, while weak connections are culled. During this period, the brain is primed for rewarding behaviors, and is marked by risk taking and impulsivity.

The brain may also be more vulnerable during childhood and adolescence because it is "wired" for marijuana. The human brain is comprised of cannabinoid receptors designed to interact with the body's natural chemicals; however, the main psychoactive component in marijuana, Δ-9 THC (delta-9-tetrahydrocannabinol), also fits into these receptors. During adolescence, the level of cannabinoid receptors peaks, and accordingly, exposure to THC may alter brain function and structure in regions rich with these receptors.

WHY MARIJUANA IS NOT AS HARMLESS AS YOUTH BELIEVE

Given this information, it is not surprising that marijuana use during adolescence has been specifically linked to deficits in cognitive performance as well as alterations in brain structure and function. Comprehensive reviews of marijuana smokers have revealed that teenage onset of marijuana use is associated with greater alterations than those who begin using during adulthood.[2] Weekly or more frequent marijuana use during adolescence has been linked to reduced performance on measures of IQ, attention, memory, and processing speed; most notably, it has been linked to reduced executive functioning, which are processes involved in inhibiting impulsivity, shifting strategies, self-monitoring, and planning.[2, 3]

Further, longitudinal studies have found that increased marijuana use predicts reduced attention[4] and some aspects of memory.[5] Neuroimaging studies have revealed that changes in brain function and structure underlie these cognitive decrements. Adolescent marijuana users demonstrate alterations in brain function across numerous regions.[6]

In addition, marijuana use during this critical period is associated with decreased integrity of white matter, which is responsible for efficient communication between and within brain regions. White matter changes may also be related to increased impulsivity. In one study, lower white matter integrity was related to higher levels of impulsivity specifically within marijuana smokers who began using regularly prior to age 16.[7]

Taken together, regular exposure to marijuana during adolescence may disrupt healthy neurodevelopment. Given the high rates of marijuana use among adolescents and teens, this may suggest that a large proportion of youth experience some cognitive difficulties related to marijuana use, which are also likely to impact academic performance.

Despite this mounting evidence, perceived risk and harm related to marijuana use is at its lowest levels since the 1970s. These perceptions are likely due to ongoing debates regarding legalization of marijuana that often underscore the benefits of marijuana, while overshadowing potential negative consequences.

In fact, the majority of high school seniors do not believe that regular marijuana use is harmful; less than 32% believe that regular use is associated with great risk, which is a sharp decline from five years ago when more than 50% reported great risk associated with regular marijuana use.[1]

In addition, the potency of marijuana (percentage of THC) is rising. Potency is estimated to have increased from 3.4% in the 1990s to 8.8% in 2008.[8] Unfortunately, national trends also reveal an increase in the use of butane hash oil (BHO) and other concentrates, particularly among younger populations, which can contain up to 50-80% THC. This raises concern about whether marijuana users may experience more pronounced cognitive deficits and alterations in brain structure and function because they are using products with such high levels of THC. This is particularly troublesome because adolescence is a critical time of neuromaturation, with increasing evidence that the adolescent brain is more vulnerable to the effects of drugs than the adult brain. **Accordingly, those at the greatest risk for adverse consequences represent a growing population of consumers of marijuana, posing a serious public health concern.**

THOUGHTS FOR THE FUTURE: IT'S WORTH THE WAIT

At this point, policy has outpaced science, with critical questions regarding the effects of marijuana still unanswered. As policy is drafted, it will be important to consider how recreational and medical marijuana use differ. For example, many who seek out marijuana for medical reasons are drawn to products high in cannabidiol (CBD), which has therapeutic potential for a number of conditions and can prevent and/or mitigate adverse affects often associated with recreational marijuana use.[9]

In fact, the director of the National Institute on Drug Abuse (NIDA), Dr. Nora Volkow, commented, "CBD appears to be a safe drug with no addictive effects, and the preliminary data suggest that it may have therapeutic value for a number of medical conditions." Research dedicated to understanding the differences between marijuana use (recreational vs. medical, adolescent vs. adult onset, THC vs. CBD content, etc.) is particularly important as more states continue to move toward legalization of recreational and medical marijuana.

Many policymakers, consumers, physicians, and the general public remain misinformed about marijuana, yet it has never been more important to understand the impact of marijuana on the brain, particularly in our nation's most vulnerable population — adolescents and emerging adults. Efforts targeted at early identification, education, and intervention regarding the potential negative consequences of recreational marijuana use are critical as the nation grapples with understanding marijuana as both a recreational substance and a medicine.

While the message "just say no" was not particularly successful, **"just not yet"** is likely a more easily adopted message, especially if paired with meaningful data that resonate personally with adolescents. Empirically sound interventions aimed at identifying, delaying, and decreasing marijuana use among youth must be consistently implemented to optimize neurodevelopmental trajectories and minimize the impact of marijuana use on the developing brain.

As states consider legislation for both recreational and medical marijuana use, it is imperative to determine safe guidelines regarding the impact of marijuana on the brain, particularly during critical periods of neurodevelopment.

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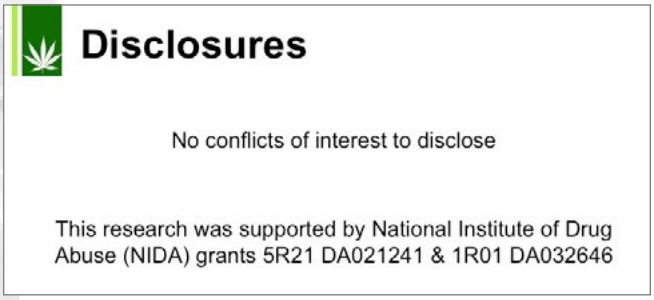
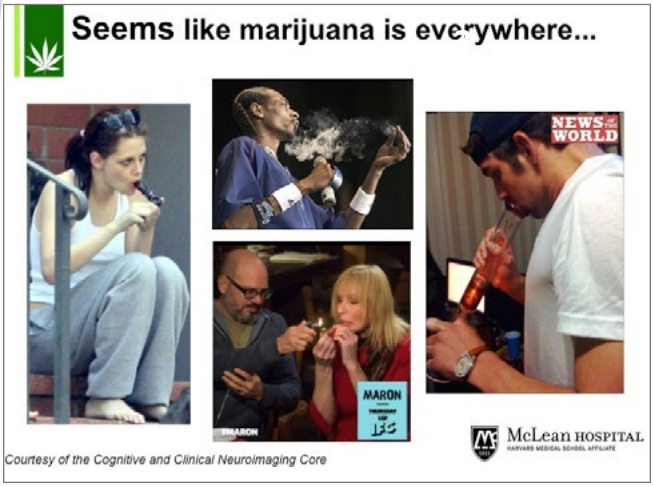
Dr. Staci Gruber is director of the Cognitive and Clinical Neuroimaging Core and associate professor of psychiatry at Harvard Medical School. Her clinical and research focus is the application of neurocognitive models and multimodal brain imaging to better characterize neurobiological risk factors for substance abuse and psychopathology. Dr. Gruber's lab has examined the etiologic bases of neural models of dysfunction in patients with psychiatric disorders as well as marijuana-abusing adults. She has published in numerous journals and been the focus of national and international symposia and press conferences.

TRANSCRIPT OF DR. GRUBER'S TALK

Today, it's an honor to come and talk to you a little bit about the ability to assess the impact of early onset marijuana use on the brain. What do we mean by that? What do we mean by early onset? What do we mean by impact on the brain? I'm going to get to all of that.



First and foremost, I have no conflicts of interest to disclose and the research that I'll present that is from my lab is funded by NIDA, the National Institute of Drug Abuse.



Courtesy of the Cognitive and Clinical Neuroimaging Core

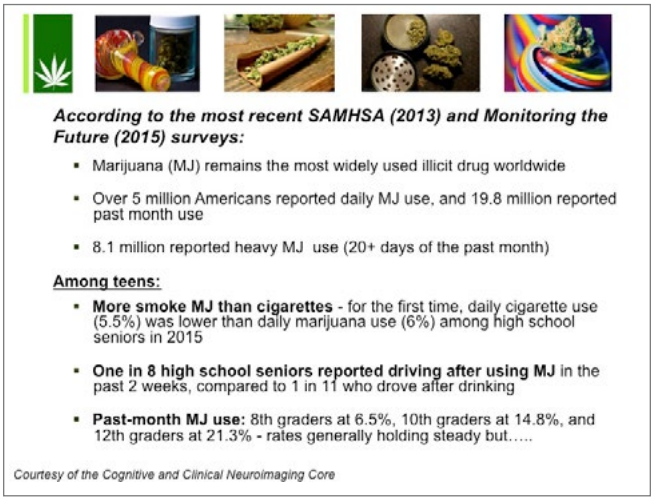
It's always nice to follow a policymaker who literally says things like, "We know people are going to use marijuana, now what do we do about it?" In fact, that seems to be true. And you basically have to be living on Mars at this point not to realize that marijuana is everywhere. It's in our newsfeeds. It's in our social media. Every day there's something new on the radio or the TV about potential negative impact of recreational marijuana, potentially unbelievable therapeutic potential of medical marijuana for yet another indication. It may cure everything.

So it really is everywhere, and I have to tell you when I looked for images to put this first slide together. I didn't have any paucity of data for people smoking marijuana pretty much out in the open. It just goes to show, it's not hard to find.

Why is that? As I think you're going to hear from our next speaker, marijuana is on everybody's mind because of course, when we consider the stakes of marijuana. We now have 23 states, plus DC and Guam, which have passed full medical marijuana laws. Another 18 have partial medical marijuana laws. Those marijuana laws are specific to one constituent of marijuana, which I'll talk about in a few minutes.

Of course, recreational marijuana is legal in four states, plus DC. Then there are nine states that have not prohibited marijuana. That's for now. A number of those nine states have pending legislation, as we do here in Massachusetts, with regard to the issue of legalizing recreational marijuana use.

This is why everybody is talking about it. It's on everyone's mind because it's across the country. You cannot escape it. I was talking to one of my colleagues earlier, and I realized that I've been at my hospital almost 27 years, and of those 27, I've been involved in marijuana research for 25. So even though we're now talking about the green rush, trust me, it's been going on a lot longer than the last few years.



Courtesy of the Cognitive and Clinical Neuroimaging Core

So that's what people know about marijuana. We're talking about it. It may be good. It may be bad. Some of the things that people aren't necessarily aware of are some of the better points that come from these wonderful national surveys.

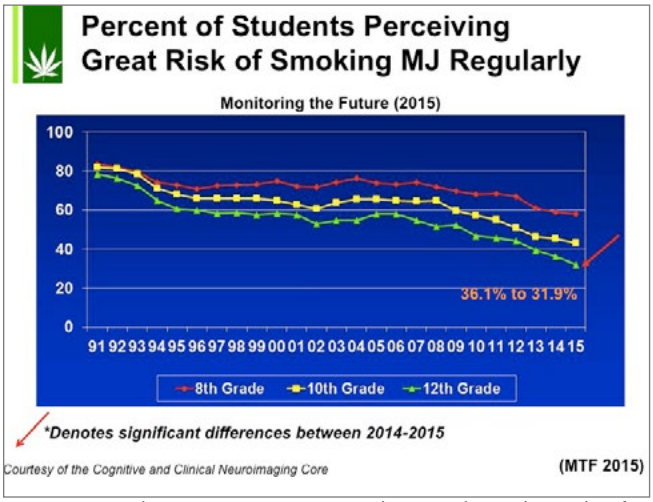
Monitoring the Future is a wonderful survey that basically assesses our 8th, 10th, and 12th graders across the country, not just with regard to marijuana use and alcohol use, but for all sorts of things. We get this great data every year, and every year we look at different use rates of prescription drugs, non-prescription drugs, marijuana, alcohol, you name it. Then of course, we have data from SAMHSA and other organizations telling us about use rates in general in the population.

What we know, currently, is that marijuana is the most widely used illicit substance worldwide, not just in the US. I say illicit because currently, let's just remember, it is a class 1 substance. So according to the DEA, it's a class 1 substance, just like heroin and LSD. It may be a little bit counter to what people think of when we think of legalized medical marijuana use in states, because in fact, it is still a federal offense to use marijuana.

However, over 5 million Americans report daily marijuana use, and almost 19 million report use within the last month. These are not small numbers of people. Of those folks who are using, more than 8 million report using heavily. What do I mean by that? Heavily is defined by more than 20 days of use in a month, in this particular case.

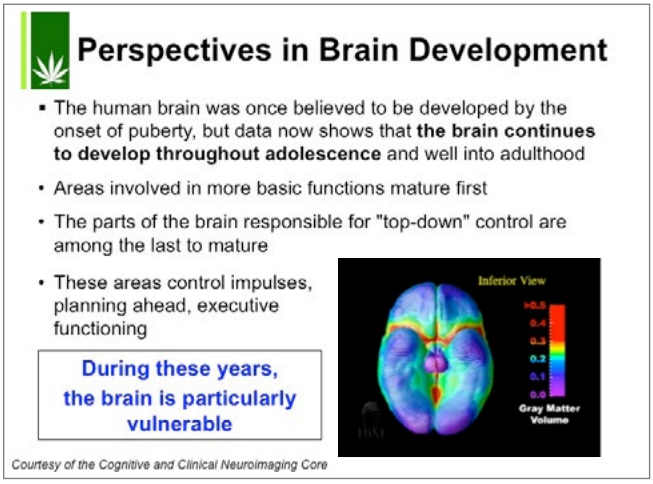
Among teens, very germane to us today, when we think about the impact of some of these things on families and our teens, our most vulnerable population. For the first time, the Monitoring the Future study has basically demonstrated that there are more high school seniors who smoke marijuana every day at 6%, than use cigarettes at 5.5%. First time. We also see about 1 in 8 high school seniors get behind the wheel after smoking marijuana. That's compared to 1 in 11 who get behind the wheel after drinking. I don't even want to talk about the numbers who get behind the wheel after doing both because it has some very special and unfortunate circumstances when you couple them together.

In the past month, marijuana use for the first time, in the Monitoring the Future Study, has demonstrated that use rates are starting to level off. I used to give talks like this and say use rates are continuing to climb. They're now starting to level off, but among 10th graders for example, 14.8% are using. With 12th graders, over 21% are using, and that number, again, is holding steady. It didn't increase. However, what's not holding steady is the perception of risk and harm associated with marijuana use.



I'm going to draw your attention to this graph on this side. If you look at the far right of the graph here, you can see that between 2014 and 2015, the number of high school seniors that perceived great risk or harm associated with marijuana use dropped significantly from over 36% to just under 32%. That was in one year. Perception of risk and harm is continuing to drop.

That's our first really important take home message. Why is it continuing to drop? Probably because of our ongoing discussions and debates about the potential utility of things like medical marijuana and the fact that four states plus DC now have recreational marijuana that's legal with a number of other states, including Massachusetts, with pending legislation.



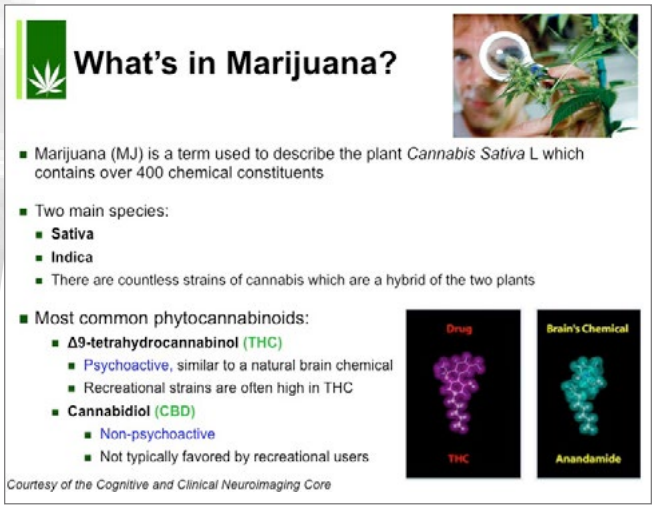
Is marijuana as harmless as our youth are led to believe? Long ago before the advent of MRI technologies which allow us to look at the brain over time in a non-invasive, non-harmful way, we believed that the human brain was done

with regard to development by the time we hit puberty. Poof. Sexual maturity. We must be done. Nothing else is really happening.

In fact, we now know that the brain continues to develop throughout the second, and into the third decade of life. So, the brain basically develops from the back to the front and from the bottom to the top. Areas involved in basic functions mature first, like senses and the ability to move: our limbic system.

Parts of the brain that are responsible for things like top-down processing, what we call the seat of executive function. What do I mean by that? What are executive functions? The frontal part of your brain is the last part to become fully developed, and in fact, the part that's responsible for things like planning, being able to inhibit inappropriate responses, being able to control impulses. Very last part to come on line. We actually have the term executive function because we think of the frontal cortex as the brain's CEO. Think of it as being in charge, pretty much of everything. So just remember, it's the last to become fully developed.

During development, especially adolescence, the brain is particularly vulnerable, not just to marijuana, but to things like drugs, illness, and injury. It is under construction. It's not fully developed, so almost anything potentially could impact the system.



We have the term marijuana, and we hear it and use it pretty freely. In fact, it's not just one thing. This is another really critical point for all of us to remember. Marijuana really is a term that's used to describe anything that comes from the plant *Cannabis Sativa L,* of which there are hundreds of constituents. We know there are different strengths and species of marijuana.

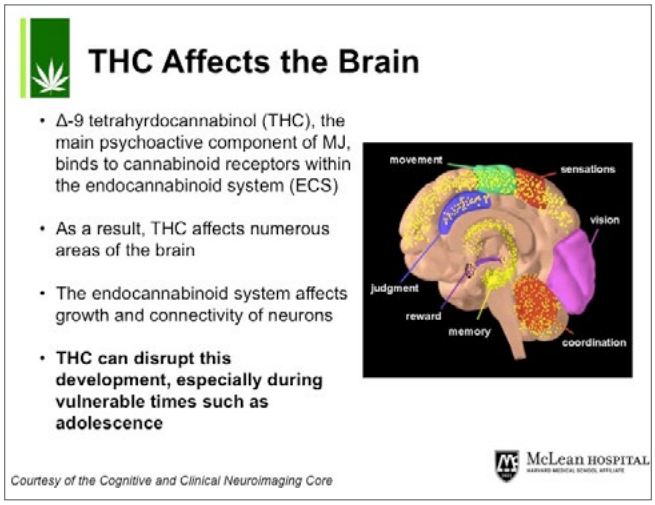
My recreational users are very happy to tell me the differences between *Sativa* strains, which are energizing ("I feel so happy"), and *Indica* strains, which tend to mellow them out and relax them. Most people use a hybrid, but the important thing to remember is that the constituents of cannabis, the actual chemicals in the plant itself, are different. They are not all the same.

The most common constituent that we talk about is Δ9 tetrahydrocannabinol. THC is what gets you high. That's the constituent that most recreational users are looking for in their marijuana. In fact, if they don't get it, they really want their money back. I heard that last week.

So recreational strains are particularly high in THC. I can tell you that over the last several years, THC levels are continuing to increase in marijuana. Our recreational users are averaging somewhere between 12% and 14% THC. I'll show you how that is different from years past.

Cannabidiol is something we've often heard about or more recently heard about in the media. It's another primary constituent of the same plant, except it's not psychoactive. It's been shown to have potentially therapeutic indications for a number of conditions. Not typically favored by recreational users. If you get something that's not high in THC, you want your money back.

I draw your attention to the bottom right of this slide. THC is in purple. Notice how similar that structure is to what is to the right of it. That's one of our brain's own chemicals called Anandamide. As it turns out, we actually have our own cannabinoid system: the endocannabinoid system, consisting of chemicals and receptors. Basically the endocannabinoid system that we have is responsible for growth and connectivity of neurons. It's responsible for keeping a pretty homeostatic environment. Mood, memory, pain, and appetite are all regulated by the endocannabinoid system.



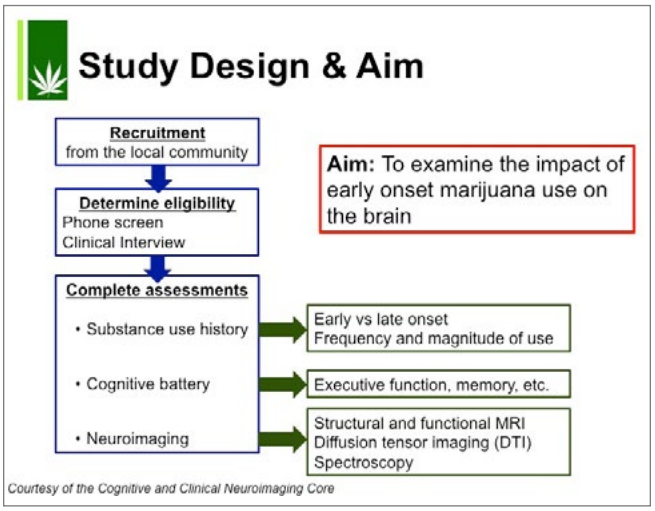
So we have these receptors, but as you saw, it's pretty similar in terms of Anandamide to THC. As it turns out, THC binds to these same receptors that we have, and those yellow dots throughout the brain basically demonstrate where we have these receptors, and there's almost no brain area that's excused from having these receptors.

When you use marijuana, especially if you're smoking or vaporizing, which is the fastest way to get high, it binds to these receptors and you get an effect. So it affects a number of different parts of the brain.

THC exposure, especially during adolescence or what we would call a period of vulnerability (remember I told you that brain is still under construction), may actually disrupt the way that neurons are supposed to be developing as a result. That's my take home point here. As a result, there have been a number of studies that are particularly focused on the impact of early onset marijuana use. Is there, in fact, an impact of using marijuana early while the brain is still under construction?

There have been studies that look at age of onset of marijuana use, but no studies until more recently had really looked at those with early onset use. What do I mean by that? For my own data, we tend to put people in classifications of early onset users as those who begin a pattern of regular consistent use prior to age 16 versus those who begin using later. Would there be a difference if we looked at them head-to-head? Not just does earlier onset make a difference, but also do people look different from those who started smoking later?

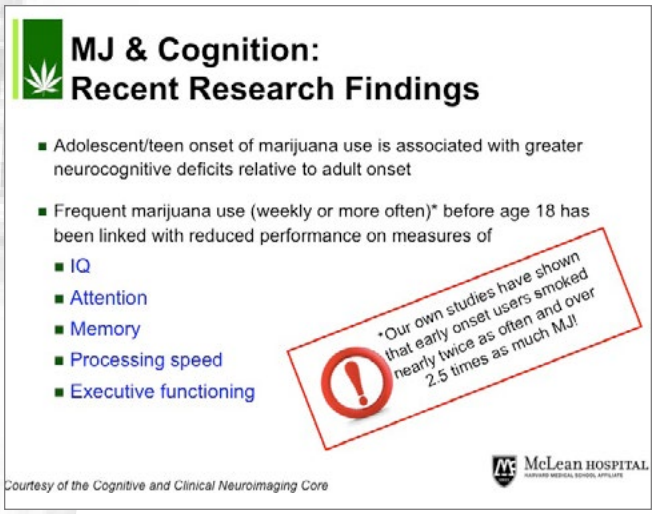
I'll show you some data from other folks' studies, and data from my own just as a way of making it a little bit more real world. Remember that these studies are basically dependent upon recruiting people from all around this area, and sadly, I have no trouble recruiting. I'm just going to say that. For our recreational studies, we have no trouble getting folks who are interested in participating, which is a great thing. But certainly we have a number of people who are using.



We recruit from the local community. We do a very comprehensive screen to make sure that folks meet eligibility. What do you have to do to get into one of my studies? For our chronic heavy smoking studies, people have to smoke a minimum of 1,500 times in their lives. They have to report smoking 4 or 5 of the last seven days. Their urine has to be positive for cannabinoids, and they can't have any other psychological or medical condition. We also recruit healthy controls and they're matched pretty well with one exception: They can't have used any substance, even marijuana, more than five times.

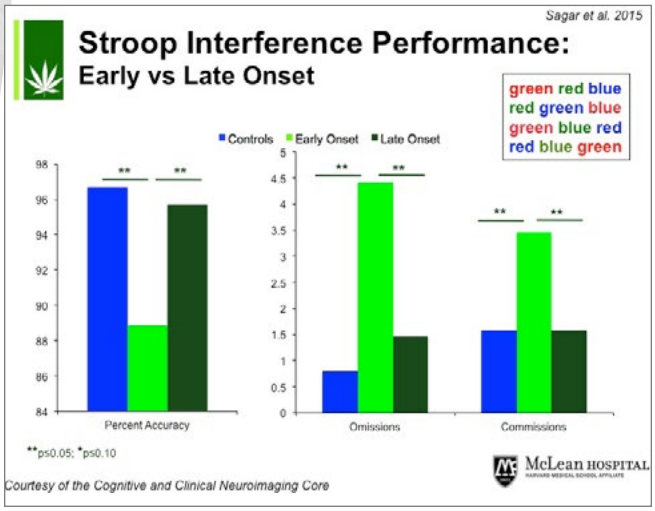
They come into our lab, and we give them a lot of different assessments from clinical and diagnostic interviews, to clinical state measures, to see how they are with regard to mood. Substance abuse history is pretty extensive for themselves and their family members. We do a very comprehensive cognitive battery where we use pencil and paper measures and computerized tasks to look at the way their brain is functioning, and, of course, a suite of neuroimaging measures so that we can look at brain structure and function and in some cases chemistry and connectivity.

Our goal is to examine the impact of early onset use on the brain. Is there a difference in frequency and magnitude of use? What if you start using early, but you don't use much? Or you don't use too often? Does that matter? These are some of the questions that we like to ask.



To summarize what we know in general from studies of cognitive performance, I can tell you that adolescent and teen onset of marijuana use is typically associated with greater deficits on a range of cognitive measures. Most specifically, the most commonly reported difficulties are in things like verbal memory, executive functions — these things mediated by the frontal cortex — and processing speed.

We also have some reports of reduction in IQ in one longitudinal study that's been reported. We can talk about that during the question and answer period if anybody wants more information about that. Our own studies have basically demonstrated that early onset users, compared to late onset users, use twice as often and almost more than 2.5 times as much marijuana per week, as those who started smoking after age 16. So that's pretty significant.



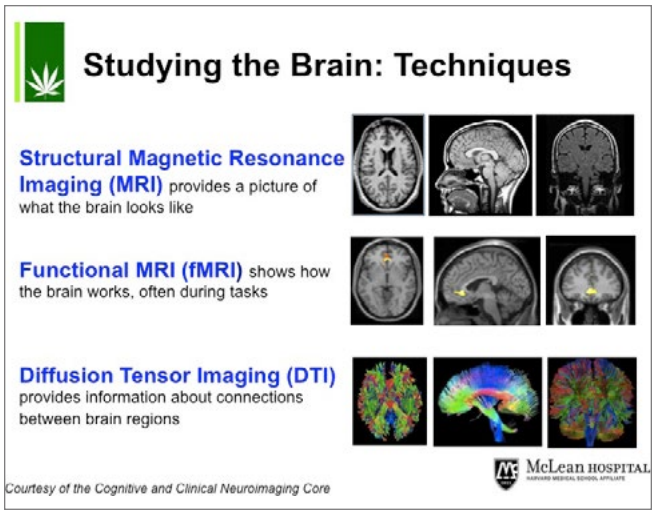
When I talk about these executive functions, what do I mean? There are a lot of different measures we give, but I love this one because it's very colorful. This is called the Stroop color word test, and some of you may be familiar with this. Some of your kids may have this app on their phone. You may have seen this in graduate school. Very simple. Three conditions. The first: color naming. Subjects simply name colors. They are red, blue, and green. Single syllable colors. Nice and easy, as quickly as they can. Then we have words printed in black ink, and subjects are asked to read the words. Reading is the most automatic process you have. You can't help but read a word printed in your native language. It's very automatic.

Then we have the interference condition. Now we have words printed in different colored ink than they'd spell, and what we'd like you to do is inhibit — use that frontal cortex and don't read the word, but name the color of the ink. It sounds very easy, and probably the first few you would do really well, and then nobody wants to be singled out because invariably somebody makes a mistake. I get a lot of different responses that are not red, blue, and green, by the way. They're also single syllable.

So we do this task, and it's very interesting because what we're really looking for is how well they do the interference condition. We look at smokers, and split them into early onset and later onset users versus controls. The controls are in blue. The late onset group is the dark green bar, and the early onset group is the light green bar.

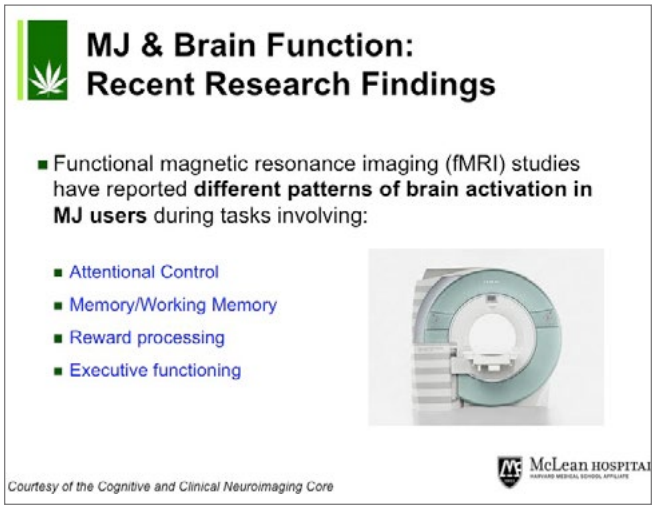
When you look at smokers versus controls, they look different. But it turns out the differences between the two groups — smokers and non — are almost exclusively driven in every case by the early onset group. I draw your attention to the first panel on the above slide: percent accuracy. Significantly lower accuracy in the early onset group compared to the later onset group and the controls.

Commission errors are a direct measure of a failure to inhibit an inappropriate response. The higher the commission errors, the worse they are doing at the task. Significantly higher commission errors in the early onset group compared to the others. This is critically important. It's not just smokers as a whole. The early onset group is really driving it.

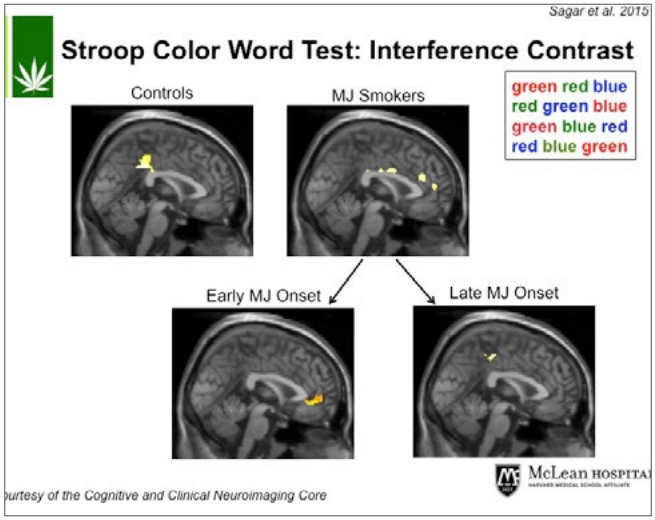


I spend a lot of time doing brain imaging and we have a lot of different techniques that we utilize. Everybody in this room definitely is familiar with MRI, right? Magnetic Resonance Imaging. It's really revolutionized the way that we are able to do neuroscientific experiments. It gives us a picture of what the brain looks like, and we can actually measure discrete areas of the brain. Gray matter, the hard working neurons part of the brain versus white matter, which connects brain regions to each other.

FMRI — pretty great technology — allows us to look at how the brain is working during tasks. Then diffusion imaging or DTI allows us to look at how organized or coherent white matter is. What's the strength of the white matter connection? Again there are a lot of other techniques. I'm just going to highlight these really quickly.

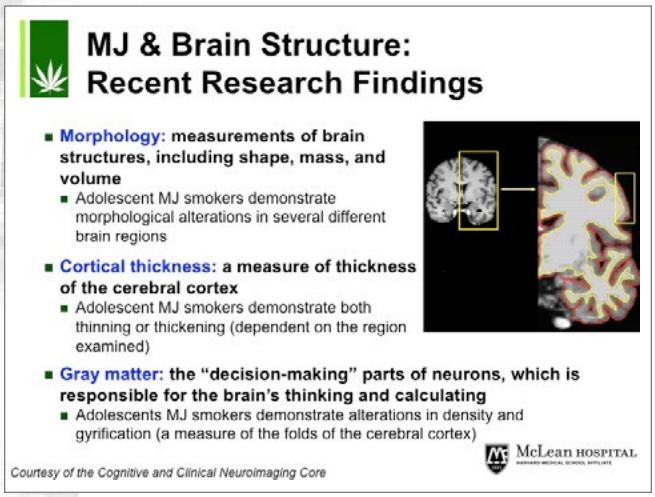


To summarize what we know in general about FMRI studies of individuals who use marijuana, specifically during adolescence: What we see are different patterns of brain activation in those who use early versus those who don't. These are predominantly during tasks that require additional control, memory or working memory, reward processing, and executive functioning, the last part of the brain to become fully developed.



This is data from my own lab. Here's that same Stroop test. The interference condition. Now they're doing it in the scanner. You don't have to be a neuroscientist to know that these two images look different, and if anybody has any questions about how these data are analyzed or acquired, we can certainly talk about it at the break.

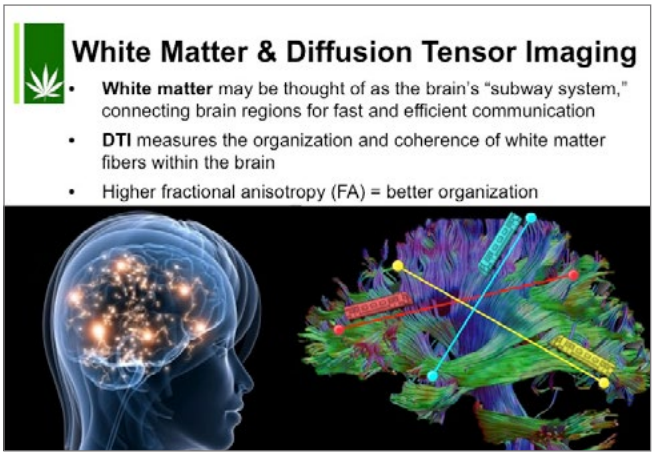
You can see that the control subjects have a very discrete area of activation — this is within the cingulate cortex — versus the smokers, which have a much more diffuse pattern. What happens when we split the smokers into those with early and late onset? I want to tell you, the early and late smokers are matched for absolutely every variable in terms of age, education, SES, everything we can match them on, except the age at which they began using and the fact that they're using more often and in higher amounts. Here we see that the early onset smokers have a very different pattern of activation from the late onset smokers. Late smokers are activating predominantly the same region as the controls, but not the early onset group.



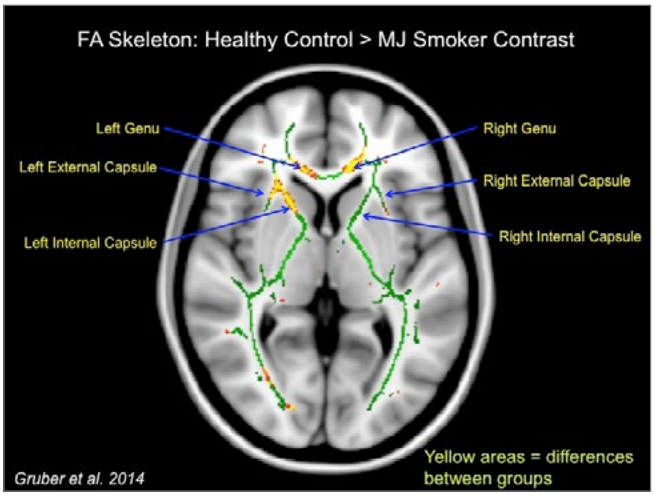
When we think about brain structure, we know across studies, adolescent marijuana smokers have exhibited changes in shape, mass, and volume in a variety of brain structures. We've also seen changes in thickness of the cortex overall. Depending on which areas you're talking about, sometimes we see adolescent marijuana smokers with thinner areas, sometimes the areas are thicker. It really depends on the region.

We've also seen changes in density and gyrification. What does that mean? We've all seen those pictures of the brain and people say, "What are those little folds?" That's gyrification, a measure of the folds within the brain's gray matter. What do all those things mean? Basically they boil down to the fact that those types of changes represent changes along the underdevelopment trajectory, differences in their development over time. And they appear to be related in each case to cognitive difficulties, relative to those who start smoking later.

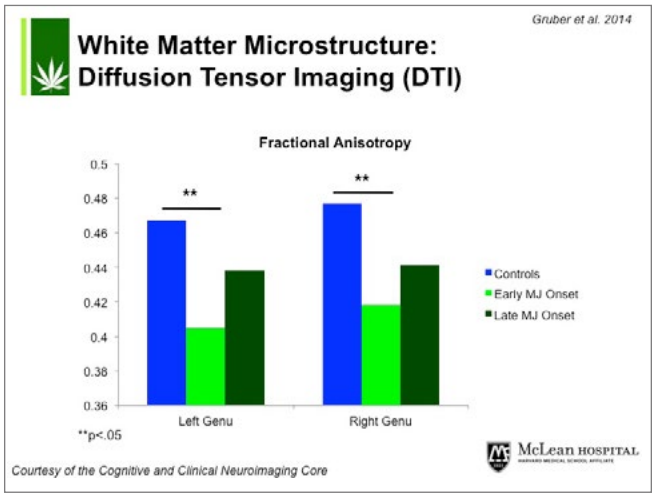
Changes in gray matter have been reported to be associated with increased executive dysfunction and poor memory. Decreased thickness areas are related to a poor ability to accurately perceive their own subjective negative emotional state, so they're less in touch with how they're feeling. Decreased gyrification, or fewer folds, has been associated with worse performance on complex attention tasks.



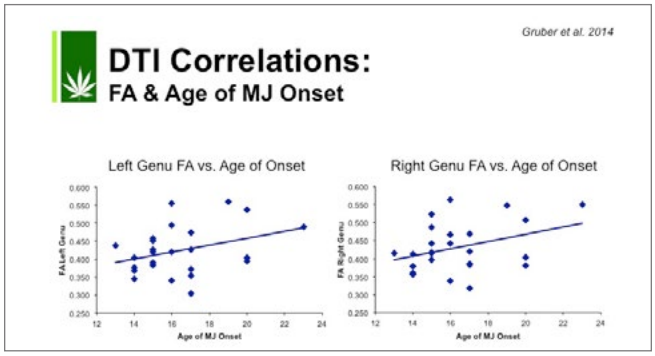
Diffusion sensor imaging is a way that we can measure the coherence and organization of white matter, and again, I think of white matter as the brain's subway system, connecting one region to another for fast and efficient communication. You can have all of the hardworking neurons from your gray matter that you can possibly have, but if there is no way that you can communicate that to another brain region, it doesn't matter. So DTI allows us to measure organization and coherence. DTI gives us a number of measures, one of which is called FA or Fractional Anisotrophy. That's just the measure of how well organized the white matter fibers are.



This is an image that demonstrates the differences between smokers and controls, just in general. What you see in green is just a white matter skeleton, and what you see in yellow are the regions that are different between smokers and controls. I draw your attention to the top part. See the big smile? That's the very front curve of the largest white matter structure of your brain, the corpus callosum, which separates the left and right hemisphere of the brain. That region, on the left and right side, also projects significantly to the frontal cortex.

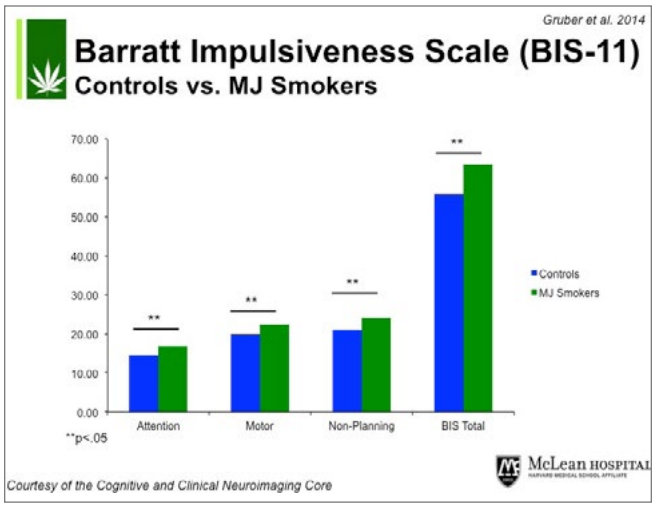


So, what do we see when we look at smokers versus controls, and smokers divided into early and late onset? Once again, early onset smokers have significantly lower white matter organization relative to the healthy controls. Not quite significant when we compare them to the late onset smokers. That's true in both the left and the right side.



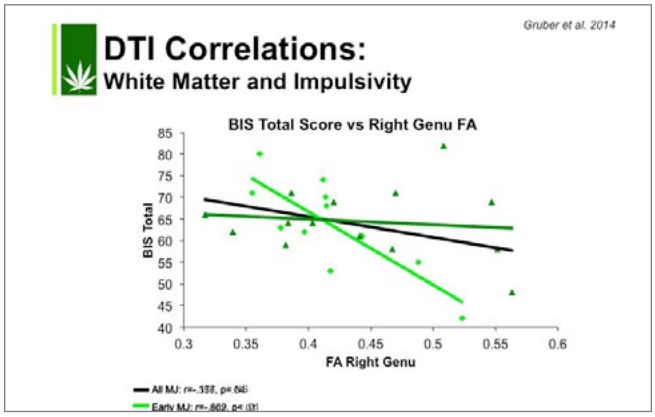
Actually, when we took a closer look, it turns out that earlier age of onset was related to lower white matter integrity across the board. This is true not only in the one region I pointed out, but in a number of regions.

Let me say this again, the earlier you start smoking, the lower the white matter organization. This is a really important point because it argues for a structural brain change secondary to early exposure to marijuana.



I mentioned that we give all of our folks a huge amount of assessments, and some of them are examiner-driven and some of them are self-report. The Barratt Impulsiveness Scale is a self-report measure of how impulsive people think they are, and there are three sub-scores: attention, motor, and planning, and then there's a total. "I do things without thinking," or, "I act on impulse": subjects rate themselves.

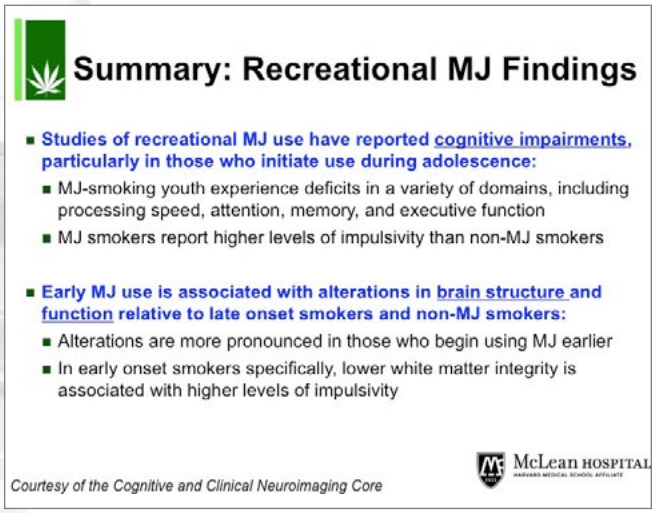
The smokers are in green. Controls are in blue. Across the board, smokers are more impulsive by self-report than the controls. I wondered, given what we know about this and the fact that we just saw early onset was associated with lower white matter, is there a relationship between impulsivity and white matter?



In fact, it turns out that there is. The black line represents smokers as a whole, and on the vertical access, what you see is the impulsivity total score and the horizontal access is that white matter measure. No relationship in smokers as a whole, but when we split them into late onset smokers, that's the green line and still no relationship — but look at the light green

line. That's the early onset group. What we see is a significant relationship between lower white matter organization and higher impulsivity.

Remember the take home message: Earlier onset of use, lower white matter organization. Now what we see is lower white matter organization is associated with higher impulsivity only in the early onset group. This is incredibly important and present in both the left and the right side of this brain region. This is something to keep in mind. In fact, the idea that it's only related to the early onset smokers really bears much greater investigation.

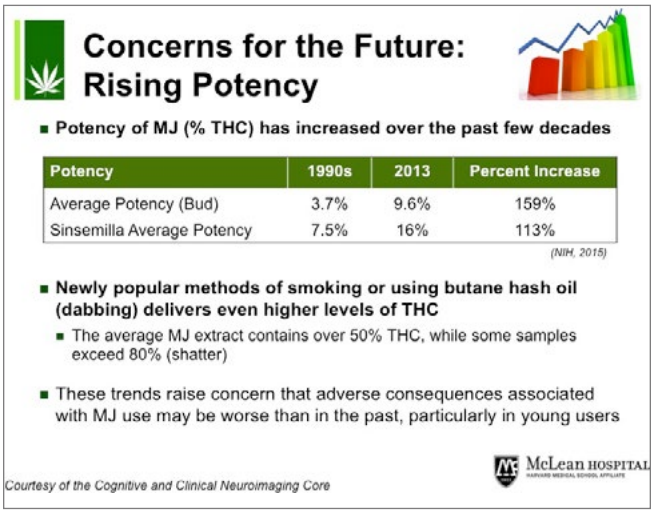


To summarize these points, we know that studies of recreational use have reported cognitive impairments, particularly in those that begin using in adolescence. We see changes in a number of domains including processing speed, attention, memory, and of course, executive function. Early use is also associated with alterations in brain structure and brain function, relative to both late onset smokers and the controls.

The alterations or changes are more pronounced in those who begin using earlier, and in the early onset smokers specifically, there's a relationship between lower white matter organization and higher impulsivity. This is like the perfect storm for families. So we have early onset exposure to marijuana, reduced white matter, maybe increased impulsivity.

We know that over time, a number of campaigns like "Just Say No" didn't really work. In fact, I have people who come in and say, "If somebody tells me just say no, I'm saying yes, just go away." I get it. We find at least for a number of our folks, "Just Say Not Yet" is a more easily adopted message. You explain to folks that we're not saying never, we're saying not now. We're saying your brain is under construction and that it's vulnerable. It's incredibly important.

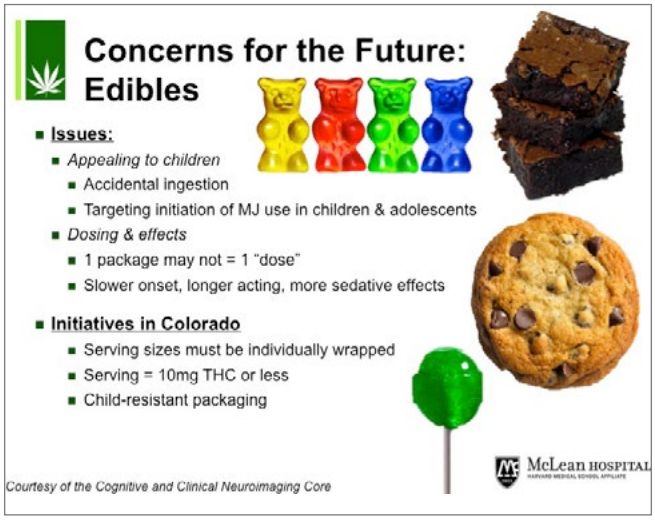
Our kids, our adolescents, our emerging adults are smart. You have to make them your allies in this and explain to them that there's data that suggests that if you expose yourself to high levels of the substance, the chances of having a negative impact are greater than if you didn't.



This is especially important given the rising potency that I alluded to earlier. We know that the average potency of what we call bud that people were smoking in the 90s, was just under 4%. The national average based on seizure data, seizure from law enforcement, was just under 10% in 2013.

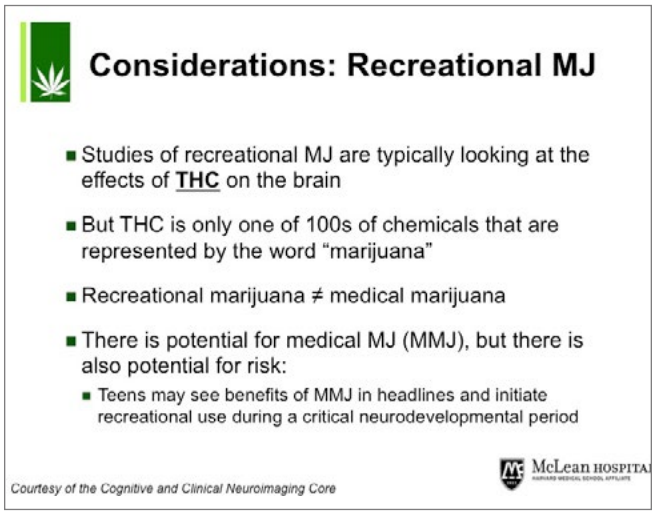
I want to make the point about more popular very novel methods. People are incredibly creative about how they're using marijuana. Concentrates, for example — shatter, budder, wax. Budder contains over 50% THC. In some cases, over 80%. Shatter, 80%.

Of course, these trends raise concern that these adverse consequences that we see with marijuana may be even worse, especially in our youngest consumers. There have been no controlled studies on the effects of concentrates on the brain. Not one. What we know is from recreational marijuana studies of primarily smoked or vaporized products, not concentrates.



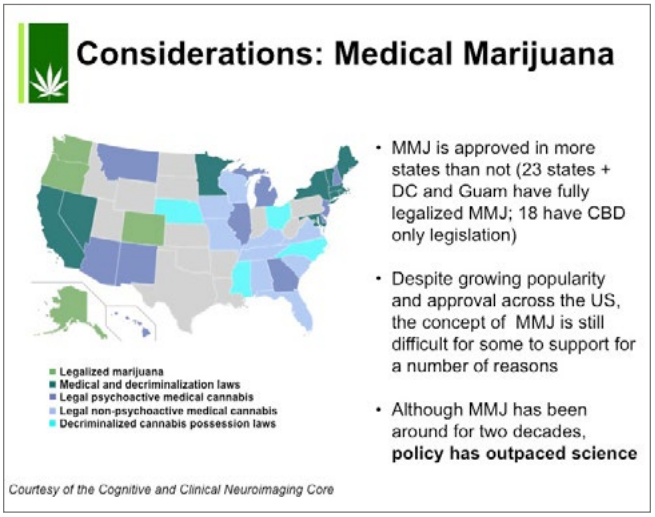
I won't get into this too much because I think my esteemed colleague will get into this, but in terms of thinking about the future, it's important to remember things like edibles. They are incredibly appealing to kids. Who doesn't want a gummy bear that looks like that or a brownie that looks so delicious? We have issues with accidental ingestion, and of course, many of these products are targeted for kids and adolescents. It's really important to remember as we encounter this next ballot initiative about legalizing recreational use. One package may not be one dose. Colorado spent $10 million going through a whole packaging thing and making sure one unit dose was 10 mg of THC only.

Remember that your body or brain does not process edibles in the same way that it processes smoked or vaporized products. There is a much, much longer rise time, the time until you feel the effect, and it lasts a lot longer. These are important things to keep in mind.

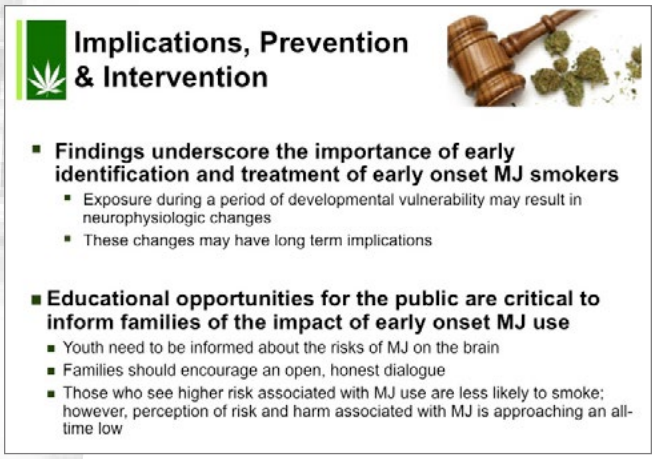


When we consider recreational marijuana, it's important to remember that what we know so far is based on studies primarily focused on THC. That's one constituent of marijuana. Just one. It's important to remember that medical marijuana products very often have other things like cannabidiol that are present which are shown to have potential therapeutic indications.

There's also the potential for risk. I can't tell you how many kids say to me, "How can something be negative if in fact they're using it as medicine? My mom's best friend uses it as medicine; why can't I use it?" We run the risk of accidental exposure because kids are misperceiving the intention of use.



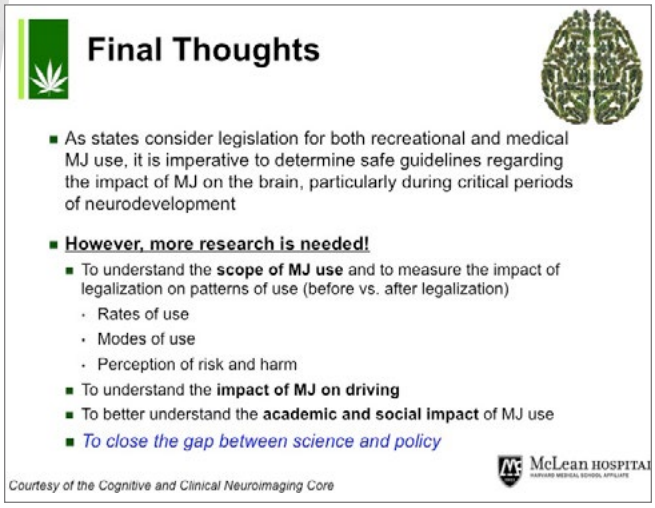
We saw that although medical marijuana has been around for two decades, policies outpace science. We do not have any empirically sound studies of the impact of medical marijuana on the brain. We have two studies ongoing in my lab, but we are in the very early stages.



Together these findings underscore the importance of early identification and treatment of those who are using marijuana early. We know that exposure during a period of development may result in long-term changes. What happens after folks stop using? We actually have a cohort that has stopped using marijuana, and they don't look the same as current smokers, which is encouraging.

Educational opportunities for the public are critical to inform families of the impact of early-onset use. Youth need to be informed of the risk. You have to explain what we really know. Those who see higher risk associated with marijuana are less likely to use, but you saw perception of risk and harm continues to drop.

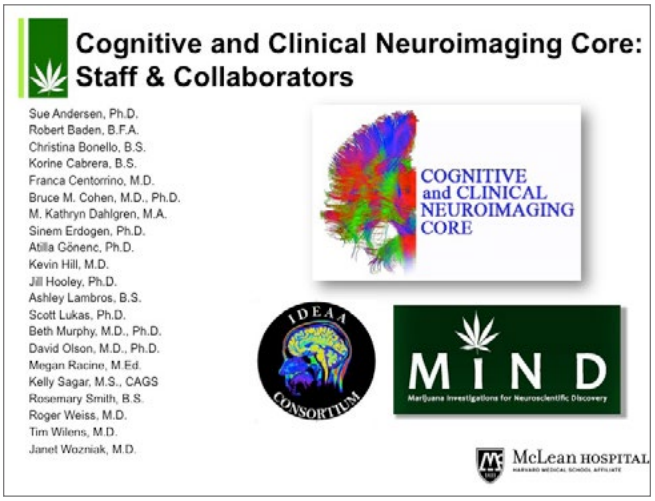
Families should encourage an honest, open dialogue, and they should engage in the dialogue. Part of the problem is a lot of folks don't want to talk about it. I have a lot of families who say my kid doesn't use it, and the kid looks at me.



So as states consider legislation for both recreational and medical marijuana, it's important to determine safe guidelines regarding the impact of marijuana on the brain, especially during critical periods of development. We need more research on the scope of use, and we have some data from other states out west like Colorado that have suggested that there may not be the biggest change post legalization, but some of the data actually says there is change, post legalization, in terms of the rates and modes of use.

We have to better understand the impact of marijuana on driving; the academic and social impact, and of course, close the gap between science and policy.

Adolescence is a time for neural maturation. Those that are at the greatest risk for adverse events or adverse consequences represent a growing number of the consumers of marijuana. Thank you for your time and attention.



QUESTION AND ANSWER

Audience: I have a question on age 16…[inaudible] early onset as the brain continues to develop until 30.

Stacy Gruber: We actually chose 16 for a number of reasons. There is some evidence to suggest that we were far enough past the second wave of these progressive and regressive events that happen in the brain during development. There were also some other studies that had used 16 or 17. And it's all about finding something that lines up with what we already know. Sixteen is also a time that kids are pretty firmly ensconced in high school, and this is when the threat of potential exposure really becomes greatest, although I've got folks in my study who are 12 and 13. So that was why we chose it. If only there was something that told us exactly what the right time was, that would be terrific.

Audience: But you picked a [inaudible] so I can smoke as much as you want.

Stacy Gruber: I think it's important to get out that we're not saying that we don't see changes in those folks. We're just seeing a specific sort of incrementally worse set of performance from folks who are using regularly prior to age 16. It seems to be worse the earlier folks are using. It's not to say you get a free pass at 17. In fact, car rental companies: What do they know that other folks don't know? They don't rent to people before age 25. Right? Okay. But you can vote and buy liquor, 18-21. It seems strange to me. I think those car rental companies have some scientific board working behind the scenes.

Audience: Do you think there's a link between earlier uses of marijuana to specific more hard line [inaudible] as opposed to other countries that have a more liberal progressive drug policy that would mean a lower, earlier usage of marijuana? A lower use of alcohol. Level of abuse. That doesn't have a puritanical very strict alcohol policy.

Stacy Gruber: That's a good question, and I think that it's a two-part question. We've heard a lot of theories related to the gateway theories. So, does early use of marijuana lead to the use of harder drugs? Does marijuana itself prime the pump that is the reward circuitry in the brain for other drugs? I think that the data for that theory, separate and apart from the psychosocial aspect of whether we do or don't allow it here, is different. I don't think there's a tremendous amount of hard evidence suggesting that marijuana is a gateway drug. It's more often that folks who use hard drugs have used marijuana, but typically, when you query them, they're around people who are using other drugs and the folks from whom they're getting marijuana are often offering them other substances. It's not that marijuana created the difference. To your other point, I think that's a great question. You know in other places where we have much more liberal views, there are lower rates of abuse. Right? We don't have abuse and dependence anymore. We have use disorders. We don't say that. But in fact it's a really important consideration. I'm not sure I know the answer to it. It's a great thought, though, and I think we'll maybe start to see some of that data come out from states that have a more liberal policy, but I don't know.

Audience: Are there other risks that you know about or other risks in [inaudible] states that may pose similar or greater risks to adolescents?

Stacy Gruber: Marijuana? Sure. I think that it's hard to come up with an absolute relativity index. Like, what's the number one greatest risk for the adolescent brain? I think certainly there have been a number of reports in terms of alcohol and other drugs that demonstrate similar detriments, and I've heard a lot of people say, "But it's not as bad as people who are drinking very heavily from the time they are kids." We don't have a huge amount of longitudinal data. We're about to start. Several governmental agencies have this great longitudinal study planned called the ABCD Project which will look at 10,000 kids age 9 and 10 to begin with, and follow them pretty much for a decade, to see what has the greatest negative impact. It's a great question. I get it a fair amount. How much more harmful is this than something else? And the answer is I'm not sure we know. I think the point is it's not harmless. I think that's the thing to keep in mind. Are there things that are more harmful to the brain? Likely, yes. In fact, we see that. Does that mean that this is a benign substance? No.

Audience: Interesting. I work with young men and [inaudible] a lot about minimizing their trauma impact and I understand that, and what I find so troubling about your data is not only are they using it to manage the trauma impact of their lives but to [inaudible] the need to [inaudible] transition and [inaudible] life. And having these [inaudible] it impacts the impulsivity to manage healthy relationships, to navigate conflict and that it manages something for the [inaudible] and the long-term outcomes for them are profound. How do you feel?

Stacy Gruber: I agree with you, and it is somewhat stunning to us as well. I think for those folks –and you know there's been a lot of talk about alternative therapies for folks with trauma histories, and in fact we see a lot of folks with a lot of trauma who are self-medicating with marijuana. We've all seen the PTSD data where people will swear to you that marijuana helps them, and it may in part be true. What's more likely true is that if we were able to isolate and allow a cannabidiol specific — a cannabidiol heavy product with just a touch of THC — we may see a very different outcome, and that's sort of poised for the future and it's something that I

hope we are able to spend a fair amount of time and energy on because we need to. The number of people who have survived trauma is staggering, and the things that they turn to, including marijuana, deserve attention.

Audience: So before this longitudinal data, how can you differentiate on looking at images and data what makes them more likely to use?

Stacy Gruber: Excellent question. Cross sectional data is limited. That is, we don't know about cause and effect. How do we know, for example, with regard to the white matter data — which I find stunning and incredibly disturbing — how do we know that those people weren't more predisposed somehow to use earlier versus the white matter now — is it antecedent or a cause? Is it causative or an outcome? And the answer is we don't really know. Interestingly, the earlier the onset of use, that relationship between earlier use and lower white matter, tends to suggest there is a relationship. That exposure is what's causing this, but to really definitively know that for sure, you need longitudinal studies. We also need longitudinal studies to follow some of these folks out. They don't all look like potatoes. You know these guys are doing really, really well, and they're well matched to our controls for IQ, which is well over 116 and 118. These are guys who are doing pretty well. These are not folks who don't have lives. They're college students. They're paralegals. They're dental hygienists. You know them and see them every day. That's the thing. They're everywhere. That's the great question in terms of what longer-term use or abstinence results in with regard to recovery of function and brain structure.

Audience: I work for [inaudible] and [inaudible] of [inaudible] but we see in so many of our cases involving violence and we get direct testimony from people who have participated in that violence [inaudible] or just were observers to that violence, marijuana is almost always present and the idea — it's an eye opener for me that your research around impulsivity. I guess impulsivity can mean different things, but impulsivity to act violently. There is a lot of research going on that I would say that might be an area where [inaudible] everyone thinks of someone smoking marijuana they're just like —

Stacy Gruber: Mellow.

Audience: They're mellowing out.

Stacy Gruber: Not everybody.

Audience: Yeah. And obviously for some people they can have very violent reaction.

Stacy Gruber: So the big question for those folks is what else is going on. What else is happening with regard to genetic predisposition or if we just take the marijuana — I hate to say this. I think some of the only folks who are getting samples of products from our medical marijuana users and our recreational users. What's in their weed? How high is the THC level? And when we think about legalizing for recreational purposes, are we going to put restrictions on the maximum level of THC and will we mandate some cannabidiol is present if you're buying before the age of X? Twenty-five? Twenty-eight in fantasyland. But it's a great question, and it's something that shouldn't go unnoticed, and I think that again, we see marijuana factoring into the equation across the board. The question is: what is it about the marijuana versus the person? And again, different strains. There are thousands of strains and hybrids. The mode of use and the way that people are using whether it's a blunt, a spliff. They're vaping. The product. The frequency and the magnitude all those things are important in terms of the outcome. We need studies to more clearly define what it means.

Audience: Do you have any plans to change the conversation with children and adolescents about marijuana as like to make it more tangible to them as opposed to just like the don't do drugs message that police —

Stacy Gruber: So really the just say no, it really doesn't work very well. We try to explain that during a specific period of time, they're particularly vulnerable. And we say, you know you're not going to be a kid forever. You have a long time. Isn't it true that for those of us who are adults, we're adults for a long time seemingly? There's no rush. And we try to explain that they may not be giving themselves the very best chance, and again, most of these guys for our recreational studies are doing pretty well. The question is how well would they be doing if they weren't using? So I think it's important to point out that this is a period of time that's a specific vulnerable period of time, and they need to wait. Like so many other things, there's plenty of time to do it, and if they're going to do it, do it responsibly. Don't hit it every single day, six times a day. Don't have a product that's 26% THC. There are things that you can advise, now that we have information. We didn't have information for many, many years.

CLARK UNIVERSITY
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Marijuana Legalization: Impact on Public Health and Public Safety

By John F. Kelly, Ph.D.

POLICY BRIEF

The social, legal, and political landscape surrounding marijuana legalization for recreational use has changed dramatically. "Medical marijuana" initiatives have culminated in laws being passed in 23 states (and Washington D.C.) and allow a medical recommendation for the use of marijuana to help alleviate symptoms of a variety of medical conditions.

Colorado and Washington have now taken a further step of legalizing the cultivation, distribution, and commercial sale of smoked and edible marijuana for recreational use. This is the first time that a signatory to the 1961 international drug treaty, the Single Convention on Narcotic Drugs (the implementation of which in the United States was the Controlled Substances Act of 1970) has had at least some of its territories legalize the use of any currently illicit drug for recreational use.

Marijuana is a psychoactive drug that causes intoxication and psychological impairment, as well as addiction and other health consequences. As such, the broader availability, accessibility, and lower prices associated with legalization and commercialization are likely to increase exposure to and use of marijuana.

Because marijuana can cause harms to public health (e.g., addiction, cognitive impairments) and risks to public safety (e.g., drugged driving), we will likely see increased public health and public safety problems associated with legalization.

Marijuana contains psychoactive ingredients, such as delta-9 tetrahydracannabinol or "THC" and cannabidiol or "CBD". THC, in particular, produces psychological and physical addiction, and is associated with changes to the structure and function of the brain. Increased exposure to the drug is associated with acute and long-term cognitive deficits (particularly among adolescents exposed to the drug), including psychiatric illnesses (e.g., psychosis) and long-term problems with memory and attention that persist even after cessation of a year or more.[1]

Intoxication with marijuana does not produce some of the severe psychological, emotional, and behavioral consequences often seen with legal drugs, such as alcohol. For this reason, it can be perceived as comparatively benign. Concentrations of the psychoactive ingredients (THC) have been increasing steadily in recent years, however, and the marijuana available today contains about 4-5 times the amount of THC that was used commonly during the 1960s.

Furthermore, even more concentrated forms have emerged in consumable products (e.g., "edibles"). Edibles can produce more profound intoxicating effects that have resulted in more emergency department visits than with smoked marijuana. This is caused in part by the delayed onset of the subjective experience of intoxication from edibles because absorption takes much longer through the stomach than through the lungs. Consequently, individuals perceiving no initial effects can continue to consume more and more, resulting ultimately, in uncomfortable and sometimes serious levels of intoxication.

From the public health standpoint, smoking marijuana is associated with addiction.[2] Approximately 9% of regular users of marijuana will become addicted. It is also associated with onset of serious mental illness,[3, 4, 5]

heart and lung complications,[6, 7] injuries resulting from car crashes,[8] IQ degradation and poorer academic achievement,[1] poorer quality of life,[9] and poorer educational and vocational performance.[10]

Increased exposure, and especially regular exposure during the critical developmental period of adolescence, is almost certain to increase the occurrence of these problems in exposed individuals and the population more generally. Importantly, like all drugs, the toxicity and harms are related to the dose and intensity of exposure as well as the length of the period of use.

From the standpoint of public safety, acute intoxication leads to psychological impairments (e.g., memory impairments, decreased attention, slower cognitive processing speed, impaired judgement, increased anxiety, and paranoia) that have obvious consequences for driving under its influence. Use of marijuana is associated with a two-fold increased risk of having a car accident while driving; the effects can last for up to three hours following consuming a dose sufficient to impair psychological functioning.[11]

Unlike alcohol, marijuana use and heavy use is not associated with violence. It is currently unclear whether use of marijuana is associated with increased risk of lung cancer, but smoking does increase risk of pulmonary harms.

While there is very likely to be increased exposure to marijuana in the population if it is made more available, accessible, and cheaper, proper regulation can reduce the degree of harm to public health and safety. The Netherlands has allowed commercial sales to occur in cafes, and it has enforced rules that limit the amount of marijuana anyone can buy in a single day, ban advertising completely, and prohibit sales to minors.

Allowing legal use, commercial cultivation, distribution, and sale, while simultaneously enforcing such restrictions, could help reduce expenditures from law enforcement and criminal prosecutions related to the drug's illicit status while minimizing escalation of use.[12] The financial savings from the eradication of costs to law enforcement and criminal justice expenditures due to its illicit status, must be weighed against increased law enforcement and legal costs that will accrue due to failure to comply with the new regulations of cultivation, distribution, and sale (e.g., illegal sale to those under age 21; driving while intoxicated, etc.). Alcohol prohibition was ended, in part, due to increased criminal activity in supplying alcohol illegally, but despite the end of alcohol prohibition, there are millions of arrests annually across the country related to alcohol (e.g., sales to minors, DUIs, violence/domestic violence)

Legalization goes much further than decriminalization. In Washington and Colorado, there are regulations in place to try to minimize harms to public health and safety. Many of these policies are borne out of the experience from alcohol and tobacco, with minimum purchase age being 21 years old and requiring licenses to sell the drug. Colorado does not allow advertising.[13] Washington does, but has restrictions.[14]

There are other issues that will need to be addressed, such as second hand smoke exposure, quality control, and consumer protection. Potency (e.g., THC content "per serving") will need to be standardized and labelled, and safeguards should be taken to ensure that the salable product is not contaminated by fungi, bacteria, or pesticides. There is also the question of how the products should be packaged and labelled and whether to list ingredients and potential health harms, including addiction risk.

Any legalization and commercialization of marijuana will need regulation, education, and taxation. Education initiatives will be needed to inform parents and young people about the potential harms and hazards associated with marijuana (especially during teenage years).

Taxes on the cultivators, sellers, and buyers of the product could be used to help offset its likely contributions to health and safety related harms. As with alcohol and tobacco, consumers are sensitive to price, and higher prices reduce consumption, particularly among those who spend a large amount of their available income on the drug (i.e., those most likely to have problems and encounter problems due to the drug).

Care must be taken, however, not to price the drug too high, as this can lead to black market sales with cheaper availability. To the extent that marijuana can cause population-level health harms and threats to public safety, price and availability are two central factors that influence such harms and threats. Lower prices and greater availability will increase use and related harms; higher prices and lower availability will have the opposite effect.

It is likely that if commercialization expands, greater financial resources and lobbying efforts by commercial growers could begin to change the policy and regulatory landscape over time, such that gradual erosion of enforcement efforts and any imposed restrictions on advertising, amount of daily purchase, warning labels, etc.,

could occur. To prevent this, a proportion of the tax revenue should be spent on an independent oversight body that can provide ongoing monitoring and evaluation of these policies and regulations, such that they are not eroded for corporate gain at the expense of public health and safety.

The journalist, Henry L. Mencken, once remarked that for every complex problem, there is a solution that is clear, simple, and wrong. Drug policy, ultimately, should be about minimizing or eradicating harms due to drugs. Given that intoxicants are threats to public health and safety to some degree and at least some proportion of the population appears to want to use intoxicants, complete eradication of all harms is unlikely.

Policies to minimize harms have been implemented in the form of prohibition, decriminalization, or legalization. Each policy position has side effects. Effective policies should be devoid of ideology and based on rational data-based solutions that minimize harms. On the one hand, prohibition works. It dramatically reduces exposure in the population and consequently, minimizes related harms. On the negative side, due to the demand, it increases illicit black market and criminal activities, and leaves consumers, distributors, and sellers on the wrong side of the law. This drives up costs in law enforcement, criminal justice, and incarceration.

At the other extreme, legalization and unrestrained free-market corporate commercialization with largely unrestricted advertising and sales likely would lead to targeting of young people and other vulnerable sub-groups, and casualties would increase (as has been the case with alcohol). Decriminalization, as has occurred in Portugal, minimizes illegal consequences, but does not eradicate the black market and associated criminal activity. Drug problems will not be completely eliminated as a result of any particular position. Rather, we are at a new juncture where we will be choosing which types of drug problems we will have.

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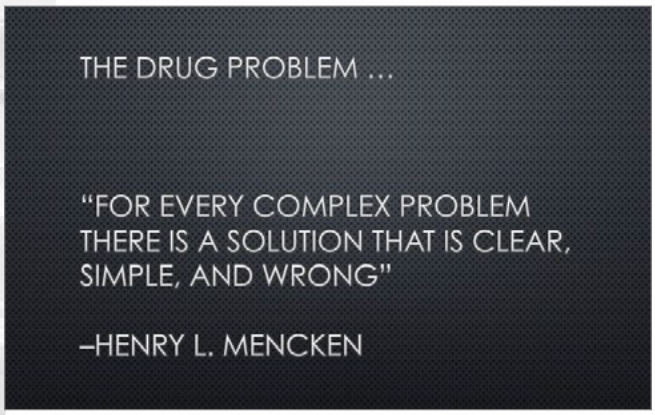
John F. Kelly, Ph.D. ABPP is the Elizabeth R. Spallin Associate Professor of Psychiatry in Addiction Medicine at Harvard Medical School, the first endowed professor in addiction medicine at Harvard. He is also the founder and Director of the Recovery Research Institute at the Massachusetts General Hospital (MGH), the Program Director of the Addiction Recovery Management Service and the Associate Director of the Center for Addiction Medicine at MGH. Dr. Kelly is a former President of the American Psychological Association (APA) Society of Addiction Psychology, and is also a Fellow of the APA and a diplomate of the American Board of Professional Psychology. He has served as a consultant to U.S. federal agencies and non-federal institutions, and foreign governments.

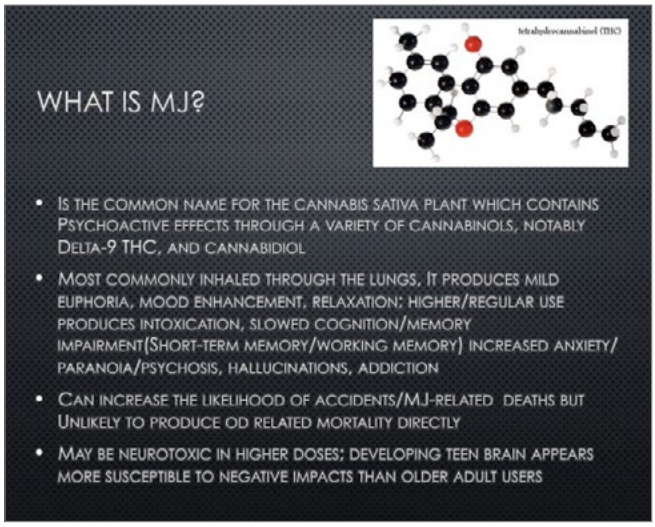
TRANSCRIPT OF DR. KELLY'S TALK

Good morning everybody. Delighted to be here. Thank you very much, Dr. Hines, for the opportunity and invitation to come along and talk to you all today and be a part of this fabulous seminar. Thank you for coming. Let's get started.

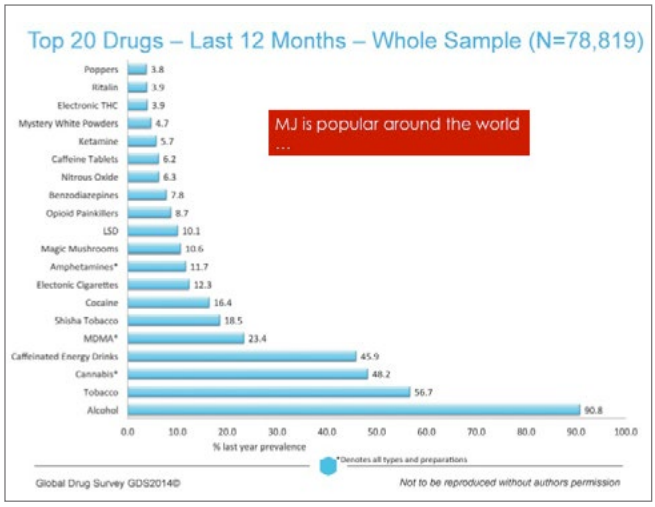


I like this quote a lot. "For every complex problem, there is a solution that is clear, simple and wrong." This was by Henry L. Menken, and applies particularly well to drugs and drug policy. Whenever you hear someone say all you've got to do is dot-dot-dot, you know immediately that that person doesn't know largely what the nuances of the complex issues are at stake in drug policy.

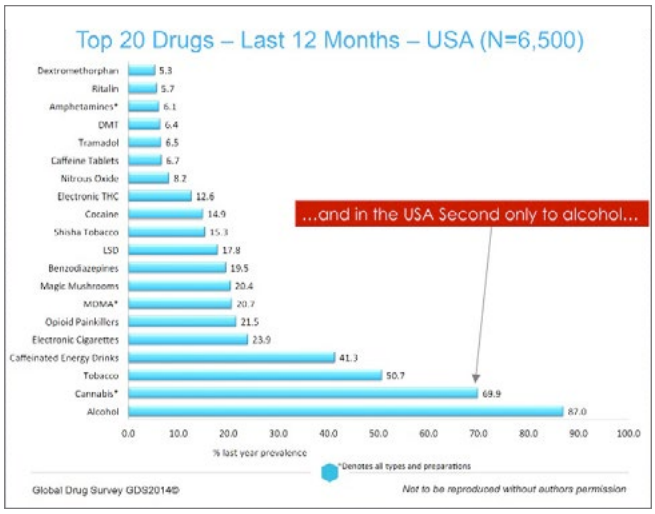
So hopefully you won't be leaving here today saying all you have to do is dot-dot-dot. That's one of the goals that I want to try to get across. I want to inform you all about some of the things that we have learned and I have learned regarding the complexity of drug policy. I think ultimately, we cannot eliminate our drug problems. What we can do is try to minimize the drug problems by taking different policy positions, but ultimately we are going to have to choose which problems we are going to have.



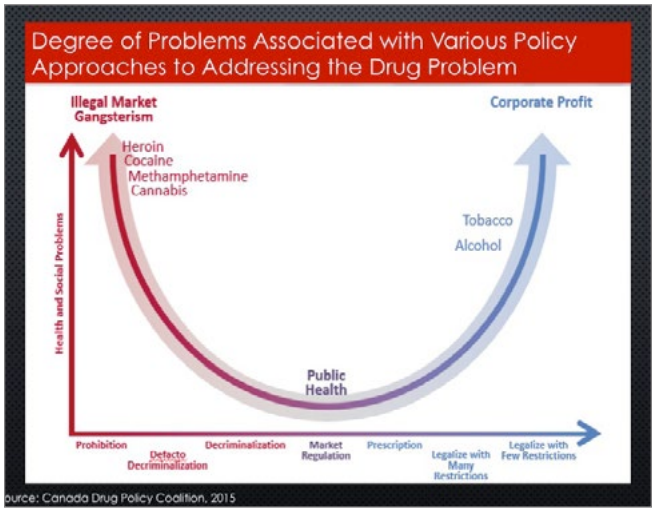
What is marijuana? It's a psychoactive drug. It produces addiction, as I'll talk about. It produces, of course, euphoria. People like the feeling when they're exposed to marijuana. It produces pleasant effects that people like to repeat. It produces intoxication. It has neurotoxic effects, and I'm going to distinguish between these three different pathways through which substances cause harm as I go through today's talk.



It is the world's second most favorite intoxicant/psychoactive drug after alcohol. Alcohol is by far the world's favorite drug.



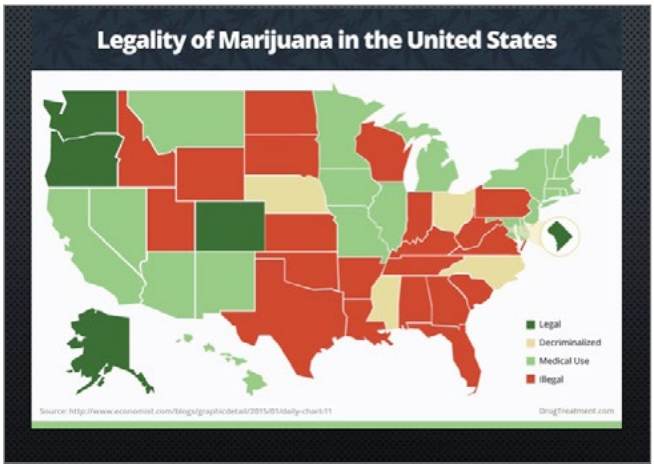
But cannabis is number two, and it is number two here in the United States.



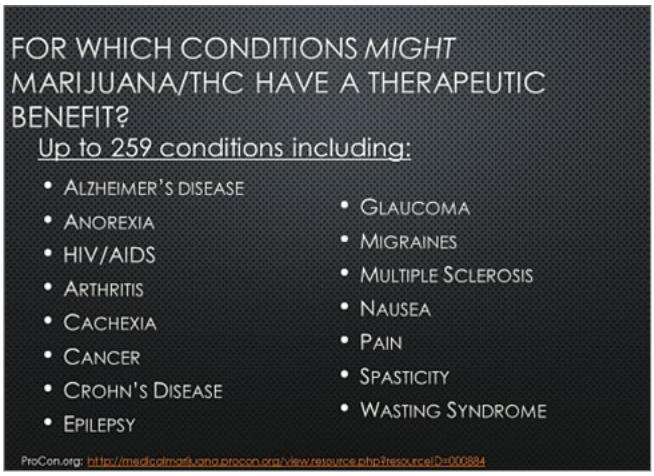
When we think about addressing the "drug problem," there are different broad policy positions we can take, and this is a nice graphic that highlights these different policy positions. You can see along the bottom of the graph, along the x-axis of this graph, on the left-hand side, is what we currently have federally: prohibition. In fact, all nations have signed onto a single narcotics convention. It was signed in 1960 prohibiting the use of illicit drugs other than alcohol and tobacco. So we have prohibition.

You can see prohibition and de facto decriminalization, decriminalization, market regulation, leading on to legalization with a few restrictions, and then legalization with some restrictions, and legalization with few restrictions. Those are the different policy positions that can be taken regarding drugs. Up the y-axis going north there, you can see these are the number of health and social problems related to each policy.

You can see the two extremes on either end here: we've got prohibition on the left with a high degree of health and social problems, but we also see a high degree of health and social problems on the right-hand side. The two extremes are prohibition with full enforcement of prohibition and on the right-hand side we see full blown commercialization, unrestricted commercialization also producing health and social problems.



So how do we get to this point in terms of legalization? The states in light green are the states that have medical marijuana laws passed. The four dark green states and the District of Columbia are the states that have now legalized recreational use of marijuana. We have quite a few states already with medical marijuana.



When we look at medical marijuana, it seems to be a magic potion that can cure many things, according to those who would advocate for its widespread use medically. In fact, this particular website said there was up to 259 conditions that medical marijuana could help with. I was immediately

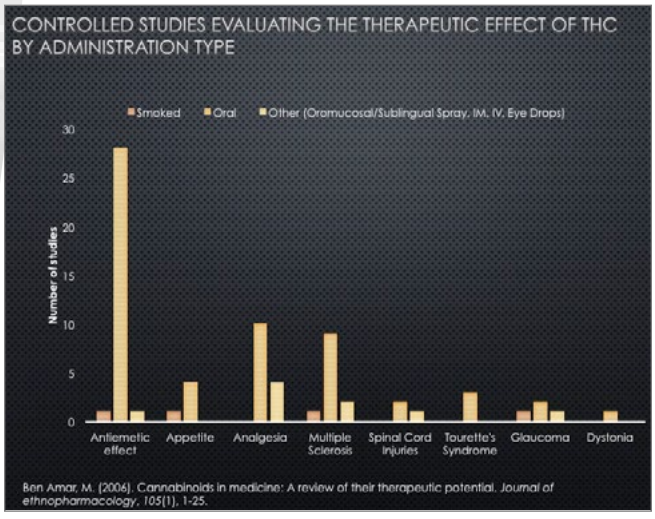
skeptical because we only have 109 known medical conditions. So I'm joking. I don't know how many known medical conditions we have, but anyway, it would be fantastic if it were true that it could have such a broad impact on so many conditions.

CANNABIDOIDS HAVE DOCUMENTED THERAPEUTIC POTENTIAL...
THC ADMINISTRATION & FDA APPROVED THC-BASED MEDICATIONS

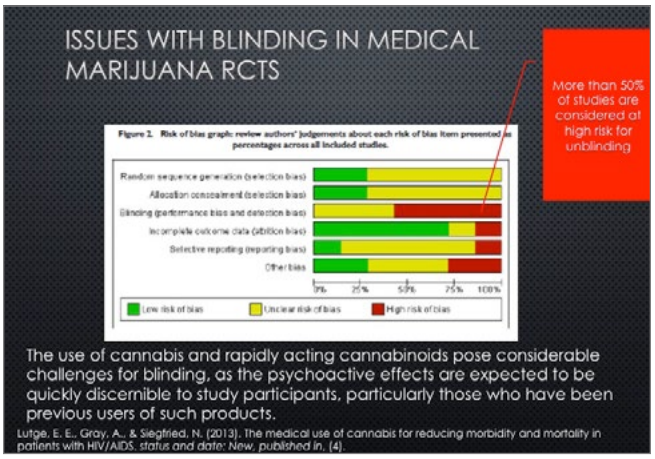
Compound	Administration	FDA Status	Approved Locations	Purposes
Dronabinol (Marinol)	Oral capsule	FDA-approved (1985)	USA, Germany	Nausea & vomiting related to cancer chemotherapy and wasting associated with AIDS
Nabilone (Cesamet)	Oral capsule	FDA-approved (1985) *Marketed in the US in 2006	USA, Canada, UK, Mexico	Nausea & vomiting related to cancer chemotherapy
Nabiximols (Sativex)	Oromucosal spray	Almost FDA-approved; late-stage clinical trials	Canada, UK, other European countries	Multiple sclerosis spasticity, cancer pain, neuropathic pain

December 9, 2010 (unpublished data).

When we look at the data, we do know that marijuana does have, like many things that we find in nature, medicinal properties. We have FDA approved medications that have THC and cannabidiol as their constituents, and these have been used and passed FDA approval to treat things like nausea, increase appetite for cancer patients, and decrease spasticity among patients with multiple sclerosis. There is no doubt that it has therapeutic properties.

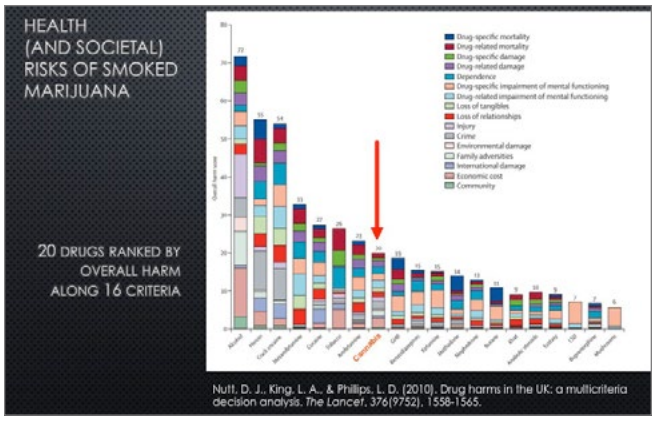


What's interesting is when we look at the scientific basis for medical marijuana, however. Remember medical marijuana is smoked marijuana. This is what we see. The left hand bar under each one of these major conditions for which it's been studied, are studies on smoked marijuana. As you can see there are very, very few studies we have on smoked marijuana. This is the scientific basis for the recommendation for medical marijuana, and when we look at the studies at risk of bias, which have actually been done with medical marijuana, more than half of the studies are at risk of biasing, by un-blinding.



In other words, when you actually do a study with smoked marijuana, people can often tell if they're smoking marijuana or not. So it's hard to find a placebo to really isolate the independent effect of the psychoactive drug. But it's interesting, isn't it, that medical marijuana has been passed by popular vote in so many states when there is so little scientific basis for medical marijuana? In fact, I can't find any scientific basis for a physician recommendation. In an era of science-based medicine, evidence-based medicine, I don't know what the scientific basis is for recommending that someone smoke marijuana. There is none as far as I can see.

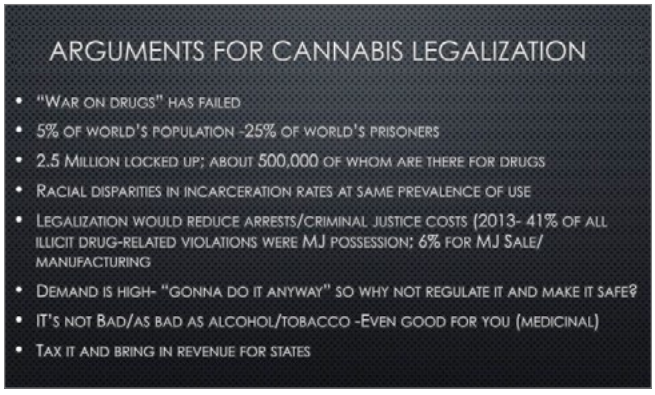
It doesn't mean that it hasn't got therapeutic potential, because clearly the constituents of marijuana do, but when we prescribe a drug or in this case recommend a drug is consumed, we should also know about things like side effects and interactions with other medications. Should you take it while you're pregnant? Etc. These are the kind of safeguards that we usually advocate for when we're recommending and prescribing a drug.



When we look at cannabis, marijuana, I'll ask you a question. Why should it be illegal? And why should it be legal? Well, we have taken a position that it's bad, right? That somehow marijuana is bad for us and it's bad for society, and therefore, it should be illegal. We certainly know it causes neurotoxic effects in the central nervous system, particularly among young people. What other kinds of harm does it do?

This is a study that was done in Great Britain. It was replicated in Europe where they had 40 different experts from across different disciplines rate the harm. Sixteen harms attributable to various substances on these 16 different dimensions across 20 different substances. These are the 20 most widely used/misused substances.

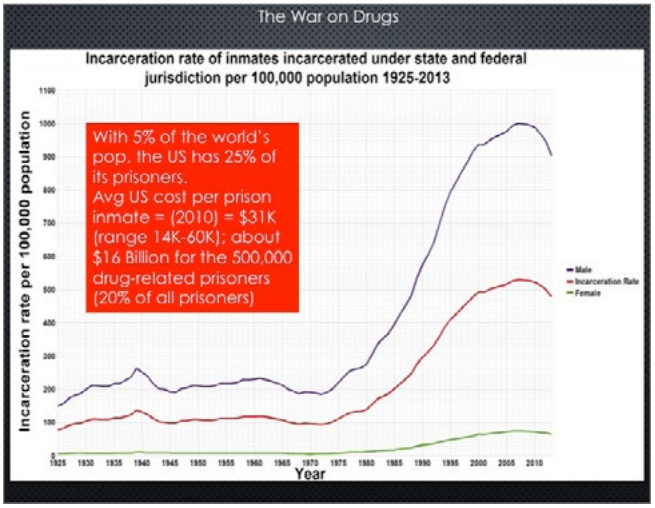
You see cannabis is right about in the middle there, so it wasn't high harm. It wasn't particularly low—somewhere in the middle in terms of drug-related effects and harms to do with toxicity and intoxication, addiction, etc. Interestingly, what they found in both of these independent studies was that alcohol was the top rated substance in terms of causing harm, overall. So this is harm to the user and harm to others. Alcohol came out top in both of these independent studies.



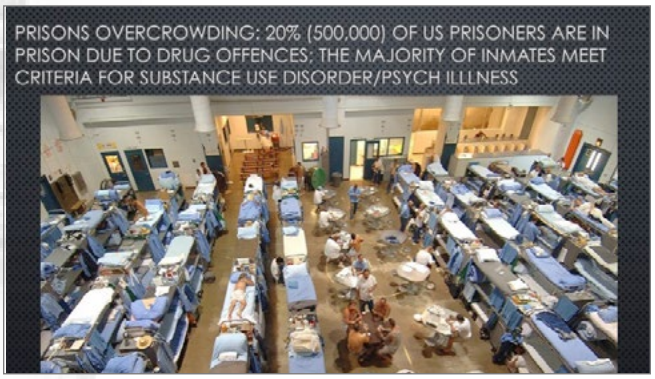
What are the arguments for cannabis legalization? Well, the war on drugs has failed. We hear this a lot. We're locking people up far too frequently. We have 5% of the world's population, but 25% of the world's prisoners. Interestingly, of the 2.5 million people locked up, about half or a million of those are there for drug-related offenses. And the issue of racial disparities, in that minorities are incarcerated at high rates, even at the same level of use and possession.

And legalization would reduce arrests, of course. It would certainly reduce arrests for possession, but it might increase arrests for violation of regulatory laws. For example, we have legalized alcohol. How many arrests do you think occur a year for alcohol in the United States? Any guesses? This is just violation of the laws governing alcohol use: 3 million every year. Three million arrests, and that's after we legalized it. So, we would decrease the 700,000 arrests for illegal possession, but we might also increase or replace those arrests with violations of regulations of legalizing it.

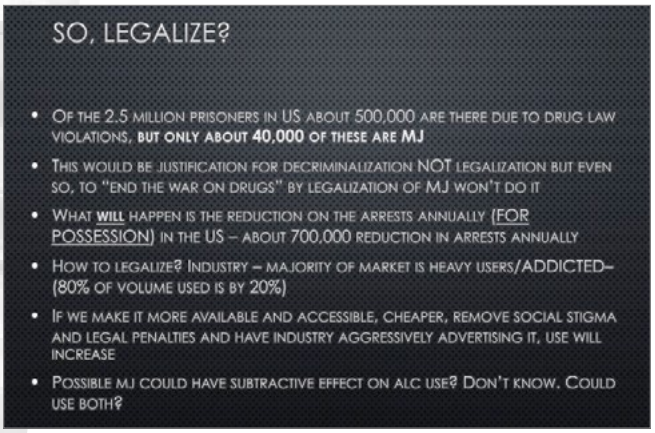
Another argument for legalization is they're going to do it anyway. People are going to do it anyway, so let's just legalize it. That's another argument. And that it's not as bad as alcohol. It's not as bad as tobacco and may even be good for you, right? It's medicinal. Also, taxing it will bring in revenues. We'll all be richer, and we can spend that money on good things, other good things that will make us a better society.



Since the 80s, we have seen a dramatic increase in incarceration rates, particularly among men and particularly among minority men.



We've had overcrowding in prisons. You can see these bunk beds stacked three high. This is actually in a California cafeteria, so we are locking a lot of people up.



If we think about the arguments for legalization based on the failure of the war on drugs, I said to you about 500,000 are in prison due to drug related offenses, but it turns out only about 40,000 of those are related to marijuana.

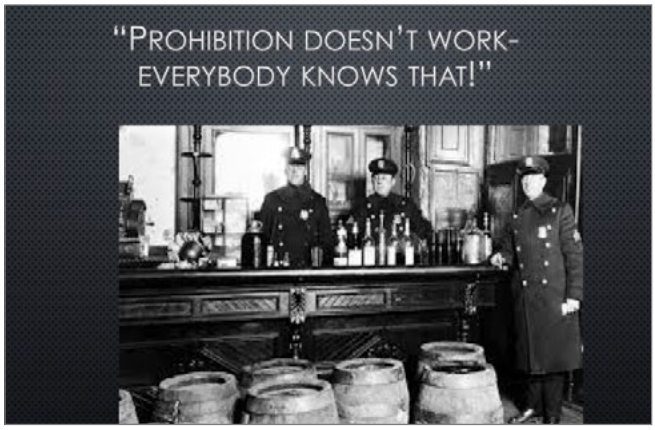
By the way, this would be an argument for decriminalization, not legalization, if we were going to prevent the war on drugs and locking people up. So, ending the war on drugs by legalizing marijuana won't do it. As I mentioned, it will reduce the arrests for marijuana possession. We have 700,000 arrests for marijuana possession, but we don't know whether those 700,000 arrests for possession will be replaced, as it has been for alcohol, with arrest for violation of laws pertaining to underage use, drugged driving, etc.

The other aspect is in terms of legalization is how to legalize. So, as I showed you on that graph before, we could legalize, have a state monopoly with no advertising. Make it legal. People can get it if they want it, but there's no advertising, and you can keep the price below a black market level, so people don't go to the black market.

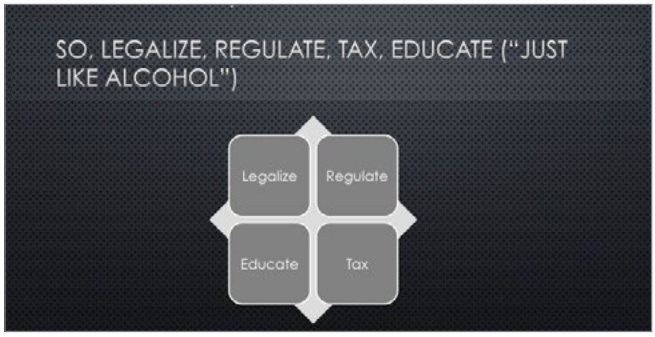
You can allow commercialization, as we have done with alcohol and tobacco. One of the problems with that is that full-blown commercialization advertising industries rely on heavy users for profit. Eighty percent of alcohol is drunk by 20% of users, and 50% by 10% of users. So, to make a profit, the industry has to rely on addicted heavy users, and they target people of vulnerable subgroups and young people to maximize the heavy rates of use that give them the profit.

If we make it more available and accessible, cheaper, and remove social stigma and penalties, and have an industry aggressively advertise it, undoubtedly we're going to see increases in use.

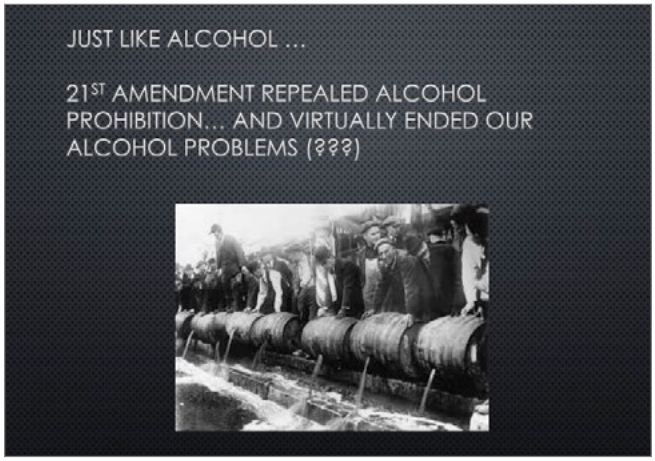
There is a question of whether marijuana could have a subtractive effect, and what I mean by that is if people were using marijuana, would they use less alcohol? And because alcohol by itself produces a lot of social harms, health harms, maybe we would see a net benefit from people using marijuana instead of alcohol? We don't know the answer to that.



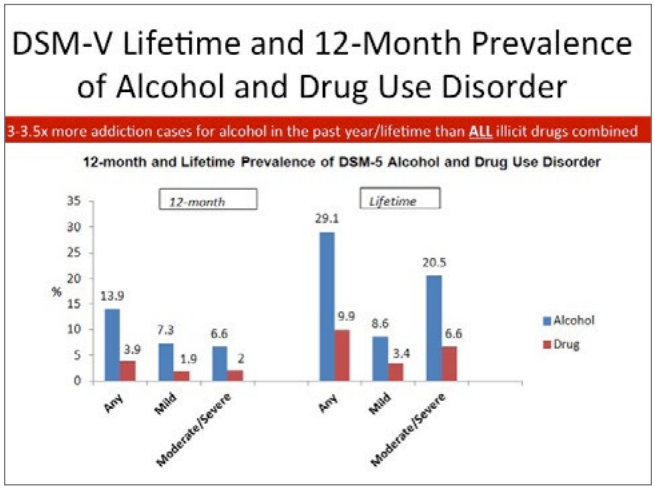
But everyone knows this that prohibition doesn't work. I hear this even from my colleagues at work. We tried that right? We tried that with alcohol. Eighteenth amendment and look at the mess that that got us into.



So we need to legalize, regulate, tax, and educate, just like alcohol.



Then we had the 21st Amendment. In 1933, it legalized alcohol because of all the problems caused by prohibition.



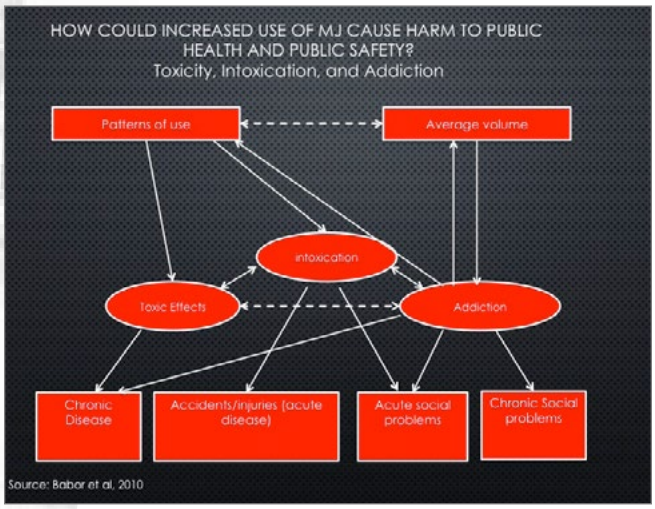
And this is what has happened: Now we have alcohol that is a legal drug, and actually the rates of addiction for alcohol are 3.5 times that of those for all illicit drugs combined. This is the latest data from a nationally representative sample, using the latest, standardized criteria for making a diagnosis of addiction, and we have obviously much higher rates when you give people access to an addictive drug like alcohol; it does produce higher rates of addiction.

So did re-legalization in this case put an end to our alcohol problems? Alcohol, as I mentioned, is an addictive drug. Of the 23 million people who have a drug addiction in the United States, about 18 million of those are addicted to alcohol.

Alcohol is a level 1 carcinogen. It causes cancer. Less than 1.5 drinks a day increases breast cancer risk by 25% in women. Not many people know that. Not many primary care physicians know that. Forty million individuals drink at levels that are harmful and hazardous. We have 100,000 deaths per year due to alcohol. It's the third leading preventable cause of death in this country.

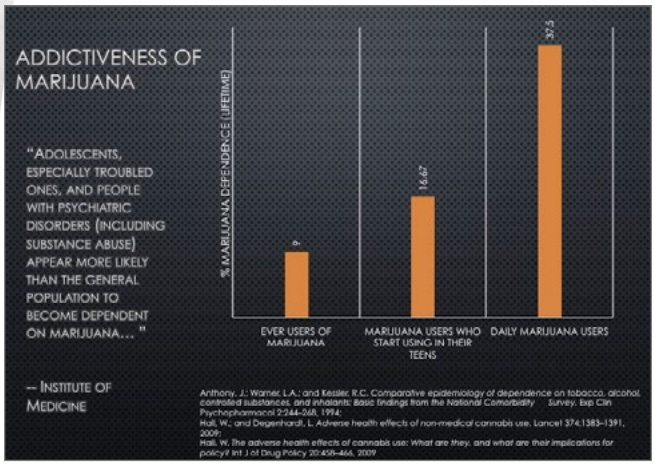
We get some money from sales tax revenue—and this is one of the promises of marijuana, that we could get some money from selling it. We get about $15 billion; $9 billion federal level and $6 billion state level tax revenue, but the cost is $250 billion. That's 17 times higher. Who's paying the tab? As I mentioned, we have 3 million alcohol related arrests each year for alcohol. So, if prohibition didn't work, it's hard to make the case from these data that somehow legalization is the answer.

Here's an interesting question. If alcohol is so addictive and the majority of addiction cases in this country are due to alcohol, why don't we have on the containers, "May cause addiction"? Any ideas? It's a level 1 carcinogen in the same category as asbestos. How come it doesn't say, "May cause cancer"? Or, "Alcohol causes cancer"? Why don't we have that on our alcohol containers? I know the alcohol industry would be in favor of that. Right? Putting those statements on them.

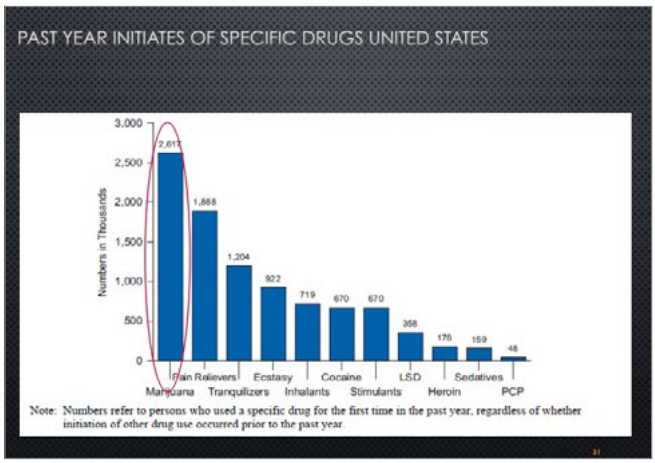


When we look at the ways that substances can cause harm, we know that drugs cause harm in three related, but distinct ways:

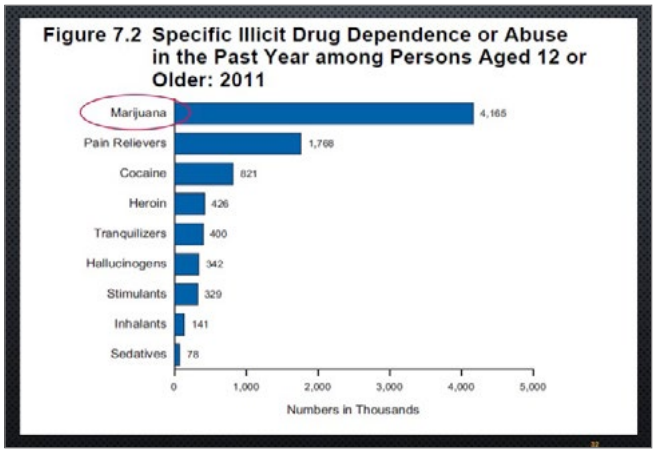
(1) Through toxicity, which Dr. Gruber talked about in terms of neurocognitive deficits, impairments produced by exposure to the substance and particularly at critical developmental stages.
(2) Intoxication is another one independent of toxicity. In other words, you can smoke a couple of joints, get high, fall down the stairs, get into a car and drive, and crash. So there are harms to just acute intoxication, independent of toxicity.
(3) Also independent is addiction, which is the one that we are most familiar with—people getting hooked on a drug. We know that marijuana does produce addiction in about 9-10% of cases that are exposed to it.



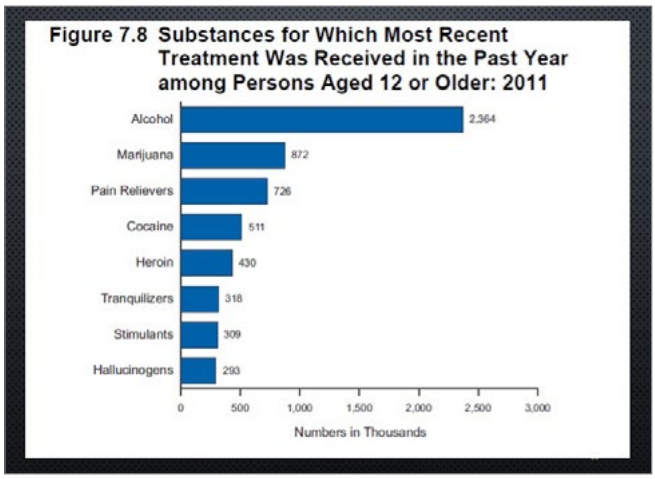
We also know that early exposure increases that risk exponentially. So we have marijuana dependence increase about 17% if they start in their teens, and if you're a regular user, you go to 38% risk of meeting criteria for a use disorder.



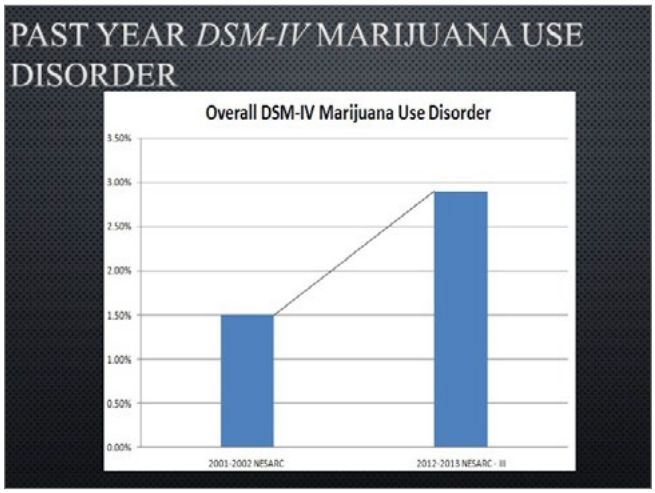
When we look at rates of use nationally, we find that marijuana is the most popular drug in terms of use.



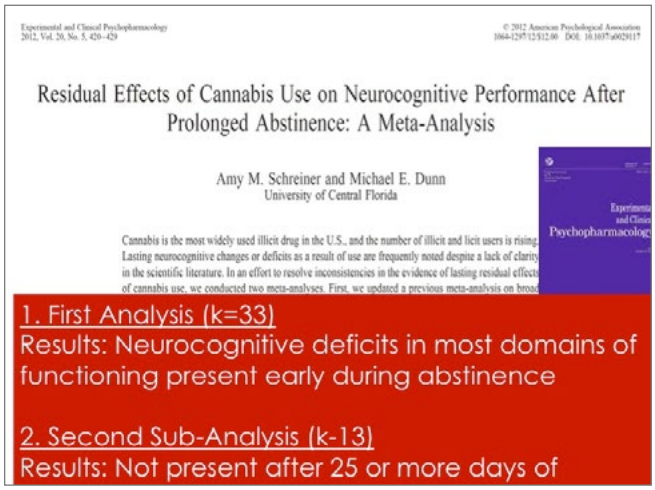
In terms of use disorders also, because it's the most widely used. Because it does cause addiction, we see a majority of addiction cases when we look at the population in terms of the type of drugs, other than alcohol, of course.



Also for coming in for treatment, after alcohol, marijuana is the most common substance for which people seek treatment in this country, among young people, adolescents up through age 18 or 19. About 90% of adolescents coming in for treatment are coming in for a marijuana use disorder.

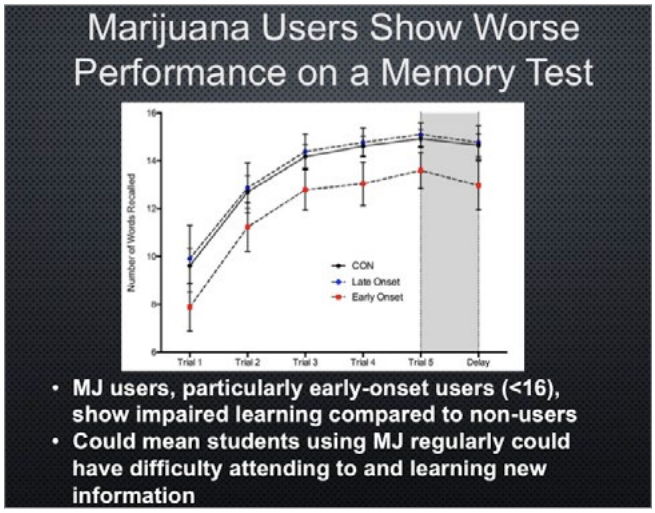


Have we seen an increase? This is again nationally representative data. When we look at marijuana use disorder specifically, we can see roughly a doubling in the incidence of marijuana use disorder between 2001 and 2013. It causes addiction.

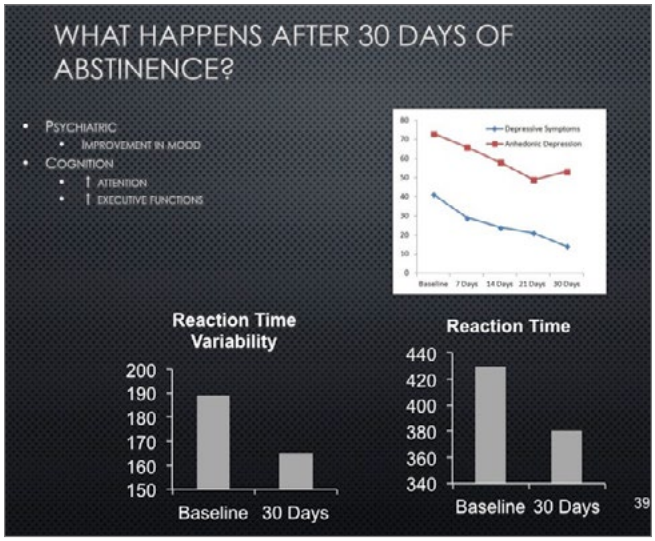


What about toxicity? That was one of the other pathways through which substances cause harm, and Dr. Gruber really focused on this very well in terms of looking at the neurotoxicity. As Dr. Gruber alluded to, we don't seem to see these kinds of neurotoxic effects with older adults. Again, the toxicity is in the dose. It's how much you use that determines what kind of an impact you will have.

This is a systematic quantitative review of the studies that have been done looking at neurocognitive deficits attributable to marijuana intoxication. When they didn't isolate those who were abstinent for about a month, they found that there was a residual neurocognitive deficit, but after 25 days, in adults they did not find any neurocognitive deficit among regular heavy users. But we do see it in adolescents. This notion of early onset and underage use given that states have legalized it at the age of 21, the way that we have with alcohol.

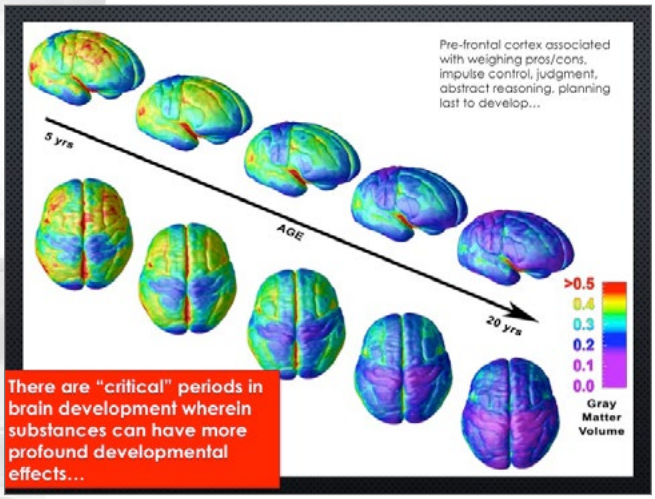


These are some studies from our lab. Dr. Gilman and Dr. Shista, from the Center for Addiction Medicine at MGH, have done some nice studies showing how exposure affects memory work and memory attention.

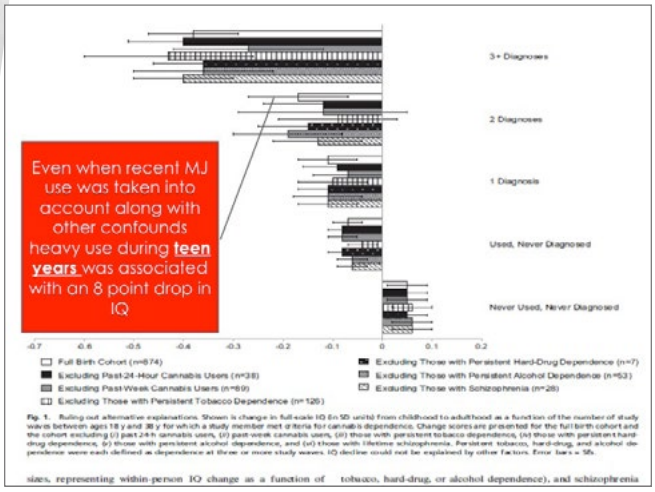


One of the interesting things about this study was what happened when people stopped—Dr. Shista was paying people to stop for 30 days. So she paid adolescents who

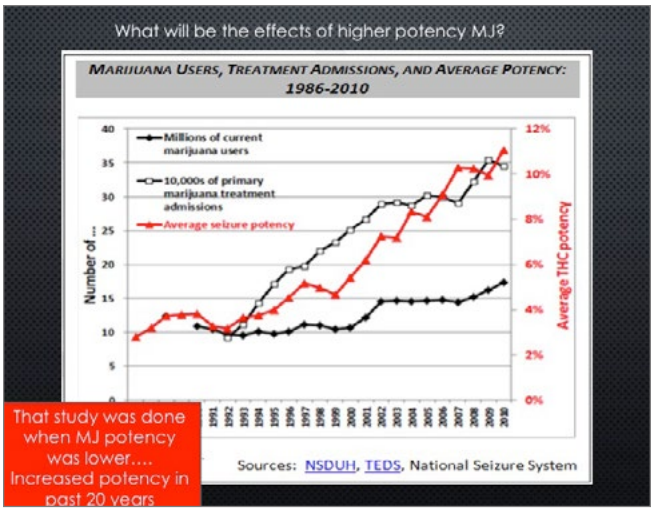
were regular users to stop smoking, and then she measured their neurocognitive function and mood, and what she found was in that 30-day period, their mood actually improved. You can see their depression symptoms actually went down substantially over that 30-day period. People will tell you, marijuana made them feel better. Objectively, it actually tends to improve mood when people abstain, at least in that sample.



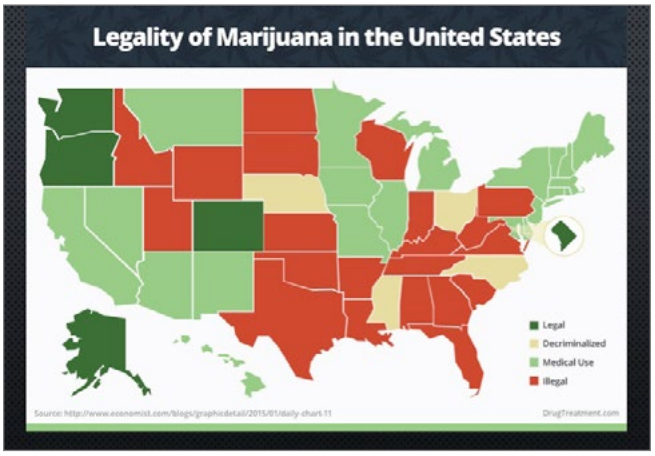
There are certain critical periods. Dr. Gruber very nicely mentioned this and explained this critical period of development seems to have unique long-term effects on development. This is a long-term study. It's the best study that we have long-term that's followed up 1,300 people from age 13, before they were exposed to any alcohol or other drugs, including marijuana. They followed them up for 25 years, up to age 38.



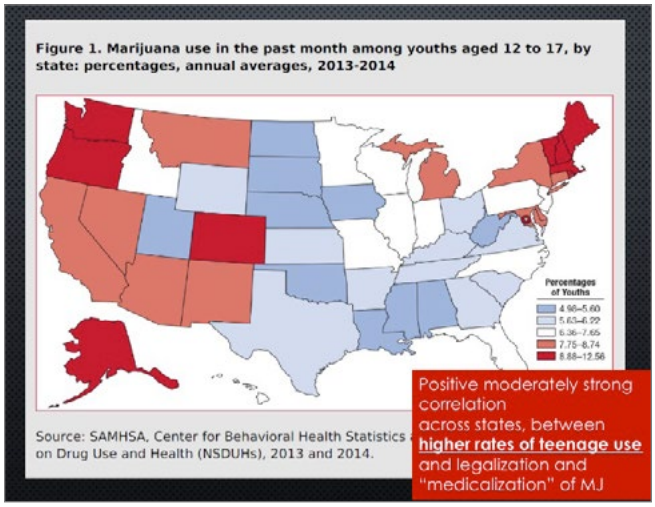
What they found is that only those who had smoked during adolescence had long-term deficits. They were heavy smokers during adolescence and had an 8-point lower IQ on average over this 25-year period. They lost 8 IQ points. That's going from the 50th percentile to the 29th. That's a pretty big drop. In fact, other people in their environment were able to notice it. It was actually discernible. People could notice the people who had smoked during adolescence even 25 years later; their attention and memory were poorer, even when they had stopped for a year or more.



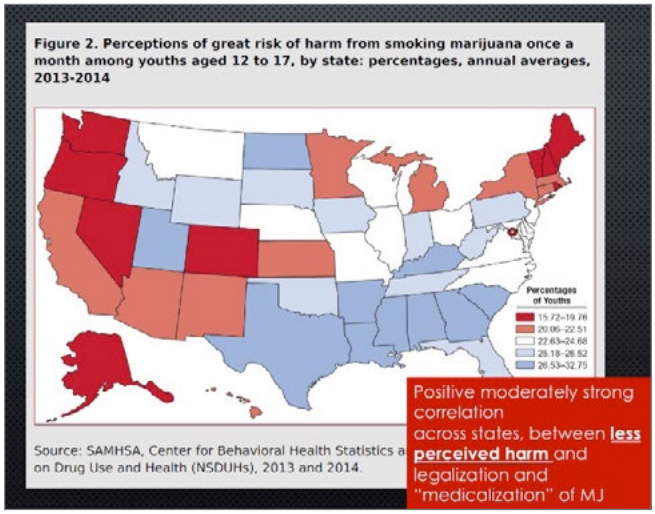
Potency has increased.



What's also interesting, regarding underage use, which is a particularly worrisome issue with potential legalization, is these are the states where you see marijuana, medical marijuana, and legalized recreational use. You see the green and the dark green. Now I'm going to show you the rates of past month use of marijuana in 12 to 17 year olds.



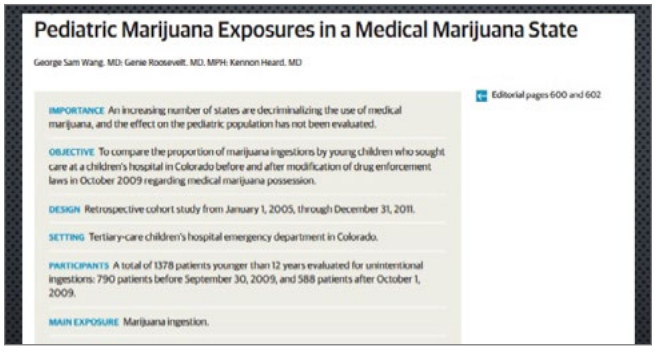
You see that? You see the relationship? The heavier colors, the red colors are the heavier rates of use among teenagers. So I would say a moderate to strong correlation between medicalization and legalization and higher rates of use in teenagers.



This is perception of great risk. Again, there is exactly the same pattern among adolescents. Those living in states where it is medicalized or legalized, you see a strong correlation between that and a lower perception of harm.

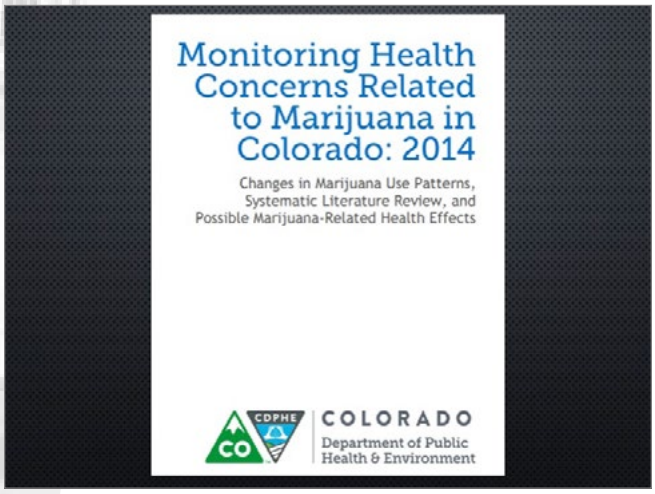
One of the other things from a public health and safety standpoint is edibles. Now we have concentrated forms of alcohol. We have hard liquor. We have beer. We have wine. We have different concentrations of alcohol. And we have the same for marijuana.

One of the things we have seen is an increase in poisoning among kids as they have picked up gummy bears, candies and consumed them. In fact, exposure among 6-year olds in terms of poisoning has increased about 148% from 2006 to 2013, particularly in states where medical marijuana is available.

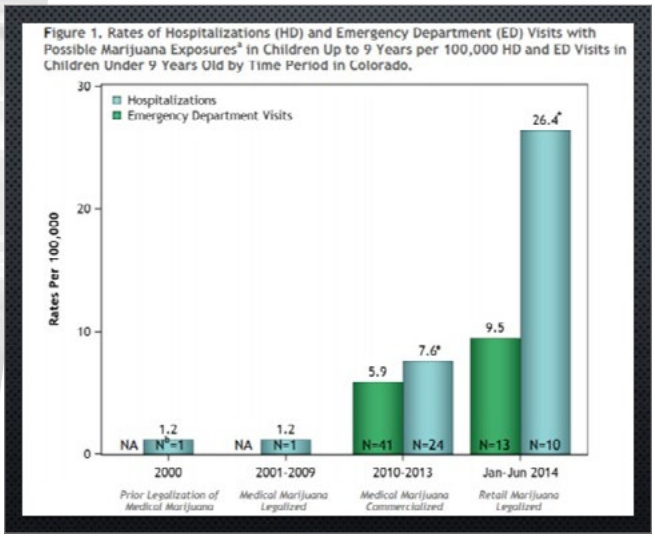


As you might suspect, as we've seen with the opioid crisis, the more you have these sitting around in people's medicine cabinets, the more likely people are to pick them up and

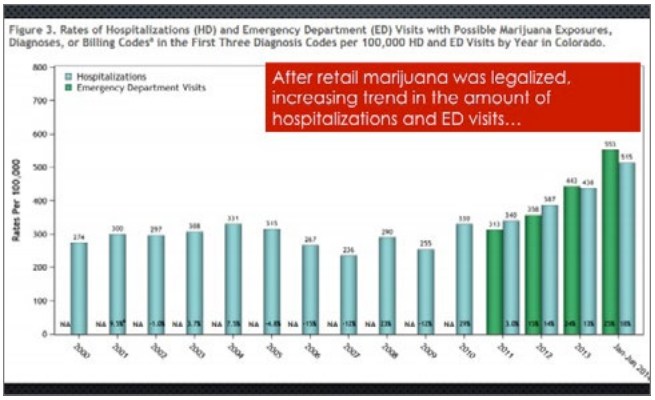
use them. The same seems to be also true with marijuana, too. The more you make it available, the more likely it is for someone to consume it and potentially have an adverse event.



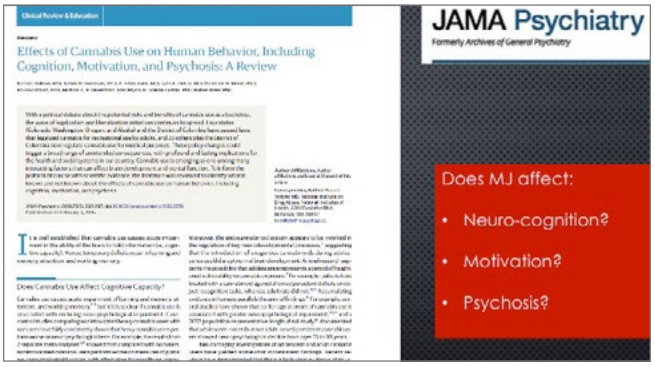
What have we learned about Colorado and Washington in terms of what's happened there with legalization?



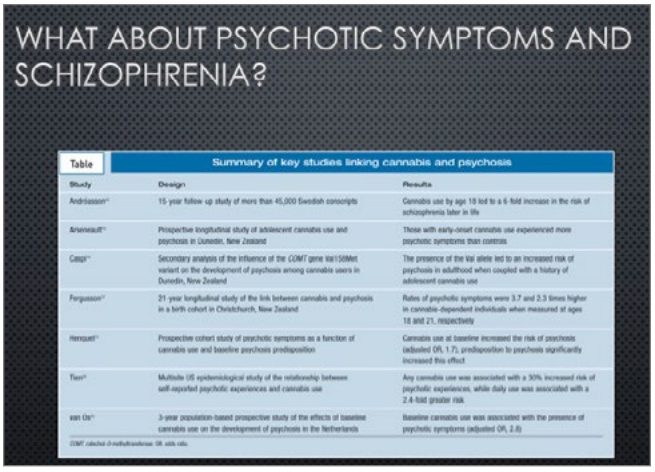
We have seen, similar to medical marijuana states, an increase in emergency department visits. Again these are small numbers. You look at the bottom, n=10, there on the right, so these are very small numbers of people, but it's going in the direction that we don't want to see, but I would expect to see given higher availability.



And the same after the legalization and commercialization of marijuana: We see increases in emergency department visits in Colorado related to acute intoxication.



Another worrying aspect of marijuana in particular is an association with psychosis. We know that exposure to cannabis, part of the pharmacodynamic effect of cannabis/THC on the brain, is that it produces psychosis.

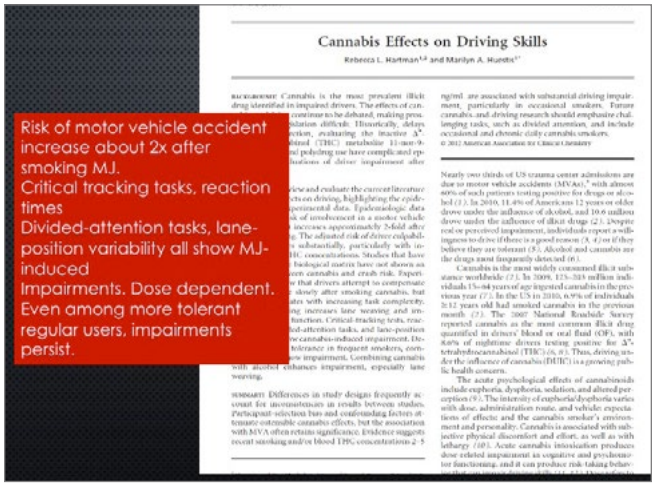


At high doses, it can produce hallucinations, and it can also produce a residual psychotic spectrum illness. Sometimes this does not go away; we call this schizophrenia. Sometimes

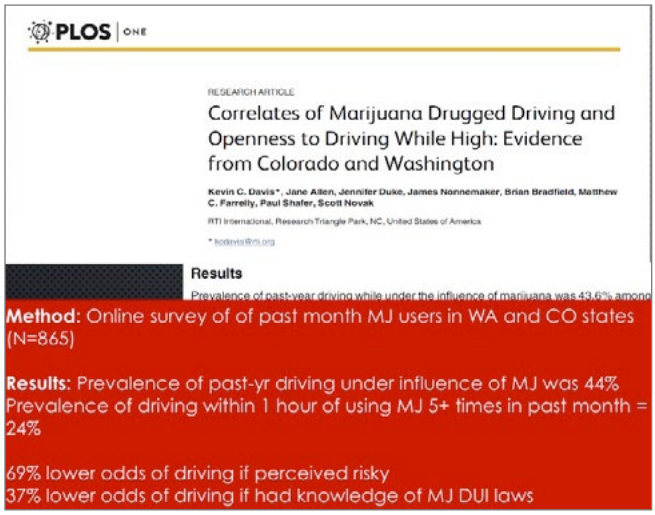
it does go away after 6 months or 12 months. I've seen many cases that have been exposed to high potency marijuana who have had one or two years of psychotic spectrum illness and not schizophrenia, but nevertheless, it's been very debilitating for individuals. There is a strong link with psychotic symptoms.

We don't really know what the true story is regarding schizophrenia, but there is an association there. About half the risk for schizophrenia is genetic, but it requires exposure to certain environmental conditions and certainly exposure to marijuana may increase the risk of the onset for schizophrenia. We need more research in that area.

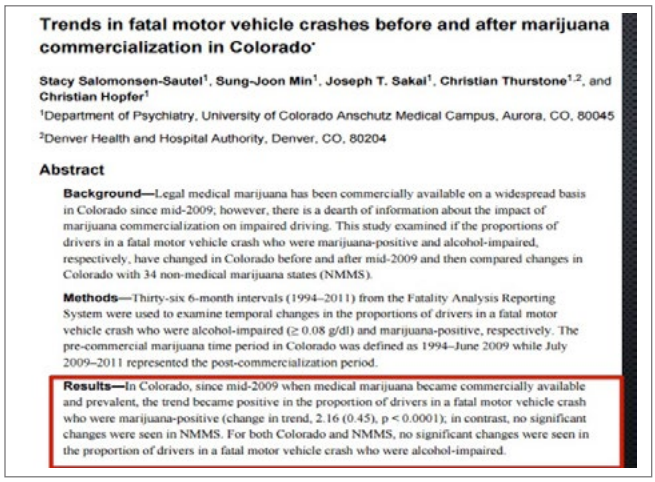
The third thing I want to talk about is intoxication. Intoxication, of course, is another pathway, different from toxicity and different from addiction. You can smoke and get high with a packet of Doritos on your couch, and there's not much of a consequence, but if you get in your car and drive, then there can be a consequence where you have to really pay attention and focus and respond quickly to things that are coming around the bend.



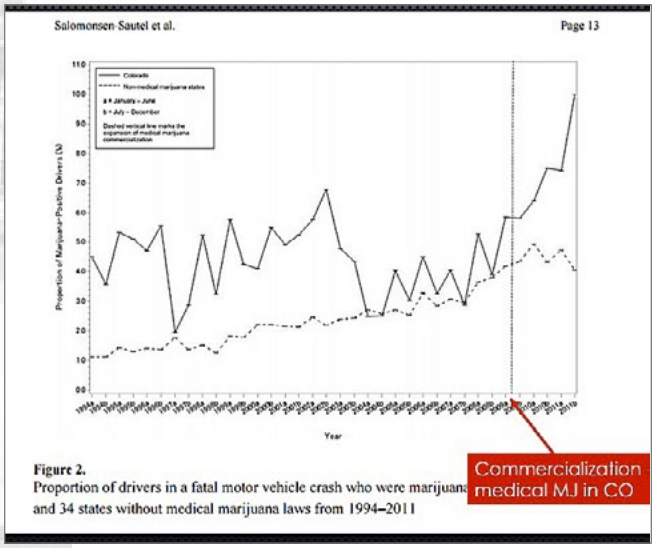
What we see with marijuana: It produces psychological impairment. It increases the risk of having an accident by about two times. There are many studies that have looked at this, and this is a quantitative review showing that because it produces impairment in reaction time, attention focus, etc., it produces accidents.



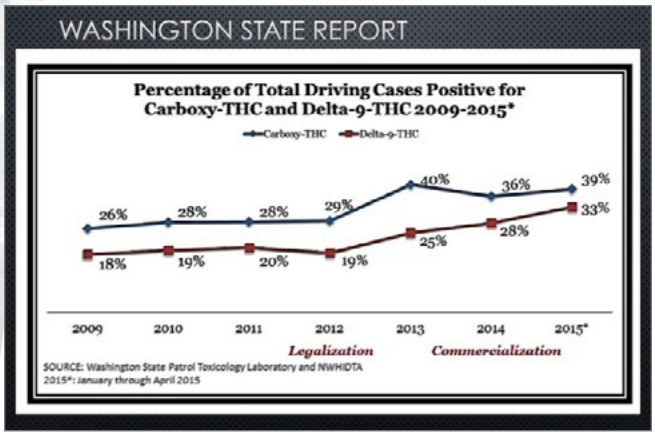
This is an interesting study that just came out looking at marijuana drugged driving and openness to driving while high, which was done in Colorado and Washington. Just published. What they found is that in this sample of roughly 865 folks, the past year driving under the influence of marijuana was 44%, and prevalence within one hour of using marijuana five times in the past month was 24%. So it's quite high when you look at a potential damage that lifelong harm that that can produce.



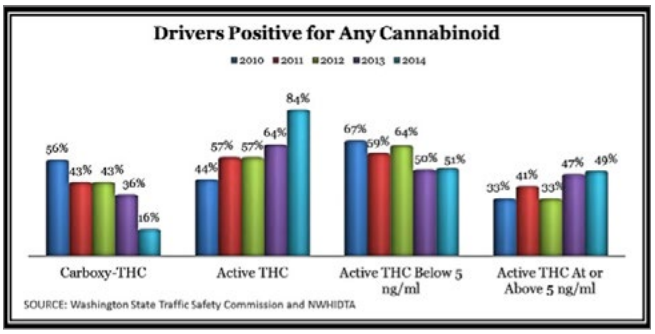
This is also a study that recently came out in Colorado looking at trends in fatal motor vehicle crashes before and after commercialization.



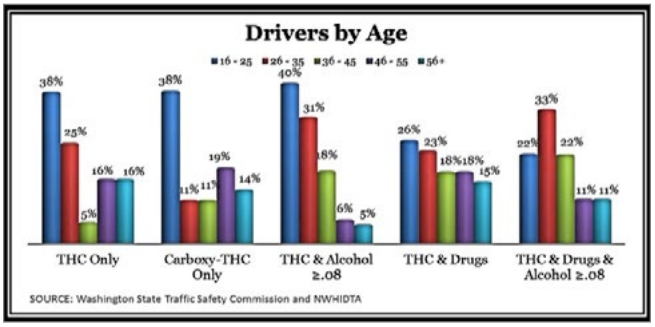
What we see over on the right hand side is an increase in Colorado after the commercialization of marijuana. There is also an association of medical marijuana with an increase in deaths, crashes related to marijuana, and testing positive for marijuana after the crash. Those on the other line below are the non-medical marijuana states.



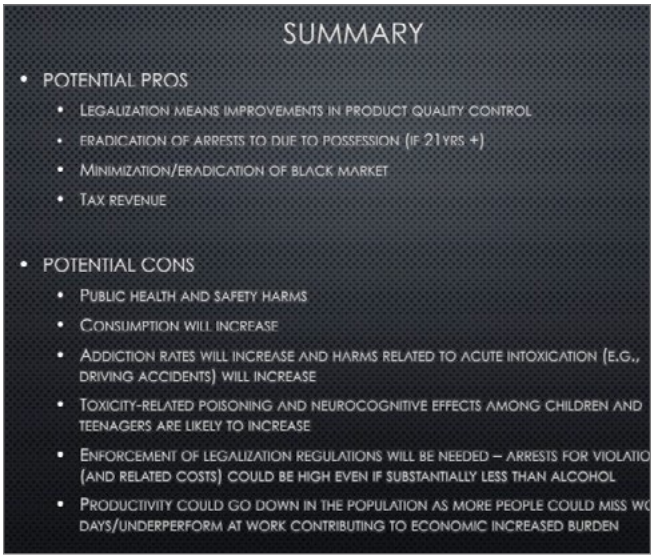
In Washington State, there has also been an increase in drugged driving cases: about a 33% increase relative to the baseline.



Drivers testing positive has gone up over time.



What's interesting is age. We see that young people are much more likely to drive under the influence. You can see here, between the ages of 16 and 25, 26 and 35—these are the highest rates. Young people are the ones who are smoking marijuana as well.



Just to finish up, when we think about legalization, there are pros and cons to each position. We think about the potential pros of legalization, and we would improve the quality control

of the product. That's what happens when we legalize it. We can eradicate arrests due to possession and we can eradicate the black market. The bad guys get put out of business. Now we have control over the quality of production and distribution, and of course it can produce tax revenues. So this is one of the arguments for it.

On the downside, there are public health and safety harms having to do with increased addiction, toxicity, neurotoxicity, and intoxication. Drugged driving. Accidents. Those will increase. We've seen increases in toxicity-related poisoning. We are likely to see that especially with edibles.

And, of course, we have to consider the enforcement of legalization. As I mentioned, there are 3 million arrests for alcohol—that's a legal drug—a year. We would reduce arrests for possession by 700,000, but we may replace that with arrests for violations of the legalization laws/regulations governing marijuana.

Another thing to consider, of course, is productivity. One of the major contributors to the burden of disease, disability, and premature mortality related to alcohol and other drugs is lost productivity: People missing work or not working to their full potential because of the impact of their psychoactive substance on their cognitive functioning. With more people exposed, we are likely to see more lost days in terms of productivity.

With that I will stop and thank you very much for the invitation and your attention. I'll take questions. Thank you.

QUESTION AND ANSWER

Audience: What do you see is driving the effort to complete legalization? Is it commercial interest? Is it other recreational business? Given that all of the problems that you mentioned, what's behind it?

John Kelly: One is supply. One is demand. One is the corporate interest that is projected by 2020. If we were to follow the path of legalization, the marijuana industry would be $35 billion a year. That's a lot of money. And these individuals want to legalize it like alcohol. This is their motto. This is in fact their name. Legalize marijuana like alcohol because the alcohol industry makes a lot of money from commercialization, so that's what they would prefer. There's going to be a lot of push to commercialize it and make big profits. There's also a demand side, so there's a lot of people who want to be able to smoke marijuana, and why should marijuana be illegal if alcohol is legal. So they make that argument. It's a both a supply and a demand, I think, but there's a lot of misinformation. As we all know, sitting here today, there's a lot of misinformation, fuzziness, and muddying of the waters out there, so it's hard to get any real reliable information on this topic, so that makes it tricky, too.

Audience: On the subject of actually [inaudible] market regulation, do we know what kind of substances are going to be [inaudible] United States [inaudible].

John Kelly: They're kind of in that sweet spot of being regulated, like opioids. That's a bad example right now, but there's one, benzodiazepines, stimulants, like Adderall. These have potential for diversion and misuse because they produce effects that people like recreationally. But there is a sweet spot here in the middle. That's what you're alluding to. Those drugs would fit into that category, but we've seen a problem with overprescribing of opioids, which we're going to hear about this afternoon. Again, it's kind of ironic, isn't it? On the one hand, we're talking about an opioid crisis which is caused by excess availability. And then we're talking about marijuana, and we want to increase availability, even though we know it causes similar issues. It doesn't cause the kind of mortality that we see, direct drug-specific mortality, drug-induced mortality that we see with opioids.

Nonetheless, it causes a lot of other problems that we're going to have to contend with. It's kind of ironic. We're going to increase availability and give them access to marijuana, while we're fighting right now to decrease availability of opioids.

But I think the sweet spot would be decriminalization. You look at Portugal. They have decriminalized the use of all drugs. Have not seen a great increase in drug use, if at all, by decriminalizing. That's not legalizing. That's decriminalizing any personal drug use. It's still illegal to sell and distribute drugs, but it's not illegal to consume them. That's what we had under prohibition for alcohol actually. It wasn't illegal under prohibition of alcohol to consume alcohol. It was illegal to sell, manufacture, and distribute alcohol. That was the amendment. But it, if you look at decriminalization, that's the pretty good sweet spot right there in terms of reducing the overall harms of both commercialization and prohibition.

Another way to go would be legalization with no advertising, state controlled monopoly, like New Hampshire does with alcohol. You have state run stores. People can get it. It's not illegal, but it's not being pushed in people's faces. There are no targeting of vulnerable subgroups through advertising, and that could be a way that we could reduce harm, too. Still be legal, but it wouldn't be the full-blown commercialization that we've seen with alcohol and tobacco and the related harms associated with that.

Audience: My question is in this statement, but you could speak on it a little bit with smoking of cigarettes when you had the 1960s and that push with cigarettes are bad. That knowledge was out there, but suddenly became more prevalent throughout the years. Some studies you've seen the rates of smoking cigarettes decline. Do you see something like that happening with marijuana eventually with the knowledge that particularly with younger people using it that there are detrimental effects? Do you see that eventually taking place?

John Kelly: I think we can see that happening, if we went the path of legalization. Now we've got a cheaper product, quality controlled. Maybe with advertising, more people are going to use it. Your rates are going to go up. I'd be shocked if rates did not go up. Absolutely shocked. I'd bet my house that rates are going to go up. Rates of addiction are going to go up, rates of drugged driving, accidents. All of that will go up. After ten, twenty, thirty years, who knows? Maybe people will say maybe we need to put a lid on this. Maybe we need to change some of the policies, like we did with tobacco, and increase the price and make it less desirable and less available. I think we have learned some lessons from tobacco that we can apply to marijuana — and from alcohol that we could apply — if this went through in more and more states like Massachusetts. But my guess is yes, I think as we start to see more harm incurred — the casualties from addiction and intoxication and toxicities — that we might start to implement some of those lessons. One of the other arguments, of course, is let's try this for a while and then we can go back, and we'll go back and ban it again. How hard is that to do? We tried that right. It was called the 18th amendment. Ever try to make something illegal that's been embedded in our culture that has tax stakes, tax embeddedness in it? In Colorado they're using that tax for schools.

Audience: I would say let's see what happens in Colorado and we'll decide five years from now. I think that's better to [inaudible], but that's not the reason I raised my hand. Did either of you hit on the [inaudible] marijuana just following up to your question, is a carcinogen that will cause like lung cancer, emphysema whereas you pointed out smoking has gone like this there's a concerted national effort to drive down smoking rates and it's worked. Does marijuana cause lung cancer? Will people die from lung cancer if they're users?

John Kelly: There aren't too many studies, there aren't too many long-term studies that have looked at this, but there are respiratory problems. Lung problems. Breathing problems with smoking marijuana. Less so with vaping. So if you're vaping without any of the bad stuff being burned and inhaled, that can reduce the risk of respiratory problems.

Stacy Gruber: There's only been one study demonstrating that there isn't a huge increase in lung cancer in folks that smoke marijuana, but again, they are pretty sparse and the one thing is that vapors and things like that are incredibly carcinogenic, so the idea is to move people to more safe ways of using.

Audience: So you talked about decriminalization as a sweet spot and one of the things that gets lost in the conversation is I do clinical work. A lot of people don't know, I'm not a policy expert, but I believe in [inaudible] small amounts of possession under 20 grams of marijuana. For people who don't know, that's a daily use for quite a while. It's quite a lot. So based on—is there any data out there or based on your expertise, why is decriminalization not good enough for people if it does seem to hit the sweet spot where we're not increasing availability but we're also not incarcerating people, and if it hits that public health sweet spot, why is that not good enough for some people?

John Kelly: I think part of it is that people don't know the difference between decriminalization and legalization. In people's minds, they think that's the same thing. That's why they think, we're arresting all these people with marijuana and the war on drugs doesn't work, therefore let's legalize it. Really that's an argument for decriminalization, which is not legalization. So I think a lot of people don't understand the maybe subtle difference between decriminalization versus legalization, and then legalization with few restrictions or with many proscriptions, versus legalization with commercialization with few restriction. I think that's part of it. People don't know in the general public or they don't even stop to think. I think that's part of the problem. But when you look at a chart like this you think oh yeah, I didn't really think about that. Right? Didn't really think about that. What's the scientific basis of medical marijuana? I didn't really think about that. I just think that this is a really a good idea. By popular vote, we've made that legal. Not based on science but based on popular vote. Interesting.

Audience: I just want everybody in the room to know that I've been [a district attorney] since 1984. I can't think of a single case in Boston where somebody went to jail for possessing marijuana in my entire career. In fact going back 30 years, the state legislature passed a statute that says if you're caught with possession of marijuana, it's an automatic disposition of continued without a finding, which means if you keep your nose clean for a period of time, the case is dismissed. And in order to be convicted of trafficking in marijuana in Massachusetts, 50 pounds. You said 20—20 grams is enough to keep you going for a month. How much is 50 pounds. Very few people even go to jail for that in Massachusetts. I just wanted you to know that.

John Kelly: And pretty much universally, that's true. Pretty much across the board, but maybe down south and places in Texas, you might see more harsh penalties, but in general where there is decriminalization, hardly anybody will go to prison just for use or possession of a small amount.

Audience: I have [inaudible] both of you mentioned the increase in drugged driving and I know from speaking with different legislators, one of the challenges is how do we know and how do we measure drugged driving the same way that we're able to measure drunk driving and be able to prosecute correctly people who are driving [inaudible]?

John Kelly: We don't have a good way right now of measuring that. Roadside. And so this is a problem that we're going to face: developing technology that can be immediately appraised and evaluated to see if someone is under the influence. The way that it's been done is post hoc. After an accident, they're taken in and taking a urine sample a blood sample a bit later.

Audience: Is there any evidence that legalization increases consumption?

John Kelly: Yes. Oh yes. Again, price and availability are two big factors which will influence consumption. Every company knows that. Price and availability of their product. If you make something that produces euphoria and pleasant feelings like Oreo cookies or something like that, or marijuana, alcohol that people like the effect of. You make it cheaper. You make it available on the corner, legally you destigmatize it, and you will see increased use. That's different from decriminalization. Right? And also it depends on, like I said, are you making it legal with full commercialization? Or are you making it legal and with non-commercialization? There's a big difference there, as we've seen with tobacco and alcohol. There are certain restrictions governing alcohol and tobacco, but the alcohol industry spends $15 billion-$20 billion a year on advertising. So they know advertising works. And it's worth the investment if they spend that much money advertising. Think how much money they're making based on the advertising. So commercialization really does increase consumption because it increases those profits.

CLARK UNIVERSITY
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The Highs and Lows of Relapse and Recovery in Opioid Use Disorder

By Kathleen M. Palm Reed, Ph.D.

POLICY BRIEF

Opiate Use Disorder (OUD) is a chronic, relapsing disorder with significant mortality, morbidity, and disability. Over 2.6 million Americans are currently living with an opioid use disorder.[1] High relapse rates[2] and rapidly increasing numbers of overdose deaths[3] highlight the urgency of the opioid crisis.

Early stages of treatment, when relapse and overdose rates are highest,[4, 5] are a critical period for setting up a successful recovery. Early lapse is predictive of full-blown relapse and may lead to treatment dropout.[6] Conversely, early abstinence in the first few weeks of treatment is predictive of long-term abstinence.[7] Being younger and unemployed increase risk of early relapse.[8] Additional risk factors for early relapse include co-occurring mental health conditions, use of other illicit substances, and chronic pain.

Fortunately, there are a number of relapse prevention and treatment options that improve chances for a successful recovery. Those who receive ongoing supportive counseling, medication-assisted treatment,[9] greater drug-free social support,[10] and who actively participate in AA/NA have better long-term outcomes.[11] Further, having positive expectations about treatment success and greater commitment to abstinence[12] influence treatment engagement and long-term abstinence. Unfortunately, barriers such as stigma may defeat any positive expectations of recovery and, ultimately, lead to treatment dropout.

STIGMA AS A ROADBLOCK TO RECOVERY

While public perceptions of OUD are changing, there continues to be a prevailing view that substance use is a moral failing. This stigma is apparent in the larger culture, but also among treatment staff and those suffering with OUD themselves.

Institutionalized stigma impacts treatment retention and engagement, and effective care.[13] OUD treatment is segregated from the rest of health care in practice and location, limiting the opportunity for communication between OUD and other health care providers, and decreasing accessibility to OUD treatment clinics. Integration of methadone maintenance treatment in primary care settings has shown greater treatment retention compared to stand alone clinics.[14]

Another source of stigma comes from treatment staff, who may regard individuals with OUD as untrustworthy and dangerous.[15] Greater stigma and rejection by treatment staff is particularly reported by patients with more prior episodes of treatment, intravenous drug use, and co-occurring mental health conditions.[16] Unfortunately, similar stigmatizing attitudes are also present in self-help groups, with many of those in recovery reporting that they do not disclose their participation in methadone maintenance treatment due to fear of stigma and rejection.[17]

Shame and internalized stigma associated with opiate use can trigger relapse and also serve as a barrier to seeking help. Among adolescents with OUD, two of the most frequently cited reasons for not seeking treatment are "didn't want others to find out," and "treatment might cause neighbors to have negative opinions."[18]

POLICY RECOMMENDATIONS

- The first few months after treatment are a high risk period for relapse. We need greater efforts to facilitate aftercare services and exposure to drug-free support networks. Vocational services may mitigate risk for early relapse.
- Peer recovery and 12-Step programs are beneficial, and may offer sustainable sources of support for those in recovery. Specific recommendations by physicians to pursue these programs may foster greater participation.
- Consideration should be given to relocating drug treatment services to mainstream health centers that address both substance use disorder and underlying medical and/or behavioral health issues.
- Improved training and support, and increasing the number of treatment providers, may reduce burnout and increase compassion among treatment staff, thereby decreasing stigmatizing attitudes.
- Educational campaigns aimed at changing attitudes and perceptions of OUD and treatment may reduce stigma. Further, educating families and schools on how to discuss substance abuse and treatment options can facilitate help-seeking.

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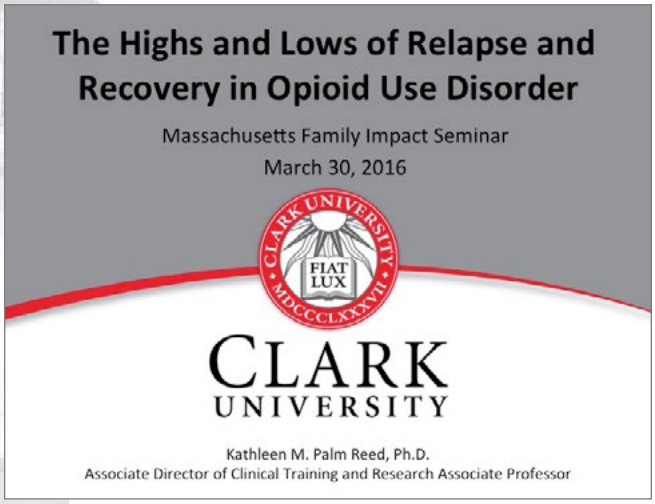
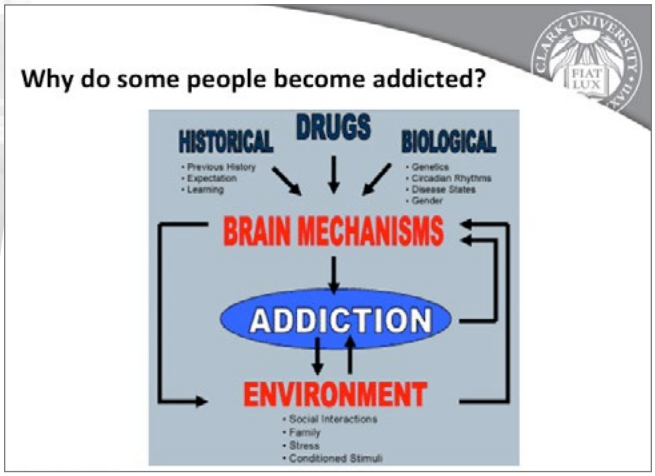
TRANSCRIPT OF DR. PALM REED'S TALK



Today I'm going to talk to you about opioid use disorders. When I talk about opioids, I'm referring to heroin and other opiate prescription medications such as OxyContin, oxycodone, hydrocodone, and others that fit that group.

I'd like to give you a brief overview of trends that we've seen in terms of opioid use disorder, with particular focus on the relapse and recovery for individuals who are struggling with opioid use disorder.

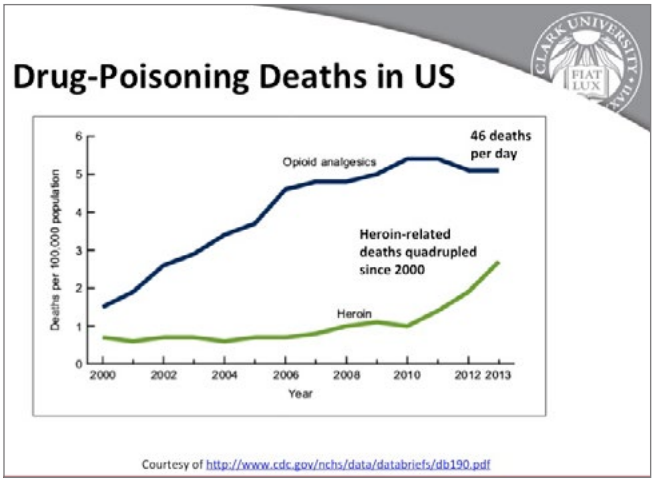


So, before talking too much about relapse and recovery, I'm going to talk to you a little bit about why people become addicted in the first place. This is usually the first question that my students ask me when I'm talking to them about substance use disorders. As many of our speakers have already alluded to in our talks this morning is, it's complex. There could be a number of historical, biological, and environmental factors that increase one's risk for becoming addicted to a substance.

Additionally, there could be factors associated with the drug itself. All of these things interact with each other to increase one's risk for addiction. There's no one defined route that leads one to addiction. People become addicted for different reasons. Similarly, there's no one simple answer for addressing substance use disorders, specifically opioid use disorder.

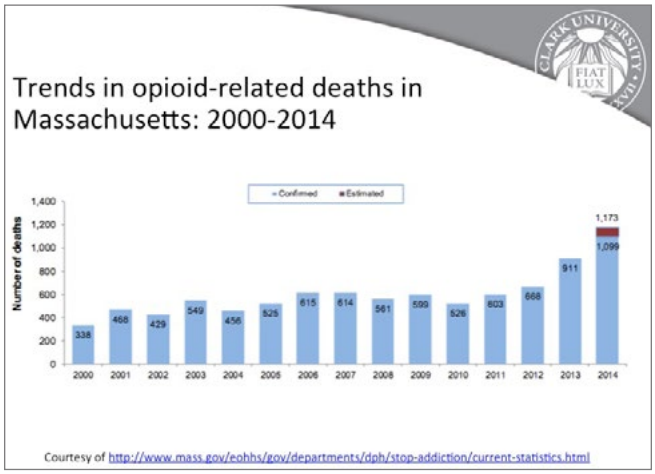
So, interventions and policies that we adopt to prevent substance use disorder, and to improve our rates of recovery for opioid use disorder, need to be multi-pronged, addressing both of these individual and these environmental factors.

It's estimated that approximately 2.6 million Americans are currently living with opioid use disorder. What's become the opioid epidemic has been fueled by a number of things; including an increase in use and abuse of prescription opiate medications and increase in use of heroin. Heroin has become more available and cheaper than prescription opiates, and so more people are using heroin. It has gained particular attention related to the increase number of overdose deaths.



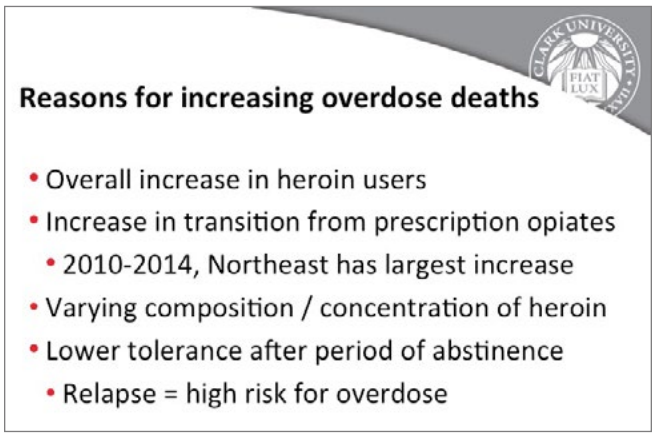
Looking more closely at the overdose-related deaths across the country, heroin-related deaths have quadrupled since 2000, and have continued to be on the rise.

If we were to translate these figures into what we're seeing on the ground every day, if we look at opiate-overdose deaths related to opiate medications alone, we could estimate there are about 46 deaths per day that are associated with overdose-related deaths.



This data is mirrored in what we are seeing in Massachusetts, as well. So there has been a steady increase in the rates of opioid-related deaths since 2000, particularly in the past five years. The rates in 2015 are still being finalized, but they're similar to what we've seen in 2014.

So the deaths — the accidental deaths related to opioid overdose, are now surpassing what we see in terms of car accidents.



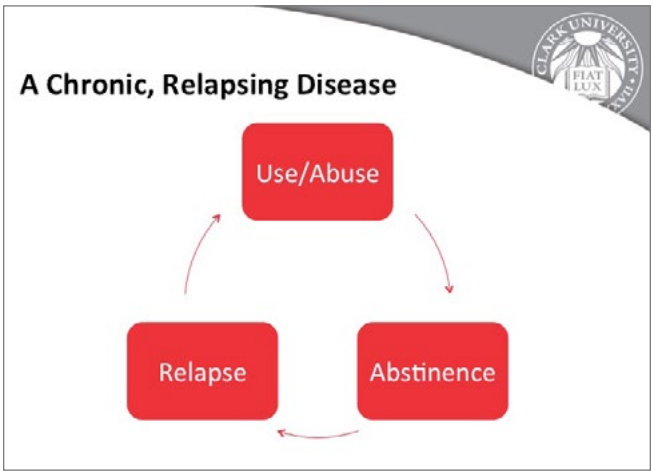
So the next logical question is, why are we seeing this increase in overdose deaths? There are a number of possible factors that might be contributing to this. First, there's an overall increase in the number of heroin users. It's more available and cheaper, and so more people are using it.

There has also been an increase in the transition from prescription opiate use and abuse to heroin. In some ways, prescription opiates have become more expensive and less available in recent years, and so some people are turning to heroin as an alternative. In particular, between 2010 and 2014, the Northeast region of the country saw the greatest transition from prescription opiate use to heroin use.

Another factor that contributes to the rates of overdose deaths could be the varying composition and the concentration of heroin that people are using. So, if people were using prescription opiates before, there's a known amount of opiates that are in there. With heroin, you don't know what you're getting. There are varying doses and concentrations in it, and plus, there could be additional adulterants that are included in the heroin.

Fentanyl, for example, is one that we've heard about on the news recently, which can be lethal. And people don't know what it is that they're injecting.

Another reason why we've been seeing this increase in overdose-related deaths is that people, after they've had a period of abstinence, have a lower tolerance. If after a period of abstinence from being in treatment or being incarcerated, they relapse and go back to the level of use that they had before they had the period of abstinence, then they're at higher risk for overdose.

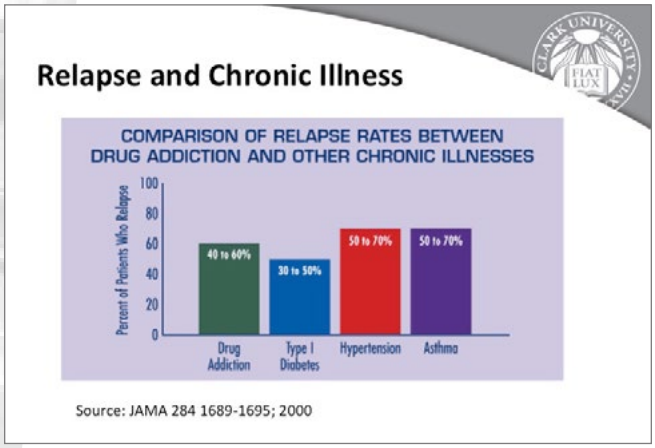


I want to spend some time today really focusing on this period of relapse—this phenomenon of relapse. There has been a lot of discussion about the prevention of opioid use, in general, which is very important.

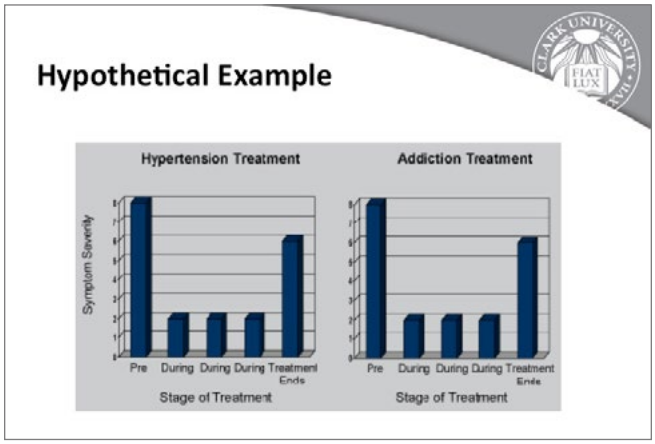
But it's also important to understand what it's like for people who are already struggling with opioid use disorder, and to understand the phenomenon of relapse and relapse prevention.

Over time, our understanding of what addiction is has changed, such that we've been understanding it more as a chronic and relapsing disease. We've come to this acknowledgement after realizing that relapse is common, with rates of lapsed opiate use from treatment-seeking individuals ranging from 60%-90% after treatment.

Relapse can happen at any time during recovery. It can happen after one year of being abstinent. It can happen after five years. It can happen after ten years, at any point — and it may take an average of nine years following someone's first intervention before they can have a full year of abstinence. So, we've come to understand recovery as a process because of this. Someone may experience multiple episodes of this use, abstinence, relapse, and treatment multiple times before they can achieve a full remission.



If we're thinking about substance use disorders or opioid use disorders, as chronic relapsing conditions, you might compare them to other chronic illnesses that we know something about. For example, other chronic illnesses are Type 1 Diabetes, asthma, and hypertension; and with those chronic illnesses, we also see high rates of relapse, affecting over half of those who are treatment-seeking.



Now this is hypothetical data; this isn't an actual study, but unlike other chronic illnesses, individuals who are struggling with substance use disorders are sometimes expected to be fixed after they have acute treatment. They go through detoxification, and that's meant to cure them. Right? We shouldn't expect any kind of relapse.

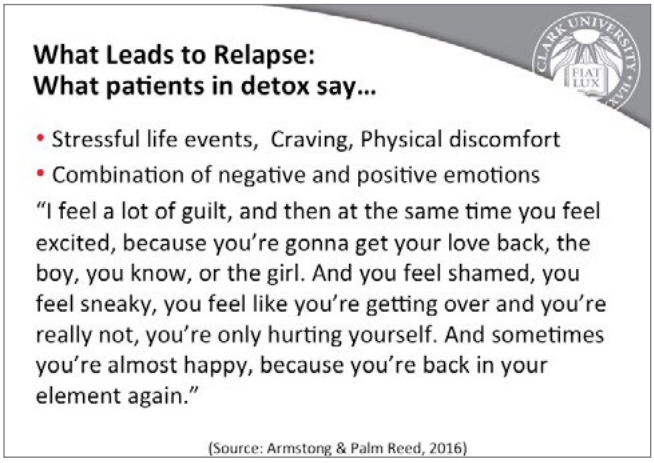
If we had that same kind of picture with someone who is struggling with hypertension, for example, and someone was really having a difficult time — they went into treatment, they were discharged from treatment, and there was nothing else that was done for them — then we wouldn't be terribly surprised if they relapsed and needed to be readmitted to the hospital.

Yet, we have this expectation with people who are struggling with substance use disorders, that they suddenly are cured from this. It's estimated that 31%-50% of opiate-dependent patients will relapse within the first two weeks after treatment. Not surprising if they're just expected to go out and try to deal with this on their own.

So, like other chronic illnesses, we should consider how we could best address the long-term maintenance of opioid use disorders, rather than just focusing on managing acute crises.

Researchers have been trying to understand what increases the likelihood of relapse. There have been a number of ways that researchers have tried to look at this. One way is they've interviewed people who have relapsed already and asked them to think back on what led to a previous relapse and to tell us more about that.

Another way that we've been trying to assess it is when people come in, we collect a lot of different information, do a lot of the clinical assessments that have been mentioned earlier, and follow them over time, to see after treatment, which one of those factors that we assessed beforehand actually predicts how well someone does afterwards, and what is predictive of early relapse.



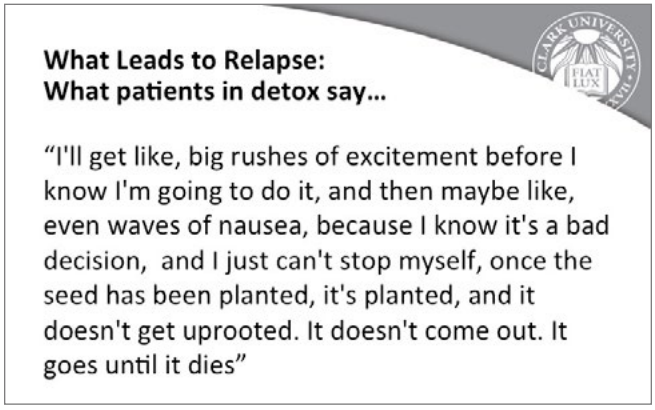
When we ask patients what they said led to relapse, they indicate a number of things. Probably some of the most commonly reported reasons are that they were exposed to triggers in some way; they might go back to their home environment or back to being with their friends who were using with them before. That might trigger a relapse.

There might be some sort of stressful life events, which could be negative; people also report positive events as being triggering and leading to relapse. Occasionally, people describe craving and physical discomfort that's associated with withdrawal.

Most often, people describe negative emotions that they experienced as triggering of relapse experiences, and sometimes it's a combination of positive and negative emotions.

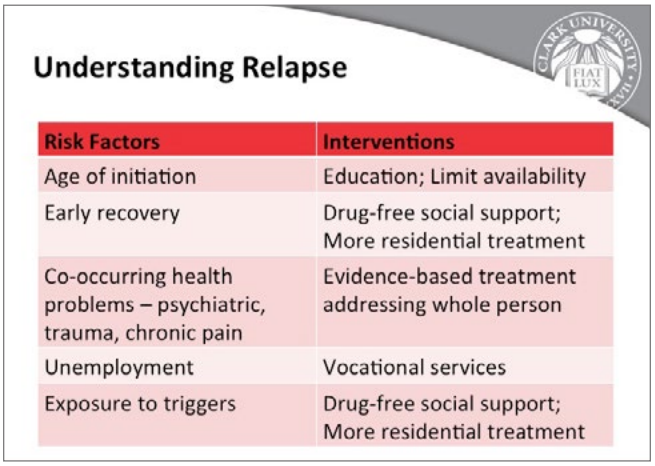
This is one study that we're wrapping up right now in my lab — Jessica Armstrong is finishing up her dissertation on this. She interviewed about 80 individuals in detox and asked them what they thought was going on that led up to their relapse experience.

I have a few quotes of what they reported was going on. One person says, "I feel a lot of guilt. And then at the same time, you feel excited because you're going to get your love back; the boy, you know, or the girl. And you feel ashamed. You feel sneaky. You feel like you're getting over and you're really not. You're only hurting yourself. And sometimes, you're almost happy, because you're back in your element again."



Another person describes a similar mix of positive and negative emotions. They say, "I'll get like, big rushes of excitement before I know I'm going to do it, and then maybe like, even waves of nausea, because I know it's a bad decision, and I just can't stop myself. Once the seed has been planted, it's planted, and it doesn't get uprooted. It doesn't come out. It goes until it dies," or until the person uses.

Through many of these interviews, we've also noticed that people know they're going to relapse before they actually relapse, and sometimes they have it planned out. You can see that they pull out of different types of support services that might have been helpful in maintaining their abstinence. So what that can indicate is that if they know that they're planning this, this might be an opportunity for treatment providers to intervene if we can recognize the signs that someone is starting to make a plan to relapse.



By looking at the research that has followed patients over time to see what factors really predict how soon and whether or not someone is going to relapse, we've identified several factors.

One is — and this is something that's come up in some of the talks earlier today — the earlier someone starts, the more difficult it is to stop, and the more likely it is that they're going to relapse. So, making sure that we address that the age of onset of substance use disorders is important in marijuana. It's also important in terms of individual's introduction to opioids.

We know that early recovery is a stage in treatment. The early stages of treatment are a time when relapse and overdose rates are high; this is an important time that we address. We also know that early abstinence is also predictive of long-term abstinence.

So this accumulating data is showing that there's something about the first several weeks, the first several months after someone has a period of abstinence through treatment; mostly that it's important that we provide supports during that time.

We also know that co-occurring health problems—whether they be psychiatric, whether there's a trauma history, whether there's chronic pain—that these are also risk factors for relapse. I do want to mention that there is some concern out there that chronic pain is a risk for substance use disorders. While some people with chronic pain do experience opioid disorders, that chronic pain in and of itself doesn't mean that someone is going to have an opioid use disorder.

However, if you have an opioid use disorder and chronic pain, it could be a risk factor for relapse because once they don't have the opiate anymore, they don't know how to really address their pain.

Numerous studies have also found that unemployment is a risk factor for relapse. So people who have a steady job are more likely to be able to maintain their abstinence. Then as I mentioned before, what the patients said was a trigger for relapse is just being back in the same environments that they were before they were abstinent. Those environments can be triggering.

Now we know that these factors are triggers for relapse—are predictive of relapse. We know a little bit about what types of interventions can be helpful, but there's a lot more that we can learn about it.

In terms of addressing the age of initiation, we can do our best in terms of education and awareness campaigns, so that we can keep our youth from becoming addicted to these substances. Then also, we can limit the availability of these substances so they don't have access to get started with them in the first place.

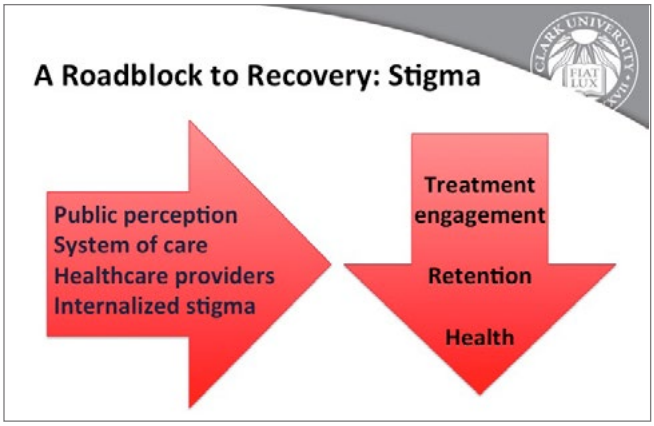
In terms of addressing early recovery as a risk period for relapse? There has been a lot of data showing that ongoing support, participation in AA and NA, and other peer-recovery networks, has been really helpful in helping people achieve positive, long-term outcomes.

There's also been recent data that individuals with opioid use disorder may benefit, even more than other people with substance use disorders, from long-term residential treatment, in helping them maintain their abstinence and recover.

So, it could be that when they are in a sober environment, they can really benefit from that, partially because they have the ongoing drug-free social support and they're not exposed to the triggers that might be increasing their risk for relapse.

There are a number of evidence-based treatments that have come out that try to address the whole person, and not just their substance use disorders. So, there are treatments out there that are addressing trauma and trauma reactions that people might be experiencing, that can help them learn additional pain management strategies, whether they be psychosocial or pharmacological. And then also, helping people learn other strategies to deal with anxiety, depression, or other psychiatric symptoms that might increase their risk for relapse. Vocational services have been discussed as a potential addition to existing treatment services, given that unemployment is such a risk factor for relapse. Adding vocational services to existing treatments might be something important to explore.

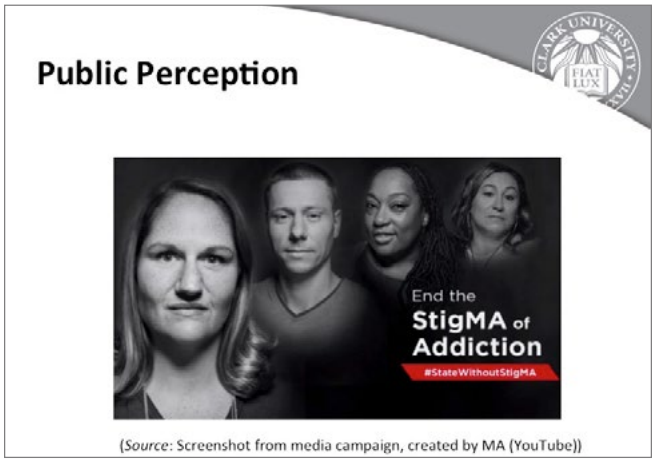
As I mentioned, a drug-free social support — attendance at AA and NA or other peer-recovery networks — could be helpful with decreasing exposure to triggers.



One factor that was not on that list that I want to spend a little time talking about is stigma. So, stigma can be another risk factor for relapse, and it can be a major roadblock in the process of recovery.

Individuals can experience stigma through the public's perception, through our healthcare system, from healthcare providers themselves, and then they may internalize some of this stigma. This experience of stigma can really impact the patient in terms of just how they're feeling overall, but also limit their engagement in treatment – in their willingness to stay in treatment — so, treatment retention and their overall health.

It could also lead to chronic stress, and keep people from asking for help in the first place if they're struggling, or if they know that they're about to relapse. If they're experiencing stigma, then they might be less likely to ask for help.

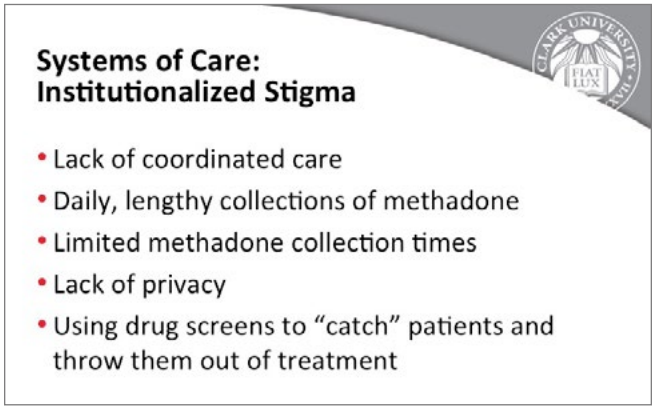


(*Source*: Screenshot from media campaign, created by MA (YouTube))

There have been a number of initiatives that have tried to address these different levels of stigma, so education and awareness campaigns can be useful. In fact, there's one — I don't know if folks have seen it yet, but it's the "End the Stigma of Addiction" campaign that has been launched by the State of Massachusetts.

These types of campaigns can be useful, but research suggests that they may also be insufficient. When looking at actual stigma reduction, research has shown that there's been minimal impact on actual stigma reduction.

The strongest evidence is found for interventions that focus on creating more personal contact between the stigmatizers and the stigmatized groups in a positive context. So, we should have these educational campaigns, but know that they're not going to be the silver bullet that addresses stigma in the public eye.

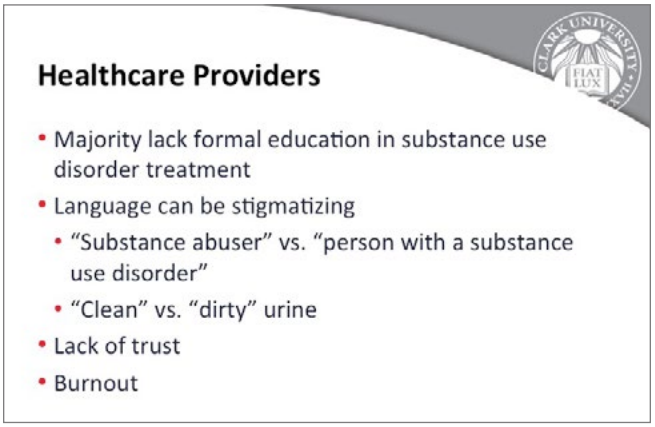


Individuals with opioid use disorder also describe institutionalized stigma. So, within the healthcare system, they experience a feeling of discrimination. First, there could be a lack of coordinated care between addiction treatment services and primary care providers, such that primary care providers might not know that someone is in addiction treatment and might be fearful of even mentioning it.

We talked about how unemployment can be a risk factor for relapse, but if someone is on methadone that means that they have to go and get it daily. It sometimes could be a lengthy task. There might be limited times where they can actually go to collect their methadone, and so it's hard to sustain full-time employment with some jobs when you also have to add that into your schedule.

There can also be a lack of privacy when going to collect the methadone. Sometimes in our healthcare systems, in our addiction treatment services, there are urine screens to test for whether or not someone is using; they're used to catch someone doing something wrong and to throw them out of treatment.

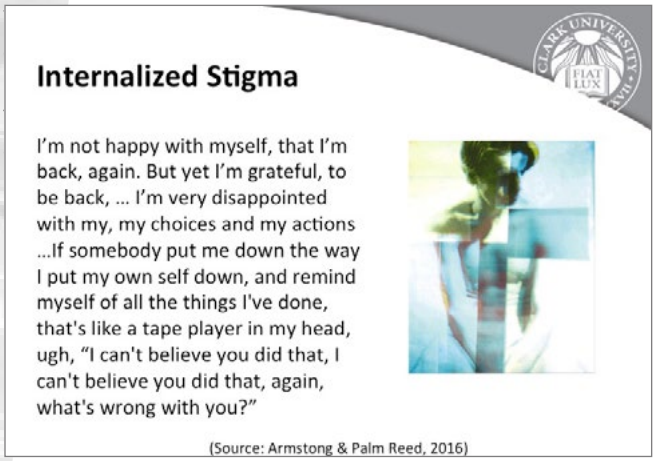
Instead, it might be useful to think of it as a teachable opportunity, especially given we know that relapse is a part of the illness. It could be expected that someone can relapse at some point, and so rather than thinking of it as catching them doing something, using it as an opportunity to teach them something different and get them the help they need.



There has been a lot of talk of making sure that individuals with opioid use disorder get access to care, but one thing that people might not know is that there has been research examining the level of formal training that physicians get, that clinicians get, that social workers get, in substance use disorder treatment. It's really discouraging because not that many programs actually offer that level of formal education. So, well-intended treatment providers might not understand exactly what the person is dealing with.

Further, our language about substance use disorders can be stigmatizing. There have been some studies that have looked at laypeople's and professionals' reactions to labels of substance abuser versus a person with a substance use disorder. People's reactions to a substance abuser: "Well, this person needs some sort of punishment." However, if they saw a vignette about a person who was described as a person with a substance use disorder, there's more of an inclination to get this person clinical intervention and to help this person.

So, how we describe people affects our response to them. Healthcare providers and researchers, too, should continue to think about the language we're using to describe the phenomenon we're talking about, and the experiences that people are dealing with. We also describe urine screens as clean versus dirty. These might seem like subtle changes in our language, but it has an impact on the people that we're working with.

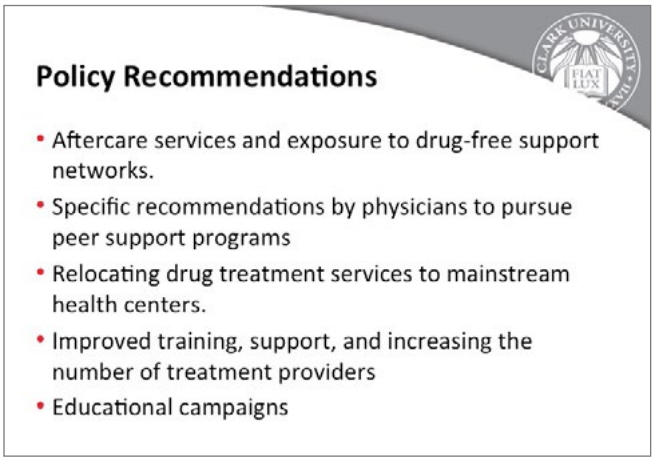


It's not surprising given these different levels of stigma, that people with opioid use disorder might internalize this. This is, again, the same study that I was talking about earlier. This person's quote really exemplifies some of this internalized stigma and what it might look like for a person who's struggling with this.

This person says, "I'm not happy with myself, that I'm back again. But yet, I'm grateful to be back. I'm very disappointed with my choices and my actions. If somebody put me down the way I put my own self down and remind myself of all the things I've done, that's like a tape player in my head. 'Ugh, I can't believe you did that. I can't believe you did that again. What's wrong with you?'"

So this internalized stigma is associated with poor mental health and a greater risk for relapse.

On top of that, the experiences of stigma for minorities and the poor can be even worse, with some individuals in treatment having to depend on other patients to translate their sessions for them, and the poor having limited access to state-of-the-art treatment.



So, what could be some possible policy implications of what I've discussed today? One is that it's important to really focus on that period of early recovery and make sure there are appropriate aftercare services so that we're working on the maintenance of the opioid use disorder.

There's been a lot of promise looking at drug-free support networks, so encouraging participation in AA and NA and other peer-recovery networks. In fact, some people have discussed asking physicians, nurses, and clinicians to make specific recommendations to patients to pursue peer-support programs.

In terms of addressing institutionalized stigma? Some researchers suggest that it might be relocating drug treatment services to mainstream health centers, so that they're not so divided. Improving training and support of healthcare providers to try to limit burnout and give them more education about what substance use disorders are and what state-of-the-art treatments are. And then, increasing the overall number of treatment providers that are out there.

Education campaigns are also important in increasing our awareness and knowledge about opioid use disorder, with the caveat that education campaigns alone are probably not going to be the silver bullet that'll address any public negative perceptions of opioid disorders.

QUESTION AND ANSWER

Audience: You mentioned that the [inaudible] time in a recovery home or — what do you mean by a long? In terms of [inaudible] two weeks? I think that's what the current is in time, six months, or a year? Like, what's the research show on that?

Palm Reed: I don't know if it's looked at, the exact length of time, but just more is better. We need to find out exactly what that kind of sweet spot is. We're not exactly sure on that. That data is hot off the presses really. So, we need to find out what that is exactly.

Audience: What's known about the relationship between the population that develops opioid use disorder and their prior use of say alcohol? Typically, the substantial proportion of the opioid abuse population also have a problem with abusing alcohol prior to becoming users of opioid?

Palm Reed: There's a lot of poly-substance use. People who use a lot of different substances, and some people do start out with alcohol, with marijuana, but it's not the only pathway to opiate use.

You hear in talking to a lot of individuals that sometimes they weren't using alcohol, but they might have started getting hooked on opiates, specifically after surgery. Or even — I've heard people talk about in high schools, people knowing when everyone's wisdom teeth are going to be taken out. So it might start there — where alcohol might have been used, it might now be pills. It might be the thing to share opiate pills instead.

So sometimes, but there's not any kind of set, gateway type of drug that gets into opiates. So some people start directly with opiates.

Audience: [Inaudible].

Palm Reed: So do we want to completely eliminate stigma because there's some kind of social control and utility to that in some way? There's been some argument about that for addressing stigma because of that reason, which might prevent opioid use disorder, not for everyone. But it's still not helping the people who are already struggling with an opioid use disorder and keeping them from seeking help.

So, it's both, you know? It's important to prevent opioid use, and also, we need to think about the impact of people who are already struggling.

CLARK UNIVERSITY
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Addiction, Overdose, Suicide: Facts You Need to Know about Treating Opioid Use Disorder

By Hilary Connery, M.D., Ph.D.

POLICY BRIEF

Opioid misuse and addiction have increased severely during the past decade. Death rates associated with heroin and prescription opioid use are rising rapidly, despite efforts to control opioid availability and distribute life-saving emergency medication. Prevention education and widespread access to quality, evidence-based treatments are needed now to stem the tide of this tragic, national epidemic.

OUT OF CONTROL: WHEN OPIOID USE BECOMES OPIOID USE DISORDER

Naturally-occurring opioids (e.g., morphine) and man-made synthetics (e.g., painkillers such as oxycodone and hydrocodone) have been used successfully to treat pain, cough, diarrhea, and mental distress associated with physical injury and illness. Opioids are potent sedatives and in high dose can shut down the part of the brain in charge of regular breathing. Thus, there is always some risk associated with opioid use, especially in those with other risk factors for sedation or compromised respiration (e.g., pneumonia or other lung disease, use of other sedating medications, or alcohol use).

Some people who are sensitive to the pleasurable effects of opioids have additional risks for taking more than prescribed or using opioids routinely to cope with stress. When this happens, repeated misuse can lead to patterns of addiction, with too much time spent seeking and using opioids, and too little time spent in normal life activities. This is referred to as opioid use disorder, and for many, the addiction cycle includes a need to keep taking opioids in order to avoid feeling sick (opioid withdrawal syndrome).

It is also important to know that anyone chronically exposed to opioids will develop physical dependence and increased tolerance to the effects of prescribed opioids, even if they don't develop addiction. Sometimes they will require higher opioid dosing to achieve the same effect, which presents more risk for sedation, reduced breathing, and overdose death.

TREATMENTS PROVEN TO REDUCE OPIOID MISUSE AND PROBLEMS OF ADDICTION

Medical treatments proven to reduce opioid misuse begin with a careful assessment of the need for opioid prescribing, and limiting unnecessary exposure to opioids for medical conditions that may be successfully treated with less risky medical approaches.

In the case of people presenting with opioid use disorder with physical dependence, three FDA-approved medications targeting brain opioid receptors will double the chance of good outcomes when added to evidence-based psychosocial treatments for opioid use disorder (individual and group therapy, peer support such as Narcotics Anonymous and SMART Recovery). These medications include methadone and buprenorphine, which activate brain opioid receptors, reducing opioid craving and withdrawal; and extended-release naltrexone, which blocks brain opioid receptors and thereby prevents the pleasurable effects of illicit opioid use.

In addition, people with opioid use disorder have high rates of co-occurring depression and suicidal thoughts and behaviors. Screening and providing evidence-based treatment for depression and suicide prevention is recommended for all people with opioid use disorder.

CAN WE PREVENT OPIOID OVERDOSE DEATHS?

Controlled clinical trials and observational clinical data demonstrate that opioid overdose deaths are reduced in people with opioid use disorder who participate actively in a medication-assisted, evidence-based treatment.

There is also evidence that the rapid administration of intranasal naloxone will reverse an opioid overdose death occurring in the community, and dissemination of easy-to-use kits to drug users, families, clinicians and first responders is indicated. Keep in mind that this approach is not treatment, but a life-saving intervention similar to cardiac defibrillation for heart attack. A person will not experience reduced risk following naloxone rescue unless that person engages in evidence-based treatment.

Educating patients on the risks associated with opioid use, screening for suicidality prior to prescribing opioids, and outlining procedures for safe storage and disposal of opioid medications will reduce unintended opioid exposures and overdose deaths.

OPIOID USE AND THE FAMILY: SAFETY FIRST, CONNECTION SECOND

Families struggle with behavioral patterns associated with illicit substance use, such as personality changes, lying, stealing to support a habit, and otherwise unreliable behavior that is out of character and a symptom of active addiction. It is important that families have adequate options for receiving education and support about opioid use disorder, and that they understand how loved ones under the influence are chemically "disconnected" from normal relational attachments.

Families need to be taught that safety is the priority in managing loved ones with active opioid use disorder, both their own safety and that of a loved one with opioid use disorder. Family connections may be weakened in the addiction cycle, and often are not a strong enough incentive for a loved one with opioid use disorder to enter treatment.

CRAFT (community reinforcement and family training) is an evidence-based strategy for family members to help engage a loved one in treatment. Once the recovery process is occurring, family connections will strengthen or be repaired if all members are supportively engaged in the treatment process. Families are thus advised to consider safety as the first priority, and family repair work as a next priority integrated within the recovery treatment process.

KEY REFERENCES AND FAMILY RESOURCES

1 Nora D. Volkow, M.D., George F. Koob, Ph.D., and A. Thomas McLellan, Ph.D. Neurobiologic Advances from the Brain Disease Model of Addiction. New England Journal of Medicine 2016; 374:363-371; January 28, 2016.

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3 Meyers, R.J. & Wolfe, B.L. (2004). Get Your Loved One Sober: Alternatives to nagging, pleading and threatening. Hazelden Publishing & Educational Services: Center City MN.

4 Narcotics Anonymous: www.na.org

5 SMART Recovery: www.smartrecovery.org

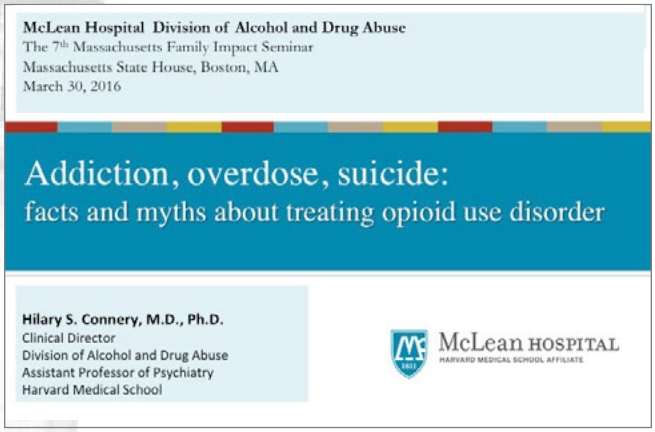
6 Learn to Cope: www.learn2cope.org

7 GRASP: Grief Recovery: www.grasphelp.org

8 Provider's Clinical Support System: www.pcss-o.org and www.pcssmat.org

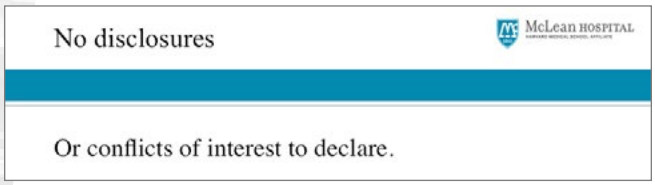
Dr. Hilary Connery's expertise includes treatment of opioid use disorders and co-occurring mental illness and substance use disorders. She contributed to American Psychiatric Association Practice Guidelines for treatment of substance abuse and is an investigator in Harvard University/New England Consortium of the NIDA Clinical Trials Network. Dr. Connery is New England director for the American Academy of Addiction Psychiatry, rotation director for addiction psychiatry in Massachusetts General Hospital/McLean Hospital Adult Psychiatry Resident Training Program, and mentor in Partners Healthcare Addiction Psychiatry Fellowship.

TRANSCRIPT OF DR. CONNERY'S TALK

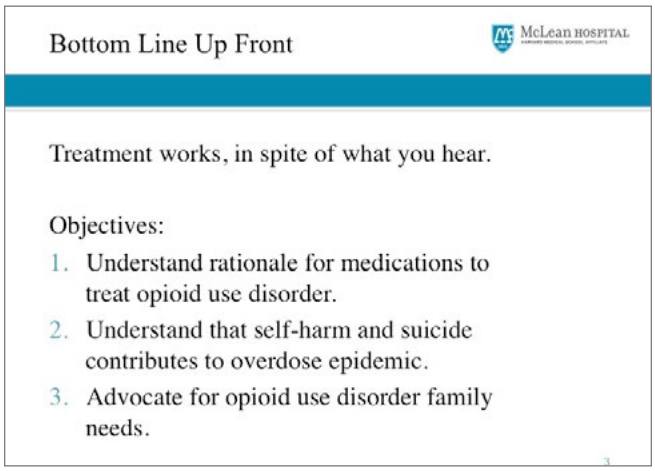


It's a pleasure to be here. Before I start, I will tell you I'm keeping this presentation intentionally brief. It's the end of the day, and there are a couple of points that I just want to make sure people have some basic knowledge about.

I did want to comment on that last question about stigma, only to point out that there is no other chronic medical illness where we use a negative stigma as a prevention strategy, and I don't think we should be thinking about mental health or substance use any differently.



So I don't have any conflicts of interest or disclosures to make.

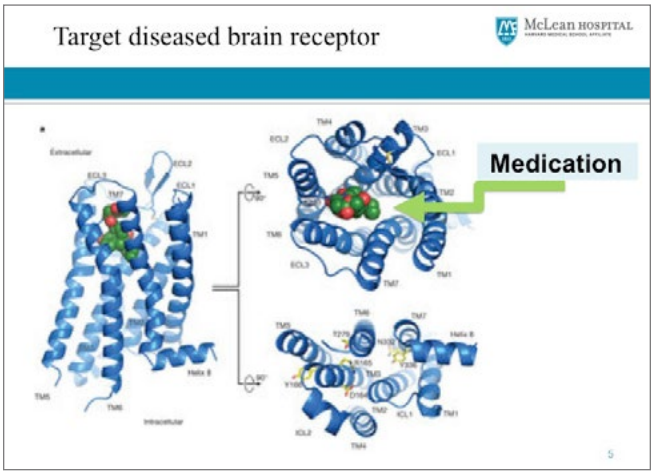


Bottom line I want you to take home is that treatment works, and we're going to talk about medication-assisted treatment.

My main objectives are for you to understand in basic terms why we recommend medications to patients with opioid use disorder. Also, to understand that the overdose epidemic is more complicated than just addiction and accidental overdose. That mental health comorbidity is significant, and there is also good data to show that self-harm and suicide contribute much more significantly than you're hearing in the public dialogue. I would like to raise more awareness around that.

Then finally, to talk about what families are worried about and the kinds of things that we know help them in terms of supporting loved ones in their recovery.

So, let's start with the myth that's been around for going on half a century. Every time I hear somebody say, "Aren't we just replacing a drug with a drug?" I think to myself, "Really? Are we still having this conversation? How much science, and how much medical evidence do we need before we're going to stop this conversation?"

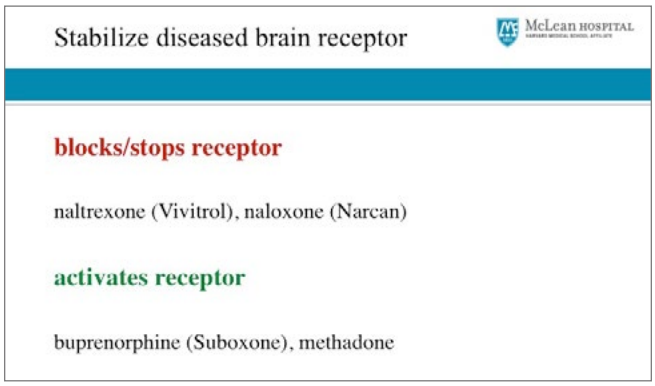


So, if you take a look at this slide, it's representing x-ray crystallography of the protein structure of the mu-opioid receptor in the brain. On the left side is a picture of what it looks like — looking front on — and that line in the middle there suggests that you have a neuron, or brain cell, that sits half on the outside and half on the inside.

The way that protein receptors work is that when you have something that binds to them and activates them — in this case, we're talking about an opioid — it binds to the outside of the cell, changes the shape of the receptor, and then the inside part of the protein has cellular activation. Okay? So that's how it works.

I've shown you where medications bind; that would be the outside of the cell. Essentially, I always feel like we're so fortunate when we treat opioid use disorder, that we understand that this receptor is destabilized in this illness. Because if we understand the site of where the destabilization is, we can actually develop — and we have developed — effective targeted medication treatments for that.

So this is what you need to know: The mu-opioid receptor in the brain is the site of the three FDA-approved medications that are demonstrated to be effective in treating opioid use disorder and helping people to get into recovery.



How do they work? We have two categories. One category blocks activation entirely at the receptor. When we talk about this, we're talking about naltrexone, and in the case of opioid use disorder, preferably extended release naltrexone, which is also known by the trade name Vivitrol. Or we're talking about naloxone, known by the trade name of Narcan, which is the emergency rescue. Both of these medications bind to that binding site, and they basically cap off the receptor; no activity can happen. That's how they work.

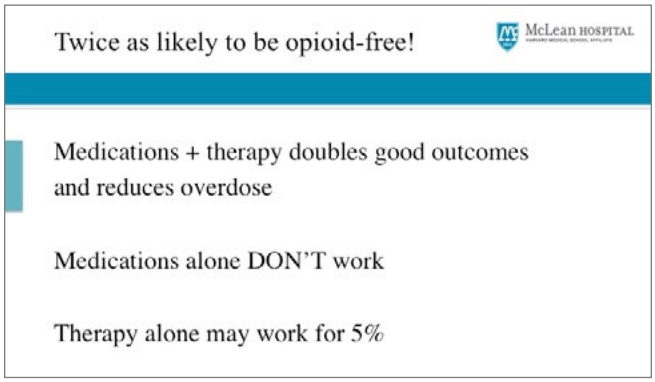
So, if you're talking about naloxone rescue, you are talking about something that rapidly displaces the activating opioid from the receptor and puts the person into an immediate withdrawal state, which is horrifically painful to the person who's experiencing it, but it saves their life.

If you're talking about medication treatment for somebody who's coming into recovery, essentially what you do is have the person stop using opioids for a long enough period of time that then they can start taking the naltrexone treatment, which just seals off the receptor. In doing so, if during the course of their recovery, they have a bad day, and they use, nothing happens. They don't get high. Essentially, they have an opportunity to say, "That didn't work, and I didn't want to do it in the first place; I was just having a bad day." So it preserves them in recovery.

The second category activates the receptor. These would be buprenorphine, also known by the trade name of Suboxone, or methadone maintenance. The way that these work is that they bind to the receptor and they activate the receptor in a controlled fashion.

So somebody who is in recovery now takes a medication that's prescribed at a very precise dose, and is monitored very carefully, and has a steady state effect, so that they're not getting high; there is no euphoria. Essentially, they're comfortable and able to get on with paying attention to all of the lifestyle changes that need to happen when you're entering into recovery.

All three of these types of medications are really effective in treatment. And of course, we know that intranasal naloxone is saving many lives in the state of Massachusetts and across the country, for those who are in an overdose state.



When you look at the controlled clinical studies, the other thing about the FDA-approved medications is that for all three of them, the evidence shows that patients who add medications to the psychosocial treatment have doubled the chance of actually sustaining an opioid-free outcome. At least double the chance. In some studies, you're looking at a six-fold improvement.

So, these are effective. Medications without the mental health treatments attached to it, without an attempt to change your lifestyle, without peer support — medications alone won't work.

We know this. Why do we know this? Because there's diversion. So, a lot of people in the community are using diverted buprenorphine, not in recovery. If it worked all by itself, you wouldn't need people like me running clinics. People would just figure out how to get it, and they'd be better. They don't work without all the supports.

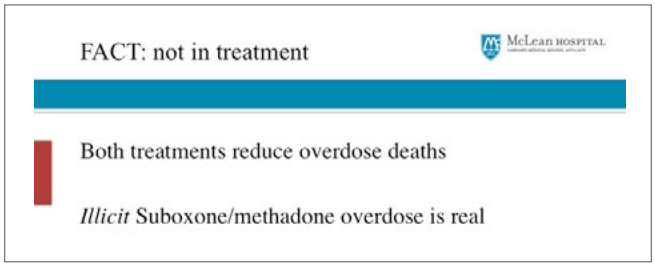
The other issue: People argue, "What about those who don't need a medication to get clean and sober?" The problem is what we know from clinical studies is that it's a minority of people who come in for treatment, are detoxified, and do not have a relapse episode.

Some people can do it. But from the medical perspective, we have no way of differentiating who's going to be able to successfully enter a sustained recovery without a medication. Because we can't tell that — and the data is such that it's probably about 5% — and because the majority of people will do much better with a stabilization period with medication, we recommend it universally.

What I would hope in the future is that we might be able to identify the subset through a blood test or a brain scan or something like that, and then be able to more precisely target not just who needs medication, or who can do it without medication, but beyond that, which medication is right for this person? We have three medications because not everybody responds well to any single one of them, and we need to have these options.

MYTH #2:
Suboxone and methadone treatment cause overdose deaths

Myth number 2 is that, "Aren't we contributing to overdose deaths by prescribing Suboxone and methadone?" The answer to that is simply: it's true if these medications are used illicitly, not so under a monitored treatment. Somebody gets it on the street. Somebody gets it from their dealer. Yes, we have data that these medications are involved in overdose deaths, but they're being used in the wrong way. People are accessing them not in treatment.



The truth is that when people are taking them in a treatment setting, overdose deaths are reduced. So, we shouldn't be afraid that treating people appropriately with these medications is going to increase overdose. It doesn't. The data is totally against that. It decreases overdose.

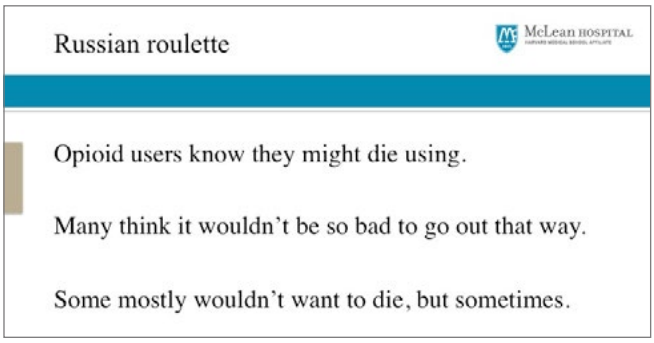
We should be concerned that when these medications get diverted into the community and people are doing who knows what with them, that they show up in forensic reports as part of a tragic overdose death.

MYTH #3:
Opioid overdose deaths are accidents

Did anybody see President Obama yesterday in the opioid summit — the National Opioid Summit? Nobody? I'm surprised. Well, it was great. It was really terrific. A lot of great stuff was talked about, and I'm encouraged that we have some of the most comprehensive dialogue around what we need to stop this epidemic. It's not just about medication, and it's not just about treatment, and it's not just intranasal naloxone, but a full-on community effort.

Although, one thing that I noticed is that we're still using this terminology of overdose accidents. It's really quite inaccurate if you think about what an accident is. An accident assumes that the person's not really aware of risk.

So when you think of opioid overdoses, the only real accidents that I know of are the ones where there's a pediatric exposure. Somebody leaves their opioids out, and a child who knows nothing about the pills, what they do, or what the risk is, takes the pills and has an accidental overdose.



For those who are using opioids, you ask any of them, and they'll be the first to tell you, "I know this could kill me. I don't think it's going to, but I know this could kill me." So, right then and there, if somebody's engaging in a self-harm behavior that they know could potentially kill them, it's not quite accurate to label a death like that as purely an accident. There was some risk assessment involved.

The other part is that the overlap, the co-occurrence of mental health problems among substance use disorders is very, very high, particularly major depressive disorder.

In the field, we sort of have this artificial distinction between mental health disorders like depression, PTSD, bipolar disorder, schizophrenia, and substance use disorders, such as opioid use disorder, alcohol use disorder, tobacco use disorder. It's a pretty artificial divide. It really shouldn't exist. They're all brain diseases. They're all chronic illnesses. There's a lot of genetic vulnerability overlap, and there's a lot of behavioral overlap—and one of the behavioral aspects that overlaps across the spectrum is suicidality.

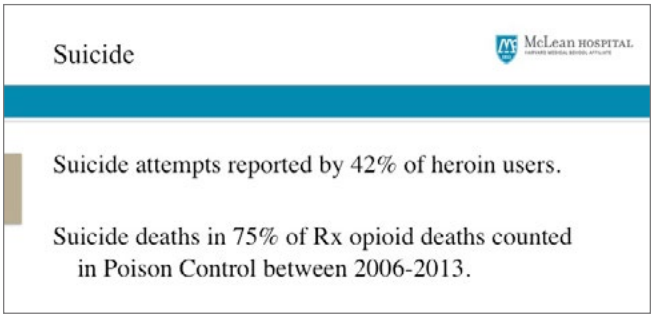
So, we have a spectrum of suicidality. We have patients that (A) are flirting with disaster in the first place. They're using a substance that they will tell you, "I know it could kill me," and (B) a lot of these people are suffering, tremendously. Their lives are chaotic. They have depression. They have trauma. And there's despair. It may not be all the time, but many of them will say, "You know, if I had to go out using and sort of sleeping into my death? Not such a bad thing. There's a lot of worse ways that I could die, especially with what's happening in my life right now." So that's not quite suicidality, but it's getting closer on the self-harm spectrum.

Then the other thing that we forget is that the way that substance users experience suicidality is quite different from the way that somebody with a melancholic, chronic, major depression experiences suicidality. The melancholic depressed patient can't get out of bed, doesn't want to brush their teeth, and is thinking about suicide as the only possible relief to this awful state that just goes on.

One of the reasons I like working with substance users is they're full of life; very resilient people. They have incredible stories. They've lived through all sorts of things. Oftentimes, they're lively and have a good sense of humor. The way they experience despair and suicidality is quite different.

It's often brief, episodic. They could be having a great day, then something shifts. Sometimes it's related to using a substance because they get more disinhibited about the despair side or prior suicidal thoughts that they've had. They can have these brief onsets of very deep despair and active suicidality that because they're using lethal substances are even more dangerous. That's suicidality. That's not just because it looks different from a melancholic, depression suicidality. It's still lethal suicidality.

So, they'll say to you, "Most of the time, I don't really wanna die. I — I have a lot to live for. But there are times when I really do wanna die." And those are really the danger times.



Why do I think this is happening and contributing to the overdose epidemic? Two reasons. Two publications this year that really got my attention that people are not talking about. One was a longitudinally followed cohort, an 11-year follow-up of an Australian study of heroin users — 600+ people, a large cohort.

Of people who entered treatment, 42% of them had self-reported suicide attempts. We know that already. We know substance users have high rates of baseline suicide attempts. But when they followed them out even at year 11, the persistence of suicidality was tremendous: 10% with still active suicidal ideation, and about 4% actually maintained a plan.

Even though they were in treatment, and getting better in certain ways, suicidality persisted. We see that in our own clinics. We see that in practice. That's the mental health component.

The other thing was that there was a national report put out this year that looked at overdose deaths with prescription opioids. It was a multi-center collection of poison center calls that looked from 2006 to 2013 at the overdose deaths related to prescription opioids. Seventy-five percent were called in with known suicidal intent. Why is nobody talking about this?

Then, if you looked at just those who are age 60 or older: 86% suicidal intent. That says something really important. I feel like we're missing this in the dialogue. I'm not saying that there aren't unintentional overdose deaths. I'm just saying that we don't want to simplify the problem as people getting prescribed too much pain medication, then they're addicted, and now, as an addict, they have reckless behavior, and they accidentally overdose.

That's not really the story here. We have a much richer story about people's lives being tough; people having vulnerability; people having co-occurring mental health problems; and suicide as a real problem.

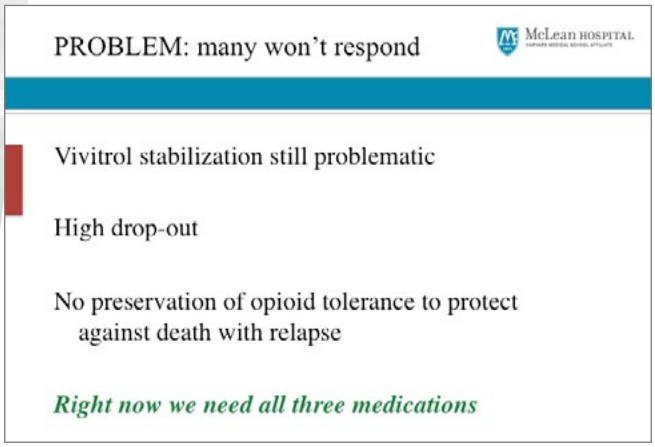
You can also reflect on the fact that suicide rates in the United States continue to go up, and are particularly alarming among our youth. So, there's something bigger that's happening here. I think that it's relevant for reducing stigma. I think it's relevant for developing programs that have more comprehensive treatment and aspects that are going to address depression and suicide prevention. It's not just looking at, "Let's get you clean and sober."

MYTH #4:
We should just use non-opioid treatment

Then the other question that has come up a lot, particularly when people talk about changing the criminal justice system: What should we do for people who have been incarcerated, who have an opioid use disorder, and are now being released in the public and are at very high risk for relapse as well as overdose?

There's a push to use just antagonist treatment, Vivitrol, and I don't really have a problem with that, as long as it turns out that we can study it, and it's effective.

Because there was a lot of interest in doing this, the question sort of generalized: why are we giving anybody agonist treatment? Why can't we just treat everybody with the blocker — with Vivitrol?



The reason for that is that there are a lot of people who just simply won't respond to that. Not everybody will do well with an antagonist-based treatment like Vivitrol. There are a couple of problems with it. For the example of the person who's been incarcerated, if they haven't been exposed to opioids (which is another story—there is a lot of opioid use in the prisons), they don't need to have a washout period.

That's straightforward. You can start them on naltrexone before they go. They can then continue to get their treatment.

However, for many people coming into treatment, they have to really go through a detoxification process, where the opioids wash out, so there has to be a significant amount of time, at least a week, before it's safe to give them naltrexone.

And this week, where they're just in opioid withdrawal, is a high dropout period. People don't tolerate it well, and they just basically have trouble making it to that first dosing. So that's one problem.

Another problem is that many people who get onto Vivitrol come in, they get their first injection, and then they disappear from treatment. Or, maybe they get two injections, and then they drop out. That's a problem, too. We're working on trying to improve retention in this treatment model.

It has been a problem because when they do drop out, they've lost their tolerance, and if they relapse, they're now at a great risk for opioid overdose.

The other treatments, while there's a downside to having activation at the opioid receptor, the upside is that it does preserve a little tolerance. They're less likely to have an overdose fatality when they do overdose.

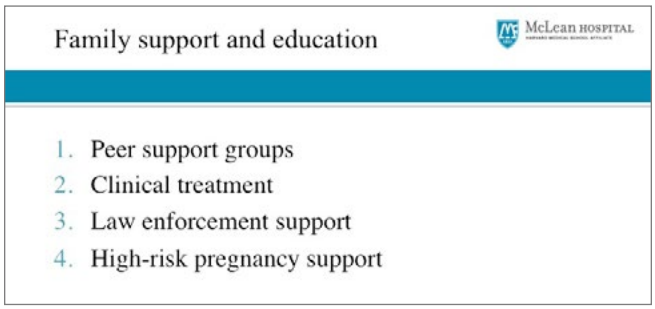
So, for the moment anyway, until we get better with all of this, we need all three medications.

What do families need in addition to naloxone training?

Then, finally, what do families need in addition to intranasal naloxone rescue training? Which I'm so pleased Massachusetts has taken up very rapidly, and access keeps improving, so I'm not going to actually talk too much about that, because we're really doing a good job with that.

I'm going to talk about the other aspects, though. In a nutshell, families are mostly suffering from anxiety of losing their loved one. They're terrified. They know that at any moment, they could get the knock on the door or the phone call, telling them their loved one is dead.

Then, there's all of the other problems of addiction that they suffer with, what I call active using behaviors, that don't reflect the person's character baseline, but is a symptom of being actively in the disease: lying, cheating, stealing, etc.



So what families really benefit from are peer support groups. That means getting together with other families who are in similar situations to share support resources and information.

I think the peer support groups can be especially helpful if you have a licensed professional facilitating it, not necessarily directing it, but being there to answer questions that may come up, or offer resources when somebody has a question that nobody can answer.

Families need clinical treatment. The families that I see? They have high levels of insomnia, anxiety, horrible depression, despair, hopelessness, fear, and trauma. The trauma of watching somebody get well, thinking you're out of the woods, and then all of a sudden, "Oh my God, are we here again? I don't know if I can live through this again."

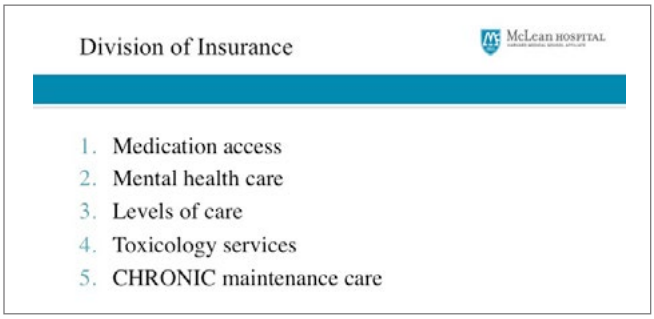
They need clinical treatment. They need therapy supports. Sometimes, they need targeted treatment for their own mental health issues: getting to sleep, depression, etc.

They need help from the law enforcement world. I can tell you, a lot of patients that I've seen, their families will say, "You know, in the worst of this, I found needles, heroin, a supply. I went to my police station saying, 'I don't know what to do with this. Can you do something with this?" Basically, you know, they're up against, "We really can't take that, ma'am, and also, your child will have drug charges if we do something about it."

So, we have to figure out some way that families can get some more and better support from law enforcement without being put in this really strange situation of, it doesn't belong in my possession, but I'm not really sure what else I can do with it.

And then, you know, unintended pregnancy, unplanned pregnancy—there are very high rates of that among substance users for a variety of reasons. But when a substance-using woman becomes pregnant and makes a decision with their family that they want to keep the child, the way they are treated in our healthcare system is awful. Just awful. This extends to families, too.

So, I think that one of the places that we could immediately do a lot of good is to train our clinicians who work in prenatal and postnatal care how to be more understanding about what the disease of addiction is, how difficult it is to break. Essentially, deliver more effective, compassionate care, which is not only going to be good for the families and the woman, but also for the baby who is developing.



Medication access. These are things that the Division of Insurance can work on — medication access for everybody. For all three medications, having the choice, so that if you try one and you don't respond to it, you can easily and rapidly be tried on another. And not have gaps in your treatment due to your requirements for pre-authorization, delays in being able to get something shipped to you, etc., etc.

Mental health care: I think I've already said enough about that, but if that's not put into the treatment planning, you're not likely to get the kind of outcome that you want.

Offering more levels of care: The gap between inpatient level of care and outpatient level of care is just too wide. We need day treatment. We need more residential treatment.

And then finally, toxicology services. Again, not for the point of policing patients, but they're the only objective data. I call them my vital signs — our breathalyzer for alcohol use disorder, and urine toxicology or other toxicology for drug use disorders. These are our vital signs. They're the only ones we have, really.

Yet, somehow, in our line of work, instead of having a technician who comes in and takes your blood pressure and your pulse and then collects some blood for routine tests, we're told, "Oh no, no. You can't have that. And we're going to put a limit on the number of times that you can use this kind of assay to inform your clinical interventions." That's just dumb.

You know, effective care needs to have reasonable access to toxicological services. It would actually benefit from having more of a medical model of payment for somebody up front to do the weight, the blood pressure, the pulse, other vital signs, and wellness checks, which would be very helpful to providing comprehensive care.

This is chronic maintenance care. That's the point. So, if those things are provided better for patients, families are also going to have a much easier time with it.

QUESTION AND ANSWER

Audience: You had mentioned the high-risk pregnancy [inaudible]. Have you seen children who are born from high-risk pregnancies, the side effects that they suffer?

Dr. Connery: In this case, we're talking about opioid use disorders, so we're talking about the awful event of neonatal abstinence syndrome, which is when you see a baby who has been exposed in utero to opioids to a level of addiction, and are born in opioid withdrawal.

As I mentioned, opioid withdrawal is miserable. It's an awful physical and anxiety depressive state. When you see these babies, it is actually very horrifying. I understand why people look at that and say, "How can we allow this to happen to these babies?"

But I ask the question, if we don't treat women, then what? The babies are going to come anyway, right? But now, these babies will not have had any appropriate prenatal care. So they'll have all the problems of addiction, including a mother who's actively addicted and probably depressed, as well as all of the health problems of having not received a stitch of prenatal care and not having the opportunity of a planned delivery. This baby is going to have special requirements. We need to be ready for it. We need to plan for it.

So, the alternative just isn't viable. I mean, leaving these babies to be born God-knows-where and without proper prenatal care and delivery planning; that's not an answer. I don't have the miracle answer, which I wish I did, which would be: Can we spare the babies from all of this?

But in reality, right now, the best we could do is really be compassionate, engaging these women who are pregnant in treatment that works, providing resources. If they can't stop using even with treatment, residential treatment, protect them from the environment. Provide for them. Provide for the child. At least give them the opportunity to become good mothers.

They may not make it, but some do. And on the point of the post-delivery part, we thankfully have medical treatments that will stabilize these babies. You know, there are some people who were babies born to opioid-addicted women, who suffered through the neonatal abstinence syndrome, and are productive members of society; happy to be alive.

So, that's my picture of it. It is an awful reality, but there's a lot that we can do to mitigate that awful reality, and end up in a better place.

Audience: You mentioned that [inaudible] users know that they're—say heroin, for example—when they shoot up, they know they can potentially kill themselves? What are your thoughts on the effectiveness of Narcan? And while it's keeping people alive, some of these [inaudible] users—they're starting to use it as a safety net. And do you think that's starting to ruin that perception of, "Oh, well, I don't have to worry about dying because I have a couple bags of this?"

Dr. Connery: Okay. I'm glad you bring that up. So the question is, is the use of intranasal Narcan actually creating a safety net for opioid users whereby they think, "Well, if I have that handy or my friends have it handy, you know, I'm not gonna kill myself. So that gives me more freedom to use." I have two answers to that. Actually, I have...

Audience: Or just maybe take away some of the danger.

Dr. Connery: Yeah. I have three answers to that. Number one, if you've ever worked with an opioid addict, they don't think that way when they're using. None of that is going on in their head at all. They're not rational. They're not thinking about anything other than my brain receptors are screaming that it's time to use, and I've got to use.

So that line of logic that seems like it would be expected from those of us who aren't addicted to opioids, you have to understand, they're not even thinking about that. That's number one.

Number two, there's no evidence that the use and dissemination of intranasal Naloxone has increased opioid use. The only evidence we have is that it's done a damn good job of preventing people who would otherwise be dead from being dead. They're still alive.

Number three, there is the very important question of, "What do we do with them once we've resuscitated them?" Because as I mentioned earlier, you give somebody intranasal Narcan, they don't wake up and say, "Thank you for saving my life." They wake up and they're in the most miserable level of opioid withdrawal that you can imagine. And they wake up screaming, angry, get away from me. I mean, literally, they're out of their minds. And the only thing on their mind is, I need to use again. Right? Because that's what's going to fix it. This is part of the brain illness aspect to it.

We've got AEDs in our malls. When we defibrillate somebody who has had a heart attack in the mall, what do we do? Do we say, "Oh, you don't want treatment? Okay, good luck. Hope you have a good life. If you're not dead in a month, maybe I'll see you at the mall again."

We don't do that. If somebody gets defibrillated in public, they get treatment. Right away, they get treatment. Right? And if they say, "Oh, you know, no thanks. I don't want

treatment," people bend over backwards trying to say, "Are you nuts? You almost died there. You need treatment." Right?

But somehow, we've had intranasal Naloxone for years, where people wake up and they're angry, they want to use. A lot of times, they just get discharged and sent on their merry way. There's a discrepancy there that's just crazy.

I think that Governor Baker's new mandate—that somebody within 24 hours gets a qualified professional evaluation for substance use disorder and offered appropriate access to treatment—is such a step in the right direction.

We may end up needing more than that, but that is just right on target, and I really applaud that.

Audience: So, to me it sounds like when we're talking about the spectrum of self-harm, there's a group that, you know, is flirting with disaster in the sense that they are suicidal and there is medical treatment for that. But there's also on the other end of the spectrum, risk-seeking individuals who, you know, might not wear their seatbelt. And then, you know, maybe this group is a potential group to target prevention, intervention as a [inaudible] for a drug use disorder? I was wondering if there's any research that goes into that? Or is the dialogue surrounding this self-harm, but not quite classified as a medical need?

Dr. Connery: There is. So, the question is, on the topic of self-harm and just risk-taking behavior in general, how can we use this for the purpose of prevention? Prevention of injury. Prevention of death. Prevention of addiction.

The dialogue is actually happening amongst the public health experts. There's a group of them who have been pretty vocally advocating that we change the way we're coding deaths.

The self-harm aspect: if we identify this as an accident, then our capacity to intervene in ways that will be effective for prevention is minimized, but if we identify this as behavior for which we can identify effective interventions for prevention, now we're doing a lot of good.

One of the points that these public health experts make is that the burden of evidence on medical examiners to determine cause of death as intentional or suicide-related is very, very high.

So, if somebody hangs themselves; somebody puts a gun in their mouth; somebody puts a bag over their head; those are pretty obvious. They get coded suicides. Somebody does something less obvious like overdose on pills or drugs, and there's a note there, "Dear loved ones, please forgive me, but I couldn't take it anymore." Okay, that's suicide.

But in the many cases of overdose — whether it's by the needle or by a bottle of pills, or a bunch of alcohol mixed with all of this — there's no note. The only way that you would really be able to call it a suicide, according to our current coding, is if there was a sufficient investigation of that case that determined pre-existing mental health problems or suicidality. And enough evidence to piece it together and say, "Yes, probably this was in the self-harm suicide spectrum."

So, the problem is that the deaths are getting captured, but not necessarily being categorized in the right bins. We're probably undercounting suicides significantly. If we change the way that we're coding these things to include deaths that are self-inflicted, or self-harm deaths, we can do a whole lot more on the public health prevention side around testing interventions that will effectively prevent this. I'm 100% behind that.

The other piece that I think is so important is that the dialogue is happening, and many people are now mobilizing to do something about this problem, but mental health is not really getting the play that it needs in this picture.

And, you know, some of the reasons for that may be people are afraid of how much it's going to cost. Right? If we can cleanly separate this as an addiction problem, then let's just get this supply of opioids out of the way and treat addiction: that seems like it's going to cost less than dealing with all of the other chronic illnesses—trauma, depression, suicidality.

Treatment is costly. Treatment for mental health and substance use is not like many other medical treatments in the sense that it often requires multiple contacts per week as an outpatient. You might see a psychiatrist. You might see a therapist. You might go to group therapy. You're going to peer support, like 12-step or Smart Recovery, multiple times a week.

This is hard on people, especially people with jobs or children that they're raising. And, frankly, it's part of what continues to fuel the stigma because you're doing the treatment that's prescribed. It's very intensive. It's what's required to get recovered, but what does your boss think of that? Another medical absence?

I mean, it's different than even having to go into an office once a week and get your vital signs monitored and something checked. It's much more intensive. So there is that perpetuation of stigma because it interferes with other conflicting responsibilities.

But the problem is, we don't have a more efficient way to get people well yet. Hopefully, that will continue with research and development. But right now, this is what it takes to get people well.

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