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**DR. SUSAN WEISS**  
**APRIL 27, 2010**

00:00:03:07 MS: -- Policy and communications at the National Institute on Drug Abuse, formerly known as NIDA. And that's within the National Institutes of Health. Prior to coming to NIDA, she served as the Senior Director of Research at the National Mental Health Association, which is now known as the Mental Health America Organization, where her role was to infuse research and science information into the organization's strategic planning, public education, and advocacy efforts.

00:00:32:20 And before that, Dr. Weiss was Chief of the Unit of Behavioral Biology in the Biological Psychiatry branch of the National Institutes on Mental Health, where she oversaw a research program focused on characterizing the evolving nature of psychiatric and neurologic illnesses to inform the development of novel treatment options for patients with affective, anxiety, and substance abuse disorders.

00:00:57:25 Her current position at NIDA includes her supervising a dozen staff working on various aspects of drug abuse and addiction, from conducting outreach and education programs for elementary school

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students, to overseeing the training of young scientists and new grantees. Also preparing scientific and policy communications for members of Congress and the public.

00:01:19:25 She has received on multiple occasions the NIH Plain Language Award, and the NIH Director's Award. Her -- she has published more than 140 scientific manuscripts and book chapters. Most notably you'll -- if any of you watched the HBO series Addiction, which was on 2 years ago, Dr. Weiss received an Emmy for her work on that series.

00:01:43:05 Finally, she graduated from the State University of New York at Stonybrook in 1975, and received her doctorate from the University of Maryland in 1982. She does welcome the opportunity to take questions during the program, so please feel free to interrupt. She is not on autopilot. If I could ask, though, if you could wait for a microphone to be passed to you so that we can get the question on the transcript.

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00:02:07:11 Then if you feel at the end of her presentation you have any additional questions to ask, please feel free to do so. And join me now in welcoming Dr. Susan Weiss, from NIDA. [applause]

00:02:21:02 Dr. Susan Weiss: Okay. Thank you very much. It's really a pleasure to be here. As Sean [ph.] has said, I'm the Chief of the Science Policy Branch at NIDA, and just for those of you who are not so familiar with NIDA, we are one of the institutes of the National Institute on Health -- of Health, and we support about 80 or so percent of the world's research on drug abuse and addiction, which includes also research on HIV/AIDS.

00:02:49:10 So most of what NIDA does is to support grants, and support training of researchers, but my office has the unique position of being NIDA's voice to the public. And that's actually a very fun job, which has allowed me to be one of the numerous people working on the Addiction project for HBO, and we also had the pleasure of working on the travelling DEA Museum exhibit a number of years ago.

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00:03:15:03      So it's actually quite a fun job for me. Okay, so today I'm gonna talk to you about marijuana and what we know from the science, and again, I would welcome questions at any point during the presentation. Next slide, please. So we have -- I can't really see the slides. So we have a number of surveys that are used to tell us sort of what the degree of the problem is. And what you can see on this particular slide, although it's a little bit hard to see, is the path -- past month use of a variety of illicit drugs from the National Survey on Drug Use and Health.

00:03:56:21      This is a large national survey. It's conducted every year. It's among people who are non-institutionalized, and 12 or older. And the main point that I want you to take from this is that marijuana, which is the line in red, is the most widely abused illicit drug. And this is probably not a great surprise to you. And our country, the United States, is also one of the biggest users of marijuana.

00:04:21:04      So we are among those -- we are among the developed nations that use -- that abuses

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marijuana the most, and it is the most widely abused drug. And you can see, looking at this overall -- this shows information from 2002 to 2008, and for the most part, the numbers have been pretty steady. They were going down a little bit for marijuana, and then in the most recent years, that -- downward trend seems to have slowed.

00:04:48:24 Just if you wanna notice on the bottom, it's really hard to see, but the -- the bottom line is methamphetamine, which actually has been going down. It's -- it's been at low levels, but it has been going down, which of course is very good news. Next slide please. So this is a slide -- so NIDA has its own survey, and it's called the monitoring the future survey, and it's a -- a national survey of 8th, 10th, and 12th graders.

00:05:13:21 And we survey both attitudes about drug use, as well as drug use. And this -- these data are from that survey. And what you can see on this slide is that if you look first at the red line, which is cigarettes, you can see that there's been a downward trend that began around the mid-19 -- mid-1990s, that

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has been ongoing since then. And actually, it's been -- it was ongoing -- we were seeing a downward trend since 1975.

00:05:43:09 And in fact, the reported use of cigarettes is at the lowest point since the survey began. But for marijuana, which you can see, is we also -- we had a -- we had the highest rates back in the 1970s, and then we'd seen a persistent decline as well since about the mid-1990s. But in the last couple of years, that decline seems to be slowing. So that is a cause for concern. Next slide, please.

00:06:10:06 This is a slide which shows something that you may kind of think is a duh, but it's that, you know, the more people see risk associated with using a drug, the less likely they are to use a drug. But this slide is such a nice image of that, and showing that lawfulness. So you can see that the blue indicates past-year use, and you can see that it's at its lowest when youth perceive risk associated with marijuana use at its highest.

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00:06:38:08      So this is something that tells us that we really need to make people aware of what the possible consequences are of using marijuana, if we hope to have an impact on preventing its use. Next slide, please. Oh, yes please. Could you wait for the microphone?

00:06:59:01      FS:    Could you explain that downward -- that very precipitous downward trend after '91?

00:07:04:25      Dr. Susan Weiss:      After '91.

00:07:06:24      FS:    Where it just --

00:07:07:14      Dr. Susan Weiss:      Just starting --

00:07:08:14      FS:    [unint.]

00:07:10:01      Dr. Susan Weiss:      In terms of why it happened?

00:07:11:05      FS:    In terms of perceived risk.

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00:07:13:14 Dr. Susan Weiss: Okay, so what you can see there is that the perceived risk started to go back -- the -- the perceived risk started to go down at that point, and at the -- and usually what happens, and that's also shown here, is that perceived risk actually anticipates the change in use. And what happened here is that I don't know why the perceived risk went down. I mean, if -- if that's the question, that's a much tougher question, and I don't know, and there may be a whole bunch of cultural factors.

00:07:41:20 It may be things that are in the media. It may be a lack of attention to messages about marijuana that needed to -- we needed to maintain attention to. I mean, this is one of the things that we -- we always have to keep in mind, that we're -- we've always got a new cohort of young people, and so we've gotta really be persistent in the kind of messages that we give them. So I don't know what caused that downturn.

00:08:04:21 And I don't know, you know, I can't really say. You know, we always take credit for the good things, so we always take credit for when they --

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when the use goes down. But in fact, there's a whole variety of factors that are involved, and I don't know what caused that precipitous downturn. Okay. Next slide. This slide just shows that prevention can work. And there are a number of evidence-based prevention methods that --

00:08:35:05 Programs that have been shown to work across -- in a variety of settings, in schools and communities. There are programs that target parenting. And there are programs that are designed really for all age groups, saying you really need obviously to have developmentally appropriate groups. So there are some that train people how to deal with peer pressure. There are some that just promote general healthy behaviors.

00:08:58:19 In general, our prevention programs don't target a specific drug. They really target healthy behaviors, and taking care of your body, and taking care of yourself, and -- but they do work. And this is just one example. This was actually a community study using a life skills training

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prevention program, and it was given to sixth and seventh graders.

00:09:21:04      And then they were looked at a year and a half later. And what you could see is, it did reduce the use of marijuana and actually inhalants, you can also see on this slide. Inhalants are a problem often among younger people, probably because they're so accessible. But it's -- it's also a problem that we often try and draw attention to, because many people aren't aware of -- of inhalants, and they are so readily available.

00:09:44:28      And there are kids that are certainly aware of it. Okay, next slide, please. Okay. So now I would like to turn to kind of what do we know about THC, which is the -- the main active ingredient in marijuana that produces its -- its mind-altering effects. And this is just a picture of the THC molecule. We were studying THC to find out about -- to find out how it worked in the brain, and in around the mid-1990s, there were receptors in the brain that were discovered that THC binds to. Next slide, please.

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00:10:22:21      And this is one of the first studies that showed that. What this is is a picture of a rat brain, and it's what's called a sagittal section, which means it's kind of a slice sideways through the brain. And what it's showing is the areas of the brain that have a lot of receptors for -- for THC. So red and yellow mean a high density of receptors.

00:10:44:10      And what you can see in this -- in this slide is that that sort of big area on the top, that's kind of the frontal lobe of the rat brain, and that's the equivalent of our cortex. So you're talking about the areas that are responsible for sensation and perception, and in humans for decision-making and for planning. And some of the other areas that are also high in marijuana receptors are the hippocampus, which is an important area for memory.

00:11:12:22      So this was one of the first demonstrations of this, and actually, it's by studying how marijuana works in the brain that we really discovered an entirely new signaling system, which is called the endocannabinoid system, which is really

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where there may be a lot of very important information as far as medications development go. So there's the endocannabinoid system is a system that's involved in a whole variety of physiological functions, including pain and appetite, reward, memory, learning.

00:11:46:16 It modulates the immune system. So by studying marijuana, we actually discovered a very important biological system that may actually prove very fruitful in the future for developing medications. Next slide, please. So this shows the human brain, and again, it's sort of showing the areas of the brain where -- where there are a lot of marijuana -- or a lot of THC receptors.

00:12:11:14 And this is important, because in fact this determines what the effects of marijuana are. And again, it's in these areas like the neocortex, which is on top, which is involved in thinking and planning. The hippocampus, which is that sort of little yellow area, which is involved in memory and learning, and some of the other -- the amygdala is important for emotions. We know that mood and emotions are affected by marijuana, and so if you look

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at where in the brain THC acts, that tells you why it produces some of the effects that it does. Next slide, please.

00:12:49:11      So we know a lot about the acute effects of marijuana. And we know that people -- people use marijuana because it makes them feel good. It makes them feel calm. It also stimulates appetite. It alters the perception of time. It can impair coordination and balance, and that's because there are a lot of receptors in a part of the brain called the cerebellum. People also can have an acute psychotic response to it, or they can panic.

00:13:17:09      And this often happens when higher doses are used, and sometimes when marijuana is taken in food, taken orally. In part because the effects kind of can come on suddenly after a while, and it's also very high -- hard to make -- to know what dose you're taking. But we do know that some people have those sorts of reactions. It increases heart rate.

00:13:39:21      And for a young, healthy person, that may not be a very significant effect clinically, but

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in somebody that's older, it could put them at risk of heart attacks. And there is a study that showed that within an hour of using marijuana, there was an increased risk of -- of heart attacks. And this is a concern that we have, particularly for now some of the aging Baby Boomer generation, where we're seeing that the rates of illicit drug use, and particularly marijuana, are higher than they were in previous cohorts.

00:14:11:07 And so there could be cardiac problems resulting from it as well. Impaired driving. So this is something that's obviously very important from public -- for the public health perspective. We know that marijuana affects judgement. We know that it affects reaction time. So we know that it affects some of the skills that are needed to be a good driver.

00:14:33:18 And in driving simulation tasks, and in some studies that have looked at what's happened with people that have been in accidents, there does seem to be an increased risk of being in an accident if you've smoked marijuana. There's also an increased risk of

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being culpable for the accident, although many marijuana users claim to compensate, and they often do compensate, they're not necessarily equipped to deal with an emergency situation or an emergency response, or to pay attention to all of the different things that are going on on the road that they need to pay attention to.

00:15:07:10 One study from France showed that marijuana is probably responsible for about 2.5% of fatal accidents. And alcohol about 29%. So it clearly is a factor. It's clearly, you know, not a good idea to drive while under the influence of marijuana. It's not as big a factor as alcohol. There are studies that show that the two potentiate each other.

00:15:30:28 So even a low dose of marijuana and a small amount of alcohol can be worse than either -- than either one themselves. And then there's the fact that marijuana affects judgement and affects decision-making, and people report being more likely to get into a car with somebody who either was driving while drugged, or driving after drinking. Next, please.

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00:15:55:14 Cognitive dysfunction. We know that because it affects the hippocampus, we know it affects short-term memory. It -- which would make it difficult to do complex types of tasks. Certainly not good to learn anything new. And again, just like most drugs, it affects areas of the brain involved with judgement and decision-making. And that means that people may be at risk of doing things that they wouldn't ordinarily do.

00:16:20:14 Increased risk of injuries. In addition to those injuries associated with driving, there -- one Kaiser study just looked at injuries in general and found a 30% higher risk of -- in people who were marijuana smokers. So that's not necessarily when they were intoxicated, but just in general. And another study found that among people that are hospitalized, there is a greater -- a greater risk of hospitalized injury from either self-inflicted, motor vehicle, or assaults among people who are marijuana smokers.

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00:16:57:03 Next slide, please. So this -- this looks at emergency department [unint.]. So there's another large database. It's called DAWN [ph.]. And it looks at the number of -- it goes through hospital records and determines whether or not there was any drug that was used at the time that a person is brought into the hospital. And this just illustrates the -- from 2004 to 2008.

00:17:24:22 Unfortunately, the DAWN survey changed between 2002 and 2004, so you can't really go back before then to make a comparison. But what the -- what the DAWN survey was showing was that the rates of emergency room visits associated with marijuana had actually gone up quite dramatically between 1992 and 2002. These data, from 2004 to 2008, do not yet show a significant increase, although it certainly looks like it's going up.

00:17:58:05 But whether or not it's a significant increase, we're still talking about 374,000 marijuana mentions that DAWN has recorded. Some of these were for mentions with marijuana and other drugs, so maybe marijuana and alcohol, marijuana and cocaine, but

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about 100,000 of them are marijuana alone. So a lot of people are winding up in the emergency room for something related to marijuana.

00:18:22:10 I actually don't know why they're all there. I'm trying to get that information. We kind of did some quick math based on the number of hospitals that DAWN surveys and the number of motor vehicle accidents that happen in a year and the number that result in hospitalizations, and this can't all be related to driving accidents. So I don't know what all of the reasons are for the marijuana-related hospital visits, but I'm hoping that we can get some more information about it. Next slide, please.

00:18:56:05 And this is just to give you a perspective on where marijuana falls relative to other drugs. So as you might expect, alcohol is -- is the largest -- largest associated with visits associated with the emergency department visits. Cocaine is second, and marijuana is third. And then heroin and other stimulants. So it's not quite -- it's not having quite the same impact that alcohol is, but it's still having a pretty major impact. Next slide.

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00:19:26:23      So then we get to the longer-term effects of marijuana, and this is where we start to kind of get a little bit more iffy in what the research has shown us. So we know that if you -- if you continue to take it long-term use, that you're gonna have deficits in learning and memory and attention, and in your ability to think and plan, because these are the effects that marijuana has on the brain.

00:19:49:05      And marijuana also sticks around for quite a while. So somebody who is using marijuana every day is probably -- is probably effected every day, and probably functioning at a lower than their normal level all of the time, which is obviously particularly problematic for children or kids who are in school and trying to learn. There seems to be greater impulsivity and -- and less ability to be kind of creative and flexible in your thinking.

00:20:18:02      But some of the studies -- well, the data so far suggests that if somebody stops using marijuana that these effects are reversible. So you

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have to think about this in two ways. One, I mean, that's great, because if you stop taking these things these effects don't last. But you can't necessarily go back in time. So if you spent 20 years of your life taking marijuana, then you've gotten to a different place than you would have had you not done that.

00:20:43:20      So you may be able to recover from a lot of these effects, but the impact marijuana has on the trajectory of your life is still there. And in fact, we know that there are greater dropout rates associated with marijuana use, and we know from a study of marijuana users, these were people who'd been using marijuana for 30 or so years, did not wanna -- people who did not choose to give it up, did not even wanna give it up, they were not treatment-seeking people.

00:21:10:26      But they were asked -- they had a -- there was a comparison group that came from a similar background, similar parental education and -- and job attain -- job achievements, and -- and what was found is that these people tended to not only have poorer

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educational outcomes and -- and lower salaries, but they themselves reported less life satisfaction, and they themselves perceived marijuana to have had a negative impact on social relationships, on their mental health, and on their physical health.

00:21:42:09      So these are in people who were not treatment-seeking, but they also felt that it was not a good influence on their life. As far as what happens to the brain, and again, here's where it's not -- we have not seen very major effects so far. Structural abnormalities have not been consistently identified. There are some functional changes. So now we have brain imaging studies, which are great because we can see what the brain is doing while somebody is actually engaging in a certain kind of activity.

00:22:12:21      And we can look in -- we can look in live, breathing humans, and not just be looking at either autopsy brains or animals. But we're not -- we're not seeing major changes yet. And there's -- the studies are really in progress right now, particularly looking at adolescents. And adolescence

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is a very important time -- is a really important group to look at, because we've learned over the last 10 years or so that the brain continues to develop and is really changing quite dramatically during adolescence.

00:22:45:16 It continues develop -- to develop into early adulthood. And it's those frontal areas of the brain that are involved in thinking and judgement that are the last to mature. So those areas are the ones that could be impacted from chronic marijuana use. The functional changes that are seen tend to be things like people that are doing memory tasks will -- will use parts -- will use a sort of greater amount of brain to do a task than people who are not marijuana users.

00:23:21:02 So the implication is that somehow their brains are less efficient in doing these tasks. It's really hard to know how -- what to make of these kinds of -- this kinds of information. It may be that they are -- they're still -- this is in tasks where the marijuana users are performing equivalently to somebody who's not a marijuana user. So engaging more

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of the brain may not be as efficient, but they're still getting there.

00:23:45:29      The question would be, what happens when they're challenged with something that's really difficult in -- in life, or in, you know, some sort of emergency situation. Would this less efficient brain put them at a detriment in -- relative to other people. And this is a question that we don't know the answer to. Or, how will this effect them as they get older. I mean, we know, for example, that the hippocampus in general in anybody that's aging starts to lose cells.

00:24:13:23      So will marijuana's effects on the hippocampus in some way make this worse, or not? And these are -- these are questions that are ongoing. They're very important research questions, and we're still trying to find out. Yes?

00:24:36:05      MS: Quick question. You mentioned when you got to this slide on long-term effects that -- you added a lot of caveats. If not yet, and still learning. Can you talk about the length of the body

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of knowledge you all are working with? How long have -- have you -- you all been engaged in these significant studies of long-term effects, and how much longer do you think it'll be before you can get a little bit more definitive in the long-term impacts?

00:25:03:23 Dr. Susan Weiss: I think that's a very good question. The -- it -- we have not really been studying it as long as we've been studying, for example, the effects of cocaine. I think for a long time marijuana was not, even by the scientific community, it was not -- it was not looked at as being as problematic as some of the other drugs that were -- that were available. And so there was -- there was not as strong a research focus on marijuana as there was on other -- in other drugs of abuse.

00:25:31:05 So that's one thing that really started late. As I said, we -- you know, we only found out how marijuana even works in the brain in the 1990s, so that's actually pretty -- pretty late in the game. The other issue is that -- the other issue is that there are -- when the initial brain imaging studies were being done, those involved radiation. So those

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were not -- those were not really appropriate studies to be done in youth.

00:25:57:29      And particularly if you wanna try and follow somebody up, you're not gonna expose them to radiation. Now we have -- we have different techniques that don't require radiation, so that means that now we're really able to do a lot more studies in young people, and sort of look at what's happening over time. And the other important variable, and this is always true in any, you know, human study, is that when you look at the brain of somebody who's a drug abuser, compared to somebody who's not, you don't know where they were to begin with.

00:26:26:12      And so you're always -- you're always stuck with, you know, was this person more vulnerable? Did they have a smaller hippocampus before they took marijuana, and maybe that's why they were more susceptible to its effects, or more susceptible to its addictive effects, which is why the animal studies -- which is why the animal studies are very important, 'cause then you can actually presumably look at those variables.

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00:26:47:04      So in answer to your question about when the long-term effects are there, I think that I don't -- I don't -- I can't really answer that conclusively. I hope that within the next ten years we will -- and probably sooner than that, that we will have more information, because there are a lot of studies going on right now to look at the -- to look at adolescence, and to look at what's happening over time, and to try and follow groups that -- that are not necessarily -- you know, have -- have a better database of people who are -- don't have drug abuse problems, and then sort of look at them over time.

00:27:20:15      So I think that, you know, we're getting there, but I think it's -- it's still gonna be a few years. The other point I would make is that the effects may be more subtle than they have been with some of the other drugs that we've looked at. And that's another -- that's another factor. So it hasn't been hard to show effects of cocaine that are -- that are longer lasting, that are sustained, as much as it's been to show effects of marijuana.

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00:27:44:00      So there may be -- there may be more subtlety to the effects. There may be -- and you know, we just don't know. So I think at this point it's something that we're gonna have to -- I would say five to ten years. You can have me come back at that point, to try and answer this question again. Was there another question? Yes. Do you wanna --

00:28:10:27      MS: Thanks. You mentioned the ongoing trial. So you're saying there are ongoing clinical trials in the United States, and if so, how many are there -- are they NIDA-sponsored, are their teenage subjects?

00:28:22:19      Dr. Susan Weiss: They're not being given marijuana, if that's what you're asking. So what -- okay, when you -- but there are -- there are studies that are looking at the brains of -- I don't -- I'd have to go back and do -- I can get you the information. I'd have to kind of go back and look at how many grants there are. But there are ongoing grants that are studying adolescent brain development.

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00:28:40:05      And that are looking at people over time, so that they can look at normal brain development, they can look at what happens when -- when things change over time. So that's -- those are the kinds of studies that are being supported, and that hopefully we will be able to use to learn what happens. There have been some studies -- Germany, I think, has some studies also, looking prospectively at -- at brain images of people that are marijuana users.

00:29:02:25      Again, the effects are not huge. They're subtle. And so what they mean functionally, we don't -- we really don't know yet. And the other -- other thing that makes these studies very hard is that it's very rare to find people that use only one drug. So you've usually got alcohol in there. You've often got cigarettes in there. You know. So there's -- there's -- you know, and this is a study -- I mean, there's also been studies looking at women who are pregnant and have been --

00:29:31:09      And their fetuses have been exposed to marijuana. But it's -- again. To find women who have been -- whose fetuses have been exposed to marijuana,

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who have had proper nutrition, good prenatal care, no nicotine, no alcohol. That's, you know, very, very hard to do. And we know that nicotine and alcohol have their own effects on prenatal development. So teasing out marijuana's effects has been very difficult.

00:29:55:14      You know, short-term effects are easy. Because then, you know, you can see what marijuana is doing to the person's ability to do things. The longer-term effects get very complicated, not unexpectedly.

00:30:07:25      MS: I don't know whether you have additional information that's coming in or additional slides, but I'd expected to maybe see something that association with depression.

00:30:17:17      Dr. Susan Weiss: I'm coming to that.

00:30:20:27      MS: Thanks.

00:30:21:08      Dr. Susan Weiss: Sure. Okay. Two more slides. So respiratory system is the other -- is

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another big effect that we are aware of. And there is clearly information that marijuana use increases -- produces a lot of the same effects as cigarettes do on the respiratory system. Increased susceptibility to respiratory illnesses, increased bronchitis, cough. Worsening of asthma symptoms or cystic fibrosis symptoms.

00:30:54:29 There's no increase in emphysema, and the research on cancers, airway cancers, have been very, very... Very inconsistent. Sort of the best studies that we have today don't show a relationship between marijuana and the airway cancers. That said, and these studies are done by one of our researchers, who's actually shown pre-cancerous types of changes in the lungs of people who are marijuana smokers. So he was expecting to see a greater risk of cancer in marijuana smokers.

00:31:30:04 There have been some studies in other countries that have shown a greater risk of lung cancer, but in many of those countries, the way marijuana is taken is that it's -- its combined with tobacco. So a lot of those studies are -- are

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confounded. So at this point, we don't have a strong link there between marijuana and lung cancer. I certainly wouldn't say we should rule it out. We don't know enough yet to do that.

00:31:55:03 But it's certainly not jumping out at us. And there may even be some protective components in marijuana smoked. Maybe not the THC. There may be other -- other cannabanoids, or it may be -- I mean, one of the things about -- about THC is that it has very complicated effects on the immune system. So it affects the immune system, but it actually suppresses some of the -- the parts of the immune system that are important for fighting illness, and then it enhances others.

00:32:23:12 And so it's -- again, so what comes out at the end is hard to know. So right now, there is not a strong link with lung cancer, but there certainly is with these other airway diseases.

00:32:45:22 FS: How long did it take, and how many studies did it take to establish that there was a link between tobacco and lung cancer?

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00:32:54:23 Dr. Susan Weiss: Yeah, I don't know the answer to that. It's -- yeah, I -- I don't know the answer to that. I'd have to check for you. But I -- I don't -- you know, they've been pretty good case control studies at this point that don't link it. That doesn't mean -- but you're right. That we still could find that out. But I think that it's -- you know, it is being looked for.

00:33:15:12 It's also -- once again, it's complicated, because you have to find marijuana smokers who are not tobacco smokers, and many are both. And so -- and many -- so the other thing about marijuana is that many people that are marijuana users when they're young, stop. So just as we know that if you stop smoking cigarettes, you know, that can start to decrease your risk of lung cancer as you get older.

00:33:35:25 You know, people tend not to stop smoking cigarettes. But many do stop smoking marijuana. So in the studies that have looked at long-term marijuana users that -- so again, we're talking about a much smaller population than we are of

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-- of tobacco smokers. So those are things that may make it different, but -- so again, I wouldn't -- I wouldn't say it has no relationship at all, but at this point I don't think that we can make a -- we can make a statement that it does cause lung cancer, or that there's strong evidence that it causes lung cancer.

00:34:07:07 FS: Following up on your reference to immune system effects. Is there a correlation between marijuana use and pneumonia in people whose immune systems are suppressed because of AIDS or cancer?

00:34:21:25 Dr. Susan Weiss: Not that I'm aware of. There are -- you know, people are using marijuana when they have AIDS, and then they have cancer. And I am not aware of that. The studies that I know that have looked at AIDS patients have just looked -- they're very short-term studies. They've looked at some different measures of immune system function, and haven't found a negative impact.

00:34:46:08 But you're asking about a specific -- specific problem, and I'm not aware of any studies,

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but it's something I'd like to look into, and -- and I can try and get back to you on it if I can -- if you wanna give me your information, see if I can find out anything. But to this point I'm not aware of anything. Okay. Next slide, please.

00:35:12:05      So, mental illness. Now, here's where things get also pretty dicey, because people have shown -- there's now quite a bit of evidence that shows that our -- from large prospective studies, they study people over time, and that they show that use of marijuana does increase -- it is -- it does increase the risk of developing psychosis. And probably that is in people who are vulnerable to psychosis in one way or another.

00:35:40:02      And these studies are -- they've been very controversial. There's been a lot of arguments back and forth. But I think the evidence at this point -- I think people are pretty clear that it does increase the risk of schizophrenia, at least in people who have some vulnerability. It is a risk factor. The links with depression and anxiety and suicidality

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have not been as strong, particularly not with respect to it being a causal factor.

00:36:06:28      However, there certainly is a lot of evidence that these things occur together. Can you -- next slide, please. Oh, okay. So -- next slide -- okay, go ahead.

00:36:18:25      MS: [inaud.]

00:36:21:18      Dr. Susan Weiss:      Behind the what? The schizophrenia?

00:36:23:23      MS: [inaud.]

00:36:24:27      Dr. Susan Weiss:      We know -- you're asking me -- there is a -- we don't know for sure, but there's a number of different hypotheses. One is -- oh, the question is what might be the mechanism by which -- by which cannabis can exacerbate psychosis? Is that your question? Okay, so we know that this is one of the things that -- I mean, we're learning -- we're still learning about the endocannabinoid and its role in a variety of different types of functions.

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00:36:51:19 I mean, one thing it does is it modulates dopamine. And dopamine is an important chemical with respect to both reward effects of drugs, as well as with respect to schizophrenia. So it could be through some sort of indirect effect on the dopamine system. And I'm gonna show you a slide, the next slide, that shows that there could be a little bit of a link there. But there may be other ways as well, because we do know for sure that --

00:37:16:07 That high doses of cannabis can acute -- can induce a psychotic response in some people, acutely, that usually resolves when the effects of the cannabis wear -- wears off. So there may be other mechanisms as well. But we're still -- we're really still learning a lot about what the -- what the endocannabinoid system does in the norm -- in the normal brain physiology. We know that it's involved in stress-related responses.

00:37:41:28 We know that it's probably involved in anxiety and depression. And this is mostly from animal studies, that show that if you modulate these

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systems, that you can -- you can get a change in an animal's response to stress, or in -- using different types of animal models that measure anxiety or depression. So this endocannabinoid system, which -- which THC is acting on, is involved in a lot of different aspects of mood and -- and with respect to psychosis, I think at this point the link -- the best link is to the dopamine system.

00:38:15:07 But so there's reasons to be concerned about this link. But it's not -- it's not that straightforward, of course. Did you have -- yes.

00:38:25:04 FS: Yeah. Can -- can use of marijuana and then the stopping of marijuana cause a permanent mental illness, anxiety, permanent anxiety, that may take [unint.] or may not take [unint.] after years and years after having used?

00:38:41:02 Dr. Susan Weiss: It hasn't been associated -- I mean, the psychosis is the one disease where it's associated as -- as one risk factor. It's probably not the only thing -- so there aren't -- there aren't data that I'm aware of that show any

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lasting effects of marijuana from an acute anxiety reaction, or an acute psychotic reaction. Those things do tend to wear off.

00:39:02:02 In people who have some sort of tendency towards psychosis, the effects of marijuana as a causal agent can then sort of be part of what triggers the disease, and then the disease could be continuing. It can also exacerbate symptoms in people that are -- that have schizophrenia. So -- and it may make the course -- it may -- it may be -- may bring the disease on at a slightly earlier time.

00:39:26:19 So there are -- there are data that suggest that it does -- it does link to this disease process. But as far as the acute responses, and for anxiety, as far as an acute response, there aren't data yet that can say that that would happen.

00:39:44:22 MS: Would it be then fair to say that it changes the base rate temporarily while it's being taken, and that people that have, if you will, a higher or lower equilibrium status with regard to dopamine levels, if they're in standard levels,

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marijuana really isn't going to have a problem, but if they're at -- if they're high or low levels, whatever is out of the normal range, that's when -- marijuana actually will have any real negative impact.

00:40:14:13 Dr. Susan Weiss: In theory, yes. But there -- the data aren't quite there to support what you're suggesting, but yes, that's one possibility of how it could happen. And there are data, not for marijuana, but there are data with -- with stimulants, like amphetamine, that do show that there's kind of an optimal level of -- of dopamine in order for it to -- to have any kind of effects on cognitive function.

00:40:40:27 So for people who have sort of very high levels, then amphetamine tends to worsen their performance. Whereas people that have lower levels, amphetamine can actually increase their performance. So there's -- there is precedent for it, but it's not that clearly shown yet for marijuana.

00:41:03:21 FS: I wanted to make another analogy with tobacco smoking. Doesn't -- wouldn't you

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consider also that tobacco-related cancer are gonna happen mostly in people who will have this or that genetic mutation that will make them more likely to have breast cancer, or I mean, isn't any disease going to --

00:41:22:08 Dr. Susan Weiss: Absolutely.

00:41:24:03 FS: So do -- does saying that it only happens in vulnerable people or predisposed people, doesn't that unfairly reduce -- reduce it as a risk factor?

00:41:38:15 Dr. Susan Weiss: No, I don't -- I don't think so. I -- you're absolutely right. Almost any disease that we can talk about has genetic risk factors. I guess what I'm concerned about is that -- I mean, we don't -- for example, we don't see the incidence of schizophrenia going up, even though we know that marijuana use in the last, you know, 20 or 30 years, particularly in some countries, has really gone up.

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00:42:01:21      So if we -- if we look at it as being, you know, the cause of the disease, then we get into trouble right away, because the data aren't there to support it. On the other hand, you know, there's probably a lot of risks that contribute. I mean, stress we know contributes. I mean, early -- you know, early types of -- of severe stress can be a contributing factor to the development of schizophrenia.

00:42:24:04      Genetics, clearly the case. So marijuana is also among the causal factors. I just don't want it to be considered -- you know, that all of a sudden that, you know, that's gonna be it. And you know, one of the things that we -- we strive very hard for in our -- in our general kind of capacity as communicators is -- is not -- you know, we want people to understand what the risks are. We don't wanna oversell, because then we lose people.

00:42:51:04      And particularly when we're talking about youth. And youth are a lot of our audience, because we're -- you know, we're an institute that's concerned about drug abuse. And so we try and be very

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careful, and try and make sure that the message is that we give them are going to really be credible to them. We're not gonna not -- you know, we're not gonna downplay it and say, no, this doesn't happen.

00:43:09:18      You don't have to -- you don't have to worry about that. We're gonna say, yeah, we now know that there is a risk. But we at the same time don't want to overplay it, because they're gonna say, all my friends are smoking marijuana. None of them have schizophrenia. And none of them may have schizophrenia. You know? On the other hand, someone who may be vulnerable, this may really push them over the edge.

00:43:29:26      So you're absolutely right, though, that genetics clearly play a role in any disease, and that's not to -- you know, it's not meant to downplay the role of marijuana. It just meant that that is one risk factor among many.

00:43:42:24      MS: Three -- three quick questions. One is, we talked about marijuana generically here. But we talk about it in speeches and elsewhere. We

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talked about how BC [ph.] bud, for example, is much more potent. That today's marijuana is much more potent than it used to be. Can you talk a little bit to that? Second, again, when we talk about marijuana, we talk about THC being the active ingredient.

00:44:06:11 But then we also talk about that there's hundreds of ingredients. Can you maybe talk about a couple of the other active ingredients that are important?

00:44:13:17 Dr. Susan Weiss: These are three small questions?

00:44:17:14 MS: Okay, the -- and the third one is short. It's a yes or no question, which is, can -- can we say, can we administer and can others say that marijuana is addictive?

00:44:26:24 Dr. Susan Weiss: Yes. You're actually getting ahead of my talk, so would you mind if I just kind wait on some of that stuff? But I am gonna talk a little bit about potency, and we definitely -- and I am gonna talk about addiction, and

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we definitely can say that it's addictive. That's incontrovertible from my perspective. And as far as the other ingredients go, that I wasn't really gonna talk about.

00:44:45:23 We don't -- we know that there are some other cannabinoids in marijuana that may actually have medicinal uses, but we really don't know what all of the other ingredients are. And that's one of the reasons why marijuana as a plant is really not a good medication candidate, even if you can see some value -- some medical value in the cannabinoid system, because for one thing, it has, you know, some 400 other chemicals in it, and we -- they're usually not well characterized in any --

00:45:12:28 They differ from one plant to another, and we frequently don't know, you know, how they're going to impact somebody's health, particularly somebody who has some sort of illness, how it's gonna affect their health. But there may actually be other cannabinoids in marijuana that have some potential medical benefits, and I forget the -- I think it's CBD is one that can -- I forget the name of it.

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00:45:34:27 But anyway, there's at least one other that we think may have some potential benefits, as far as medical uses go. Okay, so mental illness -- so let me just come back one -- one -- this is just -- this is just one example -- next slide -- oh, that's it. This slide. No, no, go back one. This one. Okay. So this is just one example showing the genetic -- the genetic predisposition and also kind of bringing in one other factor that is --

00:46:00:09 That just kind of shows just a little bit of the complicatedness of it. And this is the idea that it's not just genes, but it's also when you start using the drug, and that there's an interaction there, in terms of its affecting your vulnerability to schizophrenia. And this is a study that looked at something called COMT, and that's an enzyme, and it's an enzyme that's involved in the breakdown of dopamine and some of the other similar chemicals to dopamine.

00:46:28:02 And there are different variations, genetic variations of it. And the only thing I want you to see in this slide is that among people who used

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-- it's if you look down at the very last -- last bar, among people who used marijuana when they were adolescents, their risk for schizophrenia goes up quite a bit. Among people that don't have that genetic variant, their risk is not affected by using marijuana.

00:46:56:23 And even among people that have this risk variant, this [unint.] version of the gene, if they didn't start using cannabis until they were older, beyond 25 I think, or 21, they -- they did not show this increased risk. So there's a lot of variables that go into this. So there's gonna be -- I mean, and this is just one example, and it needs to be repeated, but it's just one example of one particular kind of genetic variant that does show that you can be --

00:47:25:08 You know, that -- that when there's an interaction between age of use, between exposure to cannabis, and having this genetic variant, that increases your risk for schizophrenia. Okay. Next slide, please. And this slide gets at sort of the other question, which really has to do with -- with

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the kind of co-occurrence of mood and anxiety disorders in people who are cannabis-dependent.

00:47:51:02      And what this slide shows is the -- the prevalence of a whole variety of depressive and anxiety disorders. And in the red bars are just in the normal population, this is yet another study, another large national study. And this study looked at the prevalence of these different disorders. And then it looked at the prevalence in people who are cannabis-dependent. So these are people who are -- meet the psychiatric criteria for addiction to -- to marijuana.

00:48:20:05      And you can see that their risk of having other disorders is also much higher. And this wouldn't -- I could show you this slide probably for a number of other drugs as well. But the point I'm trying to make here is that it's very rare that you're gonna find people who have just one particular problem, like they're just cannabis-dependent and there's nothing else going on.

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00:48:40:21 It's much more likely that you're gonna find people that have co-morbid depression, anxiety, other types of -- particularly in -- in somebody that's addicted to cannabis. It's more likely you're gonna find that they have other types of psychiatric problems, as well as other drug use or drug problems. Okay. Next slide, please. Okay. Now we get to the addiction question.

00:49:03:26 So this is a -- this is a slide from another -- another -- a slightly older study, but this was a study in which the person looked at among people who used a variety of different drugs, what percentage of them developed dependence. And again, this was looked at in terms of the psychiatric criteria for dependence or addiction. And what they found was that for cannabis it was about 9% of people who used it became addicted. It's much higher for tobacco.

00:49:34:25 You can see it's 32%. 15% for alcohol. Cocaine is higher as well. But still, you know, 9% of -- when you think of the numbers of people that are using, that's -- that's quite a huge number. And then other studies since then have shown that among

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adolescents who use, it gets down to about 1 in 6 adolescents. And among daily users, we're talking about 25 to 50% will develop addiction or dependence on cannabis.

00:50:04:23 So yes, it is definitely addictive, and this is a message -- again, this is one where we do really try to push hard, because there seems to be this belief that it isn't addictive. Next slide, please. Okay, this slide shows again the number of people who met dependence or abuse criteria for a variety of different drugs. And you can see that marijuana is quite huge. It's about 4.2 million people meet --

00:50:30:03 Met criteria in 2008. And again, this speaks to the -- the very widespread use of -- of the drug, which is why the numbers are so high. Next slide, please. And this is just to show you kind of a little bit more, but just a breakdown by age. And -- and you can see that the -- this is percentages. And so you can see that the numbers are highest in the group that's 18 to 25. In general, if you look at most drug abuse and most drug indices, it's the 18-

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to-25 year-olds where you see the highest abuse patterns.

00:51:10:20      And then it starts to go down. And again, this is looking from 2002 to 2008, and we can't go back further because of changes in -- in this survey as well. So. You -- you take what you can get. Yeah?

00:51:33:10      MS: I -- I read somewhere, and Eric also saw this, the -- a statistic that most marijuana users are under the age of 21. I think I got that right. Is that correct?

00:51:48:08      Dr. Susan Weiss: I believe that -- I believe that is correct. I'd have to go and look at the -- I'd have to go back and look at one of these surveys to tell you for sure, but I believe -- well, let me take that back. I'm not sure. I know that most people who start using marijuana are under 18. I -- I -- I don't -- I'd have to check that for sure.

00:52:10:04      It -- it wouldn't surprise me, but I would need to go back and look at it. Okay. The next

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slide, please. This just shows treatment admissions over time, just to show that they've been going down for alcohol, down for cocaine, but they've been going up for marijuana. Next slide. And this is in 2007, and you can see here number of treatment admissions for a variety of drugs, and obviously alcohol is kind of got the highest number of treatment admissions.

00:52:49:23 But marijuana is third. So many people are in treatment for marijuana abuse, and that's another point that we really try and emphasize, that it's not -- you know, it is -- you know, people do become dependent on it, and people do have to go to treatment to try and stop -- to get off of it. Next slide, please. And this just shows you a little bit about who are the people that are in treatment for marijuana abuse, and not that surprisingly, it's among --

00:53:16:27 Among people in treatment that are under 15, 61% are there because marijuana is their primary drug of abuse. And 56% for those -- for those between 15 and 19, and 24% for those 20 to 24. Then alcohol starts to become a bigger problem, as you

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start getting up in age. And also you can see from this left side -- those are males, and on the right side are females.

00:53:42:11      Marijuana tends to have higher -- it tends to be used more by males than females, and abuse and dependence is higher in males than females. Don't see that -- you see that same pattern a lot, but you don't see it quite as much for -- particularly among young people. You don't see it as much for cocaine, and you don't see it as much for prescription drugs.

00:54:01:16      But marijuana seems to be still a little bit higher among males than females, even in the youngest cohort that's 12 to 17, [unint.]. And that -- that group is actually showing much -- much fewer differences between males and females. Is there a question, please? Oh, do you wanna -- coming -- that next slide.

00:54:29:17      MS: And so my question is this. Given that marijuana is "a socially acceptable" drug to admit you're admitting and you're coming in for, the notion that we can take the [unint.] data prevalence

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estimates and say that they're good, bad, indifferent relevant to anything but alcohol may be a stretch.

00:54:52:11 Dr. Susan Weiss: Look at this slide, which I was coming to. That has to do with why people are getting -- how they're getting into TEDS [ph.] in terms of the referral source. And so what this is showing you is that a lot of people are going in because they're being mandated to go in through the criminal justice system. That said, we do -- we do -- I mean, we do have -- that said, we do have data that show that coerced treatment actually works as well as not-coerced treatment.

00:55:18:27 And whether or not people are coming in through the criminal justice system, many of them are being coerced by other people as well to get into treatment. But yes, you're right. It's not -- it's not a perfect indicator of things. But I think if you're getting people in when they're -- if people are going into treatment when they're young for whatever reason, and I think in this case most of it is through the criminal justice system, then most of them,

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marijuana is the drug that they're -- you know, that they're using.

00:55:42:28      So it does kinda make sense. But still, I don't wanna take away from the fact that, you know, people -- that again, people will blow it off and now it's -- it's just marijuana, nobody gets addicted and nobody needs treatment, and in fact there are -- you know, there are many people for whom it really is a problem. They can't stop using it. It's really interfering with their life, and they really need treatment for it.

00:56:06:05      So. But -- but you're right. There are certainly limitations as to what you can get from the TEDS data set. Did you have any other questions? Okay. Next slide, please. Okay, so what kinds of treatments do we have for marijuana addiction, and we don't -- of course, we don't have quite enough. We don't really have any medications at this point for marijuana. We do have behavioral therapies, and they're pretty much the same behavioral therapies that we know work for other addictions, which is good and bad.

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00:56:41:27 They're -- they are -- they can be somewhat effective. Many people that have marijuana problems have other drug problems as well, and so that means that having a more generic treatment is not necessarily a bad thing. The types of treatments that we have evidence for are things called motivational enhancement, which is really just a way of trying to engage people in therapy, and it's -- and it's a sort of --

00:57:06:18 It's also called motivational interviewing, and the idea is it -- for it to be a kind of non-judgmental sort of interview when you're bringing people in, trying to get them engaged and seeing how this is harming themselves, and get them to sort of come to the decision that they wanna make a change, that they need treatment. Motivational incentives is what's also called contingency management, and that's actually providing some sort of reward for somebody being clean from the drug, for --

00:57:37:02 For them staying in treatment, and this is very controversial. It gets a lot of people really

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crazy that we should be rewarding people for doing what they should be doing anyway. But the fact of the matter is that it -- it works, and that -- to some extent, it works, and that actually if you talk to the treatment providers that are using it, they really like it, because they feel like they get to catch people when they're doing good, and that's -- that helps to build up their therapeutic relationship with people.

00:58:05:18      And it -- and it really sort of kind of positively feeds back, both for the drug abuser and for the therapist. And this is just true in general about motivational incentives. And cognitive behavioral therapy, and this is something that also -- that teaches people to sort of recognize the triggers that they have for -- for going back to drug use, teaching them different ways of coping with stress.

00:58:27:21      The triggers that -- that often set off -- that set off relapse are stress, cues that are associated with drug use, so if you start hanging out with the same friends that were always using these drugs, you start wanting to use these drugs. And

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exposure to the drug itself can -- can get people back in there. So these types of therapies have shown effectiveness. Next slide, please.

00:58:52:07 This slide shows a not terribly satisfying result, which is a study that -- that shows the blue graph is the -- is the graph that you -- in fact of the group of people who received all three types of therapy, and this shows that they got 35% of people abstinent at the end of treatment. Which is not terrific. One of the -- one of the things about treatment that we've been also talking about for a long time, and it's not just about marijuana, it's really about drug treatment in general.

00:59:24:17 And actually, Tom McClellan [ph.] started to talk about it. He's the Deputy Director for the Office of National Drug Control Policy. And he's talked about the fact that when we look at drug abuse treatment and we say that it doesn't work, we kind of evaluate it differently than when we look at other types of treatment. So if somebody had diabetes, for example, and you gave them insulin, and -- and of course that worked to treat their diabetes.

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00:59:48:20      And then they went -- they went off the insulin, and they relapsed, you wouldn't say that insulin is a lousy treatment. You would say we really need to treat them longer. We really -- you know, they have to stay on the insulin. And we've been making the same statement about drug addiction. And it may not be true for everybody that they need to have chronic types of treatment or long-term types of treatment.

01:00:10:26      But for -- certainly for the people with the most severe problems, and many -- many of these people do have severe problems, and comorbidities and other drug addictions, we really do need to look at drug abuse treatment as a chronic care type of thing. Now, you don't necessarily need the same intensity of treatment all along, and sometimes, you know, different types of support groups, and you know, Alcoholics Anonymous, and these types of groups may be what helped people maintain their abstinence from drugs.

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01:00:40:13 But I think when we look at drug treatment as something that you put somebody in for a month and then you send 'em out, and then they're on their way, and you expect them to be better, we're just fooling ourselves to think that that's gonna work really well. We really do need to -- and I don't think that that's so different from marijuana. In fact, it may even be harder with marijuana, because of one of the things that you said, that it's so socially acceptable.

01:01:00:23 And that it's -- you know, that it makes it even -- it makes it even more likely that somebody's gonna be in situations where -- where they're going to relapse. So we could certainly do better with treatment, and we certainly should kinda pay attention I think to the chronic care model of treatment when we're talking about treatment for marijuana addiction just as for other addictions.

01:01:21:13 One of the other things -- well, one of the other things about marijuana addiction that people didn't realize for a long time is that there really -- there is a withdrawal effect when -- when somebody

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that's a chronic user goes off of marijuana. And it's probably at about the same degree of severity as when they go off of nicotine. And we know that it's a big relapse promoter for nicotine.

01:01:41:21      So people become irritable. They don't sleep very well. They gain weight. And it -- it tends to last for about seven to ten days, but it's often a time when they'll relapse, because the marijuana will get rid of the withdrawal signs. So treating withdrawal is also something that people have been focusing on for treating marijuana. So next slide, please.

01:02:04:09      So one of the ways that -- that they've been doing that is to look at a combination of oral THC with a drug called Lofexidine. And Lofexidine is a drug that's a little bit like... It's -- it's a little bit -- [unint.]. It's a little bit like Clonidine, which has been used to treat withdrawal for opiates. And it -- it kind of dampens the system that's kind of -- very anxiogenic and arousing and alerting.

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01:02:35:09      So the combination of that plus oral THC for a certain amount of time has some -- has shown efficacy in -- in preventing withdrawal. These are really early stage studies looking at medications. Like I said, we really don't have anything for marijuana. The whole focus on the endogenous cannabinoid system raises hope that we will be able to get something that will be specific and that will be very useful. We can also, we've also looked at cannabinoid antagonists.

01:03:05:13      So these are, these are drugs that block the receptor, that THC binds to. And I'll show you, I'll show you, actually next slide please. The next slide just shows you that if you give somebody who has smoked marijuana this antagonist, that you do in fact reduce marijuana's effects. And this antagonist, and this is on feeling high and on, as well as its effects on heart rate. An antagonist though, this is actually a drug which is called rimonabant that you may have heard of.

01:03:39:04      It's, it's anti-obesity drug that's been approved in Europe and in Canada. It's an

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interesting drug except that it's been associated with depression and anxiety which is why it hasn't gotten approval in this country. And it was particularly thought that as a treatment for obesity that many people with obesity already have depression and anxiety and that this may not be a really great treatment for them and, and could push them further along that particular line.

01:04:08:21 It's very interesting when you're thinking about how to treat marijuana dependence. So marijuana is acting at, at this receptor and a blockade of this receptor makes somebody depressed, so then shouldn't marijuana be anti-depressant, right? But no, because marijuana doesn't act, it doesn't act selectively the way the natural system does. In fact what it does is, it's flooding the system and it's acting at all of the different receptors.

01:04:36:02 And then the receptors start to modify, they start to adapt and so there's where you could get a link to how depression can start to come about because you're, you're flooding a system, the system is adapting and we do know in fact that a drug, a

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medication that blocks the cannabinoid receptors can make some people feel depressed.

01:04:59:16 So, so the kinds of medications that people are now thinking about are ones that are more subtle, that kind of tweak the natural system, that may prevent the endogenous or the natural marijuana like compounds from being broken down or keep them having their effect for a longer period of time. So... it's funny because you have to think of marijuana as sort of both activating a system and then ultimately making the system less responsive.

01:05:32:04 And so, and that's, that's why it's obviously not, you know that's where its limitations are in terms of its, its medical applications as well as, as you know relating to its abuse and other long-term effects. Next slide please. Okay, so this is just a couple of slides on the thorny issues that get a lot of, get a lot of press. Next slide please, and one is the potency issue which you brought up. And we do know that this is a, NIDA has a contract.

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01:06:02:10 We've been monitoring mostly from DEA seizures the potency of cannabis over the last, actually since the '70s, but very few samples at that point. But you can, you see quite clearly that the potency has been going up over these years and maybe it's leveled out now, I hope so, but not really sure if that's true. Next slide. So the question is, what does the increased potency mean?

01:06:32:29 And that's where we don't know enough. So you know it's possible, particularly in somebody who's young or who's a naïve user, they may get much greater exposure to THC very quickly, very early on. It may cause more of an anxiety reaction. It may cause, may make them more likely to become addicted, we don't really know that for sure. We do know that between 1992 and 2002 we knew that the ER visits were going up as the potency was going up.

01:07:06:00 The rates of abuse and dependence have been relatively stable in looking at some of the data from 2002 to 2008. We're not sure yet what that means and I think we need more time to see what happens there. But the big question is whether or not users

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titrate their intake. So do they take in less if you're talking about a much more potent drug than they would if, if they were taking in a less potent drug?

01:07:34:07 And there is some evidence for that in experienced users, maybe not so much in less experienced users, we, we don't have a lot of information to tell you the truth. I mean we don't know what doses people were taking in the '80s when there was less potent marijuana versus what doses they're really exposing them self to now. Obviously we're concerned, particularly about young users with developing brains.

01:07:56:06 There was one study that I thought was kind of interesting, it was in the Netherlands. They're really, they're very concerned about increasing potency and their potency levels are actually much higher than ours. But they interviewed people who are marijuana users and they kind of fell into three groups. The one, one group why was the, one group was kind of like, this is, this stuff is too strong, I can't, I don't like it, I'm not going to take it anymore, they just kind of backed away from it

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01:08:23:05 Another group felt that, they titrated, so they changed the way they inhaled, they breathed in more air, they took less, they did, they did a lot of compensatory behaviors and they tended to be kind of stable marijuana users. And then there was the third group and they were, you know, the more the better. And they were the ones that were younger and that tended to have more problems with abuse and dependence.

01:08:48:07 So there is potential for the higher potency marijuana to be more problematic, but again, we don't, you know a lot of it depends upon how people use it and you know, and that's something that we don't really know yet. Next slide, gateway term. That's another thorny issue. So we hate that term because we don't, we feel like it just sort of raise arguments and doesn't really get us anywhere and, and actually takes away the focus on, of marijuana itself in its own, you know, its own problems that are associated with it.

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01:09:24:07 It's true that marijuana use usually precedes the use of other substances, it's also true that most marijuana users don't go onto use other substances. We know that there are some work that's looked at you know drug using propensity and has shown that somebody who's likely to take drugs, is likely to take drugs, they're likely to take marijuana first. It's the first drug that's available to them.

01:09:46:12 It's also true that somebody that's using marijuana maybe hanging around with other kids that are using marijuana that might put them in, that might also put them in contact with other illegal drugs or that might be a sort of, you know a group that may not be as focused on their schoolwork or, you know. So it's, it's really hard to tease that out. And for us we, we really try not to even use the term because it seems to create more problems than it, than it helps.

01:10:09:27 There is, there is some data in animals that show that, that exposure to marijuana during, exposure to marijuana during adolescence does change the reward system in a way that makes those animals

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more likely to self-administer opiate drugs later on. So that's a little bit of evidence in animals showing that marijuana can be changing the brain in a way that could make using other drugs more rewarding.

01:10:38:04 But I wouldn't want to, again, so I think there, you know there certain maybe changes in the brain that marijuana causes that will make some, that will change someone's likelihood of using other drugs. But at this point that particular term doesn't really help us, I don't think. Next slide please. And this just shows that marijuana is of course the drug that's most likely to be used when somebody starts using drugs.

01:11:00:07 Pain relievers are second and that's been a really big focus for NIDA and for a lot of other places, the, the misuse of prescription drugs. And next slide, which is my last slide, no, my next to last slide. The... so the other, the other obviously thorny issue is medical marijuana. And you know there, there are certainly, there are certainly some evidence including ani, there's some evidence and there's some anecdotal evidence that it, that it has

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promise in treating in pain, in treating in nausea, in treating wasting disease.

00:11:13:16      There are very few scientific studies that deter, that show this. This was from the IOM report which is back in 1999, there are now some more studies that do show an effect, but they're pretty small and they are usually quite short-term. So it's a little bit, you know, so they're, they do an effect but it's hard to know what to make of them yet. The IOM did feel it was justified to conduct research into marijuana's active ingredients.

01:12:01:06      And again, and this is really where we are, we, we feel that marijuana is not a benign drug, that there are many adverse consequences including addiction and certainly smoking is not a great way to do things. And as I said before, using a plant product has, has certain drawbacks in its own, but our improved knowledge of the cannabinoid system is really opening up a lot of very interesting research avenues for developing medications to treat addiction as well as to treat a variety of other illnesses.

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01:12:29:20 So, so we don't deny that there's a therapeutic component to marijuana's effects, but this, but marijuana as a, as a smoked plant is really not something that we feel has a lot of potential for medical use. Okay, and my final slide, my final, final is just to sort of give you our website and to tell you that we have a lot of resources that you can download, that are free.

01:12:56:06 We have a lot, we, we try to appeal to a large variety of targeted audiences including teens, including physicians. We've actually been doing a lot of outreach to physicians lately because we want to get them involved in screening and brief intervention because they often see people before problems really develop. So we, we have outreached to a whole lot of groups, we have treatment books, we have prevention books.

01:13:19:25 And I just would really ask you to come to our website, see if there's anything that's appealing to you, everything's free, use it, reuse it, do whatever you want with it. But we, but we hope that you will take advantage of the knowledge that we

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have and in anyway that we can help you. So there was a question I think I saw somewhere, there.

01:13:42:06 Q: The next to the last slide there, are you sure that's accurate, that first colon, isn't it what the IOM study said was that, the... thank you, that certain chemical components of marijuana might hold promise as providing therapeutic value. I, I don't think that the IOM study actually said that marijuana per se...

01:14:02:25 A: I believe it did, I'd have to go back and look, but I believe that it did say that. I mean I think they still recommend it going at it from other, in other ways that you know, either through other delivery systems or through developing the components rather than to, rather than using marijuana itself. But I believe that they did say that marijuana itself did have promise.

01:14:20:21 I mean there is a lot of, you know, I mean marijuana does seem to help some people with pain, that doesn't mean there aren't liabilities to it. And it doesn't mean that that's the best choice

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for somebody with pain. The same thing with the anti-nausea effects of it, I mean that's a pretty well known effect of marijuana. There are other anti-nausea drugs and there are, and there are obviously liabilities of using marijuana that way.

01:14:45:06 But I don't think we can say that that it has, it doesn't have those properties, that it's not an appetite stimulant, it's not anti-nausea type of...

01:14:52:07 Q: But if there's no realistic probability that it will ever get FDA approval...

01:14:57:03 A: That's right.

01:14:58:14 Q: Then is it really accurate to describe it as showing promise for treating pain, nausea, waste?

01:15:07:20 A: No, you're right. I won't argue with you there.

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01:15:12:00 Q: Okay, I'm not so, so worried about this audience, but others.

01:15:15:19 A: Okay. There's another question in the back.

01:15:29:06 Q: Dr. Weiss, all of you at the beginning you mentioned there's a 80 percent of, of research on drug abuse is funded by NIDA and could you give us a general sense what's the approximation, what's the percentage of the actually funded to marijuana related study?

01:15:46:13 A: Not off the top of my head, I'd really have to go back and look. I can certainly get your that information without much trouble, but I, I really don't know and I don't really want to guess at the... and just also one other thing. So our Institute is mainly funding research on the abuse properties of marijuana. I mean we get, we get a lot of inquiries from Congress and from the public about studies of marijuana for its potential health benefits.

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01:16:13:22      And that's not what we typically do, so there may, and actually I know that there are very few other studies for marijuana's health benefits that are being done, that are being support for smoked marijuana's health benefits that are being supported through most of NIH. But our studies just, just to focus, they're really on the abuse and the health problems associated with marijuana.

01:16:34:05      Q:    And a follow-up question and recently in the United State, especially some those new, non-colosical [ph.] cannabinoid, synthetic cannabinoid like JWH and CP product, mixed with the spice and K2, is NIDA currently have any study or research or grant funding for this type of study?

01:16:55:20      A:    No we don't right now. We've been hearing about it, you know, we have something that's called the Community Epidemiology Watch... Work Group. And it's, it's a group of researchers that are in some of the major cities and, and they're supposed to be kind of an alert system for us because they look at a lot of indicators in their cities. And so we are starting, you know, we are seeing reports of this.

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01:17:17:10 But at this point we don't actually have any research on that specific variation.

01:17:28:12 Q: Help, help me square the circle on, and this is sort of a follow-up to the other question. Smoked marijuana, even if there is a medical benefit, is not the way to go because it's smoked.

01:17:37:02 A: Right.

01:17:38:19 Q: But there are drugs out there like marinal [ph.] and if you can, I think there are a couple of others, if you can refer to this, that, that have the active ingredient of THC. So does marijuana have...

01:17:54:09 A: Something beyond marinal?

01:17:57:22 Q: Or, or does, can we say that it has no... redeeming medical effect?

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01:18:08:11 A: The problem with marinal is marinal works fine for some people but it doesn't work so well for other people because it's, because of the way it's, you know, it's an orally taken medication and the way in which it hits people, they actually may feel very out of it and they may not get very good symptom relief. The smoked marijuana, the reason that people seem to like it better, is because they can titrate it, because they can take enough to... to lessen their symptoms with out necessarily taking too much so that they're really out of it and they get an immediate effect.

01:18:42:23 That's the advantage that marijuana has over marinal, that doesn't mean that there aren't better ways to come up with a way of doing that, of, of and sativex is a compound that's been developed by a pharmaceutical company that I believe is a nasal spray and it has THC in it and that may have more promise. So that's, so I mean I think that you can't just say well we've got marinal, we don't need anything else cause marinal is not satisfactory to a lot of patients.

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01:19:11:17 But there are certainly other ways to go besides smoked marijuana and I think that's really still where the focus is and that's where I think it should be. Is there another question?

01:19:36:13 Q: Do you have any reason to believe that any of the other components of marijuana allow or enable people to accelerate risk-seeking behavior? If you will, you pointed out toward the end that baseline risk-taking propensity, which I study in criminal recidivism, it's, if you will endogenous to the person. However, would you be willing to characterize marijuana as a, being an accelerant or an enabler, exacerbater?

01:20:06:08 A: I'm trying to think of, I'm trying to think of studies that have, you know there's just, there's just not that many studies. I mean there now are, they're getting, where people are getting more sophisticated with the types of tasks that they're having people do in brain imaging. But I am now aware of, there, there could be. I'm not aware of any studies that show that.

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01:20:28:11      Again, I don't, I'm unfortunately not writing these things down, but if anybody that wants me to get back to them, if you could come up to me afterwards, I will write it down and I will look, look it up and see if I can get back to you on that. So I'm not sure.

01:20:49:02      Q:    You've said that smoked marijuana is not the best delivery system for the ingredients in marijuana that may have therapeutic value. And yet we've got 14 states that have... in one form or another, approved the use of marijuana for medical purposes.

01:21:04:23      A:    Right.

01:21:05:23      Q:    And I'm assuming at least in part, the states are acting in good faith and have based that upon some scientific studies. So where are they getting the information that smoked marijuana is a viable delivery system for the therapeutic effects of marijuana?

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01:21:23:25 A: Okay, well it, it comes back again to what I said. First of all, okay two, two answers to that. So smoking does you know decrease nausea, it does increase, increase appetite so those are some of the effects of marijuana and it does seem to have some effects on pain, so people do. So, so that, those types of symptom relief does seem to happen with marijuana.

01:21:48:06 That said, some of the ways that it's being used are just you know, I mean, they're just, they're not based on anything. I mean people are using marijuana to treat ADHD, I don't, I have no idea why they're using marijuana to treat ADHD or you know, we also know that a lot of the, I mean people walk in with you know, especially in California. We're all hearing about the fact that you know it's, it's essentially a way of just legalizing it.

01:22:14:05 People can come in with anything in the world that they imagine and say I want marijuana for that. So the states are not, so I mean there maybe, you know I mean for somebody that's having cancer chemotherapy, I mean there maybe some, there maybe

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some reasons why people can you know, can get symptom relief that marijuana does offer. But the states are not necessarily, you know I don't, I don't think that they're basing these, these decisions on scientific research.

01:22:46:13 You know there are a few studies from California, they, California has a cannabis research group that was setup by the state a number of years ago and they just came out with a report to the state. They had to report back on how they're doing. And they had a few studies that showed that smoked marijuana was helpful for pain. It seemed to give increased pain relief above, this is added onto other pain medications.

01:23:12:06 So these are people that had intractable pain and that, that they were able to get something like 30 percent reduction in, in pain perception and that's clinically significant for those people. So there are some studies that do show that occurs. As I said, these studies are not large and they are very short-term so that you know whether or

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not, I mean there's a lot of things that help pain initially.

01:23:34:16      And then after you do them for awhile, they don't work and that's one of the problems with a lot of the pain medications, is that people get tolerant to the effects. So does that mean that either they get tolerant to marijuana or they'd have to smoke so much as it would be, you know, they couldn't get out of bed or something... I mean we don't really know. But you know California asked for some studies on this.

11:23:54:23      They got a report but my reading of that report was that the, the information is still very limited. So you know, states are not, I don't think states are making these decisions based on the science, they're making, they're making it based on anecdote and on you know very sort of... and on a view of, you know, their view of whether they not they feel that the harm's of having it not be legal are, are you know, are more then the harms of having it be legal... for medical use.

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01:24:35:03 No, because... I mean we're not, I mean we always, you know again, we get a lot of questions about what are you doing on the long-term benefits... alright, what are you doing on smoked marijuana's health benefits and we always say the same thing, you know. NIH is open to any application that comes in that's scientifically meritorious and that's competitive and this wouldn't come to NIDA cause we study abuse.

01:24:56:16 But if they want to look at it from multiple sclerosis for example, they could something to the, to NINDS. NIH has just never gotten a lot of studies that have actually wanted to look at that. In California the studies have not, you know, California has really been the main place where smoked marijuana has been studied for its therapeutic uses. One of the studies that they said they actually had to stop because they trouble recruiting, was for cancer.

01:25:24:26 And the reason they had trouble recruiting was that part of the, one of the conditions of being in the study was that people couldn't drive because they were taking marijuana. So imagine what

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it's like to try and recruit people and tell them, well you can't drive for the whole time you're in the study. So you know the study, and the studies aren't going to be done, I don't think, because nobody... I mean I really don't believe that most people feel that that's the way to go.

01:25:48:09 If they're going to put, there's another issue too, I mean this patent issue, you know. What drug company's going to want to come in and do this when they can't get, you know, they're not going to be able to patent it. It costs a lot of money to do the kinds of studies you would need to do for the FDA. But really I think the reason is that there is so many other, there's, there's no reason to go that way, if you're looking for a therapeutic effect.

01:26:11:16 You want to go with something that's not smoked, where you can characterize what the components are and where you can work on the kinds of deliveries... I mean what, what the smoked marijuana is telling us is that we need something that people can get you know, that they can get quickly and that

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they can, you know and that they can titrate the dose, that's important knowledge.

01:26:30:14 But that's important knowledge to be used in developing better medications that are based on the components of marijuana. So I don't think we're going to see long-term studies of marijuana's therapeutic effects, I would be very surprised, smoked marijuana.

01:26:45:08 Q: I think the study that you're referring to where they had to, they couldn't recruit because the patients wouldn't, wouldn't be allowed to drive. It was a multiple sclerosis study.

01:26:53:13 A: Was it?

01:26:55:18 Q: Yeah and...

01:26:56:10 A: I think there was also a cancer one, but maybe both.

01:26:59:00 Q: There were three studies that stopped out of six or seven, I mean...

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01:27:03:25 A: Right.

01:27:04:22 Q: The majority of the research at the CMCR had to stop because of recruitment issues, even though it's in the state that would be in theory most amenable to, to smoked marijuana.

01:27:13:04 A: Right, right.

01:27:16:21 Q: But... the, the problem with driving, if, if somebody was looking into the therapeutic uses of alcohol, you wouldn't be allowed to drive.

01:27:24:17 A: Exactly.

01:27:25:16 Q: But that, that wasn't an unfair demand or...

01:27:28:23 A: Oh no, no I wasn't trying to say that. I was just trying to say that that's, I mean, I think those studies are unfeasible and they're, and they're not really useful. So on both levels I think

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it's very unlikely that we'll see those kind of studies. But yes, certainly.

01:27:53:23 Q: Even though the, the THC content has gone up overtime, is there a long-term effect that you can extrapolate the, the use of cannabis in 15 years, 20 years?

01:28:14:06 A: That's where I'm not sure because we, we're talking and it's where it's really hard to look at changes in the rates of abuse and dependence because our survey changed between 2002 and before and then. So I'm not really sure if the rates have really gone up. Treatment admissions have... and again, treatment admissions have gone up. But that, a lot of that is related to the referral source. So that's, so that makes it a little bit trickier.

01:28:39:14 There's one study that suggested that between 1992 and 2002, there was increased rate of dependence on marijuana while this potency issue, while potency was going up. But when you look carefully at the study, it wasn't, it wasn't a general increase, it was in very specific subgroups. So there

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may have been certain cultural factors or other things that were going on that increased the rates of dependence in that group.

01:29:04:04      So I don't think we have the evidence yet to really show that, I mean it maybe that the, I mean to me the most likeliest, sort of the emergency department things, the emergency department mentions because that's where you're sort of likely to see some sort of acute response either in acute psychosis or panic or even potentially a cardiac effect because of the increased potency.

01:29:25:29      And again I think our biggest concern are in young users and new users who are really exposing their brains to maybe higher levels. But I don't think we know enough yet.

01:29:37:24      Q:    [Inaud.] longitudinal survey of the youth that's been going on since the '70s, that asked about marijuana use, that's tracking people through today, so they've got to be twice my age.

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01:29:53:05 A: I'm not sure which study you're talking about. Are you talking about...

01:29:59:04 Q: [Inaud.] medical, the earning potential, whether or not they offend, how often they offend...

01:30:09:03 A: Yeah, I'd have to, I'd have to see the study, again it sort of depends upon what they're looking at. I mean if they really are tracking, if they are tracking marijuana and other drug use and then also looking at this...

01:30:18:10 Q: They are.

01:30:18:15 A: Then I think that would be a great, a great study to look at. But I don't, I'm not aware of the data there.

01:30:34:25 Q: If you read many of the speeches of the ONDCP director recently, he talks a lot about... drugged driving. And one of the things that I've been, you know if there's an analogy to marijuana, might be alcohol in a certain respect. And

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one of the things we're able to do with alcohol is give a breathalyzer test to determine the degree to which somebody is driving drunk. Do we really have the capability to determine how inebriated if, for lack of better term, somebody is from smoking marijuana while driving?

01:31:08:16      A:    That's, that's the problem that we don't have the same sort of lawful data that we have for alcohol where you've got an easy test and you've got a, once you hit this level, we know that this increases the impairment. We do know there's a dose response effect with THC that the more you give somebody, the more it impairs driving. But we don't have an easy way to measure that at this point.

01:31:26:23      People are looking at blood levels, but, but even that is not always a very good marker of it. There's certainly a lot of work being done to try and get better tests, but what a lot of the states have done is to pass per se laws, so that means if there's any detectable drug, then you could be considered guilty of drug driving. But we're not, we don't have that as good.

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01:31:50:13      And, and you know it maybe that we also need to do some other measure of impairment, you know some other behavioral measure of impairment in combination with whatever types of test we have. Marijuana is particularly tricky but it's very fat soluble and so you can detect it in the urine at least for days after and sometimes even weeks after somebody used it.

01:32:09:25      So the fact that you detect it doesn't mean that somebody was really intoxicated when they were driving. So that's been, that's what's made drug driving a little bit of a harder sell cause we don't have as good, we don't have as good you know methods of detection that we can correlate with, you know, with the level of impairment. But there's a lot of work being done in that area cause it is a big concern of ONDCP and a big concern of everybody else I think.

01:32:45:25      MS: Please join me in thanking Dr. Weiss for her time this morning, it's been an excellent exchange. Our education coordinator, Katie Drew has a small token of our appreciation. Just two

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quick notes before we close. Our second in our series of lectures this spring is going to take place back here in the auditorium May 25th. We have forensic chemist John Casal [ph.] coming into speak on cocaine.

01:33:08:21 And then Dr. Weiss also mentioned the DEA Museum's traveling exhibit. If your travels take you to New Orleans between now and Thanksgiving, the Target America Exhibit is on free exhibition at the Louisiana State Museum in the French Quarter. Thank you all for joining us and Dr. Weiss is here take questions after the program. [APPLAUSE]

**END OF AUDIO**