

Dialogue4Health

Marijuana and Our Health
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>> Laura Burr: Welcome to today's Dialogue4Health web forum, Marijuana and Our Health: What We Do and Don't Know, brought to you by our partner CA4Health. We also thank the California Endowment for funding today's event. My name is Laura Burr and I will be running today's web forum along with my colleague, Joanna Hathaway.

Audio is through your computer speakers or headphones. Click event info to see the phone number if you need to call in to hear the event. Closed captioning is provided today by Karen of Home Team Captions. The caption window is on the right side of your screen. Click the Media Viewer icon on the top right of your screen. Or if you're on a Mac you'll see it on the bottom right of your screen. Next, locate the link in the captioning panel that says show/hide header. If you click these links you will be able to see the captioning more clearly. If the captioning window ever disappears, click the Media Viewer icon to bring it back.

Today's web forum is listen only for our audience. That mean that you can hear us but we can't hear you. That doesn't mean, though, that it won't be interactive. Please share your thoughts and comments about today's presentation by typing them in the Q&A box and we'll try to answer as many questions as we can today. The Q&A panel is on the right side of your screen. It can be toggled on and off by clicking the Q&A icon at the top right of your screen or if you are on a Mac, at the bottom right of your screen. In the Q&A panel select "all panelists" in the dropdown menu so your question gets sent to the right place.

We will conduct polls to get your feedback during the event. When you see a poll, please select your answer and click the submit button.

You'll see the poll appear on the right side of your screen. Please select from one of the four choices. When you've made your selection, just click the submit button to let us know as we start this first poll: Are you attending alone? Are you attending maybe in a small group of two to five people? Or are you in a larger group of six to ten people? Or perhaps you're in a large room today with all of your colleagues, more than ten people. We can see the responses coming in now.

Let us know who you are attending today's event with. And we will close the poll now. It will take a moment to tabulate. If you have not hit "submit" yet, please go ahead and do that. Let us know if you are by yourself, in a small group, or a larger group.

Of course, not surprisingly, most folks are attending individually. And we have a small number of people in groups of two to five. And about 1 percent in groups of six to ten. And so we will

now move along. I would love to introduce our host for today, Susan Watson. Sue is the director of CA4Health, a community of practice that works on projects with local health departments on accreditation, strategic planning. She has worked in various sectors of public health including research, government, profit, community arenas with emphasis on equity, community health, and the elimination of racial and ethnic disparities. So welcome, Sue. Thank you for joining us.

>> Susan Watson: Thanks, Laura! Thanks for joining us for this web forum. I want to share a little bit on who might be participating today. We had an amazing response to the webinar with over 1700 registrants across the U.S. plus some located internationally.

Now, the registrants were predominantly from nonprofit organizations and local or state government entities, but there was a really good mix of sectors represented showing the broad interests in this topic. Now, before we get started I wanted to share a little about CA4Health. For those who may not know, CA4Health is an inclusive statewide community of practice comprised of passionate, diverse, and committed individuals and organizations advancing chronic disease prevention and health equity across California.

We work together to provide platforms for intersectional thought, dialogue and action because we believe that increased collaboration fostering nontraditional partnerships and tackling tough challenges together will create impactful lasting change in California. If you are on this webinar and you are in California, we invite you to become a member of the CA4Health community. Go to the join now section of our website and fill out the form.

Now, back to the topic at hand. Since the passage of proposition 64 that legalized recreational marijuana for people over 21 in California, CA4Health has become increasingly aware of conversations about marijuana at the state and local government levels among community groups, and within communities. Many of which are not the same conversation. So in keeping with our roles as a capacity builder and information sharer, we are excited to provide this webinar series to look at the scientific findings, history and community impact and equitable considerations in policymaking.

Now, we recognize that this series will not address everything, but we hope that as a whole it will provide a solid foundation for answering and maybe even inspiring new questions. That it will expand some basic understandings and offer a pathway for viewing marijuana issues through an equity lens.

Now, in this first session of the series focused on what we do and don't know, we've two wonderful speakers who will provide both the broader landscape of scientific findings and a more localized set of findings from Colorado, one of the first states to legalize the adult use of marijuana. There will be time for questions and answers towards the end of the webinar. For those who submitted questions during registration, we will strive to address many of the topical areas raised there. But also feel free to type questions in the Q&A panel throughout the presentations.

Now, since this webinar is on what you do and don't know, we've got some true/false statements instead of traditional polls. We'll discuss these after both presentations have concluded.

The first statement for you to respond to is: Marijuana is a gateway drug. It generally leads to the use of more potent drugs like heroin, cocaine, et cetera. Go ahead and choose whether you think that is true or false.

The second statement is marijuana use negatively impacts mental health and can cause permanent mental illness. So select whether you think that is true or false.

So take a moment, weigh in. Like I said, we will revisit these later and have some conversation with the presenters on these.

So that will close soon. But I want to keep us moving. So I will go on to introduce our first presenter. Dr. Wallace is the Irene Ensminger Stecher Professor of Cancer Research in the Department of Epidemiology at the University of Iowa. He is particularly interested in the prevention and control of disabling chronic illnesses in older people. He served on the national academy of medicine, health and medicine divisions' committee that evaluated the health outcomes of cannabis use. We are really thankful that Dr. Wallace agreed to share the general findings of the national academy report with us today.

With that I would like to let Dr. Wallace go ahead with his presentation.

>> Robert Wallace: Thank you, Sue. So, good morning, afternoon, or evening, depending on where you are. I am going to present as briefly and clearly as I can what is really a fairly substantial report. I'll tell you how to get the report later if you wish to really see the detailed information. Here is the cover actually of the report. And there I am. I wanted to show you quickly the sponsors of the report. I think it's important not only to give them credit but to point out that there are at least four states and several federal agencies and foundations, actually, all of which was a testimony to the general interest within the United States of this issue and particularly as the states change their laws.

Let me go on. I'm going to talk about basically what our mission was, how we approach the study. Then I hope to spend most of the time on the findings.

Let me go on and I wanted to just say that the National Academies, which is what I'll call it, or the Academies, has had previous reports. We built our findings on the previous reports. Just to let you know, the marijuana cannabis issue has been around for many years and has been recognized previously as a health problem.

So what those sponsors asked us to do is to develop an in depth review of the existing evidence. So we went to the scientific literature to extract that evidence and then made some recommendations, which I'll show you at the end.

In terms of conducting the study, we basically chose a number of topics. It is not all the topics that have been related to cannabis, but enough of them so that we were able to have enough to do. We met five times to prepare this report and had two open sessions. So we invited public comments in person and we also accepted all sorts of information by any other conveyance, mostly email.

Then we developed basically a systematic review process. Went to all the scientific literature that we could find. We actually found 24,000 articles, mostly since the year 2000. And we condensed that down to 10,000 abstracts and distilled that further to get the findings that I'm about to show you.

Here are the prioritized topics. I'll go through them one by one and again try to make this as easy as I can. Because, in fact, cannabis is a pretty complicated topic.

We also graded the evidence. You can see at the bottom of the slide the levels of evidence.

I'll try to use those words, but I lapse into sometimes a little, sometimes a lot. But I can tell you overall that as in most controversial topics, the level of evidence and the amount of evidence is often far from what we need. So part of what we did was a research agenda.

And I'll just go on and so let me summarize the chapters. Let me first start with therapeutics, also called medical marijuana in the vernacular. And we basically had three findings. That

oral cannabinoids do work in-patients with chemotherapy induced nausea and vomiting. It also has a role in terms of chronic pain and it also appears to alleviate some of the spasticity symptoms associated with multiple sclerosis.

There are a couple more things to say about this. Maybe the most important is that cannabis and cannabinoids really are not -- their effects are modest. That is if I had to summarize all of this, they work but they are not necessarily the best treatments and there are many other treatments in fact that are available. So the states and the federal government are working through all of this now.

I also wanted to say that since we did the report, some randomized clinical trials have arisen in terms of controlling epilepsy, particularly in children. There are some promising occurrences there. But all of these appeared after we finished the report. So they are not in the report. I just wanted to tell you that.

Respiratory disease was very important. Most of the time we look at the effects of smoke in marijuana. Let me just start by saying that not surprisingly, people who smoke marijuana have increased respiratory symptoms and more frequent bronchitis episodes. There was a moderate association found that when you stop smoking marijuana, that there were improvements in the symptoms. Maybe that is not surprising. There was also moderate evidence, and this is physiology, but interestingly enough despite the symptoms that smoking cannabis actually was associated with improved movement of air in your lungs and airways, and moderate evidence that you could actually move more air which is called the forced vital capacity. There's this contradiction between the symptoms that people experience and the evidence of what it does to respiratory physiology. That needs to be further explored.

Further with respiratory disease there was only limited evidence that cannabis smoking increases the risk of chronic obstructive pulmonary disease, also known as emphysema, and there wasn't enough evidence one way or another about whether it leads to hospitalization for chronic obstructive pulmonary disease. There was also not enough evidence to see whether cannabis had an effect on exacerbating or developing asthma, all of which needs more research. Unfortunately, I'll keep saying that.

We looked at death and injury from cannabis, which is a very important area. Basically, what we found was that there was clear evidence that acute cannabis use is associated with increased motor vehicle accidents. That had been demonstrated a number of times. We also noted the literature which suggested that in states where cannabis is legal, there is a risk of unintentional cannabis overdose among children. That's usually where the children get into marijuana or cannabis that is around the house.

We looked at the effect on overall mortality. And there just wasn't enough evidence one way or another. We were also very interested in whether cannabis smoking was associated with occupational injury. Once again there was just not enough evidence to make a judgment. Well, one of the areas where this has been an important topic is cancer. I think back beginning in the 1980s a lot of investigators worried or wondered whether smoking of this particular plant of cannabis was associated with various cancers in an analogous manner to use of tobacco. But in general we didn't find very much. Just quickly there was no evidence of association between smoking cannabis and head and neck cancers or lung cancer. The only limited evidence we found was with testicular tumors and that also needs to be followed up. We don't believe that case is made.

There was also not enough evidence for cancer of the esophagus and in the second bullet on this slide you can read a bunch of other adult cancers, none of which had enough evidence to

make a statement one way or another.

There was a little bit of literature mostly from the '80s in which women who used cannabis during pregnancy had their children followed to see if they got childhood tumors. There were three or four of them listed below. I'm not going to read the names to you, but there is that literature. We thought these were almost always just one study and we don't think that is sufficient evidence. But this is certainly something that needs to be followed up. So this is again looking at cancer in children. It is just a hint and needs much more good research. In terms of some of the other chronic diseases, we found really no clear evidence one way or another with respect to heart attack or stroke or diabetes. Very important adult diseases, but really not enough evidence one way or another. That needs to be followed up.

We looked at the effect of smoking cannabis on the immune system and here again not a lot of scientific reward. There wasn't enough evidence about whether it affects one's immune system and only limited evidence that cannabis smoke actually has an anti-inflammatory effect. All of that needs to be followed up. Cannabis had also been studied in AIDS patients or those with HIV and there just wasn't enough evidence to suggest whether it had an effect on the immune status of those patients in fact one way or another.

We did look at birth outcomes, prenatal, perinatal and neonatal outcomes, other than the cancers which I mentioned earlier. We did find there was an association between smoking cannabis, the mother smoking cannabis and lower infant birth weight. That also needs to be followed up. And any other of the outcomes of pregnancy and childhood are just simply unclear because the studies in fact haven't been done.

So there is information on the psychosocial effects of using cannabis. There is good evidence that acute use of cannabis impairs performance of memory, learning, and attention. Maybe that's not surprising, but in fact that evidence is there. There were only a limited number of studies about what happens to those psychological performance measures after you stop. But there is a little bit of evidence that in fact those are impaired even later. There is also evidence that cannabis use during adolescence is related to subsequent social impairments such as academic achievement, education, employment, and so on. All of that in fact needs to be studied further, but we thought that this was an important finding.

So related to that, there are some mental health findings as well. They are complicated. Sometimes what we found was that there was association between cannabis use, smoking, and the development of schizophrenia and other psychoses. I want to emphasize this is a statistical association. By no means in the view of the committee does it suggest causation. It can affect people who have schizophrenia and other psychoses. Cannabis, however, does not appear to increase the likelihood of developing depression, anxiety or post-traumatic stress disorder, PTSD.

Individuals diagnosed with bipolar disease may have greater symptoms when they use cannabis and heavy cannabis users are more likely to report suicide thoughts. All of them again is important, as is mental health in general. But it needs to be followed up.

So problem cannabis use or dependence or addiction, cannabis use disorder in the current jargon, there seems to be pretty good evidence that in populations who are made up of regular cannabis users, that maybe nine or 10 percent of them have what we would call a use disorder. That means they have dependency. They tend to have more health problems and health outcome problems than those that don't have the disorder. All of this needs to be followed up to see how much of this is real. If so, what -- excuse me -- and what needs to be done about it.

A lot of interest, Sue mentioned the gateway issue. There is only limited evidence that cannabis use is associated with tobacco use. And only limited evidence that cannabis use is associated with other illicit and licit substances and only a statistical association on substance dependence. These are very complicated issues, but as of right now, as of the time the committee did the report, there was very little evidence of that.

So that is basically what we found. I understand that it is a lot of diseases and we went quickly. I went quickly. Let me just finish this with some of the research barriers and our recommendations. Then we will wait until later when we do the questions.

So we did pay a lot of attention to cannabis research and its barriers. Not surprisingly there are lots of regulatory barriers. Cannabis is a Schedule One substance. In medicine that's the most severe kind of substance. It was often difficult for researchers actually to gain cannabis, to acquire cannabis in order to do their research. Not impossible, but there is a lot of paperwork. We made a recommendation on that. We made a recommendation -- we found that it was difficult to get cannabis funding. We certainly acknowledge that national institute of drug abuse at NIH and others do fund research. That's very much to their credit. But in order to nail all of this down as I have been describing it, we think much more funding is needed. And we thought there needed to be improvement in research methods. So the recommendations just follow along. I'll just paraphrase them. We need to address the research gaps and the report talks about how to do that and where the methodologic problems are. We need to improve the quality of the research. That will come with increased funding. We need to do more surveillance, which is a public health term for monitoring how much cannabis and what kind of cannabis and so on and for what reasons, how much is being used in the community. And following those persons to see what happens to them clinically. Then as I said, we need to address the research barriers.

That basically is a report. Since this is a California production, I want to roll out the screen credits. I had 15 very capable senior scientists who worked with me on this panel. I just wanted to show you their names because they are very much deserving of a lot of the credit for this. There are the rest of them.

I don't have a list of the committee names, but there were committee staff people who really made a lot of this happen. They were remarkable staff. Also in fact deserve credit.

So I want to thank you for your attention. I will be happy to answer questions later. You can download report at NAP.edu, the National Academies press, free of charge. We would always in fact welcome your comments. So thank you very much. Thank you, Sue.

>> Susan Watson: Thank you, Dr. Wallace. It's a lot of information. I know, to digest. We have a lot of questions that have come in. Some are really specific. We will try to get to some of those. Some of those may also be addressed a little further in the following presentation. Before we move on, we've got a couple other statements here that again we'll revisit later. The first one is that legalization of marijuana leads to increased use. So go ahead and choose whether you think that is true or false.

And then the second statement is that marijuana impairs driving the way alcohol does. So go ahead and make your choice there. This will close shortly, but put your information in, submit it. We'll revisit this later. I want to move on to our next presenter.

Dr. Vigil manages the marijuana health monitoring and research program at the Colorado Department of public health and environment. He has worked in marijuana since 2014 and says Colorado has made great strides in understanding the science on marijuana and health. Monitoring important data, educating the public and refining policies. He's excited to talk with

us today and share some of their learning. So take it away.

>> Daniel Vigil: All right. Thank you, Sue. Hello, and thank you all for joining us. A couple of quick things before I start. I use marijuana and cannabis interchangeably in this presentation and don't intend them to have any different meaning.

Second, I have a lot of content and time is short. So some slides I may move quickly past.

The information is there for your reference if you want to look back.

So the health effects of marijuana and research are really a hot topic right now. Sorry, these are my older slides. Oh.

One moment.

>> Laura Burr: Dr. Vigil, can you proceed? We'll send out the corrected slides after the event. Would that be okay?

>> Daniel Vigil: Yes. So with retail -- let's see.

So with retail legalization in Colorado, we had a real increase in public interest in the health effects. And with this now being a state regulated legal market, we also had a real responsibility to determine what the research could tell us. So we have a lot of marijuana use in Colorado. 14 percent of adults are current users or past 30 day. One in 818 to 25-year-olds use daily or nearly daily and many adults use three or more times per day. 25 percent of high school juniors and seniors are current users. The top reasons for use are every day use, sleep, anxiety and just feeling good and smoking remains the most common method of use. So Colorado is not alone in the legalization. It has become a national and international topic of interest. There is a lot of information out there, both founded and unfounded ranging from it will cure everything to it will kill you. So summarizing and improving cannabis research is more important now than ever. Today I want to cover some of our literature review process briefly. Then important considerations when evaluating marijuana research. Some comparison of our findings with those that Dr. Wallace just presented. And some research gaps that we identified.

So Sue just gave you an introduction. I'm also a preventive medicine physician. I didn't have a special interest in marijuana. But as I was finishing residency, it was something that needed focus. So I learned a lot about it. And other than the hair, I think this is a good likeness for me, even though you can't see me.

So our program has three main responsibilities. We review and report on existing and emerging research along with the retail marijuana public health advisory committee. We monitor data on patterns of use and health impacts in Colorado. We administer currently 16 research grants. This is our report that I'll be presenting findings from today. It is available at this web address. Or you can simply search monitoring marijuana Colorado. It will be the first link that appears.

So our advisory committee was convened in accordance with statute. It is responsible for ongoing review of published research. It is made up of physicians, pharmacologists, behavioral health experts and epidemiologists. We met monthly initially and now meet five times each year.

We use standardized criteria and language for the weight of evidence. This should read five levels: Substantial, moderate, limited, insufficient, and mixed. And our searches mainly include 2005 forward but older for some topics. We include all relevant primary research and meta analysis identified for each topic.

These are the topic areas that we evaluated. They are very similar to those in the Academies report except we did not look at therapeutic efficacy and we looked in greater detail at some of

these which I will cover soon.

And from there unfortunately I am going to have to talk without the benefit of slides. So first I wanted to cover some important considerations that we identified in evaluating cannabis research specifically. The slides have a couple of great evaluation resources in general. The New Castle, Ottawa scale for observational studies and the grade system with criteria for more focused on randomized trials.

Specific to cannabis research, population can be a little bit tricky. You have to read a little more closely some studies to determine exactly what population is attached to a finding.

Sometimes that is because of recruiting. For example, a number of studies recruited very few subjects over age 30 even though the aim was to study all adults.

Then if a study breaks out into subgroups and reports a finding that is specific to a subgroup, it is important to be clear on what that subgroup is. An example is that decreased IQ was found among individuals with multiple years of cannabis use disorder but not among the more studied population. For exposure, marijuana use is identified with a relatively low amount of exposure. The worst is always used versus never used. Marijuana use with ongoing, a group with more ongoing use, many of the individuals in that group may be occasional users. It's hard to get good representation of heavier use in the research.

Self report is the primary method of measuring use. It's hard to get away from that, but it can lead to under reporting of use, which would tend to bias towards the null. Case control studies in particular can have recall bias depending on the individual's perception of cannabis related to their condition.

Then the last point on exposure is really about dose response. A true effect should usually be greater or equal in groups with more exposure. If you have a study that reports a statistically significant finding among less than weekly users, but that finding is not present among weekly users, you have to try to clarify that.

For analysis, tobacco use and alcohol use are very common among users of marijuana and should be accounted for. In cognitive studies they often have multiple test types. Interpreting the significance of findings can be difficult, especially when the study finds impairment in some tests but not others. In addition, multiple comparisons like this should be statistically corrected for and are in some studies and are not in others.

With mental health, there are many shared predictors of mental health conditions and marijuana use. Those should be accounted for.

Then finally, in ecological studies with marijuana these are mostly at the state level. But they really need to consider other policy and social differences that could impact the outcome that is being studied.

With that I will move on to the comparison of findings. And quick note on this. I am using the Academies report and what Dr. Wallace presented as a jumping off opinion and going to only focus on places where there was a difference. So included in these slides are topics in our report that were not addressed in the Academies' report. Places where there was an important difference in the population, the level of exposure or the outcome measure, and then findings where it was limited or lower in one report but moderate or higher in the other.

These slides do not include the places where we were really in agreement, including close like substantial in one report and moderate in the other.

So for respiratory, many of our statements are well in line with the Academies' report. We also found limited evidence that daily or near daily marijuana smoking is associated with pneumothorax and lung disease in individuals under 40. Weekly or daily marijuana smoke are

who switched to vaporizing had improved pulmonary function. For driving we looked in a lot of detail at impairments and in those studies they were almost exclusively in less frequent users. So for less than weekly cannabis users there is substantial evidence of driving impairment at blood levels of two to five nanograms per milliliter. This is important because many states have chosen five as a cutoff.

Smoking more than 10 milligrams of THC is likely to impair driving. We recommend delaying driving for six hours after smoking based on the evidence of impairment.

Ingesting 10 milligrams of THC is also more likely to impair driving and we recommend eight hours of waiting before driving. In daily or near daily cannabis users there is little evidence of driving impairment.

Both reports indicates that cannabis use increases crash risk. We found substantial evidence that the combined use of marijuana and alcohol increases crash risk and impairment more than either substance alone.

In injury, we found limited evidence that marijuana use is associated with physical dating violence perpetration by adolescent girls and victimization among adolescent boys and not the converse. When you get to young adult men or women there's a limited body of research that failed to show association between marijuana use and physical dating violence.

So then cancer. Again a lot of similarities in our conclusions with the Academies' report. We found substantial evidence that marijuana smoke contains many of the same cancer causing chemicals as tobacco smoke and substantial evidence that daily or near daily smoking is familiar with premalignant lesion in the airway. When it comes to lung cancer specifically most studies use the concept of joint days, which is -- sorry, joint years, which is equivalent to one joint a day for a year. And we found kind of a natural cut point in the research around ten joint years. So we looked at those separately. For greater than ten joint years the evidence is mixed on association with lung cancer. For less than ten joint years there is a moderate body of research that failed to show an association. This moderate evidence is failing to show an association is where the academy landed on this topic overall, but I think as we see more cumulative exposure we may end up seeing some association.

For cardiovascular we found limited evidence that acute marijuana use increases the risk of myocardial infarction, likely in individuals with other risk factors. We found limited evidence that marijuana use increases risk of ischemic stroke in individuals younger than 55 years of age.

Moving on to pregnancy and breast feeding we made some statements about biological evidence that it shows that THC is passed through the placenta and is present in breast milk of women who used marijuana and that the breast feeding infant absorb and metabolize the THC.

Low birth weight is the one place where the significant contradiction between the two reports. We found mixed evidence about use during pregnancy and low birth weight. On the Academies report found substantial evidence that there is an association. The review included one recent meta analysis and three primary studies. Our review was prior to that meta analysis and included six primary studies, several of which did not see an association. So we are currently reviewing the newer research and more information later.

Then finally, for still in pregnancy we found moderate evidence for some associations in exposed offspring during childhood. Reduced cognitive function, decreased IQ scores, attention problems and decreased growth.

So an area of cognitive effects, again a lot of similarity in our statements with the academy.

We also found substantial evidence that adolescents who use weekly or more frequently are less likely to graduate from high school and moderate evidence that young adults who use weekly or more frequently and begin a college program are less likely to attain a college degree than those who don't use.

Mental health, similarly a lot of overlap. We also found that substantial evidence that THC intoxication can cause acute psychotic symptoms which are worse with higher doses. Those sometimes lead to dangerous behavior.

Gastrointestinal there's moderate evidence that long time frequent marijuana use is associated with cyclic vomiting, called cannabinoid hyperemesis syndrome. We look at metabolism and the slide has graphs for you. Two key points are that THC blood levels after inhaling peak rapidly at ten to 12 minutes but the peak after ingesting is around four hours.

In second hand exposure, in testing there is really insufficient evidence to determine the health effects of second hand smoke. We did find substantial evidence that typical second hand exposure to marijuana smoke should not result in a failed urine test or blood test. Failed being above the standard cutoff. There may be some cannabinoids present, but it should not be above the cutoff.

On the other hand, with extreme secondhand exposure, such as an hour of secondhand smoke in an unventilated space, individuals are likely to feel the effects of marijuana, including increased heart rate and psychomotor impairment and they can test positive.

For opioids there are two levels, state level and individual level comparisons. We found insufficient evidence to determine whether or not there is an association between marijuana legalization and the prevalence of opioid use at the state level and currently reviewing recent studies on severe opioids, current assessment, it looks like there might be some reduction. He we don't have a clear statement on that yet.

At the individual level, we found studies among chronic pain patients and among patients with a history of injection drug use or Opioids addiction treatment and the evidence is mixed in both of those groups about association between marijuana use and reduction in opioids. Finally, there is credible evidence of clinically important cannabis medication interactions. The list is on the slides and I'm not going to read it. With additional research, I think the list is likely to grow as well.

Finally I wanted to cover some research gaps that we identified. First across all topics, there's really a lack of research on more frequent use, higher quantity of use and higher concentrations of THC. For driving we need to see more on frequent users and using higher doses of THC. Ideally to develop some evaluation methods that accurately correlate with impairment.

We need more research on the effects of secondhand exposure and on interactions between cannabis and prescription medications. We would like to see more on the effects of prenatal exposure, especially miscarriage, birth weight, and early childhood development.

And also the presence of cannabinoids and their duration in breast milk and the effects on exposed infants. Then factors related to adolescent initiation, a population of particular concern. On more prospective studies would be ideal. We need better classification of exposure. Collect times per day, times per week or other measures of exposure. Separate groups with occasional and heavy use or even additional gradations of levels of use and then some research on former users with different periods of abstinence could help identify the duration of effects and possible resolution.

Confounders are really important. Improved data collection is needed. For trials like driving

impairment studies we should use doses consistent with current THC levels.

This is our retail marijuana public health committee member list. I apologize for the mix-up in the slides. I encourage you to go and take a look at them and thank you for joining us.

>> Susan Watson: Thank you so much, Dr. Vigil. Actually, we apologize for the mix-up in slides. And I think you still did a wonderful job. For those of you who are listening, all of that data and that information that he shared about what Colorado has found, there are slides for those. So as was mentioned, when the recording and the slides are made available we will make sure that the complete slide set is what you will have access to.

So thank you so much for getting through that without some of those visual aids. Technology, this is human error.

So we wanted to go back and revisit some of these true/false questions it's an opportunity to have more dialogue. Some of it may get to some of the questions that came in during registration. Then we can also bring up some of the questions that have come in during the course of both of your presentations.

So I went back and looked at the poll results. And it looks like 40 percent selected true and 57 percent selected false on the gateway aspect of marijuana. So I think you both have touched on this. I want to share that one of the ways I understood this is that while most people who use more potent drugs have also used marijuana, but the majority of marijuana users do not go on to use more potent drugs.

Is that consistent with what you both have seen and know? Or how you would characterize this?

>> Daniel Vigil: I think what you just said is accurate. It is true that use of other substances is more likely among marijuana users, it goes both ways. So risky behaviors in general lead to other risky behaviors. And the gateway drug idea really tries to focus in on marijuana as a special culprit.

>> Susan Watson: Uh-huh. Thanks. I know Dr. Wallace, if you want to unmute yourself, if there's anything you would like to add?

>> Robert Wallace: No. Not much. I agree with Dr. Vigil and I think it's very complicated, particularly in young people. As those who are going to develop mental health conditions experiment with a number of things and they get more proficient, and whether abusing drugs and they get more experience as they go out in the world, I think it's very complicated. A lot of this comes with underlying mental illness for which drug use including marijuana, including cannabis, is an epi-phenomenon. So it's just very complicated.

>> Susan Watson: Okay, things. And then for the next one around mental health, it was 48 percent selected true and 48 percent selected false. So exactly split down the middle. And you know, I think we acknowledge that this question is a tough one because even as with what Dr. Wallace just said about gateway, that sometimes these things are hard to tease out. But I'm interested in how you would approach answering this one around mental health.

>> Robert Wallace: Dr. Vigil, you want to try that?

>> Daniel Vigil: Sure. The first part I think is true. I think marijuana can exacerbate symptoms of mental health conditions and there is likely a reinforcing cycle there.

As far as permanent mental illness, I would say this focuses probably on psychosis and psychotic disorders like schizophrenia. The evidence suggests that marijuana can precipitate psychotic disorders. There is some suggestion that it may be only among individuals who are already at risk. Of course, that makes sense. One concern is how do you know if you're at risk? But for other mental illnesses the evidence is really not there for any suggestion of

causation. But I think there is, as I said, that reinforcing cycle.

>> Robert Wallace: So I think that's what we said in our report. So we fully agree. I think the committee agrees that it can exacerbate acute episodes. It can make some mental conditions worse, that is cannabis. And whether it is constitutional in terms of causing the biology of serious mental illness, I personally think that's a tougher question. And I don't think -- I know that our committee didn't really go there in the kind of depth we would have liked to.

>> Susan Watson: Great. So maybe a fifty-fifty response is probably appropriate.

(Laughter.)

>> Robert Wallace: Right on, yes.

>> Susan Watson: So then around legalization, use, and Dr. Vigil this may be something you can share about the experience in Colorado. 68 percent selected that it was true and 29 percent selected false, about legalization increasing use. Have you all been able to track some of that pre-legalization to now? Or even over the years since it has been legalized?

>> Daniel Vigil: Yes. Our answer for this is not in Colorado. Both adult and youth use have been stable since legalization. I believe Washington did see an increase in adult use. Across all recently legalized states, we have been pleased to see that in adolescents there doesn't appear to have been an increase.

>> Susan Watson: Good to know. And then the last one is on driving impairments. We had 64 percent chose true and 31 percent chose false. About the impacts on driving. I know in preparing for this webinar, came across some folks -- there are some specific studies underway related to this. So I assume there will be additional richness to the data and the information that is out there. And I know, Dr. Vigil, you talked about what you have seen in Colorado. Again, there could be confounding factors and what may have been attributed to a motor vehicle accident or between how long marijuana may stay in your system or whether alcohol was also involved. And just want to see if you all have any other comments you would like to make on this.

>> Daniel Vigil: First, just want to be clear that marijuana does impair driving and increases crash risk, no question. I think the extent and manner of impairment are different, however. So both -- marijuana can cause slower driving which is not really seen with alcohol. There is certainly speeding still with marijuana DUI stops and another important factor is that the time covers impairment can be different, especially with edibles. You know, it is not quite as linear of a change.

>> Susan Watson: Uh-huh.

>> Robert Wallace: So I basically agree with all of that. Again, our committee found the crash risk that others have found. And that led us to again ask the question about occupational injuries. Again there wasn't much evidence for that.

I actually have some colleagues at the University of Iowa who are evaluating cannabis in driving simulators. And basically they see some of the correlates of driving in a simulator that are likely to be predictive of crashes, had this been in a real life experience. So I think there is accumulating evidence and so forth. It sound like Dr. Vigil and his colleagues have gone further with this and I applaud that.

>> Susan Watson: That's great. That was the end of the true/false discussion. There are a lot of questions and I'm kind of weeding through some of them. If I start with one that came in during registration and again just a reminder for participants this is how you submit a question. One of the questions that came in for you, Dr. Vigil, has the legalization of marijuana impacted crime rates in Colorado?

>> Daniel Vigil: Yes, good question. And so first, possession, arrest, have obviously gone down. That's the first clear thing. DUIs for marijuana have increased. Other marijuana related arrests have been pretty stable here.

>> Susan Watson: That is important for people to know from a state that has been operating under legalized marijuana for -- three years now? Two years? Almost three?

>> Daniel Vigil: Almost three.

>> Susan Watson: There were some --

>> Daniel Vigil: I'm sorry, almost four.

>> Susan Watson: Four, wow. Time is flying, right?

(Chuckles.)

>> Susan Watson: There were some questions for Dr. Wallace around, and maybe the two of you can answer this. When you looked at the research and you categorized things around limited, substantial, did you use the same parameters for those brackets? Like what equaled what? Some people, we went through that quickly. There were some questions to revisit that.

>> Robert Wallace: Well, let me say just to give the questioner a little bit more detail. It sounds like both the Colorado group and our National Academies committee used the same general level of evidence, five levels and so forth.

We, because of our limitation of resources, actually first started with existing systematic reviews. That is where other investigators have actually gathered the evidence that they felt was appropriate and combined the findings into larger findings. Actually, Dr. Vigil mentioned this in one instance. In order to conserve our resources and use them as best we could in this report, we actually depended on other people's summaries of research as best we could. And where we couldn't, we evaluated individual studies. There are many different ways to use evidence. We actually also used what is called the grade system where we had it available, where the evidence would allow us to do that, and where our resources did, as well as what the Colorado group is doing.

So I think the structure of evidence review is reasonably similar.

It is clear in listening to Dr. Vigil that the Colorado group has gone further in certain areas, and we went a little further in other areas.

>> Daniel Vigil: Absolutely.

>> Susan Watson: I hope that -- go ahead.

>> Daniel Vigil: I am going to answer for Colorado, but I don't know if it would add much.

>> Susan Watson: I hope that helps clarify a little bit more. And everyone will get these slides, so you'll have a chance to sit with what's on the slides a little bit more.

There seem to be a number of questions that are related either to the strain, the potency, the different types of levels of THC or THC versus CBD in either the research that was reviewed in the National Academies' report or some of the primary collection that is happening in Colorado. Have you been able to use that information to reflect or strap late or talk more about some of the different ways people are using marijuana? Whether it's with oils or with the plants, and or whether or not you are able to say anything about different levels of potency and its effects?

>> Robert Wallace: Dr. Vigil, let me start, but it sounds like you have done some more with it. First of all, I want to second what Dr. Vigil said earlier about one of the deficits in the epidemiological studies that looked at the association of cannabis use with health outcomes is that there wasn't enough attention to the level of use. And that, I wouldn't say it wasn't attended to, but I think that the amount of attention was inadequate. That's one of the reasons we pled for a standardized approach to doing these kinds of studies. It's hard to get

investigators to do that. But we asked for that.

But there are other issues. I'm sure Dr. Vigil is up on all of this. To begin with, these are plants. Like tobacco, they are different depending on the weather, the amount of year, the amount of rain fall and so forth. So different parts of the country or the world where the plants are grown and so forth. So there really is nothing, what I would call standardization. I think a lot of people refer to the fact that the amount of THC, tetrahydrocannabinol, the psychoactive drug. There is no population sampling, but in a series of seized drugs in legal actions, the amount of THC per given amount of plant has actually been going up over the last 15 years. And I don't know that I understand the reason for that, but I would only have speculations. But there isn't enough standardization. To a certain extent that is because of the biochemistry and all the substances, as was said in cannabis. Even some of the medicines don't have the level of standardization that, the medical marijuana preparations don't have the amount of standardizations that they might have.

Finally, there was a paper in JAMA, the Journal of the American Medical Association, suggesting that some of the medical marijuana preparations are actually mislabeled. But in any case, standardization and exposure is really a problem.

>> Daniel Vigil: Yeah, I agree. I'll stress that most of, nearly all of the existing research has been on sort of the use of marijuana without real clear definitions. Most of the marijuana used is going to have THC because that is one of the primary reasons that people use it. But the mix of cannabinoids can be different and we really don't have much research at all yet on different cannabinoid profiles or even on the different methods of use.

>> Robert Wallace: Right.

>> Daniel Vigil: We do have some information in Colorado, the marijuana enforcement division collects info on every registered marijuana product. So we have 17 percent is the average concentration in flower. And 72 percent in concentrate.

>> Susan Watson: Okay. So it sounds like as again as more of this is out there and the places are legalized and data is collected and monitored and surveillance, we may learn more. The current existing evidence is limited or not there to help answer this. People want the answer.

(Laughter.)

>> Robert Wallace: That is particularly for street drug, yes. But yeah, right.

>> Susan Watson: So there are a couple of questions that are linked to if you can speak to what does use disorder or overdose or dependency mean when we talk about marijuana or what that looks like.

>> Daniel Vigil: I can start on this one.

>> Robert Wallace: Go ahead, Dr. Vigil.

>> Daniel Vigil: So use disorder definitely occurs with marijuana. I think both reports have statements about marijuana being addictive. And there is a common misconception that you can't be addicted to marijuana. I think that is related to thinking about it in terms of a nicotine type of physical dependence, which is not as pronounced with marijuana. Heavier users can have withdrawal symptoms. But in general, cannabis use or any substance abuse disorder is really more broad. I would boil it down to say that continuing to use a substance despite it causing you problems, whether those are social, financial, career, et cetera, or physical health. So that is the substance use disorder. You also mentioned overdose. Most people think of overdose in terms of opioids where there is a life threatening impact and that is not true with marijuana. I would refer to it more as over consumption. An unintended effect which, of

themselves, I don't believe can be life threatening. However, they can lead to behaviors that might be life threatening.

>> Susan Watson: Okay.

>> Robert Wallace: Sue, I basically agree with all of that. I think the population studies, the cohort studies need to pay more attention to working definitions of use syndrome because the little bit of information that there is suggests that those persons actually do worse in terms of health outcomes. But some of this, as Dr. Vigil said, are just related to the amount that you use and so forth. Whether this is physiologic addiction is as has been discussed. A lot of the work needs to distinguish between again those persons who have a use syndrome and those who are otherwise just using it recreationally.

We really need those answers.

>> Susan Watson: Thank you. I'm sorry, I'm trying to read and then collapse several questions into a single question. But I'll bring up one that came up from registration that a couple people asked, around about safer use guidelines. And do you know if anyone is working to develop safer use guidelines, kind of like we might have for alcohol?

>> Robert Wallace: Go ahead, Dr. Vigil.

>> Daniel Vigil: I am not aware of any. I was hoping perhaps you might have heard of something.

(Laughter.)

>> Daniel Vigil: Really, we are just beginning to understand how people use. An example with alcohol is an understanding about binge drinking. Understanding about the number of drinks that may suggest a problem. And we really don't have that level of nuance for marijuana yet. We need a lot more research on the effects of different methods and on higher levels of use, as we've already said.

So no, I'm not aware of any safer use guidelines.

>> Robert Wallace: Let me just opinion out that the Academies' report, the sponsors that I showed at the beginning of the presentation, actually asked us not to do policy. At the time they really wanted health outcomes and the states particularly were feeling their way through all of this. Really wanted to just get the information on the health outcomes. So we didn't really go there.

>> Susan Watson: I will add, and I guess the power of an event like this with people from so many different places is that three folks have written in to let us know that Canada has lower risk cannabis use guidelines that have been endorsed federally and provincially. Then sent us the link. We will include it. We do have a list of some resources. So we will add that to the list that will be available to those of you who have participated. There is something out there in Canada.

>> Daniel Vigil: Great.

>> Robert Wallace: I'll ask this as a question, Sue. But I think Canada is pretty close to legalizing cannabis, if I'm not mistaken. Daniel, do you know?

>> Daniel Vigil: I do, yes. July 1 of 2018.

>> ROBERT: Yeah. So they are getting ready for it.

>> Susan Watson: Okay.

>> Daniel Vigil: They have also been a little bit more ready to do some attribution for marijuana on different conditions.

>> Susan Watson: So they let us know July 1, 2018 is when this should happen in Canada. Dr. Vigil, there was a specific question for you in your work about how you defined young

adults.

>> Daniel Vigil: Oh, yes. So young adults is 18 to 25. Part of that definition is focused on the cognitive and the fact that brain development is until 25, according to the well accepted literature.

>> Susan Watson: Okay.

Bear with me for a second.

There are a lot of specific questions that I won't necessarily get into.

>> Daniel Vigil: I'm happy Tom try to field some of the specific ones if you have a way to get them back to people.

>> Susan Watson: They were things like how many million meters -- oh, offline, okay.

And you've discussed the lack of clarity or con since technical assistance between studies for levels of use, what heavy use is versus moderate use. We won't go into those.

>> Daniel Vigil: I'll sale real quickly on that, we actually started with the terminology of occasional use -- I forget what the middle one was. And heavy use and realized that really we were defining them around how many days of use. That's one of the more common measures of frequency. And we've revised that now to simply say less than weekly use, weekly use and daily or near daily use.

>> Susan Watson: So you have been able to establish that in Colorado. So I think for those who may be getting ready to monitor or look at things, that there may be some already existing suggestions in place that you can refer to or have some further conversations with the folks in Colorado to see how that is, how they came to that and how it's working.

>> Daniel Vigil: Clarification or near daily, that's five days a week or 20 or more days a month.

>> Susan Watson: Have you been able to collect any information? I think we touched on this. Related to smoking versus ingesting versus vaping? And if those different ways, or using a topical application, did any of your research allude to having different impacts on the health effects?

>> Daniel Vigil: Sorry to jump in here Dr. Wallace but I'll go ahead and start.

I covered a few of the pieces of information that we do have. There was some study in respiratory symptoms where vaporizing seems to reduce symptoms among frequent smokers. Then for edibles and inhaled marijuana, the only data really is around the metabolism and driving impairment studies, which I covered some of that. Really the effects last longer and are more delayed with starting with edibles.

>> Robert Wallace: Our committee report actually, Dr. Vigil, did not really look at much in the way of mode of delivery. It was almost all smoking.

>> Daniel Vigil: There's very little out there.

>> Robert Wallace: There's very little out there and we made a pragmatic decision at the time not to go there. When we looked at therapeutics we did look at some of the extracts, most of which are oral medication like preparations. We didn't look at edibles, vaporizing, et cetera. We didn't think there was enough information at the time.

>> Susan Watson: Okay. On that, we are close to the end. So I want to move us to the close here so that we end on time.

And again I want to just say that we really appreciate all the information that has been provided today. We appreciate the questions that you all have asked. I want to extend my thanks to Drs. Wallace and Vigil for sharing so much of their knowledge and insights with us today.

Feel free to contact us for more information. If you are in California remember to join us at CA4Health.org to continue these and other conversations.

Lastly as a reminder, we have two more webinars in the series. One on November 30 talking about marijuana and communities. The other on December 11 that will be looking at marijuana and public health opportunities. You can register for those at Dialogue4Health. I will hand this over to Laura to kind of close us out. Thank you, all.

>> Laura Burr: Thank you so much, Sue. I want to thank all of our panel today: Sue Watson, Dr. Wallace, and Dr. Vigil. We appreciate your presentations.

Also a big thanks to CA4Health for partnering with us and to the California endowment for funding this event. And thank you to you, our audience. A recording of today's presentation and the slides will be available to you next week at Dialogue4Health.org. You will receive an email from us with a link to a brief survey. We hope you will take that. We really would like to hear from you.

And the survey also includes instructions forgetting a certificate of completion for this event. Thanks so much for being with us. That concludes today's web forum. Have a great day.

>> Daniel Vigil: Thank you all for the great questions.

>> Robert Wallace: Me too, thanks to all the participants, Sue, Laura, and all the other staff that made this possible.

>> Laura Burr: Thanks so much.

(The webinar concluded at 3:00 o'clock p.m. EST.)

(CART provider signing off.)