>> And we will hear from Andrew Freedman to start us off.

>> Welcome to session two of NCI's Cannabis and Cancer Research Symposium. My name is Andrew Freedman, and I'm the branch chief of the Clinical and Translational Epidemiology Branch at the NCI. Along with my co-chair, Dr. Ilana Braun, we hope we have put together a really informative and thought-provoking session titled Cannabis and the Cancer Patient. We have four scheduled talks, followed by a live panel discussion. Our first speaker is Stacey Blansky. She's a recent graduate of Cornell University with a bachelor's degree in industrial and labor relations. Stacey is also a cancer survivor, and she will tell us about her experience using medical cannabis while undergoing cancer therapy. Our next speaker is Dr. Ilana Braun. Dr. Braun is chief of the Division of Adult Psychosocial Oncology at the Dana-Farber Cancer Institute and a clinical psychiatrist with a specific research focus on cannabis use among cancer patients. She will talk about cannabis' legal landscape and the potential clinical implications. She will be followed by Dr. Steven Pergam, who is an associate professor of clinical medicine at the University of Washington and an associate professor of vaccine and infectious disease at the Fred Hutchinson Cancer Institute. Dr. Pergam specializes in the prevention and treatment of infectious diseases, particularly among patients whose immune systems are compromised due to cancer or chemotherapy. He will be speaking about the risk of cannabis use for the cancer patient. Our last speaker is Dr. Donald Abrams, who is a professor emeritus of medicine at UCSF and has an integrative oncology consultation practice at the Osher Center for Integrative Medicine. He has been conducting cannabis research for over 20 years and was a key member of the 2017 National Academy's committee that published a report on the health effects of cannabis. Dr. Abrams will be discussing the benefits of cannabis use for the cancer patient. After Dr. Abrams' talk, we'll have time for a thirty-minute live panel discussion. Thank you once again to all our speakers.

>> Hi, everybody. My name is Stacey. I'm here to provide the patient experience. I just wanted to thank you all again for virtually tuning in to the National Cancer Institute's first ever symposium on cannabis, cannabinoids, and cancer research. So why don't I just jump right into my story. So this picture here is me just moments before a lymph node biopsy that two days later would diagnose me with stage four Hodgkin's lymphoma. At the time, I was entering my third year at Cornell University as an undergraduate, and I was really shocked. I was healthy for as long as I knew before that. I followed a vegetarian diet. I exercised all the time. I got great sleep. Nothing pointed towards this. So it was a huge shock for me and my family. So immediately thereafter, this was actually the second day of classes at Cornell, I drove home for the weekend and set up an appointment with my new oncologist to get staged and get a lot of testing done. He advised me to continue going to school if I felt up to it because the way the chemotherapy worked, the first week was pretty challenging in terms of side effects but the second week usually got better and more manageable. So as he requested, I kept going to school, to beautiful Cornell University. Basically what I did was I would have a really early important on Monday mornings where I had a three-hour infusion. And then somebody from my family graciously would drive me the hour because I live an hour from campus. They would drive me back to class, and I would go straight to my first class. Usually, if I had early chemotherapy, I didn't have to miss any classes. It was definitely a really challenging year, but I was determined to make the best of it, and I was determined to really push myself and see what I was capable of. Regardless, chemotherapy is a really challenging course of drugs for your body to undergo, and I definitely felt like I was out of control of my own situation. The oncologist prescribes you the chemo. The nurses prescribe you the drugs for managing side effects. All drugs have side effects and side effects have side effects. So I wanted to try to find some sort of holistic treatment that I could kind of take the diagnosis back into my own hands with. I've always been one for plant medicines and just looking into how nature can heal us as opposed to always looking for the pill at the pharmacy. So I kind of knew -- I mean, before I even got cancer, I knew about cannabis and marijuana. I was a college student, and I had experimented a little bit here and there. But I think I always knew that it had more benefit than people might have been assigning to it in college, for example. Kids in college drink just to have fun and they smoke just to have fun, but I kind of knew deep down that there was more to this plant than I knew. So when I got the cancer diagnosis and I found out that cancer is a qualified condition for being a medical marijuana patient in the state of New York, I decided to approach my oncologist and ask him if I could get referred to a medical marijuana dispensary. He was definitely not supportive, but he wasn't against it. I think he never received any information on this in his medical school training. He's much older than I am and just didn't want to recommend something that he wasn't informed educationally on. So I had to push just a little bit and reassure him that I did my own research and that I felt that this was going to help me with my side effects. And shortly thereafter, he did refer me to somebody else in his practice who was registered to register people to dispensaries. So I went to a dispensary about an hour from my house. Waiting room looks a lot like this. It was a very, very formal looking setting as opposed to, I guess, what people might associate a street drug with. It looks nothing like that. And dispensaries are four tinted window walls that you see from the outside. But when you get inside, I found it to be a very professional experience. So I went for a few different symptoms. I went for nausea because the nausea was really bad as well as appetite stimulation because when you're nauseous you're no really hungry and you're losing weight. I also went for insomnia because I was receiving a steroid that kept me up usually the first two nights after treatment. And just stress, anxiety, depression. Just the emotional effects that happen when you have to undergo something so challenging all at once. So I presented those symptoms to really a pharmacist. They take you behind the waiting room to a more pharmacy enclosed area. And the pharmacist will recommend based on what you are experiencing the products that are right for you. So they're all color coded. The CBD dominant products -- this is a little bit misleading, because they don't actually sell flower in New York state because smoking is still unhealthy. But I received CBD-heavy oil, which was yellow. That was the color code. And then I received THC-dominant not vaporizer, a vaping pen, which is coded blue. And then anything that was equal THC to CBD is coded green. So those were the three products I had. It was two vaping cartridges and it was one oil. I also have this little chart. It's really busy, but I always thought that it was helpful in showing that there are so many different conditions and ways that medical marijuana can treat. It's not just for pain, for example, and it's not just for insomnia. There are so many different things. It's because it's ratios. So everything in a ratio will act a little bit differently on your body. So that is pretty much my dispensary experience. I was at the time taking a class at Cornell in the anthropology department that focused on the corporation. And our final research product was to write a paper, like an ethnographic research paper, on a corporation of our choosing. So I actually did choose to write on the dispensary that I was attending, that I was a patient at the time because I felt like this is a very insider-outsider perspective. You can't enter this building unless you have an approved card from an approved physician for an approved condition. So it's closed off right now, and it still is in the state of New York, to a lot of people who don't get to understand that there's a whole new side of cannabis that's coming about because we're learning medical benefits and medical therapies. That was a really fun experience. I got to write the paper. I got to present it to a group of 20 peers at Cornell. And I thought it was informative. I thought I was doing something. Yeah. That was a nice experience. I will say I have been to a recreational dispensary once. I was out in Denver. It's definitely a different feel. There's no waiting room and then prescribing room separation when you go to a recreational place. Everything's on a wall, and you just tell them what you want. They're not going to necessarily advise you what to get unless you ask for it. I did want to discuss some of the negatives, I guess, that I personally experienced. So the first would definitely be stigma. All of the awkward conversations with the doctors trying to convince them that this wasn't me just trying to get something for me and my friends at college but it was something for a very legitimate health condition. I was also living in a dorm at the time, and you're not supposed to smoke or vape in dorm rooms. But I had a talk with the woman who was head of the dorm to explain to her I will be doing this and I know I'm breaking the rules, but I need to find a way to do this so that I can still live on campus and go to college. So it was a bit challenging, but we found mutual agreement through that honest conversation. What else? So there's also the fact that this is an expensive thing to purchase monthly. It's not covered by insurance because it's not even federally recognized yet. And I had the privilege of my parents were willing to pay for this for me, but that required both my parents' support on this issue and also their financial support. Those are two separate things. The CBD oil was, I think, $150 to $170 for a 30-mililiter tincture bottle which lasts a month. And then the vaping pen was probably 80 with the cartridge attached. So it was not cheap, and I know it's not accessible to everyone, which is why I think it's important that we're doing things like this and raising awareness because people shouldn't have to pay to feel better. And I will just say my post-treatment cannabis experience now. So I'm no longer undergoing chemotherapy. I'm cancer-free since February 2019, which also means that I no longer qualify for a medical card because I no longer have that qualifying condition of cancer. I did call my oncology office maybe a month ago because I'm still having appetite issues. And I asked if I could get a new write-up for a medical card, and they declined me because I don't have that condition anymore. So even though I know that this s a treatment that has been helpful with my appetite, I can't utilize it right now because it just wouldn't be legal to do so. So that's still kind of a negative of the current situation is, again, you're only granted access if you've got one of these 10 to 15 qualifying conditions. So I just have to find other ways, which is fine because cannabis isn't the be-all, end-all answer to all issues, but it certainly is a very useful product for a lot of issues. And I would just say my goal now, there's me on the last day of my treatment, is to change the narrative and unwind people's preconceived notions and conceptions of what it means to use medical marijuana or to use marijuana. This was the girl that was using it for six months just to deal with a lot of the really horrible side effects of chemotherapy. So I really do appreciate you guys listening to my story. Definitely a little bit less scientific than all these other doctors talking about the studies. But from a patient experience, I only have positive beneficial things to say. And I'm just really glad that the narrative is slowly changing and that I can be part of that story. So thank you guys and enjoy the rest of the symposium.

>> I'm very excited to be here today participating in this first of its kind conference. Hi. I'm Ilana Braun. I'm a psychiatrist of the Dana-Farber Cancer Institute in Boston. And my hat is off to the NCI for putting on this four-day conference on medicinal cannabis. I owe a debt of gratitude to my symposium co-chair, Andrew Freedman, as well as my co-presenters, Stacey Blansky, Steven Pergam, and Donald Abrams. And lastly, I would like to thank you in the audience for taking an interest in this oncologic topic of increasing salience. Today, I'll discuss the legal landscape for medicinal cannabis in the United States as well as the research and clinical care implications of that landscape. I have no financial conflicts of interest to disclose, but I would like to be transparent that I'm not formally legally trained, although I have been asked to speak on this topic on a number of occasions. And I also would like to state that my presentation was finalized at the end of November 2020, and so is current only through that time. Let me begin with my take home messages. The United States is in the midst of a legal sea change with regard to medicinal cannabis law. Today, federal and state laws frequently conflict. But the degree to which the federal government enforces its prohibition varies from administration to administration. And these fluctuations, as well as the divide between state and federal law, influence clinical care and research around medicinal cannabis, leaving medicinal cannabis something of a conundrum for patients, loved ones, clinicians, researchers. Which brings me to my greatest take home message, which is I firmly believe that clinicians should routinely ask their patients about medicinal cannabis in order to guide care in this domain. This is my home-grown schematic intended to depict the degree of medicinal cannabis permissive over time on a state and federal level. So as you can see, in the early 1900s, state and federal law were quite permissive and agreed in this respect until the late 1930s when it was state law that led the way toward greater prohibition. And then both state and federal law yawed sharply in their course, ushering in a five-decade period of considerable prohibition. Once again, state law led the way towards greater permissiveness, and federal law has begun to follow. But the double headed arrow in red is intended to depict the divide between the two, perhaps the greatest divide of all time actually. So now let me dive in in a little bit of greater detail. Until the early decades of the 20th century, cannabis existed in patented formulas for antispasmodics, analgesics, sedatives from makers like Eli Lilly and others we still know today. It also existed in the U.S. Pharmacopeia. Then, fueled by anti-immigration sentiments and the timber interests, several states begin to restrict or ban outright cannabis use. As one example of the xenophobia, it is in the early 1900s that the term marijuana enters the lexicon, ostensibly linking cannabis use to Mexican immigrants fleeing a civil war. And why timber interests? Well, it turns out that hemp was a major competitor to wood in the making of paper. These sentiments are amplified by Harry Jacob Anslinger, the first Bureau of Narcotics chief, and William Randolph Hearst, the newspaper magnate, who together launch a very successful campaign racializing cannabis and associating its use with criminality and insanity. This brings us to our first inflection point. In 1937, the Marijuana Tax Act is proposed and passed. This is the first time that cannabis sales will be taxed. Interestingly, the American Medical Association at the time lobbied against the passage of this act and advocated for greater cannabis research, but the act passed nonetheless. And yet, global interests in cannabinoid research persists. In response to this, the United States appoints in 1968 the University of Mississippi the official federal grower of cannabis for research purposes. It remains so to this day. In 1970, Richard Nixon signed into existence the Controlled Substance Act. This act assigned cannabis a Schedule I designation. What does that mean? It means not acceptable for medical use, lacking a safety profile acceptable for medicinal use, even under medical supervision, and with a high abuse potential. To put this in perspective, the same act rendered cocaine Schedule II. In other words, it viewed cannabis as more dangerous than cocaine. I thought it would be particularly important in an oncology conference to mention that in the early 1980s, dronabinol, which is synthetic THC, is tested and FDA approved for chemotherapy induced nausea and vomiting. We come to our next inflection point in the mid-1990s. Spurred by an activist ballot initiative in 1996, California becomes the first state to legalize medicinal cannabis, and many states gradually follow suit. In 2004, in a federal versus states' rights fight, the U.S. Supreme Court rules that the feds may prosecute patients abiding by their state medicinal cannabis laws. In other words, medicinal cannabis users are not completely shielded from federal legal exposure. In 2012, there are about 18 medicinal cannabis laws on the state books. And in this year, Colorado and Washington become the first two states to approve an adult use or recreational cannabis law. Under the Obama administration, two important things happened. First, the Department of Justice issues a memo to prosecutors that medical cannabis cases are simply not their priority. And also the Rohrabacher–Farr budget amendment is passed in which the Department of Justice is prohibited from using its funds to interfere with the implementation of state medicinal cannabis laws. Jeff Sessions' Department of Justice takes a harder line towards cannabis. Sessions goes on record as saying that cannabis is hyped, maybe too much, and his Department of Justice blocks more than two dozen requests to grow cannabis alongside the University of Mississippi for research purposes. Between 2018 and 2019, two important things happen. First, the first herbal cannabinoid is FDA approved and in this context rescheduled from Schedule I to Schedule V, allowing it to stock pharmacy shelves. And the second important thing that happens is a farm bill is passed that legalizes cannabis high in CBD, in cannabidiol, and low in THC, tetrahydrocannabinol, aka hemp. So hemp and hemp-derived products are suddenly legal. However, many federal, state, and local regulatory uncertainties persist. Why? Well, one reason is that affordable, commercially available assays test for the presence of TCH but not for the quantity of TCH. And so this leads to many difficulties, and I'll give you an example. Here is a headline from CNN August 2020, so just recently. Grandmother sues after she was arrested at Disney with cannabidiol oil in her purse. And here is the filed complaint from her attorney. "Disney and uniformed local law enforcement officials arrested and detained, processed as a narcotics, and strip searched a harmless, entirely blameless American great grandmother whose only crime was her desire to lessen crippling osteoarthritic pain with a doctor recommended hemp-based oil." So you see things are not clear cut. This brings us to today. As of this election cycle, there are thirty-six states in the United States that have comprehensive medicinal cannabis laws on their books. 15 of those states have in parallel recreational cannabis laws on their books. And I might add that the District of Columbia has both such laws as well. What is less appreciated is that 11 additional states have more limited form of medicinal cannabis legislation. So typically, allowing for products high in cannabidiol and low in tetrahydrocannabinol, which means that there are only at this time three states in the United States that have no public access to nonpharmaceutical cannabinoids. This map depicts cannabis laws as of the 2020 election. So as you can see, states in green are states that have in parallel comprehensive cannabis laws and recreational cannabis laws. States in blue have comprehensive medicinal cannabis laws while states in yellow have more limited forms of medicinal cannabis legislation. And the three states in orange are states with no public access to nonprescription cannabinoids. So let me take a moment and explain what is meant by a comprehensive medicinal cannabis law. Such laws protect the user from criminal penalties on the state level. They allow access to medicinal cannabis, whether through a dispensary system or through home cultivation. They allow for a variety of strains and products to be sold or used. They allow for a variety of modes of administration, including vaporizing and smoking. And most importantly, they're open to the general public, so not just, say, a pilot program. Well, all these changes on the state level beg the question of where cannabis law is going next on a federal level. What does the Biden-Harris administration have in mind? As it happens, Kamala Harris has been quite vocal on this particular issue, and I will read two quotes from her. One, "I definitely believe that we should legalize marijuana. There was a time when I was advocating more medical marijuana, but I believe that we just need to legalize it. Period." And another. "We will decriminalize the use of marijuana and automatically expunge all marijuana-use convictions and incarcerations for drug use alone." She, along with Jerrold Nadler, Democrat from New York, have proposed the MORE bill, the Marijuana Opportunity Reinvestment and Expungement Act. This act promises to decriminalize cannabis, to expunge prior cannabis convictions from the record, and to impose a five percent federal sales tax on cannabis sales with this additional revenue reinvested in the communities greatest affected by the war on drugs. But even if such a bill passes the chamber, it's unlikely to be approved by the senate. In fact, Senate Majority Leader Mitch McConnell has gone on record as saying, "I do not have any plans to endorse the legalization of marijuana." So let's return to comprehensive medicinal cannabis laws. These laws are generally structured to identify medical conditions that qualify for cannabis. They tend to allow for what we call recommendations, medicinal cannabis recommendations, but not prescriptions. And this is intended to protect the recommender from federal legal exposure. So we all must learn a whole new lingo. They tend to stipulate permissible amounts, and these amounts vary dramatically from state to state, say, from 1 to 24 ounces at any one time. They tend to establish state registries and issue identification cards. And they tend to authorize dispensary systems which allow access to medicinal cannabis. The health conditions that qualify for medicinal cannabis vary substantially from state to state with two standout exceptions. HIV/AIDS and cancer exist in almost every state law, which is one of the reasons that a conference of this sort is so important in the oncology world. So we move on now to typical medicinal cannabis dispensaries. The nature of dispensaries varies somewhat from state to state, but in general dispensaries offer nonpharmaceutical grade products, so not of a chemical purity standard outlined by, say, the U.S. Pharmacopeia to ensure stability, safety, efficacy. They are regulated in so many ways but tend to be unregulated in a few important ones. For instance, the ratio of active ingredients they offer, the types of products they offer, their potency. And the last thing to understand about medicinal cannabis dispensaries is in most states it tends to be nonmedical intermediaries who ultimately advise patients about things like dosing, types of products, and mode of delivery. Let's spend a moment contemplating some of the differences between a traditional prescription and a medicinal cannabis recommendation. So when one writes a traditional prescription, one stipulates the active ingredient as well as the quantity, the route, the dose, the frequency, and the duration of use. When one writes a medicinal cannabis recommendation in most states, one does not specify the active ingredient. And why do I say that? I say that because medicinal cannabis is not one active ingredient usually. It's usually more than 300 active ingredients that work through complicated inhibitory and synergistic interactions, termed entourage effects. And so in most states, providers just allow access to any ratio or potency of those ingredients. And then also, providers tend not to specify things like the route, the dose, and the frequency of use. So these may be decisions that are ultimately made at the dispensary counter. So what are some of the research implications of a Schedule I designation for cannabis? Well, I know from personal experience that they are myriad. This designation leads to challenges in accessing federal funding to carry out the research. It leads to challenges in being able to source the study drug. It leads to challenges in negotiating red tape and in taking on a degree of personal, criminal, and financial liability in carrying out such research. But don't just take it from me. Here's a quote in The New York Times from Orrin Devinsky and Daniel Friedman who carried out some of the seminal work on cannabidiol for seizure prophylaxis. And I read, "The Schedule I designation hamstrings doctors from performing controlled studies. For our study, we keep the CBD in a 1,200-pound safe in a locked room in a building with an alarm system." So how does the legal milieu affect clinical care? Well, I believe it leads the medical community to assume a contradictory stance towards medicinal cannabis. On one hand, clinicians are clearly recommending the agent to their patients. In fact, more than two percent of the population in several states holds a medicinal cannabis license that in the vast majority of states had to have been recommended by a healthcare professional. On the other hand, most professional medical associations offer little clinical guidance around medicinal cannabis. Most medical practice infrastructure does not take cannabis into account. I'll give you an example. Epic systems, which is the electronic medical record that half of the clinicians watching use, has no easy way to add medicinal cannabis to a patient's medication list. Research has shown that some clinicians who recommend medicinal cannabis to their patients acknowledge that they don't understand the agent well enough to be making the recommendations that they're making, and I'll explain more shortly. And research has also shown that some patients who use medicinal cannabis perceive a lack of clinical oversight for their use. Because this is an oncology focused conference, I'll focus on evidence from the cancer world. And my wonderful co-presenter Steven Pergam recently carried out a survey of cancer patients in a comprehensive cancer center in the state of Washington. The N was 926. And he found that a quarter of those cancer patients had used cannabis in the past year, mainly targeting physical and neuropsychiatric symptoms, but that 74 percent had hoped to receive cannabis related information and education from their healthcare providers while only 12 percent had. So at the Dana-Farber, my team recently carried out a survey of a nationally representative sample of 400 medical oncologists. We found that 80 percent discuss medicinal cannabis with patients in the clinic. Almost half recommend the use of medicinal cannabis in the course of a year. And less than 30 percent felt knowledgeable enough to make recommendations around medicinal cannabis. Our most curious finding is that more than half, 56 percent of those who recommend cannabis to patients in the course of a year fell into the group who didn't feel knowledgeable enough to make recommendations. I think of oncologists as some of the most evidence-based physicians out there, and so this finding is certainly curious. To begin to understand what might be going on in the clinic, we went on to do qualitative interviews with oncology patients using cannabis in compliance with their state laws. We recruited from eight states. And with an N of 24, we came to the following informed assertions that I'll share with you. First, most of the patients we interviewed received their initial certification from a provider who was new to their care, typically through a brief transactional encounter. Every single patient we interviewed disclosed cannabis to their medical teams but found that their medical teams offered them considerably little clinical guidance. Cannabis patients left to their own devices relied on personal experimentation and commercial information sources around medicinal cannabis. And like in the Pergam study, we found that most used cannabis for symptom management. But half the patients we interviewed also used cannabis for cancer-directed therapy, not infrequently in lieu of standard treatments. So let me provide you with some illustrative quotes. This is one on the process of obtaining certification. "The guy wore a stethoscope and never used it. Nor did he examine me in any way. Nor did he ask me any really penetrating questions. I went in, gave my $200. I spoke to the doctor who said what ails you. Cancer ails me. Okay. Sign on the dotted line. And I was out the door. Helping me figure out what I needed and how to go about the process of self-medicating, none of that was provided by this doctor." And another. "Once he handed me the paper to say that it was approved, I looked at the boxes he was checking and it was talking about vital signs and if my stomach was distended. I mean, it just had all these things that he never did, no sort of exam or anything. It was more he just asked me why I wanted to do it, and that was it." Now certainly, these two quotes aren't representative of all the recommenders who are new to a patient's care, but they do suggest that this is going on to some degree. As I mentioned, every patient that we interviewed had spoken to their medical team about medicinal cannabis. What was the response of the medical team? "Most doctors, you mention cannabis, they shut right up. They don't say two words to you. They don't give you an opinion, nothing. They shut right up." "They're not voicing pro or against, just neutral." "They weren't confident or comfortable recommending different types or different dosages to me, given that they didn't know enough about it and there wasn't enough research. They said they didn't believe that it was harmful but didn't fully understand how it was helpful either." I find this to be a particularly powerful quote. "I vaped in front of my doctor the other day, and he didn't even know what I was doing." The next quote illustrates a emergent theme running through the transcripts, which is that of patient serving as teacher for provider. "I gave the doctor all the information I had on medicinal cannabis, and I ended up talking to a couple of his patients. And he said would you mind because they had questions." Another emergent theme was that of rigorous self-observation. Here's an example. "I'm documenting quantities. I'm looking at how I feel. I'm documenting how long it takes before I feel pain relief or before I nod out and go to sleep, how do I feel when I wake up. I have a table. I'm building up, okay, how much THC in this brand, this strain that I just purchased. And then is it an indica or is it a sativa. Put that checkmark in the table." Here's another example of some of the methodical self-observation that patients seem to be undertaking. "So I did a sensitivity test. I sent in Rick Simpsons Oil and found that it does kill my cancer cells. So now I know that it really works. What I do is in the morning, I just make a little capsule, and I put a little grain of rice sized in there because it keeps it very minimal during the day because I don't like the high. But what I found is you can use cannabidiol oil after you take it, and that buffers it. So that helps a whole lot. And I usually take depending on pain levels or how I feel or what I'm doing. You know, I might take a mid-afternoon dose. Then I take one before I go to bed." The vast majority of patients we interviewed cited the cannabis dispensary as a key source of medicinal cannabis information. Here is one example of a quote. "Sometimes I go in and I ask the dispensary employee additional questions. Like, you know, one of the things I'm having problems with is muscle spasms. I mean, they have a better feel from the reaction that other buyers had while they've gone through there." So that brings me to the end of my illustrative quotes. And now I'd like to finish with some suggested future directions. I believe that healthcare professionals should be first in the endocannabinoid system, the system on which cannabis operates. I believe that cannabis's risks and benefits should be included in medical education and in CME curricula. I believe that medical support infrastructure should routinely take cannabis into account, that professional societies and medical practice organizations should come together and issue consensus guidelines on clinical use of medicinal cannabis. I believe that we should all be advocating for a loosening of restrictions on medicinal cannabis research and that even in the absence of such loosening, rigorous bench and clinical research should be carried out on medicinal cannabis using either the federal product, studying what is happening naturalistically in the field, or carrying out such research outside of the United States. Most importantly, clinicians, whether you stand for medicinal cannabis or against medicinal cannabis, whether you feel knowledgeable about medicinal cannabis or could stand to increase your knowledge, please ask your patients routinely about medicinal cannabis use in order to help guide care in this domain. Here are my list of references. Thank you very much to our research team, to our funder, the Hans & Mavis Lopater Foundation, and thank you to you for taking the time to listen.

>> First of all, I want to thank the NIH committee for inviting me to speak on this important topic. As mentioned, I'm Steve Pergam from the Fred Hutchinson Cancer Research Center. And I'm here to talk about the risks of cannabis use for the cancer patient. I participated in clinical trials with Chimerix and Merck and do receive research money from Global Life Technologies Corporation. I will discuss neither non-FDA approved drugs or non-FDA approved indicated reasons. And I don't receive any funding from the cannabis industry at all. So I like to start with just a case just to sort of frame this question a little bit. So in this case, patient is a 42-year-old male with known pulmonary nodules. He's diagnosed with acute myeloid leukemia after presenting with fever, diarrhea, and mucosal lesions and was found to have circulating blasts. He received seven plus three induction. Went into partial remission. And then left care to seek naturopathic remedies. The returned four months later to 80,000 circulating blasts and was given ara-C and cladribine and then followed by HiDAC consolidation. After multiple neutropenic fevers, he had a couple of minor infections. And then he was referred to our transplant center for evaluation. He was a difficult HLA match because he was a Pacific Islander. And the transplant team decided to pursue an umbilical cord transplant. For those of you who work in the cancer space, that particular situation means they're at higher risk for infectious complications. And in the process of their pre-transplant workup found some small pulmonary nodules. And so they were referred to our clinic for assessment and pre-transplant screening. And this is an example of one of these small nodules, round with a small halo around it, which can be consistent with a fungal infection. In the chart, there were no reported risk factors for fungal infections. Clinically no symptoms, no chest pain, no shortness of breath, no fever or sputum production. He was on fluconazole, which is a smaller, lesser known for fungal prophylaxis for something like posaconazole, which we would normally use. Lived in Hawaii and had limited high risk exposures except to Phoenix and Tucson. Worked as a computer programmer and is a video gamer in his free time. And again, we went through this, and he had no reported history of exposures. Seen by pulmonary and felt to be low enough risk that he didn't need a bronchoscopy. So I noticed when I went into the room to talk to the patient this was the phone on his belt. And so as happens with our patients, we're asking a lot more about marijuana use. And I asked specifically about this. And his response was pretty consistent with what we often hear. Stated he had started marijuana a few months back after suggestions from a friend, stating you have cancer, you could start marijuana. And he really didn't want to stop because it helped him sleep and he believed it really helped him with his nausea. So was seeing some benefits of cannabis and prior to transplant we had to make a decision what to do. So I think the challenge here is what were the risks and what are the risks of somebody going into a transplant, in this particular situation, or who is going through cancer and chemotherapy who might potentially be using cannabis. And the big question that would always come up to me is how do you advise this patient and what would you say to individuals in this situation. So I think in this talk, I'm going to be reviewing what are the risks of cannabis in cancer patients. So what do we know about risks and what are specific ones that I can address? What are some theoretical concerns, particularly related to some fungal infections that I want to talk through? I'll talk about some specific side effects of cannabis that I think are really important for others to know and then some other issues and challenges that I think many times don't come to the forefront for people thinking about cannabis, but I think are important when planning your approach and how we think about how cannabis should be dealt with when we're talking about cancer and transplant patients. So I'm not going to go into the details of this, which is the pharmaceutical grade THC. I think these are well vetted. They're FDA approved and are not a major risk. There is a lot of data out there about these being used for various forms of support in terms of nausea and even as an alternate for people that are currently using marijuana, but I think it's important just to keep in mind that a lot of the studies that have been put forward for cannabis that are available in the literature really are focused on these drugs, and I'm going to be talking about cannabis proper, the actual plant and its use. So what are the dangers of cannabis? Well, I'm an infectious disease physician by training. And so this is the question, I think, most commonly came to me is what is the potential risk for a patient using cannabis and what were the infectious complications that patients might be at risk for? So I think when you ask -- and we did this through a survey for our staff who take care of cancer patients. What was the concern that was most often brought forward to those who were asking and had questions about cannabis? Our providers are saying that 62 percent of them, it's the highest risk issue that they'd like to know more information about and they worry about this with their patients who are potentially using cannabis. So one particular group is mold infection. So we know mold infections can be quite dangerous, particularly in patients who have neutropenia or who are going through leukemia therapy or transplant. But they can also be dangerous for patients with lung cancer and other complications. And so when looking at data that's available, Dr. Verweij and colleagues in the Netherlands, when they looked at marijuana in Dutch locations found that 100 percent of all marijuana was positive for fungus. And that compared to about 64 percent in commercial cigarettes, and those are mostly rolled cigarettes and not things like Marlboro Lights. They estimated about 300 to 50,000 times more CFUs of mold in marijuana compared to commercial cigarettes. In another study, they found that marijuana cigarettes from 26 users, 73 percent grew Aspergillus species, and spores were easily passed through an air sampler during the smoking process. They found 52 percent of the patients in that study had Aspergillus precipitins their blood, which suggests that they had significant amount of Aspergillus exposure. And that was compared to about 10 percent in controls. And Mucorales species, which are life threatening mold infections that require surgery often to control were also found in these, but less frequently in the marijuana samples that were tested. And then additionally, Moody and colleagues in Ohio tested three types of street marijuana, government prepared marijuana, piping tobacco, and cigarettes. And they found that all marijuana was found positive for Aspergillus. They pulled smoke through water and through seven filters and found that the water and the first filter were always positive for Aspergillus and only about a 15 percent reduction in spores. And multiple other fungal species have been described. As I said, Mucorales species, things like Scedosporium, Curvularia, all really highly dangerous molds that can be quite risky for patients. And this is just some examples that I pulled off line where you can actually see -- if you look up mold and marijuana, there's lots of pictures. The marijuana industry is very concerned about mold because it can ruin large crops. And when they've been collected and sort of held in containers, mold can sort of overgrow. It's a dying leaf. Like things throughout the community, we see autumn leaves on the ground during the fall. Fungus is really important to making vegetable matter go away. So if you leave these out for a while and they're older, they can develop mold. And these are just some examples. Mold in white, on the top in the red. And then some black mold that's on some of the buds here in the lower picture. So this is an interesting paper that came out earlier this year that really talked about cannabis use and fungal infections looking at commercially insured patient population. It's pretty small. They don't look into specific subgroups, but they can actually look at this and found that the adjusted odds ratio was 3.5 between cannabis users and non-cannabis users. And they adjusted for age and level of immune suppression. And so this is a really broad, very 10,000-foot view of this. But really difficult to know all of the different complications because the patients that may use cannabis may be more likely to be at risk for fungal infection. So it's very difficult to sort out whether this is a true association or not. I think something that we're all very concerned about that I think there's just not enough data, and we need more as we move forward. So other risks for infection that are clear I think are more understandable as we know a lot from cigarette smoke where we know that smoking can decrease function of alveolar macrophages. There can be injury to the cilia alone, particularly among chronic smokers. We have seen a number of high-risk pathogens that can grow and are often associated with marijuana, particularly how they're grown in the community. And particularly in edibles, that can be an issue for foodborne infections. And then smoking marijuana and other illicit drugs, we have seen an increased risk of bacterial pneumonias in HIV patients. This is just reported history in the past. But again, these are all really old data and we really don't have anything in the more modern era that suggests these associations. So I think it's a really interesting question when you're adding marijuana to a pathway for a cancer patient and they're directly inhaling this into their lungs. Depending on the method of how they use this, this could be a risk. And particularly those that are smoking joints and using pipes, I think this is particularly one that we are very concerned about. I think smoking is something that's being used quite frequently. So we did a survey of our cancer patients a few years back and found that around half, if not more, were using at least some form of inhalation as a method for using marijuana. And pipes, vaporizers, joints, water bongs and pipes were often used for most of our patient populations. So I think you see smoking as a primary method for how people like to take marijuana. And what we've heard time and time again from patients is they feel like they get more of the benefit when they smoke specifically. And so that, I think, is a particular risk that we are concerned of. Some others I think in the conference are going to be talking about vaping dangers, so I won't go into the details of this, but there is an increased risk with non-licensed products and cannabis containing products, particularly some with vitamin E. This has been well reported and I think important to be wary. It's not just this, but there are some additional dangers associated with vaping that does come up. So it's not just smoking and risk of infection but also potentially pulmonary disease that can be associated. So what about edibles? We sort of wonder. Mold probably is in foods. I think we've all eaten bread the day beforehand and then had mold spores growing on our bread the next day. But for some of our patients, this may be a bigger issue. And it's important to know that Aspergillus and other molds are not killed by boiling. Some organisms like Rhizopus grow best at actually 130 degrees Fahrenheit. There's other fungi that are more thermal tolerant. Cladosporium as an example is actually stimulated by moist heat above 160 degrees Fahrenheit. And it's been suggested in studies that if you bake for 300 degrees Fahrenheit for 15 minutes, you could kill most conidia, but you don't kill or destroy the THC component. There are no guidelines for this currently for how to create butters or oils or, for that matter, baked goods that are safe for cancer patients. And a lot of times when there are things that are available in the community, if they're made by a local distributor, you may not know how these were prepared, where our patients are getting their marijuana products. This can be quite challenging, particularly in areas where marijuana is not currently available and they're getting it through dealers or other locations. And I would say is it cooked throughout? And so the example I gave is when is the last time you had a brownie that was cooked all the way through. And if that's true, it may mean that there are potential pathogens in that that we don't know about. This is particularly important, again, for high-risk patients and for those potentially who might be eating marijuana and be neutropenic or be high risk, have a high risk for procedure. So I think there are particular situations where edible marijuana might be at risk for causing infections as well. I think there's some really interesting questions about emerging concern for Aspergillus resistance. We know that broad spectrum azole antifungal therapies frequently used for prophylaxis and treatment for mold in high-risk hematologic malignancy patients. From colleagues in the Netherlands, the first cases of resistance were really reported in the 1990s. The azoles inhibit fungal cell walls by ergosterol biosynthesis through interference with the activity of the 14-alpha-lanosterol- demethylase, which is encoded in the cyp51A and cyp51B. Most azole resistance comes from mutation in the cyp51A. It can also occur through overexpression of efflux pumps, which can reduce the accumulation of drugs in the cell wall. And so there are a couple of different ways that Aspergillus has become resistant. And why this is important is a lot of azoles are actually used in agriculture. And this is just a list of many of them that have been used for different reasons. Data from resistance is primarily from Denmark and Germany. And interestingly, the Denmark association appears to be for tulips. And so tulip farming appears to be linked to resistance. In South America, Colombia, which is also a major tulip distributor, also has seen a fair amount of Aspergillus resistance. And it's thought to be from some of these agricultural azoles being used in the tulip farming. But they've also seen resistant isolates throughout the world really. I think some of this may be related to azole use in agriculture. So this becomes important because there was a couple of studies in the mid-2000s that basically 50 samples of illegal cannabis taken from the community were tested for herbicides and pesticides. Seven different pesticides were detected, and four antifungal agents, including two that were agricultural azoles, were found. And then in the illicit cannabis industry in Belgium, again, they found a number of pesticides, some of which can be dangerous. But also things like propiconazole and tebuconazole, which are agriculture azoles that might also lead to increasing resistance to Aspergillus in cannabis. So some states have regulated pesticides, herbicides, and fungicides in the cannabis industry partially because they know one of the problems with cannabis is to have mold overgrowth where you can lose an entire stock. They are really interested in ensuring that these are not getting into that pathway and potentially leading to early resistance in these particular populations. But we don't actually know how much there is in active dealers or non-licensed distributors who may use this for prevention. And I have gone to some of the chat rooms to understand a little bit about this, and I've seen some people describe these agents being used to prevent mold overgrowth in supply stock. Just as an example, you can buy propiconazole in large quantities. You can do your own pest control dot com. But you can find these pretty easily online. And so these are not restricted in purchasing. And so there's a worry that these could be getting into other areas where marijuana is currently being used. Other things that I think are important to go through beyond some of what we've discussed in terms of risk is drug-drug interactions. THC and CBD undergo hepatic metabolism via cytochrome P450. Cannabis may increase metabolism of warfarin because of the Cyp2C9 interaction, resulting in increased plasma concentration. And potentially, a couple of case reports that have described bleeding. There is an opioid drug-drug interaction with things like buprenorphine. There's also concern with CNS depression. That can be compounded with barbiturates, opioids, and benzodiazepines. And I think this becomes more important as patients who are receiving cancer therapy are often receiving a laundry list of therapies. This can become concerning in those who are using cannabis because these small interactions can have larger effects on our patients, particularly if we don't know they're using these drugs. And I think there's one report of this. Hard to know exactly what this means. But there was a review where cannabis did affect tumor response rates in patients who were using nivolumab for advanced malignancies. And I think these are newer agents that are being used for cancer therapy. And if this is something we're starting to see -- and I think you have to wonder about how there could be potentially downside and downstream effects if we don't know that patients are using this. This is data out of Israel where cannabis is more available. But I think it's a pretty small study. It's retrospective. But I think it does suggest that we need to be cautious of these particular issues. So the other piece beyond just drug-drug interactions is the alternative therapy to proven medications. So we know that some of the patients are using for dealing with stress, coping with illness, and sleep. These are all the neuropsychiatric symptoms that our patients are using cannabis for. But we also found in our study that many were using it to treat their cancer. We found that 26 active users believed their cannabis would help to cure their cancer. And five percent of patients who were using stated it was their primary reason for use. And this is obviously concerning because if we're having patients going down this pathway, they may be using this instead of standard treatment therapies that we know are effective. That goes for psychiatric medications like antidepression medications, et cetera. But also for some of the reasons that are more important is actually treating their disease. And I think it's important because patients can be pressured for these reasons. So this is a Twitter account that I follow. And I copied this. But it said, "To be honest, I'm already sick of these sorts of messages. Yes, I have cancer. Yes, I'll be undergoing chemotherapy. And yes, I'll probably try a CBD oil as well. But I'm not going to go against the advice of an amazing medical team and countless clinical trials." And this comment from below from a colleague was, "Please don't do chemotherapy. Try CBD oil first. It's a cancer killer." What we don't want to see is we don't want to see patients choosing this over standard therapies that can be quite beneficial. So it's really important for teams to be talking about this. And I worry a lot about patients thinking that this is a pathway forward. I would encourage people to google cannabis and cancer. And a lot of what comes up are these miracle cures related to cancer and cannabis. So I think it's really dangerous to see this out there with the lay press. There is cannabis hyperemesis syndrome. The mechanism is a little unclear, but it seems to be centrally mediated. It's seen in long-term users of cannabis. It's a cyclic nausea vomiting that's made worse in the morning. Improved by stopping cannabis. You can you actually take hot showers and capsaicin cream seems to make this better. But it's being increasingly recognized in ER where cannabis is legal. And colleagues in ER have told me if they have a patient with leukemia who's in their teens or in their 20s who comes in with chronic vomiting, marijuana is almost always on the top of their differential because of the use patterns in local areas. So I think this is an important side effect that we sometimes can miss and is important for recognition and can be problematic. And one of the ways to deal with this and most importantly is to have patients stop using. A strange side effect of a drug that can be quite bothersome for patients. The other potential dangers of edibles and cannabis in general is, again, unclear dosing and serving size. I sometimes comment that I'm not sure how many bites a candy bar or a brownie actually meet the right amount for patients. If they're not taking it appropriately, they might take too much and might feel quite uncomfortable with that. And there are a lot of homemade preparations. There is no real FDA regulation for any of these products that are being made. And so it can be somewhat challenging to track. We worry about children and pets, other people in the home where they can get into marijuana products and it can be quite dangerous for some. In Colorado, there's a lot of children that were in the early phases of approval that were being taken to ERs with cannabis overuse or excess use because they were getting into candies. There's also foodborne illness. Again, I mentioned the drug-drug interactions. And then with PPI use or proton pump inhibitors, all the sort of infectious pathogens we're putting in potentially the stomach lining is not necessarily as protective so can potentially increase their risk for infections. And so again, when I think about dangers for household members, these are all cannabis products that I pulled offline. Many of these look very similar to a child. They would think these are things they could dive into and I think really could be dangerous for some particular groups. So really making sure we're communicating with our patients that they need to be cautious about use and guarding this supply, however they're using it, particularly as these are becoming quite like the real thing and look very appropriate for kids to dive into. I think there's also the legal risk. Cannabis is not legal in every state, and so patients may get cannabis from dealers and risk fines and may get into legal proceedings, which are important and can be quite traumatizing for patients. There's always the risk of driving while high on the way to clinic or another location. That can get our patients into trouble. There's dangers for work job restrictions and testing. So some people who work in different jobs may not have communicated with their employers that they are undergoing cancer therapy. Soldiers or security guards, doctors and nurses, school teachers, truck drivers, et cetera may undergo work testing and can lead to complications and loss of job if they're not careful. So having these conversations upfront, particularly in areas where cannabis is not legal, I think is critical when you're talking about this with patients and can be a real downside to cannabis at the moment. And then I think what we don't really talk about a lot is cost. Cancer care premiums, deductibles, coinsurance, copayments, many of these are $10,000 per month for some patients. It can be quite expensive, even with good health insurance. And it exposes patients and families to significant out-of-pocket healthcare expenses just to take care of their primary disease. Cancer and bankruptcy are often tied together because of the cost. Cannabis is an extra cost, but it's not covered by insurance. So this all out-of-pocket cost. And just to give you some examples that I pulled from some internet sources. An ounce of high-quality cannabis in Seattle is about $234 an ounce. If you go down, it goes down to 170 for low quality. In D.C., you can add an additional 200 for all those costs. So it's very different in the different states. And there's also a fair amount of taxes that are put on these in state locations because they're using this as a potential source of revenue in some locations. It does drive patients, because of costs that are in the distributors or medical marijuana facilities to go to dealers rather than medical/recreational distributors. And this has actually been shown in a study in Michigan where it is medically legal. And they found that more patients who were using cannabis were using it from community sources and not from medical marijuana distributors for two reasons. One, they didn't want to tell their providers and two because the cost was less. An example. This was a box of mints that I was given by a colleague. It's called Mr. Moxey's Mints. These are 100-milligram THC per tablet. And this is a box of Altoids. You can see the difference in price. That may not seem like a lot, but that's 20 servings. It's a small amount. And depending on how much you're taking, you may be taking multiple to get the right amount of THC content that you need. So it can be very varied for the different potential costs that would be involved in this. I think it's important to consider when you're talking to patients about this and a definite downside to cancer therapy and marijuana use. And again, I just point out that this is really hard to see. So if you're a kid looking at this, this looks like Altoids. They do look different on the inside. They're individually wrapped. But you can see how this can be dangerous again in that situation. So I think I'll stop there. I don't want to go over time too much here. I just want to thank my team who spends a lot of time on this, particularly Jesse Fann, my psychiatric colleague and Christine Lee who works in the alcohol and drug abuse group at the University of Washington who's helped a lot with these products. And I'll be happy to take any questions at the end once we're all at the meeting. Thanks.

>> Hello. I'm Donald Abrams from the University of California San Francisco. And I am here now to talk about benefits about cannabis use for the cancer patient. I greatly appreciate the prior presentation by Stacey as well as the NCI for putting on this conference altogether. I think it's really important. And my talk today will be sort of an introduction to other talks that are going to be upcoming in the next two days. Next slide, please. I am a scientific advisor to two companies and have stock options with these. It did not impact on the presentation that I'm giving at this time. Next slide, please. So this Siberian ice princess is a mummy that has been well preserved, found in Siberia. And under an MRI, she appears to be a young woman in her 20s who has metastatic breast cancer involving bone. And around her waist is a belt, at the end of which is a pouch in which are found the flowers of the female plant of cannabis sativa, suggesting to the anthropologists or archeologists, whoever makes these hypotheses, that this young woman was perhaps using cannabis 3,000 years ago to treat the symptoms of her cancer or perhaps even the cancer itself. I think this is the sort of big leap that we see on the internet because we don't really know that everybody in this tribe was not buried with a pouch of cannabis around their waist. Next slide, please. So when we look at symptoms that cancer patients experience, and I think, again, Stacey really enumerated all of them quite well, related to appetite, pain, anxiety, depression, and I would add insomnia, which we mentioned already as well today, and then nausea and vomiting. Clinicians do have one intervention that we could recommend to patients rather than prescribing four or five different medications that may all interact with each other or with the chemotherapeutic agents that we're giving the patient. Next slide, please. So I was one of the 16 folks on the committee from the National Academies of Science, Engineering, and Medicine. And in the single chapter on therapeutics, we reported that the strongest evidence that we found really for the use of the cannabis and cannabinoids was in adults with chemotherapy-induced nausea and vomiting that oral cannabinoids were effective antiemetics. Again, we also felt that in adults with chronic pain, certainly relevant to our cancer patients as well, patients treated with cannabis or cannabinoid are more likely to experience clinically significant reduction in their pain. Next slide, please. The analysis or the meta-analyses that we use really are numerous meta-analyses available of the large number of studies done with delta-9-THC products, nabilone and dronabinol in the '70s and '80s. And these studies which demonstrated that cannabinoids were more effective than the then available antiemetics again have been widely analyzed and reanalyzed. And a Cochrane Review a few years back that included 23 of these randomized control trials concluded that cannabis-based medications may be useful in treating refractory chemotherapy-induced nausea and vomiting as well. Interestingly, the three most recent meta-analyses and systematic reviews of systematic reviews are all much less enthusiastic about the efficacy of the cannabinoids in chemotherapy-induced nausea and vomiting, although they are still evaluating and analyzing the same studies that were done in the '70s and '80s. Next slide. One might ask then we know that delta-9-THC has been approved for this indication. Where are the controlled trials of cannabis? Well, because of the barriers that have been mentioned already in studying the botanical itself, there are only three controlled trials of cannabis in chemotherapy-induced nausea and vomiting in the medical literature. And in two of them, cannabis was only made available after dronabinol failed, so not likely to be effective. The third is a randomized double blind crossover trial in 20 cancer patients, the results of which I find difficult to interpret. Nabiximols is the whole plant extra one-to-one ratio of THC to CBD delivered as an oral mucosal spray. Was studied in addition to standard antiemetics in 16 patients with cancer. And it was demonstrated that compared to placebo, the nabiximols was more effective as an antiemetic. There was recently a paper published from Australia in the Annals of Oncology just very recently again suggesting that a one-to-one THC to CBD capsule added to standard antiemetics was preferred by the patients and more effective than placebo in further reducing chemotherapy-induced nausea and vomiting. I point out a study that was in the gastrointestinal literature. Not looking at cancer patients, but 153 outpatients presenting for a GI evaluation were asked to rate 29 antiemetics with the mean efficacy score of all of them as a 1.73. And you can see that after adjustment, cannabis actually rated higher than ondansetron and other currently available antiemetics. Interestingly, in my practice, my patients find that ondansetron leads to significant constipation. And I think if you have cancer and feel that part of you is dying or that you are dying, the ability to move your bowels regularly is something that is much desired. So I have many patients who have foregone the use of currently available antiemetics that we prescribe in favor or using cannabis. Next slide, please. This is just a sample of an email in the days when I had to write recommendations for patients to access cannabis. We no longer do that in California since we have adult use since 2018. This is a 48-year-old gentleman with metastatic colon cancer asking for an extension. "Although I did not use it until my last five sessions of chemo, me getting over the stigma of its use, it did what no other drug could do, completely solved the severe nausea I had. It allowed me to play with my children, attend their sports and school functions, and just function very normally in day-to-day activities. Cannot thank you enough for giving me that option. I'm currently on a chemo vacation after a clean scan, and the only time I use medical marijuana now is when I have trouble sleeping. I would like to continue to use it for that purpose instead of relying on pharmaceuticals." And again, the National Academy's report, we found second level of evidence below the more substantial ones that I first showed that cannabinoids, particularly nabiximols, is useful for sleep. Next slide, please. Unfortunately, my parent organization, the parent organization of many of us, the American Society of Clinical Oncology, had an expert committee meet a few years ago. And they recommend FDA approved cannabinoids, dronabinol or nabilone, to treat nausea and vomiting that's resistant to standard antiemetic therapies, claiming evidence remains insufficient to recommend marijuana in this setting. I find this unfortunate. Next slide, please. What about appetite? We know that the endocannabinoid anandamide in low concentrations in mice leads to a potent enhancement of appetite. It's felt that the cannabinoid 1 receptors are implicated in food intake control. And in mice who are genetically programmed not to have a CB1 receptor, they tend to eat less than wild type littermates. So it's felt that the cannabinoid one receptors involved in the motivational or reward aspects of eating. Next slide. Well, the best data that we have on the cannabinoid that is delta-9-THC and appetite stimulation in adults with cancer-associated cachexia-anorexia comes from probably one of the largest studies of dronabinol comparing 2.5 milligrams twice a day to the progestational agent megestrol, which is an appetite stimulant but predominantly produces water weight, compared to the combination of the two. And you can see that dronabinol was inferior to the progestational agent in increasing both appetite and weight. And when you added the two, the dronabinol seemed to decrease the effect of the progestational agent. This is why in the National Academies of Science, Engineering, and Medicine, we did not find particularly strong evidence that the isolated cannabinoid dronabinol increases appetite. However, most people who went to college appreciate that using cannabis, the whole plant, does produce something that used to be known as the munchies. So again, it's the difference between the whole botanical versus an isolated cannabinoid. There was a smaller randomized control trial of dronabinol alone in cancer patients that demonstrated enhanced chemo sensory perception of the food. It looked better, tasted better, smelled better. Appetite improved and calories increased, but the patients did not gain increased weight. Next slide, please. There have been two other more recent studies, a randomized placebo controlled nabilone in 47 outpatients with non-small cell lung cancer. After eight weeks, the nabilone patients again increased their caloric intake and had higher intake of carbohydrates compared to placebo. They reported significant improvements in quality of life with regards to role, emotional, and social functioning, improvements in pain and insomnia, but no statistically significant increase in weight using the isolated cannabinoid. A small Israeli study also looked at capsules containing more THC than CBD in patients with cancer over a six-month period. Of the 17 patients who began the trial, only 11 remained on the study for more than six weeks. And only six completed the six months. And that is who we have the information presented on. In that, those six, three gained greater than equal to ten percent from their baseline weight and three had stable weights. Patients reporting improved appetite, mood, quality of life, and again less pain and fatigue. Again, a very small study, but perhaps suggests other evaluation. Next slide, please. So CBD as mentioned by one of the earlier speakers has really taken off and caught the world by storm. And the question that I'm often asked by my patients again is what's the right ratio of THC to CBD that I should use for appetite, for sleep, for pain, for anxiety. And the answer is that we don't know because there hasn't been a lot of research looking at any other combination of CBD to THC other than one-to-one. But in the Netherlands where people can access cannabis from pharmacies, they have two high THC chemovars and one that's more balanced or slightly greater CBD. And what they found was that the lower THC patients reported less appetite stimulation. So it appears THC is what's modulating appetite perhaps. And this is supported by a very large study from the app Relief App where 3,300 people were asked to rate symptom improvement on an 11-point scale, zero to ten, across 27 measured symptoms. And most of the patients participating were using dried flower, i.e. the whole botanical. And this was felt to be associated with greater symptom relief. Only higher THC levels were associated with greater symptom relief as well as the prevalence of positive and negative side effects. And CBD potency levels were generally not associated with either symptom change or side effects. Next slide, please. So certainly pain is an area that we're all quite interested in, something that cancer patients often experience. Elevated levels of the cannabinoid 1 receptor, like the opioid receptor, are found in areas of the brain that modulate processing of noxious stimuli. And CB1 and CB2 agonists also have peripheral as well as central nervous system actions. And cannabinoids, as well as terpenoids and flavonoids in the plant may also have anti-inflammatory effects. It's interesting that the analgesic effects of the cannabinoids are not blocked by opioid antagonists. The largest body of evidence supporting cannabis as an analgesic is in patients with neuropathic pain. Particularly, most studies have been done in patients with HIV-related peripheral neuropathy, but there is a small study in diabetic neuropathy. And certainly pre-clinical data suggests that cannabinoids may be effective in chemotherapy-induced peripheral neuropathy as well. Next slide, please. So there is only one study as yet reported in the medical literature of again nabiximols in 16 patients with chemotherapy-induced peripheral neuropathy. And this was, again, another placebo-controlled crossover trial where panel A shows that there was in fact no difference between nabiximols and placebo. However, the investigators did a so-called responder analysis. Five of the patients did report a greater than two-point drop in their pain on a zero to ten scale, averaging 2.6. The number needed to treat for one to have a benefit then is five, which suggests that this should be further studied. And they're currently, if you look at clinicaltrials.gov, there are two studies ongoing looking at cannabinoids in patients with chemotherapy-induced peripheral. Next slide, please. Nabiximols, which is not yet licensed and approved in the United States, did not fare too well in patients with cancer pain and non-neuropathic symptoms. Six randomized controlled trials were identified for a systematic review and five for meta-analysis of nabiximols in cancer pain. And what was discovered, there was no difference really between nabiximols and placebo for the difference in the change in average pain scores. And this finding remained when only phase three clinical trials were included, as shown in the forest plot below. And the cannabinoids had a higher risk of adverse events compared with placebo. Next slide, please. Our group studied the potential pharmacokinetic interaction between cannabinoids and opioids, looking at 11 patients on sustained release morphine and 10 on sustained release Oxycodone and exposing them to vaporized cannabis three times a day before and after, doing the 12-hour pharmacokinetic curves. On the left in panel A, you can see that morphine plasma concentration absolutely decreased a bit after exposure to the vaporized cannabis. But the error bars cross, so it was not statistically significant. The Oxycodone curves were inclined. So if the level of the opioid either decreased or stayed the same, we would expect the pain to stay the same or increase. And in fact, we found overall in the 21 participants their average pain score on day zero was 40 and it dropped to 29. So that was a significant 27 percent reduction in pain with a greater reduction in the morphine recipients compared to the Oxycodone. Again, this study was a pharmacokinetic interaction study only powered for safety, which we saw, and not for its effect on pain. But again, suggesting that cannabinoids may be synergistic with opioids, something that would be beneficial for our patients living with and beyond cancer. Next slide, please. And again, this study in Israel, patients receiving botanical cannabis get a license and they're asked to complete questionnaires and surveys. And this study that was published showed that at baseline, first obtaining their cannabis, 53 percent reported pain in the eight to ten range whereas only 5 percent reported that at six months. And you can see that the symptoms that patients had at baseline were generally ameliorated significantly by six months. I'm one of the editors of the NCI Integrative, Alternative, and Complementary Therapies website. And I submitted this for discussion and inclusion onto the webpage. I missed the conversation that the committee had about it, but I was told that it was elected not to include it because there was potential for bias. And the issue here and in doing any observational study is how do we know that it was the cannabis that led to the improvement of these symptoms and not the fact that from baseline to six months the patients were actually cured of their cancer, and that's why they had less pain, nausea, et cetera. Interestingly, again, it was also noted in the study something that's been reported in other situations, that of those who are on opiates at the onset of treatment, a third stopped their therapy and ten percent decreased the dose. Next slide, please. So let me just conclude with talking about this issue of whether or not cannabis cures cancer because this is certainly something that I agree is a risk and something that pains me to see in patients who have waited a number of months to consult with me in clinic who are treating a potentially curable malignancy, foregoing conventional treatment to use highly concentrated oils of THC or CBD. And now they're metastatic and can't be cured. This social media issue has really been a problem because as you can see, more people are searching for these fake news stories compared to those who are actually looking at the reality of the situation. Next slide, please. So I looked at a group that feels that cannabis has a role in curing cancer at the isolated case reports that they suggested were convincing. Click, please. The one that seemed to the most easy to accept or potentially agree with was two young girls who had partially resected pilocytic astrocytomas. These are unfortunately malignancies or fortunately for the patient that may resolve spontaneously. Their astrocytomas were resected only partially at age 11 and 13. And over the next three years, they were stable or slightly progressed. And then three years after that, both of these young women now achieved complete remissions. And the only thing that they had in common was that they were using cannabis daily. I don't know. Again, because this is a malignancy that could regress spontaneously, it's a little unclear as to the contribution of the cannabis. Next slide or next click. This clearly is a patient who had ALL refractory therapy. Went into hospice and started using a hemp oil. Her blast count decreased, but ultimately she died of neutropenic colitis and a perforated colon, so I don't consider that to be a cure. Next. This is a 44-year-old gentleman who had a recurrent right buccal squamous cell carcinoma and a wound that was malignant that wasn't healing. He applied topical THC and CBD and sunflower oil and achieved rapid analgesia of the painful wound and a five percent decrease in the size of the wound but ultimately died. So I don't consider that to be a cure either. Next slide. Two 38-year-old men with glioblastomas, one had an oligodendroglioma, were treated with chemo and radiation and received CBD with good clinical response. But these two patients had conventional cancer therapy. Next slide, please. And then finally, there's an 81-year-old gentleman who had a left lower lobe adenocarcinoma who didn't want chemo. Treated himself with CBD oil and reported decreased size in tumor and lymph nodes but ultimately did not cure his cancer. Next slide. Next click. There are some published case series as well. In London, they collected data on 119 patients at a clinic over a four-year period who were receiving pharmaceutical grade synthetic CBD oil. Again, at a very low dose, ten milligrams twice a day compared to patients in the previous slide. And they reported clinical responses seen in 92 percent of solid tumor patients. But most of the patients also received standard therapy. Only 28 received CBD alone and no data is presented on those patients. They concluded that CBD is a candidate for treating breast cancer and glioma patients but without evidence to support that. Next slide. The other series is nine consecutive brain tumor patients in Vienna who received pure CBD at a dose of 400 milligram capsules in addition to standard therapy with resection followed by chemo radiation. Six of the patients had the most aggressive glioblastoma and three had lower grade tumors. The investigators state that the median glioblastoma survival is 14 to 16 months and the mean in their series is 22.3 months, which is longer. But they also are including three patients who had less aggressive tumors. So this is not impressive in my mind either. Next slide. The first interventional study was done by Manuel Guzman, my friend and colleague from Complutense University who we'll hear from yesterday where he dripped THC into the tumor via a catheter in nine patients with recurrent glioblastoma in the Canary Islands. He reports that the treatment was well tolerated if you don't mind having a catheter in your brain. But there was no different effect on survival from chemotherapy alone. He did show that in vitro THC inhibited the proliferation and decreased the viability of the glioblastoma cells. And it was later demonstrated that CBD enhanced the inhibitory effects as well. Next slide. And again, we're going to hear in a few days the update on this study, which was done with nabiximols and placebo in association with dose dense temozolomides in patients with recurrent glioblastoma reporting an 83 percent one year survival compared to less, I believe it's 44 percent. Statistically significant. Published as an ASCO abstract but not yet in the medical literature. A smaller study or a study of 60 patients with CBD was taken under consideration in Israel, but the investigator closed the study after only enrolling four patients because accrual was difficult and he saw no response. Next slide, please. There is again a study that Manuel Guzman and his group will conduct. Again looking at a THC/CBD combination in association with standard therapy in patients with glioblastoma. Next slide. Dylan Zylla in Minneapolis is doing a study of patients who report that cannabis has cured their cancer. And this is a national survey analyzing the impact of cannabis use on tumor control among patients with metastatic cancer who believe that their anti-cancer benefits have been achieved through the use of cannabis alone. www.catasurvey.com is what he's offering patients as a platform to share their stories. And they will then do a chart review to ascertain whether or not this is correct information. Next slide.

>> Dr. Abrams, we're going to need to wrap up so we have time for the panel discussion.

>> I'm just concluding. So one of the things that I think is interesting is that we don't really know what overexpression or underexpression of the CB1 and CB2 receptor mean in different tumors. Sometimes, it means that it's of benefit. And sometimes, it means that those tumors are more aggressive. Next slide. I'm just at the end here. The Israeli group also demonstrated that different cannabis extracts from whole plant have different effects on the same tumor but from different cell lines. So that makes this question of whether or not cannabis is going to have an anti-cancer effect also difficult to get our head around. Next slide. So again, as we heard, the oncologist's main concerns are pulmonary Aspergillosis. I've been an oncologist for 38 years. I've never seen a case in a cancer patient in San Francisco. I think a nice study, a case controlled study on HIV patients showed that cannabis use was not associated. I do worry about the drug botanical interactions. And particularly for my patients using highly concentrated CBD and THC oils, that it may impact on their cytochrome P450 and the metabolism of the cancer therapies that we're prescribing. And finally, again, we're going to hear more on the immunotherapy issue that was previously mentioned that nivolumab, both the response rate and also now the survival may be impacted in the patients who use concurrent cannabis. Next slide. In conclusion, then, despite a dearth of public evidence related to various research, botanical cannabis may be a useful adjunct to standard treatment in alleviating side effects of cancer and its treatment. Next slide. Despite promising pre-clinical findings, there's no convincing evidence in the medical literature today supporting anti-tumor activity of cannabis or cannabinoids. Next slide. CB1 and CB2 assessment of all tumor specimens might be something to do in personalized medicine so we can understand better. Next slide. More research should be done exploring the direct impact of cannabis-based interventions on malignant tumors. Next. Oncologists' concerns about the use of cannabis during cancer treatment, in my opinion, can be largely allayed. And finally, additional research and education is always warranted. With that, I'm done. Thank you.

>> Thank you so much, Dr. Abrams. And thank you to all the speakers. I'm Andy Freedman from the NCI and along with my co-chair, Dr. Ilana Braun from Dana-Farber. Ilana and I have some questions lined up, and we'll try to get some things from the chat as well. So a question to all of you, and we'll start with Stacey and then go around. Ilana will be both a co-chair of this session and a panelist. Could all of you speak to the major evidence gaps that need to be filled to understand how cannabis should be used most appropriately by cancer patients? What type of studies need to be done? What types of barriers and challenges must be overcome? From each of your perspective. Stacey, could we start with you?

>> Sure. Can you guys hear me all right?

>> Yes.

>> All right. So I would say since I'm not a researcher, I'll come from this more from a patient perspective and from my own personal experience. Study-wise, I couldn't tell you, but I think as a patient it would have been nice if the doctor had more evidence for me as opposed to me having to seek out my own evidence. So I had to read a lot of pre-trial studies online myself to learn what I knew and what I found out. And even all of those studies that I read are very preliminary and they don't really have any firm conclusions. So from my side of things and for all other patients, I'm sure they feel the same way, it would just be nice if the healthcare side of things could provide us the information so that we didn't have to go out of the way to almost teach our doctors something and feel like we have to convince our doctors that this was the right decision for us.

>> Great. Thank you, Stacey. Could we go to Ilana?

>> Sure. Can you hear me okay?

>> Yes.

>> Okay. Great. So when I think about the types of evidence that we as clinicians hold dearest, it's evidence of our agent of interest and our population of interest. And before I go on, I want to amplify two points. First, that bioactivity comparisons between, say, purified THC and whole plant cannabis are speculative because cannabis is not one active ingredient but hundreds of active ingredients that act through complicated, synergistic, and inhibitory interactions that we term entourage effects or ensemble effects. And while some of what is available through cannabis dispensaries is probably pretty purified THC, particularly, say, the concentrates used in vaping devices, the bread and butter of what cannabis dispensaries offer is still whole plant, full spectrum cannabis products. And so when I think about the clinical trial evidence collected in, say, the last two decades for full plant cannabis in cancer patients, I don't come up with a whole lot. Some studies jump to my mind. The 2006 Strasser study that I believe Donald referenced which looked at whole plant cannabis taken orally for anorexia-cachexia. And unfortunately was a very ambitious study, but lots of people dropped out. And an attempted analysis showed no effect. I think a Grimison study published just last year for chemotherapy-induced nausea and vomiting, again a very ambitious study. And it was a crossover trial that really did seem to work. And then I don't know if you include nabiximols studies in this as full spectrum cannabis products. I would argue as pharmaceuticals they are not. You don't use nabiximols the way you would use something you buy at a dispensary. But there are all those nabiximols studies for cancer pain. And of course we know from qualitative and survey research that patients are using cannabis for many indications, chemotherapy-induced nausea and vomiting, anorexia-cachexia, pain, mood, sleep, quality of life, and as cancer directed therapy. So we need trials in all of these domains. And then slicing the data a different way, we know that research has demonstrated that cancer patients use cannabis products through a wide variety of modes of administration, from sublingual to oral to vaporizing to vaping, from smoking to topical applications. Even rectal suppositories. And yet, when we examine the clinical trial evidence in oncology, by and large what we see is oral and sublingual modes of administration exclusively. All this to say is when I think of next steps, I think of this. I think we need additionally rigorously conducted clinical trials of whole plant cannabis for indications cancer patients are frequently targeting. I think we need comparative efficacy trials between different modes of administration. And I certainly think that there are methodologic hurdles. I don't think it's easy to do whole plant cannabis trials. My understanding is that concentrations of active ingredients at the top of a single plant and the bottom of a single plant are very different. So I understand there are certainly problems, but I think we still need to tackle this kind of research. And I do believe that once we have clear clinical evidence, the oncologic community will act on it. I find the oncologic community to be some of the most evidence-based clinicians out there.

>> Great. Steve, do you want to add your perspective?

>> That was sort of the tour de force of everything that's needed. I'm going to focus a little bit differently, I guess, on sort of some of the other issues. I think some of the challenges, as Ilana said, we need randomized clinical trials to better understand what we need to do next. That's what's going to drive change within the oncologic community. I think it's helpful patients can have these conversations with their providers, but without data it gets really difficult. And I think the biggest roadblock to this is our inability to do these studies. The funding sources are not necessarily focused on this. And doing work with what is still considered a level one drug makes this difficult even in cancer populations. So I think some of the challenges are just sort of the roadblocks that exist within the current structure in doing clinical research in this space. I think it will be really important to better understand in these trials, and one thing that I sort of advocate for is how we can look at negative outcomes as well. I think that will be the really great piece about this is doing clinical trials in ways that you're doing placebo controlled, you have the ability to look at complications that we think might be existing but we don't know are linked because those are hard to do. And you can actually compare and contrast in high-risk populations to see is the difference really there. So I think these are the kind of things that are going to make oncologists and those in the community who are providing access sort of that safety data. I think, finally, some of the things that are really critical is really looking at some of the data about the methods of administration and the appropriate dosing for patients. And that may be very different for patient populations. I think we don't know enough about individual responses, both in the different cancer communities and then within individuals, about how they respond to this. I think many of us can describe stories of patients who use cannabis and have negative side effects or don't like using it and then others that have great benefits. So I think understanding the individual differences in how cannabis can affect individual patients will also be really important. So some of the pharmacokinetic studies will be super interesting as we dive more into this. And I think a lot of that's going to be important as we have more ability to do these kinds of studies.

>> Great. Thanks, Steve. Donald, do you want to comment on major scientific evidence gaps and the types of studies that we need to still do?

>> Just want to respond to Ilana that, yes, oncologists are the most demanding of evidence because we deal with a very serious disease and we use very sort of potentially toxic agents. So I believe that the degree of evidence should be directly proportional to the potential for the intervention to do harm. So if I'm going to say take this new chemo and your hair's going to fall out, your bone marrow's going to be suppressed, and you're going to vomit for three days, you want the evidence. But as an integrative oncologist, if I say eat more blueberries and get a massage twice a month, how much evidence do you need? And how do you do placebo blueberries or massage? Well, I'm putting cannabis with blueberries and massage. It's a botanical that's been around for 3,000 years. And I think our attempts to pharmaceuticalize it are going to fail. It's very difficult to do randomized placebo-controlled trials of inhaled cannabis. Whenever I submit one, the reviewers say it wasn't placebo controlled. Your patients know if they're inhaling cannabis or placebo. I wrote a paper, should oncologist recommend cannabis. And the bottom line of my abstract was I don't think that this is an intervention that requires a package insert. I think patients are going to figure out how to use cannabis just as the ice princess did 3,000 years ago. So I'm not sure that we're going to make a lot of progress doing symptom management studies of the plant. Where I'd like to see more research is does cannabis have any anti-cancer activity. And I think that's something that we can start in the lab and in pre-clinical work and then move on to some clinical trials.

>> Great.

>> Maybe I will on behalf of some of our attendees ask some questions that came in through the chat box. Stacey, we're all so thrilled you joined us today. I think you really conjured for us and brought to life what it means to use cannabis medicinally. Some of the questions that came your direction are how did you handle this in the dorm? What was the agreement with the university around cannabis use through cancer treatment? How was it messaged to your peers? And then a second question, which maybe you could answer them all, is how well did CBD products work and how well did THC-based products work for you? Which worked better, particularly for chemotherapy-induced nausea and vomiting.

>> Yeah. Yeah. Thank you guys for the questions. The first one's great. So there was a dean that lived in the dorm with all of the students. And I just happened to be close with her. And I just went into her office one day and spoke with her. Told her I was diagnosed with Hodgkin's lymphoma. And I told her that I had plans to become a medical marijuana patient and that I would have vaping cartridges, and that's totally not allowed in university dorms. It was a brief conversation. She kind of just said if you don't tell anyone, I don't tell anyone. I guess it's not a great thing to say, but it's the truth and it's how it went. Cornell University at large never found out. But if anybody here is from Cornell, they know now. [Laughter] But it sucks that I had to be that way. But I never abused that power because I didn't go into the situation with any bad intentions other than helping myself. It was a very down low agreement, I guess, between us. I always tried to be respectful of the fact that I didn't want to cause any issues within the dorm. So that's the first question. I don't remember the second one, Ilana. I do remember the third one. I don't know if you want me to just get to it.

>> Yeah. I think you've answered one and two, so now you're onto three.

>> Right. So the third question. I did use the different products for different purposes. So I would take the CBD oil usually in the morning for anxiety, depression, and potentially appetite, but honestly I can't even remember at this point. I would say that just helped with my calm overall and my mindset whereas I would consume the THC dominant products at night usually to help with sleep, nausea. To the extent with which they helped, I think they were helpful. At the very least, it could have been a placebo because I thought I was doing something for myself. But I do also think that the products were generally helpful with my appetite, certainly with sleep, and just overall helping me get through it. But I have no control in my own experiment, so to say, to know whether or not it was definitely helpful or I just felt that I was helping myself. But I'm led to believe that it was a little bit of both.

>> Great. Thank you. Now we have a series of questions that came in for Steven. I think Donald may want to weigh in as well. It sounds like if we're choosing to use cannabis in the cancer setting, how can we use it most safely? So first of all, how can we store it most safely? And I hope I'm not going to butcher this word. What do you think about using Boveda humidifiers or vaporizing it with filters or water filters versus smoking, let's say? How can we store the product most safely? Also, if you could weigh in on how safe you think it is to vape now using formal sources of cannabis, so dispensary purchased cannabis.

>> Yeah. Maybe, Donald, I can go first, and then you can comment. It's a lot packed in there, so let me make sure I get all these questions. I'm going to start with the last one first. I think the real danger from vaping was clearly in these sort of products that were being developed in the community where they were using devices and filling it with all kinds of vitamin E and other things like that that caused major complications. I do think that vaping in general can have some long-term effects, but the data really isn't super well known. I think there's a lot of studies going on looking at vaping as an overall issue related to tobacco or any other products that are used to understand what long-term consequences can be. I think it very much has to do with the amount of vaping you're doing. If it's on occasion, maybe once or twice a day, it may not be as high of a risk. But I think depending on how patients are using it, that may be varied. And I think the pulmonology groups are looking at this very carefully. I think there actually may be a talk later that reviews some of the details around this. I think in terms of the other questions, one is sort of how can you sort of deal with your marijuana safely. In general, I can't give you advice about that particular product because I don't know it. It's a humified container. And I was sort of chatting with people in the chat room about this. I don't know enough about it. I do know that humidity can support the growth of mold, but there's no perfect method for storing cannabis that I'm aware of that can protect it from mold growth because all dying plants eventually grow mold. And so it's varied. I would say that some people have suggested going to reputable dealers that their stock is overturning on a rapid basis because the longer it sits there, that might potentially be risk. But frankly, I don't know the answer for the best way to manage it. In some ways, I've actually reached out to marijuana distributors, what they tell patients, to have a better understanding of what that is because I think they have more knowledge than we do. I think that's a really key piece is that some of the things that we talked about about cannabis, unless we're talking to those who are some of the people using it or involved in it regularly, it can be really hard to know what to do. And since I'm not a user personally, I can't speak to how these products are used and the potential risk. But in general, when I think about risk for cancer patients, I like to propose edibles and tinctures and oils first because I think the risk is less. And I think smoking can potentially, if anything, is associated with more risk. And if they are smoking, I do generally recommend that they use vaping devices or that they use filters on their water pipes, if possible. And that's generally the approach that I take.

>> Thank you. Donald, in our last two minutes, any points you'd like to weigh in on?

>> Well, I just want to make a distinction between vaping and vaporizing. I think vaporizing is inhaling combusted or not combusted but heated plant material. Vaping, which I'm very much against, is inhaling oils. We know the long-term effects of inhaling plants over thousands of years. But these oils are problematic. I believe that if people want more control over the onset, the depth, and the duration of the effect that inhalation is probably better than oral ingestion. And as an oncologist who's really concerned about sugar, I don't think edibles are medicine. I think edibles are mainly sugar, and I'm concerned about the effect of sugar intake on cancer. I do like tinctures and oils because you get a sort of hybrid kinetics between inhalation and oral ingestion because when you put a liquid in your mouth, you immediately absorb some sublingually, which reproduces inhalation, and then you swallow the rest. So I think that tinctures and oils are probably the best route. As far as storage, that's not in my wheelhouse. I'm not a cannabis storage expert. Sorry.

>> And that brings us to the top of our hour. I thank all of our panelists for participating. I thank my co-chair, Andrew Freedman, for organizing this wonderful symposium. And I thank the NCI. My hat is off to you.

>> Thank you all.