Sean Fearns: Ladies and gentlemen good day and welcome on behalf of everyone at the DEA museum and DEA demand reduction, cumulatively our community outreach. We want to welcome you today as we continue our fall lecture series. The museum often brings together topics that are literally ripped from the headlines, and you cannot argue that opioid addiction issue and the growing problem of opioids leading heroin, moving across the country and getting a lot of news coverage. Our opportunity today is to bring in some nationally renowned experts from all over the country, moderated by a very good friend of DEA, but himself an expert Dr. Mark Gold. Let me take a moment and introduce him.

I'll say just for those that are in the audience if you could please silence your electronic devices so that they don't disturb your fellow participants. A special welcome to those who are watching via our live webcast from around the world. If you have questions for our moderator and panelists please feel free to hold those to the end, we will have an opportunity before the program concludes for you to ask questions. If you're here in the audience in the room, please wait for a microphone so that your question can be broadcast to those watching on the webcast and if you are watching us via the webcast there's a button down in the bottom for you to submit a written question to be read here in the room.

Let's being by introducing you to Dr. Mark Gold. He is a translational researcher, author and inventor, best known for his work on brain systems underlying the effects of opioid addiction dependence and withdrawal, changing the way that opioid action was understood. What makes this very interesting is that he proposed these ideas back in 1978, certainly a man that's been ahead of the power curve on this one. During the '80s Dr. Gold developed a new theory for cocaine action and dependence, also proposed a dopamine theory for pathological attachment, has worked for more than 30 years trying to understand overeating as it relates to drug abuse and addiction models.

He has served as a consultant to the drug [ARS 00:02:15] office, the Office of National Drug Control Policy, the National Institute on Drug Abuse, DEA, other government agencies, professional sports and CASA at Columbia University. Most recently is has completed a 5 year state department study on opium and the children of Afghanistan. Please join me in welcoming Dr. Mark Gold who will now introduce our panelists.

Mark Gold: It's a great pleasure to be here and bring together such a esteemed panel of experts and discuss a problem that as Sean said is in the news and is really critical. This is the announcement that went out and these are the speakers. The main speakers are Dr. Ted Cicero and Bill Jacobs and I'm the moderator. I'll add a few points of of color here and there and also some context. Ted Cicero is the

John Feighner professor of psychiatry at Washington University in St. Louis. He's a faculty for 45 years. He's the author of over 200 scientific articles in the field of substance abuse research and generally a great person who's done really the seminal work in this area of the opiate overdose epidemic, prescription epidemic and then the most recent work, here in the New England Journal of Medicine literally last month, showing that the prescription opioid epidemic morphing into the heroin epidemic.

When I read this paper, and we'll hear in great detail from him on it, it reminded me of a finding that one of my colleagues called me about in physician addiction. We've worked for many years, I've worked since the 1970s on physicians who become addicts and we intervene and send them to treatment and monitor their treatment progress. Physician addiction treatment has been used as an example that treatment works since over 80% of physicians in treatment return to work and have negative urines. However the physician addicts of the 1970s were mostly alcoholics, alcohol misuse and alcoholics. We reported about 10 years ago on physician prescription misuse, which is disproportionate to other use, and when you match physicians with lawyers or other similarly matched controls the misuse of prescription medication is quite high amongst physicians. We reported that in the Harvard Review of Psychiatry. Most recently colleagues from physician impairment programs have been reporting medical students and other physicians who have also morphed from prescription misuse to heroin as predicted and reported in Ted's recent New England Journal paper.

Bill Jacobs is the medical director at Buff Plantation, associate professor and chief, the first chief, of addiction medicine in the Medical College of Georgia, has a recent article in the Atlanta Journal Constitution saying something like "How could we ever solve the opioid crisis without physicians trained in addiction medicine." Most people haven't focused on this issue, the fact that there's a tremendous manpower shortage and the lack of physician expertise. He's a triple board certified physician, certified in anesthesiology, also certified in pain medicine and in addiction medicine, and has been an expert on what is a pain program, what is a good pain program and what kinds of tests and measures should be used in pain programs to reduce the likelihood of prescription misuse and dependence. He's been an author of practice guidelines in ASAM and previously has served in most of the positions where we think the prescription misuse could be prevented by education and prevention. He's really done a fantastic job.

This was his Atlanta Journal Constitution, an excerpt, "Less than 10% of addicts receive treatment. The ones who do are often in a crisis mode. With nearly 8% of Georgians over the age of 12 suffering from a substance use disorder we must do a better job identifying and treating those as early as possible. At the heart of the problem is a lack of addiction medicine training, especially in medical schools. Our health care providers are the first line of defense and they actually don't know very much about addiction", about intervention and maybe

they learn. Maybe they learn a little in classrooms but imagine learning OB in a classroom. It's not transferable, physician is a practice that requires actual practice. "The most effective way of assuring the American public and our healthcare system has the knowledge and skills we need to do a better job here as well." I think Dr. Jacobs will present the case for what is a pain program, how to improve current pain programs and how to do a better job of preventing the kind of catastrophe that Dr. Cicero has reported.

This is our format, we'll have a lecture from each of the experts starting with Dr. Cicero, immediately followed by Dr. Jacobs and then I'll say a few words, ask a question or two if they come up. Then we'll open internet question as well as live questions. Without further ado, here's professor Ted Cicero talking about prescription opioid abuse. Thank you.

Theodore Cicero: Thanks for the introduction, I hope I can live to some of the words that were just said. I'm going to discuss not only our most recent article in the New England Journal of Medicine but research we have been doing for the last 15 or so years looking at the epidemic of prescription opiate abuse which has swept the country and more recent developments that have now suggesting this is spreading into users of prescription opioids, not only using prescription opioids but they're now switching to heroin, importantly, not exclusively necessarily but they're occasionally using heroin when they can't get their drug of choice. I think this is a very important distinction. Couple disclosures, my research is supported by the National Institute on Drug Abuse and there's an unrestricted research grand by Denver Health and Hospital Authority. I do serve on the board of directors of that particular agency as well.

Okay, prescription opioid epidemic. Two major developments in the '90s and the 2000s are what really are what really have accounted for where we've gotten ourselves today. The first is, and this was a very innocent well intended report by the Joint Commission on Accreditation of Healthcare Organizations, they reported that pain was the fifth vital sign. They recommended an increase use of opioids to relieve pain. Which is in some sense a good thing but this made the national news, this was on Time magazine's cover that we're under-treating pain in this country, we have good medications and we're not using them. What this actually cause was a tremendous increase in the use of prescription opiate and analgesics across the market. Some of that was useful, however in all situations no matter how well intended you might be there are always some unintended consequences and diversion is certainly part of that unintended consequences. Especially for doctors who may not necessarily be following the rules in an [identical 00:10:48] sort of way.

The next major milestone was the release of extended-release Oxycodone, which you probably know as Oxycontin. It was initially thought both by the company and the FDA that it was going to have very limited abuse potential. The reasoning was it was a slow release device as the [inaudible 00:11:08] release preparation it had to be, and therefor if you delay reinforcement, this is

an old Skinnerian principle for those of you who took psych 101. If you delay reinforcement there is less likelihood that the drug is going to be abused. Addicts are out for the immediate rush of drug. What everybody failed to recognize at the time, and this is indeed surprising if this through an FDA approval process and went through a number of committees, no one thought that this drug could be crushed. Since it's in a sustained release preparation it let copious amounts of Oxycodone that were now available to use multiple times, one pill served multiple purposes and it also served the purpose of injecting. That was a huge increase and sort of was the gateway if you will for people using prescription opioids.

The epidemic as Mark suggested has just increased over the years. It's showing some signs of leveling off at this point, which we'll discuss a little bit of that, but it's still a massive problem. We shouldn't fool ourselves, it's a massive problem. The fact that many of these people are now mixing in heroin along with their prescription opioids. Why are they so attractive? They're euphorigenic, the are legal and they're approved by the FDA and prescribed by doctors. This turns out to be a key point for most of the addicts that we interview. They're seen as safer than other drugs, they're trustworthy and predictable. The dosage is clearly specified on the pill, they know what they're getting, they know it can't be contaminated in any way, unless it's counterfeit which is increasingly more common. They exactly know what they're getting. They view this as very safe and the possibility of an overdose becomes less in their mind because they know what they've got, they know the drug and they know it particularly safe. Most importantly he doesn't have the stigma of being a junkie. I had this in quotes because most people will tell us, "Well at least I'm not a junkie." They may be [inaudible 00:13:00] prescription opioids but they're legal, they're safe, they're not the same as using heroin.

What prescription drugs are most commonly used? Oxycodone leads the list. This is just a survey, I should indicate we have 17,000 people that we've admitted into treatment clinics and we interview those directly with standardized questionnaires. But we also have a great of one on one interviews where we get a lot of information of a qualitative nature because standardized questionnaires really don't reveal the depth of the problem. We're asking people open ended questions that say what does this opiate do for you? I think you're going to see a lot of that today. I'm mixing some quantitative data which you've all seen in DAWN reports and all kinds of other things, but also with actual quotes from patients telling us why they're taking these drugs. Oxycodone is number one, hydrocodone, nothing very surprising there. Then they drop down with surprisingly few endorsers for almost any other drug out there. It's interesting Fentanyl, way on the right, is generally not a preferred drug because they view this as particularly dangerous. It's very difficult to titrate the dose and they view Fentanyl as ... They don't want to kill themselves and they view Fentanyl and Sufentanil as a little bit too potent to deal with. Not surprisingly Oxycodone and Hydrocodone are the most popular.

The initial opioid exposure is very interesting. You ask people, "What did you feel the first time you took an opioid?" First of all the source of the opiates, 62% of our patients, we're talking about 17,000 people, got their prescription for an opiate from a pain physician. Now this may not be a legitimate pain physician, this could be a pill doctor but they got it from a physician. 38% or so took it to get high, that was their primary intent. We can talk about all this later if you wish.

These are representative quotes of people related to the first use. "Minutes after doing them my first time I felt like there was not a care in the world to me. Nothing and no one existed except for me and the amazing high I was feeling." But this next quote to me summarizes in the most succinct way possible and the most elegant way possible what the initial exposure to these drugs [inaudible 00:15:08] "It was like god was petting me." I'm not sure what the definition of that is exactly, but if you just imagine it, the high, the euphoric feeling this person felt that they were next to god at this point. It's a very, very powerful motivating force, to consistently want to seek out that feeling.

There are a lot of unanticipated benefits of opioid that really lead to misuse. The high, if you really look at it the high occurs in the first couple of times but then after that that high wears off and people begin to use it for other purpose. What are those other purposes? 75% of our sample self-reported that they used opioids to self-medicate a psychiatric illness. 85% of the sample self-reported that they used opioids to escape from life. This is a group of individuals who have extremely low self-esteem, they have lots of problems with anxiety, depression and they're finding strangely enough that opiates are relieving that at least temporarily for them. They all realize that's a [inaudible 00:16:08] but they still continue nonetheless.

Again some quotes from that "I did not have any tools for coping with uncomfortable situations and the more I used the opiate the more I responded or reacted to all situations as uncomfortable which made using drugs my go to coping skill for anything from handling emotional abuse to taking a shower." "They made me feel like I could talk to people and not be scared or embarrassed to walk around and just talk and be part of society." A lot of normalizing effects, people actually feel they're better on these drugs than they are when they're not. They feel that they're more outgoing and people actually like them more. "Mask inside emotions/trauma, feelings of fear, self-esteem, self-pity, anger and avoiding the growing stress and responsibility of my life." This person is obviously finding a way to escape from something unpleasant and just wants to get away.

I think it's important we understand why these drugs are being taken because we should work on the demand side of the problem certainly, on the demand side we need to do all we can to interdict and stop the supply but as long as there's a demand for a drug it's going to be met in some fashion. We learned that in prohibition, we banned alcohol and what happened? Not good things. I

think no matter what you do, as long as you don't address the demand, what is driving the need for these drugs, we're going to have a problem for a long period of time.

"It made me feel happy and gave me the energy and want to do daily activities such as working that otherwise wouldn't have been possible due to the debilitating depression at that time in my life." "The escape was from real pain I had from back problems but it also allowed your mind to release and think in comfort, rather than in a stressful way. I have never been as successful or motivated or feel as good as when I was on opioids." Now this is a person in treatment, maybe for the third of fourth time, but still stating that first experience, "I have never felt as good as I did then." Many will say "I've been chasing it since." This is a very strong motivating factor.

I'm going to skip over a couple of these. Let me talk a little bit about transitions to heroin. There were two previous epidemics of heroin abuse. We sometimes sort of forget this. One was after the second world war and then there's a famous study of the post-Vietnam era, [Lee Robins 00:18:21] a professor at my institution actually did a study where there was a lot of heroin, a lot of smoking opium in Vietnam. The worry was that we're going to have a huge number of heroin addicts [inaudible 00:18:38] come back to this country and take drugs. Some of them did come back, but that waned very quickly, showing very situational specific factors can sometimes drive abuse and in fact the Vietnam War was such that there was a lot of stress, a lot of drinking, a lot of taking anything to numb themselves of the pain of what they were going through. Interestingly when they got back, they seemed to self-correct the problem. Both subsided, it was attributed to high cost and low purity of heroin.

The current epidemic has really gone unnoticed for a long period of time. It's taken a backseat to prescription opioids and it was not seen as important because Rx abuse was the real issue and the stigma there, again, was associated with heroin [inaudible 00:19:23] prevented prescription opioid users from wanting the drug. But again there was certainly curiosity out there and drug dealers are very clever people who make lots and lots of money and recognize the market. You'll see that shortly.

This is actually showing, this was in a paper that we just published, the top line that you see, and I can't really step behind to point at it for you, but that blue line with the open circles coming done is actual people who exclusively use prescription opioids. The bottom line or the red line is the people who used exclusively heroin. But at the blue line in the middle, this is people who use prescription opioids and heroin interchangeably. They weren't totally using heroin all the time but they used it when they couldn't find their drug of choice. They used it when they were getting sick because it was cheap and it was affordable and accessible. You now have people making the difficult jump, going from prescription opioids into heroin because they are opiate sick and they

need to in some way or other stop that sickness and the best way to stop a sickness is with another opioid.

We did a regional analysis and I think this is pretty informative. If you look at the Midwest, where I live, there was certainly a gradual reduction of the people who used exclusively prescription opioids, the top blue line. Red line again, there is an increase in heroin use but exclusive use is still less than 10% of the population. Most people fall in between, they're using prescription opioids or heroin, depending upon availability, so they can switch back and forth. The Northeast show the most dramatic example of this. Prescription opiate only use has really dropped markedly over time. Heroin use has increased rather substantially, it's actually doubled even though that number is small. But at the increase in the mixed use of prescription opioids and heroin, that's huge increase occurring over time. This is scary. This is showing an interchangeability between prescription opioids, they certainly share the same pharmacology, but you now see people overcoming the aversion to heroin that they may have once had because they now need the drug.

The South shows somewhat more modest effects than any other region in the country. I don't know whether it has to do with availability but we're looking into that right now. The West shows almost as dramatic an effect as is occurring on the east coast. I think one can explain these pretty readily just that heroin is a lot more accessible on the east coast and the west coast than it's going to be in the Midwest or it's going to be in the South, not to say that they're not there, because again heroin dealers are very shrewd businessmen and they've moved in to take a target. There's a target audience now of people using prescription opioids and they see now potential market for selling heroin.

Prescription opioids, are they a gateway to heroin? Answer is they sure are. If you look at people who started in the 1960s, '70s, '80s, '90s, up to the present time, you can see from the line at the top, the bars or the squares rather, heroin was really the first drug used in the 1960s. Prescription opioids really weren't all that popular. Now this is looking at first drug use. If you look over time, the percentage of people now using prescription opioids first and then graduating to heroin is marked. There is absolutely no question, at least in my mind, that prescription opioids are serving as a gateway to people using more dangerous drugs. I think we can over some of those mechanisms but this is a very clear-cut finding.

Why are the increases occurring in heroin? There really are practical factors if you will. Prescription opioids, some are very expensive and they've seen their prices increase over time, largely due to interdiction efforts and clamping down on pill mills, clamping down on script docs, closing the pill mills that were rampant in Florida has certainly helped. It was estimated at one point Florida, Mark's home state, was supplying about 99% of the prescription opioids used in this country. Whether that's true or not, I don't know. Many preferred opiates are really hard to find now. They really want to find Oxycontin, they might not

want to find something else but they can't find it or it's horribly expensive. The other unanticipated consequence abuse deterrent formulations are being developed, which are very good but they prevent crushing and they prevent solubilisation for IV use. As these have come along, some people have backed off, not all but some people have backed off and said "This is too much effort now expanded to actually defeat the abuse deterrent formulation so I'll switch to something else" and that turns out to be heroin.

Heroin is cheaper, it's much easier to get now, it's easier to inject, much easier to inject. It's purer than ever at this point. Really what's happening [inaudible 00:24:04] right now is this is being cut with Fentanyl as well, which is an extremely inexpensive compound. A lot of what you're seeing when you're reporting heroin overdose is really a combination of heroin and Fentanyl. Both act with the same opiate receptor but you've got a very lethal combination. Again smart business here, this is purely a business decision. Dealers are saying "I've got to make my drug attractive at an inexpensive price and have it available for these people who are taking prescription opioids because we need to compete. The drugs are too expensive, we can undercut them and sell a lot more drug, make a lot more money."

These are representative quotes of what's happened to the whole culture, as you recall I've said before people regarded when they started taking prescription opioids, they regarded these as safe alternatives and at least they weren't junkies. Something really has happened that this junkie concept seems to have gone out the window. That's a very interesting dynamic we need to know a lot more about. Typical comment, "Heroin is cheaper and stronger than prescription drugs, and the supply is typically pretty consistent. It is also much easier to use intravenously than pills and other prescriptions, which often take more complex methods to break down." "It was cheaper and easier to get heroin, which was much stronger and would get you higher than Oxycodone."

There's a lot of evidence of reduced stigma. "Once one leaves the stigma or prescription versus street drugs behind the question becomes more purely economic/pragmatic, what will keep me from withdrawal right now?" That becomes the most immediate concern. "The 2 dealers and the people around them are middle class white kids, not even kids we were all in the age range of 25 to 41. It just became easy, and we weren't really looked at as being addicts because everyone thinks that heroin addicts are all homeless, shady looking, dirty junkies." "I knew I liked it above all else, and once I had a drug dealer it became almost too easy to get. I had access to money because I'm an upper middle class family and I also became close to my dealers, driving them around so I could get paid in drugs and just becoming super close, even if it meant sexually, so I could get the drug."

What's the societal impact of these and I'll wrap this up. The changing demographics that we've seen over time and I think this important to really focus on. If you look at the demographics in the '60s, 85% of the heroin use in

this country was used in fact by men, women were a very small percentage of that number. Look what's happened over time where women have become more and more and more common among an addicted population until about there are about equal numbers now of men and women. This is a demographic we never expected to see and that women have [inaudible 00:26:40] men typically tend to be more risk averse, especially younger men, and are more willing to experiment and try things. Women tend to be a little less risk avoiders, a little more risk avoidance factors but something's happened to that as well.

If you look at the racial background of these individuals, it was in the '60s probably even divided between whites and non-whites. You can see what's happened over time now, the percent of white individuals that are being admitted to treatment has increased dramatically. Over 90% of what we're seeing now are white middle class people showing up in treatment clinics, very dramatically different than it was in the '60s or '70s. Something very large has changed, the whole demographic [inaudible 00:27:26] change. Why is that important? Because all of our efforts previously have been directed looking at urban issues, they're looking at ghetto issues, they're looking at poverty. This suggests a whole new avenue that needs to be opened to look at this population. This is not your typical heroin population. This is a group of people who had a history of prescription opioids use, who have the means to procure drugs and just simply aren't following the stereotype of someone that should be using heroin, but they're now using it I think.

All of our prevention techniques, all of our intervention and our treatment procedures need to take into account this is a different demographic of people that we've seen before. Over 75% of heroin users in the past few years resided in suburban or rural areas. Again a dramatic change, this was an inner city problem for years and years and years, it's now occurring in the suburbs and in rural areas. As one sees the overdose deaths that are occurring around the country, the ones that are making the news, and this is a very significant sentiment among the black community, had never been much of a story when blacks were killing blacks on the streets and in North St. Louis or wherever, but now that it's hitting home, it's coming out of the suburbs and kids are overdosing in parking lots, they're athletes on the team, it makes the 10:00 news or 11:00 news that evening.

But it is in fact the case, you see lots of heroin because people don't know what they're getting. They're getting a powder form that they think is a certain purity, so they take a guess, the best guess they can and then inject it and sometimes they figure wrong, especially if there's Fentanyl that they didn't realize was there and they're overdosing and dying. I sort of summarized that. I think it's sort of been a perfect storm as I indicate here. Heroin is cheaper, heroin is easier to get, it's easier to inject, it's purer than ever. It gives a better high to some people. It's a balance of what makes you feel the best versus practical issues, cost et cetera. The stigma has started to subside.

That is really a scary development and I think it's our next public health crisis. Prescription opioid abuse though importantly has not gone away, it's still the foundation of much of what starts as a prescription opioid use but we need to understand that there's unanticipated consequences [inaudible 00:29:46] moving in and making prescription opioids less available. These addicts aren't going away. They're not going away without treatment. They're going to turn to something else and we have to anticipate this turn and not being to delve into the heroin problem as it exists. It's a big problem, lots of overdose deaths. Thank you very much. I didn't use all your time.

William Jacobs: Good morning. I'm Dr. Bill Jacobs. It's great honor to be back here. I had the pleasure of being here in 2008 when we opened the exhibit at the museum that's in the back, the section on good medicine, bad behavior. I'd like to talk a little today about some definitions for pain so we're all on the same wavelength here. The most important thing about treating pain is that this is a different entity than most of us as physicians have to deal with. If I'm going to treat blood pressure, I can slap a blood pressure cover on a patient and get a number. I can treat that number. If I'm going to treat cholesterol I can draw some blood, I can measure the cholesterol and the lipids in the blood. I can give a patient Statin, bring him back in 6 weeks and have pretty good success with that.

Pain, importantly, is really very difficult to measure. It's a subjective experience. By definition it's a subjective experience. There is no [dolometer 00:31:35], there have been attempts to create pain meter, dolometers. Most of them cause more pain either for the patient or the doctor than giving us anything good to work with. Acute is pretty straight forwards and relatively easy to treat. We've done a great job in being more aggressive in treating acute pain. With our experience in Afghanistan and Iraq, the Department of Defense and the acute pain specialists particularly in the army have done a miraculous job in reducing battlefield injuries to really 10% mortality at this point. We're having patients come back from war now that in the past would not have survived. They're developing chronic pain as a result of their acute pain.

Now chronic pain is interesting because it's much more difficult to measure. The visual analogue scale as I'll show you in a bit are pretty good for using to measure the level of subjective experience of pain that a patient's having. If I break my femur and go into the emergency room and I tell them it's a 8 out of 10 pain, they can give me some pain medicine to set my leg, get me x-rayed and get me treated. I can pretty accurately report to them what my pain level is after they give me that pain medicine. Over time our ability to know what our pain was 2 weeks ago, even 2 days ago and compare it to what it is at the point that I'm in to see my doctor is very difficult.

It's very interesting, when I did my anesthesia and pain training in the University of Alabama in Birmingham back in the '80s, we really defined chronic pain as something that had persisted for more than 6 months. Then we shortened it down to 3 months. Now, and sometimes I will be called to see a chronic pain

patient that had surgery 10 days ago and got a week's worth of pain medicine and now the surgeon has decided they have chronic pain. We've really changed our definitions. One of the things that's happened is this subjective experience has gone to not really a time limited definition but something that's extending longer than we would expect for the level of pathology that the patient has.

A couple other definitions so we can be all on the same page. One of the terms that you'll hear a lot of pain management doctors about is aberrant substance use behaviors. That really doesn't necessarily mean the patient is addicted, they may be taking their prescription and because of their disabling condition have lost their job, can't pay their mortgage, can't put food on the table for their children and are selling their prescription. That doesn't mean they're addicted, it means they're breaking the law but it certainly is an aberrant substance use behavior. Then we have abuse where there's a maladaptive pattern of drug use that puts the patient in harm's way or at least at risk for harm. Then we have addiction, it's a primary chronic illness, and Dr. Gold has done great research on. It really involves both brain reward systems, motivation, memory and related circuitry. We have this dysfunction that encompasses the whole person.

In getting for this talk and only having really a few minutes to speak to you today, I wanted to think about what would be important to say. I think a lot of the audience is probably DEA and DOJ, I think maybe you'd like to know how would you try to determine what's a good chronic pain program. I had the opportunity to work with the state of Florida, Governor Rick Scott and Attorney General Pam Bondi, when we had the epidemic there with the pill mills. We were really the poster child for the nation and we did a really good job in cracking down on that and cutting back really in a 2 year period cut down the number of pill mill significantly in the state. I had the opportunity to train a lot of the agents that were going out in the field in terms of what to look for.

One of the first places I suggested they go is the Federation of State Medical Boards because for over a decade there have been model guidelines for the use of opioid analgesics in the treatment of chronic pain. These were last revised in July of 2013 and there were some pretty significant revisions. I think if we're looking from a DEA or DOJ perspective in terms what would be a model pain program, I think looking at the Federation of State Medical Boards guidelines can be helpful because we're both really looking at are the opioid analgesics being prescribed and used in a manner that's both medically appropriate and in compliance with state and federal laws and regulations.

One of the first things to look for is, is there adequate attention to the initial assessment to determine if opioids are clinically indicated and to really do a risk/benefit ratio as to that particular patient. Will this potentially addictive substances have a risk/benefit ratio where the benefit is worth the risk involved. The next place to look would be the monitoring. Is there adequate monitoring being done both before and during the treatment to look for the potentially abusable medicines? The next piece will be, as there been adequate attention

given to patient education and informed consent? This is a very difficult issue, I ran a chronic pain and addiction private practice in Jacksonville Florida for 5 years and I can tell you that most of the patients that came to me had been to see at least 6 to 10 other physicians before they got to me. As my partner and I used to like to say, all the gimme putts had been made.

When I would see those patients, they would come in and the vast majority of them had no idea how dangerous the medications that they were being prescribed were, particularly the combinations. Prescribing not just chronic daily opiates in very high doses but also adjuvant drugs like Soma, Xanax, other muscle relaxers [inaudible 00:38:47] other sedatives and sleep medications. The next piece to look at would be, really has there been attention given to dose escalation? Has there been adequate attention to the risks and options for alternative treatments? When I speak to medical students, residents, even primary care physicians, they really don't have a lot of education about other options for the treatment of chronic pain.

I can tell you as an interventional pain physician for more than 30 years, I've had great experience in providing patients good relief using interventional techniques. Now they don't work for everybody but they certainly work for a lot of people and I can't tell you the number of patients that I would see who came to me strictly on opiates and never had anything else tried. We'd do a few interventional procedures and be able to taper their opiates dramatically, sometimes completely off. In looking at a pain practice, is there excessive reliance on opioids, particularly high dose opioids for the management of chronic pain? I had the opportunity to work with the DEA in an investigation in Louisiana into some pill mills down there, where the holy trinity was being prescribed to every patient that came in the office. They were receiving Hydrocodone, Soma and Xana in almost the exact quantities every months, regardless of their diagnosis. One of the physicians that was treating those patients was seeing up to 240 patients in a day.

Now to see a chronic pain patient, I don't know how a primary care doctor can manage it. They're given 15 minutes to treat multiple medical problems, diabetes, hypertension, heart failure, asthma, COPD and oh by the way they have chronic pain and you've got 15 minutes to talk to them. I couldn't handle one of those problems in 15 minutes, I don't know how they can manage to do it. One of the quick easy solutions is to just prescribe them high doses of opiates and escalate the doses. Another issue is, does the practice make use of the available tools for risk mitigation? One of the big advances that we've had is the use of prescription drug monitoring programs. It's been a great tool.

I happen to be right now at the Medical College of Georgia in Augusta and we're right on the Georgia/South Carolina border for those of you that don't know. I've actually enrolled in the physician monitoring program in both South Carolina and Georgia because I have a number of patients that go back and forth across the state. I had to do the same thing when I was in Jacksonville

because we were only 50 miles from the Georgia line and had a lot of patients that were filling prescriptions in both states, so I was able to monitor those. It's very quick and easy to do, it's an underutilized tool to really be able to alert any physician seeing a patient on what controlled substances have been filled by that patient in the last 6 months, and by who.

Now there's a huge interaction between pain and addiction and all the manifestations that we get from it. You can see from this, we have to address all of these issues when we try to treat patients, I treat a lot of patients with both chronic pain and addiction at our residential facility Bluff Plantation down in Augusta. They almost all have sleep disturbance, they have functional disability, they have a huge [inaudible 00:42:22] increased stressors as well as depression and anxiety. An interesting thing Dr. Cicero was talking about the emotional pain and being a driver for opiate use. I can tell you that our brains don't work very well in terms of being able to differentiate between emotional and physical pain.

We did a really interesting study down in Gainsville a few years ago where we put a clamp on a patient's finger and we would let that clamp get tighter and tighter and we'd ask him to tell us when it hurt, that would be their pain threshold and then ask them to tell us when they couldn't stand it anymore and actually when we let it go a little further and they actually ripped the thing off their finger that was their pain tolerance. If you tested patients over a period of time where you've got a standard response that you could pretty well predict when they came back in what it would be, within a matter of seconds you could look at them and say "Okay, they're hitting a 4 on the pressure scale so they're going to start to say it hurts now." And sure enough it would, so we could get a standard for most patients. Then we could image them and see what their brains looked like when ... We get a kind of this is your pain, this is your brain on pain.

Then we did a very interesting little study, we put 3 patients in scanners at the same time that had video monitors above them and had them play a little very simple game where they could pass a ball on the video monitor to either of the two other patients that were being tested. If for instance Dr. Cicero and Dr. Gold and I were in the monitors, we're passing the ball back and forth and unbeknownst to me after a certain number of passes they've been told not to pass the ball to me anymore. The ball's not showing up on my monitor or I can see it going back and forth between the two of them. Now you wouldn't think that would be a very big emotional hit but when we scan those brains, my brain having been left out of this very simple little game looked almost identical to when you put a clamp on my finger and cause me physical pain.

Our brains are not really very well equipped to differentiate emotional from physical pain, so it's no wonder than when we have a patient that we give chronic opiates to and they do get some stressors in their life and develop some emotional pain, as all of us in life have, that we turn to the opiates to try to fix

that. Now I have a number of slides here on some statistics that I find are pretty interesting. Chronic pain patients who may have addictive disorder, about a third. People ages 20 and older who report pain for more than 3 months, over 50%. If you skip down a little further, patients ages 65 and over who've had pain that lasted for more than 12 months, almost 60%. If you skip down to the very bottom, people with opioid addiction who report chronic pain, anywhere from 30% to 60%, one to two thirds.

There's a huge overlap and one of the problems that I frequently see, and it goes back to my real podium stance on better education, is we have some really good chronic pain doctors that really have no training in addiction and we have some really good addiction medicine physicians and addiction psychiatrists who don't really understand pain. The patients end up being ping-ponged back and forth between these two sets of physicians. If they go see the pain doctor they will probably get some opioids for their pain. If they violate a treatment agreement and are maybe developing a potentially fatal illness addiction, they may have their care terminated.

It makes me put my hands, my head wants to explode because we have a patient that's had a bad illness, chronic pain, he's now developed a potentially life threatening illness addiction and we're terminating care at the very point when we should be escalating their care. Those patients if they're lucky get sent to an addiction medicine physician or addiction psychiatrist who frequently has no training in pain. I'm sorry but if you've had 6 back surgeries, 2 neck surgeries and can barely get out of bed in the morning, even the best 12 step program in the world, and with no treatment for your chronic pain, you are set up for relapse.

In the terms of the pain assessment, I'm going to over this briefly, but this again speaks to what you should be looking for in a chronic pain program. A good comprehensive initial assessment, not just "Oh you have chronic pain, that's the diagnosis." It's very interesting that we had no diagnosis for widespread chronic pain in our ICD-9, now ICD-10, categories until just a few years and now we have a new category simply for widespread chronic pain. They should get good looks at their personal and family substance abuse, as well as their psychiatric history and collateral information is a huge piece to this. We have to look a those co-occurring psychiatric and psychological conditions and we have to assess them for both these problems because they are very frequently going to be co-mingled.

I'm going to skip through most of these assessments, I put these in here for the physicians. I think it's important to know. This is, as Dr. Cicero talked about, pain becoming the fifth vital sign and every hospital room now has these little smiley face charts. We even put ours in multiple languages. They're really worthless in terms of looking at chronic pain. I throw this out there for the pain physicians or pain patients out there who might be looking in. I find this scale invaluable in my practice because instead of just asking them on a 0 to 10 scale I actually give

them some qualifiers. You'll not to have a 10 out of 10 pain, that patient would have to be unconscious, the pain had made them pass out. It'd be very difficult for a patient to be talking to me and tell me that their pain was 10 out of 10 on this scale.

There are tools to asses the dimensions of pain, I include them for reference. There are tools to look at the pain's interference with life activities and functional capacities, that's really what we should be looking at when we're treating chronic pain. The pain score as I said, over time that visual analog scale is virtually worthless in treating chronic pain, we should really be looking at activities of daily living and function. When I have a patient one of the first things I ask him, "What is a realistic goal for you? I'm not going to make you like you were when you were 18 years old, assuming you were healthy at that point in your life, but maybe I can help you get to a point where you can do more."

I may have a grandmother who has a 10 out of 10 pain because of back and pain, can't get out of bed, if I can do some things for her and she says "Now I'm able to go sit through a movie with my husband" or "I can go walk around the grocery store and shop" or maybe "If I'm willing to put up with some I can actually maybe spend part of a day at a theme park with my grandchildren". That person's pain may still be a 10 out of 10, if I'm looking strictly at the pain score it's not much help but if I'm looking at their functional ability you can see they've had a significant improvement in their life.

Other tools to assess coping and tools for developing, I throw these in because this is important for the pain physicians out there, there are some very good screening tool. The SOAPP-R can predict your high risks patients as can the Opioid Risk Tool, they're included in my slides for those of you that want them. Our key points here are, patients should get an initial comprehensive assessment. They should be given a diagnosis of widespread chronic pain, we should be searching for the pathology that's causing the pain and treating the underlying condition. We need to carefully ask about the family and personal history, we need to obtain collaterals on pain just as we would in a substance use and wee need to be treating the psychological co-morbidity that's there. With that I'll close so we have some time for questions.

Mark Gold: Well, that was really amazing and unbelievably comprehensive. Thank you Dr. Cicero from Washington University and Dr. Jacobs from the Bluff Plantation and Medical College of Georgia for the most current update possible. I think I'll ask a question and then we'll go to the audience. When Dr. Cicero was talking about people using both, is there any difference in treatment if a person was just an [iatrogenic 00:51:42], just got addicted to pain medicine when you evaluate and treat them, but they're there for dependence. Is there a difference between that and a person who has a different pathway to treatment.

William Jacobs: I think there will certainly be some difference and we individualize the treatment to every patient. I certainly see 2 groups of patients in my practice.

It's almost a bi-modal curve, I have that young adult population, the late teens to early 30s group, that are primarily using initially for the high, the euphorigenic properties that Dr. Cicero was talking about. Then that group that you were mentioning Dr. Gold, who maybe has naively gone to a pain physician that really doesn't do a very good job and simply just prescribe escalating doses of opioids. The treatment has to be a little different in them just to get them to buy into treatment. Putting them with peers and [norming 00:52:51] them with a peer group is one of the most important things I found in treating addicts of all kind, whether I'm treating doctors, if I can get them to norm with a peer group of doctors who are also addicts, that's helpful. Young adults, if I can get them to norm in their peer group. The older population, if I can get them to norm in their peer group. There then become a lot of similarities in treatment when you get right down to the bare basics.

Mark Gold: Your question.

Speaker 6: Thank you. I wanted to ask about office based opioid therapy. I realize there's a lot of factors that go into the effectiveness of such treatment but let me ask you about a couple of areas and get some of the thoughts of the panelists. How important do you think it is to have ... Is the number of patients being seen by the treating practitioner ... As you may know there's some discussion about increasing the statutory limits. Right now it's 30 in the first year and then it can escalate up to 100 after that and there's some who suggest there should be no limits. How important a factor is that? Secondly how important is it in terms of the training and whether it should be expanded beyond Mds to say nurse practitioners and physician assistants?

William Jacobs: I've got a lot of experience with buprenorphine in the past because when I started my anesthesia career or came in my residency in 1984 and buprenorphine was first released in this country in 1986 as Buprenex as an injectable pain medicine. It wasn't until the real first wave of the Oxycontin epidemic in 1999/2000 what we started using buprenorphine to detox these patients. I'm a big believer in medication assisted recovery, but I like to use as a bridge to abstinence. I think there are some patients that really benefit from long term buprenorphine therapy, those are mostly my chronic pain patients, they have co-occurring chronic pain.

To give you an example I have a gentleman I'm currently treating, he's just stepped down into our outpatient program, had 4 back operations with spinal fusion that has been moderately successful but not completely successful. He also has Crohn's disease and has had multiple abdominal surgeries. He's a patient that I think will be probably be on lifelong buprenorphine, it gives him great pain relief. I can tell you in my experience in my private practice we were seeing primarily patients that had both chronic pain and addiction. We went in-

Theodore Cicero: I'd have a little bit different take on that. I think the limit is 100 now for- The purpose of buprenorphine is to aid hopefully the detoxification and get people

drug free. [inaudible 00:55:44] I'm somewhat ambivalent about this overall but you've also got to remember physicians- constantly. They need counseling and they need some help with their underlying problems as I was talking about earlier. I'm afraid we use a lot of methadone programs and buprenorphine programs as sort of parking spaces for people that we've been dealing with the substance problem, but the original intent of all these programs was again just to assist in recovery. I'm afraid it's become a model where we just park people and I have some issues, some real problems with that.

The other problem we have to realize is these compounds have very high addiction potential. The more drugs we use and the more distribution we have, as I mentioned in my talk, there's always going to be some diversion of that substance into the street population. Buprenorphine is now quite attractive on the street, there are a lot of people buying and I think we need to be very mindful of it. While I see the value in it and I understand the value in it and if used properly it's useful, I don't think seeing 200 or 300 patients is going to accomplish the goals that he really needs to accomplish and we've got to be mindful there's always unintended consequences with everything we do. Some of this leak out and there's an abuse potential problem. It's a complicated answer to your question.

Mark Gold: You know, we've done a lot of work with physician addicts, it's a contact sport. You have to do a comprehensive assessment. You have to do an intervention. You have to work with the family. There's a lot of insulary services. -have your outcomes with return to work relationship and- for have everyone have the same kind of treatment opportunities and options available as physicians have rather than having physicians have their own very special treatment with the highest outcome and everybody else having something else. Do you have a-

Speaker 6: Quick follow up,

Mark Gold: Do you have a ... Oh excuse me.

Speaker 6: Yeah, if I may just quickly follow up also on the office based use buprenorphine for addiction treatment. Current law limits the dispensing to only physicians and there's been some discussion of extending that to say nurse practitioners, physicians assistants, any thoughts from any of the panelists on that.

Mark Gold: No.

William Jacobs: I would be opposed.

Mark Gold: I think there's just the general question of what is the value of specialists and specialists training. We maybe could spend an hour on what do you actually learn in addiction medicine fellowship or in addiction psychiatry fellowship that's of value? It's so tremendously valuable that most of those experts are [sought 00:58:40] to run major university, major academic and major treatment

centers because if you take a person like Bill Jacobs, here you have somebody who's done interventional pain medicine, can inject a joint in the spine and done pain management, medication assisted therapies as you suggest, as well as evaluate and intervene in an addiction in both dual disorders and in [inaudible 00:59:09] the straight forward. Those kinds of experts to me are like what we'd expect in cardiology. This is a post-residency training program, you did your medical school, internship, residency and then you trained in addiction medicine and passed those boards.

I see addiction as much more complex than other people have considered it. I go back to my early days in training, I remember when now [Naloxone 00:59:43] was first introduced and we could save someone's life. But in Florida we took the position of drug court and intervention. Yes it's true that's a wonder-drug, it was actually my book Wonder Drugs, but if that's all you have that is not going to cure anyone. Did you have another ... I'd like to say also that there have been a couple of questions that have come through from the internet, both of our speakers have agreed to make their slides available on the web and we really appreciate that. I know how much work as a lecturer goes into putting slides together and to make them available is really generous and I thank you. I also of course thank you all for taking the time out of your busy careers to fly here and do this. You have a question from the internet?

Speaker 7: Yes we do have many web questions, I will try to get a few of them. One of the first ones is, what is your thought on Vivitrol, the time released injection of Naltrexone for an opiate addict that has been off opiates for a year and a half due to being in jail and having the door closed on their addiction, now out and has cravings, regarding safety, long term use, brain chemistry while on an opioid blocker et cetera.

Mark Gold: Bill's probably the best expert as a medical director but in physician's health one thing that we thought about was mandatory Naltrexone either injectable or with adherence for anesthesiologists who came back into practice and came back into contact with opioids before their first slip is often times a death. That's been proven to be a prevention strategy. In your practice what do you do?

William Jacobs: I actually use more Depot Naltrexone, Vivitrol, in my practice than I do long term Buprenorphine. Initially we thought it wasn't going to have a great deal of effect on craving but it actually seems to in a significant subset of the patients. I think it also provides a safety factor in there, it gives the patients ... And I talked to my patients about this, it gives them an out. If they happen to be in the wrong place at the wrong time and somebody offers them drug, they can say "I'd love to do that but I'm taking Vivitrol so it'd just be a waste of that $80 for that Oxycontin that you're offering me." It also gives them some stability if, as the weather turns cooler and they pull out a jacket that they haven't worn since last winter and they reach in the pocket and there's a bottle of pills, they may look at that bottle of pills and if they didn't have Depot Naltrexone in their system, they may well use.

If they have Depot Naltrexone in their system they may well be able to put the clutch in and the break on and say "I remember that euphoric recall, it'd be great to use but it's not going to do anything. It's a waste of time. I think I'll call my sponsor and get to a meeting." I'm a big believer in both oral and Depot Naltrexone and use it in almost all my patients, particularly in transitions out of residential treatment and in the questionnaires situation coming out of a controlled environment like a jail, I think that's a huge relapse potential. I think I would certainly in most cases be recommending that.

Speaker 7: All right, this is for Dr. Jacobs. What's being done to look closely at non-opioid analgesics? What's the highest level of pain they can realistically manage, 6, 7? How is the academic and bio-pharmaceutical R&D enterprise doing in developing non-opioid therapeutics for moderate to severe pain?

William Jacobs: I think the first thing to say is what we haven't talked about yet today, and that is that there are really no good long term studies on either the safety or efficacy of chronic daily opioid therapy. Again my career has spanned the entire pendulum swing of opioid use. When I trained in chronic pain at UAB in our pain clinic no patients asked for chronic opioids, no patients were considered for chronic daily opioid therapy. We just didn't even use it. We had patients that were doing very well. I think it's an individual basis but certainly we're getting more and more medicines, particularly with research in the other cannabinoids and marijuana besides THC, cannabidiol potentially has some analgesic properties. There are 80 cannabinoids in the marijuana plant and we have not done the studies. I think that's a huge frontier and a great opportunity for us to be able to reduce pain.

Theodore Cicero: Yeah. I should just add, in 1940 the Addiction Research Foundation was established in Lexington Kentucky. It's major goal was to develop a non-addictive opioid. The purpose being all opioids have abuse potential so could we develop something just as effective that did not have abuse potential. That's I think 75 years ago or is more than that? About 75 years ago. We've made very little progress in that area. In terms of pain relief opioids still are the gold standard. There are certainly new compounds being developed but right now there is no opioid that's as effective that doesn't have some abuse potential.

Speaker 8: Thank you for coming. According to the International Narcotics Control Board the United States manufacturers, a large supply of the prescription opioids, we also consume a large supply of the prescription opioids. Do you foresee this could be a problem in other countries which would lead to addiction and also potential heroin problems?

Theodore Cicero: Yeah. I think we're doing some studies in Europe now. They're becoming somewhat like us in the sense that they're beginning to have problems in that area. Traditionally they haven't and it's been because of very stringent government regulations about the use of opioids. In many countries, like India, I may be wrong on this but the total amount of opioid use in India last year was

70 kilos for a country of 1.4 billion people, very little opioid medication. The government frowns upon, certainly in China it's frowned upon. Across Europe it's not uniform in the way it's being applied but there's becoming I think an acceptance of the fact that they are useful in treating pain, so I think as preventative measures they're gearing up to basically look at this problem. They're beginning to see it, drugs are infiltrating from various parts of the country, especially with the EU borders coming down. I see it as a potential problem but at the moment they don't have it as severe as we have it here.

Speaker 8: Thank you very much.

Speaker 9: That was a good dovetail into my question which is, my last assignment was in Germany where an 18 year old child for acute pain when she has her wisdom teeth pulled is given 2 days of Ibuprofen, with very strict restrictions and cautions about how to use that very strong drug. I think it's interesting how different countries approach, in this case acute pain management, it think the question was a very good one, what is it out there that we have to learn from our European colleagues? What are they doing right that we're not doing right?

Mark Gold: I'll just tell personally when I send patients to Bill Jacobs because I didn't know what was the story and what was going on, he took them off their medicines and the patients would complain and say "How could you send me to a doctor who took me off medicines?" I didn't really understand this hyperalgesia thing, and then the idea that rather than injected a joint we give a pill that affects the entire brain and body. It's almost in my other interest, I'm interested in depression treatment. You could treat the entire brain and body or you might find the circuit and change that circuit. What would you say to that? The kind of other taking people off ...

William Jacobs: We haven't touched on opioid hyperalgesia, which is certainly a very real phenomenon. I can't tell you the number of patients that I have reduced opioid doses on that have said they actually feel better. It's a scary thing for a patient to do because initially maybe the opioids help them, but again there have been no studies that show the long term safety or efficacy for chronic daily opioid therapy. As I said in our pain clinic back in the '80s we would give [poltz 01:10:10] doses of opioids to our very severe pain patients. Maybe 7 to 10 days at the most for somebody who had 4 back surgeries, a couple of times a year when they really needed them the most rather than the escalating doses of more and more and more. Which really causes them to come back in and tell me "It's not just my back that hurts doc, I hurt everywhere."

Targeting the cause of the pain, targeting the pain pathology I think is the most important piece. That can be done with interventional treatments as well as we can target other systems like the serotonin or epinephrine system with medicine like Duloxetine and Venlafaxine and even our old tricyclics that we've used for more than 40 years now that are still very effective. Also we're getting

more and more medicines like Gabapentin and Pregabalin which are very helpful in this widespread chronic pain syndrome that we seem to have more of.

Mark Gold: Thanks. We have time for another one or two questions.

Speaker 10: All right. How many people who use their opioids properly truly become addicted?

Theodore Cicero: That question has been impossible to answer. Part of the problem is in order for us to really get a handle on that, you have to have ... We applied for a grant and for those of you not familiar with the NIH grant process in the old day 100 was the best score you could get, a 500 was the worst. We got a 250, which split the middle and the reason for it was we were trying to study that very question but somebody, half the group decided that we needed a control group. What was the control group? Every person prescribed an opioid in this country. If you start looking at how would you even sample that population of people, because if you get your wisdom teeth taken out or you get a tooth implant you're given Vicodin, it's very, very, very common. Do we look at that population as well?

It's a very difficult question to answer. The estimates range from anywhere from .1% to 40% or 45%. The number of our truth is probably some place in between that but I don't know. Certainly if you have risk factors, and I think our data show quite clearly, if a person comes in, and certainly with a past history of abuse that's an issue, but if they have underlying psychiatric problems, not that you should withhold the medication but you should be very careful in dealing with that population because they do have this added quotes, "benefit", end of quotes, of temporarily making things a little bit better in terms of their psychological problems.

William Jacobs: One of the other things that I'd proposed for years to our dental schools and to our family practitioners and our emergency room doctors who are really the people that usually prescribe the first opioids to a person in their lifetime is that we really ought to document that patient's response to the opioid because certainly their genetic predisposition is a huge risk factor but their first response, the quote "normal" patient, I don't see very many of them, they don't come to me for some reason, but the normal patient takes a Hydrocodone after a wisdom teeth extraction and doesn't feel very well, maybe gets a little nauseated and goes to sleep on the sofa. The patients that I see who have become addicted and I'm treating them for either heroin a prescription opioid addiction later in life, when I ask them about their first response to an opioid they tell me "Yeah, I got that Hydrocodone for my dental procedure. I took 2 of them and went out and washed the car and cleaned the house and then went shopping." That first response I think is a huge predictive that we ought to build into our healthcare system.

Mark Gold: Last question.

Speaker 6: The last question is, why are there not more controls and checks put on prescribers? As a pharmacist it's very frustrating, pain contracts don't work.

Mark Gold: This is a complicated question like all the questions. Really I thank the audience and the people watching, the questions are just outstanding. The level of continuing education in pain medicine is a problem. If all prescribers can prescribe what's the CME? What's the continuing education that is required for them to keep prescribing? It's not much, maybe nothing. Part of the rise of experts like Dr. Bill Jacobs is, where are the double and triple board certified experts? The anesthesia, pain and addiction experts, where are they? I don't know that there are many. I don't know whether since the problems are common in both, it's more like child psychiatry to me. You need to be a psychiatrist but you need to have a specialty in child to be a child psychiatrist. Unfortunately we have silos and they don't communicate very well.

Pain has not been seen as requiring the most training, the most continuing education and the most attention to what can be done locally versus whole body. One of the roles and importance, I know Dr. Jacobs' program has alternative treatments, mediation, massage, exercise and so forth. These are all really important in pain programs and if you were trained at a certain time, if you were trained 40 years ago, what would you have learned about diet, nutrition, exercise, mindfulness, intervention? Without continuing education it's very, very difficult to keep up.

That's the last question, I want to thank the audience here as well as around the world for tuning in and sending your questions in. This is obviously a topic of great interest here and elsewhere in the United States. I just want to thank Dr. Jacobs again and Dr. Cicero again and their institutions for allowing them to spend the day here. They have a special gift for you and even one for me. Thank you very much.