

NAMI Ask the Expert: good News for People with Mental Illness as the Great American Smokeout Nears November 5, 2020 Presented by Eden Evins, MD, MPH, Cox Family Professor of Psychiatry, Harvard Medical School

Ken Duckworth (<u>00:00:10</u>):

Welcome everybody. As you know, Ask the Expert is our opportunity to bring the best thinkers, the best researchers, the best clinician and leading peers to you. We're interested in your feedback and input. I want to let you know next month in December, Gail Daumit of Johns Hopkins University will be reviewing the literature on reducing your cardiovascular and metabolic risk. She's well published in the New England Journal of Medicine. And again, in this time of COVID, we wanted to make sure that we make the opportunity available to review the literature on how you can take care or your lungs and how you can take care of your heart.

On the smoking front, which is today's topic, it's an absolute pleasure to introduce Dr. Eden Evins. I was incredibly fortunate to see her as a brilliant resident at the Massachusetts Mental Health Center, and I knew she had great things ahead of her. She went on to found the Center for Addiction Medicine in Mass General Hospital and became a full professor of Addiction Medicine at Harvard School of Medicine, and the Cox family funds her professorship.

Eden also had, in her spare time, picked up a Master's in Public Health. What I like about Eden are many things, but her ability to help people think about how to think about quitting smoking and what are the evidence-based strategies to do so. And she attends to people's symptoms. And she does a lot of work to make sure that people know that you can quit smoking and do quite well with your symptoms. So, Dr. Eden Evins, I want to thank you for donating your time to NAMI. We're incredibly grateful for the research and work you're doing and for giving us your time today. So why don't you take it away. And put the questions in. I'll rejoin after Dr. Evins has done her presentation. Thanks everybody.

Eden Evins (<u>00:02:15</u>):

I want to sort of plug in for Gail Daumit for next month. She's a friend and a collaborator in doing our third study together, because, of course, smoking cessation is one of the best things you can do to improve your cardiovascular health. So, [crosstalk 00:02:31]-

I bring good news, and that's really fun. The good news for people who smoke, how people with and without serious mental illness can quit smoking. There's lots of new good stuff out there. So, next slide, or first slide really. The main thing is that people with serious mental illness who take a medication to smoke do not get more adverse events. They do not have more depression, anxiety, hallucinations. They do have sometimes more trouble sleeping, that's across the board, and we know that from this study. If you look, this was the EAGLES Trial, which the EAGLES stands for, down at the bottom you can see, Evaluating Adverse Events in a Global Smoking Cessation Study. This was an FDA required clinical trial to evaluate the safety, the neuropsychiatric safety of [inaudible 00:03:40] bupropion in over 8000 persons with or without a psychiatric illness.

So we had 4000 people with a psychiatric illness, either a psychotic, an anxiety, or a mood disorder, and 8000 people without. This was at 144 sites around the world. And what you see in the first series of bars, this is the rate of adverse events amongst people without a psychiatric illness. The blue bar is varenicline, 1.3%. The green bar is bupropion, 2.2%. The purple bar is nicotine patch, which has an active control of 2.5%. And the gray bar's placebo, 2.4%. So if you don't have a psychiatric illness, you have about a 2% chance of having a moderate to severe neuropsychiatric side effect when you try to quit smoking, regardless of what treatment you take, right? You have just as much chance of having a side effect with placebo as you do with an active medicine.

And then if you look in the middle, you see these are the rates of side effects during a smoking cessation attempt. Again, in blue with varenicline, in green with bupropion, purple with nicotine patch and gray with placebo. So, you've got about a three times greater chance of having a neuropsychiatric adverse event, psychotic disorder, than if you don't have any psychiatric illness. No mystery there. That's over the course of 16 weeks, many people or about 6% of people will have some kind of psychiatric symptoms flare up during that time. But it's no different by what treatment you take and by what is exactly the same rate in varenicline, bupropion and placebo.

And then in the far right, in mood disorders, it's the same thing as there's no significant difference across these drugs, including placebo for people with bipolar disorder who try to quit smoking. And this is the reason why I think safety, people are scared to take a medication to help them quit smoking. And the idea of, I had time doing this, the biggest trial ever in the world for smoking cessation treatment was to understand, what is that risk? Is that a risk we need to worry about? Because we don't want to see people having exacerbation in their psychiatric symptoms when they try to quit smoking, certainly not due to a medicine that's intended to help people be successful quitting. Lo and behold, we don't see an increased risk in this very large study that was powered to be able to see that. So next slide.

So, I use this information to talk to, not only doctors, but people who smoke and their family members on what's the risk of having a moderate to severe psychiatric adverse event when they try to quit smoking. And it's pretty simple based on this trial, if you don't have any psychiatric illness, your risk is about 2%. If you do have a psychiatric illness, your risk is about 6% of having some kind of transient psychiatric symptom while you try to quit smoking, right? But the key is, is that rate is not different whether you're on an active treatment that actually improves your chance of success, or on a sugar pill or placebo. Critically, we looked really carefully at this and there's no pattern of neuropsychiatric adverse events that are the most worrisome, we don't see more

irritability or suicidality, or, say, aggressiveness or feelings of hostility, and we don't find any psychiatric subgroup to be particularly at this. To the next slide.

What we do see is a major difference across these medicines in efficacy, particularly for people with psychotic illness. So if we look in the middle four bars, this is quit rates. Again, blue is for varenicline, 23%, green is bupropion, purple is nicotine patch, and then gray is placebo at 4%. And this is what we see time and again for people with psychotic illness, there's schizophrenia, [inaudible 00:08:12] disorder, is without a medicine, even with the best sort of behavioral group treatment support, we only see about 4% of people being successful in trying to quit. And trying to quit is hard. We want to increase people's chances of success the first time they try.

And so, what we see here is no matter whether you're in the non-psychiatric cohort, whether you had a psychotic illness or a mood disorder, what we see is the best treatment is varenicline. And in all of those, varenicline or Chantix is statistically significantly superior to bupropion or Wellbutrin, and nicotine patch. And there's no difference, and that's been shown time and again, they're about equally effective and they're better than placebo in every group. So yes, the patch works, yes, Wellbutrin works compared to placebo, and yes, varenicline works better. And that's true in all of these groups.

So the absolute quit rates are different depending on your psychiatric status, but the relative quit rate is the same. And in fact, your odds of quitting are even or are improved more if you have a psychotic illness than if you don't, right? And that's again because the placebo quit rate is just so low. And we see that time and again, that people with a psychotic illness really seem to need a medication to sort of replace that nicotine during the time that they are trying to quit. So, next slide.

So this big study which we call the EAGLE study made a huge impact. Basically, what happened was both the FDA and the European Medicines Association, which is essentially the FDA for Europe, removed the box warnings for both bupropion or Wellbutrin, and varenicline or Chantix, right? And to me, that was huge, because what I saw is that was going to mean that doctors were going to be less hesitant to prescribe these effective medicines for people with psychiatric illness, in particular, and people and their families would be less afraid to use them, because this box warning's been removed. And that has the chance to make an enormous difference in people's health, and their quality of life and how long they live. Tobacco products are the only consumer product to kill half their users when used as directed. So that's quite a statement. So, next slide, please.

So, this slide, I think you can see all of these at once, there's no animation here, so I'll just start through with the myths. And the myths are huge. When I first started doing this, people said to me, "What! You're going to make your career helping people with schizophrenia quit smoking? They don't even want to quit smoking." And that's not true

at all. People with serious mental illness want to quit at the same rate as people without any psychiatric illness. 60 to 70% of current smokers with serious mental illness say they want to quit.

The next myth is that quitting worsens psychiatric symptoms. And that is super not true. In fact, a really nice paper came out about three years ago in the British Medical Journal, very nice paper, showing that stopping smoking, not only doesn't worsen psychiatric symptoms, but within six months, quitting smoking, improves depressive symptoms, anxiety, and perception of stress in your life with a large effect size that's equivalent to the effect of an effective antidepressant medication.

Then the next myth is that meds don't help people with serious mental illness quit smoking. Number one, they're not going to be successful people taking, so it's not worth any risk. And that couldn't be less true. Like I showed you in the last slide, smokers with serious mental illness are three to six-fold more likely to quit when prescribed a medication. That's 300% to 600% more likely, right? And that's largely because only about 4% quit with behavioral treatment alone.

And then this last one is really new information. And it says a lot of doctors think that meds should only be prescribed for smokers who are ready to quit completely, right now. And that's not true, and in fact, the official guidance has changed. And that's on the next slide. Okay, so the animation's not working. That's all right. So there are three ways to quit smoking, and all start with a smoking cessation medication. And the first is the usual way, there's a fixed quit date, people would come in, they say, "Doc, I'm ready to quit. Let's set a quit date next week. And we'll start a medicine and I'll set a quit date next Monday or next Sunday."

And so, we prescribe a medication, I explain what side effects to think about, to call me if there's any problems, and they keep smoking for that first week while they get ready to quit. And getting ready usually means setting a quit date and planning that day out, maybe sometimes going to a place where smoking is not allowed, like the public library, or the local mall or someplace where it's comfortable. And you can do something you like to do, or go to movies, back within pre-COVID days, where you can't smoke. The middle bar shows this new way that the FDA has approved for quitting smoking, and that is you have a flexible quit date. And I usually ask people to set at five weeks after starting a smoking cessation medicine.

So we start the smoking cessation medicine where you see that first green dot, and they take that medicine for a month, and they keep smoking during that time all they want. And the point of that is to get that medicine on board and they're sure that they tolerate it, that they're not having side effects. So when they set their quit date, when they have some side effects around the time that they quit, we know that those are nicotine withdrawal symptoms, we know it's not caused by the medicine.

And this is what I really recommend, and this is what we've used now for, gosh, more than 10 years as our strategies, particularly for people with serious mental illness. Because we meet once a week in that month after they start medicine and we plan their strategies, so that when they do set their quit date and try to quit, they're more likely to be successful. And then we continue the medicine for about six months after that time, particularly if they're successful.

And then the last one is really the most radical one for the FDA. And what they said is, "Start a smoking cessation medicine for everybody, even people who aren't clear that they're going to be able to set a quit date right away." Right? So start the medicine. And the idea is you start the medicine for every smoker. Just like if you've got diabetes, you don't wait for somebody to be willing to change their diet and start an exercise program before you start them on insulin, or Metformin or some medicine, you do both at the same time. And that really makes a lot of sense to me.

And so the idea is that we're trying to get doctors to offer smoking cessation medication to all smokers, and then work with them to maybe try to cut back a bit. Maybe if they're a pack a day smoker, maybe over that first month, try to cut back to half a pack a day. And then over the next month, maybe try to go down to five cigarettes per day. But to do it at the person's pace, which really makes a lot of sense.

So to me, this middle one, where some people really do well and they prefer to just set a quit date, especially if you're in a group with other people, you can all set a quit date together and support each other. So some people really prefer that. And then others just setting a quit date isn't going to work for them, and doing it gradually works. And Gail Daumit and I just finished a big study where we enrolled people who are willing to set a quit date within the first month. And also, people who said that they wanted to quit, but they weren't ready to set a quit date for six months. And Io and behold, starting a medicine right away worked for both groups. So next slide, please.

So, this is really things that you should be expecting from your doc when you go in. You should expect them to ask you each time you go in if you smoke. And people with psychiatric illness have the highest rates of smoking. And then you should expect for them to remind you that quitting smoking is your power and it's the number one, it's the single best thing you can do for your health. And in the study that Gail Daumit and I did together, we [inaudible 00:17:55], we did exercise, and weight loss, and diet and smoking cessation, all the things to improve heart health. And in our big study, the thing that really moved heart health or people's risk for having a heart attack was quitting smoking. The rest moved things in the right direction, but it was quitting smoking that made a statistically significant difference in that big study.

So you should expect your doctor, in this third panel, to encourage you to start a medication at every visit, right? So if you aren't ready at one visit, you should expect him to ask you again the next visit. And then decide together whether you want to set a fixed quit date in a week, or if you want to have a flexible quick date over the next five weeks,

or if the gradual approach to quitting works for you. And then you should expect a call back within the next week or so from the nurse or the doc where you can talk about how well you're tolerating the medicine, if you're having any adverse event and if you are having some problems where you can problem solve around that. Next slide, please.

So, there's no difference in dosing these medicines if you do or don't have a major psychiatric illness. For varenicline, it's a half a milligram a day for three days and then a half a milligram twice a day for four days. And then it's one milligram twice a week for 11 weeks. And then if you've been successful, we recommend another three to nine months of treatment. And in fact, in the study that we are about to publish with Dr. Daumit, we offered people treatment for 18 months, and people continued to quit over the course of that 18 months. And so that's where we think the field is moving. There're no significant drug-drug interactions with your other psychiatric medications. So it's a really easy medicine to add to the medications that you might be on for your psychiatric illnesses.

Nausea and headache are really common. Vivid dreams are also really common. Insomnia does happen for some people. And that's one of the reasons to sort of just start the medicine and then wait a few weeks before you actually try to quit smoking, so you see how well you tolerate it. Are you sleeping okay? Right? Did you have some nausea, but that's gone away now? And then you're really ready to set your quit date. The next slide.

And this is how, too, for nicotine replacement therapy. Now, what we recommend for almost everybody is dual treatment. Dual treatment may even be as good as varenicline. And that means you use the patch, so that's the long acting version of nicotine replacement therapy. You put a patch on every day, you move it around a different site every day, one arm, the other arm, the back, so that your skin doesn't get irritated. And then at the same time, you use either the gum or the lozenge. And that's what you do, those really help with cravings. It allows you to choose the amount of nicotine, right, that you have in your body at any time.

And one of the things that works really well is we ask people when they're trying to cut down, or quit that they make a deal with me that when they have a craving, they'll use a piece of gum or a lozenge first. And if they still want to smoke that cigarette after the lozenge or gum is done, okay, but they try the gum or lozenge first. And that works really well for folks because cravings come and go, even though they're very intense when they happen. And a lot of people tell me, "Hey, doc, the gum doesn't work for me. I've tried it before."

And there's one common reason why the gum doesn't work and that's that it doesn't get absorbed when you have an acidic oral environment. So, if your mouth is acidic, and usually that means coffee. So if you're a coffee drinker, and you're using nicotine gum, just one swallow of water after your coffee and before you use the gum will return your mouth to sort of, what we call, a neutral pH and that will help the nicotine be absorbed.

And then the main thing is you don't chew it like gum, the nicotine gum, you bite it a few times just to soften it up and then you park it between your gum and your cheek. Same thing for the lozenge, don't chew it up, because the whole point is for the nicotine to get absorbed across, what you call, the mucous membranes in your mouth. It won't be absorbed from your stomach, it'll just be digested, essentially, and will get to your brain as nicotine. So, those are the main reasons, because most smokers have tried the gum or the lozenge at some point, so I would encourage you to try again. And I think that might be in two slides coming up. So let's look at Wellbutrin on the next slide.

So this is just how to take Wellbutrin. And it's just the same as you would bupropion. SR is the same as bupropion. XL, they're really not different. And so the dosing is 150 milligrams a day for three days, and then 150 milligrams twice a day. And I think people tolerate this quite well. The only possible exception is people who feel quite anxious a lot of the time or have feelings of activation that's uncomfortable, because bupropion or Wellbutrin can make those a little bit worse. On the other hand, if people are taking sedating medicines, the kind of activation you get from bupropion can be kind of helpful sometimes. So, a lot of times we'll choose people's meds based on using the side effects to our advantage.

And this big square box in this slide is there just to remind you that we've studied these medicines in so many smokers. So, there was a meta-analysis, which means an analysis where you pull together many studies. So over 182 studies in over 70,000 smokers. And just like the EAGLES trial, it found that varenicline triples your chances of quitting versus placebo, that's in the general population. And it increases the odds of quitting by 50% over and above NRT and bupropion. So varenicline is 300% better than placebo or three times better and is 50% better than NRT or bupropion.

So, that's really my go-to, it's what I encourage people to try first. And then let's not forget, NRT, nicotine patch, and gum, and bupropion or Wellbutrin, also nearly double your odds of quitting versus behavioral treatment alone. So they really worked. 80% better chance than placebo is really good, but 300% chances is better, I would say. Next slide, please.

So this is really two different messages. So if we look at this first graph about how long to treat, this is from a study we did in 256 smokers with schizophrenia or bipolar disorder, this was published in JAMA. And what we had seen is that people on medicine were able to quit, but they fell off a cliff as soon as we stopped their medicine. I just remember that so incredibly, people worked so hard to quit and come in our studies, and then within two weeks of the study ending, they'd be smoking again, and it's like all that work. And so, we did a trial where we gave everybody active medicine, and we tried to get as many people to quit as we could.

And then at week 12, which is when, according to the FDA, you're supposed to stop smoking cessation medicines, back in the old days, we took all the people who had quit and we flipped the coin and assigned half to placebo and half to stay on Chantix or varenicline. And what you see here is just what we've seen clinically. When you switch to placebo, you started relapsing. The average time for relapse was 35 days in this group that went on placebo. And the average times for relapse was over a year, 358 days in those who stayed on varenicline. And basically, a year's worth of varenicline tripled your abstinence rate at a year, right? 60% versus, this is 19%, were able to stay quit. And that's amongst the ones who were successful to begin with.

And based on this, as the pharmacy director for MassHealth, which is Medicaid and Massachusetts, made the Pharmacy Benefit for varenicline one year for people with schizophrenia. And in working with Gail Daumit for next month speaker, Medicaid and Maryland has just done that. It took them a little while longer, but they just made it available. So, the word's getting out. And data also suggests that extended treatment or maintenance treatment, as we call it, with bupropion or NRT can sustain cessation.

And we did another paper where, I don't have the slide of it, but we compared people with schizophrenia and bipolar disorder in our paper that was published in JAMA, and people with no psychiatric illness in [inaudible 00:28:06] paper that was published in JAMA. And we basically analyzed the data together, person level data where we're able to control for sex and for how much you smoked. And we found that maintenance treatment normalized the relapse curve. So if you stayed on varenicline, [inaudible 00:28:26] study was only for six months, and we only were able to do it that long. The relapse rate was the same in people with schizophrenia and people with no psychiatric illness. But if you went on placebo, those with the psychiatric illness relapse faster. So that there, again, the medicine seems to be especially helpful for people with the psychiatric illness.

And studies have shown that those are just the people who are least likely to be given a medicine to help them quit by their doctor. Okay. So, we have this idea. So go to the other side of this slide. Oh, no, go back, please. Yeah, so the other side of this slide, this is repeat attempts, okay? So, we have this idea that I certainly learned in residency with CAM and in my fellowship at Mass General, that if you start a medicine and it doesn't really work for somebody, like an antidepressant, well, you need to try a different medicine. But that doesn't seem to be the case for smoking cessation. And that's because, I think, it takes an average of five tries before people can quit for good.

And this my colleague, Dr. Gonzalez out of Oregon, did this trial where he enrolled only people who had failed a trial of varenicline. They had had varenicline before and, either they quit and relapsed or they never quit, those people were enrolled and they were randomized to get varenicline or placebo, right? So they have had varenicline before, and they would basically be enrolled for a repeat attempt. And look at this, these people

who previously failed varenicline, 45% were abstinent at the end of this trial for the last month of treatment, versus 10% who got placebo plus or behavioral treatment.

Now this trial is not in people with psychiatric illness, but it just goes to show you just because you've tried once or twice. I tell people [inaudible 00:30:33], "It doesn't work for me doc." I ask them how many times they've tried, "Oh, I've tried three times," and I say, "Well, you're not even average, we're going to try it again. We're going to learn from what you learned before about what helps you quit for the days that you were quit, and we're going to build on that." So next slide, please.

So this is why we're here, is that 15% of the general population smoke tobacco, right? And that hasn't budged, and we need to do better for the general population. But 44% of individuals with bipolar disorder smoke tobacco, and 64% of individuals with schizophrenia smoke. And what that means is, if you look in the middle sort of column here, is that mortality for people with serious mental illness is 3.7-fold higher than the general population. What does that mean? It means that you die 25 years earlier. And if it's schizophrenia, it's over 29 years earlier. That's a generation, that's not seeing your grandkids graduate high school. That's huge. And this is fixable, right? Every quit attempt helps you move towards permanent abstinence.

So, a quit attempt where you quit for a bit and resume smoking is a success, right? Because you've probably learned something, and it means the next time you try, you're more likely to quit. So, about 20 to 30% of those who quit are able to sustain that abstinence in that try, but the ones who aren't able to quit in that try are more likely to quit the next time, all right? I'm going around trying to get doctors to understand that and encouraging and prescribing medications for people with serious mental illness is so worth it, and so, so helpful. Because, again, tobacco is the only consumer product to kill off its users when used as directed, right? That's a pretty crazy statement. Next slide, please.

So, this is super new. And I want you to bring this to your doctors, and any treaters, please spread the word. The new guidelines, these were published in January 2018, so almost two years ago, is that all smokers should be treated with a medication regardless of readiness to quit. The idea is the treatment will change the readiness to quit, right? And how this works, so you give varenicline. Varenicline [inaudible 00:33:32] receptors in the brain, and it buys more tightly than nicotine does. So if you've taken for varenicline that day, and you smoke, you don't feel much, it doesn't reinforce. You might have learned in psychology, you start to sort of get extinction, you just don't get the buzz from it.

But it also opens those receptors a little bit, so you don't get withdrawal symptoms. And nicotine replacement therapy works sort of similarly. And the analogy is that we don't wait for people with diabetes or high blood pressure to be, "Ready to change their diet and exercise before we offer them an effective medication." We try to do both. And we

certainly offer the medicine first and then we work overtime on the behavior change, because behavior change is hard, right? Habits are hard to change. So, next slide.

This is sort of a schema showing these new guidelines, which is essentially an opt out. If you're a smoker, your doc should recommend a prescription for you at every visit and make [inaudible 00:34:55], right? So rather than the way most primary care doctors and psychiatrists work now where they're not going to bring up your smoking cessation unless you do. The new guidelines are they should bring it up and if you say, "No, thanks, doc [inaudible 00:35:12]," they should bring it up at every visit, right? So that's what this flow chart shows. At the top, in purple, offer treatment options, offer behavioral support and prescribe pharmacotherapy. And first line is varenicline, or dual NRT. And second line is bupropion, or single NRT.

And if the smoker, the person accepts that, that's great, you provide some support [inaudible 00:35:41]. And then you [inaudible 00:35:43] to make sure they don't have any side effects, and if there are, you problem solve around how to relieve those. But if they say, "No thanks, not this time," then you bring it up at [inaudible 00:35:55] every and then you monitor [inaudible 00:35:58] over time. So, next slide, please.

So this is the medicine that has sort of said, this is table four in the new guidelines. So first, varenicline treatment, or a combination of nicotine replacement therapy. And we're working on actually a study where we start that in the psychiatric hospital. And certainly should be done if you're hospitalized for a cardiovascular disease. Second line is bupropion or single nicotine replacement therapy. And then down here, this is pretty cool, there are a couple of studies showing that adding nicotine replacement therapy to varenicline improves effectiveness over varenicline alone.

And then I've done now two studies [inaudible 00:36:50] when he was at Yale did two studies of bupropion... Sorry, of nicotine replacement therapy with and without bupropion, and found the two together were better than bupropion alone. And so, success rates are high, the medications are safe and available, and they increase your chance of success to 300 to 400%. And I think we've got time; I'm actually going to go through... Next slide. This will be available to you. These are all the papers that I've talked from today. The EAGLES trial is this one. This is Anthenelli, et al. I'm the senior author on this paper. It was published in the not too shabby Journal Lancet. And it really did change practice and change the regulatory environment.

The retreatment, if you want to look at that, that's the Gonzales paper. So, if at first you don't succeed, try again. So repeat treatment works. This is the JAMA paper I showed... Sorry, no, this is the paper where we showed, with our JAMA data, that... So this is the JAMA trial where we showed maintenance treatment triples out [inaudible 00:38:15] a year. And then this is the paper that showed that staying on varenicline normalizes the relapse for schizophrenia and bipolar [inaudible 00:38:24] psychiatric illness whatsoever. And then this is the new consensus guidelines that say that to treat every

smoker regardless of this readiness to quit thing, because the treatment will move the readiness to quit. The next slide.

If those weren't enough papers, here's some more. We've got best practices from the Harvard Review of Psychiatry a few years back, and then other papers coming out [inaudible 00:38:58] without the benefit of [inaudible 00:39:03] paper, that's in the Journal of Affective Disorders for the bipolar subcohort in EAGLES. This is the [inaudible 00:39:14] clinical psychopharmacology. And then there's a paper coming out just in January in psychiatric services just showing the schizophrenia subcohort from EAGLES. I'm going to go to one more slide. Ken, I see you there, but I want to show really why we're here. So the next slide.

This is classic data from a physician's health study in the UK. This was published in the British Medical Journal. I think when I, long time ago, I think it's before I was [inaudible 00:39:52], showing that low level of smoking takes 10 years off your life. And this is in physicians, and people with serious mental illness, as I showed you, it's 25 to 29 years, right? And so how you read this is, is if you're a smoker, you've got a 58% chance to live in to age 70. If you've never smoked, you've got an 81% chance of living to age 70. [inaudible 00:40:22] the next slide. Quitting works. So that dotted line is somebody who quit smoking in middle age. They've got an 80% chance of living to age 70. It's not an 81% chance, but it's sure better than 58%. This is really the reason we're here, is it fucking kills.

And the next slide shows that in a million women, that if you smoke like men, you die like men. And again, this is just that same curve flipped on its side. If you're a non-smoker and you're a woman, you got a 78% chance to live in age 80. If you're a smoker, it's 47%. And next slide, and then this will be the last one. Again, to show you that quitting really works. If you quit at age 30, it's like a get out of jail free card, your likelihood of early death is no different than a never smoker. But even if you don't quit till you're 50, you're lucky that all-cause mortality has increased 50% compared to a never smoker, but it's nowhere near as somebody who never quit, which is 300 for a smoker, right? So, quitting at age 50 halves mortality. And I'm going to show you what to expect. Next slide.

The next slide is a cover from JAMA. We got our paper in this particular issue of JAMA, which was the 50th anniversary of the time that the Surgeon General made his report that smoking caused cancer in 1964. And 50 years after, we had a paper in this journal, but we couldn't take so much solace, because adult smoking had declined by 55% in the general population, but smoking prevalence among people with serious mental illness remains 53%. And that's higher than it was in the general population in the United States in 1964. Next slide.

This is an incredible paper that came out in California showing that if you'd ever had a hospitalization in your lifetime for schizophrenia, bipolar disorder, or major depressive

disorder, you're at a 50% chance of dying from one of the 19 diseases that causally are linked to tobacco use. That's not half the smokers, that's half the people who had had a hospitalization. And this is in the statewide data from California. So, it's a major deal. And the good news is that, next slide, quitting really works. Quitting reduces all of these things. And the next slide, and this will be the last one. Quitting actually shows that you have reduction in depression, in anxiety, in stress and quality of life. And the actual data are, I think, on the next slide, which is a little hard to read, but one more spot.

Yeah, so this shows the actual data showing that for every study, the average, which is the squares and the diamonds, favors improvement in anxiety, depression, mixed anxiety and depression, and stress for quitting versus non quitting. Quitting smoking, yes, you've got some nicotine withdrawal symptoms in the first couple of weeks, but it's a better life, and only that will make you have less suffering from these psychiatric symptoms within six months of quitting. So I'm going to stop there. And I'd love to have questions. And I understand, Ken, you've got some questions?

Ken Duckworth (<u>00:44:31</u>):

I've got questions. Dr. Evins, that was a fabulous talk. And I think you make the case quite convincingly that it's never too late to quit, that you can quit. You may have to stay with it and be persistent, but it could change your quality of life and quantity of life, right? That's the best [crosstalk 00:44:54].

Eden Evins (<u>00:44:53</u>):

That's right.

Ken Duckworth (<u>00:44:54</u>):

All right. So the first question, a person wants you to go over varenicline for schizophrenia. Is that your recommendation for smoking cessation?

Eden Evins (<u>00:45:03</u>):

100%, yeah.

Ken Duckworth (<u>00:45:04</u>):

100%, yes. So let's develop that. It's the best because it's safe and effective, is that it?

Eden Evins (<u>00:45:13</u>):

That's it. It causes no more symptoms than placebo, but it increases your chance of success by five-fold.

Ken Duckworth (<u>00:45:22</u>):

Fivefold.

Eden Evins (<u>00:45:24</u>):

500%.

Ken Duckworth (<u>00:45:27</u>):

This is a doctor question. When Chantix first came out, I'm using the trade name because that's the most advertised version that you might have seen on television, there was concerns about suicidality, and I think-

Eden Evins (<u>00:45:41</u>):

That's right.

Ken Duckworth (<u>00:45:42</u>):

... physicians were quite reluctant to give it to anybody with any mental health vulnerability. That study seems to pretty definitively put that to rest. So I just want to make sure we take that up.

Eden Evins (00:45:55):

That's right. So that was the intent of that study, that was an FDA mandated study. I'll give you a little bit of history, the reason we got into that pickle to begin with, is that the FDA allowed the company to conduct [inaudible 00:46:15] safety and efficacy trials in studies that excluded people with psychiatric illness. A majority of smokers have a psychiatric illness, but yet a medicine was approved without any use in people with psychiatric illness. And so, that's just clear discrimination, right?

Ken Duckworth (<u>00:46:39</u>):

Yeah.

Eden Evins (<u>00:46:39</u>):

And so what the EAGLES study showed is if you've got a psychiatric illness, you're three times more likely to have a psychiatric side effect during the time that you quit smoking than if you don't have a psychiatric illness, right? The rate's 2% if you've got mental illness and 6% if you've got a psychotic illness. But there is no difference by whether you're on a placebo or not. I mean, in one of the first studies I ever did of varenicline, the maintenance trial, I was taking care of one of [inaudible 00:47:14] my teachers, Don Goff, a person who was working with him as their treater was in the study, and this person got more psychotic about three weeks into the trial.

And Don called me up and said, "You need to take her off out of the trial," and we said, "Of course," and we did. And [inaudible 00:47:36] she's on placebo. People have fluctuations in their symptoms, it's part of the challenge of having this mental illness. So that's what I think what those early reports must have been. And they've been laid to rest in study after study after study. And then now you think [inaudible 00:47:56] EAGLES is it confirms a large body of evidence of smaller trials.

Ken Duckworth (<u>00:48:02</u>):

And these slides are available to the listeners and participants today. Dr. Evins is a full professor at Harvard. I mean, this is exhaustively researched. It's very refreshing to see every last study laid out, you make the case quite convincingly. All right, next question. Am I supposed to use the patch or the gum while smoking? I thought that was bad for me.

Eden Evins (<u>00:48:27</u>):

It's not bad for you, and you can use the patch and the gum while smoking.

Ken Duckworth (<u>00:48:34</u>):

But why is that? Nicotine isn't bad for you?

Eden Evins (<u>00:48:38</u>):

Nicotine will give you a stomachache if you use too much of it. So, if you use the patch and the gum and you still smoke some, you're going to smoke less. [inaudible 00:48:54], a good friend of mine at the University of California, San Francisco did a... He's a cardiologist, did a fantastic study where he put one, two and three patches on smokers, and put a Holter monitor on them, which does a continuous EKG and he did [inaudible 00:49:13], et cetera, and told them to smoke as much as they want. And they smoked less, and there was no problem. This was back in the late '90s. I don't know what it is, who it is that starts these urban myths of how difficult smoking cessation medications are. I think they're only dangerous tobacco industry.

Ken Duckworth (<u>00:49:35</u>):

Well, you're crushing these urban myths very nicely. Next question; talk a little bit about vaping. And I don't know if this is an urban myth or not, but the question is, I've been told that vaping carries no risk, why should I quit vaping if it's not going to cause me lung, heart or cancer risk?

Eden Evins (00:49:57):

Great question. So, the risk of vaping is all relative, right? It's super relative. So, for that, I just put a grant in yesterday for a big trial to help kids who've never smoked quit vaping, because vaping is normalizing tobacco use and getting a whole new generation of teenagers addicted to nicotine. Again, kids don't smoke, it's almost rare, but they sure vape because it's cool. Now, if you're a three pack a day smoker, and you switch entirely over to vapes, well, that's less harmful than three packs a day of cigarettes. No shit. No question. Less harmful.

Ken Duckworth (<u>00:50:42</u>):

Okay. Possibly you know the answer to every question, fine. [crosstalk 00:50:47]. Question comes in, "I am 66 years old, is it too late for me?" And a related question, "I've been smoking for 30 years, is it too late for me?"

Eden Evins (<u>00:51:00</u>):

No. Even if you have emphysema and you're on oxygen, what quitting smoking will do is not make your emphysema better, but it will make it stop getting worse, right? It will stop the progression. So absolutely not, it is never too late. And I don't have in this slide deck, but they're wonderful graphs. Richard Peto, who's a fabulous, famous epidemiologist has made these graphs of preservation of lung function out. And I think his graph stops at age 88 for some reason. But no, it'll preserve your quality of life and it'll stop the worsening of your lung function. You've probably got some emphysema, somebody who smoked for 30 years probably got some emphysema, so it'll stop the progression.

Ken Duckworth (<u>00:52:01</u>):

I used to play in a pick-up basketball league called Never Too Late. And of course, they could have a smoking cessation sponsor for that, because it sounds like it really is never too late. Here's another sophisticated question, NAMI audience always asks great questions. "What is the current thinking about quitting smoking when you're living with other addiction? And whether that's alcohol, opiates, cocaine, whatever it is, is it the idea that you're supposed to stop all at once so they don't trigger each other, or is it more like, 'I'm ready to quit this, but I'm not ready to quit that. Don't make me give up this, I'm willing to give up that'"? How do you think about that from a behavior change theory?

Eden Evins (<u>00:52:48</u>):

That's a great question. And really, this talk that I just spoke to the opt out approach essentially works for people who have other addictions. And so, if I'm treating somebody and they're going on Suboxone for their opioid addiction, or they're going on Naltrexone to stop their craving for alcohol, I will also prescribe varenicline. Why not have less craving for tobacco, right? And tobacco essentially makes other substances more addictive. And so, if you're smoking and you have a slip, this has been shown for cocaine and heroin so far, if you have a slip, you're more likely to basically have a relapse. And that works in animals as well. If you pretreat an animal for two weeks with nicotine and then expose them to cocaine, that cocaine is more addictive.

Eden Evins (00:53:53):

And the worst thing, cocaine doesn't need a lot of help being addictive, but it's more addictive. And it doesn't work the other way around. If you pretreat with cocaine, nicotine is not more addictive. So, nicotine and heroin are the two most addictive substances we have. So, for them to put them together, your doc should be prescribing you something, and if they aren't, please educate your doc and ask for it.

Ken Duckworth (<u>00:54:20</u>):

Does it work the other way? A question is related, "I'd like to cut down on my alcohol use, I smoke when I drink." Right? So is the idea that this person would consider doing them both.

Eden Evins (00:54:36):

So, I wrote an editorial in the American Journal of Psychiatry, for Stephanie O'Malley at Yale did a study of varenicline for alcohol dependence. And the only good finding she had was varenicline, they reduce the drinking, but they're more likely to quit smoking. Again, though that's a treatment for quitting smoking, it's likely to help you. Certainly, you can keep your goals and mind better...

Ken Duckworth (<u>00:55:08</u>):

Got it. A person asked a question, "My patients, clients," so this is a mental health professional, "Says that smoking helps them manage anxiety and depression." How do you think about that?

Eden Evins (00:55:23):

[crosstalk 00:55:23]. Yeah, I actually have pictures for that too, but I don't have them here. So yes, because every time you smoke, they say first thing in the morning you're feeling anxious you smoke, and you feel a reduction in anxiety. Well, that's because anxiety is a withdrawal symptom, and between every [inaudible 00:55:43] you go into withdrawal. And so your experience is, every time you smoke, you have a reduction in anxiety. That is true. But after you quit, you stop having that spike in anxiety with withdrawal, and so your average anxiety level, actually, is lower.

Ken Duckworth (<u>00:56:03</u>):

People are confusing the symptoms with the cause. So they think smoking is addressing underlying symptoms, when in fact, it's addressing withdrawal. And this is the idea of nicotine replacement therapy, right?

Eden Evins (<u>00:56:20</u>):

That's right.

Ken Duckworth (<u>00:56:21</u>):

You deal with no withdrawal varenicline.

Eden Evins (<u>00:56:25</u>):

That's right.

Ken Duckworth (00:56:26):

That's right.

Eden Evins (<u>00:56:28</u>):

That's right. [crosstalk 00:56:28]. And that's why it's great to be able to say, "Hey, look, let's try this out. Let's go on for a month, go on duo NRT or go on varenicline for a month." Don't change your smoking. And then basically, they have replacement, and

then they can't give up the smoking, and will see in that meta-analysis of, I don't know, 40 or somewhat papers in the British Medical Journal paper tailor it all, actual anxiety symptoms go down and that's why.

Ken Duckworth (<u>00:57:00</u>):

Excellent, that's excellent.

Eden Evins (<u>00:57:02</u>):

Cool, right?

Ken Duckworth (<u>00:57:03</u>):

This person is taking bupropion for depression, has seen no effect on their desire to smoke. Is varenicline or NRT a next logical step? So they happen to be on bupropion, which has a cross-effective effect on smoking cravings, right? But it happens to be an antidepressant, right?

Eden Evins (<u>00:57:27</u>):

So I would add duo NRT to that, just because I've studied it and I know it's well tolerated. [crosstalk 00:57:34]-

Ken Duckworth (<u>00:57:33</u>):

What is duo NRT?

Eden Evins (00:57:35):

Duo, that means the patch plus, either the gum or the lozenge. So two forms.

Ken Duckworth (00:57:40):

Full monty?

Eden Evins (00:57:41):

Full monty the kitchen sink.

Ken Duckworth (<u>00:57:44</u>):

Okay, that's very helpful. Now, we haven't talked at all about therapy or support. We've been talking about the biological cravings, how you have to stay on it for a long time, that it's safe and effective and that people's symptoms don't get worse. I mean, it's been an amazing educational opportunity for all of us. Psychotherapy, cognitive behavior therapy, support groups, 1-800-QUIT-NOW. What other non-biological things are in the toolkit?

Eden Evins (<u>00:58:18</u>):

You bet. And I'll just say, the reason I talked about meds is because people with serious mental illness don't quit without them [crosstalk 00:58:27]-

Ken Duckworth (<u>00:58:27</u>):

Yes, you made that point very clearly, actually.

Eden Evins (<u>00:58:31</u>):

They don't get them. But yeah. We use a group program, we deliver a group, and we get a former quitter to come in with serious mental illness, because they've got more street creds than I'll ever have to talk about what worked for them. It's supportive. And people get that healthy competitiveness going. So if you can get a group going, we've got a manual, we'd be happy to share that, that's not available to everybody. So, there's the North American Quitline. So if you live anywhere from Mexico to Canada, you can call the Quitline. It's available through all of North America, 1-800-Trying-To-Stop. I think it-

Ken Duckworth (<u>00:59:24</u>):

Trying to stop, okay.

Eden Evins (00:59:25):

... yeah, is helpful. I've never tried to use just a medicine for folks, I feel that-

Ken Duckworth (<u>00:59:34</u>):

Got it.

Eden Evins (<u>00:59:35</u>):

Yeah.

Ken Duckworth (00:59:36):

NAMI's big on the peer movement, of course, you're familiar with the CHOICES program in New Jersey, undoubtedly, the coach peers?

Eden Evins (<u>00:59:43</u>):

Yes.

Ken Duckworth (<u>00:59:45</u>):

Is that scalable? How might we think about that? We have this amazing community of peers.

Eden Evins (<u>00:59:51</u>):

So I'd love to talk about that. We just finished the PCORI trial where we enrolled almost 1200 smokers in Greater Boston. And the ones who got a community health worker,

which could have been peer, but basically was a bachelor's non-clinically trained, we put them through the five-day tobacco treatment specialist program, so they learned something about... They memorized these slides; they'd doubled their chances of quitting. So our community health worker really was helpful. And partly what that helped people do was to go to their doc and voice what their preferred preference was, help them with any problems at the pharmacy, getting their meds filled, help get them to group, give them rides to group [crosstalk 01:00:42], but this also helped them stick to their goals. And so, I'd love to talk about scaling this.

Ken Duckworth (<u>01:00:49</u>):

Good. Other question, how come my psychiatrist doesn't talk to me about my smoking?

Eden Evins (<u>01:00:55</u>):

It's really messed up. Nobody feels well trained enough. Some places like Massachusetts encourage smoking cessation treatment to be done only by your physical health doctor, not your psychiatric doctor, and the way they encourage that is they only pay for it if it's your physical health doctor. We can't run smoking cessation groups in a psychiatric clinic or addiction clinic and get reimbursed for it. And people feel that they don't have enough training, I think. And so, we're trying to change that.

Ken Duckworth (<u>01:01:35</u>):

Excellent. I'm old enough to remember when people were given cigarettes to sit through groups with me at the Massachusetts Mental Health Center, our favorite community mental health center. That, of course, was the early '90s. There's a lot of controversy when hospitals went to no smoking, right? Let's just talk a little bit about that. At NAMI we had some complexity because some people felt like, when they were in the hospital, they didn't necessarily want to quit smoking. Although, in the main, I think we felt that it was the right thing to do. But remember, we're into people's choice, and they're like, "That's not when I'm ready to quit." Tell me your observation about how the culture has changed around smoking, where you can smoke and how that impacts people.

Eden Evins (<u>01:02:23</u>):

Yeah. So I consulted to the Mass Hospital Association who were freaking out when Jayco was going to... They were really scared that there was going to be more people leaving against medical advice in dangerous ways, more dangerous behavior on the unit for patients and staff. And in the end, I mean, I did a literature review for them and saw that essentially, in other places, it was a non-issue. As long as you give people something to prevent withdrawal, then they can be comfortable, that way you don't expose others to secondhand smoke.

I mean, the smoking room in the Lindemann was just deplorable. And secondhand smoke, we've learned a lot about how dangerous that is. So it really respects others' rights. A bit like wearing a mask, it's not just for yourself in COVID time, it's really for the health of your community. So, I'm not sure I really answered the spirit of your question.

Ken Duckworth (<u>01:03:31</u>):

No, that got to it, right? I mean, the idea is it hasn't had a big impact at all, but people do require nicotine replacement strategies, so they don't arrive ill and withdrawn.

Eden Evins (<u>01:03:45</u>):

Yeah, and it's a teachable moment. We're trying to encourage people inpatient units should [inaudible 01:03:53] to offer nicotine replacement therapy that they've been on in the hospital when they go out. People who are often entitled to a month of free meds as they walk out the door from a hospitalization. And we found real variability in our fine Massachusetts, Boston hospitals, the doctor did a great job of sending people out and hooking them up with smoking cessation resources, and our great Mass General did not. So we're working on that.

Ken Duckworth (<u>01:04:22</u>):

Is there any evidence that smoking increases psychiatric symptoms? You mentioned that quitting smoking doesn't increase them, so what about the converse? How does smoking relate to symptoms?

Eden Evins (<u>01:04:37</u>):

Smoking causes symptoms in between cigarettes when you're in withdrawal. You can feel more nervous, more anxious, more stressed, and you can feel craving, which is a sense of just the opposite of being at ease or equanimity, right? Or peace. Smoking can cause tachycardia; it causes a rise in your blood pressure. Nicotine is a stimulant; I don't know of any credible data that smoking worsens psychotic symptoms or... One of the first reasons I started doing this work was to understand whether the glutamate hypothesis for negative symptoms but we [inaudible 01:05:26] people quit smoking if they would have worked the negative symptoms, and they did not.

The thing that I have seen is, and I've published several papers on, is that nicotine can improve your ability to experience things that are rewarding, okay? Makes the blue sky bluer, if you will. And that may be the reason... And it improves some cognitive deficits that are seen particularly in people with schizophrenia.

Ken Duckworth (01:06:01):

So I was going to ask you about cognition, because that was a good question, just came through.

Eden Evins (<u>01:06:05</u>):

Yeah, and so that may be the reason that maintenance treatment is so important for staying off tobacco for people with psychiatric [inaudible 01:06:15]-

Ken Duckworth (<u>01:06:19</u>):

Actual nicotine in their bodies without all the toxicities of smoking?

Eden Evins (<u>01:06:23</u>):

Yeah, nicotine or varenicline. So I tell you, my dad, I'm from North Carolina, I'll give you a little personal... I am from North Carolina and my dad smoked three packs a day. And in the year 2000, I think it was, I got him to quit on the gum. He used so much gum, but okay. You know what? It's 2020, and he's still on the gum. [crosstalk 01:06:53]. He goes off of it before his physical exam every year, and you do not want to be around him, not for those two weeks when he goes off of it.

Ken Duckworth (<u>01:07:05</u>):

So why does he go off of it before his physical exam?

Eden Evins (<u>01:07:09</u>):

Because he wants to show that he has a negative cotinine in his urine, that he's a nonsmoker.

Ken Duckworth (<u>01:07:15</u>):

I see.

Eden Evins (<u>01:07:16</u>):

So he basically detoxes from nicotine so that his urine sample is normal.

Ken Duckworth (<u>01:07:26</u>):

Fresh nicotine.

Eden Evins (<u>01:07:28</u>):

And I felt he couldn't stop, because he can't stay off of it and he can't taper. And some people, that's the case.

Ken Duckworth (<u>01:07:34</u>):

Yeah, that is the case. It's true for a lot of medicines that you're [crosstalk 01:07:38] hypertensives or lithium. Some people just appear to need these things for decades.

Eden Evins (<u>01:07:44</u>):

And the trial with Gail was an 18-month trial that we just finished. So we'll publish that. Maybe we will try it for the New England Journal, see how we do.

Ken Duckworth (<u>01:07:54</u>):

Let's talk about the sticky wicket of weight gain.

Eden Evins (<u>01:07:57</u>):

Yeah.

Ken Duckworth (<u>01:07:58</u>):

How real is that? How much risk does that confer? Quitting smoking is great for your health. But if you picked up five or 10 pounds, how much does that compare to the benefit of smoking? And how do you prevent picking up five or 10 pounds?

Eden Evins (<u>01:08:18</u>):

Yeah. With an exercise program and diet, in our study with Gail in Hopkins, that we showed no weight gain, no significant change in weight with abstinence. If you don't make a real effort, you can gain about five pounds when you quit smoking. Now the famous Walter Willett, I don't know if you know Walter Willett from the Harvard School of Public Health. So he famously said-

Ken Duckworth (<u>01:08:43</u>):

Yes.

Eden Evins (<u>01:08:44</u>):

... I think with no data, but with lots of experience, "That you'd have to gain 100 pounds to undo the cardiovascular benefit of quitting smoking if you're a pack a day smoker." So, there's no data, but that's an expert in diet, and exercise and cardiovascular risk. [crosstalk 01:09:03]-

Ken Duckworth (<u>01:09:03</u>):

I don't know, but I think we're going to make this the last question. I have asked you every question from every angle, it's been amazing to talk to you. Let's talk a little bit about the relationship between smoking, stimulating your liver and what that does to medications. Because I have been able to convince a few people to quit smoking, because I told them they could take less antipsychotic, right?

Eden Evins (<u>01:09:34</u>):

That's right. [crosstalk 01:09:35]-

Ken Duckworth (<u>01:09:34</u>):

So, let's just talk about that and make sure we understand that a little better.

Eden Evins (<u>01:09:39</u>):

Yeah. There are 1000 toxins in tobacco smoke. It revs up your liver, which is your body's detoxification system. So, if you're a smoker, your liver is really active. So your liver is also what breaks down a lot of the psychiatric meds you might take. Not lithium, not varenicline, but certainly medicines particularly, clozapine, olanzapine, lots of antidepressants are metabolized by the particular enzymes that smoking gets revved up. So the first guy who quit smoking back when I was a [inaudible 01:10:23] Clinic was also a UVA grad. That person was [inaudible 01:10:27], 500 milligrams a day, and really annoyed by the drooling that it gave him at night. He hated that.

And I said, "Look, you can probably..." and he smokes a lot, a couple of packs a day, "You can probably reduce your clozapine [inaudible 01:10:43] dose maybe in half." And he thought that was fantastic, and in fact, he did. He went down to 200, he quit, on bupropion, and he went down to 200 milligrams a day of clozapine. And he was a happy camper. And he comes back, he's the person who comes back to this day, 25 years later, to speak to often our smoking cessation groups the week before the quit date.

Ken Duckworth (<u>01:11:12</u>):

Fantastic.

Eden Evins (<u>01:11:14</u>):

And it's another reason to try to quit smoking in the hospital and to try to... You go in the hospital because you're having exacerbation of your symptoms, often you get your meds changed, but you get your meds changed while you're not smoking. And you get [crosstalk 01:11:29] while you're not smoking. And so, really, we want if people are off... They've gone through the worst of it, they've gone through the withdrawal in the hospital. If we can keep them off cigarettes on the way out, they're not only more likely to live longer, or live better, but the med change that they've just had is more likely to continue to provide symptom relief for them, smoking again, and revving up their liver and then being [crosstalk 01:11:58]-

Ken Duckworth (<u>01:11:58</u>):

Fewer side effects because lower doses, right?

Eden Evins (<u>01:12:02</u>):

Yeah.

Ken Duckworth (<u>01:12:02</u>):

Yeah, great. Well, Dr. Evins, I just want to say it's fabulous to see you. It's so impressive to see how much you have learned about this. I mean, it's just amazing, actually. I want to turn it over to Dan Gillison, now he's CEO, to close up our program.

Dan Gillison (<u>01:12:21</u>):

Thank you, Ken. Dr. Evins, thank you. You have shared so much information. Just starting with the treatment guidelines, and the data and just helping us manage by fact, your information has just been incredible. And my takeaway is, it takes up to five times to quit. So it's not the first, the second or the third, you've got to stay, and you've got to continue to do it. So they were some real incredible takeaway. So thank you very much for that. I want to thank our board and our board president Shirley Holloway, as well as our field alliance leaders, and our staff and every one of you who have participated in this Ask the Expert.

These are very important. We try to make sure there is a good transfer of usable information to you. So we really do appreciate you joining. We also welcome your feedback because we believe in constantly trying to bring the best to you. So if you've got suggestions on topics or method in terms of how we bring the information to you, let us know. There's a production team that works on these and they're behind the scenes. And for those of you that love the theater, when you go to the theater, you see these sorts of performance, and all of the performer, you don't see the work they do behind the curtains.

So with that said, I just want to thank Teri Brister who leads the production, and Gustavo Guerrero who helped us on today, Jesse [inaudible 01:13:51], Elizabeth Stafford, Christina [inaudible 01:13:53], Jordan Miller, and really do thank them for their work to make sure... Right now we're in an unprecedented time where we're using this pipe to bring information to you. We have grade school students, we have high school students, we have colleges, we have parents, we have employees, workers, all of us are using technology. So it looks seamless to us, but to keep this coming to you during this unprecedented time takes a great deal of work. So we want to thank them. And to Teri Brister, and to our chief medical officer, Dr. Ken Duckworth, thank you, because the partnership that you all create and to bring these to us is outstanding.

Last thing is a reminder, our next Ask the Expert will be with a very good friend of Dr. Evins that she referenced a couple of times here, Dr. Gail Daumit, Daumit, excuse me, on December 10th. While we haven't titled it yet, it will really be looking at the physical health impact on mental health. And as you know the World Health Organization coined the phrase about 20, 21 years ago about there is no physical health without mental health. So, we're looking forward to that session on the 10th of December. We wish you all the very best as you close out your week. Thank you for what you do and thank you for joining us on today. Bye now.

Ken Duckworth (<u>01:15:23</u>):

Thank you, Dr. Evins. Take care.