SMOKING CESSATION AND HIV WHAT'S THE CONNECTION

Speaker: Dr. Shadi Nahvi

2/8/2017
Smoking Cessation and HIV What's the Connection

00:00:06

[Instructor] Good afternoon and welcome everyone to This Month in HIV. Our May presentation is smoking cessation and HIV, what's the connection? And will be presented by Dr. Shadi Nahvi, an associate professor in the departments of medicine and psychiatry and behavioral sciences at Albert Einstein College of Medicine. My name is Jessica Steinke I'm a program coordinator for HIV/AIDS education and training department with the Mt. Sinai Institute for Advanced Medicine. Before I officially introduce our speaker, I would like to thank our funder, the New York State Department of Health AIDS Institute Clinical Education Initiative. The Mt. Sinai Institute for Advanced Medicine served as a co-sponsor of This Month in HIV. A few housekeeping notes. For the duration of today's presentation all lines will be muted to ensure that there will be no distractions during Dr. Nahvi's presentation. At the end of the presentation you will have the ability to unmute your own line if you have a question. If you don't have a question, please do keep your line muted. Alternatively you can type your questions in your WebEx chat box which is at the top right of your WebEx window. You can direct those questions to the host, Gail Figgins, and I will read them at the end and you can do this at any point during the webinar. At the end of today's presentation you will receive an email with instructions on how to evaluate today's presentation and claim your CME, CNE, or CPE credits. Please remember that This Month in HIV is supported via our New York State Department of Health CEI grant and your participation in the evaluation process helps to keep this program free of charge for all attendees. At this point I'd like to introduce our speaker, Dr. Shadi Nahvi. As I said, Dr. Nahvi is an associate professor at the Albert Einstein College of Medicine. Her research focus is on tobacco control interventions among vulnerable populations. Dr. Nahvi graduated from the Brown University School of Medicine in 2001 and completed residency training in primary care internal medicine at Bellevue Hospital and New York University Medical Center in 2004. She then joined the faculty in the Albert Einstein College of Medicine division of substance abuse as the medical director of a substance abuse treatment clinic. Dr. Nahvi's research focuses on intervention to treat tobacco use, and to optimize use of tobacco cessation treatment among persons with substance use disorders. Her work has been recognized with numerous grants and awards. So at this time Dr. Nahvi, I'm gonna turn it over to you. –

00:02:31

[Dr. Nahvi] Great, thanks Jessica.

00:02:32

Thank you for the opportunity to present, I'm very excited to see that the AIDS Institute is prioritizing tobacco use in particular. So I'm very happy to have this opportunity.

00:02:46

I do receive funding from Pfizer through an investigator-initiated grant award, but I'm not paid to promote their products.

00:02:59

So I'll be talking about why we should focus on tobacco use among persons living with HIV and then how we can assess tobacco use and provide evidence-based treatments.
Tobacco use is the leading preventable cause of disease and death and is responsible for nearly 500,000 deaths in the U.S. annually.

The good news is that tobacco use prevalence continues to decline. The bad news is that these gains in tobacco control have not been evenly distributed and 15% of U.S. adults continue to smoke. I'm concerned about these folks.

We know that the burden of tobacco use is disproportionately concentrated in selected populations. When we look particularly among people living with HIV and AIDS,

The smoking prevalence is two to three times higher in this group, with national samples estimating that approximately 40 to 70% of people living with HIV smoke cigarettes, again compared to the U.S. population of 15%. This disproportionate burden has an associated health cost and threatens the gains made in life expectancy with antiretroviral therapy.

Specifically, tobacco use increases the risk of lung cancer among people with HIV three to four fold, increases the risks of myocardial infarction, increases the risk of pneumonia and of COPD.

Immunological and virological effects include increased risk of opportunistic infections including candidiasis, oral hairy leukoplakia, and pneumocystis, and tobacco use is associated with decreased response to antiretroviral therapy including poor medication adherence, as an independent predictor—tobacco use is an independent predictor of poor medication adherence, and then lower viral load suppression and poor quality of life.

And importantly, there is a disproportionate mortality burden, HIV-positive smokers lose more years of life from smoking than from HIV.

This is illustrated by a cohort study in which the life expectancy of a 35 year old living with HIV was 62 years, almost 63 years, among smokers and 78 years among non-smokers. So that's a 16-year difference in life expectancy. In this cohort, people lost more years of life to their cigarette smoking than they did to their HIV.

So the health burden is enormous and we need to do more about it.

So specifically how can we help smokers living with HIV and AIDS to quit?
I argue that we can do so by providing evidence-based smoking cessation treatments including both behavioral treatments and pharmacotherapy.

Unfortunately there's a scant evidence base among smokers living with HIV and AIDS. This is a summary of a number of randomized trials that have been done among smokers living with HIV. You see that the sample sizes range from 15 to a few hundred, and that the interventions vary from some sort of more intensive combined behavioral and pharmacological intervention in general in comparison to a less intensive control condition.

These results were summarized in a recent meta-analysis that concluded that overall there's a very limited evidence base for smoking cessation interventions among people living with HIV, that in general more intense interventions are more efficacious than less intense interventions at increasing rates of short term cessation, but there isn't enough of an evidence base for looking at interventions that really boost long term cessation rates over time, and that the effect of tailoring interventions to address the unique needs of people living with HIV and AIDS is unclear as of yet, given what we know so far.

So let's talk about the evidence base more generically, rather than focusing specifically on the clinical trials among people living with HIV. The Public Health Service guidelines recommend five A's. They recommend that providers Ask about tobacco use at each visit; Advise patients to quit in brief, specific, focused and unambiguous language; Assess patients' willingness to quit; Assist in quit attempts with behavioral treatments and pharmacotherapy; and then Arrange follow up to continue to address tobacco use over time. When we think specifically about asking about tobacco use, this prompts identification and treatment of tobacco use.

So how well are providers doing? Unfortunately, not very well at all. Fewer than 25% of smokers receive treatment. This is through a national survey of ambulatory care visits in which only 19% of smokers received behavioral counseling and only two percent received pharmacotherapy. There's a really big room for improvement here.

In a study looking at HIV providers and non-HIV providers caring for patients with and without HIV, HIV status unfortunately was an independent predictor of failure to identify tobacco use, and symptoms that patients had including illness, cough, and dyspnea did not impact recognition of current smoking.

So this is an important missed opportunity. If we don't provide cessation information, then people will get a lot of misinformation and a lot of marketing from the tobacco industry. So we have a lot that we can do to really help our patients.

It's important that we do so because there are a lot of misperceptions about evidence-based smoking
cessation treatments. Patients perceive that these treatments have limited efficacy, and they don't know what these medications do, they don't know that medications help to alleviate withdrawal symptoms or alleviate cravings. In a survey of current and former smokers, only 16% agreed that quit smoking medications help people quit smoking. The net result of all of this misinformation is that people really overestimate the risks of evidence-based smoking cessation treatments and underestimate the harms of continuing to smoke.

So we need to do more to provide good information to our patients.

So let's talk about providing evidence-based smoking cessation treatments, and specifically let's talk first about providing behavioral treatment.

So let's illustrate this with a case. Maria is a 56 year old woman with HIV. She has a CD4 count in the 400s on antiretroviral therapy. She was hospitalized for pneumonia recently and you're seeing her in a follow up primary care visit. She's never tried to quit smoking and she doesn't want to stop.

So you want to advise her to quit and the best way to do this is, again, with brief and unambiguous and very patient direct, specific language. Quitting smoking is the most important thing you can do to prevent another pneumonia and to prevent another hospitalization. Then you assess Maria's willingness to quit.

In this stage, she's not ready. She knows that there are harms but she's really not ready to make that jump.

So what can we offer? The Public Health Service guidelines recommend motivational enhancement counseling for patients who are not yet ready to quit. They present a five R's framework. Make it relevant, again the recent hospitalization for pneumonia. Elicit patient's perceived risks of continuing to smoke. These may be financial risks or risks of secondhand smoke exposure to their family members. Have patients articulate the rewards of being smoke-free. And navigate some of the road blocks, some of the challenges to successfully quitting so that you have a sense of what you're up against when you're trying to get your patient to quit. Then repeat the assessment. Again, this is similar to the arranged follow up of the five A's framework. This is a chronic condition that you have the opportunity to address repeatedly over time. So this is something that can remain on the problem list because it's an important health priority.

There's some evidence for interventions to reduce tobacco use over time with pharmacotherapy. The rationale for this is if somebody is not yet ready to make a quit attempt, not yet ready to stop entirely, but is trying to cut down, they're going to experience nicotine withdrawal symptoms and an escalation in cravings. Having nicotine replacement therapy or Varenicline, the two pharmacotherapies for which
there's evidence for patients who are in sort of a motivational or pre-contemplative phase, then you can help people reduce some of their nicotine withdrawal symptoms as they continue to smoke. That will help them to eventually know that once they’re ready to take that plunge, make that jump, make that quit attempt, they’ve got a parachute there that can help them with their nicotine withdrawal symptoms, with their cravings, and help potentially increase some motivation to quit and self efficacy for smoking cessation.

00:13:45
Then what about smoking reduction as an end point? This is something that my patients will ask me often. Reducing cigarettes smoked per day by 50% is a potent predictor of eventual cessation. It does have some modest health benefits, it does decrease cardiovascular risk, decreases respiratory symptoms and decreases lung cancer risk. It's an opportunity to engage smokers who are not yet ready to quit, who would not be interested in a cessation treatment intervention but may be interested in a more motivational intervention.

00:14:24
So you now see Maria back in follow up. She's been hospitalized multiple times for pneumonia. She comes in with a productive cough and she's sick of smoking at this stage and she wants to stop.

00:14:36
So now you have the opportunity to provide behavioral treatments and to provide pharmacotherapies to help her succeed in her quit attempt. So let's start with behavioral treatments. First, the brief counseling framework articulated by this five A's framework of the Public Health Service guidelines, has been shown to increase the likelihood of cessation success by 30%. So that's just brief smoking cessation counseling, three to 10 minutes.

00:15:10
And there's a dose effect between the total contact time, the more you do, the more likely that your patients are gonna quit over time. But even three minutes, which is very easily integrated into the clinical demands of a busy clinical encounter will increase the likelihood of long term cessation success.

00:15:33
You have other options for your patients including telephone quitlines. Telephone quitlines have demonstrated efficacy for increasing success in quitting attempts and long term cessation. They're effective at reaching racial and ethnic minority smokers, and they're a great resource particularly for patients who don't have insurance and can't otherwise access pharmacological treatments. Telephone quitlines offer free telephone counseling in English, Spanish, and other languages on nights, weekends, and during the day. They will mail patients without contraindications free nicotine replacement therapies, and can refer patients to local cessation treatment programs, cessation groups, and other local resources. Then they can mail patients free educational materials as well. So this is the telephone number for the New York State Smokers’ Quitline, and if you Google New York State Smokers’ Quitline you'll see a range of other resources that their website offers to help providers and patients both help the patients through quit attempts.
The New York State Smokers’ Quitline offers a proactive form of the quitline where providers can refer patients to the quitline and then the quitline will call the smoker who’s interested in treatment. Then they will send the providers a progress report detailing the counseling and whether nicotine replacement therapy was provided, so that you have some feedback about what your patient is doing over time, and have a feel for what other services they’re receiving above and beyond the services that you’re offering to them.

So those are some of the behavioral treatments, let’s talk about providing pharmacotherapy.

Specifically, how can we optimize smoking cessation pharmacotherapy to ensure that it’s efficacious?

So first we can use efficacious evidence-based agents.

We should use enough of them, use them for long enough, and we should troubleshoot adverse effects, all the while talking to our patients to try to help dispel the myths and the misperceptions about these medications. So let’s talk about using efficacious agents. There are seven FDA-approved smoking cessation treatments. Five are nicotine replacement therapies which include the patch, the gum, the lozenges, oral inhalers, and nasal spray. The patch, the gum, and the lozenges are all available over the counter and the inhaler and the nasal spray are by prescription only. There are two non-nicotine medications, they’re both pills, oral medications, and these include bupropion, the trade name of which is Zyban, and varenicline which is known as Chantix.

But Maria says, "Eh, I don't want to try medications. "I know I can do this on my own."

So how efficacious is cold turkey? Unfortunately it's not. 72% of quit attempts are without medications or without provider counseling. Only three to five percent of these self quitters achieve prolonged abstinence, and the vast majority relapse within eight days. So my approach to patients is look, quitting smoking is really hard to do. I want to give you all of the tips and the tricks that I can to help you quit and help you stay quit.

If you compare the quit rates of cold turkey to the quit rates of evidence-based smoking cessation treatments, and here I include the different medications sort of in isolation, but all of these are based on clinical trials in which these medications were combined with either a five A's-based counseling or a motivational counseling, so these are medications in combination with some degree of behavioral counseling as well. If you compare cold turkey to evidence-based treatments you see that rates of cessation are just much much lower.
And why is that? It's because cigarettes are the most addictive drugs of abuse.

They're engineered to maximize their nicotine delivery. This is illustrated by a quote from a focus group of smokers with opioid use disorder, one participant of which said, "The experience of smoking "for me, when I'm jonesing and I take in that first hit, "it's like scratching an itch. "It's like taking a drink on a really thirsty day. "It's like taking a breath of air when you've had "your head under water and you pop back up." This is incredibly profound, and this is what we're up against, this is what we're asking our patients to give up. The air that they breathe and the water that they drink. This is not a small task for them to do and we need to be mindful of that as we navigate this challenge with them.

The converse of the sort of reward properties of this drug is the adversive withdrawal symptoms that happen every two hours after somebody has smoked their last cigarette. These include anxiety, irritability, poor concentration, restlessness, craving, depression, and this is miserable. Of course people are gonna want to go back to smoking another cigarette to alleviate some of these symptoms. So you've convinced Maria not to go cold turkey, and she asks you, "My friend has one of those "metal cigarettes, what if I try one of those?" So what's the evidence base for electronic cigarettes or electronic nicotine delivery systems? This is an illustration of a first generation e-cigarette, sort of a cig-alike. The technology has evolved considerably since this time. You see that there is a battery, a heating element, and then a little chamber that allows for concentrated nicotine liquid to be heated up and then aerosolized or vaporized and then breathed in.

Electronic cigarettes have unclear efficacy for cessation, the industry has successfully argued in court that they don't want to meet standards of efficacy and safety that are demanded of medications. So they now fall under the regulatory authority of the FDA which has the regulatory authority to oversee tobacco products. So their efficacy for cessation is unclear and can't be studied well in the U.S. because you can't study a therapeutic outcome or end point because these companies cannot make therapeutic claims. But the majority of the users, despite the lack of evidence base, use electronic cigarettes for smoking cessation. Electronic cigarettes have variable levels of nicotine delivery from device to device and puff to puff. With the diversity of products on the marketplace now, this variability is only increasing. There is theoretical safety concerns that are now being explored in the research literature, but we're sort of a step behind given how novel these product are and how rapidly they're evolving. But there's concern that these could lead to use initiation, particularly with the marketing that really tries to present these in many of the ways that the tobacco industry used to present images of sexiness and coolness and counter-culturalism. That combined with the flavors in these products raise concern for potential use initiation. There is poisoning concerns associated with lack of safe storage of the concentrated nicotine refill liquid. There's concern that if people use the electronic cigarettes rather than evidence-based cessation treatments that this may, in the end, be a barrier to ultimately quitting and staying quit. This is challenging to evaluate without randomized trials because cohort study samples
may be confounded by sort of very highly dependent smokers who've tried many many treatments before and are now turning to electronic cigarettes because they've been unable to quit before. So our ability, methodologically, to tease this out is limited.

00:24:54
Electronic cigarettes have been compared to nicotine replacement therapy in two large randomized trials, one of which I've shown here. The cessation rates were comparable between electronic cigarettes, placebo electronic cigarettes, and nicotine patches.

[00:25:16]
So you've convinced Maria not to waste her money on the electronic cigarettes, the evidence is not there yet. But she tells you, "You know, I've tried the patches and the gum before," "and they didn't work for me." Well, why is that?

00:25:30
One is that a cigarette is an incredibly efficient drug delivery device, it's designed specifically to maximize the nicotine yields, which is to say the rapid onset of the nicotine highs. So this is a cigarette and you get to very high nicotine levels pretty much instantly, and that's because the nicotine is absorbed so quickly through the enormous surface area of the alveolar capillary system. All of the nicotine replacement therapies can't compete. You've got nicotine patches hitting their peak effect after about two hours, and gums, inhalers, and lozenges hitting peak effect after about 30 minutes. None of these, even at full dose, reach the level of nicotine delivery that's provided by a single cigarette. So if you think about the fact that we tend to under-dose and that patients tend to adhere to only a proportion of what we've prescribed, we can be really under-dosing people. Even still, also, not at all mimicking the nicotine delivery to which people are accustomed through their cigarettes.

00:26:59
So let's talk very specifically about the different nicotine replacement therapies, how to prescribe, how to instruct patients in their use. The patches come in three doses, 21-milligram doses, 14, and seven-milligram doses. The prescribing guidelines classically are that you smoke until your target quit date and then you throw away your cigarettes, throw away your lighters, ashtrays, put on a patch and go. We'll talk a bit about variations on that in a few minutes. The classical duration of patch treatment is eight weeks. Four weeks of 21 milligrams, going down to two weeks at 14 and then two weeks of 7 milligrams. The patches again are available over the counter and Medicaid and Medicare do pay for patches as well.

The gum comes in four milligram and two milligram strengths and the dosing is dependent on the number of cigarettes smoked per day. The way that you instruct patients to use the gum is to chew on the gum until a peppery taste comes out, then to park the gum in between the cheeks and the buccal mucosa. That allows you to absorb the nicotine mucosally. Then you chew again til the peppery taste comes out again, then you park again until the peppery taste goes away and you've absorbed the nicotine. The dosing for the gum is that you take one to two pieces an hour at the beginning with a maximum of 24 pieces in a day. You, over time, decrease the frequency of the gum, increase the interval between the pieces. The lozenges are similar in their pharmacokinetics to the gum, the dosing is based on time to first daily cigarette. So if you smoke first thing in the morning before you do anything else, you get four milligram lozenges. If you can hold it for a half an hour you'd have the two millgram
lozenges. Again, you start at one to two pieces an hour at the beginning and then decrease the frequency over time. The inhaler is prescription only. It comes in a 10 milligram strength but that 10 milligram dosage delivers a total of four milligrams. It basically comes with a little plastic mouthpiece and little cartridges, and each of those cartridges delivers four milligrams of nicotine over 20 minutes of puffing. So if somebody puffs on it for 10 minutes, puts it down, they've got sort of 10 more minutes worth of nicotine in that cartridge. You use six to 16 cartridges a day and as with nicotine replacement therapy products, the short-acting products, you can sort of decrease the frequency over time. The nasal spray is also prescription only. It's administered by giving one spray in each nostril. Each spray delivers .5 milligrams, so one dose, one spray in each nostril, is one milligram. You use that sort of frequently at the beginning and decrease over time.

All of the nicotine replacement therapy products have roughly similar efficacy in terms of treating withdrawal discomfort, urges to smoke, and long term abstinence. Adherence is best with the patches, lower with the gum, and very low with the nasal spray and the inhaler.

Bupropion is an antidepressant that was found to have independent effects for smoking cessation. There are multiple potential mechanisms of action including sort of dopaminergic activity as well as reducing negative affect that's associated with tobacco abstinence. The net results is that Bupropion serves to reduce withdrawal symptoms and reduce craving. Varenicline is a partial agonist of the alpha-4 beta-2 nicotinic receptors. Its partial agonist activity means that it sits there in the nicotinic receptor and decreases the craving and the withdrawal symptoms. Then, because it's sitting there, you don't get that reinforcing effect when you smoke because it's blocking the nicotine binding so you don't get that, "Ooh, I love that cigarette" sort of instant gratification and hit. The dosing for both Bupropion and Varenicline starts one week prior to the target quit date in sort of classical prescribing. Bupropion you start at 150 milligrams daily for three days and then increase to 150 milligrams twice daily and you continue that for 7 to 12 weeks. Varenicline you start at .5 milligrams a day for the first three days, go up to .5 milligrams twice daily for the first week, and then at the end of the first week you go up to the full dose which is one milligram twice daily. That was based on the early clinical trials that showed dose-dependent gastrointestinal side effects.

So Varenicline, Bupropion, and placebo were compared in identically designed pharmaceutical industry sponsored clinical trials that included smokers who had no medical problems, no psychiatric problems, and no substance use disorders. So you can see the problems with generalizability to our clinical populations, but Varenicline outperformed Bupropion with cessation rates of 44% at the end of treatment compared to 30%, compared to 18% in placebo. By one year follow up, about 50% of people in all three treatment groups had relapsed which is very common, and the cessation rates were down to 22%, 16%, and 8%.

Given these problems with the sample and concerns about potential neuropsychiatric side effects, which I'll get to later, the FDA made these companies conduct an adequately powered clinical trial with
a sample including people with psychiatric illness, so including people with major depression, psychotic disorder, bipolar disorder, and other mental health diagnoses. They recruited over 8,000 people of whom over 4,000 had mental illness. In that clinical trial that was just published at the end of last year, you see again similar efficacy rates both in the cohort that did not have psychiatric disease and lower abstinence rates, but still better in the Varenicline group compared to the other treatments in the group that had psychiatric illness.

00:34:40
But then when you look at sort of primary care settings, Varenicline compared to patch compared to combination nicotine replacement therapy, all in primary care settings, have roughly equivalent efficacy. A major driver of the sort of disappointingly low cessation rates compared to the early clinical trials is probably medication adherence which was only about 45% two months into treatment.

00:35:03
When we go back to the clinical trials looking specifically at people living with HIV, again the cessation rates are lower than seen in those early clinical trials of people with nothing else going on. Varenicline alone was associated with about a 6% cessation rate compared to 16% when combined with text message counseling, support, and adherence counseling trying to remind people to take their medications. So in real world settings, we likely need much more intensive packaging of interventions in order to get adequate cessation effect.

00:35:48
So when we think again about evidence-based treatments, they boost the likelihood of success.

00:35:56
and we have a lot of different options. The good news in HIV treatment is that there are not a lot of drug-drug interactions. Bupropion is the one place for concern where there are a number of antiretrovirals that have the potential to decrease Bupropion levels. The recommendation in this case is to monitor clinically for clinical effect. But there are no described interactions between nicotine replacement therapy and with Varenicline and antiretroviral therapies.

00:36:39
So we talked about using efficacious agents but we need to use enough of them. So let's talk more about what I mean by that.

00:36:48
This is an illustration, "It took 279 nicotine patches, "but I no longer have the urge to smoke." We may need to do more than the standard doses of smoking cessation treatments that first came to market and that have demonstrated efficacy, but still modest efficacy.

00:37:10
Again that's partly because of the pharmacokinetics and the delivery of nicotine with cigarettes compared to the nicotine replacement therapies.
One cigarette delivers between one and three milligrams of nicotine, depending on how deep a breath you take in, how slow, menthol versus not. So there are a lot of different factors.

The clinical trials show that combining nicotine replacement therapy products, high doses of patch versus standard doses of patch, so for example 42 milligrams, 35 milligrams, compared to 21 milligrams, is more efficacious than standard doses of patch. Then combination nicotine replacement therapy, patch plus lozenges or patch plus gum is more efficacious than single agents alone. So these effects are clinically modest but they are statistically significant and they can sort of boost efficacy over standard dose nicotine replacement therapies.

The combination of Bupropion and nicotine replacement therapy was evaluated in an efficacy trial in the 1990s and suggested that Bupropion plus patch was more efficacious than patch alone, didn't out perform Bupropion alone. In an updated study of this, and I didn't add a slide about this, but in an updated study of this looking in primary care settings in a more generalizable population, they had roughly equivalent effectiveness rates. Again speaking to that translation between the efficacy seen in clinical trials and the real world effectiveness in our clinical settings.

Varenicline has been evaluated in combination with Bupropion and with patches. So there was a randomized trial looking at the combination of Bupropion plus Varenicline compared to Varenicline alone, and there was some benefit to combination treatment. It did increase prolonged abstinence rates, but it didn't increase point prevalence abstinence rates and there was no difference at long term follow up. In a placebo-controlled trial comparing patch plus Varenicline versus placebo patch and Varenicline, so patch and Varenicline versus Varenicline alone, the cessation rates were higher in the combination treatment group but these results were not replicated in other separate randomized trials looking at the combination of nicotine replacement therapy and Varenicline. So from a pragmatic perspective, in New York State, New York State Medicaid does not pay for the combination of Varenicline in combination with other smoking cessation pharmacotherapies because the evidence is scrawny.

I apologize, this is not Jorenby, this is the wrong label, it was a study by Jed Rose and colleagues. But the combination of treatments was evaluated recently in a pretty novel way, looking at adaptive treatment paradigms where they offered people nicotine replacement therapy for a week, and those 222 clinical trial participants who didn't reduce their tobacco use by 50% at the end of a week of the patch were randomized to escalate treatment with Varenicline plus Bupropion or Varenicline alone. The abstinence rates were higher in the combination treatment group among the sample of people who had been pretreated and unsuccessful with a week of nicotine replacement therapy. So as we think about how to optimize therapies for our patients, this is an interesting example.
So in general, pharmacotherapies outperform cold turkey, and combination therapies may outperform standard treatments even more.

So we need to use efficacious agents, we need to use enough of them, and we need to use them long enough both to increase their efficacy and to prevent relapse.

"I know I shouldn't smoke if I have the patch on, right? "You can get a heart attack from that."

This is a very common misperception among our patients, and it's important to point out that nicotine is the addiction. Nicotine is the pleasure and the pain. Nicotine is not the cardiovascular risk. That is largely mediated by carbon monoxide and combustion products causing endothelial damage and oxidative stress.

So nicotine replacement therapy has been shown to be safe and efficacious among the people with stable cardiovascular disease, and is not associated with increased cardiovascular risk.

When they've done clinical trials looking at pre-cessation patch treatment, so like I said earlier the classical prescribing guidelines say smoke until target quit date, then stop smoking and only then should you start the nicotine replacement therapy. But if you start the nicotine replacement therapy two weeks before that or four weeks before that, it actually doubles the likelihood of long term cessation and doesn't have any adverse cardiovascular consequences.

Similarly, pre-cessation Varenicline treatment, so giving people varenicline for four weeks prior to the target quit date rather than one week prior to the target quit date, increases the likelihood of longer term cessation success.

So you've convinced Maria to use quit smoking medicines but she's still concerned. "Even when I've quit smoking before, I've gone "back to smoking a month later."

So what can we do to prevent relapse? Extended pharmacotherapy has demonstrated efficacy at reducing lapses, reducing the likelihood that a slip will become a full-blown relapse, and increases the time to lapse and the time to relapse, and increases rates of tobacco abstinence overall. This has been evaluated in clinical trials looking at two months versus six months of nicotine patch and Robby Schnoll has actually published a more recent paper looking at two months versus six months versus 12 months. At 12 months out, adherence is more of a concern. So six months seems to be the magic number in this regard. Then this has also been evaluated with Bupropion and with Varenicline comparing three months versus six months of treatment.
So you can use evidence-based efficacious agents. Use an adequate dose of these agents. Use them for long enough, both to promote cessation and prevent relapse. Then you can help to troubleshoot adverse effects.

"I just don’t know about putting chemicals in my body." "Aren’t the side effects of those medications" "worse than my cigarettes?" I hear this very very very often.

It’s important to help patients navigate and anticipate what the actual adverse effects of these medications are. With patches, local site reactions are very common so it’s important to instruct patients to switch the sites of their patch placement; legs, arms, belly, back, to not develop rashes at the site of the patches. Insomnia can be a side effect, so patients can take the patches off at night before they go to bed and apply a new patch in the morning. The trouble with that approach is that the first daily cigarette is a very challenging one to give up and so if you’re not having the patch on at night, you’re not having that nicotine in your system, the nicotine withdrawal in the morning can make that even more challenging. Bupropion also can be kind of activating and can cause insomnia. Varenicline, nausea is very common in about 30% of the phase three clinical trial participants and potentially even more among our patients who are living with HIV and taking a lot of other medications that might also cause gastrointestinal effects. So the best advice here is to space out the dosing, taking two milligrams daily causes more GI side effects than splitting the one milligram twice daily, and taking medication with food can help. You can also reduce the dose to .5 milligrams twice daily if necessary.

The precautions and contraindications to nicotine replacement therapies include a myocardial infarction in the prior two weeks, serious arrhythmia, serious angina, uncontrolled hypertension, and nicotine replacement therapies are pregnancy category D. Bupropion is associated with decreasing the seizure threshold, so a history of seizure disorder and eating disorders or medications that can predispose to seizures are all contraindications. Varenicline requires dose reduction for people with creatinine clearances less than 30.

So the FDA issued a black box warning about Bupropion and Varenicline in 2009, which they removed in December of 2016, but let's take a moment to talk about that black box warning. They warned of the risk of serious neuropsychiatric symptoms including changes in behavior, agitation, depressed mood, suicidal ideation, and attempted suicide among people who were taking Bupropion or Varenicline for smoking cessation. They highlighted the benefits of using medications to help people quit smoking and the benefits of quitting smoking, and recognized that these neuropsychiatric effects were potentially confounded by nicotine withdrawal symptoms and recommended that if patients had these effects that you stop medications and monitor until resolution.

The early clinical trials excluded people with mental illness. In my talks until the EAGLES trials came out, I included all of the results of now a couple dozen clinical trials among people with major depression,
psychotic disorders, substance use disorders, which all very consistently showed no increased psychiatric risk or increased neuropsychiatric side effects with Varenicline. But the EAGLES trial, which included over 4,000 patients as I said earlier, with mental illness, found no difference in composite end point of moderate to severe neuropsychiatric adverse events with Varenicline, Bupropion, nicotine patch, and placebo. So there was no statistically significant difference between Varenicline and placebo or between Varenicline and patch. This was very reassuring and really alleviates a lot of your initial concern that came out of the initial case reports, and really importantly eliminates a traditional barrier to use of these medications.

00:49:21
So in conclusion, there is a significant burden of tobacco use among people living with HIV and AIDS. We need to identify tobacco use and provide evidence-based treatment.

00:49:36
To do so, the New York State Department of Health has a new HIV tobacco cessation improvement campaign where they are trying to facilitate tobacco screening and tobacco use treatment among people living with HIV and AIDS. They recommend, I recommend, that you check out their website, HIVtobaccofreeny.org, which includes a number of resources that you can use as well as resources that your patients can use to help patients quit. It has linkages to the New York State Tobacco Control program and a lot of other resources there. There are patient handouts, patient materials, provider handouts, including what do you do with your patient if you have no time? What do you do with your patient if you have one minute? What do you do with your patient if you have three minutes? So I recommend that you take some time to check out the resources on their website.

00:50:47
Then there are more resources at the hivguidelines.org as well as the New York State Smokers’ Quitline website as well, so in addition to the quitline itself there are tons of pamphlets, brochures, educational materials and tools that you can use for your patients.

00:51:15
So I’d like to thank the Clinical Education Initiative and

00:51:21
I welcome questions.

- [Jessica] Okay great, Dr. Nahvi, thank you so much that was really fantastic. So we've got a little under 10 minutes left for questions and to have a facilitated discussion. So if people have questions at this time you can unmute yourself by pressing on the red microphone in your WebEx box next to either your call-in name or where you see your name, and that way you can ask a question. Alternatively, you can click open your chat box which is in the top right-hand corner of the WebEx window. You can type your questions there and send them to the host, Gail Figgins, and then we can read them out for Dr. Nahvi to answer. So as people start doing that I can start with a question that I had. Dr. Nahvi, one of the things you mentioned was with the nicotine replacement therapy, that there was quite a variation in terms of adherence. So I was wondering if there’s evidence and information on why there’s those differences in adherence or if you have your own thoughts on that?
- [Dr. Nahvi] Because the patches are just much more straightforward, they're unobtrusive, and they're once daily, all of the other nicotine replacement therapies require very frequent dosing in order to get enough nicotine into your system. So if you need something twice an hour, the likelihood that you're gonna adhere and get adequate dosing to that is just gonna be much much more challenging. That's part of why combination nicotine replacement therapies are so great, because you have sort of the basal level of nicotine administration through the nicotine patches, and then get sort of an additional boost from the shorter acting nicotine replacement therapy products. The nasal spray is kind of poorly tolerated. Because it has the most rapid onset of action, it's also kind of irritating, so it can cause nasal congestion and sneezing and irritation. So that's another factor. The nicotine inhalers are not Snoop Dogg branded and fancy carrying case-y like the electronic cigarettes are. They're plastic and they're visible and they're ugly. So those are some of the considerations that can potentially impact adherence.

- [Jessica] Great, thank you. Does anyone on the line have a question? Alright, I can ask another one. So I know one of the things you mentioned was that it's possible, depending on individual use, that they might need more than maybe what's recommended as the standard dose, again for the nicotine replacements, so I'm wondering especially for primary care providers if this is a new area for them, what kinds of ideas do you have on how you would judge that, how do you assess that in terms of dosing?

- [Dr. Nahvi] What my first line is will really depend on the patient in front of me and what they are willing and interested in taking. I have patients who are very emphatic that they don't want another pill to swallow because they're on multiple medications already, and they're not interested in doing anything else. For those I'll start with combination nicotine replacement therapy. In general I do combination nicotine replacement therapy rather than single agents alone, just because it is more efficacious and I want to give my patients all the help they can get. Or I'll do Varenicline if they're interested in that. In terms of what nicotine replacement therapy agents I use, that tends to be guided more by pragmatic considerations, does the patient have teeth or dentures, what's their dentition like, will help to inform whether or not we can use gum. And then what insurance formularies will pay for can be variable with respect to nicotine replacement therapy, so I'll do whatever I can get.

- [Jessica] Okay, great, thank you. I'm happy to keep asking questions, please if anyone on the line wants to jump in please do. Again you can unmute yourself and ask a question or alternatively you can chat in a question. Oh, we just got a question. Alright, so we have a question from someone on the line, they're asking is there a limit of times a patient should continue to take Chantix after the initial six month treatment?

- [Dr. Nahvi] Pfizer conducted a study looking at 12 months of treatment and it was safe and efficacious. It was a trial sponsored by the maker of the drug so you know, you can take that into consideration as well. The six months is, in the clinical trials looking at six months of Varenicline, those were for relapse preventions, so they were open label three months of treatment. Then among those people who had successfully quit in that last month of treatment, they were randomized to receive either an additional three months of Varenicline or three months of placebo. So it was six months only for people who had really established an initial abstinence and to sort of maintain abstinence over time and prevent relapse over time. So that's the major group for who there's an evidence base is among people who have established initial abstinence, to help maintain that abstinence over time. That said, if somebody says,
"I'm taking whatever "smoking cessation pharmacotherapy and I'm now "down to one cigarette a day from two packs a day "and I really think that this is helping me to do that," from a harm reduction perspective as long as they can continue to procure the medication I think that the risks of the medications are much much lower than the risks of continuing to smoke. So it's less evidence-based but I might continue it in that setting as well.

- [Jessica] Okay, great, thank you. One thing you just said, you know, if they're able to continue to procure the medication, so that's something I wanted to ask about for cost of the nicotine replacement therapies, both over the counter as well as the prescription ones, what the cost tends to be, if insurance covers it, and if you've had patients just have difficulty even being able to access or afford those nicotine replacement therapies?

- [Dr. Nahvi] For one thing, I will again give a plug to the New York State Smokers' Quitline. People can get a two week supply of nicotine replacement therapy free of cost from the quitline, and they can call back and get another two week supply once that's done, so that's a great resource in the first place. Unfortunately, nicotine replacement therapies are not cheap, they've targeted the pricing to sort of be calibrated to a pack of cigarettes, the sort of daily cost of a pack of cigarettes. But daily cigarettes feel great and give a lot of reward, so patients can't necessarily justify the costs of nicotine replacement therapies compared to continuing to purchase their packs of cigarettes. So they can be challenging for people to afford. If they're sold in boxes that are two week supplies or four week supplies, then it can be an up front investment rather than a three day starter pack, try it out, put it on, see how it works. New York State Medicaid does pay for, and does mandate among all of the Medicaid managed care programs, that they do pay for nicotine replacement therapies, Varenicline, and Bupropion, without limits to the number of treatment courses over a year. It used to be that you could get a six month supply over the course of a year and they recently eliminated that. So for patients with public insurance in New York State where we have relatively generous benefits, that shouldn't be a concern.

- [Jessica] Okay great, thank you so much. So that brings us to one o'clock. Dr. Nahvi's email is there on the screen, if you have questions you can reach out to her at that email address. So thank you again Dr. Nahvi for leading this presentation, it was really fantastic. We did have somebody not with a question but who did chat in a comment to say thank you so much, this was incredibly informative.

- [Dr. Nahvi] Great, thank you.

- [Jessica] So thank you to you, Dr. Nahvi and thank you again to our funder, the New York State Department of Health AIDS Institute Clinical Education Initiative.

[Video End]