U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
National Center for Chronic Disease and Health Promotion
Office on Smoking and Health

Public Committee Meeting of the Interagency Committee on Smoking and Health

Youth Tobacco Cessation

U.S. Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Ave SW
Washington, DC 20201

October 15, 2020, 12:30 p.m. – 4:00 p.m.

Record of the Meeting

OBJECTIVE

Identify federal actions to prioritize areas of research that can be expedited to support tobacco cessation treatments for youth.

OPENING ANNOUNCEMENTS AND WELCOME

Kathy Gallagher, Associate Director for Policy
Office on Smoking and Health (OSH)
Centers for Disease Control and Prevention (CDC)

Ms. Kathy Gallagher: Welcome and thank you for participating in the 2020 Interagency Committee on Smoking and Health Meeting. My name is Kathy Gallagher. I serve as the Associate Director of Policy in the Office on Smoking and Health at the Centers for Disease Control and Prevention and I am the Designated Federal Official for this Federal Advisory Committee. This meeting is being recorded and is open to the public. Information for the public to attend the meeting via Zoom was published in the Federal Register in accordance with Federal Advisory Committee Act regulations and rules.

This is our first year holding this meeting in a virtual capacity. We would like to remind all Speakers and Committee Members to refer to their "Zoom Webinar Attendee Guide" for some helpful meeting etiquette. Though this is a public meeting, conversation and questions will be confined almost entirely to the Committee and presenters. Speakers and Committee members may use the "raise hand" function during discussion, to signal that you wish to make a comment. To raise your hand, please click on the "participant" button in the bottom of your tool bar, and then click the "raise hand" button in the bottom right corner. We ask that you lower your hand when you are done speaking.

For those who pre-registered, there will be an opportunity for public comment this afternoon at approximately 3:15 PM. Please note, we will not be responding to or answering questions during the public comment period. If you need Zoom-related technical assistance during the meeting, please contact one of the individuals listed on the screen.

I will now call each Committee members' name and ask them to introduce themselves. I ask the Committee's public members to disclose if you have any conflicts of interest.

ROLL CALL AND DISCLOSURES

The following individuals were in attendance:

Committee Chair

- Vice Admiral Jerome M. Adams, MD, MPH, U.S. Surgeon General, U.S. Department of Health and Human Services (HHS)

Public Members in Attendance

- Jasjit Ahluwalia, MD, MPH, Professor, Department of Behavioral and Social Sciences and Center for Alcohol and Addiction Studies, Brown University School of Public Health
  - Disclosures and/or conflicts of interest: Lucy Goods, manufacturer of generic nicotine gum
- David Dobbins, JD, MPH, Chief Operating Officer, Truth Initiative
  - Disclosures and/or conflicts of interest: None. Will refrain from providing comment on presentation from Dr. Amanda Graham, a colleague from Truth Initiative
- Lisa Henriksen, PhD, Senior Research Scientist, Stanford Prevention Research Center, Stanford University School of Medicine, Department of Medicine
  - Disclosures and/or conflicts of interest: None
- Suchitra Krishnan-Sarin, PhD, Professor of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center
  - Disclosures and/or conflicts of interest: I do not have any conflicts of interest, per se. I do lead the Tobacco Center of Regulatory Science at Yale, which is funded by the U.S. Food and Drug Administration (FDA) and the National Institutes of Health (NIH) to research tobacco products and to support regulation.
- Dennis A. Henigan, JD, Vice President, Legal and Regulatory Affairs, Campaign for Tobacco-Free Kids
  - Disclosures and/or conflicts of Interest: Campaign for Tobacco-Free Kids, 1% funding from pharmaceutical companies

Federal Members in Attendance

- Peter J. Ashley, DrPh, Director, Policy and Standards Division, U.S. Department of Housing and Urban Development (HUD)
- Gina Bowler, Lead, National Smoke-free Low-Income/Affordable Multiunit Housing Initiative, U.S. Environmental Protection Agency (EPA)
- John Howard, MD, Director, National Institute for Occupational Safety and Health (NIOSH), HHS
- Rosalind B. King, PhD, Associate Director for Prevention, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, HHS
- Deirdre Lawrence Kittner, PhD, MPH, Deputy Director, Regulatory Science Center for Tobacco Products, FDA, HHS
- David M. Murray, PhD, Associate Director for Prevention; Director, Office of Disease Prevention, National Institutes of Health (NIH), HHS
- Letitia Presley-Cantrell, PhD, MEd, Acting Director, Office on Smoking and Health (OSH), CDC, HHS
- Rosemary Rosso, Esq., Senior Attorney, U.S. Federal Trade Commission (FTC)

- John Snyder, MD, MS, MPH (FACP), Chief Medical Officer, Health Resources and Services Administration (HRSA), HHS
- Douglas Tipperman, MSW, Tobacco Policy Liaison, Substance Abuse and Mental Health Services Administration, HHS
- Kim Hamlett-Berry, PhD, National Program Director, U.S. Department of Veterans Affairs (VA)
- Michael Toedt, MD, Chief Medical Officer, Indian Health Service (IHS), HHS

Speakers

- Brian King, PhD, MPH, Deputy Director for Research Translation, OSH, CDC
- Kevin Walton, PhD, Chief, Clinical Research Grants Branch, Division of Therapeutics and Medical Consequences, National Institute on Drug Abuse (NIDA), NIH
- Susanne Tanski, MD, MPH (FAAP), Associate Professor, Pediatrics, Geisel School of Medicine, Dartmouth
- Wilson Compton, MD, MPE, Deputy Director, NIDA, NIH
- Jonathan Bricker, PhD, Professor, Public Health Sciences, Fred Hutchinson Cancer Research Center; Affiliate Professor, Psychology, University of Washington
- Yvonne Prutzman, PhD, MPH, Program Director, Tobacco Control Research Branch, Division of Cancer Control and Population Sciences (DCCPS), National Cancer Institute (NCI), NIH
- Amanda Graham, PhD, Chief of Innovations, Truth Initiative, Professor of Medicine (Adjunct), Mayo Clinic College of Medicine and Science
- Kimberly Horn EdD, MSW, Professor and Scientist, Virginia Tech-Carilion Fralin Biomedical Research Institute
- Steve Kelder, PhD, MPH, Professor, University of Texas Health Science Center at Houston, School of Public Health, Austin Campus, Co-Director Michael & Susan Dell Center for Healthy Living, Co-Creator, CATCH Global Foundation

Ms. Kathy Gallagher: Thank you all for introducing yourselves and for being here with us today. Our first speaker, who will call the meeting to order and give the charge to the Committee is Vice Admiral Jerome M. Adams, MD, MPH, U.S. Surgeon General. Dr. Jerome Adams is the 20th Surgeon General of the United States. His mission, as the nation's doctor, is to advance the health of the American people. Dr. Adams leads with science in a way that facilitates locally led solutions to the nation's most difficult health problems. In his role as Surgeon General he works to advance tobacco prevention and control, including issuing the first ever Surgeon General's Advisory on Tobacco Product Use, and joining Generals of the Air Force, Army, and Navy to issue a joint letter, entitled *Tobacco Product Use Threatens Military Readiness.* Earlier this year, he released *Smoking Cessation: A Report of the Surgeon General.*

CALL TO ORDER AND CHARGE TO THE COMMITTEE

Vice Admiral Jerome M. Adams, MD, MPH
U.S. Surgeon General, U.S. Department of Health and Human Services

Vice Admiral Jerome Adams: Good afternoon everyone. Thank you so much for joining us. For those of you on the west coast, I believe it is still good morning. We officially have a quorum. So, I am calling this meeting to order. I'd also like to highlight that I put out an advisory on e-cigarette use among young people (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/surgeon-general-advisory/index.html). I want you to know how committed I am to make sure we are looking both at preventing people from starting tobacco product use, and also looking at how we can help more people quit. As was mentioned, I put out a report earlier this year on smoking cessation—the first one on this topic in 30 years.

I want to thank you for joining us today for the first ever virtual Interagency Committee on Smoking and Health meeting. It's a testament that nothing stops us in our fight to protect Americans from the harms of tobacco product use. I'd also highlight that, at least as far as I can see, we've got close to 200 people joining us today. So maybe this will be the most well attended meeting that we've ever had.

I want to thank our speakers for taking time to contribute their extraordinary expertise to our discussion today, to members of the public for taking part, and to our public members on the Committee, Dr. Jasjit Ahluwalia, Mr. Dave Dobbins, Dr. Suchitra Krishnan-Sarin, Mr. Dennis Henigan, and Dr. Lisa Henriksen. In particular, I want to welcome Mr. Dave Dobbins and Dr. Suchitra Krishnan-Sarin, who are new Committee members joining the meeting for the first time, as you just heard. I want to extend our gratitude to Mr. Dennis Henigan for his service as he rotates off the Committee this December. Thank you so much for all your work.

I want to recognize Kathy Gallagher, Associate Director for Policy in the CDC Office on Smoking and Health for serving as the Designated Federal Official for today's meeting. It is a really a tremendous task, and oftentimes a thankless task. So, thank you, Kathy, for all that you're doing.

And finally, I want to take a moment to acknowledge two individuals who have been integral to the Interagency Committee on Smoking and Health. First, Simon McNabb, who technically works for and belongs to the CDC. For those of you who've had the privilege of knowing and working with Simon, you know that he belongs to the mission that we all share. Simon had served as the Designated Federal Official for this meeting for the past eight years, and we will greatly miss his leadership and guidance and want to share our appreciation, not only for his deep commitment to our mission. But also, Simon, thank you for your leadership, your depth of management expertise, your abiding friendship in the face of unthinkable obstacles, and your unfailing good humor.

I also want to thank Monica Swann, who is also with the CDC. Monica recently accepted a new position within the Office on Smoking and Health. So, this will be her last meeting as our Committee Management Specialist. For more than a decade, Monica has been critical to the planning and execution of each meeting. Her knowledge of the Federal Advisory Committee process and her project management skills are truly incredible. We're here because of you, Simon and Monica. So, I just wanted to give the two of you, in particular, a special shout out and thanks.

It's critical that we gather today to focus and redouble our efforts, especially in light of the ongoing challenges that we as a nation are tirelessly working to overcome. I want to acknowledge that while we're continuing to learn each and every day about COVID-19, a disease that we've seen in stark relief lately which can affect anyone. The available data tell us that certain underlying medical conditions can increase the risk for severe illness from COVID-19. When it comes to tobacco use, the evidence indicates that people who smoke cigarettes might be at increased risk of severe illness from COVID-19. However, we don't know whether e-cigarette use is associated with COVID-19 severity. We also don't know for certain whether secondhand exposure to tobacco or e-cigarette aerosol is associated with severity of COVID-19. There is still a lot we don't know about the health impacts of tobacco product use in relation to COVID-19, but we have decades of science on the well documented and irrefutable evidence of the adverse health effects of smoking. I just want to remind us that quitting smoking is one of the most important actions people can take to improve their health. There's never been a better time to quit smoking than now. You may notice I took pains, particularly in a gathering like the one we're in, to say things as precisely as I could. We know that if you've had a stroke, if you have cardiovascular disease, if you have kidney disease, if you have lung disease, all of these things put you at risk for complications from COVID-19. That's been shown, and we know that tobacco product use increases the chances that you're going to have those diseases. So again, while we search for direct links between tobacco product use and COVID-19, we know that indirectly, it's highly plausible, that quitting smoking is going to increase your chances of being able to fend off COVID-19.

There's never been a better time to quit. This is true, regardless of how long a person has been smoking, and regardless of their age, as was highlighted in the first Surgeon General's report on smoking cessation in over 30 years, that came out in January 2020. The report documents how quitting smoking can reduce the risk of diseases and summarizes the latest science on interventions that have been proven to help people quit smoking. It notes that despite substantial progress in the area of smoking cessation, 34 million Americans still smoke, and disparities persist in the prevalence of smoking and cessation behaviors across certain populations, including by socioeconomic status, health insurance status, race, ethnicity, and geography. Tobacco dependence is a chronic, often relapsing condition, that is driven by an addiction to nicotine. But while quitting tobacco product use may be hard, one of the things we have to keep shouting from the mountaintops, is that it is possible to end nicotine addiction. The report documents an array of effective clinical interventions that can help adults successfully quit smoking, including counseling and FDA-approved medications. The report also highlights important interventions that increase access to treatments and resources for quitting, including health systems changes that make it easier for healthcare professionals to deliver cessation treatments and comprehensive barrier-free insurance coverage that increases the use of cessation treatment services.

The report reinforced the importance of population health interventions, such as smoke-free policies, that create an environment that motivates people who smoke to quit and makes it easier for them to do so. I often say the choices people make are 100% dependent on the choices that are in front of them, and we need to make the healthy choice both available and easier for people to pursue. And that's a lot of what this report details. How can we make it easier, so that when an individual decides it's time for them to quit, they can have the best chance of success?

While effective cessation treatments exist for adult cigarette smokers, the report reinforces the need to identify effective cessation treatments for all tobacco products and cessation treatments for youth. This is particularly true for e-cigarettes, which have been the most commonly used tobacco product among U.S. youth since 2014. We think of these as new, but again, going back to 2014, they have been the most

commonly used tobacco products for young people. In 2019, more than 85% of the youth tobacco product users in the United States reported using e-cigarettes. Although the latest data from the National Youth Tobacco Survey showed a decline in e-cigarette use within the past year, it still remains prevalent, and clinicians, schools, and parents are seeking effective ways to help youth quit tobacco. I also very much wonder what we're going to see as kids go back to school post- pandemic, because one of the challenges is that we know that a lot of the access the kids are getting to these products is occurring in school environments. So, the fact that many kids across the country have been out of school since March may impact the numbers this year. I do think it's good news anytime we see a decrease in use, but we have to make sure that decline continues, and is not just a snapshot that then comes rebounding back to higher levels of use in the next year or two.

In 2020, about 3.6 million U.S. youth reported currently using e-cigarettes, including one in five high school students and one in 20 middle school students. As a dad of two high schoolers and a middle schooler, that's shocking to me, and it should be shocking and concerning to all of us. As summarized in the *Surgeon General's Advisory on E-cigarettes*, most e-cigarettes contain nicotine; the same addictive drug found in cigarettes. Nicotine exposure during adolescence can harm the developing brain, which we know continues to develop until about age 25, and it can prime the brain for addiction to other substances. The widespread use of e-cigarettes and popularity of certain products among youth, have been driven in part by use of appealing flavors and development of new e-cigarette products. For example, the latest data from the National Youth Tobacco Survey showed that one in ten e-cigarette users reported using flavored varieties and that disposable e-cigarette use increased 1000% among high school students within the past year.

But it's important that we don't lose sight of the fact that the tobacco product landscape is constantly evolving with new products continually being introduced into the marketplace. We're really seeing that phenomenon of squeezing the balloon – you've squeezed down in one place and it pops up in another place. Therefore, tobacco cessation treatments and interventions that address all types of tobacco products are crucial – not just ones that address cigarettes or e-cigarettes. And that brings us to today's topic.

The charge to the committee today is to identify federal actions to prioritize areas of research that can be expedited to support tobacco cessation treatments for youth. We've invited our speakers today in recognition of their expertise and contribution across the domain of youth cessation, including clinical treatments, treatment extender strategies, and school- and community-based treatments. Despite known gaps, we hope that their excellent work will serve to move the discussion forward within the Committee on steps that can be taken next. We're not going to solve all of the problems today, but hopefully we can move the ball down the field a little bit and figure out how we can divide and conquer, and how we can continue to push for more and better research to guide our strategies as we move forward.

Working together, I know we can protect our nation's youth from all forms of tobacco product use. As a dad, we don't have any other choice. We've got to do this. And so, I look forward to today's presentations, and I look forward to engaging in the discussion and working to advance a research agenda for youth tobacco cessation.

Kathy, I'll turn it back over to you.

Ms. Kathy Gallagher: Thank you, Dr. Adams. Today's agenda will consist of an overview of opportunities and barriers to tobacco use and cessation, followed by three panels. The first panel is on clinical treatments. The second panel is on treatment extender strategies. And our final panel is on school- and community-based treatment programs.

After each panel, we will hold a 15- to 20-minute discussion with Committee members and the presenters. Now, I would like to introduce our first formal speaker. Brian King, PhD, MPH, is the Deputy Director for Research Translation in OSH within the National Center for Chronic Disease Prevention and Health Promotion at CDC. In this capacity, he is responsible for providing scientific leadership and technical expertise to CDC/OSH, the lead federal agency for comprehensive tobacco prevention and control. Welcome, Dr. King.

Brian King, PhD, MPH
Deputy Director for Research Translation, Office on Smoking and Health
Centers for Disease Control and Prevention

Dr. Brian King: Thanks, Kathy. I'm pleased to be here. This is always an exciting meeting every year.

I know I've said it before, but I compare this meeting to the tobacco control equivalent of Game of Thrones, where we bring all the different tobacco houses together. But I'm very hopeful that our meeting will end with a far better finale than the Game of Thrones series. So, with that, I'm going to get started.

On disclosures, as you've probably surmised, I am an employee of the U.S. government. So, depending on who you ask, that may or may not be a conflict of interest. But other than that, I've no other conflicts to disclose.

So, we know in the United States, that cigarette smoking has declined markedly since the Master Settlement Agreement in the late 1990s, which is a very commendable public health achievement. I've argued for many years that declines in smoking among adults and youth are among the greatest public health accomplishments of the past century. When it comes to youth smoking rates, they were 36.4% back in 1997, the year before the Master Settlement Agreement, and since that time they've declined all the way down to 5.8% among youth in 2019, specifically among high school aged youth.

But what we don't want to be doing is playing this game of public health whack-a-mole. And so, it's important to note that we have a diversified tobacco product landscape. Although we are seeing a commendable decline in cigarette smoking, we have to remind ourselves that we are in the business of tobacco prevention and control, not just cigarette prevention and control, when it comes to kids. To that end, we've seen a diversification of the landscape to include a variety of different products. These data are from the National Youth Tobacco Survey for all tobacco products from 2011 onward. We included the e-cigarette estimate for 2020, which was just recently released by CDC and FDA a few weeks ago. You can see that it's been a bit of a roller coaster ride when it comes to e-cigarette use in this country. Whereas use of other tobacco products has remained fairly stable or declined in recent years, when it comes to e-cigarettes, we saw marked upticks through 2015. E-cigarette use then declined in 2016 and 2017. Then we saw that marked uptick through 2019. That was the result of the further diversification of the landscape with emerging products, such as pod mods that were particularly appealing to youth. We have seen a decline in use within the past year, which we are cautiously optimistic about. We know that

these data were collected before a lot of the school disruptions related to COVID-19 took place. So, we believe that it's a valid estimate, but it's important to monitor moving forward, and keep in mind that we cannot rest on our laurels. It's a very volatile landscape when it comes to tobacco product use. E-cigarettes are not the first novel product and they will not be the last. We continue to have a diverse array of tobacco products, which is important to acknowledge, not only in terms of research, but also public health practice and treatment in the context of cessation.

This slide shows the trends among middle school students in grades six through eight, whereas the previous slide was on grades nine through 12. You can see they're fairly comparable trends. We've seen this continued increase in e-cigarette use over the past several years. So, we've seen a marked and hopeful decline within the past year, but otherwise the use of other tobacco products has remained the same, perhaps indicating that we are playing a game of public health whack-a-mole. And when it comes to our tobacco prevention and cessation activities, we want to ensure that our messaging, evidence, public health practice, and work all address the diversity of tobacco products that American youth are using.

So why is it a problem? Well, you've already heard Dr. Adams outline the various adverse effects of tobacco product use to youth outside of the known risks of continued use of combustible and smokeless tobacco use into adulthood and acute health effects, particularly coronary outcomes. We also know that most e-cigarettes also contain nicotine. E-cigarettes have been the most commonly used tobacco product among kids since 2014, and 85% of youth tobacco product users are using e-cigarettes. Certainly, right now, the greatest burden in terms of prevalence of use is on e-cigarettes. And even though e-cigarettes have a lower risk profile than conventional products, that doesn't mean that the risk isn't great. We know that e-cigarettes contain nicotine, which is highly addictive and can harm the developing adolescent brain in the prefrontal cortex, which is responsible for learning, memory, and cognition. We also know that nicotine can prime the brain for addiction to other drugs. There is a robust body of science on the adverse effects of nicotine specifically in addition to all the other harmful ingredients that are in tobacco products, including e-cigarette aerosol. The bottom line is there are absolutely no redeeming aspects for use of these products among kids, and it's critical that we decrease use of all of these products among youth.

Benjamin Franklin said it very well. Back in 1736, in a fire ravaged Philadelphia, he said, "an ounce of prevention is worth a pound of cure." It's very appropriate here when it comes to tobacco control. Of course, we know that addressing something and preventing it from occurring is a heck of a lot cheaper than having to clean it up on the back end. And so, the bread and butter of tobacco control for many years has really been in this context of prevention.

One way that we have articulated this is through this depiction of the tobacco control vaccine, which shows population-based preventive strategies, including tobacco price increases, smoke free policies, increasing cessation treatment access, and hard-hitting mass media campaigns. These are the interventions that, at the population level, really help create an environment where tobacco products are less accessible and less acceptable to use. It primes the population at the environmental level to really help prevent initiation, but also to promote cessation.

Now, we see that we have an emerging tobacco product landscape as well. In addition to the tried and true strategies that we know work in this population-based prevention vaccine, we also know that there are emerging strategies, particularly when it comes to the retail environment, which is a very critical

intervention point. I recently wrote a commentary in the past year with one of my colleagues, Amanda Kong – it's the King Kong commentary – that pushes even further on this issue of the vaccine and highlighting the importance of retail strategies around availability, pricing, promotion, and advertising. It emphasizes display bands, age of sale policies, and restrictions on resale of retail license to prevent tobacco product use. But again, also at the population level, to promote cessation in terms of making these products less accessible and acceptable. When you have this comprehensive approach, which has been the hallmark of tobacco control for many years, it helps to address these multiple levers.
But it's important to note that although we've focused on prevention for many years, we now have over six million US youth who are currently using these products. We cannot lose sight of the fact that it's not just prevention, but also cessation to address youth who may be dependent or addicted to tobacco products. Frequently we focus on this measure of people who have ever used the products which addresses the prevention lens, but we also have to be mindful of the fact that we do have millions and millions of youth who are using these products. We can't get pigeonholed into this notion of just preventing use when it comes to youth. Now that we have over 6 million tobacco product users, we have to address those levers of cessation as well.

So, when it comes to addressing cessation behaviors among kids, we do have some limited data, and the good news is that a sizable portion of kids are seriously thinking about quitting use of all tobacco products. It's not that different from adults. The data from the National Youth Tobacco Survey show that about 60% of both middle and high school students who are using tobacco products are seriously thinking about quitting the use of these products. Importantly, a sizable portion have actually stopped using all tobacco products for one day or longer in the past year. If you look at these numbers, you can see that they're fairly comparable between youth and adults. So almost all the kids are thinking about quitting, and they actually tried to do so. That's a very good sign. We see far more variability when it comes to adults. But when it comes to kids, there's certainly a desire to do so, and there have been attempts to do so based on the available data.

When it comes to adults, we have a variety of evidence-based resources. So, we know advice to quit from a healthcare professional; counseling in individual, group, and telephone/web/text formats; seven FDA-approved medications; barrier-free insurance coverage of evidence-based treatments; and health systems changes all increase cessation. All of these were nicely articulated in the recent Surgeon General's report. But an important caveat there is that the science underlying these efforts are focused on adults, and specifically on combustible cigarette smoking. So, there's really this dearth of science to address not only youth, but also the emerging tobacco product landscape and the new products that are out there.

The question that always comes up is "What is the evidence-base for youth tobacco cessation treatments?" This question is something that the tobacco control community has only recently started to vigorously address in terms of the science. There is limited evidence, not nearly as robust as when it comes to adult cessation treatment. The U.S. Preventive Services Task Force has been a guideline body that has put out some messaging on this issue and noted that the evidence is insufficient to recommend for or against providing interventions to youth for cessation of tobacco product use. And they noted that the existing studies on behavioral interventions to help youth quit tobacco have been too heterogeneous and too small to detect a benefit, and that no medications are currently approved by the FDA with regards to tobacco cessation in children and adolescents. Importantly, they also note that you can use clinical judgment to decide how to best help youth who use tobacco to quit. So, what does that mean?

This is what they articulate in terms of using clinical judgment on these issues. Pharmacotherapy for moderate to severely tobacco dependent youth: the risks and benefits should be explained to youth and their family prior to utilizing pharmacotherapy; and pharmacotherapy should be utilized with close monitoring and follow up by their healthcare provider. Again, this would be off label use of these products. So, we do know that pharmacotherapy is being used, but again, the evidence base is not there. It's very important for us to use a data-driven approach when it comes to recommendations. That's why we're here today to hear where the data are on these issues in terms of both behavioral counseling, which the U.S. Preventive Services Task Force has an "A" rating for prevention, but nothing similar for youth cessation. So, we can't, to date, utilize cessation levers. I look forward today to a fruitful discussion in that regard.

In the meantime, we do know that many youths who are using tobacco products report that they're receiving some of these cessation interventions that have been proven effective among adults, including screening by healthcare providers. We do know that among students who visited a healthcare provider during the past year, close to half of high school students, but only one quarter of middle school students, report that they were asked if they had used tobacco. So, a clear gap here. We know that in order to treat something, you have to know whether it exists. There is a clear gap in terms of screening for tobacco product use. We also know from other surveys that there's also variation in what products are assessed. We know that it's an evolving tobacco product landscape. If healthcare providers are not asking about the products that youth are using, and using the terminology and language that is relevant, you may get an underestimation of use, even if you believe you are appropriately screening for tobacco product use. We do know from the cigarette literature that students who smoked cigarettes in the past 30 days have been advised by a doctor to quit. But again, it's only a third of high school students, and slightly less than a third of middle school students as well, who are being advised to quit. Even though there is some screening, in terms of advice and intervention, they are not necessarily occurring. That could be for a variety of reasons, but also most notably, because we lack clear evidence-based recommendations about what works best for this population.

So, when it also comes to the use of counseling and medications, we do have some trend data as well. These were released in the recent Surgeon General's report. You can see among the middle school students and high school students, there are self-reported data on their use of programs, counseling and/or medication - including the use of nicotine gum, nicotine patch, or any medicine to quit - which again is off-label for this population. You can see that there has been an uptick in this measure in recent years among middle and high school students, but it's still very low. What is particularly concerning is use of counseling is particularly low given that we know that it's effective for prevention. Again, reinforcing that we're not necessarily reaching youth in terms of healthcare provider counseling, but also other methods of prevention.

It is important to note that the times are changing and so must we. You've heard me say before, we cannot behave like we live in a cave. The landscape is changing, and we have to be nimble to ensure that we communicate in ways that youth communicate. That also points to novel strategies that reflect the ways that youth communicate. We're going to hear more about that later today from several experts around things like online and web-based interventions and mobile texting, both of which have been found effective among adults. Also for emerging strategies, like mobile-based apps, the available evidence is limited, but this is a novel strategy that really reaches youth in the way that they

communicate and can help supplement the existing tried-and-true interventions such as tobacco quitlines, which have been highly effective in terms of getting evidence-based resources to adults

So, here is the take home message. Progress has been made in reducing youth cigarette smoking, but the tobacco product landscape continues to evolve. Remember, we don't want to be playing a game of public health whack-a-mole. We need interventions to address the diversity of existing, but also emerging and novel, products. More than half of the youth who use tobacco products are thinking about quitting and have tried to quit. The problem is we're not necessarily reaching the populations with the resources that can help them do so. That's complicated by the fact that the evidence is insufficient to recommend for or against providing interventions to youth for cessation. With that said, we need continued research to inform data-driven decisions. That's why we're here today, to really discuss where we are concerning the state of the science and what we can recommend given that there is definitely a dearth of information out there and a continued need among a variety of stakeholders - whether it be clinicians, public health practice professionals, the educational sector, and others.

So, with that, I'll close with some resources related to this from CDC around a variety of products. I really encourage you to examine these resources and public health messaging, which we know is a key component of reaching key populations, including the general public: both Smokefreeteen.gov, and also the Surgeon General's website that Dr. Adams already duly referenced, and CDC's youth cessation resources.

I hope that this helped kick us off today for some fruitful dialogue. I'm pleased that we've chosen this topic for today's ICSH meeting. I think that we're going to have a very fruitful dialogue with a lot of qualified experts to really broach a lot of these issues - that I've hit on from that thousand foot view - to obtain a more nuanced discourse about where we're headed in this field and to get some actionable items moving forward. So, thank you for your time today, and I look forward to today's discussion.

PANEL SESSION #1: CLINICAL TREATMENTS – BEHAVIORAL AND PHARMACOLOGICAL TREATMENT

Ms. Kathy Gallagher: Thank you, Dr. King. Our first panel is on clinical treatments, and our first speaker is Dr. Kevin Walton. Dr. Kevin Walton is the Chief of the Clinical Research Grants Branch in the Division of Therapeutics and Medical Consequences at NIDA at the NIH. The Branch manages the grant-funded clinical studies exploring new medication, behavioral, device, and digital therapeutic development for the treatment of substance use disorders.

Kevin Walton, PhD
Chief, Clinical Research Grants Branch
Division of Therapeutics and Medical Consequences
National Institute on Drug Abuse, National Institutes of Health

Dr. Kevin Walton: Thank you very much for that introduction.

I am going to be focusing on what we know about pharmacological treatments for youth tobacco cessation. Dr. King gave a very good overview, but as he mentioned, we'll be doing a deeper dive into the details.

I have nothing to disclose.

What I want to focus on first is “What is the landscape for treatments for adults for smoking cessation?” There are seven FDA-approved pharmaceutical treatments. Five of those are nicotine replacement therapy and they function to basically replace the nicotine that you're getting from tobacco products. The three that are the most popular are: the nicotine patch, which provides a constant level of nicotine; then you have nicotine gum and nicotine lozenge, which can be used in addition to the patch (meaning at the same time), to address acute craving effects. Bupropion is a medication that functions by increasing signaling of some neurotransmitters and blocks nicotine binding to its receptor. Varenicline, which is the most recently approved (in 2006), functions specifically by blocking nicotine binding to its receptor. Many studies have been done looking at the efficacy of these treatments. In 2016, a rather large study was done with a thousand individuals per arm looking at the efficacy of these treatments as well as their safety. In this study, in the placebo group, 12.5% of the people quit smoking, nicotine patch and bupropion worked equally as well (about 23%), and varenicline has consistently been the most active helping about 33% of the people quit smoking. These studies are focused on adults and cigarettes, not electronic cigarettes. All of the data that we’re going to be talking about today are focused on combustible cigarettes. I'm not sure of any controlled clinical studies that actually have looked at quitting of e-cigarettes.

Medication studies for youth tobacco cessation, in comparison to adults, are actually very limited in terms of the number of large studies that have been conducted to date. In 2017, Cochrane published a review on these studies. Cochrane published this review on clinical pharmaceutical trials, and they looked at the entire literature and identified those studies that were large enough and had good controls to really help determine whether the treatment is efficacious or not. The Cochrane review only found four studies of sufficient quality to be included. Two of the four studies were on NRT, one of them on bupropion, and another one examined the combination of NRT and bupropion versus the use of the nicotine patch alone. Since the Cochrane review was published, in just last month, a large study of varenicline was published. Because we have so few studies on pharmacological treatment for youth, I thought it would be worthwhile to look at each one of these studies in terms of how they were designed, what their challenges were in conducting the study, and their results. I'm going to be looking at the two NRT studies, the one study on bupropion, and the one study on varenicline.

This first study was published in 2005. It had three arms: a nicotine patch arm; a nicotine gum arm; and placebo. The age range was 13 to 17 years. It was a good-sized study of 120. It took four years to recruit, which is a reasonable length of time for academic studies. It had individuals who had a high dependence for nicotine. And we know that because they smoked about 19 cigarettes per day and had a Fagerstrom test of nicotine dependence score of seven. Both of those indicate high dependence. It was a 12-week treatment, and what we saw is that only 46% of the individuals completed the trial. Over 50% of the adolescents who participated in the study had dropped out. That's one issue that we see with treating of this age group. They'll sign-up, they think they want to quit, but then they don't realize how much is involved in a clinical trial. You know, it is three months long. You’ve got to come into the clinic very often. You have to keep records of how much you smoke. And so, it's more work than they were really bargaining for when they signed up. You can see that, for the nicotine patch, it had about a five- to six-fold increase in cessation compared to the placebo. That was a significant effect. Nicotine gum did not have a significant effect over placebo.

Here is a larger study looking at nicotine patch and placebo with a similar age range to the previous study I discussed. It had 257 participants. In each arm was about 120, which is three times the size of the

previous study. This actually took four months to recruit which is incredibly fast. This was done in the Netherlands and participants were recruited through the schools, which in the U.S. has been very, very difficult to do. They had moderate dependence and, as you can see, they had a six-week treatment, nine weeks for heavier smokers. They had a 91% completion rate which is incredible not only for adolescents but for any for adult clinical trials as well. Their results indicate no significant effect of the patch. However, when they broke out those who quit by level of compliance—I mean, how often they used the patch—if they used it most days, they are considered high compliant. If they use it fewer days, they were considered low compliance. If we look at placebo, the number of actual quits show there is really not much of a difference by compliance, but with NRT there is a threefold difference in those who were in the high compliant group versus those who were in the low compliant group. This is not an issue unique to this age group. Among adults it is the same thing. Compliance is a big issue, and this points out that compliance can make a big difference. It is something that when we run these kinds of studies that is something that we need to pay attention to.

This next study is a study looking at bupropion done in 2007. They had high dose, low dose, and placebo. Similar age range to the previously discussed studies. Good study size – 300 participants. It took three years to recruit, again that is a reasonable length of time. There were moderately dependent, but they required the kids to have two previous quit attempts, because they wanted to make sure that they were motivated to quit. They had a six-week treatment with an 85% completion rate. That's actually very good. The results indicate that the high dose had a significant effect over placebo at 29% quit vs.16%. That's really good. But when we look now at the follow-up, so they stopped treatment at six weeks and then they looked at 26 weeks, there was no longer a significant effect. We have seen that once the intervention stops the quit rate goes way down because of relapse. And so, again, it's not an issue related specifically to kids, but it's something that we need to think about when we try and help them quit.

So, this is the fourth study which involved varenicline. This was actually just published last month by Grey. It was a study supported by Pfizer which produces varenicline. This also had three arms: high-dose varenicline; low-dose varenicline; and placebo. It had the same age range. A really good size, 300, about a hundred per arm. This took a very long time to complete; six and a half years to complete and over 57 sites. Some of the sites weren't able to recruit at all. Some of the issues around that might've been that although they smoked an average of 12 cigarettes per day, they had to smoke every day. For this age group, they're not always smoking every day and so that's something that we think about. What is the population we need to recruit? They also had to have at least one quit attempt. Again, they wanted them to be motivated and committed to quitting. It was a 12-week treatment and 60% completed the study. That is a big dropout rate of 40%. That is the same issue we saw in the previous study. The results indicate that there is no significant effect by varenicline either at the low dose or the high dose. I was at an FDA meeting when these results were first presented and somebody from the FDA who was involved in addiction studies said, “This is the first varenicline study I ever saw fail.” So, this medication really works well for adults, but why didn't it work for kids? Well kids are a special case. I want to get into that explanation in a second but first I just want to recap a little bit. So, we have all those medications for adults, but they don't seem to be working in kids in the way the studies were designed. How are kids different? What are the issues around treating this age group?

There are a couple of issues. I broke them down into two large groups. There's something about the environment and their peer groups. So, in the bupropion study, over 70% had smokers in their household. When adults try to quit, they'll usually have nobody else at home who smoked, so they can

go home, it's a safe place. They are not tempted to relapse. If you're a kid and you're going home and there are people smoking and, if it's your parents, just think about how challenging that would be for you to not start smoking again. If it's your parents who are smoking, then you have to think about the family support too. That's always brought up that you need to stop hanging out with the people that also use those substances, because you need to find a different group of friends. But now, these kids, their peer group, and their best friends are smoking. You know, imagine them trying to find a whole new friend group. That's very, very challenging. Another issue is motivation. So, in the bupropion study, they needed to have two quit attempts before they could enroll. So, the most common reason for exclusion in the study was the lack of motivation to quit. If you're going to have a really motivated group, how are you going to measure motivation? In the varenicline study, they had fewer smoking years, an average of three years, which meant that they had fewer quit attempts than older long-term smokers. You know, if you've been smoking 10, 20, 30 years, smokers usually have at least four quit attempts before they are finally successful. They have that experience with frustration of not being able to quit. Kids don't have that. They don't realize what the challenge is going to be. They don't often consider themselves as long term smokers. They think, well, you know, maybe I'll quit next year or the year after. It's not a big deal. Lastly, they are years away from any of the serious health effects of smoking and they don't have lung disease, cancer caused by smoking. They don't have mortality issues to think about that older smokers might have. One other issue I want to bring up is whether the quitting criteria are appropriate. In the varenicline study, they were not considered abstinent if they had smoked any cigarettes, even a puff. If they smoke a cigarette and, and then decide, no, I'm not going smoke anymore, they were not longer abstinent. We need to think about the idea of lapsed versus relapse. Relapse would be, going back to smoking at your previous level. Just one lapse or two lapses well may not be a failure and maybe we need to think about different ways to categorize what success is. The last point I wanted to make is that the safety of all these medications is the same in adolescents as in adults. We need to think about different ways to do these studies, to help find approved ways of design that can help these kids quit. As Dr. King noted, kids do want to quit, and so their doctors need to think about ways to help them do it.

The American Academy of Pediatrics has put out a fact sheet for using NRT for helping kids quit. They recommend the use of NRT for moderately or severely addicted youth who are motivated to quit. They also talk about how to think about e-cigarette dependence. Again, I want to emphasize that these studies that I've been discussing are just focused on cigarettes. We don't have good studies about e-cigarettes. The last point is that in the UK, their National Health Service has also recommended the use of NRT for youth. So, there's a lot of opportunity out there, and the challenges are very big in working with this group. That sums up what we know about the approved medications for youth.

Ms. Kathy Gallagher: Thank you, Dr. Walton. Moving to our next presentation. I'd like to welcome Dr. Susanne Tanski. Dr. Susanne Tanski is an Associate Professor of Pediatrics at the Geisel School of Medicine at Dartmouth, Section Chief and Vice Chair of general pediatrics and a practicing primary care pediatrician at the Children's Hospital at Dartmouth-Hitchcock. Dr. Tanski's current research includes a focus on tobacco use among adolescents and young adults, tobacco cessation for patients with cancer, media/marketing influences on adolescent drinking and smoking and the effects of corporate interests on health. Welcome Dr. Tanski.

Susanne Tanski, MD, MPH, FAAP
Associate Professor of Pediatrics,
Geisel School of Medicine, Dartmouth

Dr. Susanne Tanski: Thank you so much. Good afternoon everyone. My name is Dr. Susanne Tanski, and I am a primary care pediatrician and tobacco control expert with about 18 years of experience researching tobacco issues and counseling youth and their parents who were using tobacco products. I'm also here today speaking on behalf of the American Academy of Pediatrics, which is a nonprofit professional organization of over 67,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists. The Academy believes that all children should lead tobacco-free lives, free from the use of all tobacco products, and free from exposure to secondhand smoke and vapor. And I really appreciate the opportunity to speak to you all today.

I have nothing to disclose.

As we're all quite aware and as articulated so well by Drs Adams, King, and Walton, youth tobacco cessation is challenging. There are a great many reasons for this, not the least of which is the dynamic developmental stage that youth represents. In our context today, I'm going to use the term youth very broadly. It's based on a time period prior to brain maturation, which occurs as Dr. Adams mentioned, in the mid-twenties. I'm going to be interchanging the terms youth, adolescents, and teens in my remarks. I hope we can all agree that youth and adolescents are not just little adults. There is really quite a lot happening during youth and adolescence. They are really works-in-progress. As the mother of two teenagers, it really resonates with me. They're developing their decision-making skills in the context of ongoing brain development. There is more active reward-seeking behavior at the very same time that their harm-avoidance skills and impulse control are still very much less active. The result of this is the discounting of risks and accordingly greater risk-taking. Simultaneous to this, as mentioned by Dr. Walton, they are really tuned in to peers and social influences and less so to adults. Peers are a very powerful motivator for the risk-taking behavior. And emotionally, as we're all very well aware, youth are much more labile than adults. This yields a cohort that overall has less ability to control, self-monitor, or regulate their own behavior. Unfortunately, this creates the perfect storm for experimentation with addictive substances such as tobacco which can lead to routine use and its substantial morbidity and mortality. Not surprisingly, it is challenging to change behavior during any point of adolescence, and it takes different approaches across this age span; working with a 14-year-old is usually quite a bit different than working with a 19-year-old.

Adding to the complexity and challenge of tobacco cessation in this population is that, as mentioned, tobacco use in youth and adolescents is different than use among adults. As shown in Dr. King's slides, in 2019, more than 31% of high school students reported having used any tobacco products in the last 30 days. Adult data from 2018 found that fewer adults overall are currently using any form of tobacco. Prevalence is 19.7% among adults. In addition, as mentioned, adolescents typically don't identify as smokers or as being addicted to nicotine even among young people with pretty significant use. One of the most common phrases I hear from my patients who are using tobacco is, “I'm not addicted or anything, and can totally stop at any time.” And then they can't stop when they try. Our young people are often also using multiple tobacco products. They're using disposables, vaping pens, their friend’s tank, smoking a few cigarettes here or there, maybe some JUULs or Puff Bars when they are available. For some it is an opportunistic pattern, but each exposure potentially leads to dependence. Indeed, in young people, nicotine dependence develops from unstable and infrequent use to begin with. This is where behaviors are being reinforced, and as such, this is a really problematic part of their trajectory. This unstable or infrequent use, however, presents an early and important opportunity to intervene. As a pediatrician I try hard to intervene whenever I can before significant dependence has developed. As

we pivot to talk about what's been done to date that has been successful specifically with regard to behavioral interventions, it is notable to bring up what Dr. Walton has already mentioned—that defining who is eligible for an intervention may vary from study to study. What makes a tobacco user? Is it use of a pack of cigarettes a week? A pack of cigarettes in a day? One cigarette per week? One cigarette per day? A pod per week? A pod per day? When is the best time to intervene and with what intensity? How do we define what it is to have quit? Our young people may view cessation really differently, as mentioned, with a puff or a hit not perceived as not-quit. We need to think of those as slips and perhaps not as a relapse.

So, what do we know about behavioral interventions for tobacco control? Again, I begin with a caveat that nearly everything we know so far with regard to tobacco cessation and youth has been around cigarette smoking. We don't know yet what will work for other forms of tobacco. Many different behavioral interventions have been conducted with many different designs, including group interventions, individual therapy, in-person therapy, computer-based programs, text-based programs, and combinations of all of these. These interventions have been carried out in multiple locations, maybe in school classrooms, in school-based clinics, medical office settings, community settings, and in their own homes. And they are built on a broad range of behavior change theories and techniques, cognitive behavioral therapy (or CBT), motivation, enhancement, social cognitive theory, contingency management, and combinations of these and more. With all of these designs and attributes, it has been really hard to identify the specific attributes that work more often in this population. There have been more than 15 reviews and meta-analyses to date and not surprisingly there is significant heterogeneity that makes comparisons really difficult. As mentioned in the last slide, studies use also vastly different definitions for inclusion criteria and cessation, duration of cessation outcome, and also verification of cessation with either biochemical verification or self-report.

From the 50,000-foot view, behavioral interventions do show some modest promise. Looking to Steve Sussman's most recent comprehensive review from 2009, looking at 64 different studies, overall cessation was achieved by 11.8% of participants in a behavioral program, as compared to 7.5% in control conditions. This is an overall advantage of 4.3%. The conclusions from this review found that motivational enhancement plus cognitive behavioral strategies fare best and that there needed to optimally be repeated sessions. One shot didn't take; there needed to be at least five sessions as a minimum. He further noted the importance of formats that are engaging to teens, which of course is critical to retain this group in any intervention.

The more recent meta-analysis, that was also discussed by Dr. Walton, was conducted in 2017 and looked at randomized clinical trials only. The authors found, overall, a low quality of evidence across behavioral intervention studies using the GRADE criteria. But overall, they found that group counseling as a design was favored. The relative effect of group counseling on cessation was 1.35 (95% CI 1.03 to 1.77). Computer- based interventions were the least effective designs across these studies. Multiple delivery methods demonstrated a relative effectiveness of 1.26 (95% CI 0.95 to 1.66) with a confidence interval that was nearing significance of 0.95 to 1.66. Outside of this meta-analysis and other reviews, there have been additional recent studies that have shown some promise. For example, contingency management, which in this study was monetary awards for abstinence, combined with CBT or cognitive behavioral therapy showed real promise, but this type of intensive intervention is not very scalable to reach the unfortunately increasing numbers of young people who are tobacco dependent. So where do we go from here?

Simply put, we need more investment in youth tobacco cessation. Until we optimize each aspect of youth tobacco cessation design, we will not be successful. We need to find better ways to motivate young people to understand that their tobacco use is something that warrants intervention, which will then hopefully facilitate recruitment and enrollment into cessation studies, and then these will not take three or four years. We need to invest in creative methodologies to increase the appeal of these interventions and thereby the level of engagement from our young people. With this we will have greater capacity to retain youth in our studies and cessation programs, which we hope will then yield a better chance for successful tobacco cessation. And finally, we do need to be mindful of scalability. The ideal program will be able to be delivered with as few barriers as possible so that we can shift this tide of 6.2 million youth tobacco users to non-users. We truly have more to do.

In summary, the American Academy of Pediatrics and I recommend that we urgently fund additional studies regarding behavioral pharmacological and combination interventions for youth and adolescent tobacco users that can be implemented and tested in real time. We just don't have years to wait, given what we know right now. We need enhanced investment in virtual treatment using digital platforms to facilitate engagement and retention and treatment, and to increase capacity and capability to deliver effective interventions and services. We need to use these novel strategies that our youth are already engaged in, as Dr. King was mentioning. We need additional assessment of patterns and trajectories of nicotine dependence among users of different and combined product types, and we need assessment of short- and long-term harms and risks of vaping specifically as a critical motivator for behavior change among this population who is using vapes.

Finally, I would be remiss as a pediatrician with a focus on prevention if I did not conclude by encouraging our ICSH partners to continue prevention efforts. To build on Dr. King's Ben Franklin axiom, we need as many ounces of prevention as we can provide. We must support enforced strong regulations aimed at eliminating youth access to all tobacco products, including e-cigarettes and vaping products with enticing flavors and high nicotine content. This is critical to prevention as well as cessation. We must prevent youth use of all tobacco products and nicotine addiction before it starts, while also supporting cessation for our youth, young adults, and older adults who are currently addicted to nicotine. Thank you so much for your time and attention. And I look forward to this robust discussion.

Ms. Kathy Gallagher: Thank you, Dr. Tanski. We'll now hear remarks from Dr. Wilson Compton. Dr. Compton serves as Deputy Director of NIDA at the NIH, where he has worked since 2002. NIDA supports most of the world’s research on health aspects of drug abuse related to preventing drug abuse, treating addiction, and addressing serious health consequences of drug abuse. Welcome Dr. Compton.

Wilson Compton, MD, MPE
Deputy Director of the National Institute on Drug Abuse,
National Institutes of Health

Dr. Wilson Compton: Thanks very much. It's a pleasure to be here today and to follow the last few speakers. NIDA is certainly interested in developing and supporting research that can address this important gap in clinical care for youth who are addicted to tobacco products. We have a long portfolio of observational studies understanding the trends in tobacco use. We also have significant investment in prevention interventions. I do think, as we talk about cessation interventions for youth, we might think about prevention as a platform for some of the cessation work. Some of the tools in terms of social interactions and social behaviors that have been so powerful in prevention may play a key role in

cessation as well. In addition, let's think about some of the challenges in the cessation research in particular. Why are the results for adults not replicated in adolescents? We heard something about this from Dr. Walton and I think this is an important issue for us to consider. Certainly, adolescents may be somewhat less motivated to want to quit. As highlighted, they haven't suffered the health consequences and their peers may not have suffered the health consequences that at times become a motivator for adults. Brain development is of course a key issue, and certainly NIDA is supporting studies, like the Adolescent Brain Cognitive Development study, to help us understand adolescent brain development and the response to the start of substance use, like tobacco use, alcohol use, marijuana use, and others in a large sample of adolescents. Can we use that information about brain development to help guide better cessation interventions? We certainly hope so.

One of the issues is that medications may have a different effect on adolescents. As a psychiatrist, I've certainly witnessed this in the broad psychiatric field where antidepressants have a different impact in adolescents than in young adults and certainly in older adults. Do we see some of the same impact in these treatments for adolescents? I don't think we know the answer to that. That is something that is worth considering and exploring. I also wonder if, as we're seeing a shift into new forms of tobacco, and really away from cigarette use by adolescents, are we witnessing such a shift in the risk factor profile of adolescents that they may not respond to tobacco cessation, because they are really such different individuals than the adults that do respond to these medications? What I mean is that studies which rely on their adolescent subjects being cigarette smokers are really recruiting a sample that is at an extreme when it comes to risk factors related to externalizing behavior and general problem behaviors. That might reduce the overall response to virtually any treatment. If we looked at adults who had that same risk profile, we might have seen the same lack of response. I think some of that may be able to be examined. On the other hand, the increases in vaping and the marked popularity of vaping by youth may have shifted the dynamics in terms of the adolescents who are now using tobacco products.

I certainly heard the message from Dr. King that we need to think about changing our targets from cigarettes to tobacco more broadly. And when it comes to cessation, we need to be thinking about that as well. It's not just a matter of helping kids, helping youth, and adolescents quit smoking cigarettes or quit using traditional leaf tobacco of one form or another, but also considering what can we do to reduce the use of all tobacco products including, in particular, the vaping products. That's a key issue for NIDA and one that I look forward to hearing thoughts from this group about what are the most promising approaches to help youth quit vaping.

I certainly remember the meeting of this group last year. What we heard during that meeting were some very dramatic stories about how serious the addiction to vaping products has become among many youths and what can we do to make sure that our cessation efforts really target the newest forms of tobacco. These are some of the issues that I highlighted on this topic and I look forward to a further discussion with the whole group.

Ms. Kathy Gallagher: Thank you, Dr. Compton. We will now enter into a 15-minute question-and-answer and discussion period from what we had heard to date. I want to remind you that the purpose of today's meeting is to identify federal actions to prioritize areas of research that can be expedited to support needed youth tobacco cessation treatments. The Committee's mandate is to focus on the federal government’s actions. We are eager to hear from the experts. I'm going to first turn to our public members, to see if they have anything that they’d like to say to kick us off.

PANEL DISCUSSION

Dr. Jasjit Ahluwalia: Thank you, everyone, for those wonderful presentations. To Dr. King, I'm always amazed at the graph that shows such a rapid decline in youth usage of combustible cigarettes, but yet the adult prevalence slowly going down. There was an article last week that shows that while there is this rapid decline in youth, there was actually a significant increase in combustible tobacco use in 18- to 25-year olds. This was a very interesting article, because something has to explain this, right? If youth aren't starting using cigarettes and adult prevalence is just going down slowly, something has to explain that increase in young adults. I would make an overall comment on that. We have the youth researchers and we have the adult researchers and, typical of clinical medicine, those people age 18 to 25 years are sort of forgotten about. Also, I have a comment for Dr. Walton and Dr. Tanski on your wonderful talks. This idea that it is hard to get youth to quit. It reminds me of when I started in 1992 with looking at cessation interventions for African-Americans and smoking when no one was doing that work. It was very hard to find ways to get them to quit. I think we need more work, you know, that's the bottom line. Dr. Walton showed that there are only four randomized clinical trials (RCTs) of good quality for pharmacotherapy. We need a lot more then. I would just caution us that… I know this will sort of rile people a bit, but we just completed an e-cigarette trial in African-Americans and Latinos which has been accepted for publication, and it should be published within a matter of days or weeks. There are some good data there with regards to biomarkers of harm and exposure and quitting or substituting. What if kids can't quit on all these products and behavioral techniques and they start using e-cigs to quit? That will really upset a number of people, but what if this occurs? Should we be doing that work proactively to better understand this possible scenario?

Dr. Suchitra Krishnan-Sarin: Thank you everybody. That was a wonderful series of talks. It's always nice to see the data. I just wanted to highlight a few things. One is we are seeing decreases, like Dr. Ahluwalia just pointed out, in cigarette use among youth, but let's not forget the other combustible tobacco products too. We have a lot of kids who are now starting to use other products like cigarillos and blunts have always been very popular. Which brings me to this very interesting question that I think everybody is grappling with—which the intersection of marijuana and nicotine use, which comes up a lot. In practice, both can be used in vaping products as well as in blunts. This is not something we should lose focus on because today many youths are using vaping products not just for vaping nicotine but also for vaping marijuana. I think there is this interesting intersection that we are coming up on that we need to keep our eyes on. I completely agree with all the speakers that understanding whom to provide these interventions to is something that I have been struggling with for years. How to classify dependence? There's a very nice recommendation of providing pharmaceutical products to those who are more dependent and how we determine that dependence. That is a very basic question that I don't think we really have answered very well in this field which really needs to be answered. My last point I want to raise is that the presence of COVID-19, as bad as it has been for everything else, has actually highlighted for me the importance of digital interventions and social media as evidence-based interventions. I think you should take this as an opportunity to really develop interventions that are based on those platforms that can reach a lot of youth knowing that a lot of them use all these digital platforms very easily compared to adults. The one thing we need to keep in mind is the huge social media influence. Many of these products are now advertised on social media. When I think about web-based platforms and online platforms, I think we need to target the social media presence of these products in reaching out to kids. Then we need to learn how to use social media to our advantage to provide interventions with kids. I think if we can target these two approaches, we could make a significant dent in terms of provision of interventions to youth.

Dr. Wilson Compton: I'd like to support some of your comments, Dr. Krishnan-Sarin, before we keep going. You mentioned cannabis as a key comorbid feature, and certainly for NIDA that has been a major theme for our work. I would highlight research out of the Monitoring the Future Study documenting a marked increase in cannabis vaping just in the last couple of years. Kids don't keep the behaviors neatly packaged in one substance at a time. Once they learn one technique, they will try it with other substances. I think that is a reminder in some ways in that as we're focusing on tobacco, we need to think about how tobacco is related to all substance use by youth. And so just like you're talking about expanding prevention and possibly treatment to cover a broader range of tobacco products, some of the most effective approaches may be those that cover a broad range of substances as well.

Dr. Kimberly Horn: I just wanted to make a couple of points and follow up on these extremely informative presentations. In thinking about some of the variability that we've seen with youth tobacco cessation trials over the years, and I've been one of those folks who's conducted many of them, I think one of the things we've been challenged with, going on two decades now, is standards for measurement and outcomes. There are a handful of meta-analysis studies (on teen tobacco cessation trials) which are important, but they underscore that the way we measure quit reduction and a whole host of other potential outcome variables are wildly different. I think we need to move closer to some standards for adolescent and youth studies; otherwise we're going to continue to grapple with being unable to appropriately synthesize findings across studies. I think that moving towards standardized, multisite trials would be beneficial. In the adult literature, when pharmaceuticals are tested or in other adult cessation intervention trials, multisite trials are common and expected. In these trials, facilities and institutions run trials with similar, monitored standards. Researchers use the same methods, measurement, and terms as well as similar types of analyses. In some cases, it is a regulatory requirement. We don't see that very often with youth intervention trials; in part because we haven't had the RFAs, the mechanisms, or the funding directed towards those kinds of studies for youth. Further, available, scalable tobacco interventions to test with youth are sparse. I think all of these factors are very important to consider to move us in a different productive direction on this research. We don’t hold our youth trials to the standards in the same way we do adult trials. Granted teens are a changing population and we have to work hard and a bit creatively to keep up with the rapid changes that happen during adolescence. However, I think that if we could move toward more intervention trials that are multisite-oriented with standards that we can apply collectively then we can make better determinations, faster, about what is working and what isn't. Without this movement, we are left as we are right now, synthesizing research in a way that seems very random.

Mr. Dennis Henigan: These were just excellent presentations and it underscored to me how challenging it is, once the kids are addicted to nicotine, to deal with that reality effectively. Right now, we have the reality of mass nicotine addiction among kids. There has been, as has been commented on, a decline in the last year in the number of kids using e-cigarettes, but it has been a decline to the level that was reached two years ago when Surgeon General Adams declared an epidemic of e-cigarette usage. What we're seeing from the most recent data is that those kids who are using these e-cigarettes are using them more often, indicating that there are a lot of kids being addicted and that prevalence of addiction is increasing. I want to go back for a moment to Dr. King's discussion of the importance of prevention and the tobacco control vaccine that he delineated, which I thought was all very valid. But I wanted to suggest an added component to that vaccine which has not been discussed at length yet. That is robust federal regulation of the tobacco industry and of the cigarette industry. The FDA, as we all know, has broad regulatory authority in this realm. It has authority to change the nature of these products to make

them less addictive, to make them less attractive, to kids by eliminating the flavors that attract kids, etc. They have the authority to actually review each product before it reaches the market. There is the authority to adapt the regulation to the introduction of new products in order to prevent exactly what has happened over the last several years, which is the emergence of a new tobacco product that is inflicting enormous suffering on our kids. I come to the conclusion that it is almost a moral responsibility on the part of the federal government to effectively address this issue of youth tobacco cessation, because frankly the federal government bears a great deal of responsibility for the creation of this youth e-cigarette/nicotine epidemic. There's very little that is more important to be discussed today as to how the federal government can be mobilized to deal with this crisis not only from a prevention standpoint, but also to give some hope—some treatment—to those kids who have already been victimized.

Mr. David Dobbins: I wanted to repeat what Dennis just said. He kind of stole my thunder. Federal regulation of these products, particularly e-cigarettes, include products that are on the market illegally and public health standard hasn't been applied to them. As a result, we see these addiction numbers. The other thing I was reminded of is that this epidemic is really only about two years old and the landscape is changing incredibly quickly. As far as advice for what the federal government can do, it's finding more nimble approaches to funding of cessation interventions because I worry sometimes that by the time we get results, the landscape has changed so much that those particular results are no longer useful as a practical matter for people who are trying to treat kids that are addicted to the current generation of products. That is my suggestion.

PANEL SESSION #2: TREATMENT EXTENDER STRATEGIES

Ms. Kathy Gallagher: We'll now move to our next panel. Our second panel is focused on treatment extender strategies. Our first speaker is Dr. Jonathan Bricker. Dr. Bricker is a professor of Public Health Sciences at the Fred Hutchinson Cancer Research Center and the University of Washington. He is founder and leader of the Health and Behavioral Innovations in Technology (HABIT) Research Group. His research group focuses on developing and testing innovative behavioral interventions for tobacco cessation and weight loss, especially those delivered in widely disseminatable technology platforms.

Jonathan Bricker, PhD
Professor, Division of Public Health Sciences, Fred Hutchinson Cancer Research Center;
Affiliate Professor, Department of Psychology,
University of Washington

Dr. Jonathan Bricker: Thank you for that introduction, Ms. Gallagher. Surgeon General Dr. Adams and members of the Interagency Committee and fellow speakers, it is a great honor for me to be here today. When I started my tobacco research career in 1999, 29% of high school students smoked cigarettes and by today that has dropped to 6%. But as Dr. King showed us earlier, the rate of any tobacco use among high school students has only slightly declined from 35 to 31%. My modest hope is that my presentation today on technologies for tobacco cessation plays some role in shaping federal research priorities so that we, as a community, can drive it down to a rate of tobacco use that is near zero.

Here are my disclosures. I have no conflicts and neither does my research group. The Fred Hutchinson Cancer Research Center does license our quit smoking smartphone app to 2Morrow, Inc.

There are a variety of behavioral models for smoking cessation that I want to talk about. The traditional behavioral models follow the U.S. Public Health Services' Clinical Practice Guidelines for Treating Tobacco Use and Dependence. The first behavioral model is motivational interviewing, which is where a counselor provides feedback and reflection to increase one's reasons to quit smoking. That is often combined with cognitive behavioral treatment strategies that teach people how to avoid or change their thoughts and behaviors that trigger smoking. Then there is the mnemonic, the five A's, that's often used in medical practice. It's a way of sequencing interventions where you ask a patient about their smoking status, advise them to quit, you assess their interest in quitting, you assist them in getting treatment, and then you arrange for follow-up. There have been emerging treatments that have been coming out in the research literature in the last 10 to 15 years for smoking cessation. The first one is acceptance and commitment therapy (or ACT), which I'll talk more about later. It increases your openness and willingness to experience cravings to smoke, and it focuses on your personal values as the driver and motivator to quit smoking. There is a behavioral economic approach called contingency management which is about giving rewards, conditional on making progress, and quitting smoking. Those rewards can come in many forms such as vouchers, money, and quit-and-win contests.

So, these behavioral models can be delivered through technology platforms meaning any population-level reach platform that is technology that can be useful for delivering an intervention on a broad scale. There is telephone coaching, such as providing phone calls delivered by trained coaches and the most prominent example is our national quitline. There are websites. Those have been around about 30 years and they provide informational and skills-based training programs. Then, in about the last 10 to 15 years, there are smartphone applications. They provide skills training. They also provide tracking of one's progress in quitting, and they give the user personalized feedback on their smoking. There have been text messaging interventions. So, you can have one- or two-way messaging that occurs pre- and post- quit. They can be tailored or not tailored, and they can either be automated or have some type of human coaching assistance. The most recent technology is chatbots. Those use natural language processing, machine learning, and cloud computing to create digital coaching. We were recently funded by NCI to test one of these chatbots for smoking cessation. There is social media that provides peer support and training through YouTube, Instagram, Snapchat, and Facebook, and so forth.

So, there are two technologies I want to focus on specifically today. The first one is the telephone-delivered quitlines. These interventions, as we know, are delivered in all 50 states. They are available to youth as young as age 13. They're free, confidential, and are delivered by trained coaches. They can use a proactive model, where you can reach out to the user who has called in and proactively call them back, or a reactive model, where you wait for them to call you. They range from one to nine calls and each call is typically about 15 to 30 minutes. They typically use motivational interviewing and some form of cognitive behavioral therapy. They'll assist you in finding your reasons for quitting, help you set a quit date, and give you relapse prevention skills training. In the 2017 Cochrane review on adolescent smoking cessation, which primarily focused on telephone delivered RCT, there was no overall effect of telephone or other treatment programs for tobacco cessation in youth. The confidence intervals are outside the significant range. What do we conclude from that? The efficacy data are lacking. For youth tobacco cessation, there have been no RCTs on e-cigarettes or vaping for any age range and there is a problem of a lack of reach of telephone coaching intervention. I think research needs to focus on how to improve the intervention reach, especially for youth, but there is a notable exception that I want to talk about.

It is an eight-year study that Art Peterson, my colleague, and I published in JNCI that was funded by NCI. It was an adolescent cigarette smoking cessation program that partnered with 50 Washington state schools. In half of the schools, students were assigned to the intervention and in the other half of the schools, students were not given an intervention. We surveyed all high school juniors about their smoking status and then in their senior year we delivered a proactive telephone smoking cessation program. We had a very broad inclusion criteria – high school seniors who identified as at least monthly smokers; this was 2,151 high school seniors. Half got the intervention and half did not. We retained 89% of them in a 12-month follow-up. This was a six-session treatment program. What we found is that the combination of motivational interviewing and cognitive behavioral therapy did increase tobacco cessation, especially among the daily smokers. We doubled the quit rate. What this study tells us is that it is possible to partner with schools. It is possible to successfully engage with adolescents proactively; 67% of adolescents who were eligible for this study completed at least one telephone coaching call. It is possible to retain them and show efficacy. The challenge now is would this work for e-cigarette cessation? Could this model be broadly disseminated?

Turning to smartphone applications for smoking cessation, these provide personalized, step- by-step guidance, skills training, tracking, feedback, and reminders. There are nearly 500 tobacco cessation applications for smoking now available in English. Since 2013, they've been downloaded 33 million times. There's been only one study of young adults from 18- to 30-year-olds. It was a pilot study and it did not show efficacy of their smartphone applications compared to texting, but that is just one pilot study. In the broader scope of studies, the 2019 Cochrane review, which covered five trials and all ages showed broad heterogeneity in the study qualities and had no definitive evidence for smartphone applications for any age for smoking cessation. Despite their ubiquity, there has been very little evidence of effectiveness for tobacco cessation from smartphone applications, and no RCTs on vaping for any age range… until now.

This is a trial we just published in JAMA Internal Medicine. It is a study of acceptance and commitment therapy (ACT) of adults, where we compare the ACT iCanQuit program versus the U. S. Clinical Practice Guidelines-based Quit Guide. We recruited 2,415 adults in all 50 States, and we followed them at three, six, and 12-months with an 87% retention at the 12-month follow-up. What this study shows is that the ACT intervention was nearly one-and-a-half times more effective at quitting smoking than the Quit Guide. The three-month, six-month, and 12-month follow-ups all show that the ACT treatment was more effective than the Quit Guide. If you zero in on the cessation of all tobacco products, which has been a theme of our discussion so far, you'll see that the ACT intervention was approximately 1.6 times more effective than the Quit Guide. We were very encouraged to hear that Dr. Tim McAfee, former director of the CDC OSH, called this a landmark study that fast forwards the field of digital health. The unanswered questions are whether an ACT approach would be effective for youth tobacco cessation, especially e-cigarettes, and we're encouraged that the smartphone-delivered ACT approach to quitting smoking, has already been disseminated to 75,000 people throughout the United States. We're hoping to increase that with the iCanQuit program release and a version of ACT for youth vaping cessation. The ACT smartphone application for youth vaping cessation has already been released in Washington state.

In closing, these are the federal research priorities that I see. One is that we need to test a US Public Health Services' Clinical Practice Guidelines-based model for youth tobacco cessation and emerging treatments such as ACT and contingency management. We need to look at all of the technology delivery modalities that youth are now using including smartphone applications, telephone coaching, chatbots, texting, and social media. We need to test different methods of reaching youth, including proactive

methods and reactive methods. We need to look at novel communication and marketing strategies. We need to integrate these cessation programs within schools and health care systems. We need to look at not only the traditional study designs for testing these treatments, such as the randomized control trial, but also newer methodologies such as just-in-time adaptive interventions to test specific treatment components at the times when youth need them. We need to look at ways to step-up treatments through methods such as the SMART designs that can start with the least intensive interventions, such as technology, and then stepping-up to the more intensive ones for those who need it. We need to look at MOST designs as ways to optimize treatment components and then we need to do qualitative research, such as user-centered research designs, to identify treatment components users would be the most receptive to before we launched these full-scale trials. There are enormous methodological challenges before us in terms of how best to recruit youth, how to retain them, how to prevent fraud and how to measure abstinence, which has been discussed earlier. Our outcomes need to look at all tobacco use not just smoking but also vaping and e-cigarettes. I think in particular if we look at behavioral approaches that focus on the processes (as opposed to the outcome), that leads to tobacco cessation in all of its forms - that can prevent us from playing the whack-a-mole game that Dr. King referred to earlier. We can try to identify those basic processes that lead to these different outcomes of tobacco use Finally, I would like to challenge the Committee to consider mechanisms of funding that are high-risk and high-reward, what I would call "warp-speed funding mechanisms" that span from intervention development to pilot testing, to full-scale randomized trials, and finally to dissemination - all in one funding mechanism. I think by taking this high-risk, high-reward funding approach, my hope is that it will not take 20 years for us to see the high school tobacco use prevalence move from 31% to near zero.

Ms. Kathy Gallagher: Next, we would like to welcome Dr. Amanda Graham. Dr. Graham serves as the Chief of Innovations at the Truth Initiative where she leads a cross-functional team that develops, evaluates, and markets digital products for tobacco cessation. She is a Professor of Medicine at the Mayo Clinic College of Medicine and Science and Professor of Oncology at the Georgetown University Medical Center/Lombardi Comprehensive Cancer Center.

Amanda Graham, PhD
Chief of Innovations, Truth Initiative,
Professor of Medicine (Adjunct),
Mayo Clinic College of Medicine and Science

Dr. Amanda Graham: Thanks again for the opportunity to present to this very distinguished group. The focus on youth cessation is one that I feel very strongly about and one that we've been focused on for several years now at Truth Initiative. It is my honor to participate. My talk is going to review the state of the science around vaping cessation among young people, and the role of digital interventions to reach and engage them in the process of quitting.

By way of disclosures, the Truth Initiative is a nonprofit public health foundation that delivers a free quit vaping program to young people throughout the U.S. I'm going to be presenting data about this free program today, but I also want to acknowledge that we partner with youth serving organizations to deliver an enterprise version of this program to support our mission driven work.

Let's start with the state of the science. You've heard reference to this before. You heard from Dr. Bricker about the wealth of evidence that exists for smoking cessation interventions for young people

and the most recent Cochrane meta-analysis which synthesized data from 41 trials involving over 13,000 young people. For vaping cessation, the story is quite different. To date, there have been six peer-reviewed publications. Two are case studies involving young adults seen in a clinic. Three report data from observational studies. One is a study protocol for a randomized controlled trial that I'll be describing shortly. What this means is that we know very little about how best to help young people quit vaping.

We do know a lot about treating nicotine dependence in young people and you've heard some of that evidence from previous speakers. We also know that digital and social media are the ways to connect with young people for ongoing and personalized support throughout the quitting process. Smartphone ownership is nearly universal among teens. It cuts across gender, race, ethnicity, and socioeconomic background. Text messaging is the preferred communication modality among teens and almost half of teens say that they are online nearly constantly. In short, this is a generation of what we call digital natives. They've grown up with technology all around them. They've never known anything other than this and they're extremely adept at using it. Dr. Adams noted in his opening remarks that the key is to have treatments available precisely at the time that a young person makes that decision to quit and technology-based approaches clearly have advantages here. A number of organizations have responded to the vaping epidemic with digital resources taking the best of what we know from smoking cessation and adapting it to vaping cessation. These include web- and app-based programs, new coaching approaches being rolled out by state quitlines, school curriculum for middle- and high-school students, and the text message program that we developed at Truth.

This is Quitting is the quit vaping text message program we launched at Truth Initiative in January of 2019, almost two years ago. I've previously spoken to this Committee about the development of the program and, in the interest of time, I'm going to direct you back to the publications that I showed on slide three for more detail. Briefly, This is Quitting is delivered entirely via text message. There is no need to download anything. Young people can enroll discreetly and anonymously by texting “ditch vape” to our designated short code. The program is currently 60 days long and we continually evaluate and optimize its delivery. More than 200,000 young people have enrolled in This is Quitting to date (and this number is already outdated now): more than 83,000 teens and 121,000 young adults. These are not kids who are passively receiving messages: 70% set a quit date, and the majority of them set that quit date for the day that they enroll. As we've heard from previous speakers, motivation can be a challenge and a barrier for young people. In contrast what we're actually seeing is a very large volume of very motivated young people who are wanting to break free from e-cigarettes. We also just published a paper in the journal *Addictive Behaviors* that showcases the reasons behind this motivation. I'll refer you back to slide three for that reference. About half of our enrollees are using keywords to get extra support beyond the scheduled messages. Sixty-eight percent complete the full two-month program. In our observational analysis, we see 20% reporting 30-days of abstinence at a three-month follow-up. I'll be talking about a randomized trial that we're currently conducting in the next couple of slides.

One of the interesting things that we've learned in promoting This is Quitting is that a cessation campaign can have very powerful effects on prevention outcomes. This past year, for the very first time, the **truth®** campaign aired a series of cessation-focused ads. They showed young people getting rid of their e-cigarettes in creative ways. You can see them on this slide. At the end of each of these ads, there was a call to action to enroll in This is Quitting. Pre-market testing evaluated the extent to which ad exposure made it more or less likely that regular e-cigarette users would quit and the extent to which ad exposure made it more or less likely that never users or occasional users would start or continue vaping.

We had a sample of about 1,500 young people ages 15 to 24 years: about half had never used e-cigarettes, one-third were triers or occasional users, and 20% were regular users. What we found is that about half of the regular users said they were more likely to quit after seeing these ads and about half of the never users and the triers said they were less likely to start using or to keep using. We've heard previous comments about maybe there is an arbitrary delineation between prevention efforts and cessation efforts. What our data are starting to suggest is that messaging around quitting vaping can simultaneously promote cessation among regular users and have a powerful impact in delivering a prevention message as well.

We're currently conducting a randomized trial to test the effectiveness of This is Quitting among young adults. We have been very fortunate to have the support of CVS Health Foundation to do this work and have done it both rigorously and nimbly. The sample that we've recruited is 2,600 18- to 24-year-olds. We've recruited them in just over three months earlier this year. We have a sample that is divided evenly between men and women, 11% identify as racial and ethnic minorities. Twenty percent are a sexual minority and roughly a third report financial struggles. I've listed just a few of the metrics to give you a sense of their tobacco use: 93% say they vape daily or almost daily and, 82% say they're vaping within 30 minutes of waking, which we know has long been a marker of nicotine dependence. The median intensity of vaping is 50 hits per day, and we do see significant comorbid substance use. Sixty percent have used marijuana in the past 30 days and 32% reported past 30-day smoking. Our primary outcome is 30-day abstinence at seven months post randomization. We will finish data collection this month and anticipate submitting our results for publication before the end of the year. To our knowledge, this is the first randomized trial of a vaping cessation intervention. We recognize that there is a lot of interest in understanding the potential impact and effectiveness of this broad reach program. I want to harken back to the really nice diagram that Dr. Tanski had in her talk that showed all the different drivers that need to be optimized when we think about enrolling young people into an intervention and conducting this kind of research. From this slide, you can see that first and foremost, we had a large volume of young people who were willing and interested in participating in vaping cessation research. We heard from Dr. Walton earlier that this field has struggled with recruitment challenges. We have a large volume of people who were interested and engaging in a text message intervention. This is certainly an efficient and very scalable approach, running a fully digital trial.

To wrap up, some of these recommendations are a reiteration of what you've heard from other speakers. I've identified seven research priorities for the Committee's consideration. The first is to stimulate collaborations to ensure adequately powered trials and shared IRB guidance across research groups. We know that current federal regulations allow for the waiver of parental permission in certain types of research, but we've seen that IRBs are inconsistent in their application of the relevant regulations, which can often be a barrier to doing this kind of work. Second, we need cessation interventions that address the unique challenges posed by vaping cessation designed specifically for young people, and I would argue that incorporating input from young people is equally as critical. Our experience over the past 20 years with the **truth®** campaign has really shown the power of a peer-to-peer approach in engaging youth. Third, we need research that evaluates the reach, the uptake, and the effectiveness of digital interventions integrated into clinical settings and schools. Dr. Bricker mentioned this. We've heard that medication adherence can be a particular challenge, and text messaging has a very solid evidence base in being effective for prompting and cuing medication adherence. That is just one example of a potential integration and just one of the ways that digital interventions can extend support and assist with specific challenges. As I've talked about previously, research that addresses prevention and cessation on a continuum rather than as discrete endeavors or separate funding

mechanisms should be considered. We need to understand how factors at multiple levels of influence interact to promote cessation. For example, mass media in certain policy environments may be more or less impactful in driving cessation among young people. Dr. King talked about the vaccine. We need to understand how the components of the vaccine can leverage each other. We need research that builds our understanding of cessation in this changing product landscape. I'll give a plug again for Dr. Bricker's call for warp speed funding mechanisms. Lastly, you've heard from a number of speakers about the need for consistency in defining quitting and measuring abstinence.

I'll wrap up with my deep appreciation for the opportunity to participate in the discussion today. I look forward to the question and answer session.

Ms. Kathy Gallagher: Now, we will have remarks from Dr. Yvonne Prutzman. Dr. Prutzman is a Program Director in the Tobacco Control Research Branch within the DCCPS at NCI. Her research interests lie broadly in the prevention and treatment of tobacco use. Much of her current research focuses on the population-level dissemination of tobacco cessation interventions via internet and mobile platforms.

Yvonne Prutzman, PhD, MPH
Program Director, Tobacco Control Research Branch,
Division of Cancer Control and Population Sciences,
National Cancer Institute, National Institutes of Health

Dr. Yvonne Prutzman: Good afternoon. I want to start by thanking Drs. Bricker and Graham for a very informative set of presentations, and for their leadership and scientific contributions in the area of technology-delivered cessation interventions. I want to highlight a few important themes.

Firstly, what we're hearing is that engaging people with cessation treatment is very challenging. We know that youth and young adults underutilize evidence-based cessation treatment. The technology-delivered approaches that we have heard about today really represent the type of innovation that's needed to extend and expand the reach of cessation interventions.

The second theme is that the technology interventions have the potential to significantly increase young people's participation, retention, and treatment because they align with the way that youth are communicating today, and they have very low barriers to entry. We can see from data that Drs. Bricker and Graham presented that these approaches can successfully engage larger numbers of motivated youth, and that is something new and exciting.

Thirdly, from an administration perspective or an implementation perspective, these approaches are scalable and cost effective which means they also have tremendous potential to expand our capacity to deliver cessation interventions to this important population.

We heard a very comprehensive research agenda presented already in the set of presentations. I'm not going to reiterate all of it but just want to underscore a couple of points. Broadly, I think we do need continued research on quitting behaviors among youth, understanding the prevalence and predictors of quit attempts, and also the strategies that youth are using. This will help inform treatment development. We also need to understand how to adapt our existing cessation interventions, which have been developed for cigarette smoking, to be responsive to the changing tobacco product

landscape. I know we're all looking forward to the results of the This is Quitting RCT. With respect to digital interventions, specifically, we need continued research on what the content of the interventions are. We heard from Dr. Bricker about a variety of different treatment approaches and modalities or models that could be used. We need to understand how these work in youth and to understand how the features and functionalities of technology-delivered interventions can promote cessation in this population. Finally, it's not enough to have treatments that work. We also need to understand the real-world implementation and scaling up of these treatments. That means understanding, in real world circumstances, who is using them, how they're using them, and exploring models for integrating digital treatments with existing infrastructure including schools, health systems, and state-managed cessation programs to expand the reach of the treatment. Finally, we need to understand the role of promotion. One of the slides in Dr. Graham's presentation about the cessation ad campaign and the halo effects on prevention was really interesting. I think this is a rich area for further exploration.

Ms. Kathy Gallagher: Now it is time to enter into the second 15-minute discussion period for Committee members and presenters. I'll first turn the floor over to our Committee members to begin the discussion.

PANEL DISCUSSION

Dr. Suchitra Krishnan-Sarin: Those were tremendous presentations. I have been a big fan of what the Truth Initiative has been doing in this area for a long time. I'm very glad to see that they are doing an RCT. I look forward to seeing those results. And, Dr. Bricker, your acceptance commitment therapy results were also very interesting and exciting. Did you mention that there was some work going on with youth with ACT and the digital interventions? If so, I hope it's an RCT, and I'd love to see if ACT works for you. That would be wonderful if we had strong behavioral interventions like that.

Dr. Jonathan Bricker: Thank you for asking. That is something we're preparing to do. We are looking at first conducting the user testing, looking at early results on receptivity to be able to modify the ACT iCanQuit program for youth. We are planning an RCT in the future and I think that it holds a great promise. We have seen from a colleague's work the ACT approaches working among young adults in a pilot research digital intervention. I think that also has a lot of promise.

Dr. Suchitra Krishnan-Sarin: Dr. Graham, I was curious, what about other tobacco product use? Have you been assessing that as well in your intervention? And do you have any findings on that?

Dr. Amanda Graham: We do. My presentation was limited only by space on the slide. We've collected a whole panoply of measures of other combusted use, other vaping behaviors, other substance use. We have a manuscript underway that we will be submitting shortly that characterizes the sample recognizing that that is of interest to people in and of itself rather than trying to jam in a description of our young adult sample in our main outcome paper. So, "Yes" to your question, and hopefully we can get that out quickly.

Dr. Lisa Henriksen: I wanted to make two points. One, I also applaud the new vaccine booster about the retail environment. I wanted to underscore that about 50% of U.S. teens ages 13 to 16 are visiting convenience stores at least once a week. Many of those stores sell e-cigarettes, and any effort to extend the FDA's campaign at the point-of-sale that is currently aimed at adult smokers and their cessation

efforts to teenagers and cessation from tobacco, especially e-cigarettes, would be a very welcome. It is a perfect target channel for this population.

The other point I wanted to underscore is an important remark that Dr. Graham made in her recommendations. As somebody who has served on four scientific advisory boards for the Tobacco Centers of Regulatory Science, I can assure you that IRBs are making very different decisions across institutions as to how to handle research, especially with adolescents. They make different decisions about informed consent and have very different procedures across institutions. This is an obstacle to creating an evidence base that is badly needed. If there is any way to intervene with IRBs to make more consistent recommendations across different institutions on the same protocols, this would be a really welcomed change for science.

Dr. Suchitra Krishnan-Sarin: This comment goes out to all those doing work in this area. I would really encourage all this wonderful work to take into consideration adolescent-specific behavioral traits that we have known for a long time: their involvement in substance use behaviors, risk-taking behaviors like impulsivity and sensation seeking, etc. Also, the need to take into consideration adolescent-specific disorders, like conduct disorders and ADHD, because I strongly feel that we need information like this to move towards a treatment-matching model, if we can. I think keeping that in mind is an important issue as well.

Dr. Jonathan Bricker: Thank you for bringing that up. I think that there are different trajectories of tobacco use that youth follow. There are some children that start very early. Those are the kids that are more likely to have conduct disorder, ADHD, or be higher on measures of poor impulse control. Those kids often start early and then they escalate more quickly, and they become addicted more quickly. Those children are different than kids who start smoking or other tobacco use later, like the end of high school years, where more social influences are more important for them. I think understanding the trajectories of tobacco use in youth is important for how we tailor the interventions, because interventions that are more focused on internal experiences, like how to cope with feelings of impulsivity, would be more central in these kids who are early starters. Not just in tobacco use, but other substance use as well, and other delinquent behaviors, as opposed to more social media influences and peer influence-focused interventions for the children that started later. That is also very different than the youth who started in college or in the military or in other vocational settings when they leave the high school setting and are becoming young adults but still lack the behavioral disinhibition. The prefrontal cortex is not fully developed. For those people, perhaps normative influence and some combination with psychological skills training would be useful. I think understanding those phenotypes are helping us do some treatment matching. That's why I brought up the issue of the just-in-time adaptive interventions. To be able to know what works best for what individual, and in this case, at what time does that work most effectively, using ecological momentary assessment could help in knowing what in that moment is triggering the use in that context. How much is it social? How much is it internal psychological factors? I think these emerging approaches can be helpful, but also social influence approaches have been useful as well. I think taking a more tailored approach is going to hold much more promise. That's why I think digital is so important, because with digital you could do things you could never do in a group intervention or in a school-based tobacco curriculum delivered by teachers. You just couldn't do those things and now you can by having these highly tailored interventions that can use sensors and can look at things and factors in real time to know when to treat the person.

PANEL SESSION #3: SCHOOL- AND COMMUNITY-BASED TREATMENT PROGRAMS

Ms. Kathy Gallagher: Our third and final panel is on school and community-based treatment programs. Our first presenter is Dr. Kimberly Horn. Dr. Horn is a scientist at the Virginia Tech Carilion Fralin Biomedical Research Institute and a professor in the Department of Population Health Sciences at Virginia Tech. Dr. Horn co-developed the Not On Tobacco (N-O-T) teen smoking cessation program.

Kimberly Horn EdD, MSW
Professor, Virginia Tech – Carilion Fralin Biomedical Research Institute,
Virginia Tech University

Dr. Kimberly Horn: Taking a little bit of a different angle, I am going to talk about the importance of place-based factors in understanding adolescent tobacco use and, in particular, cessation outcomes. I will summarize the study where we looked at the application of a place-based model to try to understand the predictors of school-based adolescent cessation outcomes, and the interplay of how personal and place-based factors work together. As was mentioned, I am one of the lead developers of the N-O-T program, so I'll talk a little bit about that as well. The N-O-T program just celebrated its 20th year, which means that I developed a program when I was about 13 (kidding, of course).
The study that I'm going to talk about has been published. If you want to dig a little bit deeper please take a look at the article, *School-level disadvantage and failed cessation treatment among adolescent smokers.*

These are my disclosures. This was funded by an NCI grant. And again, I am a lead developer of the N-O-T program.

Most of the youth who are currently using some form of tobacco want to quit. Unfortunately, few succeed with intentional quitting, and most of them actually fail with those efforts.

One of the things that we don't do often in our studies is look at failure. We don't like to publish and talk about our failed results. Instead, we seem more likely to report on our successes. Anything other than complete abstinence, as has already been addressed today, can be not favored. I think that, yes, it's important to look at factors that lead to success, but it's also really important for us to understand those factors that contribute to failure.

A typical focus on adolescent and individual level data that underscores failure might be perceived as pointing to something innately wrong or lacking in the adolescent's capacity to quit, but we think that an alternative and novel view of looking at failure is really examining the failure. We are not looking at it as a failure of the adolescent, but as a failure on us; our deficiency in providing the right type of treatment and treatment environment to meet that adolescent's needs.

We have done a lot of work. It has been established in some of the presentations we have heard today that adolescent tobacco use is influenced by a range of socio-demographic, biological, and other factors. We have a solid evidence base on that, and we know how some of those individual-level factors influence quitting or not quitting.

We also have done some work on environment. Looking at socio-environmental factors, or external forces, such as kids' schools, places that potentially affect outcomes in cessation or tobacco intervention programs.

If we have done all of this work, why do we still not fully understand why Sarah fails to quit tobacco?

To better understand it, I think it's important that we really start to look more at the critical interplay or the contribution of factors beyond the individual to try to understand in more depth about why kids are struggling with quitting tobacco.

Just imagine if we could understand the specific domains even better, the factors within those domains that explained the reasons for cessation failure. Even more so, if we could identify those factors that were malleable, those things that we could control or change.

Think about it as a puzzle or as pie sections, and that we can make intentional contributions to those sections or domains that lead to the bigger picture of quitting. Then we could make remarkable real progress in the overall targeting and packaging of our tobacco interventions.
We talk a lot about multi-level interventions. I'm not putting anything new on the table here in terms of us believing that when you intervene on a variety of different levels, we can achieve better results, but we've been really slow at implementing those types of interventions. That has been in part because the requisite research hasn't been done. Part of the reason the research has not been done is because we need certain types of data in order to better understand the environment. We also need interventions to test, like N-O-T and others that are scalable. Dr. King and I have had these conversations even as recently as a couple of years ago, about how challenging it is to get the types of data that help us link GeoIDs or place-based information to youth who are enrolled in cessation or other intervention programs.

Through NCI funding, we recently had the opportunity to study place-based factors a bit more precisely and to look at the adolescent proximal environment, in particular schools, to help us better understand how the environment moderated the relationship between an individual, risk-factors, and their cessation failure.

More specifically, we looked at youth who enrolled in the N-O-T program and the extent to which their school environment moderated their cessation outcomes. The study included youth who were enrolled in the N-O-T program across the US. But, at the same time, the study findings bring in a little closer focus to the individual faces of tobacco users who struggle with quitting.

The study included data over the course of several years from the N-O-T program. That was our key data source. We also had some location, rather GeoIDs, for all participants. The youth were enrolled in either the brief or intensive N-O-T treatment; they were moderately addicted daily smokers.

We were fortunate enough to have the GeoIDs that allowed us to take on the socio-spatial approach, allowing us to relate a lot of different data and bring into our models.

The data set includes close to 9,000 adolescents. This was over the course of several years in over 800 schools and from five different states.

We used a series of higher-level multilevel modeling which I won't go into detail here. We looked at "intent to treat" as our primary way of examining the outcomes and a host of predictor variables that were well established in the literature – not only at the individual level but at the school level as well.

There were no surprises at the individual level; we found that being in the low dose, or brief, treatment, having a high nicotine dependence, and having a low self-efficacy for cessation predicted cessation failure. At the school level, there were some things that really jumped out and were related to socio-economic status and low economic resources within the schools. Both independently predicted failure.

When we started to look at interactions, there were some economic factors, such as free school lunch and other factors, that showed how those factors interacted between self-efficacy for cessation, and failure. That was one of the findings that really stood out.

For example, we found that a significant proportion of the variance in cessation outcomes, about 10%, was attributed to the conditions in the school, and that was regardless of the individual's self-efficacy to quit. The relationship between the smoker's propensity to quit and treatment success was weakened among individuals in schools with the higher prevalence of factors associated with economic disadvantage.

The novel finding here is that adolescents in resource-limited school districts are at increased risk of failure despite their individual self-efficacy to quit. I don't want that data to be interpreted to mean that students in poor districts are destined for cessation failure. I think that these data draw attention to the opportunities to minimize the proximal effects of the school environment on individual cessation outcomes through tailoring programs. Some tailoring possibilities have already been discussed today.

The bottom line is, yes, environment matters in our cessation intervention outcomes. Past research would say that adolescent tobacco users with the same motivation, confidence, readiness, and ability to quit would be equally likely to succeed with quitting. But our findings suggest that it is just not true. It's not that simple. Our findings suggest that despite high motivation, there is a need for to shield or bolster the self-efficacy of kids in schools or areas with socioeconomic disadvantages. Programs, particularly when they're school-based, need to consider how we buffer those school factors that put adolescents at increased risk failure, and perhaps we even need to increase the dosage and concentration of cessation offerings in those areas.

I have a few take-home points. Some school factors are more malleable than others; I think that if we could start on those factors that we could have some control over creating environments that are more favorable to cessation success. Findings imply that it is important to advocate for increased funding in low resource, affected school districts, especially those that are at higher risk for health disparities. Funding could be used for issues like teacher workloads and student-teacher ratios, factors we don't automatically associate with poor health outcomes. In considering intervention programs, we need to enhance student teacher relationships as means to improve health behavior efficacy. Tobacco-related programming that offers wrap-around services that we have already talked about today should also be considered.

These are the types of things that are critically important to make sure we foster favorable cessation intervention in schools, specifically. While 10% seems like a relatively small amount in terms of explaining youth cessation outcomes in school-based programs in comparison to the remaining 90% that

we may need to still understand, I think it is a piece of the environmental landscape that can be modified to improve cessation outcomes. This socio-spatial, place-based model shows not only the interactions that occurred at the school level but the factors within schools that were the greatest contributors. This is one example that shows that with the right model and the right data, we can gain new insights into adolescent cessation outcomes. We certainly owe that to our youth.

Ms. Kathy Gallagher: We'd like to welcome Dr. Steve Kelder. Dr. Kelder is a professor at the University of Texas, School of Public Health, Austin Campus, and professor of the Division of Epidemiology, Human Genetics, and Environmental Sciences. He has over 20 years' experience in design and evaluation of child and adolescent research and an emphasis on intervention design for substance use.

Steve Kelder, PhD, MPH
Associate Regional Dean, University of Texas School of Public Health,
Austin Regional Campus and Professor, Division of Epidemiology,
Human Genetics and Environmental Sciences

Dr. Steve Kelder: I'm going to extend this conversation with what Dr. Horn put on the table and in a little bit of what Dr. Bricker did too and think more about innovation and about what's happening in schools. I'll admit most or all my research has been in the prevention realm, but when you start talking to schools about e-cigarette and tobacco prevention, you inevitably start having conversations about cessation. I think schools, in combination with the digital platforms, is an interesting idea to put together. Today's world is very different, and I imagine everyone who is doing research either in schools or with kids, it's a different world than it was nine months ago or so. Which I think—someone mentioned it earlier today—that it presents an opportunity to try to do a better job with a digital education. If you do work in schools you already know that schools are overburdened, underfunded, and many teachers are underpaid. At least in Texas this is happening, but I hear it from other states too. COVID just made it worse. What that means is you need to be innovative and creative with the amount of time you get to present your ideas in a program format at school. Schools are strapped.

I just displayed a logic model for a program that I did a few years ago. Back in 2016, I developed a program called Catch My Breath which was a middle school prevention program. We published a paper earlier in the year in *Public Health Reports*, showing some initial program effectiveness over 16 months. This is the roadmap for our new project in high schools which we have conducted already in several formative settings. This, I think, reinforces what Dr. Bricker and Dr. Horn were talking about. That schools are small communities and that there are communities within communities. Schools have their own set of norms, their teachers, etc., and there are prevailing community norms as well that vary depending on where you live. I really love the paper Dr. Horn presented which picked up on those factors and then looking at the higher-order levels. One thing that we haven't heard is the word "parent" much during today's presentations. I do think that there is a lot of work that can be done with parents. I'm discovering that in my career in working in schools, we have said that it is really hard to reach parents. If you are going into schools, the school personnel will say it is really hard to reach parents, at least a high proportion of them. That is not true anymore either because we now have a digital connection to parents. In some of the schools that I'm working with now in a formative way (I'm just starting an RCT which is on hiatus because of COVID), we are able to get on the consent form the parent's permission to reach them either via text message or e-mail.

We are creating a series of videos which correspond to some of the family systems therapy concepts, about what parents need to know and how to reduce the amount of substance use. It is in the neighborhood of ACT therapy, but it is trying it in video and text form. In the classroom lessons we get peers involved. I have trained the PE teachers, the teachers, and the parents. My view is that hitting on many dimensions in schools will help create that norm, and some of those ideas can spill into the community through the parents that you're trying to reach too. At the upper grade levels in high school, I've prepared some advocacy service projects, because many schools require service to the community, and we train kids to go out and talk.

This slide depicts part of Dr. King's vaccine; I just put more pieces on it. Enforcement or pre-market review, I am pretty sure it would work if we reduce the amount of nicotine in the e-cigarettes. There is a lot of different ideas which are in that category, which I think would dramatically change the landscape, and I only hope, as one of the previous speaker said, we acknowledge the moral imperative of getting with this work and getting the job done. We have been dithering for too long in this area with e-cigarettes and tobacco too. Age of sale and flavor restrictions: these are local community policies which could be enacted. That is part of what I think school-based programs can teach. Especially high school kids – how laws, policies, recommendations are created, so that then they can advocate for the ones that they choose to try and deploy. Of course, taxes, mass media, advertising restrictions, package labeling, and then school and community involvement are all part of the vaccine.

Dr. King covered some of this already. I want to make the point that there are kids who want to quit. There are lots of kids who have made a quit attempt in the past year or who are thinking of quitting. The numbers for those who have 30-day cravings and who use in the 30-minutes after waking, which are indicators of some level of dependence, are also relatively high. The conclusion is that kids who smoke want and try to quit and a subset of those are reasonably highly dependent. So, we need to tailor our programs to set of facts.

Data on high school students from the 2019 National Youth Tobacco Survey shows that a fair number of youths are using tobacco six to 19 days or 20 to 30 days in a month. I think these students could reasonably be considered addicted. The point is there are addicted kids, and when we think about cessation, we have to think about how they are going to handle the withdrawals from their dependence. I think the ACT therapy does that rather well. So, I'm really happy to see the results that Dr. Bricker has been able to achieve with young adults.

There is a website where you can find for all 50 States the regulations about what to do with kids that they catch either smoking e-cigarettes or combustibles. It ranges from doing nothing (I talked to a lot of schools that just don't want to deal with it because they'll stigmatize kids, upset parents, possibly criminalize the kids, etc.) to confiscating the device, have an escalating series of detentions, and/or suspension. I have seen restrictions of extracurricular activities, and I've seen issues of where different sports have different restrictions. For example, football players get detention whereas other less popular sports would get a higher level of restriction or get kicked off the team. I have seen some schools go as far as putting smokers in alternative schools in combination with community service. I have heard of schools that use expulsion. If you're a multiple offender with tobacco you possibly could get expelled. Oftentimes the school police are involved. Many campuses have school police. Many states have state laws. So, if you catch a kid who is smoking, there's a variety of consequences from paying a fine to doing community service, to seeing a court mandated cessation program. I just want to run the gamut of what I've heard that schools are doing. The controversy that I see in schools is the difference

between disciplining kids and offering some sort of treatment and support. That can come in the form of drug counseling. Many school districts will have an internal drug counseling team and intervention often involves as a first step a parent-teacher conference so they can talk together as a family and address what they are going to do about this substance use. Often, there's a referral to a doctor. Sometimes there's a referral to inpatient rehab. I've seen and heard it all with the kids and e-cigarettes, and that's partly because some kids are puffing on it so much, they are nearing a nicotine overdose and having high degree of anxiety and heart palpitations while they're in school. You can see that on the PAVE (Parents Against Vaping) website.

I'm going to end with an idea that I've had that may be worth testing. I was actually going to test this model but then COVID hit. I had a school district near Houston who was willing to try this. Let me just say that we have recruitment issues sometimes. Although, I must say, the Truth Campaign, good on you for getting that many kids so fast. I'm envious of your abilities to be able to do this. Up until now it was said that it's hard to recruit kids. Schools are having a hard time deciding what to do with kids caught using tobacco at school. I just showed you the variety of things that schools implement to address this. At the moment schools are dealing with kids who are caught using tobacco, you could recruit the kid into a study because you're having parents involved anyway. I think we could apply motivational interviewing in a different sort of context. That is to convince the teen who got caught to understand that it's in their benefit to try to quit. A lot of kids just don't want to quit. They're not thinking about quitting; they are very much in pre-contemplation. School counselors could be trained to deliver motivational interviewing. Many schools will have one or more, especially in high school, school counselors who often are the ones that counsel the kids about academic performance and where to go to college, but many may also have an interest in trying to work in programs like this. I've been training school counselors, PE teachers, and nurses in motivational interviewing to try to get teens to try different things. I have not assessed this yet. I've just been in the process of trying these ideas out.

After convincing teens to get into a program, you could go with what we have been talking about – cognitive behavioral theory therapy and mindfulness. Mindfulness as a component of ACT therapy. I've been talking to people who are using mindfulness in many dimensions, not just for substance use but for kids who have had difficulty at school. There's a professor at the University of Houston whom I'm working with who is having an entire school cover mindfulness. He is finding very positive results. Some schools are merging mindfulness in with social-emotional learning. If you haven't been paying attention to what schools are doing, social-emotional learning is a concept has been around for 15 years, but it is catching on now because they are understanding that this can assist with discipline problems, attention difficulty problems, grade improvement, etc. I think it can assist in cessation strategies because kids who are dependent on e-cigarettes are taking hits throughout the day in the classroom, in the bathroom, and outside. We've seen the epi evidence that kids are becoming dual users. They might start with an e-cigarette, which they can puff on all day, and then they might try a regular cigarette. That may lead to use of other substances like marijuana. Mindfulness will get them in a proper mental state to withstand the withdrawals. If they fail at that level, then we can start introducing nicotine replacement therapy. In a small study, I had a physician who was ready to receive the kids from the schools who would then be willing to do the off-label nicotine replacement therapy. You can do many of these things in digital formats; the mindfulness and cognitive behavioral therapy could be done digitally. The nicotine replacement could be prescribed digitally through telemedicine with the physician to make it more seamless and easier on everyone. Schools have a challenge to get things done unless you find a true champion.

The last box of potential treatment strategies would be bupropion after NRT. It is a challenge to prescribe bupropion to kids for cessation. I've talked to a number of different physicians; there have not been studies which support that treatment, but it could be worth researching more. Mindfulness can be thought of as taking the place of the bupropion. That's the way I view the mindfulness and it could be a step in what I think might be a worthwhile sequence of things to attempt.

Going back to the school as the community, if one introduces prevention and gets a lot of kids talking about it, this then gets parents talking and thinking about it, and gets the teaching staff talking and thinking about it, I think that will make an environment that will make kids more likely to engage in cessation. Getting back to the Truth Campaign and some of the other programs, I'm a believer in schools referring kids to these digital resources, so that schools can act as a guide to where they can find credible information. Rather than them finding cessation resources on their own, we can have someone in their life, their parent, school counselor, teacher, PE teacher, or coach telling them that they can go and visit the Truth Campaign.

Ms. Kathy Gallagher: Now it is time to enter into the third 15-minute discussion period for Committee members and presenters. I'll first turn the floor over to our Committee members to begin the discussion.

PANEL DISCUSSION

Dr. David Murray: I want to first thank the presenters today for all the suggestions that they've made about, things that we can do to address this problem. I want to assure you that NIH is very interested in this. Certainly, the Office of Disease Prevention is very interested in this. We monitor and collaborate with the U.S. Preventive Services Task Force closely and watch when they have an insufficient evidence statement. Dr. King's comments early on about the Insufficient evidence statement on adolescent smoking cessation is certainly one that we're familiar with. We are having conversations with colleagues around the NIH campus about what we might do to try to help generate scientific evidence to fill in some of the gaps. Thank you all for your many useful suggestions today.

Dr. Jasjit Ahluwalia: I have a general question as a follow-up to Dr. Dobbin's comments. Someone brought up a bit earlier, the idea and concept of multisite, large clinical trials. This is somewhat of a selfish question, I guess, because I work in this field, but I have always been intrigued that NIH has funded large multimillion dollar trials in diabetes, hypertension, asthma, you name it; these have been in the $50 to $250 million range, and it seems like unless I'm missing something, the maximum that we have had for tobacco is $500,000 a year from an RO1. It gets challenging to look at the more complex issues, like cancer biomarkers or other harmful products and things like that with funding of that level because biomarkers are budget busters. Any comments from NCI or NIDA?

Dr. David Murray: If we look historically, there certainly have been many large and expensive multicenter trials in smoking cessation among adults including COMMIT, ASSIST, and others. NIH has invested large sums in some of those studies, but maybe not in recent youth projects.

Dr. Jasjit Ahluwalia: Fair enough. I guess these studies haven't been recent. David, maybe I'm wrong again. You're bringing up very good points. Those were large trials in the nineties, but maybe not in the last 10 years, 15 years although I could be wrong.

Dr. Wilson Compton: When we're focusing specifically on adolescent treatment, I would ask you Dr. Ahluwalia, what's the most promising approach that deserves a large-scale investment? Are we ready for that?

Dr. Jasjit Ahluwalia: Wow, very good question. I guess I would want to think about it some more. I just saw an announcement today from NCI on Grand Challenges at $25 million each to fund four grants a year, every year, for five years. And one of the nine topics they're focusing on in the Grand Challenges is e-cigarettes, both their harm and their benefit. When I saw that email, I was triggered to think about sort of large trials and was also thinking about someone's comment on this earlier. It is worth thinking about some more. I don't know that I have the perfect answer. But I think specifically about the work I'm doing for these novel nicotine products, when you are including things like inflammatory biomarkers, tumor necrosis factor and when you have to pay for products, including e-cigarettes or others, your budget is going to go way beyond $500,000.

Dr. David Murry: I would not look at the budget as the main barrier. First, we need to decide if we are ready to do a big trial. Nobody here is going to be very excited about a project, big budget or small budget, that proposes a big study if we don't have the preliminary evidence to support doing that particular kind of intervention with that particular population in that setting, and so forth. We need all of that to fall into place. Increasingly there is interest in seeing the evidence that the intervention can affect some of the intermediate outcomes so that we have some promise that it's going to have an effect on the outcomes that we really care about further down the road.

Dr. Kimberly Horn: I think that it seems we've been having this discussion for many years in the adolescent arena and I think that we need to be really clear about what we're defining as successful enough for a large-scale trial. We certainly have a few programs in the field, the N-O-T program being one of them, and I've disclosed my biases there, but there are others that have been around for many years that have a solid evidence base, as would be considered under most standards. I think that we need to decide what is it that we're looking for in order to deem something successful or successful enough to move towards broad scale trials. Trialability, translation, scalability, those sorts of thing. I think this is an incredible group of people to have those discussions with, to start making some of those concrete decisions, or otherwise we're going to end up 10 years from now still having this same conversation.

Mr. Dennis Henigan: I wanted to go back to something that Dr. Kelder emphasized, which is schools taking an exclusively disciplinary approach towards these kids who were caught vaping. It is so regrettable; although, on some level, it is understandable given that these schools were so overwhelmed by this phenomenon that they didn't expect and didn't know how to deal with. We weren't giving them treatment alternatives. It is so regrettable that these kids, first of all, suffer from an addiction that they do not want and, secondly, suffer because their education is being compromised by the disciplinary actions being taken against them. To try and put this in a broader context, what has happened here is that the federal government has allowed a predatory industry to prey on our kids by promoting, through social media and other marketing techniques specifically designed to be effective for adolescents, to encourage their use of products that are highly addictive and highly profitable to the companies that sell them. That is what has happened, and the federal government had the tools to prevent that from happening and did not do it. It is part of the sad story, that the ultimate result is kids being expelled from school because of this activity which was made possible by a failure of our federal

regulators to curb a predatory industry. That's the context in which all of this I think needs to be discussed.

Dr. Suchitra Krishnan-Sarin: Wonderful series of presentations. Having worked with schools for a long time, I know all the nuances and the problems associated with getting into schools. Overall, I think we've heard today that education to parents and teachers is very important especially since this vaping epidemic started. We have repeatedly found that parents and teachers are very ill-informed in terms of what they need to do because they do not know enough about the products. I think educating them about that is the first piece of what needs to happen. Enforcement of rules is very poorly done in schools. I think that is something we can certainly support. Active referrals to programs. I think this is where the questions of interventions come in. But I would really encourage everybody to think about when you're putting things into schools is sustainability. We train all these teachers on how to do these things, and we leave them thinking they have the tools to do it, but schools are so strapped on resources now that, in most cases, it is not sustainable. This work doesn't continue after we provide them with the tools. Thinking about that is important. And in response to an earlier question about whether we are ready to do a large trial, I think the idea of doing a multisite, large scale trial, using a smart design can be picked up on. We have the tools to actually start with simple interventions, like quitlines and education in the beginning for all students, and then it could be ramped up to provide more individualized behavioral interventions like CBT, and then again ramping the intervention up even more to provide medications. That is the way we should be approaching youth cessation. That is the way adult cessation was approached. Why have we not approached youth cessation the same way?

Dr. Lisa Henriksen: Thanks to all our speakers today. I miss the ability to applaud you and your work and your marvelous presentations. Just a comment and a quick question for Dr. Horn. In case anyone thinks that explaining 10% of the variation in any outcome is small. Across 30 cities with different local tobacco policy contexts, the percent of variation at the city level for a 24-hour quit attempt is only 6%. So, 10% across school contexts sounds like a really important opportunity to intervene on and it made me wonder about whether you are looking at the environment that surrounds schools as well. One of the things we know about low income schools is that they are in communities that have a higher density of tobacco retailers and therefore there is much more exposure to the cues in terms of advertising and discounts that encourage tobacco use among youth and make cessation more difficult. I'm just curious if you have that kind of information in the data set.

Dr. Kimberly Horn: Yes, we do. We haven't published that information at this point. That is part of the level two of our reporting. We can actually report on level three data as well. That is how the overall study is set up. We have another level coming in to look at. I'd love to talk with you about that further. We have all sorts of data to be able to relate to this, including the lack of green space and food industry measures as well as a whole host of other variables that we could take a look at. It is the kitchen sink issue though. Your work is incredible, and I'd love to get your advice on how we look at that a little bit more systematically to make sure we are not getting so much noise in there in case we're either missing something over overestimating something.

Ms. Kathy Gallagher: Thank you for that great discussion. We're going to move onto the public comment portion of the meeting. All people who are interested in making an oral public comment were directed to send an email request to the CDC/OSH. Our operator will call on you in the order your request was received. Please remember each speaker will be limited to two minutes and each speaker may only speak once. Operator, please call the first requester.

PUBLIC COMMENTS

Donald Kenkel, PhD, MA, Health Economist, Department of Policy Analysis and Management, Department of Economics, Cornell University: I am a health economist at Cornell University in the Department of Policy Analysis and Management and the Department of Economics.

Youth smokers of combustible tobacco are beginning an addiction that will reduce their life expectancy by 10 years. Although abstinence from tobacco is a public health ideal, harm reduction is an achievable goal. E-cigarettes and other noncombustible tobacco products can play an important role in youth smoking cessation. The National Academy of Sciences' consensus report on e-cigarettes states that there is conclusive evidence that completely substituting e-cigarettes for combustible tobacco cigarettes reduces a user's exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes. The FDA Center for Tobacco Products has authorized the marketing of Snus as reduced risk and heat-not-burn as reduced exposure.

High quality randomized controlled trials have found that e-cigarettes are twice as effective for smoking cessation than nicotine replacement therapy. While the popularity of e-cigarettes among youth and young adults is often viewed with alarm, e-cigarettes are already helping young adult smokers to quit. In data from the 2018 to 2019 Tobacco Use Supplement to the CPS about 40% of young adults who quit, aged 18 to 24, used e-cigarettes when they quit smoking. We always need more research, but the current evidence base supports federal actions that treat e-cigarettes and other non-combusted tobacco products as part of a harm reduction strategy to increase youth smoking cessation.

Ms. Kathy Gallagher: Our next speaker will be Jennifer Folkenroth.

Jennifer Folkenroth, National Senior Director of Tobacco Programs, American Lung Association (ALA): My name is Jennifer Folkenroth. I am the National Senior Director of Tobacco Programs at the ALA. ALA is committed to eliminating tobacco use and tobacco-related disease. Data show that over 30% of high school students report using tobacco products, at least one tobacco product in 2019. It is clear that more must be done to halt the number of youth initiating tobacco use and the ALA is committed to ensuring the full and robust implementation of the Tobacco Control Act, including halting the sale of all flavored tobacco products including mint and menthol. But in the meantime, millions of kids are addicted to tobacco products including e-cigarettes. Proven and effective treatments to help the kids that are addicted to nicotine to quit are urgently needed. The federal government should fund studies on quitting all tobacco products among Black and Brown youth, LGBTQ+ youth, and rural youth including e-cigarettes, cigarettes, cigars, and smokeless tobacco. Our entire community, including government agencies, public health organizations, researchers, teachers, parents, and others must do more to work together. There needs to be more treatments under development, more clinical trials that are sizable enough to extrapolate the results onto the broader population, and more widespread adoption of counseling programs that we know help kids quit.

Medicaid, CHIP, and private insurance should cover these tobacco cessation counseling services for kids. In addition to our policy and advocacy efforts, the ALA also has programs aimed at helping youth quit. Our Not on Tobacco program gives youth ages 14 to 19 a voluntary cessation program designed for teens and their quit journey.

Preventing more kids from starting to use tobacco products must happen but we need to take a look at finding solutions and treatments to help kids who are currently addicted quit for good.

Ms. Kathy Gallagher: Our final speaker during the public comment section is Dr. Rose Marie Robertson.

Rose Marie Robertson, M.D., FAHA, Deputy Chief Science and Medical Officer, American Heart Association: I'm Rose Marie Robertson, Deputy Chief Science and Medical Officer for the American Heart Association. I wanted to highlight our relevant funding activities, but primarily outline suggestions for additional support central to research. We recently invested $17 million in research to fund work that would end nicotine addiction in children and teens. Our awardees are fast-tracking studies on the health effects of nicotine and e-cigarettes in particular in youth. Specific to today, these research teams are also testing current behavioral interventions and developing further technologically innovative ones like virtual reality and gaming to help youth in diverse populations stop vaping. But more funding is needed for:

1. Evaluation of the combination of program content and technology that can best maintain the engagement of youth who want to quit tobacco products. Youth need to help develop this and it needs to be sufficiently powered. Since a single failed quit attempt isn't called failure in adults it shouldn't be counted that way in youth either. This evaluation must be done across diverse populations—those most burdened by use and by health inequities.
2. More work on pharmacologic intervention such as NRT and/or other medications especially in users of high volume, high concentration, nicotine products. Are new alternative NRT products needed?
3. Assessing which cessation approaches work best in the intersection of school and home-based interventions, and the role of influencers and of supportive rather than punitive policies in each setting.
4. New surveillance tracking that is critical to evaluating policies such as Tobacco 21 or flavor bands as well as the impact of cessation interventions. Since the landscape shifts quickly, we encourage the coordination of surveillance efforts and the rapid articulation of their findings and their implications to the public.

Ms. Kathy Gallagher: Thanks to all our members of the public who provided comment. We will now enter into a final discussion period. Let me start by asking my federal colleagues if there is anything that you would like to speak to about a program or anything else.

PANEL DISCUSSION

Dr. Peter Ashley: I would like to propose that researchers consider adopting research on youth cessation and public and other federally assisted housing that has smoke-free tobacco policies. In public housing these policies have been in place for about two years. They target lit tobacco products. Public housing authorities had the option of including e-cigarettes in those policies. Research that has been done has shown that adult smokers have been motivated to quit and to reduce the amount of smoking from these policies. I don't know of any research that has been done with youth. There are about a million people living in public housing and, as you might expect, this includes a higher proportion of ethnic and racial minorities and by definition persons with low income. In addition, quite a few multi-family housing units at HUD have voluntarily adopted smoke-free policies and these present another opportunity for research. I would like to encourage research done in those settings.

Dr. Rosalind King: First I want to speak in praise of Dr. Horn for publishing null findings because I think that is a huge lack in the literature. Dr. Horn and everybody who dares to publish them should be applauded because they're so necessary.

I also wanted to say a few words about the social environment. We heard early on today with the results of the varenicline trial about the influence of parents and peers and the inevitability of the social context in which youth are embedded. They are going to go home to where they live and who they live with and they go to school with who they go to school with.

Starting in the 1990s, NIH and a consortium of federal partners funded a data collection called the National Longitudinal Study of Adolescent Health. The sampling frame was schools. It was a nationally representative set of schools, and so the investigators collected data on students embedded in schools and in neighborhoods, and across numerous outcomes. Findings from the survey showed that among students in resource disadvantaged settings, the student's own individual characteristics, such as resilience or motivation, had less room for expression because of being embedded in these resource deprived contexts. I think that you could generalize this principle to many aspects of the research that was discussed today where kids are motivated, but they just can't achieve those goals because of these interactions. We see a lot of segregation in this country in terms of neighborhoods and schools and segregation of opportunity across levels. I think that is a lot of what you're seeing here as well. Going way back to fiscal year 2011, the NIH had a FOA, a funding opportunity announcement, on the effects of the social environment on health. That effort focused on measurement and methods. There may be some useful tools or lessons that came out of that initiative for furthering this kind of research.

CLOSING REMARKS

Ms. Kathy Gallagher: Thanks to everyone for the excellent presentations and the thoughtful discussions throughout this meeting. We've benefited from a comprehensive summary of the landscape of tobacco product use, including the emerging epidemic of e-cigarette use, nicotine addiction, and an overview of what is known about behavioral and pharmacological cessation treatment for youth.

I want to highlight some of the key points as well as some questions for us to think through for a federal research agenda. We have heard throughout the day that we need to think broadly about youth tobacco cessation. Within the context of clinical trials and other research studies this work is not just focused on one or two tobacco products but encompasses the full span of tobacco products available to youth.

What are issues that we can think through in terms of inclusion criteria for study participants and how we define relapse in this work? How can we improve our understanding of whether and how FDA-approved pharmacological treatments may interact differently in the brains of adolescents versus those of adults? Given the challenges with retention, what are the new and promising strategies that can be employed? How do we maximize the use of technological interventions which have lower barriers for entry and are how youth today communicate? How do we address low motivation to quit tobacco use among youth? What are the influential factors that affect motivation such as peers or family members?

Also, a number of you noted the need to address prevention and cessation in a continuum instead of making an arbitrary distinction between these strategies. Within the context of school- and community-based programs, insightful questions have been raised about looking more closely at surrounding factors that can help us understand why certain cessation interventions may fail and also help us think through the issue from a health equity lens.

And finally, several participants commented about the benefit of identifying new and emerging approaches and modalities, and then thinking through what implementation looks like in a real-world context and how we might be able to take things to scale despite the challenges that have been raised.

I want to reinforce that we know that many youth who use tobacco products are interested in quitting and try to quit each year, which is very promising. Throughout today's discussion, we've heard a number of suggestions and recommendations on research opportunities that can move us forward in a significant and expeditious way. As we bring today's discussion to a close, I want to again thank Dr. Adams, our speakers, Committee members, members of the public who provided comments, and everyone who joined us today.

This meeting of the Interagency Committee on Smoking and Health is adjourned.

CHAIR'S CERTIFICATION

I hereby certify that to the best of my knowledge; the foregoing minutes of the proceedings are accurate and complete.

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Date

VADM Jerome M., Adams, M.D., M.P.H.
U.S. Surgeon General
Chair, Interagency Committee on Smoking and Health