

Good afternoon. I'm Commander Ibad Khan, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call, Evaluating and Supporting Patients Presenting with Cognitive Symptoms Following COVID. All participants joining us today are in listen-only mode. Free continuing education is offered for this webinar. Instructions on how to earn continuing education will be provided at the end of the Call.

In compliance with continuing education requirements, all planners and presenters must disclose all financial relationships in any amount with ineligible companies over the previous 24 months, as well as any use of unlabeled product or products under investigational use.

CDC, our planners, and presenters wish to disclose they have no financial relationships with ineligible companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients with the exception of Dr. Talya Fleming, who would like to disclose that she received a research grant from NuStep and served as co-principal investigator for stroke rehabilitation clinical research trial. All grant funds are received and managed by the hospital organization.

All of the relevant financial relationships listed for this individual have been mitigated. Content will not include any discussion of the unlabeled use of a product or a product under investigational use.

CDC did not accept financial or in-kind support from ineligible companies for this continuing education activity. At the conclusion of today's session, participants will be able to accomplish the following: describe cognitive symptoms associated with post-COVID conditions; determine which clinical assessments and tests are needed for an individual patient with cognitive symptoms; and apply health equity considerations to clinical care, activity management, and reconditioning long COVID patients.

After the presentations, there will be a Q&A session. You may submit questions at any time during today's presentation. To ask a question using Zoom, click the Q&A button at the bottom of your screen. Then type your question in the Q&A box. Please note we receive many more questions than we can answer during our webinars. If you're a patient, please refer your questions to your healthcare provider. If you're a member of the media, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov.

We have introduced self-knowledge checks throughout this presentation. We hope you enjoy these opportunities to assess your understanding of today's session. Please do not type your answers to the self-knowledge checks into the Q&A box, as this may disrupt the Q&A portion at the end of the session.

I would now like to welcome our presenters for today's COCA Call. We're pleased to have with us Dr. Jennifer Cope, who's a medical officer working on the Post-COVID Conditions Team on the Epidemiology Task Force as part of CDC's COVID-19 Response; Dr. Michelle Haddad, who's the Director of Post-COVID Neuropsychology Clinic and the Director of Inpatient Neuropsychology in Departments of Rehabilitation Medicine and Neurology at Emory

University School of Medicine; Dr. Jeffrey S. Fine, who's an associate professor and the Vice Chair of Rusk Rehabilitation in the Department of Rehabilitation Medicine and Department of Medicine at NYU Langone Health; and Dr. Talya K. Fleming, who is an assistant professor and the Medical Director at JFK Johnson Rehabilitation Institute in the Department of Physical Medicine Rehabilitation at Hackensack Meridian Medicine. It is now my pleasure to turn it over to Dr. Cope.

Dr. Cope, please proceed.

Thank you. To begin our discussion, we need to address the variety of terminology currently in use on this topic. The term long COVID is one most used by patients and the general public and is actually the term now being used by the White House in their communications about this topic. CDC uses post-COVID conditions similar to the World Health Organization or WHO. NIH uses the term post-acute sequelae of SARS-CoV-2 infection or PASC.

While there are minor differences in what is meant by each of these terms, they are often used interchangeably. In any discussion of these conditions, it is best to start with a description of what is being covered. I'm sorry. Next slide and now next slide.

Post-COVID conditions refers to the wide range of physical and mental health consequences present four or more weeks after SARS-CoV-2 infection. These conditions occur for patients with severe disease but also for patients who had mild or even asymptomatic acute infection. The patients can be medically complex, and a variety of processes may be occurring. We have been using a general framework shown here on the right for describing these processes, with the understanding that this is likely to change as we learn more and that these groups are also not mutually exclusive.

On the left, you see conditions that occur as a result of any severe illness, hospitalization, or treatment, such as post-intensive care syndrome. On the right are processes that are more specific to infection with SARS-CoV-2, the virus that causes COVID-19. These include system-specific pathology and clinically significant symptoms with unclear pathology. Multiorgan effects following acute SARS-CoV-2 infection include new or newly identified neurologic conditions, renal failure, diabetes, cardiovascular damage, and skin conditions. Symptoms with an unclear pathology involve a range of problems that can last for months after first being infected with SARS-CoV-2 or can even first appear weeks after the acute phase of infection has resolved. This unexplained group has features similar to myalgic encephalomyelitis chronic fatigue syndrome, or ME/CFS dysautonomia; postural orthostatic tachycardia syndrome, or POTS; and other postinfectious syndromes. Next slide.

There are a number of challenges in research and surveillance of post-COVID conditions. As noted in previous slides, there's a wide range of symptoms, effects, and spectrum of severity. A wide variety of new conditions may be identified, whether from worsening of an underlying condition or a direct effect. Studies have varied in the symptoms and conditions that are considered in methods for evaluating them and the time after acute illness that is used for data collection. Studies to date include different patient populations, some focusing only on hospitalized patients, others on outpatients, and others in some both.

Many of these studies do not include control groups, making attribution to SARS-CoV-2 infection difficult in preventing an estimate of risk of post-COVID conditions. And, importantly, few studies include measures on the severity and impact of symptoms on quality of life or day-to-day activities for people. Next slide.

Given the wildly different -- widely different study designs used in patient populations included, there's a wide range and estimates for the prevalence of post-COVID conditions that have been identified using self-report or based on what's available in the electronic medical record. Based on self-report using a mobile app, 13% of over 4000 people with incident cases of COVID-19 followed prospectively in the United Kingdom reported ongoing symptoms more than one month after COVID-19; and over 2% reported ongoing symptoms three months or more after COVID-19.

Using electronic health data, even among adults who are not hospitalized with COVID, over 7% have one or more of 10 common post-COVID conditions. Severity of acute COVID illness is associated with occurrence of at least one symptom at six months. Among a VA population, the burden of post-COVID conditions increased from 44 per 1000 non-hospitalized patients to 217 per 1000 hospitalized patients, and over 360 per 1000 for ICU patients. Next slide. The duration of post-COVID conditions can vary and is still unknown.

Most patients appear to recover from acute illness within four weeks. And this is the reason CDC considers illness persisting beyond four weeks as warranting at least an initial clinical evaluation and supportive care. However, as highlighted in the figure from the UK Coronavirus Infection Survey, the proportion reporting ongoing symptoms continues to decrease from 4 to 12 weeks. Improvement slows around 12 weeks after infection. This slowed recovery after the 12-week point is the reason the World Health Organization uses persistence beyond 12 weeks to define post-COVID conditions. Next slide.

Factors associated with an increased occurrence of post-COVID conditions are just now being identified. As noted earlier, severity of initial infection is associated with increased occurrence of persistent symptoms. A higher proportion of females than males report post-COVID conditions. Preexisting medical conditions that are often risk factors for severe COVID are associated with increased occurrence of post-COVID conditions.

Age is a factor as well. Adults are more likely to experience post-COVID conditions than children, and among adults older -- older age is associated with increased post-COVID conditions. Finally, unvaccinated persons who get COVID have an increased occurrence of post-COVID conditions. The known drivers of increased susceptibility to severe COVID-19, which are illustrated on the figure in this slide, will likely extend to the higher risk for post-COVID conditions. Related to this is the fact that many of these groups also experienced more challenges and difficulties in accessing care. Therefore, health disparities associated with acute COVID-19 illness will likely persist with post-COVID conditions. Next slide.

Another factor to consider with regards to risk for post-COVID conditions is vaccination. Vaccines are effective against post-COVID conditions by protecting against initial infection

from SARS-CoV-2. In some initial studies, while post-COVID conditions do occur among those who are infected after vaccination, the frequency appears to be lower.

In addition to the data shown on this slide, a new review by the UK Health Security Agency shows that people who have had one or more doses of a COVID-19 vaccine are less likely to develop post-COVID conditions than those who remain unvaccinated. Next slide. We do have evidence of disability associated with post-COVID conditions. And for those who may not have heard, under the Americans with Disabilities Act, long COVID is recognized as a physical or mental impairment that can substantially limit one or more major life activities. However, an individual assessment of whether long COVID does substantially limit a major activity is required when determining disability.

The extent of associated disability is still unknown, but one study from China found 12% of patients did not return to their original work by 12 months. Further, this analysis excluded 62% of COVID patients who are retired or not employed before infection. Given the size of this pandemic, even 1% associated disability at one year will have a significant societal impact. Next slide.

At this point, we'll stop here for a quick Knowledge Check.

The question is, What factors are associated with an increased occurrence of post-COVID conditions: A, female sex; B, younger age; C, severity of initial infection; D, both A and C; or E, all of the above. Next slide.

The answer is D. Both female sex and severity of initial infection, along with older age, preexisting conditions, and infection without prior vaccination are associated with increased occurrence of post-COVID conditions. One thing to note about severity of initial infection is the observation that many people with post-COVID conditions had mild or even asymptomatic infections. Because the majority of COVID cases are mild, by extension, most patients with post-COVID conditions will be in those who had mild acute illness, even though those with severe acute illness are more at risk to develop post-COVID conditions. Next slide.

Finally, while we're still learning about post-COVID conditions, there are a few takeaways. First is the importance of the s on post-COVID conditions. The post-COVID clinical outcomes are complex and are not one entity.

This makes simple case definitions impractical and presents challenges for standard disease surveillance methods. In addition, the clinical complexity precludes detailed and specific clinical guidance. Studies characterizing the different phenotypes, risk factors, and biomarkers are needed. Second, due to the long duration of illness, post-COVID conditions will remain a public health concern long after the acute phase of the pandemic has ended. Increasing clinical capacity to meet the needs of patients with chronic illness following COVID will be needed.

And this needs to be done with a focus on assuring equity and access to care. Follow-up times will be measured in years, not weeks or months. Finally, it's clear that the patient advocacy community has concerns about how the government and healthcare systems are meeting their

needs. Improved collaboration is necessary to provide better integration of the range of services that are needed. Next slide.

At this point, after reviewing post-COVID conditions broadly, I'd like to focus us in on today's topic. As previously mentioned, post-COVID conditions are heterogeneous and can present with a wide array of symptoms. Today we will be focusing in on cognitive symptoms. Along with fatigue and shortness of breath, cognitive symptoms are frequently reported by patients experiencing post-COVID conditions.

Those symptoms are often reported as brain fog by patients. Specifically, brain fog might mean difficulty thinking clearly or concentrating, forgetfulness, and memory loss. These symptoms can be debilitating in some people. Cognitive symptoms are frequently reported in post-COVID studies of both hospitalized and non-hospitalized patients. In one study among a large Norwegian cohort, 18% of those who were moderately to severely ill with COVID-19, including those who had been hospitalized, reported cognitive symptoms, compared with 9% who were mildly ill during their acute COVID illness. As the scientific evidence continues to build on post-COVID conditions, some studies have focused specifically on cognitive symptoms.

In a prospective multicenter longitudinal cohort study of 81 COVID-19 survivors, 25% reported cognitive symptoms at one year of follow-up. This study also used a standardized battery of tests that showed objective cognitive deficits in 18% at one year. And, finally, a UK study that used an online series of cognitive tasks found evidence of cognitive deficits among those who had had COVID-19 compared with general public controls, who reported never having COVID. At this point, I will turn it over to Dr. Michelle Haddad, who will share her experience working with long COVID patients with cognitive symptoms.

All right. Thank you, Dr. Cope. Like Dr. Cope mentioned, I have been working in a post-COVID neuropsychology clinic for about the past year, a little over a year now. And I'm going to share a sample of what I have learned from doing that.

So to just kind of set the stage, the data that are presented here are from 50 patients seen in 2021 in my clinic at Emory University. This data is not yet published but is in the process of being published. The sample mean age is 49 years plus or minus a standard deviation of 12. It's predominantly female by a factor of about 4 to 1. And it's approximately split between people of color and people who are white. A couple of important caveats, on average, patients in the sample have at least a college education.

And it's important to note that this is both a care-seeking sample and one that has been referred to me through a prior specialty clinic. So they were seen at the Emory post-COVID main clinic and then referred on to me as a tertiary referral. So, you know, they have more access to healthcare than perhaps the general population. So it's just kind of important to keep that in mind as a limitation. Next slide.

All right. So like Dr. Cope mentioned, when we think about possible impact of COVID-19 on the brain, we think about both direct impacts and indirect impacts. And these are just a few of the things that have been proposed in terms of mechanisms for cognitive symptoms, and we're still

very much in the process of learning about this etiology. So direct impacts that you see on the left includes direct viral invasion, cerebrovascular accident, hypoxia, inflammation, or alteration or reduction in neurotransmission. And indirect impacts include organ or metabolic dysfunction, hypotension, glucose dysregulation, and nutritional deficiency. And all of those things can give rise to cognitive symptoms. Next slide.

But I think it's important to note that the prevalence of self-reported brain fog in patients with post-COVID conditions, at least in my clinic, does not correlate with hospitalization treatment or acute severity of COVID-19 illness as measured by ventilation status. So looking at what these pie charts are showing is the breakdown of patients seeking care in my clinic by severity of illness. So mild here means no hospital admission. Moderate means admitted but not intubated, and severe means that mechanical ventilation was needed. So the main point of this slide is that the percentages of patients with post-COVID conditions reporting subjective cognitive problems overall mirrors the severity of COVID in the general population.

So it's definitely possible, as Dr. Cope mentioned, that people who had severe initial illness certainly could have a higher risk of cognitive symptoms. But I think it's important to note that it's not just confined to people who had a severe or moderate acute course. We have a large proportion of people who have had mild or even asymptomatic acute illness who develop post-COVID cognitive symptoms. Next slide.

All right. Among patients with post-COVID conditions who self-report brain fog, the most common subjective impairments they report are in memory by far; also in attention, in cognitive fluency, and in executive functioning. Next slide.

So, in terms of attention, this is actually the most common objective impairment that I find on testing. So whereas patients most commonly report that they feel like they're having problems with their memory, in terms of objective deficits, it's actually the most common that I see attention impairment.

Again, at least in my clinic sample. Many patients with post-COVID conditions have difficulty with sustained attention, particularly when there's also a speed component. They also have problems with working memory. So that's the ability to hold information in one's mind and manipulate or work with it. And I think it's important to note that, even though it has memory in the name, working memory is actually a piece of attention, not memory.

It's important to remember that attention is important for all other cognitive functions. So, you know, first we need to be able to fully process information and engage with our environment and the situation in order to really accurately be able to respond to anything else. So if there are sort of holes or gaps in our attention, then there are going to be gaps in our learning, our memory, our reasoning, all of the above. Patients with attention problems will often describe them as memory problems. It feels like functional memory difficulty such as losing track of tasks, losing their train of thought, or missing steps in a routine.

But, in fact, these functional difficulties are actually caused by attention deficits. And, as you can see what this pie chart is showing you and you're going to see them on the next several slides as

well with the different domains represented, this is a breakdown of the objective cognitive deficits seen in my clinic. And in terms of the descriptive labels for levels of impairment, that's based on Z scores or standard deviations below the mean. So that borderline category is minus .6 to minus .9 standard deviations below the mean. It's not quite in the clinically impaired range, but I included it because people still notice it functionally. Mild is minus 1 standard deviation, moderate minus 2, and severe minus 3. Next slide. All right.

So the next most common objective impairment that I see is in cognitive fluency. So we might be a little bit less familiar with this term. This is the ability to efficiently generate and articulate novel thoughts. So you can kind of think about it as the efficiency of overall thinking. Many patients with post-COVID conditions have diminished speed and efficiency of thinking.

Functionally, that presents as feeling slow or confused, taking longer to complete familiar tasks, and struggling to find the right words or feeling like they're saying a wrong word so that kind of tip of the tongue phenomenon. Next slide.

And then, finally, we get to learning and memory. So the interesting thing here is you might recall that over 90% of my patients come in telling me that they feel like they are having problems with memory. But it's actually only the third most common difficulty that I see on objective impairment.

Now, that being said, these things often go together. So it's important to remember that attention is the first part of learning and memory. So patients with impaired attention will very likely also have impaired encoding of new information. The analogy that I like to use with my patients is, for example, if you're trying to record something on television and your cable is going in and out during the recording, then when you go to play back the program, you're going to have gaps in it. So that's analogous to trying to remember information that you learned with a deficit in your attention.

So that poor encoding leads to transferring too little information into your long-term memory. But that's different from forgetting information that you did initially encode. And it's important to make that differentiation between encoding problems versus retention problems because the management strategies are very different. Next slide.

So what this slide is showing in these figures is that some individuals with post-COVID conditions have significant difficulty learning new information.

So, on the left, you can see that in some cases as low as 20% of information being presented over multiple trials is learned by these patients. However, most of these patients you can see on the right do comparatively better at retaining what they initially learned. Sometimes they even recall more after some time has passed than after the initial learning trials. Like I mentioned on the prior slide, this is important because it changes management strategies. So in these cases, we need to work with people on compensatory strategies for attention and learning rather than for retention and recall. Next slide.

And then, finally, we get to executive functioning. So for most patients with attention problems, a further consequence of this is difficulty with planning, organization, and problem solving. So if one can't pay attention to all relevant details, it's difficult to adequately plan, prioritize, and so on. If you're constantly losing track of what you're doing, you can't exactly function well in a situation that's complex or requires you to kind of figure out a lot of new situations.

In a smaller proportion of patients, I do see also difficulty with strategy generation and problem solving specifically, but that is a much smaller percentage compared to patients who have difficulty with attention and fluency. Patients will usually describe executive function difficulty as difficulty with making decisions, or often others may identify it as errors in their judgment. So, for example, a supervisor at work might point out mistakes in judgment or say that they're making poor decisions. Next slide.

So, so far, I've only mentioned cognitive symptoms. But it's important to take a minute to think about adjustment related mood symptoms, as well, because they are extremely prevalent in patients seeking care for post-COVID conditions. So when asked about mood disturbance specifically around their symptoms, and their current condition, over 80% of my patients report anxiety, and almost 70% report depression. So it's important to note that this is new onset emotional distress, and it's specifically about their changes in health and their changes in function. I do want to take a second to note here, emotional reactions to that type of a stressor can be perfectly appropriate. You know, this is a really extraordinary situation that we as a society are living through and that these patients specifically are living through.

It doesn't have to be disproportionate or anything like that. But that impact emotionally can still have significant consequences on functioning, so it's worth paying attention to. Next slide. Mood disorders are also associated with deficits in attention, fluency, learning and memory, and executive function. So people with primary mood disorders can have difficulty in all of those areas.

So there is some overlap. However, we don't think that psychological symptoms account for all post-COVID cognitive symptoms or even most of them. It seems to be two distinct entities. However, these adjustment-related emotional symptoms can definitely worsen functioning. So something that I see commonly is a vicious cycle of catastrophic thinking in my patients.

So they'll make a mistake, then it's kind of down the rabbit hole of negative thoughts like my brain is broken, I'm such idiot, I'll never be the same again, I'm never going to get better. Those catastrophic thoughts distract them more, they make more mistakes, and so on. And so in this cycle it's also really easy to discount any time that you're doing well and really only pay attention to that cycle of catastrophic thinking and mistakes. So it's really important to help patients recognize and break that cycle. Next slide.

And, to wrap up my portion here, it's important to keep in mind that neuropsychological data aren't everything. I know that's a little bit counterintuitive as I'm a neuropsychologist. But I think it's important to recognize that neuropsych assessment usually occurs under ideal circumstances, so you're in a lab or a clinic setting. You know, things are hopefully quiet. They're very structured.

We try to get patients when they're feeling their best. These formal evaluations are intended to capture maximal cognitive ability under ideal circumstances. But of course, most daily activities don't occur under ideal conditions. So if you have a patient who's doing relatively well on formal evaluation, you still need to consider how that function may decrease during daily activities, you know, when things are more distracting, especially if they have physical or mood symptoms that wax and wane. Functional performance may differ quite a bit from performance on a formal evaluation, and that's something that we as providers need to be sensitive to. Next slide.

Finally, I have my Self-Knowledge Check.

So the post-COVID symptom commonly referred to as brain fog may be comprised of A, post viral fatigue; B, objective cognitive deficits; C, mood disturbance; or, D, all of the above. Next slide.

All right. So the correct answer here is D, all of the above. And, like I mentioned, the reason for that is because our ability to perform our daily activities is impacted by that complex combination of physical, emotional, and cognitive factors, all of which may be affected in post-COVID conditions.

And, on that note, I'm going to pass this along to Drs. Fine and Fleming.

Okay. Thank you very much, Dr. Haddad. And thank you for inviting us here today to present our work. I'm Dr. Jeffrey Fine. I'm a Physical Medicine and Rehabilitation physician from Rusk Rehabilitation at the New York University Grossman School of Medicine.

I had the unique experience as working as an acute care COVID physician when our rehab unit became a medicine COVID unit for the month of April 2022 and then reopening our rehab unit, primarily servicing patients with catastrophic disease following the COVID infection. We treated over 120 patients on our rehab unit post April 2020. Today, we will be sharing insights from the American Academy of Physical Medicine and Rehab, Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Cognitive Symptoms in Patients with Post Acute Sequelae of SARS-CoV-2, hereafter referred to with the acronym of PASC. That's the endorsed, NIH-endorsed term, otherwise known as long COVID. This guidance statement has a specific focus on the cognitive-related symptoms of PASC that can occur in people who have been diagnosed with acute COVID-19 infection or those presumed to have had the infection.

This scope includes patients with severe symptoms that required hospital acute care, as well as the many patients with mild to moderate symptoms that were managed in non-hospitalized community settings. Next slide.

This consensus guidance statement is one in a series extending across the breadth of the most prevalent PASC sequelae. Published and in-process guidance statements from this collaborative include the assessment and management of PASC-associated fatigue, breathing and respiratory disorders, cardiovascular complications, autonomic dysfunction, mental health manifestations, pediatric conditions, and neurologic sequelae. These statements are intended to provide

consensus-driven practice guidance to clinicians in the assessment and treatment of individuals presenting with often heterogeneous PASC symptomology. Next slide.

The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the CDC. Next slide.

At the time of this report, worldwide tracking from the Johns Hopkins COVID-19 dashboard reveals that over 515 million people have contracted the virus since 2019. Over 6.2 million people worldwide have died from COVID-19, and we're currently approaching that threshold of 1 million deaths in the United States alone. This yields an estimate of approximately 510 million worldwide COVID survivors. The absolute percentage of individuals who have completely recovered remains evasive.

Current literature suggests that approximately 30% of patients surviving COVID-19 infection will develop the symptoms of PASC, creating a probable downstream pandemic of PASC-related functional disability, impacting over 125 million people worldwide. Hence, the importance of this AAPM&R PASC rehabilitation consensus work. Next slide.

Our learning objectives, so these are partially covered by Dr. Khan. For this section will be to apply the PASC consensus guidance statements into everyday practice, identify and diagnose cognitive symptoms and individuals with PASC, utilize the PASC assessment and treatment recommendations, differentiate and apply appropriate PASC-related cognitive symptom treatments, identify health equity considerations for this population, and summarize the future directions for assessing and treating PASC-related conditions. Please note these consensus guidance statements are intended to reflect current best practices in patient management, testing, and treatment. They should not preclude clinical judgment and must be applied in the context of the specific patient with adjustments for patient preferences, comorbidities, and other factors. Next slide. The consensus methodology, the AAPM&R Collaborative that now includes 35 PASC clinics across the country is following an iterative developmental approach to achieve consensus on assessment and treatment recommendations for PASC symptoms.

The PASC Collaborative sought input from patient representatives with a history of PASC and from patient-led research initiatives to inform these recommendations. As guidance statements are released, education will be provided on a rolling basis. Next slide.

Prominent neurological and behavioral symptoms have been reported in the growing PASC literature. Common neurological and neuropsychiatric symptoms in individuals with PASC include fatigue, myalgia, headaches, sleep disturbance, anxiety, depression, dizziness, anosmia, dysgeusia, and cognitive symptoms often subjectively characterized as a brain fog.

It is important for clinicians to recognize that disease severity may not be a predictor of PASC symptoms, as many patients presenting to outpatient COVID Recovery Centers experienced only mild initial SARS-CoV-2 infection. As referenced by Dr. Haddad, primary cognitive symptoms had been further characterized as a dysexecutive syndrome and include deficits and attention, reasoning, problem solving, spatial planning, working memory, and difficulty with word retrieval. The incidence of post-COVID cognitive symptoms has been estimated anywhere from

20 to 40% of patients. The assessment and treatment of cognitive symptoms in patients with PASC is the focus of this review. Next slide.

So, from the collaborative, these are our cognitive system -- cognitive symptom assessment recommendations. Patients should be screened for signs of cognitive symptoms using validated tools and instruments. Patients should be evaluated for conditions that may exacerbate cognitive symptoms and warrant further testing. Patients should have a thorough neurological examination to identify focal neurologic deficits.

Initial lab workup if not already completed should include a complete blood cell count; a comprehensive metabolic panel; B vitamins, including B12; thiamine; folate; 25 hydroxy vitamin D, a correction to that slide; liver function tests; and thyroid function tests. And for many of the participants today, you may recognize that as a very typical workup for the metabolic conditions that may contribute to reversible cognitive impairments. A clinician should conduct a full patient history with reviewing preexisting conditions and a comprehensive medication and supplemental review to identify those that may contribute to cognitive symptoms. Patients finally should assess the impact of cognitive symptoms using standardized patient reported assessments. It's important for clinicians to recognize individual patients symptom timelines vary widely.

It is possible that initiating treatment earlier will result in earlier resolution of symptoms. The absolute duration of PASC-related cognitive symptoms should not dictate the management approach. Next slide.

Patients should be screened for signs of cognitive symptoms using validated tools and instruments. The standardized general cognitive screening assessments form the foundation for the initial cognitive assessment.

Commonly used instruments include the Montreal Cognitive Assessment, MoCA; the Mini-Mental Status Examination; the St. Louis Missouri Mental Status Exam, the SLUMS: The Mini-Cog; and the Short Test of Mental Status. The attributes of these screening instruments are further defined in the consensus guidance manuscript and can be administered by a variety of clinical professionals including primary care. It should be noted that cognitive screening measures are not a substitute for more in-depth cognitive testing for selected patients, and the solitary finding of abnormal scoring on cognitive screening measures does not implicate a formal cognitive disorder. Because of the varying presentations of PASC and often a constellation of overlapping syndromes, consideration of additional studies and referral options for common manifestations is warranted. Next slide.

This table describes other potential overlapping diagnostic categories and common findings related to PASC cognitive symptoms, including referral options to consider. These symptoms screenings, initial workup, assessment tools and referral recommendations are more thoroughly defined in the consensus guidance manuscript. For each of the categories, nuance and neurologic symptoms such as persistent headache, focal or generalized weakness, numbness, abnormal cognitive screening, cognitive dysfunction, and ataxia warrant further testing and/or referral to neurology or brain injury physiatry. Endocrine symptoms such as irregular menstrual cycles,

poor diabetic control, excessive thirst or urination warrant further testing and/or referral to endocrinology.

Autoimmune symptoms such as rash, joint, and muscle pain, joint stiffness, Raynaud's phenomenon warrant further testing and referral to rheumatology. Mood disorder symptoms such as anxiety, depression, fatigue, mood swings, irritability, changes in memory or recall, warrant further testing and referral to either psychiatry, psychology, or neuropsychology, depending on the resources in your community. Sleep disorders such as difficult sleep initiation, waking frequently, early awakening, nonrestorative sleep, and daytime fatigue warrant further testing and possibly referral to pulmonology or sleep medicine. Next slide.

Individuals experiencing PASC may present with a broad constellation of cognitive and neurobehavioral symptoms, including reduced attention; diminished processing speed; and word finding deficits, as outlined by Dr. Haddad.

These findings are quantified on objective testing that are typically done by neuropsychology. A recent study here in New York City of 740 patients, patients presenting to a PASC clinic quantified cognitive deficits in memory encoding and recall from 23 to 24%; processing speed deficits of about 18%; executive functioning deficits, 16%; and language fluency, 15 to 20%. A battery of cognitive tasks that measure performance in domains administered by licensed psychologists may include assessments of complex attention; processing speed; executive functioning; memory and learning; numeric reasoning; motor function; language, including word finding and fluency; visual spatial assessments; and social cognition. Next slide.

I will now pass the baton to Dr. Fleming who will present the PASC cognitive treatment recommendations and health equity considerations.

Thank you very much, Dr. Fine. Good afternoon, everyone. My name is Dr. Talya Fleming, and I'm a Physical Medicine and Rehabilitation physician at JFK Johnson Rehabilitation Institute at Hackensack Meridian Health in central New Jersey.

Today I will be discussing the treatment recommendations and health equity considerations for cognitive impairment in post-COVID syndrome. We have already reviewed the assessment recommendations. As mentioned earlier, it is important for clinicians to recognize individual patients symptom timelines will vary widely, and the duration of PASC-related cognitive symptoms should not dictate management approach. Alternatively, individual symptom and clinical presentation, preexisting and COVID-19 exacerbated comorbidities, as well as changes in function and quality of life, should guide an identification and intervention approach. The following are PASC cognitive treatment recommendations established by the PASC Collaborative.

Number one, for patients who screen positive for cognitive symptoms, refer to a specialist with expertise in formal cognitive assessment and remediation.

Number two, treat in collaboration with appropriate specialists underlying medical conditions that may be contributing to cognitive symptoms.

Number three, in collaboration with a primary care provider, reduce medication polypharmacy and wean or de-prescribe medications if medically feasible, with an emphasis on medications that may impact cognition. Next slide, please.

Number four, reinforce sleep hygiene techniques, including nonpharmacologic approaches as first line of sleep remediation.

And, number five, similar to patients experiencing physical fatigue, patients should be advised to begin an individualized and structured titrated return-to-activity program. Based on brain injury research, cognitive rehabilitation is an effective treatment for cognitive symptoms and should be tailored to the individual patient. A rehabilitation team approach for patients with cognitive issues and fatigue can be considered with pacing and energy conservation strategies such as dividing up a longer task into small increments with judicious breaks. For memory and organization issues, application of established techniques used for patients with concussion or traumatic brain injury include taking notes, using a planner or phone app to record information, and setting electronic reminders. Other tactics include reducing screen time, proper sleep maintenance, managing stress, and increasing physical activity as tolerated without causing overexertion. Next slide, please.

In addition to physical function, sleep is an important component of restoring and maintaining cognitive function. Listed are several interventions to help improve sleep. Establish the opportunity for 7 to 8 hours of sleep duration per night; behavioral and nonpharmacological interventions; behavioral sleep hygiene strategies; treating potential sleep apnea; nutritional supplements; and referral to sleep specialists. Should conservative interventions produce incomplete effects, then pharmacological interventions may be indicated. Next slide, please.

The American Geriatric Society Beers criteria was initially created as a list of potentially inappropriate medications for use in adults aged 65 years and older. This guidance on medication effectiveness and safety management may be extrapolated to help patients with PASC of all ages by assessing the potential detrimental impact of prescribed medications on cognitive function. The Beers criteria identified medications in the following classes that have been shown to have depressed central nervous system effects such as sedation, confusion, and possible cognitive decline. They are anticholinergics; selected antidepressants; antipsychotics, both conventional and atypical; benzodiazepines; as well as nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; and, lastly, skeletal muscle relaxants. These criteria should not be used in isolation to supersede clinical judgment in individualized patient care. Next slide, please.

Regarding behavioral health and resilience, patients with PASC should be encouraged to maintain social engagement and rely on support systems during this challenging period, which may include patient advocacy groups. Life stressors, such as social distancing, lifestyle modifications, and coping with ill family members and peers, as well as new or worsening mental health conditions can also negatively affect cognitive function and need to be adequately assessed. Next slide, please.

In the context of PASC, clinicians are encouraged to consider the integration of health equity, health disparities, and social determinants of health with the evaluation and treatment of

individuals with PASC cognitive symptoms. The Collaborative developed several health equity considerations and examples in PASC-related cognitive impairment. The list is not intended to be comprehensive but, rather, to provide clinical examples as they relate to health equity. The literature demonstrates that many marginalized groups face socioeconomic and access to care barriers, though these may or may not be barriers for a specific individual patient. It is also important to recognize that individuals with intersectional identities, for example, those who identify with more than one underrepresented group, often face higher levels of bias and discrimination.

The categories explored for the cognitive impairment group include racial and ethnic minority groups, biological sex, gender, age, environmental exposure, disability, religion, and immigration. Next slide, please.

The following is an excerpt from our table included in the appendix of our manuscript providing additional information for clinicians who are treating patients with PASC-related cognitive impairment. The category in this example is racial and ethnic minority groups, specifically as defined by the United States Census Bureau. Communities of color have been especially impacted by the global pandemic.

As a result, these groups have worse outcomes after COVID-19 infection, including hospitalizations, morbidity, and mortality. Both testing and treatment of cognitive function may be biased or inaccurate for people who identify with certain racial and ethnic groups or other socially and historically underrepresented groups because of a variety of issues such as not having English as a primary language, not properly accounting for variations in dialect or education level, and stereotype threat. Stereotype threat refers to an important psychological phenomenon in which concern of following negative stereotypes about one's group impairs task performance. Clinicians administering cognitive testing that may elicit stereotype threat should be aware of factors that may affect test scores and clinical recommendations. Next slide.

A second example from our health equity table includes the category of age, with older individuals having among the highest rates of COVID-19 infection. In addition to PASC-related cognitive impairment, older individuals are at higher risk for preexisting cognitive conditions, such as Alzheimer's disease, stroke, and Parkinson's disease. Age-related disabilities such as impaired vision or hearing may also affect cognitive testing. As such, cognitive testing should be conducted by clinicians experienced in working with older individuals. In all age groups, mental health conditions and substance abuse have increased during the pandemic and may additionally contribute to cognitive dysfunction. Next slide, please.

This is an example of how Diversity, Equity, and Inclusion content is integrated into the main text of the Cognitive Impairment Consensus Guidance Statement. This portion is extracted from the manuscript. This section summarizes that older individuals with both direct and indirect cognitive-related issues should be evaluated for cognitive impairment; worsening medical conditions such as cancer or quickly progressing and time-dependent diseases; as well as degenerative conditions, were also noted to be a concern of older individuals who may not have received the routine care they needed during the pandemic. Medications such as benzodiazepines

or antihistamines should be prescribed judiciously, as they may affect cognition, particularly in older patients. Next slide, please.

In conclusion, the goal of this PASC Collaborative guidance statement was to create a coordinated and systematic approach to the evaluation and treatment of patients presenting with PASC-related cognitive symptoms. It is important to recognize the emerging knowledge and recognition of cognitive symptoms as a significant outcome of COVID-19. The AAPM&R Multidisciplinary PASC Collaborative recognizes that patients with PASC typically present with a cluster of symptoms that cross multiple body systems, and our focus in this statement only touches the surface of emerging evidence. Next slide, please.

The duration and recovery trajectories of PASC-related impairments have yet to be characterized, and some post-COVID patients may experience long-term disabilities. Beyond cognitive symptoms, case studies provide evidence that patients with COVID-19 can develop a range of neurological complications, including those arising from stroke, headache, encephalopathies, and neuropathies. Future PASC Collaborative Consensus Guidance Statements will further examine and offer guidance on mental health and neurological symptoms in patients with PASC. Next slide. Tables from this manuscript can be downloaded using the websites listed on the slides from the AAPM&R website at aapmr.org/longcovid and from the CDC website at cdc.gov/coronavirus/2019. Next slide, please.

We have come to our first Self-Knowledge Check question.

Common cognitive symptoms in patients with PASC may include subjective or objective deficits in, A, reasoning and problem solving; B, attention and working memory; C, spatial planning and word retrieval; D, A and B only; or, E, all of the above. Next slide.

The correct answer is E, all of the above. Patients with PASC may experience a subjective brain fog that has been characterized as a dysexecutive syndrome. Primary cognitive symptoms in PASC include deficits in reasoning, problem solving, spatial planning, working memory, difficulty with word retrieval, and poor attention. Next slide.

Self-Knowledge Check question 2: Cognitive screening assessments include all of the following except, A, Montreal Cognitive Assessment; B, Mini-Mental State Examination; C, St. Louis University Mental Status Examination; or, D, Wechsler Adult Intelligence Scale. Next slide.

The correct answer is D, Wechsler Adult Intelligence Scale. Commonly used cognitive screening instruments include the MoCA, MMSE, SLUMS, Mini-Cog, and STMS.

In contrast, The WAIS is used for assessment of intelligence and cognitive abilities but is not a screening examination. Next slide.

This concludes this portion of our presentation from the American Academy of Physical Medicine and Rehabilitation. We thank you for your time and attention. We would also like to thank the CDC COCA group for allowing us to share the work from our PASC Collaborative on this Call today.

This disclaimer was introduced at the beginning of this presentation. And, at this point, I will now turn the next portion of the presentation over to the moderators.

Thank you so much. And, presenters, thank you for providing our audience with such timely information. We will now go into our Q&A session. Audience, please remember to ask a question using Zoom. Click the Q&A button at the bottom of your screen. Then type your question. As you can imagine, we receive many more questions than we can answer during our webinars.

So, for our presenters, our first question asks, In your experience or your studies, have you found any association between these cognitive symptoms and sensory symptoms?

I can answer that. It's Dr. Fine. The primary pathophysiology of the acute COVID storm, it's such a exaggerated cytokine storm is an inflammatory mediated injury. And there's been a lot of talk about ACE-2 receptor mediated virus translocation into cells.

But not every tissue that's damaged has ACE-2 receptors on the surface. The numbness and tingling oftentimes is related to a small fiber neuropathy, which is the same fiber diameter as the autonomic nervous system, which may be from the same mechanism that we get autonomic dysfunction as well. That's related to inflammatory injury of the nervosum vasorum, the blood vessel servicing the nerve.

Thank you for that. Our next question asks, When is a formal neuropsych evaluation indicated?

I'll take that one. So, I mean, obviously, ideally, I would love for neuropsych to be part of, you know, all preventative care for everyone to have access and baseline and all of that. Unfortunately, that's not the case. So, you know, I think that a formal evaluation is most important when the cognitive symptoms are significantly disabling and when having, like, a primary care provider, even, you know, someone at a pulmonologist driven specialty clinic directing patients to, like, self-guided compensatory strategies is not enough. In those situations, I think it's very important to have that formal evaluation done.

And at the same time, you know, I'm involved with several efforts to sort of disseminate the ability for primary care and other types of providers to be able to manage these things because we know that not everyone has that access.

I would like -- this is Dr. Fleming. I'd like to just add to that, too, as Dr. Haddad mentioned, access to care is an important component, especially when we discuss health equity. There are certain situations where the neuropsychology evaluation is ideal.

However, there are other situations if your particular setting has easier access to a speech and language pathologist, we are using those services, as well, as they are trained in cognitive dysfunction and can give certain treatment recommendations as well. So utilization of speech and language pathologists is also an important part of the rehabilitation team.

Thank you very much for that. And we have time for one last question. And the question asks, You discussed a lot of information about health equity. Are there racial or ethnic biological differences that you found to be the case in the incidence, severity, or duration of these cognitive symptoms a la other conditions such as, say, heart disease?

I'll take that question. This is Dr. Fleming. It's actually interesting that you mentioned that. The majority of challenges that we're finding is really relating to those social determinants of health.

So it's relating to the places where we eat, sleep, work. So in terms of access to healthcare, in general, access to clean water, access to clean environments, access to a walking neighborhood, access to not only healthcare within the hospital itself but also within the community, access to a local pharmacy. Those really are where the difference is. And that's really the area that we need to focus in. It's not specific for cognitive impairments and COVID.

It really is a problem that exists among many different aspects of healthcare. So it's less about the biologic differences, more about the social determinants of health as a place where we can intervene and have a really -- an important impact.

Thank you, Dr. Fleming. I want to take this moment to thank everyone for joining us today with a special thanks to our presenters. Please note that all continuing education for COCA Calls are issued online through the CDC Training and Continuing Education Online System at <https://tceols.cdc.gov>.

Those who participate in today's live COCA Call and wish to receive continuing education, please complete the online evaluation before June 6, 2022, with the course code WC4520-050522. The access code is COCA050522. Those who will participate in the on-demand activity and wish you receive continuing education should complete the online evaluation between June 7, 2022, and before June 7, 2024. And use course code WD4520-050522. Again, that access code is COCA050522.

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