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Conference Title: **National Disability Forum - COVID-19 & SSA Programs - Long Term Health Effects**

Conference ID: **6520071**

Moderator: **Melanie Farmer**

Date: **November 18, 2020**

Operator: Good day, and welcome to the National Disability Forum COVID-19 and SSA Program's Long Term Health Effects Conference Call. The National Disability Forum is a public forum and may include representatives of the press. So, any statements or comments made during the forum may be considered on the record.

Today's conference is being recorded. During this conference, you will be in listen-only mode, there will be a five-minute break, and during this break, we ask that you do not disconnect your phone line. At this time, I would like to turn the conference over to Mark Warshawsky, Deputy Commissioner, Office of Retirement and Disability Policy. Please go ahead, sir.

Mark Warshawsky: Thank you very much. Good afternoon, everyone. Thank you for joining us today. My name is Mark Warshawsky. I'm the Deputy Commissioner for Retirement and Disability Policy at the Social Security Administration.

I have the pleasure of welcoming you to our 16 National Disability Forum. On behalf of Commissioner Saul, SSA executives, and everyone at the Social Security Administration, we hope each of you are safe and doing well during this challenging time.

Indeed, the topic of today's forum is COVID-19 and SSA programs that specifically as it relates to long-term health effects. As the operator indicated before we dive into some important and critical topic for our agency, I want to let everyone know that the National Disability Forum is a public forum and may include representatives of the press so, any statements or comments made during the forum may be considered on the record.

This call is being recorded and will be available on the National Disability forums website within two weeks after today's forum. I would also like to extend a sincere thank you to our moderator, Dr. Carlos Del Rio and to all the panelists for making time out of their very busy schedules to prepare their presentations and presenting before us today.

Then we're going to turn it over to Steve Rollins in the Office of Disability Policy. But before we welcome Steve, I would like to welcome and introduce Commissioner Andrew Saul.

Commissioner Saul was sworn in in June of 2019. Prior to becoming the Commissioner, he served as the Chair of the Federal Retirement Thrift Investment Board, which administers the Thrift Savings Plan, the retirement savings plan for federal employees.

He has also served in state and local government and nonprofit organizations. The state ones Commissioner Saul has been committed to and driving everyone in Social Security to improving the agency's customer service.

And as we have faced this unprecedented pandemic, he has also been laser-focused on protecting the public by developing campaigns and how to report scams calls and fraud, extending deadlines for requests for information, stopping adverse actions, and implementing innovative ways to continue servicing the American public.

Social Security has not been closed; we continue to do our work. If you wish to learn more about our services deadlines and how to contact us during the pandemic. Please visit our web page at www.socialsecurity.gov/Coronavirus. That's socialsecurity.gov/Coronavirus. We are constantly updating a web page with new information.

In addition, Commissioner Saul has made this forum and other engagements with stakeholders a priority for our agency. Commissioner, thank you for joining us today. And please go ahead.

Andrew Saul: Mark thanks a lot. You know, when I looked at the notes for this meeting, I was really impressed. I mean, you couldn't help but be impressed. Mark and his team have assembled a really fantastic panel. And obviously, it couldn't be more timely.

So, it should be very exciting. And I can't wait to share the ideas and thoughts that come out of this conference. It should be quite interesting. And I promise you; I will spend time with it. With this kind of a distinguished group of people, I'm sure we're going to get a lot of constructive ideas, which will help us better navigate the pandemic and also serve our customers.

So, I want to thank you and Mark, and everyone for participating in today's National Disability Forum. These forums are an important way that we exchange ideas and obtain valuable input from stakeholders and experts.

I'm very excited about the accomplished panel we've assembled today. I know medical experts and researchers are working feverishly to learn as much as we can about the COVID-19 virus, and we are eager to hear about your experiences and research to date, and especially now with the great discoveries of these two vaccines; this should make this panel even more interesting.

From this forum, we plan to learn about the medical impact of COVID-19, the effectiveness and availability of treatments, gaps in access to treatments, recent medical developments, special considerations for those with preexisting conditions, and ultimately, how it affects people's ability to work or return to work.

By doing so, you will help us strengthen our disability programs. I encourage your comments and suggestions. More importantly, we thank you for your continued participation. And I want to not take any more time from this exciting program.

So, I'm going to turn the program over to Steve Rollins, who will share some important information about today's forum. And again, I thank you sincerely for everybody for attending this important event. Steve, go ahead.

Steve Rollins: Okay, thank you, Commissioner Saul. And also, thank you, Deputy Commissioner Warshawsky. For the opening remarks. I think hearing from both of you really does highlight the importance of this forum.

So, my name is Steve Rollins. I'm the Deputy Associate Commissioner for the Office of Disability Policy here at the Social Security Administration. I, too, would like to welcome and thank you for joining us on this teleconference for our 16th National Disability Forum, discuss topic of COVID-19 and its long-term health effects risk with respect to the Social Security Administration's programs.

Some housekeeping matters before I continue, I would like to go over a couple of things. First of all, our moderator, Dr. Carlos Del Rio will guide us through the discussion with our panelists today. There will be an open discussion segment after the last presentation.

The participant line will not be open during the discussion segments. We are accepting questions and comments from the audience but only via email. If you wish to ask a question or provide a comment by email, please include your name, your affiliation, and your location in your email question.

The appropriate email address is National Disability Forum. And that's all one word @ssa.gov. Again, that's NationalDisabilityForum@ssa.gov. Please remember when submitting a question, do not include any personally identifiable information such as your social security number.

We are monitoring the inbox, and we'll make sure that the questions are shared with the panel. Feel free to submit questions at any time. Our moderator Dr. Del Rio will present the questions to the panelists as time allows.

As a reminder, the call is being recorded. So, any statements or comments, you know, made during this forum certainly can be considered on the record.

The last housekeeping item I would like to mention is that we will have a short break today. Today's forum is slightly longer, and we'll - and therefore we'll take a short break about five minutes around two o'clock. Please do not hang up. Keep your lines open during the break.

Now in terms of the purpose and overview of this forum, as with all National Disability forums, to give our stakeholders an opportunity to share your insights directly with us. These forums really do provide an opportunity for stakeholders to hear from one another, and it really is open to anyone interested.

By doing so, you will help us shape the future of Social Security, which you all care about, hence why you're on. It'll help strengthen our disability policy development and certainly enlighten our continued effort to address, you know, COVID-19 within our disability program, which certainly is a challenge for all.

Now today's forum is to hear from the medical experts and researchers about the medical and functional impact of COVID-19, including special considerations for people with preexisting medical conditions and multiple diagnoses. The effectiveness and availability of treatments, any

possible gaps in access to treatment, recent medical developments, and, you know, certainly not exclusively, but also the long-term impact of the virus on survivors' ability to work and survivors' longevity.

So, now as I prepare to turn it over to our moderator, Dr. Del Rio, a couple words to introduce him. Dr. Del Rio is a distinguished Professor of Medicine at Emory University School of Medicine and Professor of Global Health and Epidemiology at the Rollins School of Emory University.

Dr. Del Rio works on emerging infections, epidemics, and pandemics. Dr. Del Rio 's been a leader locally and nationally, doing research, developing policies, writing scientific publications, and making numerous media appearances.

To learn more about Dr. Del Rio and all of our panelists today, please visit the National Disability Forum website, which you can find it www.ssa.gov /MDF, and once there, click National Disability forums on the right panel and select the 11-1820 tab.

So, we would like to extend our sincere appreciation to Dr. Del Rio, as well as all of today's panelists, for their participation in today's forum and discussion. So, with that, welcome, Dr. Del Rio, and the floor is yours.

Dr. Carlos Del Rio: Thank you very much. And I appreciate, first of all, the invitation and the opportunity to be with you at this really important forum focus on the medical impact of COVID. And specifically, to talk about the long-term health effects and how it's related to social security programs.

Let me just say that the COVID pandemic has had an unprecedented impact causing significant morbidity and mortality globally in our country. But in addition to the acute illness, we have seen

increasingly individuals have recovered from COVID, acute COVID, develop long-term health consequences sort of a post-acute COVID syndrome.

And in today's conference, we will discuss what we know about the topic today. And for that, we have a truly outstanding panel of experts that are going to be discussing this issue.

I want to start first by introducing the panel. This includes Dr. Steven Deeks. Steve is a Professor of Medicine in Residency at the University of California, San Francisco, and somebody who has been a leader in HIV research and particularly in the area of cure, a very innovative investigator.

Following Dr. Deeks, we have Dr. Mercedes Carnethon. She's the Mary Harris Thompson Professor and Vice-chair of Preventive Medicine and Professor of Medicine at the Northwestern University Feinberg School of Medicine.

And next, we have Dr. David Putrino. He's the Director of Rehab Medical Innovation at Mount Sinai Health System. And he's an Assistant Professor of Rehabilitation and Human Performance on the Icahn School of Medicine at Mount Sinai.

Then with us, we have Dr. Paul Auwaerter. He's the ((inaudible)) and Ken Fisher Professor of Medicine at Johns Hopkins School of Medicine, Clinical Director of the Division of Infectious Disease, and he's also a past Chair and past president of the Infectious Society of America. And one of the - probably one of the top infectious disease clinicians I've ever met in my life.

And last but not least, we have Dr. Laurie Jacobs, who's Chair and Professor in the Department of Internal Medicine at Hackensack Meridian School of Medicine at Hackensack University Medical Center.

And you can find extensive bios of the executives and panelists by providing - by going into the National Disability Forum website that was previously mentioned. And again, you go to ssa.gov/MDF, and under today's forum tab, you look for the panelists.

The speakers we'll let you let each one of you, you know, start your presentations, and then we'll have a discussion. So, why don't we go ahead and transition to Dr. Deeks, and why don't we have - Steve you can start the presentation. So, the floor is yours now.

Dr. Steven Deeks: Okay, hey, Carlos, thank you for that introduction. As Carlos mentioned, my previous life, basically back in February, I was an HIV clinical researcher. And actually, we had developed a cohort, which was really focused on identifying some long term health effects of HIV. And so, for us, it was natural to sort of shift that work to the issues of what's happening in terms of long term issues with COVID. So, I'm going to share my perspective on that as I go through the slides pretty quickly to give a broad overview of what's happening.

So, I hope enough people are following along online that they have access to the slides. My second slide, I basically just make the point. That, you know, early in the pandemic, probably, I don't know, April or so there began to emerge some reports that a subset of people, initially it was thought to be 30%, 50%, a couple of reports came out from MMWR there was a high-impact, very controversial paper in JAMA around that time suggesting that 30, 50% of people at some long term consequences. It was all quite vague.

And I think if you go to slide number three, you begin to sort of see some of the data, which I think is of higher quality here. And I'm particularly fond of this ongoing app-based study that's actually happening in Sweden, the United States, United Kingdom, where basically millions of people, some really early on - really early in the disease process, are entering on a frequent basis, their symptoms, what they feel, and so, forth.

And in this study, which has now been published in Science and some other publications and got a lot of media attention, they went in, they identified these millions of people they're participating, this app identified about 4000 or so, people who were quite healthy beforehand, who began to enter data in real-time. And they began to sort of get a sense of what's happening in a population level, how frequent is this?

And these data, I think, are basically it's consistent with emerging data suggests that about 15% of adults who acquire SARS-CoV-2 are symptomatic for four weeks, that drops down to about 5%, depending on how you define about eight weeks. And then there's a subset, maybe two, two and a half percent or so, in these studies that have persistent symptoms that are lasting out three months. Of course, whether or not this continues indefinitely is unknown.

We go to the fourth slide. They actually begin to address the question of who among these people who are entering the data on the app, and it's a pretty broad population of individuals, who was at most risk for developing so, called long COVID, or the post-acute COVID syndrome, or PACs or whatever you want to handle, long haul and so, forth.

And the data would suggest that being a woman, female sex is associated with a higher risk than male, particularly in their 50s and 60s. People who presented with very symptomatic disease, defined as having multiple symptoms are more likely to have persistence in symptoms out past four weeks, as expected.

Your BMI, your body mass index is also sort of a predictor of outcome. And there's an algorithm that's been defined. But the bottom line is, some of these risk factors, not too surprising, the group that is at highest risk for developing something long symptoms are women in their 50s, particularly those who were quite symptomatic, and may actually have a higher BMI.

And what are these sequela? Again, going back to this app-based report, they've actually been able to use machine-based learning to sort of dig down deep into what people are coming up with, and they come up with these sort of clusters.

In our clinic, and now I'm on slide six, here in our cohort, we more or less have seen the same thing that there are these subsets of people who are coming in, and they have these symptoms that persist. Some are focused primarily on respiratory type stuff, cough, you know, persistent shortness of breath, my own sense of that some of that stuff gets better slowly with time.

And then there's a whole other different cluster of symptoms in which there's more systemic, and I think far more disabling symptoms. But again, we are early stages and trying to describe these phenomena.

These symptoms really, basically, I think, is the heart of what this forum is all about. Who's disabled, who can work who cannot, how frequent they are, and so forth.

But another way to take a look at this as a dig down deep into what's happening on an origin basis, right, and that's what we do as physicians, and as medical scientists, for the most part, we're really good at digging down into specific system, specific organs, and deciding and trying to figure out what's happening, and a lot of research that has emerged, probably one of the higher-profile, certainly more controversial papers that occurred over the summer, was this report that I described on page eight, in which it was described that among patients who were quite sick at a hospital in Frankfurt, who were discharged and had follow-up, cardiac MRI, this and this report suggested that a significant proportion of people in that post-recovery period had evidence of ongoing cardiac inflammation, mild carditis.

And this led to a lot of concerns and a fair amount of discussion in the media, and people have been trying to figure out whether this is real or not. At the same time, there's been some

pathogenesis work trying to figure out what's going on, and is more than I expect with an acute viral infection, strong evidence that there's persistent inflammation in the heart tissue and other tissues. The virus actually can often be found weeks after infection, so forth.

I will say that - and around this time was another high-profile report, that came out also in JAMA suggesting that even people who were asymptomatic young adults, college athletes, a subset of patients had cardiac - mild carditis, weeks after infection. So, this, of course, led to all sorts of concerns about what's going on the heart.

You know, I think many of us that's been in this business before we saw this with HIV, we always expect that these first reports that come out are going to be the dramatic ones, are going to basically generate the most attention. There's certainly kind of publication bias along those lines.

If you go to slide nine, this is actually a more recent study. An autopsy study was done at multiple centers throughout Europe, and it suggests that, in fact, yes, indeed, SARS-CoV-2 can result in significant cardiac dysfunction, but it's not as common as initially predicted. And a lot of it actually has to do with the standard stuff that happens, and people are quite sick in terms of the direct harm to overworking the heart.

Suffice it to say that the collected data from the work on the heart, as with all the other tissues that you can look at, clearly there's something happening in the acute setting. Most people resolve there are persistent diseases might be related to ongoing virus production might be related to ongoing inflammation. It's early stages.

That's the heart. Similar types of reports have emerged about what's happening in the lung. And these reports are actually quite similar to what happened in previous pandemics or previous epidemics, including the first SARS one, and Ebola and SIRs and so forth emerged. There were

these reports out early on that patient's post-acute setting, we're having persistent symptoms, and a lot of that early work suggested that there was some ongoing damage to the lungs.

So, this is perhaps not too surprising. But clearly, there's evidence of persistent pulmonary issues. As I said earlier, in our clinical cohort of post-recovery people, it's the most common symptom that we're seeing some of this persistent shortness of breath and dismay type symptoms. And again, how long this is going to last is unknown.

A lot of concerns, of course, what's happening neurologically other people on the panel have far more expertise in this area. This is, of course, probably, ultimately is going to be some of the more disabling type of symptoms that the Social Security Administration and others are going to have to deal with. They're vague. They're hard to define. They're hard to quantify.

A lot of it gets mixed up with other sort of things that might be happening in people's lives. There's a fair amount of stigma associated with some of this stuff. But I will tell you, from my experience on the front line, this is to me some of the more concerning persistent symptoms, certainly some of the more disabling and clearly something that this group is going to have to work with in the future.

Other symptoms other organ systems are clearly affected. The endocrine system, we actually have, we were struck again, in our cohort, about 200 or so, people who recovered, that there was actually, you know, three or four people who were actually coming in with their first diagnosis of diabetes. And there's been some concerns also about that emerging literature.

I can go on and on, liver, kidney, bone, and so forth. But suffice it to say, there's evidence in the literature that almost any organ system can be affected. There's biological reasons for why this might be. There are certainly historic reasons to suggest this might happen from previous epidemics that I've mentioned, and so forth.

And so, I think the consensus now is that that it's clear this is happening, it's real, and we get to figure out what to do with it.

Moving along quickly here. And again, I'm just sort of giving the big picture because other people in the panel going to be too scared to be digging deeper into some of these issues.

From my perspective, you know, once you've identified the syndrome, which we have, the next step, of course, is to figure out the mechanism, and from that, treatments actually emerged.

And so, what might be the mechanisms here, the biologic mechanisms, why would actually people who are developing an acute infection have persistent symptoms that lasts for months, if not longer?

And then obviously, this is not a lot of data, and we're just beginning these studies, but again, basically taking some of the experiences that we've had and studying long-term consequences of HIV and other people have had long-term consequences other human chronic virus infections. One question on the table is whether or not there is persistent virus replication production, causing direct tissue damage.

There are reports emerging now that you can actually find evidence of the virus many, many weeks after the acute phase, particularly in people who are somewhat immunocompromised. Should this prove to be true, probably not likely - the most likely mechanism, but certainly one that's actionable. We can give people anti-virals.

I think if you were to actually take a - you were actually asked a button, and now I'm on slide 15, which is a busy slide. It just illustrates some of the data emerging. If you were asked a group of panelists or a group of experts, potentially what the mechanism is, certainly what the media

suggested mechanism is, you got this sort of vague sense that chronic inflammation is the major player, it's bad for you.

We know from other diseases that chronic inflammation can drive chronic disease. This has been worked out pretty well in chronic HIV infection. It's actually been worked out quite well on chronic cardiovascular disease where they've actually shown in controlled studies; if you block inflammation, heart disease gets better.

So, you know, SARS-CoV-2 causes a really massive acute inflammatory condition. So, one might expect that there's going to be persistent inflammation. If so, one might expect that there will be persistent harm. If so, one might expect ultimately that we can develop anti-inflammatory drugs to reverse that.

Another big area of research in terms of mechanism is digging down deep into what's happening in the blood vessels. There's a conceptual model, one that I prefer, that in terms of how we're beginning to think about long-term treatments, you know, that the lining of the blood vessels, the cells that line the blood vessels, actually express high levels of the receptor that the virus uses to get into the cells. There's clear evidence that you have an inflammatory effect that affects the endothelium, the lining of the blood vessels, you get damage.

This actually results in tissue being expressed that that should not, which leads to clots. These clots actually can happen in the big vessels, but they can happen in the small vessels.

Of note, the kind of people who are really at risk for developing significant consequences from some of the - from SARS-CoV-2 are people who, at baseline, are expected to have underlying vascular disease, particularly diabetes, and so forth. And so, this is a conceptual model that links tissue damage from the virus, inflammation, and clotting, and one for which there are multiple interventions.

In another sort of initiative that's emerging, it goes after some of these sort of symptoms that we've seen with other chronic consequences of infectious disease in the past. And there's a concern that there's damage to the autonomic nervous system and that this, in fact, can lead to some of the chronic, somewhat disabling symptoms, including things like amputation and so forth. And this is also sort of a distinct area in terms of mechanistic work.

So, enough of the biology, what should - what's the plan right now? How is this going to be managed? Since we don't really know the mechanism. Since we don't really have a good sense of how to quantify the symptoms, since we don't know how to define it? There's not a lot right now happening in terms of treatment.

If you go on clinicaltrials.gov, there's some emerging studies looking at anti-inflammatory drugs. There's a study of prednisone ongoing and so forth.

But right now, I think what's happening in the medical field in terms of management of the syndrome is that we're coming up with these algorithms. There's actually been some really complicated ones that have emerged on how to sort of diagnose and manage people who might have cardiac implications. This is now slide 19.

And, and, of course, I think in addition to these algorithms and these guidelines on how to manage it, there are popping up all over the world, now on to slide 20, we have one in San Francisco.

I think most major urban centers have multiple now sort of post-COVID clinics, post-acute COVID clinics, whatever you want to call it, that are emerging, and they're actually thought to be sort of a one-stop-shop for people who have these persistent symptoms where they can go. They can get

access to knowledge about what's happening, engage with other people who are suffering the same kind of problem. Learning about management issues in terms of rehabilitation and so forth.

And I think, really importantly, contributing to the research evidence database and also hopefully also being available for the clinical trials that I'm hoping will merge that will help treat this and so forth.

If you go to slide 21, right, there's also the big problem right now that the medical field, those that are involved in rehab, those involved with insurance, and in fact the Social Security System Administration that's involved with disabilities.

No one really right now knows how to handle this. It's not like it's there's a specific syndrome that's easy to diagnose. I think the consensus is this is a real problem. If it's 2% of the population and millions of people become infected, well, you can do the math. This is going to be a big, big problem coming forward. And so, we need to deal with this in terms of the healthcare clinic systems, but also in terms of what the payers do, and so forth.

So, my final slide, slide number 22. Just a quick summary, and I'll hand it back to Carlos. You know, they're obviously, you know, this is a new phenomenon, it's only been around for six months. There's really limited data. It's really hard to even talk about long-term consequences of something that didn't exist six months ago.

So, there really are no really high-quality data, but I think everybody involved thinks this is real, that's no longer really questioned. How common it is, who gets it still to be defined. But it certainly is reasonable to think that this is going to be an issue.

We've seen this with other acute infections before. And there's a lot of biology that I've tried to summarize that provides real strong rationale that the issues that we're seeing are real and also targetable.

Anyway, that's my perspective. Hope I didn't go too fast. And you guys can reach me by email if you want to access those slides or have any questions. And Carlos, I'll send it back to you.

Dr. Carlos Del Rio: Thank you, Steve. I think that was a really terrific presentation and a lot of data. And as you say, I think the challenge here, it's very hard to talk about the long-term care of the consequences of something that is so new, but I think it really I agree with you. I think this is real, and we're seeing it.

And I would encourage people on the call to read - there is a perspective published just a couple weeks ago in JAMA, one of my colleagues at Emory, who's an emergency room physician, wrote a perspective about him having COVID long-term and how he essentially, you know, as an ER physician, he talks about his experience. And he basically says, you know, I'm unable to go to work, I'm unable to have a normal life. (James Ito) is his name. So, I would recommend you read his article, because it really is a good reflection of what's happening and what kind of problems people are presenting.

I want to now turn the presentation on to Dr. Carnethon. Please take a take over from here, and you'd have five minutes for your presentation.

Dr. Mercedes Carnethon: Well, thank you so much. I really appreciate the invitation to speak today. My life prior to COVID was primarily studying the chronic illnesses that ultimately, we have identified as predisposing to worse outcomes from COVID-19.

So, I'm on my second slide now. And you know, as the previous speaker discussed, we are seeing a rapid spread of COVID-19 across the United States that's affecting individuals across the (life course). And we know with aging that chronic disease rates go up. And it is these chronic diseases that I'm going to focus on today, their distribution in our society, and how that may influence outcomes from COVID.

Right now, an estimated 85% of individuals with known COVID do not require hospitalization. And, you know, for a large proportion, the experience is time-limited, and they recover pretty rapidly. But these long haulers present a unique challenge and situation for us.

And so, the question I do want to discuss today is how these preexisting conditions influenced the likelihood of experiencing long-term complications. So, I'll just discuss a little bit about the Association of preexisting conditions with COVID severity, and then describe the socio-demographic characteristics of adults with these preexisting conditions and discuss the appropriate targeting of resources for prevention and long-term management.

So, there's consistent evidence worldwide, initially coming out of Asia and Europe who preceded us in the timeline of the pandemic, spreading to the United States based on our experience that those individuals who have cardiovascular diseases of the heart and vascular system, diabetes, hypertension, obesity, chronic kidney disease, moderate or severe asthma, or who are immunocompromised, tend to have more severe outcomes from COVID. And when I refer to severity, I mean hospitalization, as well as death rates.

There is also compelling evidence for additional chronic diseases that may predispose to worse outcomes. Those conditions are also more common among older adults, which could be why we see this pattern of worse outcomes in older adults, as well as individuals with mental and physical disabilities, many of whom have a cluster of the conditions that I discussed above.

The risk for hospitalization among people with chronic conditions has shown that having more than one of the chronic conditions I mentioned, the severe asthma, hypertension, obesity, diabetes, and chronic kidney disease is associated with a higher risk for hospitalization. And if you're following along, I'm on slide five right now, which is demonstrating how much higher.

So, for example, individuals who are obese with diabetes or hypertension are three times more likely to be hospitalized with COVID. Individuals with chronic kidney disease four times more likely. And what's very concerning is that we know certainly that many of the chronic cardiovascular diseases follow obesity.

So, it's not likely that an individual has freestanding diabetes or hypertension. And those individuals with two or three or more conditions are four and a half to five times more likely to be hospitalized with severe COVID. And, you know, the shared characteristics that I described are shown on slide six.

So, for example, individuals' normal weight, the incidence rate of heart failure, for example, is nearly three times higher among adults who have severe obesity. So, BMIs above 40. As compared with those who are normal weight. The rates of coronary heart disease and stroke are twice as high among individuals with severe obesity, or even regular obesity, a body mass index of 30 or greater, as though as compared with those who are normal weight.

Over 90% of adults with type two diabetes are overweight or obese, and 40% of new-onset hypertension is attributed to obesity. Similarly, 57% of adults with severe asthma are also obese.

And so, we think about next, who is likely to have these preexisting conditions, and how is that contributing to what we see are the disparities in the severity of COVID-19. And what does that tell us about long term disease.

So, in the United States, this is slide eight, we see clear and fairly consistent socio-demographic patterns in obesity, whereby rates of obesity, based on reports from NHANES 2017, 2018, which is the National Health and Nutrition Examination Survey, nearly half of black Americans are obese with a body mass index of 30 or higher.

And that compares with 48% of Native Americans, 45% of Hispanics, 42% of whites, and 17% of Asians. Although of note these data often aggregate Asian groups and don't disaggregate by subgroup, and we see marked variability in rates of obesity as comparing East Asians, so, say, for example, Vietnam, China, and Japan, to South Asians from the continent of India, and Filipinos who tend to have much higher rates of obesity.

So, these demographics who are more likely to have obesity are also, as we've seen, quite consistently, more likely to have severe COVID. Quite unfortunately, and coupled with that, the occupations, and the socio-economic correlates of race in this country have these same individuals working and living in situations where they're also more likely to contract COVID.

Adults with disabilities, roughly grouped as both physical and mental disabilities, are also more likely to be obese. And I focus again on obesity because it is the root cause of many of these other chronic diseases. Obesity rates for adults with disabilities are 58% higher than for adults without disabilities.

So, as we couple that on to, you know, what's going to happen with the chronic conditions and the severity of COVID. This is a population that is at severe risk.

So, there are multiple pathways by which obesity leads to more severe COVID. First, it makes COVID more difficult to manage. Experiences demonstrated that moving patients to the prone position so on their stomachs can reduce the need for ventilation and improve outcomes with ventilation. But that's very difficult in obese patients.

Obesity, as well as an inflammatory condition, it interferes with the innate immune response to other viruses, including influenza, leading potentially to worse outcomes. Preexisting inflammation may also be at the root of the hyperactive immune response when exposed to SARS-CoV-2.

And I think even more importantly, and I'll discuss this a little further, the organs that are damaged by the inflammatory response from the SARS-CoV-2 may already have been compromised by obesity and its complications.

So, on slide 11, I'm showing the results of a meta-analysis. And this is where we pull together multiple studies in order to enhance our sample size and thus the reliability of our findings. So, in five studies that looked at the contribution of overweight, not even obesity, so, body mass index of 25 or higher, in these five studies that included 867 patients, patients with body mass index greater than 25, so, overweight were seven times more likely to need advanced respiratory support than those with normal weight body mass index.

And in a meta-analysis of six studies, patients who were overweight were 3.7 times more likely to die from COVID-19 than those who are normal weight. So, you know, by extension, we know a little less about what's happening with the long term COVID. But we certainly know that overweight and obese individuals are facing many starker outcomes.

So, how do preexisting conditions contribute to long term sentience or disability from COVID-19? And you've already seen this slide on slide 13. So, I'll just quickly acknowledge it, that obesity damages the heart, the blood vessels, kidneys, the brain, lungs, and intestines.

And, you know, my experience is primarily in the cardiovascular and respiratory space. And we know that diabetes, hypertension, these vascular diseases are independent risk factors for these

types of complications in the heart and in the brain. And this could be magnified from COVID-19 and possibly lead to persistent longer-term symptoms.

So, heart damage, as highlighted earlier, maybe an early severe side effect of COVID-19. And we are certainly learning as we go, the inflammation that can damage the heart muscle leading to a mild carditis, or the covering of the heart pericarditis could explain some of the longer-term symptoms such as shortness of breath, chest pain, or racing heart rate.

They are the examples from the athletes that were cited earlier, including an unfortunate death among the young athletes. But we are only eight months into our collective experience, and we don't know yet how long this inflammation in the heart persists following infection.

We do know that other viruses leading to acute respiratory distress are associated with longer-term symptoms, and you know, 5% of COVID-19 patients do experience acute respiratory distress that is managed in the ICU and requires mechanical ventilation, even ECMO extracorporeal membrane oxygenation. These ICU stays, Intensive Care Unit stays are associated with complications that can persist beyond the length of the initial ICU stay, including muscle weakness, depression, cognitive decline, poor quality of life, and physical functioning.

There was a study published in late July that sampled, and this is a slide 16, 270 adults sampled by the CDC, whereas two-thirds reported a return to their usual state of health within seven days. Among those who did not, the following characteristics were more common; they were more likely to be older. Notably, they were more likely to have two or more chronic conditions, and participants with obesity as well as psychiatric conditions were 2.3 times less likely to return to normal.

There was no association with race - of race with a prolonged return to normal. However, we do know that certain racial and ethnic groups are more likely to have chronic conditions.

So, how do we target resources to manage long term COVID? I think resource allocation is going to be critical. Prevention remains the most important strategy, particularly since we do have experience to know what's coming. Finding ways to protect those populations and those socio-demographic groups who are more likely to contract COVID will be our best long term strategy, particularly if those resources are not available.

And I think to make this really work well. There needs to be culturally competent prevention messaging coupled with practical supports, both economic and equipment. You know, when asking somebody to quarantine to protect their health and protect others, you know, that can be very challenging for hourly-paid workers who are losing income, or who have nobody to watch their children. I think advocacy for them to take vaccines when they become available needs to as well be culturally competent and aware of historical mistrust of the medical system by particular groups.

I think managing the burden of preexisting conditions remains very critical. We've had on slide 19 a lot of discussion right now about the medical system becoming overwhelmed. As the medical system becomes overwhelmed as individuals become fearful about following up on preventive care visits, individuals are losing - are not following up to manage their disease. And they're statements and hypotheses that it is poorly controlled chronic disease that's particularly problematic. I hear this in the case of diabetes, which is what I look at most often that poorly controlled disease is the problem.

So, really trying to find ways to manage the burden of COVID-19 right now in the healthcare system so that individuals can continue their chronic disease management will serve us well over time. And also, the integration and promotion of telehealth to maintain continuity of care. And also, really helping individuals understand how to use these telehealth tools.

So, you can build it, but trying to teach individuals, particularly those with chronic conditions or individuals with disabilities, how to use a video conference is going to be critically important.

And finally, enhancing discovery by supporting these longitudinal studies of survivors. The previous speaker discussed the long term care clinics of post-acute COVID sufferers. Really tracking what's happening in those groups with systematic data collection about behaviors about health history, and regular management can help us to identify some of the hints and clues about who's going to become a long hauler.

So, I do think support for longitudinally - longitudinal epidemiology studies is critically important. So, with that, I thank you so much for your time and look forward to taking questions.

Dr. Carlos Del Rio: Thank you very much. This was a terrific presentation. And I think we're already starting to hear some things, but I also want to emphasize what has been said about chronic conditions, what has been said about obesity as a major problem. And I think it really emphasizes how much we need to take care of chronic non-communicable diseases because they're really increasing mortality from this acute infectious disease.

And it's not the only one we've seen this in influenza and with other acute infections. So, the superimposition of chronic non-communicable diseases and infectious diseases is something that I want to emphasize and need to continue to address. We're going to take now a five-minute break, and my time is 1:48. So, let's say that at 1:53, we will come back online, and we will go to the next presentation.

So, please, at this point, don't hang up and just rejoin in five minutes.

Operator: Ladies and gentlemen, as a reminder, we are currently on a five-minute break. Please do not disconnect at this time. Thank you.

Recording: You are now re-joining the main conference.

Operator: All parties are now back in conference.

Dr. Carlos Del Rio: Thanks for keeping the break down to five minutes. We're going to go to our next speaker. Our next speaker is Dr. Putrino. And please Dr. Putrino, take the floor.

Dr. David Putrino: Hi, everyone. Thanks so much for having me. And I'm really honored to be here to discuss this really important topic. I thought what would be really helpful, and complimentary to some of the already amazing conversations that we've had so far would be to give a bit of a narrative review of some of the operations that I was involved in in terms of COVID management during the first COVID surge in New York City.

And then subsequent efforts to deal with people who are experiencing persistent symptoms after their acute COVID-19 infection. Since everyone has been doing this, I think it's probably worth mentioning that my, you know, pre-COVID day job is it's a really odd title. I'm called the Director of Rehab Innovation.

And what that really means is for the Department of Rehabilitation, human performance, I work to develop all sorts of new and bleeding edge technologies to treat different conditions like stroke, spinal cord injury, traumatic brain injury, as well as working with high performance athletes and really viewing wellness as a spectrum, so we get to work with all sorts of interesting technologies.

And I think that that leads into the first couple of slides which, which really, slides two and three are just images of what it was like in New York in March, showing a large part of our atrium and the main Mount Sinai Hospital being turned into ICU beds showing Central Park being turned into overflow hospital beds and hospital space for acutely ill individuals.

And what was really a point of friction for us in the early stages, moving on to slide four is, this very stark choice that we had for a disease that was largely unknown in March, where people would people would show up to the emergency department or they would show up to virtually to their choice or urgent care.

And they would list their symptoms, the symptoms sounded very COVID-like, and the poor physicians, nurses, health professionals that were trying to field these were stuck with this very stark choice. They were too sick to be at home, so they had to come and be admitted in the hospital, or they were not sick enough for the hospital. There was nothing in between.

And this issue was forcing a lot of difficult decisions about hospital capacity. We didn't -- we were very concerned in the initial surge, that we weren't going to have enough hospital beds. This is a barrier and a challenge that many people are facing right now in other parts of the country.

And so, we decided in March to quickly stand up a remote patient monitoring program that would allow us to virtually improve our health care system capacity by tracking people on a daily basis in the home, and making sure that their symptoms were not escalating to a point where they were out of control. We called this program the Precision Recovery Program, because it was actually a rollout of a program that we were running for stroke survivors already.

It used very low-cost efficient technology. It was compatible with all smartphones. We had strategies in place to assist people who did not have smartphones, so that they could still enter data on a daily basis, and it could still be monitored by health professionals. And for cases that we were particularly worried about certain biometrics, we had blood pressure cuffs and pulse oximeters so that we could track people.

We had a basic pathway, which I've noted on slide seven, where people could reach out to us directly or they could be referred to the program through being admitted into hospital and then being discharged or arriving at the emergency department not being able to be admitted into the hospital and so, therefore being referred over to us.

In slide eight, I really just go through the protocol, which is on a daily basis, we ask people to monitor a brief survey of their symptoms and provide us with some biometric data. After monitoring around 60,000 days of data, our average was around three minutes to actually, you know, it was a burden, a time burden of about three minutes on our patients to track these things.

And then, we would do weekly check ins with patients and monthly check ins with patients to make sure that they were doing okay. So, the first point of data that we recently published that I really want to hone in on is this idea that after monitoring thousands of patients, for, you know and gathering over 60,000 days of data, the first thing that immediately struck us was there was no significant difference in symptom presentation in people who were PCR positive, PCR negative, or PCR unknown.

So, regardless of testing status, people who were enrolling into our program, were presenting with the same symptoms and we were managing them in exactly the same way. This will become important later, but I just want to point out that early, we were already seeing that PCR tests were not really necessary for us to see presumptive positive signs and symptoms of COVID-19.

So, as we move forward to May 2020, we were hearing a lot of chatter that, you know, as we were learning more about the COVID-19 virus, we were hearing a lot of chatter of two weeks of symptoms if you were not sick enough to be admitted into hospital, and then you should be starting to be on your way. This was and we all now know that this is incorrect, but this was conflicting strongly with our data.

Where the median number of days that people were enrolled into our Precision Recovery Program was around 28 days and many people were still feeling quite unwell for much longer than that. We started to see that, you know, absolutely a majority of patients from our data, around 70% of cases were fully recovering and being fine. In most cases, it took more than in two weeks, it took more like a month, but 70% of people were recovering and doing and doing okay afterwards.

I think it's important to acknowledge there's around 5% of cases that have what we call post ICU syndrome PICS. So, these individuals who got very sick were admitted, were intubated, spent time in the ICU and after being discharged from the ICU, they have multiple organ issue -- organ system issues and they have a syndrome which is well documented in the literature, which requires a multidisciplinary care protocol to make sure that people manage. And we have rolled out a recovery program in collaboration with the Center for Post-COVID care at Mount Sinai to manage this roughly 5% of cases.

We also had individuals around 10% to 15% of cases that showed significant pulmonary damage or cardiac damage when tested and we are respectively placing them into pulmonary rehabilitation and cardiac rehabilitation. I also want to you know, take this this opportunity to mention that individuals who are showing these signs and symptoms, these people, when we give them standard clinical testing, we are seeing clear signs of cardiac damage and pulmonary damage that affects function on their testing.

And so, that differentiates them from this final 10% to 15% of cases, which we are calling post-acute COVID syndrome. You've also heard it being referred to as long haulers, long-COVID. These are individuals who more or less test normal in every clinical domain that you can think to test them, or it's at least they're not consistently testing abnormal in any clinical domains, but they are showing a lot of symptoms.

As we started to dig into this cohort, we saw some demographics that were interesting. The some of these have been mentioned by previous speakers, but interesting to see that they were primarily female, median age was 42, the majority of these individuals reported being previously fit and healthy. They had a healthy, you know, BMI. We don't have enough time for me to list all my issues with BMI as a metric, but they had a more or less, air quoting wildly healthy BMI.

However, so this differentiated them from the typical at-risk cohort that we would talk about, but this was really skewing the data. This is what post-acute COVID syndrome survivors look like.

In addition, on slide 12, you can also see the fact that these individuals overwhelmingly did not know their antibody status, did not know their PCR testing status, or had negative testing in the medical record, very few people had positive antibodies, or positive PCR testing. From 1,200 cases that we were initially studying, we were seeing a large constellation of different symptoms.

And you can see this on slide 13, where we were seeing many different symptoms, but an overwhelming majority of people were reporting, exercise intolerance and extreme fatigue. Also, in the mix was chest pain, heart palpitations, high heart rate, difficulty with concentrating and COPD and other cognitive difficulties, as well as a number of other symptoms.

As we move down, we dug deeper into around 100 people that had confirmed cases of post-acute COVID syndrome. This figure here is actually part of a preprint of a manuscript that's currently under review for publication and we can provide links to this manuscript, because we've pre published it on (Medara XIV).

But what you can see here is, individuals with post-acute COVID syndrome have extremely, you know, a very large constellation of symptoms. So, now we're tracking close to 40 symptoms. Other groups are reporting tracking 65, 70 symptoms, but it is a very complex picture. Again, similar to what has been discussed previously, we know that inflammation is a big part of this

story. We think that inflammation influencing autonomic function is a big part of the story and were rapidly working to manage these cases.

But as we work to manage the cases that are emerging, I think it is so important that we acknowledge how many people have negative tests, PCR tests, or negative antibody tests, and how there is extremely strong scientific rationale for why someone might present with these symptoms, and a negative PCR test and a negative antibody test.

We know that the PCR tests have extremely high false negative rates, we know that the antibody tests once they are if they if you were tested, a few months out from your COVID-19 infection, that it is likely that your tighter levels of antibodies will be lower than the threshold required to show that you have positive antibodies.

So, these are all good reasons why these patients are showing up with negative tests, yet these sorts of symptoms. So, we must not deny people medical care, this is happening all across the country, it needs to be stopped. We should not deny people medical care based on negative PCR tests and negative antibody tests.

And the final reason for this the reason why is if we look at slide 16. This is what we're calling the approach model that we've developed to address post-acute COVID syndrome. We anticipate that we're looking at 9 to 12 months of rehabilitation here. The reason we are anticipating this is based on data from previous post-viral syndromes that look similar in nature to what we're seeing here.

And so, I think it is really important that we stress that individuals who are being told you don't have (PACS) because you don't have a positive PCR test, this is catastrophic to their livelihood, this is catastrophic to their ability to work, because many of these individuals are coming to us extremely debilitated.

Our approach model begins initially with evaluation, we take an initial look at their level of function. We have them fill out a number of forms to really get a sense of where they're at. Our next step is to optimize and stabilize, so this is working with them on small things that can improve their symptoms initially. So, we work with nutritionists, we work to improve their sleep, we worked to improve their mood working with psychologists and psychotherapy.

Cardiac clearance is a must at this point. So, ECHO and EKG, I use to clear them from a cardiac perspective before we move into more aggressive health coaching and reconditioning. It's important to point out because I know that somebody mentioned the JAMA article that focused on cardiomyopathy and cardio myocarditis.

It's important to point out that we believe that not everybody needs a heart MRI. We only think a heart MRI is necessary if an EKG and an ECHO show abnormalities. The study that was published in JAMA we think was somewhat flawed in that it did not use like Lake Louise protocol, diagnostic criteria to diagnose myocarditis. It used a cardiac MRI, which showed some cardiac inflammation.

Now, this is something that is more or less common with many viral infections that some inflammation will show up on a cardiac MRI. So, we are really using these other tests, the echocardiogram and the EKG as our gating mechanism for who might need cardiac MRI, or who can move straight on to our recondition protocol.

It's important that we get this right because we do not want to delay reconditioning of these patients, because that can lead to much longer recovery times. And so, we should not have a mandatory cardiac MRI, for every single patient is our current protocol.

Multidisciplinary care is incredibly crucial for this cohort. We would not be getting as far as we are with our post-acute COVID patients, if we did not have an incredible and deep interdisciplinary multidisciplinary team.

And finally, slide 17, please reach out to this email address, healthcare providers, patients, whoever we are disseminating information as rapidly as we can. We are happy to share any and all of our protocols. We're happy to share the slide deck and all of our publications. Thanks so much for having me. And I'll give up my time.

Dr. Carlos Del Rio: Thank you very much Dr. Putrino. That was fantastic and I think we're beginning to get a picture here. I would like to ask Dr. Auwaerter to please start his presentation, Paul, go ahead.

Dr. Paul Auwaerter: Yeah, thank you so much, Carlos. And again, I wish to thank the Social Security Administration for the opportunity to present. I was charged with a discussion of whether treatments that have been developed and widely used for COVID-19 may have some impact on people that have symptoms that are prolonged after their initial recoveries from COVID-19.

Now, by way of background, I'll say that in my younger years, I trained as a biologist, an immunologist, examining measles virus, but then pivoted to tick borne diseases, specifically Lyme disease. And I have to say Dr. Putrino's talk resonated quite a bit.

For many years as an infectious diseases physician, we have dealt with post infectious what I would call fatigue syndromes. Many of these patients have debilitating fatigue, they may have migratory musculoskeletal pain reminiscent of fibromyalgia. They may have a headache syndrome, poor sleep as mood alterations and subjective neurocognitive dysfunction.

Interestingly, if you look at a broad range of infections, Lyme disease, primary EBV infection, Epstein Barr Virus, also known as infectious mononucleosis, Q fever, for example, or (Brucella), on average, about 10% of people have symptoms that are persisting beyond six months in those conditions and we're starting off with well-defined infections.

And this consistency I think, has always baffled me that bacterial or viral illnesses can have such an effect and of course, it's not universal. I mean, rhinovirus infections, the common cold, for example, doesn't seem to precipitate this, but it but it's poorly understood. Maybe a heterogeneous set of issues, but it's Dr. Putrino mentioned there is a predilection this group towards women, often in middle age and the sense of frustration, the lack of our understanding, and also defined ways to help has been really problematic.

But I agree that multidisciplinary approaches are often very fruitful and we borrow little bits of approaches from here and there, whether it's using conditioning programs, cognitive behavioral therapy, we might use neuromodulators, for example and we often try to unfortunately individualize many of these patients do have autonomic dysfunction as well.

So, I think the novel coronavirus is probably joining this rather wide and diverse group here, but this virus itself the coronavirus, has indeed, we know quite immunologically active early on and it may I'm sure have many tricks yet to teach us.

As I go on to slide number two, if I were asked what impact treatment has on long term symptoms, I think this would be a very short presentation, because we really don't have any direct evidence. All I have is indirect aspects that I might try to convince you would impact and there's been a lot of attention with treatment on mortality. This is because almost all attention, as many speakers have talked about have focused on the most ill patients, the hospitalized patients and how to improve their care, get them out of the hospital and avoid death of course.

What you see on slide two is a brief report from New York City area hospitals that speak to just changes since the start of the pandemic. Here in New York, the mortality rates were on average about 25% to 26% in March and April and this fell to approximately 7 1/2% by July and August this summer there.

In our own experience here in Baltimore, Johns Hopkins had very similar findings. In April and May we are a little behind York City, in terms of the number of patients our mortality rates, those months were 24% to 28%. Now, I can tell you in September and October, our rates are 4.9% to 7.1% over these last two full months.

So, why the mortality is decreased is likely representative of many factors. Here, I'm just showing some Centers for Disease Control data that shows you the proportion of people that are in the most at risk age groups and really the greatest risk factors is indeed age for mortality, or serious illness, but certainly comorbidities add up, but this is strictly stratified by age.

And what you see is that there is a more people who are younger, who are hospitalized and they're going to be less likely to have the most severe illness or death, so, there are many factors do include some shift to younger patients. Others have suggested that if you're acquiring the illness with lower viral loads, this may be due to mitigation efforts such as wearing masks and social distancing. This may cause a less severe illness.

Certainly, our health systems are in less chaotic form, although with a recent uptick in cases this is again becoming a challenge. I think patients are no longer avoiding the hospital or presenting as late. There's already been some discussion about pruning and how this helps patients who are quite tenuous in terms of improving their ventilation, as well as just our intensivist improving on approaches to intubation and ventilator management.

The only treatment that I think as most people would agree is substantial mortality benefits so far, is an off-label use of corticosteroids, namely dexamethasone, which is really reserved for patients that seem to be more ill with severe COVID-19 or critical COVID-19 in intensive care units.

As we move on to slide number six, early on, there was a tremendous promise that there were so many agents that seemed to be effective against this virus based on what we call invitro or test tube studies and this is not unusual for viruses. Many times, you put substances into experiments in the lab and so culture and these seem to impair viral replication. But this may also be because it's impacting cellular growth and so on in these very limited circumstances.

But this has fostered a tremendous number of clinical studies that are therapeutic in nature for COVID-19. That count keeps changing but I had 1900 that are registered worldwide.

But unfortunately so few of those actually work in human trials because of the more complex systems. And drugs such as hydroxychloroquine ,or ivermectin, or indomethacin, and so on just don't really translate in the human body to be an effective against the virus.

So initially there was great interest and there remains some for drugs that are considered antivirals. Antivirals will inhibit virus. Now viruses are not alive. They're not like bacteria and you can't kill a virus.

But antivirals work by hopefully impairing parasitic ties, co-cells from making new virus because the virus has to co-opt a host cell to make new viruses that then go on an affect other cells.

The drug of most attention has been Remdesivir initially developed against the Ebola virus. But had a number of early - The one that's made the most impact has been the Act 1 NIH sponsored trial that looked at Remdesivir versus placebo

Unfortunately this trial published in The New England Journal in its final form just earlier this month that I appear on slide 7 was unable to show any mortality benefit which was a secondary outcome. Although there was a trend toward mortality benefit.

However the main reason the Food and Drug Administration approved this drug for use is that it lowered the length of stay from 15 to 10 days. So no observable impact on keeping more people alive that we could say is likely true statistically but people got out of the hospital.

Whether this means that there's some amelioration of some of the symptoms that have already been discussed, cardiac effects and so on, not very clear. We really don't even have virologic data yet from this particular trial.

And as we move onto slide 8, other trials that have looked at Remdesivir, in short, have not had any impact on disease or appeared to have any reduction in coronavirus levels.

One of the more widely known articles that have been advanced in the press have dealt with WHO trial -- the Solidarity trial -- which was quite large with over 11,000 participants of whom 2750 got Remdesivir. But there was no placebo in this trial. It was all compared with other drugs.

But their conclusion was that Remdesivir had no impact on mortality. And some in the European Union and groups are not advocating for its use. So it remains a bit controversial this way as to whether it's, you know, really worth the bang for the buck. But it really has been adopted as the standard of care here in the United States but unknown whether the drug impacts any long-term sequalae.

Other antivirals are under study. And the reason I'm just putting up here are the oral antivirals. The analogy would be to Oseltamivir which is an anti-influenza drug. We know that the earlier you take that drug the greater the impact on illness.

Remdesivir is an intravenous drug only approved and given in the hospital. If we have an effective oral therapy then I would say there is far more potential to abrogate the illness before it becomes more severe.

Now whether this will have any impact, of course, we know from just early studies that whether you're in the hospital or have mild symptoms, both sets of people can have long-term symptoms after COVID-19. And whether trials may be shown over time to develop and get some sense whether any of these treatments have impact remain to be developed.

In terms of anti-inflammatories, I already mentioned that the dexamethasone has become a standard of care in the United States for certain groups of patients who are hospitalized for COVID-19. This is based on the United Kingdom Recovery trial, a pragmatic trial, that did suggest a rather striking mortality benefit in ventilated patients.

Early in the UK experience, their mortality rate was among the highest in the world and among their ventilated patients, had a rate over 40%. As you can see here on slide 10, this was reduced to 29% with the administration of dexamethasone.

Even patients that were not in the ICU but required oxygen had a more modest mortality benefit from approximately 26% to 23%. But those who are not ill enough to require oxygen had a trend towards worsening.

So this is reserved for people that are more ill, perhaps had more intense inflammation, the so-called hyper inflammatory phase of COVID-19. Other corticoid steroids probably have this effect too that had been outlined in a meta-analysis by the WHO seen here on slide 11.

Overall, of course, the reduced mortality is important. We still don't know if there is any impact long term other than just more people surviving and the improved mortality that we see overall as we stated.

Unfortunately as you look at slide 12, there was great hope that so-called targeted amino modulators would have an effect on COVID-19 especially this more sever inflammatory phase. The one that was perhaps given the highest hopes was Tocilizumab. This is an anti-interleukin 6 receptor monoclonal antibody that was originally developed for Cytokine release syndrome seen in CAR-T therapy.

However, the long and the short of it is the experience to date in trials has been rather disappointing. Only one trial, the EMPACTA Trial, which was a bit different than others, suggested some benefit.

However, overall, as this editorial by Par in JAMA Internal Medicine noted last month, overall the data is rather unconvincing. And I believe most centers have stopped using this.

There are a number of other monoclonal antibodies or other strategies that are amino modulators that are in clinical trials. There's intense interest here. Some are likely to show benefits such as the oral drug (barasistenid). There are others that are being used in different stages of illness.

So many of these trials will come out over the next three to six months. They probably are only going to be impacting the most severely ill of patients or those that have the greatest risk of becoming quite ill.

So I think as the Social Security Administration looks at the treatment landscape, keeping some of the patients who are at greatest risk for severe illness from becoming more ill is important. Of course, these tend to also be amongst the most fragile patients, those who are elderly for

example and have multiple co-morbidities. So this may have some impact as well in terms of need for support in recovery.

Convalescence plasmas is another strategy that's had a lot of interest and advocates. The Food and Drug Administration has approved it under emergency use as an investigational agent because it may be effective.

To date, there really hasn't been a single randomized controlled trial that has looked terribly effective. A lot of observational data has suggested that early use, especially in the first two to three days of hospitalization and before you require high amounts of oxygen or any intensive care unit, may benefit.

There is also trials ongoing now for outpatients who are ill as well as for prevention. So depending on how these studies work, there may be opportunities to again, staunch disease that would become more severe. Whether this will impact on long-term outcomes remains unclear.

There have been two monoclonal antibodies in the press. These work much the same way as convalescence plasma. Is what we think is an antiviral therapy but using antibodies.

This Eli Lilly monoclonal antibody seen here on slide 14, bamlanivimab, was approved earlier this month again for emergency use. This particular agent, why it was approved is that it appeared to reduce hospitalization and emergency room visits at Day 28.

So those that didn't get the drug, about 10% ended up in the ED or hospital versus 3%. These weren't people with defined positive molecular tests for the coronavirus. They were over 12. And they were also now approved under the EUA only for patients at high risk for severe outcomes of COVID-19 primarily because of the rather limited supply of this drug.

This drug won't be studied any further. There is a defined amount that I don't think Lilly will go for full FDA approval. They're going to be making not a single monoclonal antibody but a combination.

This will be very similar to the Regeneron monoclonal cocktail. This is the same that the President received earlier in October. We only have press release data here.

This is a drug that's easier to administer subcutaneous. And at least in the preliminary data that was announced by Regeneron, looked like it reduced medical visit needs through the first month of hospitalization with a rather significant 58% reduction from 6 1/2% of patients on placebo down to 2.8% who are in the active arm.

And those that had risk factors for COVID-19 for severe disease had a 72% reduction. The people that benefitted seemed to be those that got the drug early enough that they hadn't yet eroded their own immune responses.

The drug seemed relatively well tolerated. So this is a strategy that certainly again, may help patients not proceed to severe illness. And if severe illness correlates with long-term outcomes and complications, which I'm sure it would be in a percentage of patients, then this approach may have an impact as well.

Many have already mentioned cardiac and lung effects. Many of those especially in critically ill patients have been because of anti -- sorry -- because of thrombosis, clots and strokes. Data so far is quite mixed and only expert consensus on the right approaches for anticoagulation in these settings and parameters.

But I just wanted to point out I'm not a hematologist. I'm not an expert in this area. But this is potentially another avenue that might reduce severity and complications of illness as well.

So in treatment summary, the key points I would say are that trials are very much focused on what we know so far on acute disease outcomes relevant to survival as well as hospitalization length of stay. We know very little about the long-term effects.

Dexamethasone in certain groups of severely ill patients has the most convincing mortality benefit so far. But we know, compared to early on, the mortality rates have decreased generally. It's not all due to Dexamethasone, for example. So how much impact this drug truly has at this point in time, I would say is different than what was studied and reported in the recovery trial.

Other than survival, unknown. If other treatments impact long-term health so there is, as others have articulated, a clear long-term need.

Lastly, I was asked to talk about treatment but obviously vaccines have a much greater potential. And really I think most of us in the infectious disease and public health communities were absolutely wowed by the three Phase 3 trials that we know preliminary results to date that look highly effective at least in the short term for avoiding COVID-19.

That's the Moderna vaccine also the Pfizer MRNA vaccine both with those technologies. But even the adenovirus vaccine, Russia has reported their Sputnik vaccine, a combination of two different adenoviruses, also more than 90% effective in prevention of disease.

So these are clearly where you'll have the greatest bang for the buck, the greatest impact keeping our citizens healthy and out of the need for disability support for recuperation. Thank you.

Male: Thank you Paul that was incredibly comprehensive. We're going to go now to Dr. Jacobs and then after we'll open the Question and Answer session. So Dr. Jacobs, please take it from here.

Dr. Laurie Jacobs: Thank you very much. So I have the opportunity to finish up the comments and reinforce the important points that my esteemed colleagues have made.

I really want to focus on what syndromes characterize chronic COVID-19, how they impact function and the ability to work, who is affected and how will this impact long-term survival. But more who might be in need of disability which is why we're here today.

In northern New Jersey we were part of the New York metropolitan outbreak that began in March. We now have an eight month perspective. And at our post COVID recovery clinic, we are seeing patients eight months out.

So most of us are defining the period of the post COVID syndromes as the early post COVID syndrome, the first couple of weeks, maybe a month, maybe even six weeks. And then we move into a more chronic syndrome, in the literature up to 12 weeks. But now we are observing patients up to eight months and expect that this will continue.

The chronic symptoms of chronic COVID-19 are different than the symptoms of acute infection and are listed on slide 4. My colleagues have described them. They include shortness of breath, extreme fatigue.

And the symptoms seem to go up and down, vary from day-to-day and from morning to night. Chest pan syndromes, cough, fevers, arthralgias, myalgias, insomnia, dizziness, etcetera

I would define the long-term medical consequences of COVID-19 into two groups. The first group are individuals who are experiencing symptoms that are nonspecific to COVID-19 but are the result of being acutely ill. And then syndromes that are associated directly to viral infection.

So the nonspecific syndromes and, there is one that I have left off here, is first the post ICU syndrome that several of my colleagues have described. This affects patients that have been admitted to the ICU and intubated for a period of time due to any underlying condition be it sepsis, a stroke.

Many patients emerge from the ICU with physical weakness, dysfunction, cognitive dysfunction that can last from months to years impairing their ability to return to work and to function independently. Associated with that can be pain and depression.

Secondly, as another colleague mentioned, there may be the beginning or the exacerbation of pre-morbid chronic conditions. Diabetes was mentioned earlier. I would add to that renal disease, lung disease.

And the third I would put in the group of nonspecific medical consequences is that due to the thrombotic syndrome. We believe that this is an effect of the inflammation and the acute illness and not specific, perhaps, to COVID-19 but can produce a panoply of long-term conditions.

Those that are associated with COVID-19 we'll spend a couple of minutes on. But are multisystem disease and you've seen these lists with my colleagues as well.

One theory of the post-COVID, long COVID syndrome has been presented by Dr. Deeks. Actually he presented two theories. I'm going to present a third theory which is that it may be an autoimmune phenomenon in which, as a result of the viral infection and the immune response, there's an altered recognition of our proteins. And our body begins to develop inflammation and attack our own proteins.

This is seen in other autoimmune diseases which are much more prevalent in women particularly in middle age. And that is the population that we've been describing in this syndrome.

I don't know if this is correct. I think we need to do further study but it is one hypothesis that I'll put forward.

So the organ based chronic COVID-19 syndromes fall into basically these six groups, pulmonary syndromes where patients continue to complain of shortness of breath. Their performance on exercise testing such as the six minute walk may actually improve to normal. And yet they feel limited in their activities due to shortness of breath.

X-ray findings persist. Pulmonary function studies do show some resolution of restrictive disease in most individuals. But patients are still coming in at eight months complaining of pulmonary syndromes.

Cardiovascular syndromes have been discussed in great detail. None of us know how long the myocarditis might persist. And it was described in asymptomatic individuals not individuals who are complaining of symptoms initially with a high prevalence. But the autopsy study as was mentioned showed a low prevalence.

The arrythmias that patients complain of -- this is where individuals feel light-headed and complain of palpations and rapid heart rate -- has been quite disabling and described as associated with autonomic syndromes. Again, likely inflammation of the conduction system and may persist. It's not entirely clear.

The thrombotic syndromes we mentioned before. I would put in the bucket of autoimmune like syndromes. People who complain of persistent fevers, joint pain, muscle pain, tremendous fatigue that varies day-to-day. And the now described multisystem inflammatory syndromes seen in children and most recently described in adults.

In addition, during the acute COVID illness, a lot of individuals developed renal dysfunction and severe disease resulting in the need for renal replacement therapy and dialysis. It appears that about a third of those people have persistent chronic kidney disease and a third of them who are on renal replacement therapy at hospital discharge now continue to need dialysis and have joined the group of disabled individuals with end stage renal disease.

Neurologically, many individuals complain of headache, cognitive impairment both of which have impeded their ability to return to work. And we hear this day in and day out in our clinic.

Stroke syndromes have been from thrombosis and obviously the intensity of that determines their ability to return to work or prior levels of function. I'm going to speak in a moment about the chronic fatigue like syndrome.

But I want to end on this slide on the psychiatric syndromes. Because these are in our experience the most profound that we're seeing in our clinic's patients eight months out.

People are anxious. They're depressed and they're presenting with post-traumatic stress like syndromes. And these are just as disabling as having chest pain and shortness of breath.

In terms of heart disease, I'm just going to return to this for a moment, the Social Security Administration has a blue book listing heart disease categories and those that qualify for disability. I don't know what the result of the post-COVID-19 heart disease syndromes will be.

But I would suggest that if they become chronic that they will fall into a similar ultimate symptom description to those that are in your blue book in terms of the presentation of patients with heart failure, patients with peripheral arterial disease or venous insufficiency due to thrombosis during COVID-19.

And those who have these arrythmias, tachycardia, dizziness syndromes, it sounds like PoTS syndrome, are similar probably to some individuals described in your recurrent arrythmia group. So I would assume that the number of individuals in these categories will rise over time.

Predictors for returning to work with individuals with heart disease include their self-rated health and their sense of being symptom free and also higher social economic status.

Barriers, therefore, for returning to work with individuals with heart disease include co-morbidity and we've heard much about that today, diabetes, obesity, etcetera, duration of disease and associated psychological symptoms, depression, anxiety. In addition, older age, over education and female gender.

These are issues in the population that we see suffering from post COVID syndromes. But we don't know if these syndromes will persist or not at this juncture.

This is on slide number 12, data from Canada about individuals with mood disorders and their need for or their inability to return for work, inability to return to work and need for disability and then those who cannot continue to self-care and need long term care admissions, this data was from before COVID. But it's clear demonstration that those with psychological and mood disorders suffer disability at very significant rates, again, similar to some of the more physical syndromes.

The chronic fatigue syndrome or myalgic. encephalomyelitis is a very poorly described syndrome. It’s just described by symptoms, we don't really understand it very well, it has an association with EBV, but not in everybody. And it sounds awfully like the chronic fatigue syndrome in COVID-19, but it may not be the same.

There is a description of it here on slide 13, I think it's as good as we get for what we're seeing currently with chronic COVID-19. However, I don't know the long-term course, for those who are complaining of chronic fatigue, insomnia, pain, the COVID fog have difficulty with concentrating, dizziness, as we've talked about, and functional impairment.

Many of these individuals have such serious functional impairment that they become house or bed bound. If there are a lot of individuals with a similar persistent syndrome, after COVID-19, we will definitely see an increase in this non-specific category of chronic fatigue like syndromes for the disability group.

So, who has chronic COVID-19 syndromes? I think we don't actually know that well, because we're basing our knowledge of social media reports, and they have an inherent bias as in terms of who is reporting on those apps or those social media sites. And then the medical literature also has reflected frankly, local populations, and they differ from place to place, but broader studies are underway and I'm very hopeful that we'll have a much clearer picture of who has chronic COVID-19.

We don't for sure know if the individuals who have disabilities or chronic disease who are more susceptible to COVID-19 will also have a higher risk for chronic COVID-19. Although many of us suspect that.

In addition, I am up to slide 17, a series of patients seen at a clinic in the United Kingdom, early on characterize those who had chronic symptoms that 8 to 12 weeks, and those who had mild symptoms where they required no oxygen at all 59% of them continued to have chronic symptoms at two to three months. The numbers increased with the severity of illness, but it is very clear that those who had illness in the community and very mild symptoms in the beginning may go on to have one of these persistent syndromes.

In terms of individuals in long term care, I'm a geriatrician, so I've had an eye to this from the beginning. Long term care, patients have made up a smaller percentage of cases as time has gone on, but that's not a hopeful sign, it just means that the pandemic has spread now to a wider population.

Though it does appear to me in my study of the geriatric population, that the persistent chronic COVID-19 syndromes are less common in older adults, the residual of being ill affects them further. So, my guess is that individuals who are middle aged with a female predominance as you've heard from the other speakers, including those who have been in the ICU and have a post-ICU syndrome, will be the ones who develop chronic COVID-19 syndromes.

Skipping ahead, if we learn from our example from SARS, one year out after SARS in a small sample of 107 patients on slide 21, 66%, were able to return to full time work, 74% of that group worked at the same level that they had prior to their infection, and 17% at one year had not returned to work. Their use of physical therapy and psychological services as well as medical services was significant.

And I think that the implications for post-acute COVID-19 syndromes for disability will be in the subsets of those who have limited mobility due to shortness of breath, or inflammatory joint and muscle syndromes, those who have cognitive impairment. And that may impact the ability to live independently and self-care. So, I think those are the four groups that will increase.

How much they will increase, I can't guess at this juncture, but the road ahead for us is to define the underlying pathophysiology causing the chronic COVID-19 syndromes, identify who is at risk for these syndromes, try to prevent these chronic syndromes and treat them. If it's an inflammatory syndrome, there may be therapies that are not applied in the acute syndrome that may be of assistance here.

And finally, we need to assess and address the increase in related disability. These patients do not feel that people are listening to them except for except for the press. And they have real disease, and they need our help. So, I thank you very much. And I'm going to turn it back to Dr. Del Rio.

Dr. Carlos Del Rio: Thank you so much. I appreciate your presentation tonight. We're going to proceed now, with the with the question and answer on the discussions. We have roughly in my mind about 30 to 35 minutes for the discussion. So, we're going to proceed right to it and ask some of the questions that have already come in.

So, I'm going to start first with the question about there was a question that came about could the differences in obesity rates, explain the apparent differences in the infection rate and severity of impact of COVID across geographic areas? And maybe, Mercedes maybe that's a good question for you to start. You're muted, we can't hear you.

Dr. Mercedes Carnethon: Yeah, thank you. I apologize. You know, I think that's a really thoughtful question, particularly the geographic aspects of it. We do know that there is a geographic -- that there's geographic patterning to obesity. There tend to be higher rates of obesity and lower income areas. socioeconomically, which, you know, those are socioeconomically deprived.

We're also learning a great deal about rural areas and higher rates of obesity, potentially in rural areas. It would be a little difficult, I think, to tease out the aspects of access to care as contributing to mortality and obesity when we look at geographic patterning. I believe, and my medical colleagues can speak to this.

But I believe that just as with many other chronic conditions, the more often a hospital system has an opportunity to treat that condition and become familiar with it, ideally, the outcomes improve.

In economically deprived areas where rates of obesity are likely to be higher, the hospital systems may not have the same experience in managing COVID and that could also be feeding into outcomes, and really helping to, I guess, further lead to worse outcomes among those who are obese, but I would invite me the other speakers to chime in on that.

Dr. Carlos Del Rio: Okay, well, thank you for responding. Let me move on to another question, because we have a lot of pretty interesting questions coming here today. One of the questions is, now that there is some -- now that we recognize our long-term health effects with COVID, is it considered a pre-existing condition in itself? And I don't know who wants to take that, maybe, Dr. Putrino, this a good one for you.

Dr. David Putrino: Oh, sure. It's a tough one. I mean, I think that I think that a really important element here has to harken back to, you know, what I was speaking about during my presentation, which is if we want to start thinking about considering long-term effects of COVID as pre-existing conditions, that is a slippery slope if we're not appropriate in the way that we identify who had COVID and who did not have COVID.

So, if I would say that this may be an appropriate thing to do if we follow World Health Organization guidelines of using medical history to identify individuals with presumptive positive cases of COVID-19 based on symptoms they experienced at a certain time, as opposed to PCR tests or antibody tests, but I do not think it's appropriate, if we just saying, we're just going to go by PCR tests and antibody tests.

Dr. Carlos Del Rio: Okay. That's great. (Steve), this is a question for you. Are there any guesses as to why women are more likely to have persistent symptoms?

(Steve): Yeah, Carlos, great question. And I think, well, first of all, let me just say that I was struck by these presentations and how internally consistent they were, particularly since they came from a

group of people who have diverse geographic areas and experiences and so forth. And to be honest, the fact that everybody has a very similar perspective to me, provides internal proof that that this is all real.

But anyway, the question about women? Yeah, so this, you know, we, I think another speaker mentioned this as well., although immunity is much more common in women, and their third, there is both a sex effect, and there's an age effect. And so, one might a priority to have expected that there's going to be a chronic inflammatory condition that actually arises out of this, that would be probably more common in women than men.

We've seen these in other chronic diseases, particularly rheumatologic diseases, certainly in the HIV setting, we've seen similar. So, I suspect at the end of the day, it will prove to be something related to the chronic inflammatory state that I think is quite different in women versus men, but that's a guess.

Dr. Carlos Del Rio: No, I think it's a really good guess. But again, it goes, it goes back to this whole issue of I love the term that (Judy Aberg) uses about inflammation, right, about how a lot of the progress of aging is inflammation, and a lot of what we're seeing, you know, inflammation is really something that we really, we talk a lot about it, but we truly don't truly understand how it all impacts after a disease and an infection and long term impacts of inflammation.

And I think it really talks about the need for a more robust research agenda. Dr. Carnethon, this question comes back to you. As you decide BMI is not a great measure, a very muscular person can have a high BMI and be in great shape. Is there a difference in fat tissue as a cause of high BMI versus muscle?

Dr. Mercedes Carnethon: Yeah. I'm really curious about this and have been trying to give this some thought to determine how best we could study this question. So, you know, the question comes

down to the reality that body mass index is a crude tool. It is a valuable tool, because it can be used broadly by the population and it does not require special equipment and it is merely fool proof to measure.

But what it doesn't tell us is what proportion of one's body weight to height ratio is muscle versus fat. And furthermore, when it's fat, it doesn't tell us whether it is a healthier type of fat, so healthier being, you know, the subcutaneous fat, right under the skin versus visceral fat, that would be surrounding the organs and more likely to release factors that can promote inflammation and endothelial dysfunction.

So, what puzzles me about the obesity question is on the one hand, the worst outcomes among older adults could point to me to say that, with aging, we see a loss of muscle mass and a growth of fat mass, something we call sarcopenic obesity. So, I could say, gosh, maybe it is the adipose tissue that's driving this worse, inflammatory effect and worse outcomes, but then if I could see data, to tell me whether the death rates are similar in women and men at the older ages, and I do think I could see this now, I think they're now good enough data to see this.

Because, you know, during the life course, women tend to have more adipose tissue relative to muscle than men. Yet, we see worse outcomes in men, at least early on, I think this is still persistent and that puts a little bit of a monkey wrench in my original what I would hope to have be a simple hypothesis, that it's the -- that having more muscle would be beneficial, but having more muscle is beneficial. why do we see worse mortality among men who should have more muscle?

Now with aging, perhaps that shifting a little bit and making it go away, which is why an analysis looking at differences by sex across the age range might provide a hint, I would be very curious in finding out a little bit more about the role of the adipose tissue and whether muscle could protect against certain outcomes.

But I think the reality is we don't have, we don't have good enough measures prior to illness to be able to measure this fat to muscle ratio, because if we take those measurements after somebody is already ill things may have changed. And so, I don't know how, I actually could think of way, but there's not an easy way to test this hypothesis right now.

Dr. Laurie Jacobs: If I can just add, I think that obesity is a risk factor for infection, that's very clear. Obesity has always been a risk factor for death in acute illness and in primarily pulmonary acute illness, obesity has presented a huge problem in terms of compounding restriction on lung function and lung disease in proning, in pneumonia, so I think the acute outcomes related to obesity don't necessarily predict the outcomes of the relationship of obesity to the chronic COVID-19 syndromes.

I am not entirely certain that obesity is a risk factor for product COVID-19. I am completely convinced that is a risk factor for acute COVID-19 and poor outcomes of hospitalization, I think that remains to be determined. With aging, frankly, the outcomes are poor due to comorbid conditions and the impact of the respiratory illness and not all of those individuals are obese any longer, though some of them are.

So, I'm not sure that it's playing a role even there in the oldest old population in nursing homes, or frail older individuals. So, I think we have to be very careful in thinking about what leads to an acute COVID-19 infection, and what we're observing in our minority of those patients who survive.

Dr. Carlos Del Rio: I agree. Dr. Jacobs. I think that was very well put, I'm going to then follow this question to you, and also the Dr. Auwaerter. Many that are infected are symptomatic and is there any research in terms of characteristic of those individuals, for example if somebody with COVID

experiences loss of sense of taste or smell are they more likely to have long term sequela. Is there any correlation between symptoms and sequela, basically?

Dr. Laurie Jacobs: In my experience, and the hundreds of patients that we're seeing in our clinic, I haven't seen that yet. Loss of taste and smell is as good as a COVID test to say you have COVID, but it doesn't predict the other long-term syndromes. And in terms of recovery from that symptom, it's quite variable, about a third of them get better right away, a third get better over a little bit of time, and about a third persist and having continued loss of taste and smell and I'm not sure it relates to some of the other symptoms.

Dr. Paul Auwaerter: Yes, this is Paul Auwaerter. I would entirely agree. I don't have a systematic viewpoint, but in the experience it there's not any clear-cut correlation, once you get beyond recovery phase for patients that might be in the severe and critical ill phases of illness and recuperation from such.

Dr. Carlos Del Rio: Thank you and I want to stress with what Dr. Jacobs said, and I tell people that I do in fact, have it at home, I do a rapid test at home every morning, I prepare a cup of coffee and if I can smell it, I'm good to go. Home testing is already happening in my house pretty regularly. Anyway, I'm going to move to another question.

Is it common for patients to be admitted late in the progression of disease because they did not realize your symptoms such a headache or insomnia were related to COVID and does that have anything to do with sort of late presentation?

You know, in my experience and I'll start by saying that early in the epidemic, we saw people presenting very late. Now we're seeing people present a lot earlier, there's a lot more awareness, but I don't think -- I think the late presentation led to a lot of deaths early on, I'm not sure naturally leading to chronic manifestations. But what others think?

Dr. Laurie Jacobs: So, early when COVID hit northern New Jersey, in the very first weeks, we were getting a lot of people with early stage and late stage because we didn't know what we were dealing with. I would say we've got an increasing number of cases now, but people are admitted later on and with more severe symptoms and those remaining in the city.

And so, the severity has changed, but the numbers of individuals has changed. And I lost track of the second part of your question.

Dr. Carlos Del Rio: That was permanently related to that, but if you present later, are you more likely going to have because you didn't realize you have it, are you more likely to then develop chronic conditions? Right?

Dr. Laurie Jacobs: I don't think that's true. I think that there we're going to find some underlying reason why individuals are some sense of why they're developing chronic symptoms. There's an enormous number of people with COVID-19 infections, but the chronic syndrome is much less prevalent as one of my colleagues here described. I don't know if it's 2.5%, or what percent it is, but it is a minority of patients.

We had 13,000 COVID-19 tests positive in the first three months of the pandemic here, but I have hundreds only in our clinic. So, most people go on and to do very well. Some of them were readmitted early on with continuing shortness of breath or continuing symptoms or thrombosis, after they were discharged, that caused stroke or other syndromes, pulmonary embolism, but that is all part of the acute syndrome, not part of the chronic syndrome, per se.

Dr. Carlos Del Rio: Agreed.

Dr. David Putrino: I also just have a data point of view that, you know, simply the fact that the majority of individuals who, in our cohort have now you know, knocking on 600 cases of post-acute COVID syndrome, the majority of these individuals did not require hospitalization, they did not require any additional specific, you know, COVID related treatments which leads us to the point of, you know, regardless of when it was diagnosed as COVID, it didn't really influence the care, the level of care they received, and has not influenced the fact that they did or did not then progress to post-acute COVIID syndrome.

Dr. Carlos Del Rio: Sounds good. So, I want to ask, you know, when to throw a question out to the group, but, but see, what do you think. So, as we were concluding the discussion. I think, Dr. Jacobs, you said that, and I want to emphasize that we talked about a lot of the organ chronic complications, but I think some of the most prevalent and common long-term impact we'll see is mental health.

And with depression So, the anxiety, you know, with substance abuse with increasing in alcoholism and opiate use disorder, we're going to see as a consequence of this pandemic. So, I want to talk a little bit longer discussion about the mental health complications, and how do you guys see that currently and into the future?

Dr. Laurie Jacobs: So, we've been seeing a tremendous number of psychological symptoms in our recovery clinic, but just also in general, in the community, as part of our system, similar to Dr. Putrino said at Mount Sinai. It's a funnel, and we have a big behavioral health section and part of that is just counseling through telemedicine, and part of it is psychiatric care, should it be needed, including medication, but that's the minority, the majority are wanting to talk about what's going on and I think it's all compounded by isolation.

So, it's not only that you have symptoms, and you're chronically ill, but you're at home, and you don't see anyone else and your support system is far away. And I think this all compounds to make the psychological impact of this disease very significant.

Dr. Mercedes Carnethon: And can I jump in to say that I think the psychological aspects are particularly critical for vulnerable populations, who don't have the education and possibly don't have the infrastructure to be able to connect with communities virtually, you know, and I'll give the example.

You know, thankfully, my parents are healthy, but you know, my mother has been able to enjoy social interaction with her church through Zoom, you know. She was -- a neighbor was kind enough to help her set up her computer to be able to use Zoom, so that she can stay connected.

Now, I anticipate that that is not that simple for individuals who are recovering who live in homes that don't have internet connection, where the health literacy levels aren't high enough for them to even be able to engage with telehealth in a video manner.

One of my cardiologist colleagues pointed out that for him the biggest loss of in person clinic was being able to lay eyes on the patient, to observe their fatigue, to observe some of their symptoms and I can imagine that for mental health providers, managing patients post COVID to be able to visually engage and to have regular appointments and visits you know can be done well by a video conferencing if individuals have access to that. And so I wd say that a long-term priority and strategy would be to try to ensure that mental health supports are in place for the most vulnerable populations who may not be digitally connected.

Dr. Laurie Jacobs: I would totally concur.

Male: I agree, yes, a hundred percent. The - a question comes up and this is for you, Paul. Are there currently any clinical trials -- any clinical trials representative of the U.S. population? And do the underinsured or uninsured have access to participation in clinical trials?

Dr. Paul Auwaerter: Yes. You know, this has been an issue certainly for vaccine trials. I think there have been for acute hospitalization merely because people are presenting, you know, the enrolments are occurring at centers where people are coming into the emergency room and so on and so forth. But there certainly have been efforts in vaccine trials to make sure that we have a sufficient representation of citizens across our country. And we - I know at John Hopkins, we've had outreach to communities speaking with community leaders, religious leaders trying to have questions and answers, trying to help engage as much as possible because, as you know, there is skepticism about vaccines. But this also translates to treatment trials, you know, that experimental agents and participation in vaccine -- I'm sorry -- in treatment trials is very difficult especially with an acute disease. And efforts to try to help foster a wider enrolment amongst a particular city or region. You know, there have been some 4As, but I don't know of any specific trials specifically focused in that way for acute treatments.

Male: Thank you. There's a good question here about, you know, obviously the question we're all asking ourselves, you know. When will we have conclusive-- fairly conclusive and reliable data -- about long haulers? And I will start by saying that this disease hasn't been along for too long so it's hard to talk about long-term consequences in something that has been short or less than a year with us. But anyway, I'd love to hear your opinions about this.

Dr. David Putrino: Yes, I think this is a fair question and it's an important question. Suddenly, the first thing that we need to do as a group is get some consensus on diagnostic criteria. I think that we can learn a lot from fields such as Lyme Disease, fields such as (MECFS) and (Prox) and (Disordinomia). These are groups of professionals that have come up with rigorous ways of

identifying and diagnosing the system as a syndrome. I think that is in absence of the biomarker. I think that is a really responsible and clever way to go about it.

I think that at this point we can conclusively say that it is a thing, you know, it is a syndrome. It is something that is being acknowledged with the medical consensus. The World Health Organization has acknowledged it, the NHS has acknowledged it, the CDC has kind of acknowledged it. So I think that definitively it is acknowledged as a condition. And now the next thing that we need to do is start some coordinated research on identifying biomarkers that will either give us an indication of progression of the condition or give us an indication of diagnostics or both hopefully.

Dr. Paul Auwaerter: May I jump in for a moment? This is Paul. You know, speaking for the Lyme Disease perspective and experience there, I think I would divide this into two -- two groups of thought. One is from a pure research perspective. You like to have a very well-defined group that everyone is very comfortable fix and has had the SARS CoV-2 infection. And, you know, there are people that don't have much antibody responses, but perhaps there will be other (SAs). There's already a commercial T-Cell (SA) that might serve as a marker of legitimate infection.

So you have a well-described research cohort that could be informed making sure you're not dealing with a wider set of people that might have, you know, things that are syndromic but not due to COVID. And that's been a frightful problem for both Lyme Disease and chronic-fatigue syndrome and others where you don't have anything, of course, in the syndromic disorders.

And then you have the larger clinical aspect. I think many have argued that you don't want to necessarily require a test to have someone attribute, but for research purposes it should probably be better to ((inaudible)).

Male: Yes, so there's a question here. "Please provide comments on the Pfizer vaccine effective with long and short-term side effects." I mean I can start since I'm not a Pfizer investigator but I'm one of the Moderna investigators.

I think, you know, this has been pretty exciting to have two vaccines -- both MR&A vaccines -- come out with similar results. And then 90+% efficacy in the interim analysis. I emphasize to people two things; number one, it's an interim analysis; number two, all we've heard about in both vaccines are press releases. And I don't like to do science by press release; I want to see data.

So it's very hard to comment beyond that. We need to see data to really understand it. So far, there's not a lot about side effects. But of course, and I can tell you in the population that we've - that I've enrolled, most of the side effects we've had is primarily significant pain and discomfort at the sight of injection -- primarily in the second injection. But other than that, people have tolerated very well.

So we'll have to see. But again, we need to see data. But I mean it's very encouraging to see a vaccine giving such high efficacy in their end points.

(C. Biggs): (Crouse), (C. Biggs) here; just curious. So these vaccines prevent hospitalization and mortality and death and significant disease, but not infection.

(Crosstalk)

Male: The prevention of infection is a secondary outcome, and again, when we see the data we'll know that. I mean the primary outcome is progression of the disease. So the disease, and again, I don't even know how exactly we're looking at that. We need to look at the data to see about at least one of the vaccines, and I'm kind of confused right now, I think is Moderna or maybe Pfizer says that none of the severe cases occur in the (Vaccine R).

(C. Biggs): Yes I'm just throwing out the possibility that some of these long-term consequences may still be a problem even for people who get vaccinated…

(Crosstalk)

Male: I think that's true. I think, you know, I'm not sure the vaccine is going to prevent the infection and we need to see what happens with viral loads and other things. But at the end of the day, you know, you may still see people who have developed long-term consequences even after being vaccinated. We need to understand that better.

So I mean I think there's a question here which I think is pretty interesting about - you know, we've all seen mortality rates declining across the board. But at the same time, we're seeing, you know, mortality go up in many places. I mean right now the highest mortality place in the world in actually North Dakota. The rates for mortality in North Dakota is highest in the world.

So part of it is overwhelming the healthcare system. Part of it, I do think, there's a degree of experience. I mean when you get more experienced you're better at managing the patients. And part of it is what Paul mentioned is the population is getting younger, etc.

But any comments -- any further comments about, you know, is there any specific issues in why populations are - some populations the mortality is declining versus others?

Dr. Laurie Jacobs: Well, I would comment -- this is Dr. Jacobs -- that there's a larger prevalence in disease, so the rates of mortality have declined because of the younger patient, and the most vulnerable in certain ((inaudible)) communities have the population was reduced certainly in nursing homes in the beginning. I think we have become better at caring for these patients. And now in New Jersey, unfortunately, the rates are going up and we're seeing it in the hospital again.

I will say that the number being admitted to ICU is less than the intense wave we had in the spring last year.

But I'm not sure that we have improved that much. I just think there's a larger pool of young people who have done better. I'm not sure we've made that much of an impact on the disease. Remdesivir is a very mild effect. Most of us gave steroids from the very beginning for patients in the ICU for ARDS because that's what we do with sepsis at times when we don't know what to do.

So I'm not sure the therapeutics have really moved us very far. We were pronging here in March in New Jersey. So I just think it's a shift in wider and younger patients that the mortality rate is less, but the numbers of mortality are enormous and very disturbing.

Dr. Paul Auwaerter: Yes I think the - I want to add to that which I agree with everything that was just said. But I'm sort of a proponent of the virus inoculums theories which have emerged. I think in the first wave and early on, no one knew what was happening. Healthcare workers in particular were getting high exposures of high amounts of virus. You know, now people are masking, social distancing and infections are still occurring but with lower viral inoculums and less progression of the disease, and one would hope, less of this long-term stuff. I mean so I hope those that are getting effected nowadays, yes, in addition they're younger, they have better therapies, but there may be a dose affect as well.

Male: Great. Well there's a question here I think we need to address because I think it keeps on coming up and I think we need to give clarity on this for the listeners.

You know, the question says, "It appears that there is a great variation of manifestations. Does the initial onset and treatment providing the occasional how severe specifically would we see

someone with severe or ongoing impairment, and they were not hospitalized or experiencing such acquiring care on the onset?"

Dr. David Putrino: Yes I think we got to say right now that we cannot predict long-term symptoms based on the initial presentation. Many, many of our patients have incredibly exceedingly mild symptoms when they - you know. And these are confirmed cases of post-acute COVID in that they tested positive, they have all of, you know, that they've jumped through all the hoops. And they did not go to the hospital, they did not feel the need to go to the hospital. They barely felt short of breath; their symptoms were exceedingly mild. And now, you know, if you compare some of these patients of ours now to someone who was incubated even and is going through pulmonary rehabilitation, they're more debilitated than the person going through pulmonary rehabilitation because the level of fatigue that we're seeing in this patient cohort with post-acute COVID syndrome is if I walk up a flight of stairs, I'm crashed out for the next two or three days. That's the level of debilitation we're looking at in many of these patients; either the extreme fatigue; it is inability to work, it is inability to do cognitive work in addition to physical work. And so that level of being completely debilitated compared with someone who experienced a pretty severe acute infection and is not getting on a treadmill going through their pulmonary rehab, there's no contest.

So I don't think - in my opinion from our experience from the cases that we've seen, no, we cannot predict how debilitated someone is going to be long-term based on how acutely intense their symptoms were.

Dr. Laurie Jacobs: So I would agree with Dr. Putrino. Mild disease can lead to this or severe disease. But I would reinforce the notion that the vast majority of people recover. These syndromes are seen in a minority of patients. And these syndromes, by and large, have not so far caused many mortalities. Yes, some people have died of arrhythmias, ((inaudible)), but not like you're seeing mortality from acute infection. It is these syndromes appear if they persist to cause long-term disability due to fatigue, psychological symptoms and the other conditions that we've described in

addition to those who have chronic renal disease and dialysis or have heart disease, et cetera. So I would reinforce that.

It's very hard to see into the future, to see if they will persist. But there are now growing number. There's, again, a minority, but growing number at eight months. That's a pretty long time. And these aren't people who reappear at the hospital. In fact, they feel embarrassed to call and complain, but they just feel awful. ((Inaudible)).

Dr. David Putrino: I really want to reinforce that point right back that Dr. Jacobs just made in that there have been a small amount of deaths, but it's a very small amount of deaths. And making sure that people are cleared from a cardiac perspective, making sure that people are cleared in checking their organ system systematically is really important in identifying people who are going to have life threatening issues. These are people who are having non-life threatening but very alarming issues such as cardio, the feeling of palpitations, et cetera, et cetera.

(Crosstalk)

Male: I mean let me ask a question around a mental health consequence. I mean we talked a little bit about this brain fog that some patients are experiencing. Do you think this is going to be very similar to sort of young people's sort of learning disability? I've seen a couple of young people -- college students who have been infected -- who say, "I can't go back to class, I really can't follow the class."

Anything that you've seen or heard about that?

(Crosstalk)

Dr. Laurie Jacobs: …learning disability because that has certain patterns and relates to certain parts of the brain function. This is more like a chronic delirium and encephalitis -- a general state of confusion and headache. And that we see after other viral infection sometimes as well as other illnesses. I just think we're seeing it a lot more here.

Dr. David Putrino: A hundred percent. We're managing it like a post-concussion syndrome.

Dr. Laurie Jacobs: Right.

Dr. David Putrino: That's how we're thinking about it. It can be rehabilitated. It is scary while it's happening, it's disturbing while it's happening, and it needs to be addressed. But it's addressable.

Male: So I'm going to have just each one of you because we have a couple more minutes, just say what would be your sort of next step. What is your wish list going forward of what we need to do? Maybe we'll start with Dr. Deeks and the order in which you presented. So just, Steve, can you start? I think you're muted. There you go.

Dr. Steven Deeks: My wish list - yes, you guys there? Yes, so my wish list, right, I think it was said earlier is that there has to be consensus, some kind of statement from above that this is a syndrome, this is how we're going to define it and this is how we're going to measure it. And then from that, everything flows, right. That's - then you get the cohorts to figure out who gets it -- the natural history. You get the NIH and others to invest and understanding the biology. And you get, you know, you get clinical care systems designed to actually provide support. You get the Social Security Administration who can then actually begin to provide the kind of help that they can provide. And ultimately, the industry gets involved and ((inaudible)) therapies.

Male: Excellent. Dr. Carnethon?

Dr. Mercedes Carnethon: Yes. As an epidemiologist, I really like data and I like data to be collected in as systematic a manner as possible. You know, what my wish list would be would be that we start to aggregate some of this data so that we can identify the correlates, both the behavioral correlates, the medical history correlates, even treatment correlates that might help us to identify the patterns to that we can pick up on these individuals early. And possibly, depending on what the correlates are, help to really manage those factors that appear most strongly associated with the likelihood of a prolonged syndrome. So better data collection across the board both within the hospital and post-COVID clinics, and even starting new cohort studies where we can systematically collect a set of plausible characteristics that could be associated with long-haul COVID.

Male: Excellent. How about Dr. Putrino?

Dr. David Putrino: Yes, I think first and foremost, prevention, social distancing, everyone wear a mask. I think, you know, we're belaboring the point but clearly we are not because people are not doing it. So I think we need to really get the message out that death is not the only outcome that is, you know, life altering of COVID-19 infection. And we really need to get it out there that young and healthy people won't just be okay as a result of sustaining COVID-19 infection. This is the really strong message that needs to get out because I don't think it's being said enough or often enough. And we can't support a whole lot more people getting ill and then requiring 9 to 12 months to rehabilitate and get back to preinfection functions.

So awareness has to be a big piece. Understanding, as I said before, the idea that (PCR) and antibodies should not gate access to care. These are okay measures of understanding who was sick and who was not. But they're not gospel, they are not the ((inaudible)) and indoor, and we need to make sure that everyone is cared for; not just people who have these specific biomarkers.

And then from there, total lockstep with what Dr. Mercedes Carnethon: just said. We just need data -- well collected data -- so that the epidemiologists can do their thing and actually point us toward effective care and treatment.

Male: How about you Paul? Any comments?

Dr. Paul Auwaerter: Yes, just briefly. You know, with the public health emergency and millions of people infected although a small percentage developed long-lasting problems, there may be a tremendous burden of illness and an opportunity to truly understand some of the mechanisms especially for people who look well, have no objective findings, labs are normal. But why are they so functionally impaired?

And I think much as of other conditions have really made great advances with resources applied to it. Hopefully there will be a recognition of this problem and enough funds essentially to attract the right kind of investigators after there have been, you know, registries, longitudinal cohort studies and so on with bio repositories so that we might truly understand mechanisms that might inform therapies -- different than what we've been using in the past years.

Male: Thank you. And Dr. Jacobs, why don't we conclude with you?

Dr. Laurie Jacobs: I think I would say my wish is that all of these people's wishes come true. We understand the biology, the genetics, the path to physiology, that we describe the syndromes much more carefully, that we have longitudinal data, that we understand how to rehabilitate these patients before we understand all the rest of it, and that some light is shed on this. Although it is infrequent as an outcome, the number of people who have been infected thus far with COVID-19 is enormous. And I think physicians have to recognize the syndrome. And as we get more recognition we will be able to move towards all those goals that have been mentioned.

And I want to thank everyone today for inviting us and speaking on this very important area.

Male: Yes, thank you very much. I want to thank all of you -- Dr. Deeks, Carnethon, Putrino, Carnethon and Jacobs for valuable time and incredible presentations. And the information you provided will definitely assist Social Security in strengthening their disability program.

I now want to give it over to Dr. Steve Rollins for his conclusions.

Operator: Thank you. Ladies and gentlemen...

Male: Okay, go ahead.

Operator: Thank you Ladies and Gentlemen. This concludes today's teleconference. You may disconnect.