Dr. Lekshmi Santhosh:
I'm hopeful that people will get their boosters, children will get vaccinated, folks with kids under five will soon get vaccine approval, there will be global health vaccine equity, and that we can have this pandemic simmer down and eventually go away. That is what I hope for. That is my dream.

LuAnn Heinen:
That's Dr. Lekshmi Santhosh, founder and faculty lead at the specialized OPTIMAL Clinic at UCSF for patients with persistent pulmonary symptoms after COVID infection or hospitalization. A pulmonary medicine and critical care specialist, she graduated from Harvard Medical School and completed her residency and fellowship training at UCSF. She also has a Master's in Health Professions Education, and publishes extensively on women and leadership development, clinical reasoning, and subspecialty career choice.

I'm LuAnn Heinen, and this is the Business Group on Health podcast, conversations with experts on the most important health and well-being issues facing employers.

My guest is Dr. Lekshmi Santhosh, a pulmonologist focusing on long COVID. We'll be talking about that and her conviction that great medical care starts with hearing the patient's story. Today's episode is sponsored by Spring Health, the emotional wellness provider that makes mental health services more accessible. Spring Health does this by combining clinically proven technology with high touch care navigation so that every employee has fast and easy access to the care they need.

Dr. Santhosh, welcome to the podcast. So excited you're here today.

Dr. Lekshmi Santhosh:
Thank you so much for having me. I'm delighted to be here.

LuAnn Heinen:
This is a topic that's perplexing and of great interest to our audience and to everybody. Can you explain how you came to work with people experiencing what we now call long COVID?

Dr. Lekshmi Santhosh:
Absolutely, happy to share that. I am a pulmonologist by training. I'm an adult lung doctor, but I also work in the inpatient side in the intensive care unit. I'm one of those rare doctors who works both in the hospital and in the outpatient clinic. So when my clinical chief, Dr. Leard, asked who in our group would actually be interested in following patients recovering from COVID, as we started seeing these early reports coming out of China and Italy and we knew that this was inevitably coming our way, I leapt at the opportunity because I thought I wanted to be of service and to use my skills, both inpatient and the intensive care unit seeing these patients with COVID, as well as the outpatient clinical setting to help them throughout their recovery process. That's where it all began. We started our post-COVID, post-ICU clinic, which we call the OPTIMAL Clinic. We started the planning process in March 2020, when we started hearing about this and we started seeing our first patients in May 2020.

LuAnn Heinen:
How did you define long COVID?

Dr. Lekshmi Santhosh:
This is a question that many studies and scientific groups have struggled with throughout the pandemic and fortunately the World Health Organization, the WHO, just came out with a pretty good definition a couple of weeks ago. The new term they call it is post-acute sequelae of COVID or PASC, which of course does not have the same ring to it as long COVID. Of course, long COVID is a great term as well that I really like, because it is a patient-generated term. It is a term that the patient community themselves generated to talk about their own illness experience and their own experience of what they were dealing with. The WHO definition of PASC or

long COVID, which I'll use interchangeably in our talk today, really refers to people who are about three months out from the onset of COVID-19 with symptoms that last for at least two months, and critically, they add at the end of that clause that cannot be explained by an alternative diagnosis.

I think a lot of scientists and clinicians really like this WHO definition. Of course, like any definition it is imperfect, but the reason we like it is that it's quite inclusive, it has a clear time point, and then they also have that caution that we should make sure that there's no other diagnosis that's explaining the symptom. The reason why I mentioned that is because many times when I talk to patients and families and clinicians, I emphasize that if you have recovered from COVID or your family members recover from COVID and you're experiencing new symptoms that have come up, a new rash, new headaches, new shortness of breath, something that's new in your recovery journey, don't assume that that's long COVID. It actually could be something totally unrelated. I've seen personally in our clinic, cases of metastatic cancer, cases of auto immune conditions, etc., that patients or their clinicians have actually erroneously attributed to long COVID because they weren't putting that broad thinking cap on.

LuAnn Heinen:
If someone is more than three months out from the onset of a COVID infection, let's say they're healed, they feel fine, they think they're back to normal and they have new symptoms that seem like COVID symptoms, you're saying by definition that it's not long COVID.

Dr. Lekshmi Santhosh:
I wouldn't say that necessarily. What I would say is that all of us should be cautious and should be extra thoughtful that new symptoms that arise may not necessarily be long COVID symptoms. They may be symptoms of a new process. Statistically, when you have such a huge swath of our American population, of the world population, affected by this illness, at the same time, people are going to have other things that are true, true, and unrelated. We just have to be careful and keep our thinking caps on and keep our minds broad to those possibilities.

LuAnn Heinen:
Got it. How many people experience long COVID?

Dr. Lekshmi Santhosh:
This is another challenging question without an easy answer, because many of the research studies on this topic to identify what is the prevalence or incidents or percentage of people affected, varies widely because there wasn't a broadly accepted definition, at that point in time, until we got this WHO definition. Studies have ranged from everywhere between 2% to 90% incidents, depending on what population you look at. When you look at the larger studies, the more kind of rigorously done studies, those seem to vary between 5 to 20%. But when you think about 5 to 20% of millions of Americans, that's a huge number of our worldwide population that is being affected by this.

LuAnn Heinen:
When you're in the long COVID clinic, what are the most common symptoms you're seeing?

Dr. Lekshmi Santhosh:
There are many symptoms that can manifest. Just as COVID-19 can affect multiple organs in our body, in the earlier acute setting, similarly, in this chronic or long COVID setting, multiple organ systems in our body are affected. The most common ones that we see that are supported by the research studies are shortness of breath, cough, fatigue. Those kind of are the top three, but also we're seeing that sometimes people have kind of clusters of symptoms or as we call it, ‘phenotypes.’ What that means is that some people may seem to have a little bit more cardiac or lung symptoms. Some people have a lot of chest pain and shortness of breath. Whereas other people seem to have more neurological symptoms like headaches, brain fog, or difficulties with concentration. Some people have an alternate between prominent symptoms like the loss of smell, loss of

taste, while others have more GI symptoms. It really depends and one thing that I often say is that there is no one long COVID experience. What I mean by that is, just as I've shared that people have different symptoms, the other thing that's important to know is that that's a huge spectrum, a huge range of severity of illness. You can have an elderly person who's frail, who is admitted to the hospital, admitted to the intensive care unit, who's getting out and recovering, that person is going to have very different symptom collection than somebody who is a previously young, fit, healthy, marathon runner, who also has new debilitating symptoms, even if they weren't hospitalized. There's a huge spectrum of severity of illness, both in the acute, early setting, as well as in this persistent symptom setting, and therefore we can't really treat all these individuals the same. We really have to adopt an individualistic approach.

LuAnn Heinen:
Isn't it fair to say that anxiety and other mental health symptoms are commonly associated with long COVID? I'm wondering if that's true, is it just as they would be with any potentially life altering diagnosis, something that's frightening and scary and it creates anxiety in anyone, or is it something more than that?

Dr. Lekshmi Santhosh:
We are still learning a lot about the effects of COVID-19 on the brain. The brain has always been a little bit of a black box for scientists and researchers. It's so hard. We are seeing in many studies that there's increased incidents of both neurologic symptoms and psychiatric symptoms like PTSD, anxiety, depression, psychosis, sometimes after COVID-19. Again, that varies depending on if that person was hospitalized in the hospital, if they were not hospitalized, but we are seeing an increased symptom burden of mental health conditions throughout the world population, of course, in these pandemic times, but it's increased in people who have COVID-19 as well. I always tell people that I believe patients, I believe you, I believe your symptoms and your symptoms are valid. Symptoms include symptoms like chest pain, and some symptoms can include things like depression, anxiety, and PTSD, and both of those are equally valid and both of those should be treated equally.

We know that our mental health and our physical health can affect each other as well, which is why a holistic treatment approach, you know, treating your chest pain, shortness of breath, and treating your anxiety and depression is equally important. Mental health coverage and care of mental health conditions is imperative during this pandemic, especially for people who have gone through long COVID. I will say this is particularly devastating for people who have been hospitalized, because not only are you dealing with the challenges of coping with the pandemic, like everyone, the challenges of COVID on mental health are also significant. There's a lot of stigma still around the infections. There's a lot of isolation. You have this quarantine period, you have this isolation period that is very detrimental to mental health. On top of that, you can have the virus effects on a physiologic, virus effects in the brain as well.

Particularly for people who are hospitalized, they're truly isolated where you can't have hospital visitors. You see your doctors, nurses, physical therapists. You really only see their eyes because they're in full personal protective equipment and you can't see their faces. You can barely hear them. For people who English is not their first language, they have difficulties with communication. The mental health impact is huge of COVID on the world, of course, but particularly on people afflicted with COVID and particularly on people who have been hospitalized with COVID. Some of the leading researchers in the field have said that being hospitalized in COVID times is like a ‘delirium factory.’ That's a quote from Dr. Wes Ely. He is a world-class researcher at Vanderbilt University who studies ICU's impact on brain health and on this phenomenon called delirium. So really being hospitalized in COVID times is a setup for having mental health impacts, neurological impacts, and physical impacts, and all of those should be treated holistically.

LuAnn Heinen:
Thank you for that. It's so sad. We've had so many of those stories about the impact on ICU patients and also on their care providers and how incredibly challenging it is for all of you who work in that space. Let's turn to treatments for people who are vaccinated and who aren't vaccinated, who are struggling with long COVID.

Dr. Lekshmi Santhosh:
For anyone who's had COVID, one of the things that we're urging them to do is still get the vaccine. The reason why is because your natural immunity actually wanes, it goes down after time, particularly after that three-month mark. Even if you've had COVID, it's not too late to get vaccinated. In fact, we encourage you to get vaccinated even if you've had COVID already. There's no time limit to wait or anything like that. You can do it as soon as you're out of isolation. For people who've had those monoclonal antibody infusions, the ones who have to go to the infusion center, those folks have to wait a little bit longer to get the vaccine, about a 90-day period for that because of side effects and because you don't want it to interfere with the antibody treatment. But otherwise, anyone who's had COVID should still get the vaccine to protect you from getting reinfected, which definitely happens and I've definitely seen that happen where people have had COVID, they didn't get the vaccine, and they get COVID again. Often it can be more severe the second time around. I would urge you that "natural immunity" is not enough, that actually the immunity of the vaccine is much more longer lasting than your natural immunity, and that it's not too late, you can still get the vaccine. You should get the vaccine. It will protect you from getting reinfected, which is a thing, and can be worse.

The second part of your question is to treatments in general. Like I mentioned, there is no one long COVID experience because people are going to have different symptom clusters. What the CDC recommends, which I really like in their guidance, is they say that treatment should really be symptom focused. As of now, we don't have sadly one pill, one infusion, one protocol to treat long COVID, per se. What we're doing is aggressively treating people's symptoms. If they have chest pain and shortness of breath, let's treat that, let's investigate that and treat that. If they have headaches and fatigue, let's treat that. If they have brain fog, let's treat that. If they have weakness after hospitalization or an ICU stay, let's treat that. If they have anxiety or depression, let's treat that. It's really a symptom-focused treatment approach.

LuAnn Heinen:
I've read that rest, frequent breaks, and personal energy management are universally offered or suggested. Do you see that in your practice? Is that accurate?

Dr. Lekshmi Santhosh:
I think what you're alluding to is that some people with long COVID have a cluster of symptoms that has significant overlap with chronic fatigue syndrome or myalgic encephalomyelitis. Some of those patients will have this classic symptom that they call post-exertional malaise. What that means is unlike the traditional paradigm of just exercise a bit more every single day to build up your tolerance, to build up your endurance, instead, that traditional classical advice could be harmful for the subset of patients who have this chronic fatigue syndrome overlap, where in fact excessive exercise or excessive activity can trigger actually a relapse of symptoms. Those patients actually have kind of a waxing and waning, kind of undulating course that gets better, gets worse, there might be flares, or there might be relapses. For that particular symptom, and for that particular patient population who's experiencing that, definitely we have learned from the chronic fatigue syndrome patient community and practitioners, that the concept of resting and pacing yourself is critically important. That doesn't mean be bed bound in your home forever. What it really means, and I talk to patients about this, is finding your activity threshold or finding your floor. What activity can you do that you know comfortably you can do without any difficulty that won't trigger a relapse? Is that walking for five minutes? Okay, so you can stick with walking for five minutes and really master that walking for five minutes every single day for a week or two, before you challenge yourself, only very gradually to say, walk for six minutes. Then once you've mastered that for a week or two, you challenge yourself very gradually, and for whatever reason, if you get up to 10 minutes and you have a relapse, it's not good. Then you know to drop that activity, so rest and pace. That is really, really important. Again, that advice, that overlap of chronic fatigue syndrome and long COVID, is not in everyone, but for people who have that overlap, this concept of resting and pacing to manage post-exertional fatigue or post-exertional malaise is really important.

LuAnn Heinen:
That’s so helpful. I'm wondering what advice you'd offer to people struggling with what may be long COVID, but they're not able to access a specialized long COVID center, such as you have at UCSF or I know exists at Mount Sinai.

Dr. Lekshmi Santhosh:
What I urge patients and families is to really think about what is the most bothersome symptom to you right now, and to ask for a specialist who deals with that. For example, if headaches are really the worst symptom for you right now, ask to see a neurology specialist. If shortness of breath is the worst symptom, ask to see a pulmonary specialist. If chest pain is the worst symptom, ask to see a heart specialist. That's what you can do if you don't have a comprehensive COVID clinic in your area.

LuAnn Heinen:
What do you think about how busy primary care clinics best serve long COVID patients? I mean, in terms of chronic disease management support, are they set up to offer that? What about a role for virtual care, self-monitoring, or are there other strategies that come to mind?

Dr. Lekshmi Santhosh:
Obviously, our health care system in America is really not a system per se. It's quite episodic care. It's quite diseased focused. We excel at acute management, at hospitalization, and for chronic disease management, we have a lot of room to do better. What works well in centers of excellence like ours is that we have a physical therapist embedded in our clinic. We have a social worker who helps with disability paperwork, embedded in our clinic. We have mental health support that is accessible to our clinic. We have sub-specialists like neurology, geriatrics, etc., as I mentioned, that are one call away from us as opposed to staying in a queue with hundreds of other referrals. That is the challenging part where when you look at our fragmented health care system, it's really not set up to address a huge burden of disease like we're experiencing right now. So what can we do within the constraints of our health care system and the constraints of what we have right now in the absence of holistic care everywhere? What we can do is try to build our capacity.

Many other clinicians in this space, just like myself, spend a lot of time on outreach. We do a lot of education to primary care providers, to community health centers, to clinicians outside of the ivory tower, to basically spread this expertise, spread this knowledge, and limit harmful practices, limit non evidence-based care. The other thing to be aware of is that if it sounds too good to be true, it probably is. What I mean by that is that unfortunately, because this is an area of uncertainty and ongoing research, right, long COVID, because of that unfortunately, there's a lot of unscrupulous people who are preying on patients’ vulnerabilities and fears and offering “cures” - long COVID resort experience, infuse these five vitamins and you'll be fine through IV. There's a lot of quackery out there and that can be very harmful to patients and also erode trust between patients and the medical community.

I always tell people to be skeptical of misinformation, to vet information with their doctor, to ask their practitioner, their primary care provider, about is this a reliable resource, is this a reliable treatment, have you heard of this, etc. In the meantime, we're trying to build capacity, build information, publish articles and how-

tos to spread awareness. One of the things that I did with colleagues from Johns Hopkins University who are close collaborators of ours, from who we learned a lot about how to set up our long COVID clinic, is we published an article together, basically a how-to guide on how to establish a clinic like ours in the journal CHEST. That is a how-to guide for different community health systems, academic medical centers, community hospitals, etc., to try to build the nuts and bolts of consolidating this care under one roof, to make it more patient centered, and potentially to save costs right down the line to consolidate that care. We even put out our electronic medical record templates that you can download and use so that people are not recreating the wheel and not reinventing the wheel.

LuAnn Heinen:
Is it unusual to have a condition like COVID that is relevant to so many specialists? I mean, originally we thought about infectious disease, pulmonology is central to it, and you've mentioned cardiology, obviously mental health and psychiatry. Is there anything unique about COVID in that regard?

Dr. Lekshmi Santhosh:
I'm glad you asked. The closest analogy that we have that many of these long COVID clinics are based upon is this framework or this experience called post-intensive care syndrome. Post-intensive care syndrome or PICS refers to the phenomena that when people are recovering from being hospitalized in the ICU, people often will have issues with four domains: physical health, cognitive health, mental health, and pulmonary health or lung health. What post-intensive care syndrome clinics do is they ask systematically and provide systematic support, holistic support, to all of those four. Because if you don't ask, people may not volunteer that, and again, they're all connected - your physical health, cognitive health, mental health, pulmonary health - are all connected. We really have to treat them all and manage them all. Many clinics like ours are actually based on that post-intensive care framework, even though not all patients with COVID, in fact a minority of patients with COVID are in the ICU, we know that many of them will suffer from issues in that constellation of domains, as I mentioned - physical, pulmonary, cognitive, and neurological and psychological. So asking holistically about those is important. Many universities, even before COVID hit, had dedicated post-intensive care clinics that they pivoted to long COVID clinics, because they already had networks where they had a psychologist embedded, they had a social worker embedded, or pharmacy embedded. This was a very natural, organic pivot.

LuAnn Heinen:
Very interesting. Can you tell me about individual patient recoveries? Is there good news there? Are you seeing people get over long COVID and especially those frightening cognitive symptoms?

Dr. Lekshmi Santhosh:
What I tell patients and clinicians is that to not lose hope. That most people are getting better over time. That is what the research shows and that is what our experience shows, too. These are scary stories, absolutely. With support, with recovery, with treatment, people can get better, and so to not lose hope. The pace of that recovery, the trajectories of that recovery, may look different for different individuals, which is challenging because currently it's hard for me to predict. We still don't have the scientific tools to predict you, Mr. Smith, are going to recover within six weeks, and you'll be back to normal. Whereas you, Mrs. Smith, are going to take about 12 weeks. We just don't have that information. We don't have that crystal ball. It really is often a very individualized recovery journey and recovery trajectory. Early on in the pandemic, I was hearing from even our own occupational health colleagues, right? People who deal with doctors and nurses who are sick, oh gosh, you know, they just need to get back to work right away. They're trying to get out of work. That is simply not true. What we know is that different people have different paces of recovery, different trajectories of recovery, because, as I mentioned earlier, there is no one long COVID experience.

LuAnn Heinen:
Yeah, so there's no one profile and it does create a challenge for employers because long COVID does affect working age people, even maybe disproportionately compared to older people. Maybe older people are more

likely to get COVID, but my understanding is that younger people may be more likely to experience long COVID.

Dr. Lekshmi Santhosh:
It is very tough. It is very tough because we're seeing a huge chunk of our working age population, as you mentioned, be dealing with long-term issues like new disability, new cognitive impacts where people may need temporary accommodations, people leaving the workforce altogether. In addition to that, there's of course the regular pandemic stressors of difficulties with child care and difficulties with elder care. You have so many different layers of stressors for employees and employers, so it is quite, quite challenging.

LuAnn Heinen:
Are there any policies or practices that you'd recommend to employers? Anything you've seen as a model?

Dr. Lekshmi Santhosh:
Yes, I think a couple of things. One thing that I would recommend is reassuring folks that you believe them, that you believe their symptoms, and that you value them as employees, and that you want to support them to return to work. I think when people get into a very negative antagonistic relationship with their employer, where it becomes kind of a, he said, she said. They don't believe me. They think I'm making it up. That's really tough and that erodes trust. Secondly, is prevention is way better than cure. Anything employers can do to incentivize vaccination. We now have the best way to prevent long COVID, is to not get COVID at all. Now we have a great tool at our disposal to try to minimize COVID. Ensuring that employees have protected time, have sick time, have dedicated space and time, feel reassured that they can go get the vaccine, do on-site vaccination drives, incentivize vaccination, you know, make it a gamification of vaccination, have happy stories of people who got vaccinated and they're fun. Now with the kids getting online, getting vaccinated, encouraging people to get their whole family vaccinated. Anything that employers can do to encourage vaccination and encourage prevention of COVID is way better than losing employees later to long COVID or to COVID related complications.

LuAnn Heinen:
There's a vocal and active advocacy community around long COVID. What does the patient voice contribute to the research agenda, to the patient experience in health care? Talk a little bit about that.

Dr. Lekshmi Santhosh:
It's tremendous. The patient experience, the patient voice, the patient community has been tremendous. The patient community has been amazing at partnering with research, at raising awareness about this condition, at de-stigmatizing this condition, at like we mentioned, coining the very name for this condition of long COVID, that's a patient-coined term. So extremely helpful. I tell my patients that peer support, engaging in communities of peer support, the biggest two communities that are out there on Survivor Corps and Body Politic. Those are just two of the many, many peer communities available online, on social media. Peer support is tremendous, especially in this pandemic where we're all isolated. Knowing that someone else is going through this experience, knowing that you're not alone, is invaluable. Like you mentioned, patients are leading up in a way by advocating for more research, advocating for more funding, saying what they want to hear, raising the alarm about new symptoms, things like that.

LuAnn Heinen:
That is great and so helpful to people who are going through this challenge. Recent articles have also highlighted a potential tension between activist groups and the medical and research establishment. Is that something you're seeing?

Dr. Lekshmi Santhosh:
It’s a really good question. I think that we sometimes will see prominent voices or disagreements publicly, on social media, or with controversial articles and in the news, etc. I do think that is more rare than what's

commonly experienced and seen. I think most commonly this is a spirit of mutual respect, mutual collaboration, mutual trust. Of course, there have been instances where that respect has been broached, that trust has been broached, and then it's upsetting, it's distressing, of course. But I am hopeful that actually the research communities, the clinician communities, the patient communities, have done so much work together, have collaborated so well together, so I'm hopeful that those disagreements, those broaches of trusts, cannot be irrevocable and that those can be overcome, and that mutual collaboration respect can continue.

LuAnn Heinen:
Right, so much to be gained from collaboration and cooperation and sharing. How hopeful are you that long COVID as a syndrome will fade away or will we continue to be challenged with lingering effects of this like other post viral infections?

Dr. Lekshmi Santhosh:
In my profession, what we say is we hope for the best and we prepare for the worst. I'm hopeful that people will get their boosters, children will get vaccinated, folks with kids under five will soon get vaccine approval, there will be global health vaccine equity, and that we can have this pandemic simmer down and eventually go away. That is what I hope for. That is my dream. I would love to close down this long COVID clinic and continue seeing patients with post-intensive care syndrome in a post ICU clinic. However, we also have to prepare for the worst. We have to prepare that if there's a critical mass of people who will not get vaccinated, and if that's a large critical mass of people who will not get vaccinated, that this will be a long-term pandemic where this is going to drag on for years, because the virus is still finding hosts available, and then we'll still be dealing with COVID and we'll still be dealing with long COVID, as well. I'm hopeful for the best, but we're preparing for the worst. My take home is, of course, get the vaccine, get your friends, get your employees, get your relatives to get the vaccine. That's our ticket out of this.

LuAnn Heinen:
Thank you, Lekshmi, so much. This was a wonderful conversation. I so appreciate having you on the podcast.

Dr. Lekshmi Santhosh:
Thanks so much for your time and for your great questions.

LuAnn Heinen:
I've been speaking with Dr. Lekshmi Santhosh, pulmonologist and intensivist at UCSF, where she founded one of the first post-COVID, post-ICU clinics, for long COVID patients.

I’m LuAnn Heinen. This podcast is produced by Business Group on Health, with Connected Social Media. If you're listening on Apple Podcasts and like what you heard, please rate us today and leave a review.