Ruth Adewuya, MD (host):

Hello, you're listening to Stanford Medcast. Stanford CME's Podcast where we bring you insights from the world's leading physicians and scientists. If you're new here, consider subscribing to listen to more free episodes coming your way. I am your host, Dr. Ruth Adewuya. This episode is part of the COVID-19 mini series addressing up-to-date insights on COVID-19. In today's conversation, I'm joined by Dr. Michael Snyder, an American genomicist, systems biologist and entrepreneur. He is the Stanford B. Ascherman Professor and Chair of Genetics, and Director of Genomics and Personalized Medicine at Stanford University's School of Medicine.

Ruth Adewuya, MD (host):

I'm also joined by Dr. Tejaswini Mishra, a research scientist and a post-doctoral research fellow. Her interests lie at the intersection of biomedical research, precision medicine and bioinformatics. I am very pleased to have doctors Michael Snyder and Dr. Tejaswini Mishra with me today to share their insights on the use of wearables, especially in COVID-19. Thank you both for joining me today.

Tejaswini Mishra, PhD:

Thank you for having us.

Ruth Adewuya, MD (host):

A great place for us to start is maybe to ask the question first to you, Michael, and then Tejas is, why are we looking at wearables as a mechanism for early detection of disease?

Michael Snyder PhD:

Well, it's because they measure you 24/7. They're really powerful devices when you think about it. They make 200,000 measurements on you of all types. They're measuring your physiology all the time, things like resting heart rate, heart rate variability, skin temperature, even your respiration rate. So, all kinds of measurements can be made from a wearable. As such, then they can tell when things are going off. So first signs of illness that can get picked up, because you'll see a shift from people's personal baselines.

Michael Snyder PhD:

If you think about it, this is very much like your car. Your car has a dashboard and it has all kinds of signals when things aren't going well. Your engine light might go off, might be running low on gas. Other kinds of events can be occurring. You can't imagine driving a car without a dashboard. If you think about for people, that's what we do all the time. The only sensors we use are internal sensors, and quite frankly, they're a bit slow. These wearables really provide an opportunity to be sensing you all the time and giving you real-time feedback just like your car dashboard, and we think that's very, very powerful.

Tejaswini Mishra, PhD:

Yeah. As Mike was saying, these devices measure things continuously, and so, wearables measure things in a real-time continuous and its fast at monitoring. All you have to do is really just wear a wristwatch and the device is continuously measuring. If you think of a clinical test, it's sort of a one-time snapshot where you go into the doctor's office and you'll find out whether you're sick right now, but what wearables give you is just this continuous information and you don't really have to do anything again. You just have to wear it. We think of these as sort of digital vital signs, and as Mike likes to say, it's kind of like using a thermometer where it'll tell you that your temperature is high and you've got a fever, but

you might not know exactly why, but if they tell you that something is wrong. There's somethings going on.

Ruth Adewuya, MD (host):

Michael, I listened to a lecture that you gave, I think for Medicine Grand Rounds, where you talked about your own background for utilizing wearables as a mechanism for early detection for you personally. Can you tell us a little bit about that story?

Michael Snyder PhD:

Sure. Well, backing up even one notch, I think the way we practice help these days is quite flawed. That's really sick care. We don't spend enough time trying to keep people healthy. The wearables project really stems from that, where we've been using advanced technologies and big data to follow people while they're healthy with the goal of keeping them healthy. We got very interested in wearables back at a times, it's probably about seven or eight years ago, when these are mostly being used as fitness trackers and people put them on, they'd wear them for three months and then they'd understand the patterns and throw them in a drawer. We realized that they're actually pretty powerful physiology monitors. So, we put them on me and a small cohort of about 100 people we were following. I think it was about a year into the study.

Michael Snyder PhD:

I got Lyme disease and the way I figured it out was from my smartwatch and something called a pulse-ox where actually my resting heart rate jumped up and my blood oxygen dropped. I later learned my skin temperature changed again, all measurable with these wearable devices. That told me before symptoms even, that something was wrong, that something was up. I later got a low grade fever, got measured and sure enough, it was Lyme disease, but it was my smartwatch that clued me in that something was wrong. That prompted us to look at a lot of data we had collected at the time and we realized that look at my data and that of several other people's, that every time someone got ill, even if they were asymptomatic and that part's important, even if they were asymptomatic, we could see this jump up in heart rate prior to symptoms.

Michael Snyder PhD:

So that we think is a big deal. It tells you something's going on before you realize you're ill. That's really how we got started again from Lyme disease and then studying regular respiratory viral infections, and then along came COVID. As you might imagine, we were building out the study further, building an infrastructure to be able to follow people in real time, which is not trivial. We were also trying to improve the algorithms and then COVID came and sure enough, as you might imagine, we just ramped up full blast.

Ruth Adewuya, MD (host):

How was that conversation with your clinician when you said, "Okay, I've come up with this based off of what I've ascertained from wearables." Because I imagine that could have been a new conversation with your personal physician, right? Or how did that go?

Michael Snyder PhD:

It really was, yeah. As you might imagine, I showed up and kind of warned him ahead of time it might be in Lyme because I had been in a Lyme infested area two weeks earlier. I kind of warned him that there was a good chance this is Lyme, just because of the timing. When he went in and he measured me and saw my immune cells were up that yep, you have some sort of bacterial infection. He recommended penicillin. And of course I said, well, I think I need doxycycline, which is what you take for a Lyme, and I don't think he was very pleased to be perfectly honest. He seemed a little put off to say the least. But he did give in, and I kept saying, I need this. And he was about to go away and I didn't want to be sick at the time. So, he did give in and gave me doxycycline and it cleared it right up.

Michael Snyder PhD:

When I got back, I got measured and true enough, it was Lyme, and it's a very well controlled experiment because I had given blood before I'd even gotten the symptoms. I think he was a little surprised and even when we first presented the surround to folks about how to use wearables for illness, the reaction was pretty, not so positive actually from physicians. Let's face it. Medicine is pretty conservative business, and these folks really didn't like the idea. The first push back because they'll say, well, actually these devices aren't that accurate and I would have to say, well, actually, they're more accurate than what you're measuring in a physician's office because they're measuring you 24/7. They're much more consistent, much more reproducible than what you'll measure in a physician's office back to what Teja said. I think the medicine's conservative, but that's what we're trying to change.

Ruth Adewuya, MD (host):

That's fantastic and I think it's such a powerful story of how something that is ubiquitous in a way can be utilized in medicine. Let's talk about the COVID-19 infectious disease study around wearables and Tejas, I'm wondering if you could set the stage up for us in terms of what was your method there? What were you trying to achieve? What were you studying?

Tejaswini Mishra, PhD:

The background for all of this was just us realizing that you can use wearables for Lyme disease. When COVID hit, we just immediately realized that you can use it to do early detection and diagnostics for COVID-19. The idea for the study was that we would recruit a bunch of people that have smart watches and then look at their heart rate and steps and sleep data and see if we are able to detect significant elevations in heart rate prior to symptom onset for COVID-19. So, we collect all of this data from them about symptoms and their diagnosis date, and also these wearables data through our custom study app, the MyPHD app, and develop algorithms, and then see whether we are able to detect a significant elevation in heart rate before or at symptom onset.

Michael Snyder PhD:

What was very reassuring to us as we launched this study was the very first participant who signed up, who had COVID it turns out, when we looked at their data, we could see this jump up in resting heart rate signal nine and a half days before they reported symptoms. It was very, very clear signals. I think that told us we're on the right track. The wearables would be a great way for following when people are getting ill presymptomatically. Then we went on to show that 26 of 32. So it was 81% of folks had this jump up in signal, and so we think it can be a good general mechanism for following people who are getting ill. So on average, four days before people are getting symptoms, they get this jump up in signal, which we can pick up. We think that's quite powerful because then we can potentially alert people so that they're not running around spreading this illness while they're in this pre-symptomatic period.

Ruth Adewuya, MD (host):

Were you using a particular type of wearable?

Tejaswini Mishra, PhD:

Most of our study participants were using Fitbit. We like to be device agnostic, our algorithms work on all of the devices, but for the study that we published, just the reality was that a large number of the participants had Fitbit. So we developed our algorithms for the Fitbit devices, but now we've expanded into Apple Watch and Garmin as well, and hopefully to other devices as well.

Ruth Adewuya, MD (host):

What was most encouraging to you in looking at the data from this study and Michael I'll start with you before I go to Tejas?

Michael Snyder PhD:

Yeah, well, I guess two things. One is, in the first part of the study, and it won't come to what we're doing now, but in the first part of the study, the fact that we could see this jump up in signal in most people. So like you say, 81% of people gave a positive signal and a median of four days before symptoms. That was very encouraging. The second part, which wasn't so trivial, it was how do we set up an online alarming system or online detection system. It's fine to go retrospectively say, yeah, we see how he got ill, but if we really want to have impact, what we want to do is tell you in real time, if you're getting ill. We devised some algorithms to be able to do just that. That they follow you in real time, they follow your normal baseline on an hour by hour basis, and if you get a jump up over several hours, that's statistically significant with our algorithms, it can actually ping you, and so we could show that. That census could really work as a potential alarming system.

Tejaswini Mishra, PhD:

For me personally, also the potential of this is exciting. Thinking of where it's going to be used, by consumers, by healthcare providers? How this information is going to be used by maybe public health officials, despite emerging outbreaks to bring back employees into the workforce and augment sort of standard COVID testing or PCR testing with this type of tests as well. That stuff for me is definitely really exciting to think about.

Ruth Adewuya, MD (host):

What were the challenges though, with setting such a study up?

Michael Snyder PhD:

Getting the data, actually we'd like to even get more data. It turns out some companies are really great at sharing data and others, not so great. In the end we didn't even get all the data we wanted. That is to say, we built a lot around resting heart rate and steps and sleep because those were the data we could get, but we know there's other data types out there that we are going in and some which we're now getting, but at the time we weren't able to get it. So sharing data was a big one.

Michael Snyder PhD:

The other is the privacy. It's interesting. I hate to say it, but the IRB's they're pretty challenging on us. They're worried about how sharing of data, how secure is it, all those stuff. We actually have spent a lot

of time over the last several years, building very, very secure systems. People aren't used to doing wearable study. I think they didn't really know how to evaluate us, even though we were hyper secure. There was just getting IRB approval and then scaling the infrastructure, which is where we're going now and I can talk about that more in a minute.

Ruth Adewuya, MD (host):

Yeah, no, that's a great segue to that. What are you currently doing with the study? What's next around this initiative?

Michael Snyder PhD:

Yeah, we're hitting what we call phase two, which is where we're now alarming people. Before we were collecting data, proving our algorithms, trying to get them optimized. Now we're hitting the phase of the study where we want to tell you, we see something's off. There's a number of challenges there. One is that you needed infrastructure. Imagine you're trying to pull in data on tens of millions of people. That's what we want to do in real time and ping them back, that something's on. We had to improve our algorithms even further, so they didn't break the bank, so to speak in terms of costs, which we've done. We've just built this whole infrastructure for there being able to do it. We did have to get IRB approval, which we did, and now it's working even some of the first people who have come in, we've shown that the alarms are going out before they've reported symptoms.

Michael Snyder PhD:

In fact, we do think this is working in real time. Another challenge is that we know it works for detecting COVID. It's not specific for COVID, as I mentioned earlier, it will detect other kinds of viral infections too. In fact, we've seen that from this new part of the study we've rolled as well, but we want to be able to filter out other kinds of events too. There are other things that can trigger these alarms. They're not that common, but they're there. For example, if you drink too much, not just two drinks for dinner, two wine glasses, but if you really tied one on and you were hang over the next day. Your heart rate may still be high and that may trigger an alarm. Or if you go hiking in the mountains, your elevation will increase your heart rates.

Michael Snyder PhD:

There other things that can trigger the alarm. That's why we need your data. We're trying to improve our algorithms so that we can filter the different kinds of events. This looks like a really infectious disease event, that looks like you overexercised and it lingered for several days. So again, modest things that trigger your heart rate won't do it, but if you do something like a marathon, that will trigger the alarm in the subsequent days. So we want to catch all that.

Ruth Adewuya, MD (host):

Is it essentially that in this phase two, you're trying to look at, should I say sensitivity or specificity of the signal? Is that essentially what you're trying to achieve in this phase?

Michael Snyder PhD:

Yeah. We want to improve the sensitivity and the specificity. I think these are real events. Every time your heart rate does jump up, it's signaling something real is going on. We'd like to just distinguish that. Well, this is a stress, psychological stress versus, this was really an infection versus say you drank too

much last night. It'd be nice to distinguish those possibilities if we can, because quite frankly, all that [inaudible 00:15:55] they'll trigger different kinds of alarms, when we want to report back. Again, these are really health monitoring systems we're trying to build. If we can distinguish the kinds of events going on, we can signal to the person to ultimately seek the appropriate health.

Tejaswini Mishra, PhD:

One thing we didn't mention earlier is that in the phase one of our study, one of the categories of people that we had trouble detecting COVID was people that had lung disease. I'm really excited to see as we scale up and we get more and more people in the study, are we able to do this just for sort of healthy people or people who are on various types of medications for various chronic illnesses, because that's kind of the reality is that people come in with all sorts of comorbidities and how well we're able to detect COVID and look at the sensitivity and specificity in all of these populations, I think is also really important.

Ruth Adewuya, MD (host):

What would you say to a physician, a healthcare provider around the use of wearables and medicine?

Michael Snyder PhD:

Get on the train because you're going to miss it. Otherwise, this is where everything's going and don't be so afraid of these technologies. These technologies, they're not going to put you out of business, they're going to help you. This information can relay back to you before your patient shows up in the doctor's office with the parameters already distilled there. Some of them are going to be much, much more accurate than what you measure in a physician's office and heart rate is a good example. When I go get my heart rate measured in a clinician's office, it can vary by as much as 40 beats a minute, depending on what's going on. Depending whether I rode my bike or drove or various things, or how quickly they took the measurement after I arrived, all that impacts things. But if I get my heart rate, first thing in the morning, it's pretty consistent except on a meal, something will shift. These devices, they can really augment healthcare and it's really the future.

Tejaswini Mishra, PhD:

We're in the research phase right now. I haven't seen any sort of standard medical care using wearables on a very sort of large scale basis. But to medical providers, I would say it's coming and we want to work together and do these research studies in a way where we can bring them into the healthcare setting, and that's really what we need to figure out is once we've shown that you can do diagnostic monitoring, you can do prognostic monitoring. How do we then incorporate them into kind of regular healthcare settings? That's also something to think about.

Ruth Adewuya, MD (host):

I think it's a great opportunity for healthcare providers to partner with folks like you, who are doing their research in order to enhance the work that we're doing in medicine. I'm really excited to see more of what you do and how it can influence medicine and potentially change the face of how we approach medicine and patient care. So again, thank you both for your time today.

Michael Snyder PhD:

Thanks for having us.

Tejaswini Mishra, PhD:

Thank you for having us.

Ruth Adewuya, MD (host):

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