Dr. Brian Walitt
Behind the Mask
July 29 2021

Barr: Good afternoon. Today is July 29, 2021. My name is Gabrielle Barr, and I'm the archivist at the Office of NIH History and Stetten Museum. Today, I have the pleasure of speaking with Dr. Brian Walitt. Dr. Walitt is the Medical Officer in the Symptom Management Branch at the National Institute of Nursing Research [NINR], and today he's going to be speaking about COVID symptoms and long-haul symptoms. Thank you for being with me. [In 10/21, Dr. Walitt left NINR to become a Supervisory Physician at the National Institute of Neurological Disorders and Stroke (NINDS), where he continued this effort.]

Walitt: My pleasure.

Barr: One of my first questions is: what sorts of chronic pain and symptoms do those with COVID-19 or those who just recovered from COVID-19 experience?

Walitt: All right. Those sorts of details are starting to truly emerge now. For acute COVID-19, a lot of headaches and neuropathic pains have been associated with the acute onset. But now that people are having problems after their infections, it turns out that a variety of different types of pains are being seen. Headaches tend to still dominate the picture, but we're seeing a fair bit of organ specific pain like gastrointestinal pain. Some people have chest pain; some people will find that they have pain all over. In our own particular cohort, it looks like around 35 percent of the individuals with problems would probably meet fibromyalgia criteria if one were to look, and of course there are ongoing neuropathic problems and ongoing pain from the acute issues. If you had a stroke with pain, you continue to have that; if you had a heart attack with pain or pericarditis with pain, you continue to sort of carry those with you. But I think a lot of headaches and generalized musculoskeletal pain will be pretty common afterwards.

Barr: Were you surprised at the spectrum of conditions that people are dealing with afterwards? You know gastroenterology pain and headaches; they seem very different; so were you surprised by that?

Walitt: No, a lot of the disorders that follow viral infections have a wide range of symptoms that accompany them, and so when you look back at people who had flu, SARS, or MERS, you saw a wide array of symptoms that followed: fatigue, pain, gastrointestinal distress, changes in the ability to concentrate and think clearly, sleeping changes, and things like that. It's not really much of a surprise. Our work here at NIH is to study post-infectious ME/CFS – Myalgic Encephalomyelitis/Chronic Fatigue Syndrome – and so we had been interviewing people who developed these kinds of symptoms after different infections. The idea that somehow this would be novel or totally different, I didn't think it would be. I was pretty sure that it would look like all the problems that follow other infections too, and it seems that, with a few exceptions, is how it's working out.

Barr: Yeah, that's really interesting. I realized that I was interested in the eye pain and the throat ulcers that you spoke about in an article that you wrote. You said some patients experience that particularly

when they're dealing with the acute stage of their infection. Can you talk a little bit more about that situation?

Walitt: I can't really say that I'm the one that would know the most about this; however, because we were fielding lots of calls from different individuals – the way that our protocol is set up is that we take calls from the community – we have been able to collect a lot of different stories from patients. We did this so we could hear about the wide range of different problems people had and then refer them to different places at NIH that might be interested. We made a collaboration with some of the National Eye Institute investigators so when we would get calls about patients with eye pain or eye symptoms, we could refer them to our collaborators there who would follow up and have even brought some of those patients to campus to study. I haven't really been following that story closely, partially because it doesn't sound like to me that those are lasting problems. We're hearing that people have these issues, but they seem to disappear. They're not the ones that seem to be causing problems in our patients when we follow up with them, and they aren't making it into the news. [Dr. Walitt adds in July 2022: Looking today at our unpublished data, it suggests that this might not be true. Blurred vision appears to be a lasting problem.]

Barr: Can you talk a little bit about the lack of taste and smell that many COVID patients experience? Some even have that situation following their acute stage.

Walitt: That was one of the things that was a little bit of a surprise. Every new illness is going to have its own unique brand of problems, and smell and taste was an interesting one that isn't as commonly reported from typical infections – not like this. No one was really sure what was causing it at first, and a lot of people thought it was related to nerve infiltration by the virus – like direct injury to the nerves. Time has shown us that a lot of the injury that comes from acute COVID infections actually is its impact on the blood vessels. The sustentacular cells of the nose that nourish nerves of olfaction get injured by the COVID virus, by SARS-CoV-2, and it's the injury of these cells that leads to the injury of the nerves. It's like a second hit. You injure the caretaker cells and the blood supply, and then the nerves take an injury. That's where the changes come from. Depending on the severity of the injury and individual factors, that can lead to differences in how people lose their sense of taste or smell and how long it takes to recover. We are collecting data right now about that. When people realized that this was going to be a problem, the smell and taste people internationally created a questionnaire to try to collect data in a standard way. One of our collaborators at NIH is a smell and taste researcher, Paule V. Joseph, one of our Lasker scholars. She was able to point me in the right direction, and so we'll be following it. We have the data on how people were when they presented to us, and we'll have data over time for over three years to see what the course is for some people. More on that to come.

Barr: Has tinnitus been a symptom that COVID patients or long-haulers have experienced?

Walitt: I haven't heard a whole lot of reports of tinnitus, in particular from our reports in our interviews. I wouldn't suspect that. It will be there. Tinnitus tends to travel with all these kinds of symptoms that are being reported to us, but when people report their main issues, it's not like the first or second most horrible thing happening to them. It sort of falls to the bottom of the list. If you're having headaches and you're tired all the time, the ringing in your ears sometimes doesn't get reported. We may find that later

on that people are reporting that in these larger data sets, but it's not really coming out in the data we have at the moment. [In July 2022, Dr. Walitt adds: Of note, our unpublished data suggests that tinnitus is not a major issue.]

Barr: Did you realize at the outset of the pandemic that COVID-19 may cause chronic health issues, especially looking at some other diseases? Can you talk a little bit about that and how that informs how you plan your own protocol?

Walitt: I certainly expected this from reading about prior epidemics. We study post-infectious problems that occur that are similar to what is being seen to happen after COVID, so it seemed pretty obvious that we should be expecting something like this. Every epidemic the more modern times has something like this written about it; earlier epidemics are less clear. The flu epidemic of 1918 doesn't really have a robust history of these chronic problems, but later on people that have studied other flu outbreaks of H1N1 have actually shown that it did cause these problems. There may be historical reasons why it's not well recorded, and I think that's really has more to do with the culture at the time than it does with what actually happens to people. So we were expecting chronic problems to happen, and once we realized that it was really going to be a pandemic, we started to shift our research focus to pull together a study platform to try to study the long-term problems from COVID in phases.

Barr: Can you talk about that? About your protocol? How you designed it, and how you're going about doing that?

Walitt: I figured that COVID-19 would create a lot of morbidity in its wake. I figured that a lot of that would have to do with the direct damage it caused to different parts of the body – your lungs, your heart, (if you had a stroke) your brain. That would sort of follow what typically happens in those medical problems. Then, I figured there would be this sort of post-viral ME/CFS or fibromyalgia or long-haul symptoms that would follow along the narrative of those disorders, but we weren't really sure. We wanted to start talking to people as soon as possible. We also knew that with COVID in full bloom, it would be very hard to bring people to NIH to study them in person, and so we figured that we'd have to create a phased protocol. The types of measurements that we would make would be chosen to match that is actually allowable according to COVID-19 restrictions. Then as restrictions loosened up, in terms of being able to directly interact with people, then we would start to bring people to NIH campus and study them deeper and deeper with the goal to ultimately understand if there is a unique post-COVID syndrome or not? Is it just like other post-viral issues or is there something going to be distinctly different from this particular virus? The first phase, Phase A, was a survey phase. What we did is we created a scripted telephone interview and an internet questionnaire battery designed from our experiences with ME/CFS and fibromyalgia and other disorders to try to capture the full range of people's experience both in their words on the phone and in a way that can be easily scored and compared using internet questionnaires. We tried to make sure that it was as accessible as possible, so the questionnaires are optional. Nearly everybody can talk on the telephone, but not everybody can navigate the internet. That way we would try to be open to the widest range of experiences that we could be. We've had something like 480 inquiries to date and about 250 people have qualified to participate, and we've been collecting data on these individuals. The questionnaires are also given every three months for the next three years, so we have a sense of how people were when we captured them,

and we try to get people pretty early after COVID, within their first six months, and to follow them over time to see what happens to them, who gets better, what percent gets better, what changes, what gets worse.

Barr: What are the qualifications that they have to meet? How many patients do you hope to enroll? I know these are a lot of questions. Are you covering both adults and children in the first phase of your study?

Walitt: We have three cohorts right now that we're recruiting. We have one cohort of people that tested positive for COVID within six months of contacting us. We are interested to get people early in their course of COVID, and they're usually within six weeks to six months of having active COVID. Most of them have some sort of symptoms because that's why they reach out, but some of them reached out even though they're better, just because they want to be involved in research. We're happy to have people that are fully recovered. We think understanding the normal course of improvement is important too. We have a second cohort or people who have neurologic problems after COVID, and there's no time limit on that, but they have to have a positive test. As you can imagine, neurological complications are of interest to NINDS [National Institute of Neurological Disorders and Stroke], the neurology institute. My work is actually sponsored by the neurology institute, and so in this way it's serving as a gateway for bringing in patients with post COVID neurologic problems to NIH. This allows our program to act as a referral site to help patients get to different protocols at NIH. The third cohort are people who report having COVID but having negative tests. We added this cohort soon after we started to enroll people because testing was terrible at the beginning of the pandemic. Tests were not available, hard to get, unreliable. There were a lot of people who were test negative that were certain they have had COVID, or their doctors were convinced they had COVID. We're not really sure exactly what to make of all of those folks or how best to study them. When you don't know, the best thing to do is to talk to a bunch of people with the problem and to collect data, so we're enrolling about 50 patients who had what their doctor believes was COVID that tested negative, both on the PCR [polymerase chain reaction] test or never had a PCR test but had negative antibody testing, to see what are those persons' experiences. Is it different? How do they compare to the people that test positive? There's going to be a lot of people like that because –

Barr: I was just going to ask a follow-up. I was listening into some long-haul or patient advocacy groups talk, and some of them are very angry that they weren't allowed to take part in NIH research because they tested negative for COVID, but they were convinced that they had COVID. They feel like they're being left out.

Walitt: Well, you know there's a strict divide between clinical care and research. Sometimes that is a tough one for people to navigate. If you have problems, you need to have those problems dealt with, right? If in March you got sick and you're having issues, people need to address those issues. Insurance companies need to pay for those issues; doctors need to treat those issues and take them seriously, right? A doctor's job is to take care of people with health issues. It is different when we do research though.

Research requires you to define what you're studying, and some of the people who believe they had COVID did not have COVID. That's just statistics. Not everybody is correct about how they view themselves and their health. We can't just take people's word on it for doing research – and rigorous science requires knowing for sure and being able to demonstrate that to other scientists. A hope is that we can take some of these test negative folks and develop other tests that would be able to understand if they really had COVID. People talked about T-cell assays that might be able to tell if a person has had COVID in the past and help. In how you take care of a person, whether or not a person's problems are from COVID or from something else, it usually doesn't really matter because you're going to deal with many of these chronic problems the same way – whether you got it through COVID, whether you got it through a different infection, or whether it has a totally different cause – most of the treatments for these types of health problems are going to be the same regardless of the cause. I could understand and empathize with some people feeling left out because they do not qualify for a research study, but the needs of science and needs of medicine are not the same.

Barr: Can you speak a little bit about the second phase of your study?

Walitt: The second phase will bring in patients who had tested positive for COVID within six months to get a snapshot of what they look like clinically. We suspect that it's going to be a lot of different reasons for people to have ongoing symptoms: that some people are going to be feeling terrible because they still have ongoing problems with their lungs, some people may have had heart damage they didn't realize, some people may have damage to their nerves they didn't realize, and some people may fit into the post-viral syndrome phenotype. The purpose of Phase B is to bring 240 people to NIH to just take a very close look at them and try to sort through all the different types of problems people may have. The goal is to find people that have post-viral fatiguing syndromes that we can't attribute to their lungs or their heart or their nerves or other well-described medical problems, because that's where my interests lie. While we do that, we'll be able to better understand, in part, the individuals that are coming to see us. We'll also be able to collect samples and to do research, including comparative research to other disorders such as ME/CFS; we'll be able to understand how the severity of illness impacts persistent symptoms and start to do some exploratory research on the post COVID syndrome. All the work of Phase B is really to find 50 patients and 50 healthy volunteers that had COVID to do deep phenotyping (Phase C). We kind of measure everything that we can about a person in that approach. This is the approach we've taken with Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome already and so we'll be able to, at the end of all this, compare the post-COVID patients to other patients that we have measured with ME/CFS and to understand some of the similarities and differences.

Barr: Have you started the Phase B part of your protocol yet?

Walitt: We're so close. Right now, it's undergoing its last reviews with the Institutional Review Board. All the preparations to get started are in place. I'm hoping that we will bring our first patient by the end of August or early September.

Barr: Oh, that is really close. Who did you reach out to in terms of recruiting patients for your Phase A part of your study? How did you spread the survey?

Walitt: I work with Dr. Avindra Nath who is the clinical director at NINDS, and we've been working together on the ME/CFS protocol for many years. We've been discussing, at the beginning of all of this, like this is what we expect to happen. Avi has been out there talking to the media about, “We expect this to happen. These are kinds of problems we anticipate. This is a way to think about these problems.” That's been enough to point people in our direction, just word of mouth and people doing Google searches. At this point in time, we haven't done any focused recruitment; we've just been sort of leaving it open for people to find us and come to us that way. We plan on doing more focused recruitment once we have our Phase B open to get patients and to bring them from wherever they are in the country. That way we can get people early in their course of disease to understand it better, because a goal is to watch it emerge and to try to understand it early, so we can figure out how to intervene in the future.

Barr: Your protocol currently covers the patients for three years, but do you feel that you may want to extend that at all or set up new studies? Symptoms could last for longer or situations could arise from COVID that we don't know about possibly later.

Walitt: That's certainly possible. There have been some really good epidemiology studies for post viral ME/CFS kind of symptoms. If I were to be a betting man, by a year I would say only about nine percent of people will still have symptoms after the infections. Within the first three months, thirty percent of people have symptoms – a lot of people have them – but a lot of people are going to get better. Nine out of ten people will get better. The pandemic is so huge that ten percent is a lot of people. I assume that some of them will get better or become stable or get comfortable in their new reality within three years. There’ll be people that will have problems; somewhere between one and five percent will probably have lifelong problems.

Barr: Yes, I had a question about that because there have been studies that have shown how those with chronic diseases like diabetes and autoimmune diseases paired with COVID-19 as well as reports on how COVID-19 may end up causing long-term conditions or may exacerbate existing chronic conditions. What light can you shed on that?

Walitt: Well, I really don't know yet. It's pretty obvious that people have a lot of comorbidities, and people with comorbidities will develop problems. I mean our own data shows strange things that we still need to look into. The highest comorbidity condition in our initial analysis of like 150 people was actually seasonal allergies of all things, where two-thirds of our cohort had seasonal allergies, and you'd only expect about a third of a population to. So that was odd. A third of the people had pre-existing anxiety or depression. There was a lot of pre-existing pain and irritable bowel kinds of problems, but there's also people with diabetes and hypertension and coronary artery disease. Part of what would be interesting to unravel is if the problems that you had before COVID dictate the flavor of your post-COVID problems. That's something that we're going to be trying to understand. How does co-morbidity shape the problems you have down the road? It may not all be the same. What you already have may shape what comes, so we'll be able to look at that a little bit. In terms of the weird things that COVID may create down the road, our cohort is probably not the best one to answer those questions. I know the NIH has its PASC [Post-Acute Sequelae of SARS-CoV-2 infection] program, the RECOVER Initiative, I’m sure you're familiar with it, and that giant meta cohort of like 20,000 people is probably a better way to look at it. You would want something that's really representative of the population at large – more than my study

population is. And you would need to follow large numbers of them to find rare events that may happen.

Barr: Yeah. Like reports that COVID may cause malignancy and cancer. It was unclear to me like what's circumstantial and what can you directly attribute from the COVID, because some of these things are common in and of themselves.

Walitt: Yeah. One of the enduring questions that I came across when I was looking into that literature – people are not clear on pulmonary inflammation's relationship to cancer. It seems people go either way on it. I'm not a pulmonologist, so I can't really weigh in what I think about it, but with so many people infected with essentially a pulmonary bug, there is going to be a substantial group of people who develop ongoing lingering pulmonary inflammation and pulmonary fibrosis from the injury of the virus. If there is a spike in cases of cancer in the lungs, one would be able to say "Well, COVID kind of looks like it created that". I think like five and ten years from now, some of the epidemiology itself, just looking at the entire population, will give us some hints. COVID started February 2020, and if three years later there's a spike in cancer, you're pretty sure that you might be able to look back to COVID and say, "This is probably what did it." Some of the larger studies down the road will get at some of those questions, I would believe, but they are interesting questions.

Barr: They are. How do you tease out some of the chronic symptoms that people are experiencing either during their active infection or long haul? Or some other health issues that patients may have? Or common things like headaches or I think fatigue is relatively common? People do a lot in their lives, so I was wondering.

Walitt: The due diligence is really, really what it requires. When you study the consequences of an infection, you have to understand how people were before they got sick, and that's a that's a tough one, right? You can't go back in time, and people are only as reliable as their personal stories are. Each of us see ourselves in a certain way, and we tell our story from that perspective. But you can always get medical records from people from before they got sick and review, and you can see if a person had the same problems beforehand that has not really changed or if the problems have changed in their severity or frequency. So, for some, they are not exactly new problems, but they've grown into a larger problem that is different for them. With some people, you'll look at their old medical records and you'll be like "This person was absolutely healthy, and all this is new." Diligence can sort of help sort of untangle the issue of "Have these problems evolved from what they were before or these new problems?" Then, in terms of the question "Where in the body are these problems coming from," that's what we're hoping to achieve in Phase B. By examining people very closely and using a standardized, rich clinical protocol to evaluate somebody's lungs and their heart and their nerves, we can hopefully investigate each of the pieces and say, "Okay, this looks like it's from the lungs. They're having the shortness of breath, and they feel like they can't get air and their chest is tight and it causes pain. Well, that chest pain really seems to be related to this lung issue." Things like that.

Barr: How do you account for culture and other socio-economic determinants when assessing the numbers of people who may be experiencing these effects, the effects that people have, and the types of people who are dealing with them?

Walitt: There are many standard ways of measuring different social demographic factors, and scientists have come up with all sorts of Common Data Elements that one can refer to and use in studies. We measure a lot of common data elements for demographics and social status and work and family dynamics as best we can, and then we can determine how those factors impact outcomes. Are we seeing certain types of people in our study? Do the problems being reported look different in people from different backgrounds? We already said that we can look at people in terms of premorbid problems, such as "Did they have cardiac disease beforehand? Did they have pulmonary disease beforehand?" We can also look at sociodemographic factors in the same way – "Were they working beforehand or not? Were they married? Were they divorced?" All those different social demographic and cultural factors can be estimated and used in analyses. We can see how do people who fit into one of those categories look compared to the other category. You can get into the sense of how much are demographics and cultural factors affecting the problems after COVID – are people having more severe symptoms or certain types of symptoms if they're coming from different backgrounds?

Barr: In the past, you said that it was part of the times – not really reporting the after-effects of infection with the 1918 flu. Do you worry at all that people may attribute too much with COVID now as people are talking about possibilities? There's a lot more ways to communicate. Society has definitely changed a lot, and how we talk about illness and ourselves. Also, this is a follow-up, do you worry that people may stop reporting their symptoms or talking about them when it comes in later years with insurance? That's a big thing for people – not reporting them if they feel their premiums will go up or things like that.

Walitt: These are difficult questions. What is right for society is far more than I can pretend to be able to know… but the issues surrounding the COVID pandemic won't be forgotten the way it was back in 1918. Simply the way that we are able to record and document has changed that enormously. We're leaving a very rich history behind us, and many of the post-infectious issues being described are not going to just go away when the pandemic ends. They'll be just as vigorously advocated for by the community and by doctors and by all the stakeholders involved as they are now. I do think that there will be a drop-off in stakeholders though because people will get better. Early on after COVID, a lot of people have symptoms. Within the first three months, you expect 30 percent of people will have post-infectious symptoms and will voice them. Over time, many will get better and many of these people are going to get quiet about their prior problems. They don't have a battle to fight anymore, and they'll believe the problems are real, but they'll also try to get put the experience behind them. All people really want to do when they are ill is to go back to living their normal lives, so it's perfectly understandable to want to move on and so in some ways it will be "forgotten" by those who manage to get past it. However, those who don't get better, they don't have that option. They will advocate for themselves, and they will organize, and they will work to make sure that they get the things they need to ensure that they are seen as having a legitimate problem.

Barr: What would you like to learn more about with this situation and how do you think patients will need to be studied to have the most complete picture of the variety of issues that they could potentially face down the road?

Walitt: The real hope is to find what I would call “therapeutic targets”. If you understand what's biological changing, the different mechanisms that have changed their function in people because of COVID, you can potentially make a treatment to restore function to what it once was. You know you can't always tell what happened to individuals because you don't have any measurements taken before they were sick – but if you can look at people who recovered normally versus those who don't, you can look at the converse of those differences. What is different in people who recover normally compared to those who don’t? In biologic pathways, where are the differences and are these differences amenable to be changed? Could we block the mechanisms or increase them? If we change how the process works within people, will they get better? That's the main focus of our exploration. It'd be nice to understand why people develop these problems, but answer “why” is often harder than finding places where you can intervene and make change. And what people really want is for us to help them get better. I'm fine with making people better, even if I don't know why they get sick in the first place. The focus really is on trying to find targets that we can try to intervene and change the quality of people's lives, even if we don't know exactly why. Of course, then the second hope is to understand the mechanisms so that we understand the diseases and we can shed light into those sorts of questions of “Why?” Was there a second part to your question?

Barr: No, I think that that that covers it. In terms of your current study, it sounds like there are a lot of different people who are currently involved and will be involved in Phase B. Can you talk a little bit about your role and some of the other people's role in your current protocol?

Walitt: I serve as the lead associate investigator, and so I'm like the grand organizer. I put together the protocol, and I’m supervising all the different pieces to get them in place and make sure that they happen. I have a team of people – Elizabeth Bartram is a nurse practitioner who I work very closely with and helps me with a lot of the organization and day-to-day management of the work. Angelique Gavin, Anita Jones, and Jun Yi are members of the staff in terms of coordinators and nurses and nurse practitioners that have been working to develop the program. I have a qualitative researcher, Barbara Stussman, that's worked very closely with us especially in the questionnaire development to make sure that the questions that we invented for this are easily understood by everyone. It's been ridiculously important in putting this together. I have some trainees that work with us, Bryce Calco, Sean Horan, Snigdha Chigurupati, have been very helpful in helping me organize the data. There's a statistician, Gina Norato, who's been working with us both in sort of database design and analysis of the data that we've been collecting. I'm sure there are a lot of people that we've been missing. And there are a lot of other collaborators, people who have given us advice about the patients that we're going to see and people that we send patients to and are sending patients in our direction. Leighton Chan's rehab protocol, COVID care, is one of those. Anthony Suffredini has a pulmonary protocol where they were seeing acute patients with COVID, and they've sent people our way. We've had discussions with them. I'm sure there's others that I'm missing right now.

Barr: A variety.

Walitt: Yeah. There's just been a lot of different people doing different parts, and I think my job is just to help sort of manage and guide people. I guess I did most of the protocol design.

Barr: When did you all start this? Like Phase A, you started in the spring of 2020?

Walitt: We started developing it in the spring of 2020. I think that we were able to enroll our first participant with telephone interviews in September and bring them into our online questionnaires I think in November. Developing a whole set of online questionnaires that anyone could access from home – it took a while just to implement some of these things.

Barr: Does everyone see the same questions or are the questions different based on your responses?

Walitt: Most of the questionnaires, especially the ones that we developed just for COVID, they're really the same questions for everybody. Some of the patient reported outcome measures use this computer-assisted technology, CAT technology, which is a way of asking different questions to reduce question burden. For the most part, everybody sees the same stuff.

Barr: For the people that just do the phone, do they get read the questions or do they do both the phone and the computer?

Walitt: Everybody first does an eligibility interview to understand whether they can be in the study, and then a survey interview is performed, which uses a guided script but also has a lot of open questions. People are given an opportunity to describe their experience and then afterwards tell us what they want our team to know about their illness experience. Just to give participants some time to say, “This is what I think is really important for you to know. This is my experience. This is what I want you to know about.” That's all collected in the survey interview on the telephone, and then the questionnaires mostly use fixed responses, but we also put text boxes in there so people have opportunities to say, “Before I had COVID, this was really how I saw my health. During COVID, this was the worst part of having COVID, and after COVID this is what really surprised me. These are the things that really bothered me.” We hear all sorts of different experiences. There are a lot of people learning who were never really ill before learning about the nature of health care delivery in the US that they did not expect.

Barr: How many questions are on the questionnaire?

Walitt: Oh, there are several hundred. There are 22 different questionnaires that are part of the packet. It takes about three hours to complete.

Barr: That's a lot of questions to create.

Walitt: That's why it took us so long to get it tested and operationalized to make sure that it worked and before we went live. It's a lot, and a lot of it we've sort of had to invent whole cloth. There are a lot of common data elements that we're able to take in from other disorders, but there's some just unique aspects about COVID or even asking about a person's experience around an infection – there’s not a lot of standard questionnaires about how were you before, how are you during, and how were you after an infection. That took a lot of effort to decide what did we really want to know and to make sure that we're asking a broad range of questions to capture as much as we can but also not ask everything in the world to make it like a 10 hour ordeal of questionnaires. It's gone pretty well, I think.

Barr: Have you translated the questions into other languages for participants like Spanish?

Walitt: The telephone interview has been translated so we can interview people in different languages. We have not translated the questionnaires into other languages. The amount of cross-cultural validation and computer programming that would be required would be extensive and take a considerable amount of additional time for such an urgent to start project. That's part of why we made the questionnaires optional, so that if you do speak a different language and you want to participate, it's easy enough to find somebody that can translate on the phone. That way anyone can be involved. We can find somebody that can translate an interview. Translating questionnaires is a much more difficult task.

Barr: Yes. Have you been involved in other COVID related initiatives at NIH or outside of NIH?

Walitt: I was part of the PASC initiative. I was asked to be part of a committee for there. I was part of the common data elements project that came up, I think through the National Library of Medicine in fact. The International Association for the Study of Pain convened a Presidential Advisory Committee help figure out how they're going to respond to COVID and figure out the responses and the problems that pain may create. I've been part of that and other different little pieces. Then at NIH, within the intramural program, we all talk to each other and help each other out, so I've been helping other investigators by looking at their protocols and synchronizing some of our tools and our efforts to make sure that what we are collecting can be compared to what other people are collecting. Sort of sharing knowledge – there's been a lot of that too.

Barr: COVID has affected you as a clinician and as a scientist but also as a person who's living through this pandemic. What opportunities and challenges has COVID-19 presented for you personally?

Walitt: That's a great question. You know, I have a family. I have a 16-year-old and a 13-year-old, both daughters, that had to live through this and the no school and the tele-school. I have a wife that has had to work from home. Our lives have not been too bad. I have a house; both my wife and I work for the federal government, so we had job stability. Some of the real hard parts, you know the health and welfare parts of surviving COVID, weren't such an issue, but how to keep people engaged and keep people mentally sane amongst the challenges of COVID have been interesting for my own family. I realized pretty early that the pandemic was going to be a mess and that being able to leave your house and feel safe was going to be important for people's mental health, and so I bought a used RV like a month in or two months into the pandemic, knowing that this way we could be self-contained and go places. If we had to visit family, we could actually get there. It actually came in handy. We were able to go down to Florida and see my parents in fact. It's very nice. When other people were all holed up, we were able to have a change of location and that did wonders, I think, for my family. My daughter was really funny. I asked her how the trip was when we got back, and she goes, "It was mostly boring." But looking back now, she's like, "I'm so happy we got out of the house." [Laughter] It wasn't what we did; it was not doing what we were doing that was more –

Barr: Yeah definitely.

Walitt: I think the biggest challenge for me has been handling work. The pandemic has affected everybody I work with one way or the other, and I find that especially the 20- to 25-year-olds, the trainees who are not in a stable house with their parents, don't have stable income, and have all the issues that young people have been terribly affected. A lot of them had very difficult experiences. Trying to be there for them to help them navigate it and help all the people that I work with navigate the pandemic has become a focus of my work. How do you hire people and get them to be involved and feel valued when you've never met them in person? Those aren't unique problems, but I found these issues to be the hardest parts. People were having a lot of hidden anguish, and helping people express that anguish and address that anguish and overcome that anguish, I think that's been the hardest part of this pandemic for me – helping others.

Barr: Does it vary by person, or did you figure out a certain way to help certain subsets of groups that you deal with?

Walitt: Early on, I carved out two hours a week for what we named the "personal development" meeting for my trainees. That way once a week they had to just have a place where they could talk and voice their problems and be comfortable. It became a comfortable place, and I don't know if they look forward to it – that's asking a lot – but they were able to talk about things and talk about what they're doing, whether they're feeling good or bad, in a way that no one's judging them. I felt that was something I really had to do, because they were having all sorts of problems that would creep out. Then with other people, you'd have to take some time aside and call them in person. Everybody needs something a little different, so it's finding ways to bring it to the surface so that they can express it or just giving them opportunities to express themselves. That was the hard part because everybody needed to be seen as strong, even if they were hurting inside. Not that it's over quite yet, but when some people allowed themselves to show weakness, you ended up wallowing in it. This kind of thing could break a person, and so showing other people you're strong was important even if you were hurting. That's very difficult; to try to be strong all the time. There's no good way to be strong and also be vulnerable.

Barr: Definitely. Was there anything else that you would like to share about your COVID research or activities or experience?

Walitt: I guess what I would like to say is "these things happen". If you look at the history of epidemics, it was pretty clear that these kinds of problems would happen when the pandemic came, that there would be a long haul. That was an assumption that should have been made at the start rather than a remote possibility or an afterthought. Thinking forward, there will not be another pandemic during my career, there won't be another one of these for me, but if we learn one thing from this point in history, it should be to put research protocols in place that are ready to watch people prospectively the next time. The best way to study COVID would have been to study people before they were sick and store samples. Then you could watch them and when each person becomes ill, you have an opportunity to do a prospective study on what COVID does to them, how it changes people. There was just so many people who got COVID that could have been studied this way but were not. To put some sort of surveillance system in place so that when the next time here is a major epidemic, that researchers are ready to go. If it's all worked out beforehand, it will be simpler to study people and understand what really is

happening to them as it happens. That would be fantastic right? If history teaches anything, putting a illness surveillance system in place that could provide the answers to questions about causality would be the one thing I'd want people to think about going forward.

Barr: Well, I wish you and your family and those that you work with all the best and safety. Best of luck on your Phase B part of your trial. I will be very interested to hear how it goes.

Walitt: Thank you so much for taking the time to ask these questions. I really enjoyed it and hopefully these answers will be useful.

Barr: Definitely.