Academy of PHYSICAL MEDICINE

Transcript

333 – Decode M.E. with Sonya Chowdhury & Dr David Strain

Steven Bruce
Hey, good evening and welcome to November. We're looking at me this evening myalgic encephalomyelitis and that's an expression which no matter how hard I try, I'll have real difficulty remembering. So I'm gonna stick to say me this evening or chronic fatigue syndrome. We've all had patients who've told us that they have me I know I have I'm sure it's the same for you. But I've also had my suspicions that it's a convenient late over a basket of symptoms, which might or might not actually be me, I've also felt that chronic fatigue sufferers are difficult customers. You know, it is you want to do everything you can to help them but there's no clear answer. Well, I'm hoping that this evening's guests will help us navigate our way through that, as well as telling us about the progress in researching me. And we can all play our pup. I've got two guests with me tonight. In no particular order. They're Dr. David string, who is Associate Professor of cardio metabolic health at axon University's medical school. He's also the chair of the BMS board of science and a member of their COVID 19 Response Team. He spent a lot of his career his PhD, in fact, was looking at diabetes. And he tells me that that is closely related to me. We'll hear more about that I'm sure later on. But he's also another medical advisor action for me. And he's been there for the last two and a half years. David, thank you very much for joining us this evening. It's obviously been a bit of a rush for you what was traffic and you arrived here in your scrubs? Straight from the medical school. So really appreciate you coming along. It's always a pleasure. And my other guest is some your children who is me, action for me is Chief Executive Officer, Chief Executive Officer, I'm having real trouble again, my words this evening. She's been in post for just over 11 years. And she's got a background in senior management as you can imagine. And part of her role that action for me is to chair the management and PPI groups for decode me, which is the world's largest study into me. And the main part of tonight's discussion, Sonia, welcome to you too. I think you probably have to give us a bit of background on action for me. And you. I mean, I think I read on the website that most of the trustees have got, either me suffers or have got some connection with it. Can you expand on the whole project?

Sonya Chowdhury
Yes, no, absolutely. We're coming up to our 40th year in a couple of years time. And as you say, over 50% of our board of trustees have a direct connection with me either themselves or a close family member. But we've also got a significant part of our team that have direct experience of me to say we're an organisation, run by people with personal and professional experience

Steven Bruce
yourself. Do you have personal, real personal relationship with me?

Sonya Chowdhury
I didn't. When I joined the charity, I took the role because I wanted to be a chief executive. And I was quite ashamedly, I didn't know very much about me. But year after I joined the charity, my son who just turned 11, got a chest infection through lots of antibiotics just didn't seem to recover. And he was subsequently diagnosed with me. That's 10 years ago now last month,

Steven Bruce
right? So in some ways, fortuitous that you took on the role you did, but I said, obviously,

Sonya Chowdhury
yeah, I mean, it was horrendous time, and you wouldn't want to wish it on anybody. And rather embarrassingly, I never thought it could happen to me or my family. And, and obviously, we're in that situation. But it did give me access to people that I could talk to I could seek advice from, we had a whole range of resources and support. So I was in the best possible place to do the best job I could as a as a parent,

Steven Bruce
and DVD. I mean, I only scratched the surface of what you do in that, that brief introduction. But like any consultant, you're a busy person on you, I think, just before the show, you were saying that you're still waiting to sign off today on the training of your junior doctors for their one stage of their professional development anyway.

David Strain
Absolutely. I mean, it's a busy time for anybody working in the NHS, and I'm quite privileged that I got a 5050 job, I will spend half of my time working for the NHS and the other half working for the university in a research environment. And that that really spans across the both the clinical service in front of patients on a daily basis, but then being able to take problems that we identify in the clinical sphere, into the academic world and say, Okay, this is the question, this is a big problem. What are we going to do about it, how we're going to tackle this problem. And actually, that's really how I got involved in myalgic encephalomyelitis in ME research, because when I was seeing patients who were experiencing this disease, and you go to the textbooks, and you go to the literature, there was just so little known about this tendon disease and and as you say, very often, patients who are experiencing this have had pretty raw experience at some point during their career between developing the disease and actually being identified, because there is no as yet diagnostic test for it. And therefore there are still a lot of doctors who believe in an era where we can get a vaccine out in 10 and 12 months, that well, if we can't find a test for it, then it's not real, as opposed to we haven't got the technology right yet. In old spy identify and therefore manage these patients properly.

Steven Bruce
You've already brought up one of the difficulties because for years and years and years I've always pronounced the hard see and in Kefalonia but before The show I thought I'd better check home right? So I looked it up on the internet, whatever it was, and it said saucy encephalo. And you've just corrected me and it's now in kefalonian.

David Strain
I think it's however you pronounce it.

Steven Bruce
Like Greek isn't terrible. But actually,

David Strain
one of the big elements is it is that name. It's there, the my algae can kefla My eyes are in Cephalo myelitis. It is a disease process. And I think one of the big problems that a lot of individuals have suffered is been decades of stigmas of stigma, the name chronic fatigue, and it's like, well, everybody experiences fatigue at some point in the life, what's the difference between them and me? And the reality is, this is a very difficult and different biological and pathological process.

Steven Bruce
That's going to be something which everybody watching this evening is really interested in, because you called it a disease, widely recognised the disease, but it's hard to work out what the hell is actually going on? And can you see a virus can you see something specific happening and so forth?

David Strain
Well, actually, the the recent research has taken place around long COVID, which is another disease that's very, very closely related, has really advanced the recognition and the understanding of both conditions dramatically. For many sufferers of long COVID, Amin at the moment in the UK, it's estimated as 2 million people with long COVID. And of those at about three quarters of a million, who've got a disease that is incredibly similar to the myalgic encephalomyelitis that we've been looking after, for the last 3040 years. And actually the does appear to be a massive breakthrough into research into both areas. Because without with long COVID, they've effectively got me with a known trigger. And because there's are therefore no trigger, we know a little bit more about what we should be looking for. And therefore we can identify the outputs there. Whereas if you go to me, we think that Emmy is associated with multiple different viruses. So Epstein Barr Virus, the one that causes glandular fever, that's the one that's most commonly cited. But as many other viruses that have also been implicated the HHV six, a human herpes virus six A, for example, is highlighting about 20 to 30%. In those individuals, then specific treatments for that actually cause a resolution of symptoms. But problem is because we've got disease with so many different parameters, it's then become very difficult to find a single diagnostic test for what may be multiple different viruses, different viruses in different people. So effectively, you've got a collection of different triggers, causing the same outcome at the other side.

Steven Bruce
And you said don't think that your son's trigger was was it flu virus producing,

Sonya Chowdhury
he had a chest infection, and three, lots of antibiotics just didn't recover. We

Steven Bruce
actually had a something sent in already by Christina who said that she was hoping to learn a lot. He's going to learn a lot from tonight, I'm sure. But she's got three close friends who've been diagnosed with me. And interestingly, all three were teachers. Maybe that's the trigger, I don't

know. But she says one was diagnosed shortly after home was after her home was twice fumigated for cat fleas in the 1970s, or 80s. Is that a known possible truth?

David Strain
There have been many different possible tricks along that and there's a lot of stuff organophosphates that were still widely used by them today cause a syndrome very similar to me, and that causes a lot of those symptoms. And therefore people have this diagnosis of me based on that now, today, if she was to come along, we'd say she has organophosphate poisoning that's triggering this myalgic encephalitis type picture, but her primary diagnosis would be organophosphate poisoning. Actually, if you go back historically, you know, 5060 years ago, before we had the MRI technology that we've got today, patients with diseases like multiple sclerosis may have been treated called as chronic fatigue syndrome patients with diseases like myasthenia gravis, that we didn't fully understand that pathology, we would say, well, they've got a chronic fatigue syndrome. I think as we go through the research we're doing at the moment, what we'll end up finding is many of the patients today with a diagnosis of me will have a different trigger. And I think in about 1015 years time, we'll be in a position where we say that actually this person has the fatigue associated with EBV or the fatigue associated with an immune immunoglobulin trigger or something along those lines.

Steven Bruce
Why don't you just answer this question Victoria says, Is there a link between me and glandular fever?

David Strain
Absolutely. Epstein Barr Virus is by far and away the most common trigger that we see as identification for it. And actually Epstein Barr Virus, the thing that causes glandular fever, we know that that hangs around in the brains of people we know that that hangs around in the spinal fluid. There's a very tight association between active Epstein Barr Virus and other neurological conditions that have been difficult. Ms and schizophrenia, for example, have both been associated with that virus. And we think what we're looking at here, for some of the individuals there me is that the glandular fever finds its way into different parts of the brain. And when it's in that part of the brain, it will trigger this disproportionate fatigue associated with any sorts of activity. I think it's the disproportionate nature, that is the bit that we really have to highlight, you know, someone could spend 20 minutes doing a crossword puzzle, and ended up in bed for days afterwards, with the level of fatigue that you or I might experience if we just run a marathon or done something heavily exertional.

Steven Bruce
So the other categories of effectiveness, if you like,

David Strain
it's like any disease it is has a spectrum of severity of it, we can people who've got a mild to moderate disease, these people might have periods of profound fatigue, but actually, they can go through periods where they actually lead a normal life and can get on with things. But the slightest trigger will put them back to where they weren't before. We then have people right at the other extremes where the slightest exposure to light, for example, would trigger a day's worth of fatigue, just that sensory stimulation, these can find themselves lying in darkened rooms, minimum sensory experience. And even the the effort of brushing your teeth or having a wash can cause days worth of

fatigue afterwards, let alone eating. And at the really severe end, that's what can cause problems down there.

Steven Bruce
So just to interrupt this flow for a second, I've just got a noise in my earpiece, which I couldn't interpret so far, I just want to just in no means to tell me something, someone's going to have to tell me by another method, because I can't understand it. And when I was going to say then is if Epstein Barr Virus is associated with me, what's the what's the ratio of those who get Epstein Barr without me to lose? You do?

David Strain
It's very difficult to say that one, because just about all of us, at some point, have experienced Epstein Barr Virus, just about all of us will have come into contact with it when we've done the epidemiological studies, it's about 98% of people have got some antibodies for it. And that's what causes a lot of problems. Now, there's been some research recently into lung COVID, that might actually help us identify those who caused it. And if we look at the slide that we've got here, this is looking at the immunological signatures of people who've got lung COVID. And what we can see, we've got people here in these boxes on the left hand side, on the right hand side, rather, we've got people with post acute COVID syndrome in the red box, and people without post acute COVID syndrome. And we see a very different immunoglobulin spectrum. And what we've got here is we've got people, people who've got just their people with lung COVID, caused by the COVID virus, they have a very high immunoglobulin level, to the spiked protein of COVID, compared to people who've had COVID, but then made a complete recovery. Now, what that's telling us is that these people are having ongoing exposure to that particular virus. And this has been great with COVID, because we knew what the viral trigger word was. We are now looking to find out, can we create a panel of immuno globulin tests. And if we then would be able to look for a panel of tests against HHV, six A and Epstein Barr Virus and the other viral triggers that we know about, could we then get to a position that we say this person's me was caused by Epstein Barr Virus, or this person's me was caused by patient facing say, I keep going for those two? Because both of those are viruses that we already have recognise antivirals that will do the job.

Steven Bruce
So what do you have to do these days to be diagnosed with chronic fatigue syndrome or me?

David Strain
So for many people, it's a quite a long and slow and arduous process. Because one of the biggest problems that we still face is that when I graduated, me was one of these disease diseases that was talked about as a functional disease. There's nothing actually wrong with the patients, we just need to talk them through it. And therefore, there's a lot of doctors out there that still have that knowledge base that was given them in medical school 2030 years ago. That said, the underlying cause of me is all in the brain. Right now. We've moved on from that a long way. We have now taken out some of the causes of EMI and we've now started talking about other forms. And now to Have me there are four very important diagnostic criteria that that you need to fulfil. And we need to fulfil all of the four, and then possibly some of the additional bits that go in it,

Steven Bruce

people are going to worry about, you know, not be able to make these out while we're talking while you're talking and so on. But I will share these as a handout, as I always do after the show. So they can be reassured that they'll get the slides.

David Strain
Yeah, I just so people know, I've put together an entire slide deck, depending on where the conversation goes. And individuals Yeah, so we will make sure that you get copies of them. But there are four key criteria that are debilitating fatigue that's made worse by activity, but it's excessive compared to what you would expect. Then there's this condition post exertional malaise. And that's a phenomenon where you might do a little bit of activity today. And that could be both either cognitive activity or it could be general activity. For example, I saw one of my patients today, the he went to His granddaughter's first birthday party. Now he really knows how to control he really knows how to pace himself, how not to exert themselves, he went to the granddaughters party, and didn't do anything that apart from interact with a few people, but just that social interaction, put him into bed for two days afterwards for to recover. And it's post exertional malaise doesn't necessarily happen immediately. It's disproportional, and it's prolonged a lot longer than you would expect. The to display and refreshed sleep or sleep disturbance, or, or possibly both. And, again, we've all had an unrefreshing night's sleep from time to time. But this is the way of life. And these people's with anyone that's got children at home, for example. And they know what it's like to have that and child who's sick, and they're up all night, and they feel a couple of nights sleep and they feel terrible after a two nights disturbed sleep from the child who's sick. That's what our people that may experience every day of their life.

Steven Bruce
Interestingly, by sheer coincidence of our scheduling, a couple of days ago, we did a show on obstructive sleep apnea. And I asked the speaker there, Neil Stanley, who's asleep. But yeah, and he was saying that, yes, that could be mistaken for chronic fatigue, because people could be exhausted during the day and not realise why because they won't know that they've got sleep apnea unless someone tells them is that a problem that we have. So you've got to be able to separate these these non viral causes are non CFS causes?

David Strain
Well, that's a whole area. So Right. And that's the very first stage of diagnosis of me that we look at, to have a chat with a patient, we talk through what the differences may be. And there's a whole series of blood tests that we'd also do, because there's lots of other diseases, like obstructive sleep apnea, that can cause this disproportionate fatigue, or could cause exertional difficulties or could cause the difficulties that with unrefreshed sleep. So certainly Sleep apnea is great for that unrefreshed Sleep, we've got people with celiac disease who don't have proper absorption of the nutrition nutrients, and therefore they will feel disproportionately fatigue that they can't account for. But once you identify celiac disease, you then make the change to the diet and everything gets better. And there's diabetes, there's a whole host of vitamin deficiencies. Simple anaemia will make you feel fatigued. So we need to make sure that there isn't any of those conditions. But for it to be M E, it has this post exertional malaise and that's something that is characteristic. That is something that actually exercise itself makes people with M E on the majority of people with me, it makes them worse,

Steven Bruce

as you emphasise, it's not just being tired after a session in the gym, it's exhaustion for a couple of days.

David Strain
And if we go to the gym, if we exercise, we will feel tired, we'll feel fatigued. And then the next day we'll feel refreshed and we'll feel slightly stronger than we were before. If a person with me goes and exercises and tries to push through it, they will then have three or four days in bed, which means they will effectively decondition more from those three days in bed than any benefit that they would have got from the exercise. And so it's this post exertional malaise. And it's really important that we emphasise that this is not a deconditioning disease. This is an inappropriate response to the exercise in the first place. Right.

Steven Bruce
And I interrupted you after bullet point to there but you've just led me down another thought train here that the pace trial of however many years ago said graded exercise was an appropriate response to me.

David Strain
So yeah, the pace trial has triggered lots of controversy. It's it's probably one of the most controversial studies that's taken place in me. And actually one of the big problems with the pace trial with a criteria for people to enter the study. And that's the problem. The diagnostic criteria. These were the Oxford criteria that didn't include post exertional malaise, which is now one of the cornerstones of this diagnosis. So me is today it's a data set. positive diagnosis, if you've got post exertional malaise, you are you up towards me, when this study was designed chronic fatigue syndrome, as it was called then was a diagnosis of well, if you're feeling disproportionately fatigued, you've got chronic fatigue syndrome. Now, there are many other causes of chronic fatigue, without that post exertional aches and just having young children at home, that will cause you to be fatigued. Now, if you take people with other causes of fatigue, and you exercise, they do get better. Whereas if you take people with true M II post exertional malaise, then the exercise will not give them the benefit that they need. Now, that has been one of the most controversial results that we look at. And, and actually we have a slide here that just as a quick overview, from the study that looks around these, these 641 people who've got this Oxford criteria for chronic fatigue. And then they were randomised to this graded exercise therapy, the cognitive behavioural therapy, and then they adapted physiotherapy versus usual care. And the key outcomes that the reported were 22 people return to 22% of people returned to normal with the CBT. And with EG the graded exercise therapy, but it's very important that we look into this in a little bit more detail. So looking at face value, if you take a whole group of people who've just been diagnosed with fatigue, then you will get 22% of people will get better.

Steven Bruce
And this response, the CBT and graded exercise is just what you said, Isn't it this belief that it was a psychological problem? Absolutely. And that exercise improves everything. Yes.

David Strain
Now, the first thing to think about is that's one in five people who received the GT or received the CBT got better. Now, when you've got good recruitment criteria, that includes anyone with fatigue, many of those will have had diseases that potentially would get better from that exercise therapy. And for those of us that don't ever on exercise is good for the vast majority of diseases out there

Steven Bruce
when you're preaching to the converted. Physical Therapist.

David Strain
Actually, even for people with an E, exercise within the energy envelope within the amount of energy that they've got is good for them. We do not tell people with me to curl up in a ball and never leave the home, we say find out what you can do, and then do 80% of it. Don't push it beyond that. Because if you do 80% on a regular basis, actually your angel energy envelope does get a little bit bigger. But it's keeping within

Steven Bruce
the psychology of doing a little bit of exercise is good for them. If they've been told that you mustn't do anything, stay at home or stay on the couch. That could affect people very badly. So do it do as much exercise as you can is helpful. So

David Strain
absolutely. But it's not as much as you can, it's just just less than you can. And it's always just less than you can, because you still didn't get some benefit from it, you get psychological benefit. Many people with particularly severe me are going through a mourning process they are they're effectively mourning their children that they never had, or if they do have children. I mean, I say my pain. But another patient I saw today misses the fact that she can't play with her children. It's such a simple thing. It is a privilege to be running around with the kids. And not to be able to do that to see your kid running around and know that you have to pace yourself to just to make dinner for them, you're going to have to do it in four stages with a rest in between, let alone going out to play. So for them CBT is useful. But it's not a useful as a cure is useful as a way of helping them to deal with everything that they're missing out on with other things and dealing with

Steven Bruce
the consequences of me rather than the causes of me. Interesting to know. I mean, you're probably familiar with this particular doctor, Dr. Sarah Myhill. Now, we had her on the show several years ago, and she was very active in her campaign against the results of the pace trial saying this is complete nonsense that you could give people exercise to get over a thing, which is labelled chronic fatigue. But I wonder how many people are aware of what you've just told me, I'm talking about GPS here or other medical professionals. I suspect there's quite a few people in the audience this evening. And we think what is quite a revelation that we've suddenly discovered potential routes into the cause of me,

David Strain
it is and if we think about these as antivirals of the viral load, if you imagine that you've got a virus hiding in your brain somewhere, and you do just enough exercise to trigger that virus to circulate around the body. That's why it takes two or three days to recover every time you exercise. If you've got another cause of fatigue, actually, exercise has helped them and we've got through everything. That's another big difference between the people in the pace trial and the people that we see in with me the natural response for all All of us, if we're feeling fatigued, everybody, when they're feeling fatigued, they try and push through it, they try and exercise the way out of it. Now paced trial would have recruited all of those people when they first presented with fatigue, people that we see today, you know, me clinics, the people who have Ma, well, actually, they're the people that have

self selected because they have already tried to push through it, and realise that it made them worse. And that's the point that they ended up getting referred. So that's why the people diagnosed with me are so anti paced trial, because they have self selected as being the 78% of the people who were not going to benefit from GT, and many of whom would get take home from it.

Steven Bruce
GM into has asked whether antivirals are therefore useful in dealing with the ongoing symptoms of me, but I'm guessing from what you've said, yes, they might be. But they have to be the right antivirals for whatever potential trigger was.

David Strain
So we are just starting studies now looking at antiviral therapy in long COVID. Now in long COVID is great, we've got the trigger, we knew which virus it was, and therefore having the right antiviral is very much the feasible thing to be doing. And we've got in Exeter, we've got a study that starting in actually collaboration with Darby, just down the road from here, we've got a study that's running, that's going to be giving the remdesivir the antiviral for COVID. For people who've got long COVID to find out for got the benefit. Impact. The data that I showed you about the immunoglobulin, I'm hoping is going to be the first step towards figuring out what the right antiviral is. The problem is that the antivirals that we get for COVID, they're all based around RNA viruses. COVID is an RNA virus, and they they will not work for people who've got Epstein Barr Virus, because that's a DNA virus. So it won't be effective. The antivirals against Epstein Barr Virus may not be effective against HHV, six, eight, and so on. And that's why the first step has to be identify what's the underlying cause? Before we start looking at antivirals, and again, not everybody has gotten a viral cause, or many patients who have got low levels of immunoglobulins. There's many patients whose and the T cells or cells that help tackle viruses don't work properly. And for those that may be therapy is about giving immunoglobulin therapy, or maybe therapies about stimulating the T cells, there's therapies that are around that can be used to stimulate T cells, and the American Army uses one when they drop their soldiers behind enemy lines in order to boost their immune systems against whatever they may be facing. These are all therapies that if we figure out what particular group of people with me, are suffering from, we may be able to offer, but the randomised control trials that have been done in all of those therapy, taking me as a single disease have universally failed. Because if you give a therapy that is going to work against an immunoglobulin deficient patient, but only one in five of your patients is immunoglobulin deficient, then by definition, only one in five will benefit, and therefore it will never get the success. So what we do now are the good diagnostic tests of subtyping, finding out the underlying causes, and then we can start using therapies that will be of benefit to those individuals.

Steven Bruce
So Sonia, we still need to go to bullet point to theory for me, I knew that we were starting to talk about how we find out more about the underlying causes. And where does the decode me study fit into all this?

Sonya Chowdhury
So decode me study is the genome wide association study. We're recruiting 20,000 People with a diagnosis of me over the age of 16. In the UK, how are you recruiting? So we've had a very complicated approach to this, using a lot around social media. We used a marketing agency to be able to reach beyond our every community that we're in contact with. We have engaged with health professionals, people like yourselves, who no people with me and are able to signpost to the study.

We've used the me community themselves people with lived experience to help us reach out. We've had a press strategy, so that we've had coverage in the news, and that was particularly successful. think one of the Guardian articles reached a large number of people because we included a link within that. So it's been quite quite a big piece of work. And that's the part of the study that the charity has been responsible for. So we have we have done very well with our recruitment numbers. And I think the slide that may be shared in a moment will indicate the large number of signups that we've had. We're around the 37,000 that have signed up and the processes Have you complete a questionnaire, and it's a very detailed questionnaire or designed with people with lived experience, it takes a lot of energy for some. And it can be done over a period of time when we've particularly focused on those with more severe me who are often bed bound. And so we've had somebody that will talk with them and elicit a few answers at a time and complete the questionnaire. You get to spit kit. So a proportion of people will be invited to provide a DNA samples, we post those out, spit into a tube, pop it back in its box, and you send it to a centre where they extract the DNA. And the

Steven Bruce
proportion of people is that based on people who meet the criteria for me properly, or

Sonya Chowdhury
so everybody has to have a diagnosis of me, we have developed an algorithm that enables us to identify who meets very specific criteria, scientific criteria for this study, we're not sharing that detail enough to until after study has closed and so just if people aren't invited to provide dinner, it doesn't mean that they don't have any, just means they don't meet this very strict, narrow criteria, which we're using for this study. So

Steven Bruce
give me some strong clues that this is a fairly rigorous study that you're doing and it meets all the requirements of a proper piece of medical research.

Sonya Chowdhury
Absolutely. I mean, it's been through all the peer review and everything that you would expect it to go through. It's funded by the Medical Research Council and National Institute for Health Research. So we've had to meet all of their standards. We have a fantastic Scientific Advisory Board who hold us to account and of course, the me community hold us to account to and the people's lived experience that are involved in in the study,

Steven Bruce
who's involved in this that this is a cheeky question, who is involved in the study who might have an interest in skewing the results one way or another? Nobody. So this is a former pharmaceutical body who's interested in flipping a drug

Sonya Chowdhury
or no, so the University of Edinburgh working with action for me, and then a group of people with lived experience, we we have, we are very rigorous in our results in the process, and also when we produce results, that we are not going to produce results until they've been tested and looked at by others. The slide shown at the moment is the analysis that we've done on the first 17,000 questionnaire results. And already David was talking about the subtypes, we are starting to see that in the questionnaire results, we anticipate, you know, we're now over double that number. When we look at the next batch that we will start to see more, but we've, you know, identified that it's a

five to one female bias within the results that we've looked at. And interestingly, being female, older and more severely affected, increases. So being older female and ill for longer increases the chance of having a greater severity of the illness, we know that around one in four people are so severely ill their husband and bed bandhan actually for them, exercise could be moved turning over in bed. So they are very, very severely affected.

Steven Bruce
One of the questions that doesn't arise in my mind here is just looking at the validity of the results is a real possibility that more women are reporting or getting a diagnosis than men.

Sonya Chowdhury
And that's we you know, clearly that's something we see with other illnesses. But actually the there are various studies and the these results. Rep these results replicate what we see elsewhere that that isn't the case. We're looking at the team and looking at comparing different ethnic groups, there's some really interesting findings that are emerging there that will be published fairly soon. We've also looked at the UK Biobank, which is held by Edinburgh University is over half a million and a half a million people have contributed to that. And so there's been some genetic analysis within that. So we can't see evidence from our study and other studies that that is the case, we do see more women coming forward

Steven Bruce
with some degree of blinding in this in making sure that nobody is skewing the results according to their own personal perceptions or SIBO. Control of some sort.

Sonya Chowdhury
So with the genome wide association study, I think on one of the other slides, I think one of the earlier slides, there's what we call a Manhattan plot for the back. Yes, hello. So we have a Manhattan plot here, then this isn't me just point out but what we will look at we don't know the details. They're separated from all the data collected from the questionnaire. So once the DNA has been extracted that goes into university, it's blinded in terms of the questionnaire data and what we are expecting to see these peaks. So on a Manhattan plot and that gives us a genetic signal. And we are hope ping that we will find several genetic signals. Later on, we will then couple it with the other data, we will compare it with healthy controls from the UK Biobank, but there is no way that we can skew the results in this type of study. And so it's the largest study in the world because we've got over 37,000, to Around 37,000 people completing the questionnaire. And that data itself gives a huge amount of detail. So the only people 37,000 At the moment have started the questionnaire. And we're hoping that all of those will finish their questionnaires. And then we're looking at up to 25,000 people that will provide a DNA sample that we will then analyse as well. And

Steven Bruce
more if you had 120,000 People who completed the questionnaire with you,

Sonya Chowdhury
we will take as many as we possibly can. The study closes at 5pm on the 15th of November. So those watching tonight can help us recruit and encourage people to, to come forward, we have we don't have an infinite amount of money

Steven Bruce

to serve when there's a deadline on some sort of offer. Maybe you will,

Sonya Chowdhury
absolutely. And we are now pushing really hard, we've had some press coverage, we've had some great national press coverage, media coverage. And that always increases a surge in numbers. So we will get close to our 25,000 figure. But it's unlikely we're going to hit the 120,000 at this stage. But we do need those numbers. We want this to be the beginning, you start to see and there are some fantastic graphs, if you look at when you go from 10,000 people to 20,000 to 50,000 to 500,000 people that genetic hits that you get become clearer. So we do think we do expect to find some genetic hits. And there has been a piece of work that's indicated something called you know, in another study, but actually what we really want to lots of people to replicate this study. So we get that big number.

Steven Bruce
Well, I guess my question was going to be how many do you need for the study to be valid.

Sonya Chowdhury
So there's the scientific calculation, the scientific power has been done, we can, you know, we were not giving out that as as a number, if we hit 25,000, will be very well powered. But we know we're going to hit the numbers that we need. But we still want as many people to come forward, because the bigger the number, the more we're likely to see

David Strain
that cost because we think that MD is multiple different diseases, it is very likely there are different signals in different groups. So for example, it may well be that the one out of the six, who is male, had a very different underlying cause from the five who are female, or the younger patients may be different from the old or they may be different predictors. So that's why they're those numbers as to guessing it or not just a simple case of this is a number we need to see this gene in this peep people, we need to look at the across a range of different potential causes. And hence, the large numbers required.

Steven Bruce
It sounds as though to me and then when it's all come to fruition and you've made all these decisions, and actually, you won't be treating me you'll be treating a range of different diseases, it's, you know, you'll be you'll either be treating epstein barr, you'll be treating HLA 27, or you'll whatever

Sonya Chowdhury
different types of diabetes to get different types of breast cancer. So, you know, if we're aiming for personalised medicine, then we've got to understand what it is people are suffering with. And what we've seen with the analysis of the first 17,000 questionnaires is there are definitely subsets that are emerging. And so, you know, we hope that as we get the DNA samples in and the larger numbers, then we will start to understand that more, what then happens is that then opens the door for future studies, we can start to understand I think there's a slide in the deck that that we can start to understand the different parts of the system that being affected. So this one has got rats on it this one. Yes, that's what's the end, when you're looking at drug testing, we're not testing on animals. That's not the type of study that we're doing. But what we can start to see, it may be that one person has, you know, something that's impacting their mitochondria for another subset, it might be

at, you know, immunological, and therefore, that opens the doors for drugs, either to be repurposed or for trials to start happening. And that's certainly something that David and I have been looking at around drug trials and what's happening in the states so that we can start to think about how quickly can we move towards treatments. Whilst we're still doing the genetics, we need this basic science, but people with me have waited for decades for the research and so we need to accelerate that as much as possible. When

Steven Bruce
do you think it will all come to completion it closes on the 15th of November.

Sonya Chowdhury
So people can still send their DNA kits into the end of January. We've then got the analysis work to be undertaken. The funding is until the end of August next year. We have it Parents massive delays because of COVID it down to Amazon buying up all the boxes. So no boxes for the big kids. I mean, you would not believe the amount of difficulties we've had. So we're still dealing with some of those difficulties. But we want to get the results out as soon as possible. But only when they've been, you know, when people have looked at them, we've had any other peer review. And we are assured that what we're reporting is correct, because we don't need any more misleading research.

David Strain
One of the things is, when you say research coming to the end, this is very much the start of a very long journey, the DNA is going to give us indicators of which groups and what markers we should be looking for, in the physiology. The step after that will be saying, Okay, we've no other diseases with this gene signature respond to this sort of medication. And that's where the animal models come in that you start saying, well, that gene signature plus this marker, maybe that's the therapy, and we've got, there'll be literally hundreds, if not 1000s of different trials, molecular or a modelling computer modelling phase, before we then move to the stage after that, which would be the animal which would then be the humans. And then we have treatments that will be offered to people, we're looking at a good 15 year, event horizon before we really see this study, having the benefits on the patients by treatment options. But between now and then just being able to identify, but you know, these are the signals, these are the magnet pathways, and that hopefully, getting a good diagnostic tests out of this, they are the things that we can be looking for that will have the real, the real power for the when it's finished.

Steven Bruce
And so you mentioned peer review a couple of times because that's a very imperfect start to this whole process, isn't it? Once it's been peer reviewed, YHOO push it out to a wider medical community or research community and they can start really picking apart what the details of the programme should should offer and ignoring my audience. So go back to a few questions. And I'm Simon says if the most common causes for CFS are viruses, does that mean there's no role at all for antibacterials? I guess there's a hidden agenda behind that question. There are

David Strain
one or two bacterial diseases that do leave long term fatiguing illnesses. And a couple of those can in turn, could translate to me, we are still at a stage that that is by far and away the minority of patients that we see. And we usually have had a good handle on the bacteria that caused it actually getting bacterial identification bacterial culture in the UK, and actually across Europe, states and most of it most of the world these days, you can actually identify the bacteria. And if there has been

a bacterial trigger, we know what it was. And therefore we tend to be able to identify it better and treat it better. That's not to say every bacteria is and there are a few patients that still have weird and wonderful diseases. I love to call them they're not actually for people that suffer and they're just horrendous but people are suffering them. But there are they are represented minority.

Steven Bruce
I'm wondering if the question was provoked by what we're led to believe by the press and other sources that antibiotics are handed out, perhaps unnecessarily is a sort of a knee jerk reaction to unwell patients. In some places,

David Strain
we would never be recommending the antibiotics be given unless you've got bacterial infections. I mean, in my hospital practice, I spend longer stopping antibiotics than I do starting them. Because it because as you say it's a knee jerk response almost got a bit of an infection. But if you're doing that,

Steven Bruce
that means that there are people out there who are giving antibiotics unnecessarily, which is

David Strain
I think we could have an entire about antimicrobial resistance and the stewardship of the antibiotics.

Steven Bruce
We probably could do some says is there a link between mitochondrial damage or dysfunction and CFS? Yes, or association? Oh, that's

David Strain
an easy answer. Yes, if we head back after a slide somewhere, looking about all of the different things that have already been demonstrated, hold on, hold on, where are we? That's one of these ones. So now we have a fatiguing component. Now that is very clear evidence that you have improved increased in reactive oxygen species. So that's part of the defence mechanism that our body produces when you're sick, that are generated by the mitochondria of people with me. And that is one of the key triggers of inflammation and this is basically one of the one of the ways that our body protects itself from any infection. Actually, this is coming back to the the basics. Your body protects itself from any infection knowing that these infections mutate and therefore specific things are difficult by produce flooding your body with toxins, and then giving your body the appropriate anti toxin to healthy cells, and allow the unhealthy cells to be killed off by these toxins you produce, you produce reactive oxygen species in the mitochondria, that toxins that poison, and then you give the antidote to healthy cells. Now this was the actual the perfect example of this was COVID COVID, broke that pathway completely. It allowed our body to flip itself with toxins, but broke the system of giving anti toxins. And that caused a very specific mitochondrial dysfunction. But with the knowledge we've gained from that, we're starting to see more and more patients with M E, have got the similar sort of mitochondrial dysfunction, as we've been very, very accurately diagnosed in lung COVID. Even pre COVID, there was a well awareness that in exercise testing, if you put somebody on a treadmill, and you do exercise tests, and they use exercise, the loosest possible sense of the word, they're the most common exercise they use was just a dynamic to the grip strength metre. And what we would see is people with an E would move to anaerobic metabolism, a good 30 or 40% earlier than people without me. Now they could achieve the same power, same grip, but they'd moved to anaerobic metabolism much earlier, suggesting the mitochondria were not able to keep up with the

demands. If you then go to do the same diameter grip strength the following day, they would move even earlier. So that mitochondria hadn't recovered in the same time period that the people without me have. So it wasn't a grip strength issue, they have the same strength. It's just the fatigue ability was there. And we believe that's due to mitochondrial dysfunction. Now, again, this is a nonspecific test. The problem is there are lots of other diseases that cause mitochondrial dysfunction, and frailty that we see in the more mature adult is associated with it. People with diabetes have a not as severe but a similar sort of mitochondrial dysfunction that we see in me. And there's many other diseases that have a similar process. So that gives us a very nonspecific thing to be looking at. Not good enough for a diagnostic test, but definitely good enough for us to be looking at potential anti inflammatory treatment pathways.

Steven Bruce
So you got neuro inflammation on the slide here. We did a whole show on your information some time back, is the is there an approach to addressing neuro inflammation which will influence the severity of CFS,

David Strain
the whole new aim for Neuro inflammation access is something that's only just being looked at. And obviously, it is incredibly interesting because neuro inflammation has seemed to be the route to prevent dementia, if you can give the immunoglobulins reducing that, then you can, early enough, the hope is we can reduce dementia. Now there are those who would say that the cognitive dysfunction, the brain fog that people experience with me which, by the way, we're now up to the third of our criteria, that brain fog is a symptom of the neuro inflammation. The difficulty is, we're not sure if it's got the same trigger. The problem is that inflammation in order to get rid of a virus is entirely appropriate. Spontaneous inflammation is inappropriate. And the question then comes as In future, if you get if you break down the inflammation that is there to try and get rid of a virus that's causing problems, will you make things worse, rather than better? We know in Alzheimer's type dementia, it's neuro inflammation that's triggered by amyloid. And there are specific tests that we can actually do in the saliva for that, that might be able to pre identify and reduce the inflammation. But if if let's say that the Epstein Barr is living there, having inflammation to try and reduce the spread, might be the right thing. And therefore, although unfortunate that inflammation might be the thing that's stopping, it's spreading through the whole body.

Steven Bruce
Well, there's another interesting complication to our diagnostics. If one of our other speakers Tracy Whitney talked at length about B 12 deficiency on the show. She's not medical, which is probably one of the country's leading experts on B 12 deficiency because she's got it and researched it and so on so forth. But that produces being brain fog, and it also produces fatigue and a whole range of other symptoms. Is that something you'd want to eliminate before you said we've actually got CFS?

David Strain
Absolutely, we would be 12 tests, fine in folic acid folate test. These are all things that we know affect the brain function. And before people get through the door of a clinic, we will be doing those sorts of tests to find out do they have a potentially recognised treatable condition that we can do for this and I say recognise because M E is a disease and we are really hopeful that the next 10 years will offer treatments for it. But it's if we know what we're diagnosing, then we know how to treat it. And again, Going back to the earlier point that you made that I love the concept that me isn't one disease, we won't be having me in the future will have a chronic epstein barr virus will have chronic

immune globulin deficiency, for example, go back 20 years ago, 30 years ago, B 12 deficiency probably would have fallen into this category of chronic fatigue, because we weren't routinely testing it and therefore we might not be detecting it.

Steven Bruce
Interesting. Amanda says there's a relationship between me and migraine, she's just wondering about triggers, central centres, central sensitization, and mentioning that some cannot stand light and need a darkened room. Brain fog and fatigue are common features as part of migraine prodromos.

David Strain
So headache, migraine is type headaches and cluster headaches are very common symptoms in people with me, they have common triggers and and that tends to fit in with an aligned condition called the mast cell activation syndrome. Now, mast cells are the cells that produce non inflammatory immune responses to allergens, they go crazy for people who've got hay fever, they go crazy, and people who've got ATP. So to get eczema, for example, there is a group of people with IE who get a similar low grade mast cell response to just about anything in the environment. And when they get that response, a headache, migraine would be a very common feature. And they can often try to find out what the triggers were. Now the difficulty is, the triggers are anything that would produce a histamine response. And therefore today, it could be tomatoes. Tomorrow, it could be soft cheese the day after, it could be that dark chocolate. So if you just look at a diary, they can't see where the trigger is, until they do a map of this is the amount of histamine that I would have got from this, this and this, oh, yes, if I reach a certain histamine load, then that will trigger the migraine. And that's where the complexity starts to arise. But I

Steven Bruce
suppose that a lot of migraine sufferers or B 12 deficiency sufferers, they would probably fail your first criteria, they really wouldn't have that post exercise fatigue.

David Strain
They don't get this post exertional malaise? Yes, they will. I mean, if you're having a migraine, you feel terrible. People can be wiped out for days. But that's been a very clear, I had a migraine, I was fatigued. What we're talking about the difference here is that post exertional malaise component that they wouldn't experience. Yeah.

Steven Bruce
Moving on to Victoria. She says, Are there any preventative measures, she says she had glandular fever at least 24 hours in hospital for six weeks and bed bound for around eight months, she lives in fear of me purely because she had such a severe case of glandular fever.

David Strain
That's a really interesting concept. And one of the difficulties we've got is there are many, many cases like Victoria who have really severe me, really severe glandular fever spent six 812 months feeling absolutely terrible than men complete recovery. There are just as many people who had a very mild viral illness almost undetectable for some, but then two or three weeks, two or three months later, that's what triggered the the the Emmy was triggered, we genuinely yet don't know what the difference between those individuals were, some of that we're hoping to code me will bring out. But there are other components of that, that we need a good strong database of people

with me. And that's one of the big failings that we've have the coding for M E, in the general practice database in the NHS database in the big databases is very, very variable, shall we say, depending on actually one of the best predictors of how good your diagnosis of me is, is how close you are to a centre that the GP uses. And very often people just be diagnosed with fatigue, without having the next step of this person actually has me, they haven't been coded. Without that database knowledge, we don't really have a true idea of the total number in the plate in the UK with it. We estimate between 250 and 280,000. But that number could be twice as high, or it could just be spot on. I think that's one of the advantage that long COVID has given us that we've seen the number of people who got sick. And if you got long COVID, about half of people got better from that in the first six months, half of them, the ones that were still sick got better at 12 months, and of those who were left at 12 months, the majority of those have got an M E type illness, and they are getting better at a much, much slower rate. And I think that will give us a lot more about the natural history there.

Steven Bruce
Victoria, the question was about what she can do to excuse me, prevents me. Now I don't know how old Victoria is at the moment. She had glandular fever at 24. Would you say there's a there's a cutoff period where you say well, if you haven't had me, I'm got me by now. You're not going to get it.

David Strain
It's very rare for people to present more than three months after their trigger infection barrier. It's not impossible. But it's very rare. And I think if you had glandular fever more than three months ago, and you're completely back to normal, that's a point that you can confidently say yet again,

Steven Bruce
that should be reassuring for Victoria anyway. Simon says, Is there a link between CFS and fibromyalgia, and I've had quite a few patients diagnosed with both CCS.

David Strain
Now that this is a really difficult one, this is a controversy one, and you will get lots and lots of hate mail, whichever way we come down on this. There are some people that will say that fibromyalgia and M E are different parts of the same spectrum of disease. And for many, there will be a similar trigger in both the same things that make an E worse, makes Fibromyalgia worse.

Steven Bruce
And they tend to present in clinic as a similar similar character of patients, I think,

David Strain
and they do present with a similar character. And one of the difficulties that both conditions have is that there is no good diagnostic test for them yet. And therefore, very often, people with fibromyalgia and people with me have been dismissed by multiple different healthcare practitioners, before they actually got their diagnosis. So that automatically gives them a certain characteristic that we we see a lot and just being listened to just being said, Yes, this is your diagnosis, we don't have a treatment, here's what we're going to do try and accommodate them is is very useful. There is an overlap, and it's greater than the overlap, you'd expect to get by chance. But we still don't know whether that's shared risk factors, or whether that is the same disease, because from maps, there are other people that the ones that will be writing in because I've just said that the opposite spectrum to the same condition that there will be they're the ones who will believe that these are

similar diseases with overlapping risk factors, in the same way that the risk factors for stroke and the risk factor for heart attacks are very, very similar. No one would say a stroke and a heart attack is the same disease, but the risk factors are overlapping. It may be that the risk factors for fibromyalgia and the risk factors for me are overlapping. And therefore if you get one, you're more likely to get the other.

Sonya Chowdhury
Right. Okay. I was just going to say as well, one of the things that we'll be able to do with the decode Emmys study data, the questionnaire data, it's actually start to get some real figures around the diagnoses that people have. And you know, we've we've already got some from the initial analysis, but it is quite stark, there's the number of overlapping illnesses and the percentages and where they sit. I think we're gonna get some very interesting data on that. We just don't have it at the moment, because of the issues with diagnose, what's

Steven Bruce
your sense at the moment that there are more people not getting a diagnosis of me that should or that there are people being over diagnosed?

Sonya Chowdhury
I would say so. The there's some research that came out fairly recently that indicated 50, at least 50% of people with long COVID Have me like symptoms, slightly different figure from one David referenced early on. So if you add that to the 250,000, that's 1.3 million people, those people aren't being diagnosed with me. They're being diagnosed with long COVID. And, and actually what we found with dakoda me study, we wanted 5000 people diagnosed with me, after you know, having had long COVID And we're just not getting those we've had 1000 people I think that have come forward because they're just not being diagnosed.

Steven Bruce
David, you said your likelihood of being diagnosed diagnosis is directly proportional to your proximity to a centre. What are those centres?

David Strain
There are many MECFS services up and down the country. Yes, because the diagnostic criteria, we've got these positive diagnostic criteria now since that most recent nice updates, but previously, the diagnosis was a diagnosis of, of exclusion. There's no proven treatment for this actually, it's very similar to lung COVID. There is no proven treatment that fixes this. And therefore the majority of the treatment is about what supportive care is available, how we can help people live with the disease, how we can educate people into pacing. And because of that there is a massive disparity in the services that are offered up and down the country. If you take a disease like diabetes, there are very clear, you get the diagnosis when you HPMC is this, you then get this tablet then this tablet, then this tablet, and therefore diabetes clinics up and down the country all look the same. If you take a disease like me, then diagnostic criteria, we've got to have these four parameters and then you can refer to a service that's going to help you live with it. Some of them will have a doctor and those doctors will be happy to try different therapies by Based on low grade sea level data, so, mast cell cell mast cell activation syndrome, for example that we spoke about, there are many doctors that will try anti histamine drugs or sodium cromoglycate. mast cell stabiliser. There are doctors that will try that because we think it might work without a good evidence base. But the low risk drugs in other centres will say, well, there's no evidence base for it. So let's wait until there is an evidence

base before we do anything. Because of that the service itself differs. The engagement between the service and the primary care differs

Steven Bruce
from one that was kind of the thrust of the question, how do you get to the service from primary care presumed you've got to be referred by a GP? GP? Yeah, they're all NP referrals, right. And the GP is going to look at the NICE guidelines, which still talk about CBT and graded exercise. So they do I looked at them before they show, they don't say they don't say this is the remedy, but they still talk about them sort of somewhere towards the bottom of a page. And then there's a long list of tests, including ESR, and CRP and all sorts of other blood tests, are those tests designed to exclude other things, or they used to indicate me,

David Strain
so those tests are all designed to exclude me mimics. So the things like chronic low grade inflammation from polymyalgia, rheumatica, for example, then a test to exclude Another cause of the fatigue illness. So they're all there. CBT is still in there. But CBT is a supportive tool, right? CBT is no longer dealing with the consequences dealing with the consequences. Rather than trying to say Come on, pull your socks up and get out of bed. And the graded exercise therapy, actually the most recent review, so graded exercise therapy in the way that it was originally designed, is not fit for purpose, because it doesn't achieve the goal. Now what we now talk about a personalised Activity Plans, you find out where the energy envelope is, creates the right activity plan, based around where that energy envelope is. Now, actually a lot of this terminology, because a graded exercise treatment versus a personalised activity plan. If the activity goes through different stages, different levels based around a growing it is great, but it's a lot about terminology, anything. The words graded exercise therapy, are enough to trigger antibodies in a lot of people purely because of the concept. This thought process that people say, You go away for an in the first week you do this in the second week you do this the third week you do that people follow that plan,

Steven Bruce
without interference from other places even worse for psychology. I don't

David Strain
know any healthcare practitioner today that would say, Do this exercise, irrespective of how it makes you feel. But the whole concept of great exercise therapy, the terminology is a bit that's definitely been dropped now.

Steven Bruce
It's been early two lights on the horizon. But what are the what are the lights on the horizon for the current sufferer of me but you said there's no proven treatments. So they're going to be told to do 80% of whatever their exercise Limited is? What is the what are they recommended to do currently? What does the GP or the or the service offer? Well,

David Strain
at the moment, a lot of the service that we offer is talking about the how to live within the NG Envelope How to deal with it, we spend a lot of time discussing things around it. There are therapies we can trial that are based around extrapolations from other and restriction of these are. These are low evidence grade. But if you've got the muscle activation syndrome, if you've got evidence of any clots in the body, if you've got evidence of inflammation, we can give you therapies based around

those individuals. However, long COVID has been a big turning point long COVID. And then the similar sorts of time the the NHS and II action plan that was brought in place but a lot to do with work that Sonya had been heavily involved in this. This 10 Plus they were the PSP. Lately, priorities. We now have very clear respect research priorities, but also both a political desire to do it and political drive to do it. A growing recognition that this is a serious disease that it needs both the brains and the money being thrown at it. The will is now there to do it. And these partnerships are currently being established to look at research platforms to test drugs like this this T cell booster that the states use to use different antiviral therapies to use low dose Naltrexone and anti inflammatory Oh opioid that people use that drugs are out there that can be repurposed. And also, I know you mentioned it before we decode it but big pharma are getting interested. Now, there is pros and cons of Big Pharma BrainPOP pharma are interested in selling drugs, don't get me wrong their business businesses. In order to do that they need to see is there a market? Yes. Now there is now recognised market of at least a quarter of million people with me, plus those with the me type of long COVID which is making up to about 1.21 point 3 million people in the country. Big farm will get interested if you've got 1.3 million people in the UK, that's looking at 70 million people minimum worldwide, that with access to treatment, then they will get interested then they will start saying what molecular markers have you got? Can we put are the same brains that produce monoclonal antibodies against this in MS or something can rheumatoid arthritis can put the same technology to being into patients living with

Steven Bruce
this is a reassuring and correct way for remedies to work, isn't it rather than big pharma saying well, I've got this drug, let's do a study and prove that it works for something so often seems to have been the case in the past. And I

David Strain
think Big Pharma and particularly the technology that's been massively advanced during the last three or four years, are now interested in looking at truly personalised medicine. For example, if we can identify an immunoglobulin signature of an individual with me, and we want to boost that to tackle a vaccine to tackle a specific trigger drugs like the Maderna vaccine, the mRNA vaccines are the biontech mRNA technology, they can actually be used to provide a personalised mRNA vaccine that will then hopefully be able to boost an unnecessary immune response. Now, I know that's a long way down the line. But this mRNA technology for the vaccine was actually created in order to produce personalised cancer treatments, we've got a similar immunoglobulin signature, we may be able to get to a stage in 1015 years time, where we can offer personalised vaccines to help at least suppress

Steven Bruce
the symptoms and I assume that you're less likely to get that visceral polarised approach to the vaccine that we had for COVID because it was pushed out in such a short space of time. And, you know, the one end of the spectrum said he can't possibly be saved from the other side, I'll take it anyway.

David Strain
When it comes to the vaccine technology, I don't want to start going down vaccines and the polarising nature. There were mistakes that were made in the marketing of that vaccine, the mRNA, we said this big new technology and everything actually, it's not a new technology had been around for 10 years, the only thing that was new is that it worked at doing what it was supposed to do. And I

think that's that was the new component, but it wasn't particularly well marketed when he went forward. And there were antibodies to the vaccine for want of a better term. But what we're talking about here is a personalised jab of a stimulant of an immune system that is designed for a person about their disease. Those individuals people living with moderate severe or even mild me will take anything if they think is going to help if we can get to a stage where we can actually have a probe and therapy that's going to offer them three or six months released from being bed bound in a darkened room, unable to even speak to your family, let alone socialise with your friends. And we can get them to a state where they can at least socialise again, they will take that and that often.

Steven Bruce
I hadn't realised perhaps because they're not the sort of patients that would come to our practice in my practice or other chiropractors and osteopaths that are watching. We wouldn't see people at that end of the Emmy spectrum. And it's quite shocking to realise that there are people I don't know how many of the million or so that you talked about are likely to be at that end of the spectrum. But that's a that's a lot of economic benefit that the country has lost, not to mention the quality of life for those people.

David Strain
Absolutely. I mean, they're the economic argument for getting me right is massive,

Steven Bruce
which is what counts for the government? Yeah.

Sonya Chowdhury
Yeah, there's, I mean, there was a study that's done a few years ago that said 3.3 billion on the 250,000. It's very conservative estimate. So if you multiply that up to 1.3 million people

Steven Bruce
is that the opportunity cost of people who are sick or the cost of dealing with those people,

Sonya Chowdhury
the opportunity costs the cost to the economy, so not not in work. Carers often didn't even look at carers having to give up work. But I think to your your question around hope is a really important one. Then the other area is AI, artificial intelligence. And so there are some companies that we've started working with tech bio companies that are now applying AI to look at specifically as David was talking about that precision medicine. There are also companies in the states that were in discussion with who are wanting and their financial investment companies that want to solve this problem. So it's a scientific problem that needs to be solved, it's waiting to be solved. So if we can reduce that 15 years to 10 years or five years, because we get so much money that goes into the research, it brings, you get the money, it'll bring the researchers you know, we're lucky. We've got David and Chris Ponting at Edinburgh University, we need to we need a massive people. So I do think there are things that can happen that can reduce that that timeframe. But it is that precision bit that is really important.

David Strain
And the cost to the economy is massive amount. I think this this 3.3 billion is actually a massive underestimate. Because if you remember, the younger females and these are five to one female ratios, I've got patients have quit for university because of it. These are the big high fliers, that

should be out really pushing the economy. And instead, they are at home, unable to engage. And we've got, I've got a patient who was a championship hockey player who is now no longer able to leave the house. These are people that should be right at the forefront. And they are the missed opportunity costs, but also the bit that's never measured in these figures, the impact on their family, they're the sister or the mother that's given work in order to help look after them, the carers, the additional community costs, let alone the fact that this is a really first of first grade students, all of a sudden, is unable to put all of this education to its form.

Steven Bruce
Actually, there are still some questions here that I need to answer ask you, but you've made me think there about how it is the we are osteopaths, chiropractors, you know, we are our primary health care practitioners, how are we likely to be able to help people with me? And one of those perhaps is the conversation with a healthy parent or family member who says oh, yeah, my my brother, sister, son, daughter has got me, should we be looking for those clues and saying, Well, have they gone down the right route? Have they got the right help?

David Strain
Absolutely. I mean, that one of the things that since I've been involved in the charity, since I've been involved with the clinic, as soon as you start talking about openly, everybody knows somebody who's got it. Now quarter million people, that's us. That's a lot of people at a conservative estimate of got this. I suspect there'll be a lot of the parents, a lot of brothers sisters, who are actually coming to visit a chiropractor to help relieve stress. And we have the conversation. Well, actually, I did the back that was helping to turn my sister because she can't turn herself in bed. She's got me

Steven Bruce
haven't got me that mean, someone's told her she's got it. So presumably she's in the pathway are we are we likely to find ourselves with either patients who haven't been diagnosed or with patients who know someone who they think might have me that we should be giving advice to?

David Strain
I think the advice for someone who hasn't been diagnosed, make sure they get checked out, there are still lots of other treatable causes of significant fatigue that should be looked. So

Steven Bruce
we're gonna ask your four questions and read on the fourth one, the post

David Strain
exertional malaise is by far and away the worst, and actually feel the practitioners when they see somebody, they see someone and said, How was your last treatment that will actually have to go to bed for two days afterwards, exhausted by doing by doing it, but I felt great. It fixed that problem. But I was really worn out afterwards. That's the sort of trigger that my suffering, okay, that's unusual. We don't normally have people needing to go to work for two days afterwards. Is this a disproportionate response? The sorts of triggers that you might start thinking Have you thought about, and that's where it comes in. Because very often, you know, if you get significant fatigue or patients, that posture may not be as good because they are fatiguing. They get unexplained pains that they can't account for. That might be the route that they come through the services and that's why you might be able to pick them up.

Sonya Chowdhury
There's also an action for me website, we've got lots of resources, there is a booklet, half of it is for somebody who thinks they might have me the other half is for a doctor so you know if you've got people that are watching there are resources available anybody can access free of charge, but also you can signpost people to the website and our services

Steven Bruce
when a simple search for action for me we'll bring that up we'll send it out with the email after the show as well. We cover your fourth criteria and we have the fourth was the brain fog it was the fourth was the brain fog was the third one. So no brain has gone

David Strain
that's the brain fog so refreshing sleep is a debilitating fatigue number two's post exertional right three was a threat sleep for is a brain fog. Okay,

Steven Bruce
so we've got those some more questions. A reminder again asks What do you think David of the use of Coenzyme Q 10 or other supplements in dealing with me?

David Strain
There has not been a good run mice control trial of any of these supplements. Many people try lots of different supplements. My standard advice for these they have all been demonstrated to be safe as a food substance. If a patient feels better taking them, take them. If they take them and it makes no impact, don't take them on I've had lots of different patients who presented I mean their Coenzyme Q 10. The vitamin K 2k Seven rather, which is a vitamin D subtype be able to take in turmeric, people taking v 12. Yet v 12. Works for some, even though they've got a normal B 12 level it take a little bit extra that makes them feel better. If a supplement works for you, take it but remember, this is a food substance. But when you're visiting your doctor or your healthcare provider, make sure you do declare all of them they should be asking anyway, but taking them with you because some of those do interact with more proprietary medication, they use similar pathway so Q 10 is a great example that patients from Q 10 And then the statin therapy that they might take posthaste are more likely to get the muscle aches and pains that if they don't if they don't take it.

Steven Bruce
Right. Okay, thank you. Lots of questions that some are not strictly related to me. Phil says, first of all, what are antiviral what antivirals are effective against Epsom Epstein Barr Virus?

David Strain
So the Tamiflu is actually quite effective, but it doesn't have particularly good brain penetration. So it's not one that we're going to be using. There are many of the antivirals that we use in hospital for the HIV therapies that may have used ganciclovir, for example, is one. But these are things to be that we need to be trialling and cautious to start naming the ones that can be bought over the internet, purely because I don't want to be a Donald Trump sending hydroxychloroquine sales. They need good clinical trials. And we need careful criteria before we start using them.

Steven Bruce
So you're not either presumably recommending Boris Johnson solutions as a specialised hairdryer, they'll blow up you'll know ultraviolet light this is our government we're talking about. You kind of

touched the kind of consider this already with John says does nutrition have a place in the list of ameliorating factors?

David Strain
Absolutely. Absolutely. And actually, there is good evidence that the microbiome the gut microbiome, particularly is different in people with me. Now there's a really good evidence for that. And remember, the gut microbiome is responsible for how we metabolise most of our vitamins, and getting nutrition right is essential to stabilising that gut microbiome. Actually, there's a group in China that suggested that it was the other way around, and impaired gut microbiome led to deranged metabolic pathways that lead to the mitochondrial dysfunction that we saw. And actually, that is a train of thought that we are now revisiting, because there are some diseases that we can now do a good bacteria transplant, Clostridium difficile, where ever we won't have any adverse effects, and we basically give them capsules of different grades of

Steven Bruce
effects. I remember reading about this, it's tasteful therapy.

Well, hopefully, John anyway, Rebecca's asked about what you said about inflammation, should any sufferers have an opinion about taking anti inflammatories,

David Strain
the low dose anti inflammatory tablets are one of the therapies that we're going to be trialling, again, we're in the difficult phase that inflammation against a long standing bacterial infection or viral infection or parasitic infection is an appropriate response. And there is a risk that if we give an anti inflammatory, but actually we make make that worse. And a classic example for that, the shingles shingles will get worse if you give steroids because then it lowers your immune response against it. If the inflammation isn't appropriate inflammation, anti inflammatories could make it worse. And that's why we don't make any recommendations until we've got the good trials that we need to be doing over the near future.

Steven Bruce
Right? I shouldn't do quite a few people will find that helpful, because very often our patients will come to us with whatever they've come to. And so we should be taking this particular anti inflammatory. Now they might not, might not be coming to us. For me, that's not we're not the first port of call for a disease like that. But again, we can at least we can least point them in the right direction. So I

David Strain
think there'll be very few patients that haven't trialled and anti inflammatory medicine, regular paracetamol is a really potent anti inflammatory. And one of the good questions Well, the good indicators that might make you signpost to them towards a different route is if they took an anti inflammatory and actually they got worse as a result of it. rather than getting better,

Steven Bruce
okay. Ken says we're going back to excluding other diagnoses RME patients screened for Lyme disease?

David Strain

Yes, most patients will have their Lyme disease tests before they even get to us. And it's one of the tests that we do routinely when we see them in clinic.

Steven Bruce
And this comes back to what I think you said a moment ago, sooner, Christina says it prevalent amongst high achievers,

Sonya Chowdhury
there's no evidence to suggest that

Steven Bruce
come out of your study, you're getting that sort of information. It's

Sonya Chowdhury
not that level of detail. I mean, going back to what we were talking about before, in terms of pushing through, and it's a natural human thing a bit under the weather, a new push through. So there, there has been, we've seen stuff in the papers and elsewhere, people saying, you know, people are pushing themselves, they've overdone it, they've stressed their body, all of those kinds of things. Now, I'm not a doctor. But I know that if you want to overcome something, some illnesses, some assault to your body, having your body in the best possible place to be able to do that is helpful. But you know, sort of saying that somebody is a high achiever. And that's what's led to me is not something that we would we would say, and there isn't the evidence base of that. But of course, people are naturally sort of, you know, attuned to trying to pursue that illness. And that bust and boom, can be very, very unhelpful because you're not sticking within your 80% Energy envelope.

David Strain
The Navy a difference in recognition of it, though, that's something that we really noticed in lung COVID. Recognition of lung COVID in high achievers was much more prevalent. And the other phase if you remember, when we started hearing about it, it was always a triathlete or an Olympic rower or something that we said, This person had mild COVID, but then they've been massively debilitated. And a big part of that is if you are used to having a body that runs at that sort of level, even a mild difference is noticed, if you're used to being a first class honours student, and then all of a sudden, you can't do a, you know, five minutes a buco puzzle that's really noticed. There are preconceptions in the healthcare practitioner that you see, if you've been an Olympic rower if you've been a world class, first class on a student, and then all of a sudden, this thing, it's a very clear apparent difference, and they're far more likely to recognise it. Whereas if your entire life is playing with the Gameboy, or Playstation, and then all of a sudden your thumbs not quite as active as it was, it is less likely to get recognised by the practitioner.

Steven Bruce
I remember years ago, when I was studying sports, osteopathy and sports that somebody put forward the hypothesis at least that if you are an elite athlete, you've got very little margins in your health, one slight injury can be catastrophic. So if somebody who's pushing their psychological stresses or whatever the High Achiever are, the more likely then to perhaps suffer the result of a minor infection and end up with me.

David Strain

It's very difficult to say, because the converse argument is true that somebody who is that fit that active that well looked after that actually, their immune system is the one that's going to clear that minor infection very, very rapidly. So he could be the converse of that. But as you say, I think it's because they are using 100%, that if they're running at 90%, and they'd be very clearly monitored, it's more likely to be picked up.

Speaker 4
Right. Now, this is almost certainly likely to be the last question because we're running out of time, but also because I think there's quite a bit to this. Peggy's asked if it's a diet change, but she's asked whether taking sugar out of the diet can help but I wanted to ask about this connection you mentioned to him diabetes, and me so.

David Strain
So sugar after the diet is a very difficult concept. One of the difficulties that anybody has in the first stages of a fatiguing illness is the Reach for the sugar that carb and processed food, that caffeine drinks and all of the stuff that's supposed to make you feel good. Now there are some of these things that do have a very significant boom burst effect on mitochondria. Sugar is a great example. Now, if you don't have diabetes, you won't get a big surge of sugar after you've had that picture of the deep drink. So it doesn't do if you do have diabetes, then get me that is a disaster because you then do get these mitochondrial boom bust presos processes going up, which down down. One thing I would say is changing any food out of your diet is unlikely to have as a dramatic change as people give it credit for. One of the big problems that we face now is the effect that changing the diet rapidly has on the gut microbiome. And that gut microbiome is is essential for all of those nutrients and the absorption. We can't make many of the vitamins without the bugs that live inside us. If we suddenly go from a very healthy, you know, solid meats, but rapidly digestible processed carbohydrate rich foods and caffeine, microbiome changes of gut metabolism changes, and we will feel different for many of our individuals, that is a change for the worse, because they get this boom bust process.

Steven Bruce
Right? And so is the connection between diabetes and me simply what is what do you just described there? Or is there something more technical,

David Strain
that the similarities in diabetes and me are very much about how it interacts with the very, very fine blood vessels in our body, talking about the microcirculation, the capillaries, the vessels that actually deliver the oxygen and nutrients to the tissues? In diabetes, we know that that causes impairment of the microcirculation, because of the chronic sugar exposure, we also see impairments in the microcirculation in people with me. Now, I think that's very unlikely to be the same pathological process. But it's the same effect. So a different cause, but same effect leads to similar consequences.

Speaker 4
Thank you, David. Certainly, thank you very much. We are we are out of time. And we've had just shy of 500 people watching this live show. So we've got a lot more watching the recording as well. It's clearly a topic of interest to the people in my circle as it were. So I'm sorry, sorry that we're out of time, as usual long before we run out of questions or things to talk about. That is it for this evening. See you soon I hope good night