# Tackling COVID TACTICally: Transcript

**Dr Stranks:**

Good evening, everyone.

Welcome to our event this evening and thank you very much for joining us.

We hope that you have enjoyed the Cambridge festival events so far and that you'll enjoy spending time with us tonight.

We're going to start our event this evening with a discussion about the TACTIC-R trial and about the local research that we've been doing on COVID-19.

We invite you to submit your questions to us and there will be a live Q&A part at the end, so do submit your questions using the Q&A function at the bottom of your screen as we go along and I'll be able to take those at the end.

Joining me this evening I have three distinguished researchers, all of whom work both in clinical care and research, and who have played active roles in our local research effort throughout the pandemic.

I'm joined tonight by Professor John Bradley, by Professor Ian Wilkinson and by Dr. Frances Hall.

Professor Bradley is the Director of Research at Cambridge University Hospitals, Professor Wilkinson is the Director of the Cambridge Clinical Trials Unit and Dr. Frances Hall is the chief investigator of the TACTIC-R trial that we're going to be discussing this evening.

*(Dr Stranks addresses Prof Bradley)*

I’m going to open our questions this evening with a question for you, Professor Bradley. As Director of Research at Cambridge University Hospitals, you would have been involved in a lot of the preparations that we made when we were leading up to the first COVID patient being admitted at about this time last year.

Can you tell us what was going on at about that time and what preparations we were making to be able to support the research effort?

**Prof Bradley:**

You have to remember the uncertainty, actually the fear, and the courage of everybody: patients, health professionals and researchers.

At the time we were really very unclear what lay ahead.

In fact there were two parallel processes that we had to undertake.

One was thinking about the existing research on the campus and how safe it was for the participants.

We normally would have about 1000 studies running across the Cambridge Biomedical Research Campus and we had to pause many of those.

That means notifying the patients and notifying the regulatory authorities and obviously thinking, particularly around clinical trials where people were receiving drugs, about the relative safety of pausing the study, or continuing.

Then in parallel with that, we were thinking how can we, through our research effort, help the COVID research?

The early work focused an awful lot on diagnostics.

People were arriving in hospital; we needed to know very rapidly (if we could) whether they were infectious or not and one of the earliest studies was around using a point of care test.

In fact we were the first to report on the use of point of care testing to diagnose people within 90 minutes of undertaking a test, so that we could get them to the right environment to protect them and others.

We were also looking at the diagnostics as even at the early stages we were aware that there were variants emerging.

We weren't so worried at that stage about whether they were susceptible to treatments or vaccines because we didn't have those.

What we were more worried about was whether the diagnostic tests would still detect them, so we were doing those sort of studies in parallel.

And then we wanted to try and better understand the disease and there we exploited a resource or infrastructure that Cambridge leads called the NIHR BioResource.

This is a vehicle for people to become involved in research.

It is a national resource - there's around 200,000 people across the country involved in it.

Essentially what they do is tell them a little bit about themselves, allow us to have a look at their medical records and collect a sample from which we can extract DNA and learn about their genetics.

Then if we have a research study that we think they might be interested in, we contact them about it.

What we did was establish the COVID BioResource and that allowed both patients and staff who were interested in participating in research to join the COVID BioResource, and that way we could learn about how they responded to the disease, and about the actual mechanisms of disease.

They were the early studies but of course while all that was going on we were also setting up to run clinical trials.

**Dr Stranks:**

Fantastic, thank you.

*(Dr Stranks addresses Prof Wilkinson)*

Professor Wilkinson, you're the director of what we call the Cambridge Clinical Trials Unit (CCTU) here in Cambridge.

Can you tell us briefly, first of all, what does the Clinical Trials Unit usually do, and how is it different during this period of set up of lots of different studies?

**Prof Wilkinson:**

Thanks.

What we normally do is help people develop new treatments to improve patients’ outcomes, be it a drug or device, etc.

So, our role in that process is to work with people who have ideas and help them realize that idea: to put together a protocol (which is a set of instructions about how the trial is going to run); to help them get the permissions which they need to run the trial and navigate that; to help input into design and statistics; collecting the data; and then analyzing it.

That's our "normal job" and we would normally run about 40 to 50 trials at any one time and be closing some of those down and setting some of them up.

They might just involve Cambridge, or there might be several sites in the UK, or they could be international sites, so we do all sorts of trials but we're particularly keen on running early phase trials and developing really novel interventions or repurposing drugs, which you mentioned earlier on.

So as Professor Bradley said, when we were all concerned about the pandemic, two things happened really: the trials unit took a decision that it wasn't going to open any new trial not related to COVID and we worked with investigators to determine whether they should be closing down or pausing ongoing trials.

Initially, there was a different type of response from different investigators, so some investigators just stopped everything, whilst some wanted to try and continue.

But as the pandemic progressed, virtually everything stopped that wasn't critical and there was some critical cancer trials that had to continue.

Then we set up a number of trials designed to look at COVID, including TACTIC-R with Frances Hall, and a number of things changed.

So a lot of our staff are working from home - we embraced something called zoom, that I can't say was familiar with before we started.

We brought critical staff back because sometimes that's the only way to get things done and we prioritized our efforts against COVID.

Whatever people were working on, they started working on the COVID studies and the regulators had changed the framework that we have to work in.

So they are the people who give you ethical permission or the government agencies that allow you to do a study with a drug.

They were working to much tighter timelines, so gone were the 30 days for a response - you probably got a phone call the next day.

And we went from setting up trials in what would be three to six months to setting up trials within a month, etc.

So it was a Herculean effort by all the staff in the trials unit.

Dr Stranks:

Amazing, thank you.

*(Dr Stranks addresses Dr Hall)*

Dr Hall, in your usual role, you work with patients with what we call rheumatoid conditions.

On the University Hospital website you are listed as the connective tissue disease lead.

I think many of the people who are joining us tonight and many of the public think of COVID as a condition of the lungs and the respiratory system, so where does your expertise come in here?

**Dr Hall:**

Yes, I realize it's not an obvious connection to a rheumatologist!

What I normally do is look after people with multi-system autoimmune disease, so these are diseases where the immune system does something it's not supposed to do.

So what it's supposed to do is attack bugs like viruses and bad bacteria and fungi.

What it sometimes does, unfortunately, is makes the wrong call and attacks and bits of yourself, bits of people, and people get sick as a result of that.

That's my day job really: it is working out how to best control these conditions where the immune system goes a bit off of piste and starts attacking itself.

So it wasn't obvious to me at the outset of this that COVID was going to be a disease I have a role in researching, but I started reading about the implications of COVID for my patients, thinking about my patients taking a lot of medicines which damped down their immune response.

I'm thinking initially that this would probably be a bad thing because it might be going to make them more susceptible to getting a bad dose of COVID.

And then as we really started looking at the data coming from China and coming from Italy, it became apparent that it wasn't really quite following that model.

So, although most people get COVID as a viral infection and handle it as a pretty standard viral infection - they get on well and then their immune system attacks the virus and then they get better - as we all know now, a minority of people go on and get very sick.

Unfortunately, some of them died as a result of it.

But what became clear was that people were getting sick at the point where their learned immune response to the virus was kicking in.

So this is the time when we expect them to start being protected, but a minority of people started to get even more sick at this point.

As data flowed more and more, it became clear that we were dealing with a condition that was predominantly due to the immune system causing damage rather than the virus causing damage.

So this started to look a lot more like my day job and really that's how I got involved.

**Dr Stranks:**

Fantastic, thank you.

And after you had the idea for the trial, how did the TACTIC-R trial team put together to run and deliver the trial?

**Dr Hall:**

Well, when I when I started thinking about COVID as an immune mediated condition I started thinking: well we should really be looking at damping down the immune response.

The focus has changed a lot over the last year, but the majority of focus at that stage on the research front was to think of it as a viral infection, to think about tackling it in that sort of standard way.

So I went to Ian Wilkinson and Joseph Cheriyan in the Clinical Trials Unit and said "Well look, what about doing this?" and they immediately understood the importance of the question and why that was a sensible approach.

Of course we then talked to John Bradley and the Biomedical Research Centre infrastructure came in behind.

But then we also engaged with a lot of other clinicians up and down the country who have expertise in dealing with immune mediated diseases, many of them rheumatologists.

Many of those were supportive and many of those people became our investigators and our clinical trial leads in hospitals up and down the country.

Two centres particularly became very heavily involved with the design and running of the study - James Galloway at King's College London and Andy Cope at Guys & St Thomas's.

Together with us they formed a key Consortium.

So the Clinical Trials Unit in Cambridge, and the statistical and clinical trials units, those centres as well became involved with the design.

And then of course we had to talk to pharmaceutical companies as we were thinking about which drugs we might want to try and have discussions to set up collaborations with them.

So that was really the starting point and then behind all that there's an army of doctors and research nurses, and of course, a very large number of very courageous patients who've stepped up to the plate to make this work.

Dr Stranks:

Fantastic, thank you.

Professor Wilkinson, I know that researchers can't just go and start up trials whenever they think it's a good idea.

So when they do have an idea for research, how do they go about getting started?

You mentioned some of this before, but what checks and balances are in place to make sure that the trials that we run are safe and that they're actually able to answer the research questions that we're looking to answer?

**Prof Wilkinson:**

It's an interesting question.

It depends what type of research you want to do really.

All research requires ethical approval, even if you want to ask people some questions.

But what we're talking about here is drug trials and they are highly regulated to ensure safety for participants and to the protect medical staff as well running those trials.

And I have to say the UK has really led the way in the regulation of trials over the last 50 years or so, so it's got a very well-oiled machinery for doing that.

So if someone comes with an idea like Frances, the first thing is to have a chat and see whether it's a sensible thing that we think we should be investing time in from the Trials Unit point of view.

Then you've got to make a protocol to describe in some detail what you want to do and why you want to do it.

Then you've got to go and get some money, because you've got to have the funding to enable you to do the trial and that's I guess where the BRC can be very helpful, as it has a lot of infrastructure and expertise in helping you to design that trial, and also the NIHR has various funding streams that you could apply for.

Once you've (hopefully) been successful and got the money, then the hard work starts from the Trials Unit point of view, in that there's an inordinate amount of paperwork.

It's still actually largely paper even in the modern era!

You have got to put together information for patients telling about the trial, much more detailed protocol forms to collect all the data, we have to make a database, and then we go out and get the regulatory approvals.

So Professor Bradley as head of R&D would need to approve what we want to do before we do anything else.

Then we go to an ethics committee, and lots of different people with expertise (lay people, statistics expertise) will ask us questions and review what we're going to do and usually make some suggestions about how things might be modified.

And then we go to the regulator, so for drug trials the MHRA (Medicines and Healthcare Products Regulatory Agency) and they review the safety of what you want to do.

If you're repurposing a drug, often that's easier because there's established data about the drug - it's been into people before.

If you're working with a new chemical entity, then you have to produce a lot more data to convince the regulator that it is safe to do.

And then you can get going.

The Trials Unit will monitor the progress of the trial and make sure everyone's compliant with the various regulations to make sure that it's done safely and that we have faith in the findings of the trial.

**Dr Stranks:**

Fantastic, thank you.

Professor Bradley, we are really really fortunate in Cambridge because we are home to some of the world's best scientists and clinicians.

And yet, since the start of the pandemic, there's only so many patients even through Addenbrooke's. This is a good thing for healthcare, of course, but for research can present some problems.

You mentioned today about the COVID BioResource earlier, but how are we making sure that we learn as much as possible from each patient that comes through our doors and also so that there aren't more trials than there are patients?

**Prof Bradley:**

Right from the very beginning, we reorganized the research staff.

We have a very active clinical research facility on the campus embedded in the hospital and we redeployed many of those staff onto the wards, so they could help with the recruitment of patients.

We hope that we offered virtually all patients the opportunity to participate in research and indeed at the beginning we would have a review meeting every morning, where we would try and check that we had given all patients that opportunity.

They could, should they wish, join the BioResource and that would allow them to provide us with samples.

The real advantage there was that because we are on a Biomedical Campus with many research facilities, and indeed, some of the very high level of containment facilities that are required, we could rapidly analyze fresh samples.

And indeed, many very experienced researchers changed from their roles in the lab to being couriers and running samples between the patients and the lab so that we could analyze them as quickly as possible.

That gave everybody the opportunity to participate in research.

As we move on, and we're able to enroll people into clinical trials, they would have different entry criteria.

And really, again, we hoped that we could offer all patients the opportunities being a clinical trial and joined up, as you've heard from Frances, with other centres, so that we could share our experience, and make sure that the right patients got into the right trials.

**Dr Stranks:**

Fantastic, thank you.

So, most clinical trials that have come across all come with their own fancy acronym and TACTIC of course is no different. I think it suits it to a tee.

Dr. Hall, could you tell us what does TACTIC stand for? How did how did you come up with the name?

**Dr Hall:**

Well, I have to credit my colleague and CCTU Joseph Cheriyan with this name but the full name of the study is 'Multi-arm therapeutic study in pre-intensive care patients infected with COVID-19'.

Obviously we don't want to say that every time we want to talk about the study!

This isn't actually the first letter of each word, but Joseph concocted a scheme of borrowing letters from words in there to come up with TACTIC and of course that has an additional significance in that this kind of immune modulatory approach is a distinct tactic from the dominant tactic a year ago, which was antiviral.

**Dr Stranks:**

Of course.

In the trial at the moment there are two drugs that have been selected.

So how were these two drugs initially chosen and what does each drug do?

**Dr Hall:**

I mentioned before that we felt we were dealing with was a condition that was predominantly driven by the immune system behaving inappropriately.

So we sat down and considered candidates for the drugs that were already out there being used to treat autoimmune conditions or in conditions where the immune response is known to behave badly and cause disease.

We looked at what was known a year ago about the mechanisms under that broad umbrella of immune-mediated damage and we could see that one set of problems seem to be caused by chemicals in the immune system called cytokines, which were being upregulated inappropriately.

And each of these cytokines is a sort of immunological WhatsApp group of its own.

Each one triggers a whole pile of other messages to all of its friends and kicks off a whole range of different processes and several of them are going haywire at the same time in COVID-19.

So we thought that we should choose an agent which interfered with these WhatsApp groups.

We became aware that several other groups were thinking about using surgical strikes on individual WhatsApp groups by using monoclonal antibodies.

But we decided to take a slightly different route by choosing baricitinib, which is a medication which actually dials down the chatter in several of these WhatsApp groups all at once, rather than taking an individual one out.

There are several drugs in baricitinib's family but we chose baricitinib because it also, quite separately, has a bit of a direct antiviral action because it reduces the uptake of the virus into cells.

We thought that was very useful to have, so that's how we chose baricitinib.

Baricitinib is repurposed because it's used in rheumatoid arthritis.

It's used as a severe end of rheumatoid arthritis so obviously as a rheumatologist I was very aware of baricitinib.

Ravulizumab was the second one we chose and that targets a completely different mechanistic strand.

This inhibits a molecule in what is called the complement cascade.

The complement cascade is a group of molecules in the immune system that acts as a tag team, so they kind of pass on the message from one to the next, activating the next person along.

So they amplify inflammation, but they also end up producing a little molecular hole-punch, which really does what it says on the tin - it punches holes in cells and it kills them.

Now that's a that's a good antiviral strategy and actually antibodies can focus this hole-punching activity on infected cells.

But we knew that because antibodies could focus this and that people were getting sick when they were making antibodies to the virus, that actually this complement cascade might be important and indeed over last year, a lot of additional evidence has come to the fore to show that's the case.

So that's why we chose ravulizumab, and that's also repurposed as it is used to treat a kind of anaemia which is caused by the immune system going haywire and making these hole-punches in red blood cells.

**Dr Stranks:**

Amazing.

Professor Wilkinson, I've heard that TACTIC is called a 'platform study' which I think is the same as some other well known trials across the UK such as RECOVERY.

Can you tell us what a platform study is and why is it being used so often in the pandemic?

**Prof Wilkinson:**

Traditionally when we did a trial, you might pick a drug and a placebo and put them head to head and run what's called a randomized controlled trial.

What a platform trial does, is it allows you to add drugs or take drugs away as you go along.

It's generally considered to be a much more efficient way, because you have one control group, but you can have different drugs added in as treatments or taken out if they're not proving to be effective, based on some early readouts.

In a pandemic, where as I said to you before, you're compressing the paperwork and approvals that might take six months into weeks, it's just much more efficient to put all the effort into creating a platform and then you add in drugs.

Now having said you can't just add in drugs, there's some checks and balances around that.

I won't bore you with the details but there's some statistical methodology you've got to be aware of.

The other point is you have still got to put each of those new treatments past a regulator and the ethics committee as well before you can do it.

So it's ideal for pandemics.

**Dr Stranks:**

Excellent, thank you.

Professor Bradley, as part of your role as Director of Research, you need to ensure that the research that we do in Cambridge complements the research that's happening across the UK, and indeed internationally.

So, how does TACTIC and other Cambridge-led trials fit in with the wider national and international efforts?

**Prof Bradley:**

As we've heard, TACTIC is a national trial and indeed we hope we may be able to open sites internationally.

So it does need to be coordinated and there are a number of other centres that are working with us on TACTIC - we've heard about some of them.

Then there will be other centres that are doing different platform trials.

There's one national platform trial that virtually all centres are involved in - that's the RECOVERY trial, which is fairly unrestricted in terms of the entry criteria.

Whereas in the TACTIC trial we are looking at a select group of patients, particularly those that we think may not do so well and are perhaps more likely to respond to the drugs that are in the trial.

For the other studies, we obviously collect a lot of samples and we are analyzing those to learn about the disease.

In many cases we're part of national consortia that are actually doing perhaps immunological studies looking at the response to the COVID virus.

So it is all joined-up and has been joined up very rapidly by this remarkable national research effort.

**Dr Stranks:**

Fantastic, thank you.

Dr. Hall, with Cambridge and so many other participating hospitals supporting TACTIC-R, can you tell us where are we up to with the TACTIC trial?

Can we expect any any results anytime soon?

**Dr Hall:**

We have 416 patients who've been randomized to one of the arms, so that's either standard of care alone, or standard of care plus baricitinib, or standard of care plus ravulizumab.

At the moment, recruitment is obviously slow for all sorts of good reasons like the fact that the case rate has gone right down, which I think most of us are very happy about!

So we're gathering the data and generating queries if there are any problems or issues with the data and getting all that clean, so that it can go into the statistical analysis part of the study.

As Professor Wilkinson mentioned, this is designed as a platform study and part of that design is what's called 'adaptive' so it allows us to look at the data and do an analysis at predetermined points, so we are now at the first predetermined point where we need to look at the data.

We anticipate having the data cleaned and ready to do this analysis in May.

And then, based on what we see from that and what's happening in the country at large, we then need to make a decision on what happens next.

**Dr Stranks:**

Okay, very exciting.

Professor Wilkinson, whatever happens next with the outcome of our interim analysis, what will the next steps be?

What happens to a treatment that appears successful in a in a clinical trial?

**Prof Wilkinson:**

So if you have a signal suggesting that treatments working, in a normal situation you might want to test that in a different trial, and certainly a regulator before they gave a licence may want two different trials to prove the drug works.

It's slightly different with a repurposing study, where a study on its own may be enough to grant you a licence or to grant you an indication.

Certainly what we've seen in the pandemic, for example, with some of the drugs that RECOVERY has looked at, or in some of the American trials, those drugs have been fast-tracked, helped because they’ve got a licence already and we know they're safe and we've made them already.

They've been fast-tracked to us and they've really got into patients incredibly quickly.

If we saw strong signal of efficacy (that means it's working) with baricitinib for example, then I hope that that would get fast-tracked and we make it available to patients rapidly, because the whole point of clinical research is to improve outcomes for patients and we need to therefore work very quickly, particularly in the context of a pandemic, to do that.

**Dr Stranks:**

Well, fingers crossed it's good news when the time comes to do those final calculations!

Professor Bradley, today we've had hundreds of patients and healthcare staff participate in COVID studies right here in Cambridge.

Certainly my team have been overwhelmed, and I know researchers right across the campus have been overwhelmed, by the response of the public in their willingness to participate in these and other studies.

What would you say to our patients, and anyone who's considering taking part in clinical research?

**Prof Bradley:**

We would encourage people to do so!

If they visit our website they can find out a little bit more about the research that we are doing and how they could get involved.

I think it's important.

I said at the beginning, when we started on this journey we were very uncertain about things - there was a lot of fear, also a lot of courage.

We really are tremendously grateful to everybody who has contributed to the research effort.

We've got over 6000 people now in the COVID BioResource and many of those were recruited in hospital.

They were people who were sick and who were frightened, but they were still prepared to help us with the research effort to understand, and ultimately treat the disease.

So it's really a very big thank you to them.

**Dr Stranks:**

Fantastic.

Well I think that's probably about enough questions from me, so I think it's time to open up to questions from the audience.

Thank you very much to all of you who have already sent some questions in.

I've been watching as we've been going along and there's some really good questions that have been put in the Q&A section.

Starting with one that could be either Professor Bradley or Professor Wilkinson, and is a very good question for the many different acronyms that we started using at the beginning!

Rob has asked us what is the difference between the Cambridge Clinical Trials Unit and the Cambridge Biomedical Research Centre, and how do they work together?

**Prof Bradley:**

I'll start by telling you a little bit about the Cambridge Biomedical Research Centre, which is an infrastructure across the campus funded by the National Institute for Health Research (NIHR) over a 5-year cycle.

Including funding for the BioResource, it receives just under £150 million and part of that is the Cambridge Clinical Trials Unit, which, as we've heard, Professor Wilkinson is the director of.

**Dr Stranks:**

Fantastic, thank you.

And we've had another person put in the chat: Do you think that COVID has changed how we carry out research? Do you think that we could now speed up cancer or dementia research or research into any other subject?

Professor Wilkinson, do you think you'd like that one?

**Prof Wilkinson:**

Yes, I read that in the chat as well - it's very interesting question, and I absolutely agree with that.

I think what it’s shown is that we can move more quickly.

I'm not sure we could work at the frenetic pace that we've done in COVID permanently, but it has, not only in trials but in the health service in itself, tested the system.

I think what it has proven is that if we want to we can move more quickly and actually we've done that safely, which is the real important thing here.

So I think there will be very important lessons to be learned about making the system more efficient, because if we can get the drugs tested more quickly, but robustly and safely, we can get those treatments into patients.

And I really feel this is something that the UK needs to capitalize on after this.

It has led the way with innovative treatments for COVID and it should be able to do the same for other diseases, as was mentioned.

**Dr Stranks:**

Actually that leads quite nicely into the next question, which says: If you could go back in time, what is one thing that you would have done differently to handle COVID or that you would do first in another pandemic?

Dr. Hall or Professor Wilkinson? Either or.

**Dr Hall:**

I'll just unmute myself.

I can start off with that.

I think Professor Wilkinson has mentioned how relatively quickly things got done.

I think it would be really hard to improve on that because it's perhaps not obvious, but many people worked through evenings and weekends for many, many weeks to get this off the ground and of course, the landscape has changed very much over the year.

So, looking back we might have changed things but it would have been impossible to quite see which direction things were going to go in and at the outset.

I think one thing we have done that we should have done more of, that we want to do more of, is dock together every step of the process with basic science research.

Well we have done that and realized that was a priority, it was a huge rush to get all of this up and up and running, but it is so important that as we gather clinical data, we also gather as much data as possible to not only see what works, but to understand what's going on and why it works.

And that relates to some other questions that are coming up later.

So I guess that's one thing that we would do differently and I think another thing that we've done well but perhaps could do more of, is brokering cross-centre collaboration so you pull together the strengths of not just the researchers in one centre, but actually across different centres as we've done with King's College and Guys & St Thomas's.

We have had input from some other centres as well, for example, Glasgow, so I think that's been powerful and that's something we could do more of.

**Dr Stranks:**

Fantastic.

I've got one that's about the immunology of COVID-19 that says: Why do some people get sick from COVID and others don't?

**Dr Hall:**

I'll take that.

In fact that is fascinating and I wish we could give you a full answer!

There are a lot of people working on that including people who are working with BioResource material in Cambridge, as Professor Bradley has mentioned.

It's clear that there are very big differences between people and we know that the immune system is highly variable between individuals.

That's actually generally a great strength, because if we were all the same, a pathogen would be able to find our Achilles heel and exploit it and wipe us all out.

The fact that we're not all the same and the way our immune response behaves actually is a great strength for us as a group, but unfortunately for any given scenario, some people's immune systems perform better and some worse.

We are starting to understand the basis for some of those differences but we're way off others.

Underneath a lot of this is something called polymorphism.

So in genes like those for hair color for example, there's some people that have fair hair, some people have got black hair, some people have ginger hair.

With the immune system, there a lot more variants than just those.

In many genes controlling processes, there are multiple different variants and this gives rise to different behaviours when the immune system’s challenged in a particular way.

So some of the cytokines (chemicals I mentioned, these WhatsApp groups), some of the WhatsApp groups in some people have a few followers and some of the WhatsApp groups have large numbers of participants and so people very enormously.

So what happens when that chemical gets released is that some people have a little response, some have a moderate response and some have a big response.

One of the key chemicals is a form of interferon, so many of us will have heard of interferons and be aware that they tend to go up when we have viral infections and that's part of our rapid response system to viruses.

Well it turns out some people tend to put a little bit out and some people put a lot out.

And, for example, people who put a lot of interferon out early on seem to do better with COVID.

They tend to get SARS-COV-2 infection and resolve it more like a standard viral infection.

People who don't put out so much the beginning might actually not feel so sick early on, but then they bring in other parts of the immune army and some of those sometimes go wrong.

The chances of them going wrong again will depend on all sorts of genetic settings.

So there's genetics, but then there are also environmental things, so we know about age but also whether you're thin or whether you're a little bit overweight or a lot overweight - all those things will change the way the immune system works, the way that you handle the virus.

So we've learnt a lot but we've got an enormous amount more to learn.

**Dr Stranks:**

Excellent, thank you.

We've got just a few minutes left so I think we've probably got time for two more questions.

Someone in the audience has asked: In your opinion, will COVID be here to stay and is it something that we'll just have to live with?

Do you think we will have to have medicines ready at all times or will it just go away on its own?

**Dr Hall:**

I can take that again.

I'm afraid I think it is here to stay for the foreseeable future.

Hopefully, rolling out the vaccines will increase the protective immunity in the population but of course, we've got to think globally not just nationally to do that and the problem is the longer it takes us to roll that out, the more the virus carries on replicating and the more chances it's got to mutate and get itself into a configuration that can evade the antibodies that the vaccine has raised.

I know the vaccine teams are working on making new versions of vaccines to cope with this but it's an arms race - the virus is evolving and we're evolving to catch up with it.

So I think we've got it for some time to come - probably permanently.

Because of that we need to know not only how to immunize people against it, but we also need to know how to treat it, so running clinical trials to figure out how to treat COVID isn't just something that's useful until we have a vaccine.

We're always going to have a group of people who get COVID because they haven't responded to the vaccine or because there's a new variant of COVID, so understanding how to deal with that and indeed what's going on in the immune system is really important for that reason.

**Dr Stranks:**

Fantastic, thank you.

I think for one last question, someone in the audience has asked whether or not we are considering research into long COVID?

Now that we're having so many survivors, is there any research being done in that area?

Professor Bradley I think that's probably a good question for you to finish on perhaps.

**Dr Bradley:**

The answer is yes, in two ways.

Firstly, anybody enrolled in the BioResource, we are following over time and so we're just starting to see people a year after they first presented.

We also set up a clinic that allows people to be referred in from the community who may not have been to a hospital.

Some of them may not have been positive in terms of diagnostic tests for COVID and we can do more detailed analysis, looking not just at antibody responses but cellular responses and in particular, what we call T-cell responses to the virus.

So, yes, we are.

Obviously that inevitably came after the initial research, but it's something that we're really starting to build.

**Dr Stranks:**

Hopefully that will be along with the focus of the next phase of our research.

Well thank you very much to everyone who's joined us tonight.

I'm afraid that's about all we've got time for.

We certainly hope that you found the discussion interesting!

Could you tell us whether or not you feel like you have learned anything from what we have shared this evening?

I've just put a poll up where hopefully you can tell us if you've if you feel like you've learned something.

Thank you very much to my panelists for joining us tonight.

We really appreciate the time that you've given us and your extremely thoughtful answers so thank you very much for your time.

And I would also very much like to thank the members of the NIHR Cambridge BRC PPI and Comms Team, who were my co-pilots for this evening and without whom I would never have been able to set up this event, so thank you very much to them.

They've also been working very hard on an animation that we have about the TACTIC-R trial, where you get to meet Baz and Rav, the two treatments that we meet in the trial.

And we very much invite and encourage you to check out that animation on YouTube and to download the associated quiz and colouring sheet, if you've got some kids who might like to learn a little bit more.

We also hope that when you leave us tonight you take a few minutes just to fill in our feedback survey and help us to learn what we need to know if we run a similar event next year, so we do hope you take a few minutes to do that.

If you are interested in research, we also invite you to consider becoming involved in research as a member of the public.

Here in Cambridge, you are very very welcome to join our patient and public involvement panel, which is a group of people from in and around Cambridgeshire who are interested in research and who provide feedback, ideas, and life experience to support research into a wide range of conditions.

We don't expect you to have any experience of healthcare to be able to join us and we really are looking for people from as wide range of backgrounds as possible.

So if that does sound interesting to you, then we hope that you will use some information on the slide that we're about to put up, and that you'll consider joining us.

I know Georgina is going to put some information about that in the chat.

So thank you all very much again for coming and we wish you a very safe and pleasant long weekend.

So good evening and good night.