

Full list of questions and comments shared before, during and after the 'Let's Talk About Long COVID Research' (REACT-Long COVID) event hosted by Imperial College London on 29th April 2021

Several of these questions were addressed during the session. However, many will continue be used to develop a FAQ page to sit on the REACT-Long COVID study website (<https://react-ic.net>) as well as help to inform future communication. Others will be used by the research team to help inform both the research plans and analysis. As a result of the session, the team are already further exploring several things that people raised, including:

- how we might be able to identify people affected by Long COVID even if they do not have a positive PCR or antibody test (e.g. using reported symptoms, whether they suspected COVID, free text etc)
- new areas of analysis (e.g. looking at age differences in symptom experiences)
- exploring the possibility of adding additional items to our investigations, including whether it would be possible/feasible to monitor sex hormones as part of the clinical assessment and revisiting what questions are currently asked around menstruation

When	Question
RE. INCLUSION/SAMPLING – PARTICIPATION VS INVOLVEMENT	
Before	Would you consider patient researchers working alongside you in your study e.g. developing questionnaires, undertaking interviews, supporting data analysis?
After	I'd love to know how to get involved in any trials or research projects. I already use ZOE app but would be interested in anything further.
After	I'd like to be involved in the study, design, analysis etc as I'm a senior pathologist/scientist (married to a Prof of Immunology!) and feel I have much to offer as an individual with a huge amount of directly relevant experience, in more ways than one. Plus, as someone with such experience it will help me feel better as I'm helping as a Dr to investigate this new disease that I happen to be suffering from. I'll get in touch via email/VOICE!
After	Missed how to get involved in research, I was hospitalised last March and have been under Wolfson Neurological Rehab clinic since. On phased return back to work 3 mornings a week. Happy to get involved in any way I can
Before	Development within Pediatric PostAcuteCovid-19.
Before	What is known about Long COVID in children? 5 months on my daughter (10yr, 9 when positive) still has very disrupted smell and taste. I worry what the lifelong implications may be for her from a neurological point of view.
Live	WP1 involves people travelling to centres, but if you're too bad to travel this would cause ascertainment bias. Any domiciliary visits?
Live	Are you interested in people living outside England? I live in Glasgow and have had long-covid symptoms for 1year
After	How can I be included in your research please, and does it matter that I live in Wales?
Live	Others have asked, but are you recruiting or working with centres in Wales, Scotland and NI?

Before	Can people who have been ill for over a year be included in a study?
Before	Please do not discount people who didn't get a covid 19 test or tested negative, from your long covid research.
Before	How can patients with Long COVID without a positive PCR test get involved in research easily?
Before	Are there any current research plans that we can be part of?
After	Can you only be involved in the clinical study if you were involved in the original study, i.e. you have the proof that they had Covid-19. I had a positive test in November and have long covid symptoms so wondering if I can be involved?
Live	I would be interested in participating in any trials of new medicine or treatment, how would I sign up for this? Long Covid patient for 6 months.
Live	What about including those who didn't develop antibodies and got ill in the first wave (like myself) and are still ill with long covid? Including them might help us understand if there are differences in their long covid illness?
Live	I too was in the first wave of infections and testing was unavailable for 3months. Many first wavers did not develop antibodies so I feel that we are being excluded from many research projects
Live	I'm also untested, but diagnosed by my GP and 111 in March 2020. I have all the classic symptoms of Long Covid and my GP has diagnosed Long Covid. It is frustrating that people such as myself are considered to be irrelevant to research, especially considering that many tests are likely to be false positives.
Live	Long Covid patient here, untested in wave 1. I've participated in REACT via throat swab in Jan 21, which was negative. Is there any way for patients who haven't tested positive for antibodies/PCR in REACT to participate/contribute to this research?
Live	Lucas, Carolina, et al. "Longitudinal analyses reveal immunological misfiring in severe COVID-19." Nature 584.7821 (2020): 463-469. suggests those admitted have a different immune response to those with mild-mod COVID-19, and subsequent LongCovid development, so good that you are concentrating on those not admitted - otherwise one simply repeats prior ascertainment bias!
Live	Many Long Covid sufferers test negative for Covid antibodies. In some, could there be something potentially deficient or dysfunctional about the initial immune response? How will this specific population (clinical LC diagnosis/negative antibodies) be captured in this programme?
Live	Is there underascertainment in men, who it is well known often only present when things get very bad, and tend to shut up and put up? Any ideas on how you will address this?
Live	Sorry if I have missed this but are you looking at patients with LC who had mild disease and then had no ongoing symptoms at first but are now experiencing relapses? My sister and I are in this boat, had covid last March (no tests) and are now experiencing relapses with each

	one being worse than the one before. It seems to be hard for this set of patients to get diagnosed with LC due to not having symptoms continuously.
Live	Looks great. How will you engage minority groups? Especially if we know inequalities are present in covid, e.g. BAME community with worse health outcomes, women more affected by long covid?
RE. COMMUNICATION + COLLABORATIONS	
Live	<p>Many frontline doctors still have very little knowledge of Long Covid, resulting in lots of gaslighting and dismissal of patients, compounding suffering. How will you communicate your findings to them?</p> <p>To address the lack of understanding in healthcare staff is easy, make teaching about LongCovid part of mandatory training, just as with dementia care etc!</p>
After	Please can the results be more widely distributed in the NHS because currently there is still a lot of resistance to the fact that long Covid even exists.
Live	How quickly do you hope that WPs2-3 might lead to potential therapies?
After	The only key message that I did not perhaps pick up from the session, on how long the study will last (or take) before findings will be published. And perhaps, how these findings will be shared with policy makers to influence effective health care management going forward.
After	Can you perhaps create regular newsletter update? I would argue that Long Covid is such a huge problem it warrants the recruitment of a dedicated comms team.
After	Could a centralised source of support be offered to sufferers? We have our support groups but no centralised resource for support - be it medical or research or just up to date information. We do feel abandoned by the authorities, even though different groups are trying to help.
Live	Are you collaborating with other studies/apps for example COVIDENCE and ZOE app and the NIHR range of COVID studies that are happening currently? Zena
After	Long Covid patients are desperate for answers. I hope we won't have to wait years for answers like HIV patients-referred to - did.
RE. UNDERLYING MECHANISMS/AND WHAT WE WILL BE EXPLORING/INVESTIGATING	
<i>HORMONES/ENDOCRINE SYSTEM</i>	
Before	<p>Are you researching the effects of oestrogen and covid?</p> <p>What do you know about the role of oestrogen and covid?</p>
<i>IMMUNITY/INFLAMMATION</i>	
Before - on behalf of LC gp	<p>Is this Viral Persistence or Immune Dysfunction (or both)?</p> <ul style="list-style-type: none"> Viral particles have been found for those a year after infection and some feel that there may be viral persistence or immune dysfunction. We know that auto-antibodies are also being found and also that waxing and waning of symptoms often

	<p>relate to auto-immune dysfunction. There has been some exciting research from several sources into double negative B cells recently</p> <ul style="list-style-type: none"> • Examples of research (but not limited to): <p>> Manchester University (Lydia Becker Institute of Immunology and Inflammation) are conducting research into double negative B cells and long covid at the moment. Collaborative studies.</p> <p>> Alterations in T and B cell function persist in convalescent Covid-19 patients 31.3.21 https://www.sciencedirect.com/science/article/pii/S266663402100115X</p>
Live	How will you be looking to understand whether or not Long Covid is associated with ongoing viral antigen persistence?
Before	How does having long covid affect the chance of re-infection and the outcomes of re-infection?
Before	Are the striking similarities and potential links to Mast Cell Disorders (specifically Mast Cell Activation Syndrome, MCAS) being considered by the research? Are sufferers of MCAS and the organisations/charities that represent them being consulted or involved going forward?
Before	How do you plan for this Long COVID study to build off existing expertise in post-viral conditions, with regards to treatments, clinical definitions, potential pathology, etc. ME/CFS being the obvious example
Live	Hello, you suggest there are two main categories. Do you think one might be similar to what is commonly known as ME, or is Long Covid completely its own thing?
Live	Will existing long-term research that has been undertaken on conditions that show similar patterns of symptoms (eg Mast Cell Disorders) be considered - and will patients in such groups be identified/involved in the research?
Live	Any plans to look at increased autoantibodies - eg increased TPO, lupus, diabetes happening in LC patients....?
Before	<p>I'm a GP with Long Covid who's symptoms (>1yr duration) resolved within prednisolone. There is a small number of doctors who have shared similar experiences. Seemingly Covid has caused an inflammatory disease but my inflammatory markers and autoimmune profile have always been normal.</p> <p>I'm concerned that many people with normal tests will be dismissed.</p> <p>What immunological tests are you looking at? Should we be trialling everyone on 5 days of prednisolone to see if they improve? I am now on weaning dose and on hydroxychloroquine.</p>
Before	<p>Incelldx in the US, led by Dr Patterson, have stated that Long Covid sufferers have continually elevated cytokines, probably due to viral persistence. They are measuring this in individuals according to a 'Longhauler Index'. To reduce cytokines, their personalised treatment involves Maraviro, Ivermectin, Prednisone and other drugs.</p> <p>Are there plans in the pipeline to do cytokine panels on Long Covid sufferers in the UK and to offer treatment to reduce cytokines along these lines?</p>
Live	Incelldx in the US claim to have identified specific blood markers in Long Covid sufferers that are able to distinguish those with Long Covid from those who don't have it. This includes

	elevated CCL3, Interleukin-2, Interleukin-4, VEGF & decreased GM-CSF & CCL4. Will you be building on this research and looking at participants' cytokines as part of your research?
Before	I want to see research into medium and long term consequences of Long Covid such as cardiovascular problems (eg. stroke, heart attack, fibrosis, etc), neurological and brain problems (eg. Parkinsons, dementia, Guillain-Barré, etc), autoimmune problems (eg. MS, Lupus, vasculitis, etc)
Before	Are you looking at causes and / treatment of post COVID autonomic dysfunction?
Before - on behalf of LC gp	Cytokines and auto-immunity are not currently being tested for routinely with long covid – are these tests planned, perhaps in a trial?
Before	What studies are being done on the immunology of Long Covid?
Before	What is the effect and risks of vaccination in those with Long Covid?
Live	I still have high antibodies 14 months on and have seen a paper suggesting that in ~5% of people their antibodies persist. Have you found this?
Live	As for many others when I got ill not PCR tests where possible and the antibodies came back negative - but gamma-globulines high. What do you think about T cells involved ?
CARDIOVASCULAR	
Before	<p>Is anyone exploring the vascular aspect of long covid? Many symptoms point to vascular damage but patients are being refused testing for this.</p> <p>Also, micro blood clots. A long covid patient was diagnosed with micro blood clots in the lungs via a VQ scan at The Royal Brompton, despite blood tests and MRI being clear. Again, patients are struggling to access proper testing for this.</p> <p>I have requested these tests on four separate occasions at my Long Covid clinic but have so far been ignored.</p>
Before - on behalf of LC gp	<p>re. Myocarditis</p> <ul style="list-style-type: none"> • Active and Resolving Myocarditis - We were expecting myocarditis symptoms to resolve within 6 months approximately but for many this has not been the case. • How does Coverscan distinguish between active and resolving myocarditis on cMRI. Some of us have been told ours is active and others were told theirs was 'likely resolving'. Is this just differing emphasis in how the news is relayed to us, or are you able to definitively determine whether the inflammation is ongoing or historical? • Is this Chronic Myocarditis? Chronic myocarditis can be caused by fibrosis (causing remodelling), cytokines and/or auto-immunity. We know that we have ongoing cytokines and chemokines from Dr Bruce Patterson and Dr Yo's excellent research (Incelldx) into long covid. • If there is a form of chronic myocarditis, perhaps early diagnosis and treatment for inflammation or auto-immunity is key to preventing long term disability?

	<p>https://www.myocarditisfoundation.org/research-and-grants/faqs/chronic-myocarditis/</p>
	<p>Re. Vasculopathy – especially Endothelial Dysfunction</p> <ul style="list-style-type: none"> • We’re not aware of anyone being tested for this, yet many of us have the combination of symptoms relating endothelial dysfunction and microvascular problems such as chest pain, fatigue, relevant neuro symptoms, SOB, 'bruising' or marks on skin etc. • How can we get tested and treated for this. While the ongoing research is very heartening. We can’t wait for all the research to be done to be treated for what many of us believe to be the primary cause of most of our symptoms.
GUT	
Before - on behalf of LC gp	<ul style="list-style-type: none"> • We’re wondering about how covid affecting the gut can alter hormones and metabolic markers. What does this mean if it has? What are the impacts on diabetes risk and why is cholesterol being affected? • Some diabetic and non-diabetic sugar level results are very erratic • Are there links between fatigue and disrupted gut biome?
NEURO/BIOCHEMISTRY	
Before - collated on behalf of a Long Covid Group	<p>Re. Fatigue and Post Exertional Malaise (PEM)</p> <p>If a common link has not yet been found by the research so far regarding organ damage or blood markers and extreme fatigue, perhaps there is more to research, such as perhaps:</p> <ul style="list-style-type: none"> • links between an imbalance of dopamine, serotonin and acetylcholine to both post viral fatigue and PEM. Are there other severe viruses that share neurotransmitter disruption? • Are there links between fatigue and disrupted gut biome? • B12 deficiency?
Before	Why is there long lasting and painful nerve damage to limbs etc after having covid?
Before - on behalf of LC gp	<p>Re. Syncytia – Cell Fusion – Repurposing existing drugs</p> <ul style="list-style-type: none"> • More interesting research regarding the virus causing cell fusion linked to the TMEM16 protein Research paper in Nature 7 April 2021 which appears to demonstrate that drugs that inhibit TMEM16 proteins block spike induced syncytia. They looked at repurposing existing drugs. Calcium at a cellular level appears to be important. https://www.nature.com/articles/s41586-021-03491-6 • Repurposing existing drugs is an exciting opportunity for those with long covid – cheap and quick! • Calcium signalling is important for the following processes as far as we know: syncytia (TMEM16 protein), mitochondria and ATC uncoupling (especially under

	<p>ischemic/reperfusion stress), endoplasmic reticulum (sigma 1 receptor), muscle contractions (including cardiac muscle) & endothelial dysfunction</p> <p>Re. Mitochondrial dysfunction</p> <ul style="list-style-type: none"> • Ditto re few tests but symptoms which relate to mitochondrial damage
GENERAL	
Before	In the last 12 months, I've lost count of the number of near identical questionnaires I've filled in for different researchers. It's good to see research moving on to look at the pathophysiology of the illness and how to help those suffering (and not just with 'rehab').
Before	Long Covid and the link between physical and psychological symptoms
Before	What are the underlying physiological mechanisms of Long Covid?
Before	Will you be doing any research to establish whether COVID-19 was already present in the UK in 2019?
Before	The effects of long covid on complicating long term underlying health conditions.
Live	Do you feel the psychosocial neuroticism model of Long Covid curable by positive thinking and graded exercise suggested by Sharpe, Garner et al is discredited by your findings of definite physical symptom clusters as causal for Long Covid?
Live	Are there any potential blind spots in the clinical testing protocols which could obscure accurate results? There is one hypothesis for example, that some protracted illness may be explained by viral persistence in sensitive areas of the body (spine, testes, etc). Could etiologies like this be difficult to detect without extremely targeted diagnostic techniques?
RE. TESTS / TREATMENT / MANAGEMENT	
Before	Please update on pharmacological treatment interventions (proven or positive case studies) as post 13 months simply being told to pace and rest with little improvement is quite frustrating- thank you
Before	How is mental health being dealt with in relation to long covid, loss of work, stamina, ability to exercise in open air, lack of sleep? Vicious cycle of despondency with major change in lifestyle and health.
Before	<p>Is there the possibility of a national MRI screening programme for long covid patients to check for organ damage (basically, the MRIs Coverscan is doing, but for all patients)?</p> <p>Many of us have never had proper investigations and are worried about increasing our activities or doing prescribed physio exercises given the heart-related symptom cluster of the initial "acute" 3-month phase of covid.</p>
Live	Do you have plans to do MRI scans for organ damage in your sample? E.g. Coverscan found 70% of their non-hospitalised long covid sample had damage to at least one organ at 4 months post-covid.

After	Do MRI scans of a sample of patients to check for organ damage. Few patients are being offered this at long covid clinics, and many common issues (e.g. myocarditis) are only being picked up this way. The Coverscan study is a model for long covid research and the gold standard (as far as long covid patient groups are concerned) of what research should be being done to understand the disease(s) and help patients quickly.
After	See 6. Please could you do MRI scans of a sample of your patients (as per Coverscan) to understand the prevalence of organ damage and link this to symptom clusters and the other data you are collecting. To patients, money spent on MRI scans is infinitely more valuable than spending money on artists to draw pictures of our pain.
Before	I'm worried that a lot of us with Long Covid have organ damage, which is seen in a lot of research (coverscan etc) but won't be discovered in many patients due to the lack of access to the right tests. How are your views of national guidelines for investigating patients w. Long Covid? To check possible organ damages before i.e. physio treatments.
Before	How can we make sure treatment protocols get to patients quickly, even if treatments are in research stage?
Before	To include discussion of the many benefits of Singing for Lung Health (and whole health)
Live	Great question Jo [re. identifying early approaches/interventions associated with recovery and feeding them into recommendations/trials]. Thx I'd just like to echo Jo and say that those stats that show recovery after 9 months looking unlikely, is very disturbing for people like me, 13 months on from initial infection.
After	Do you expect the short-medium term mortality risk of LC patients to be significantly increased? Do you think it's realistic to hope for the determination of the cause of ongoing LC symptoms and therefore treatments in the near future, or should patients be resigned to being unwell for years?
After	Long Covid patients are desperate for answers. I hope we won't have to wait years for answers like HIV patients-referred to - did.
RE. SYMPTOMS / EXPERIENCES / RECOVERY	
Before	Is there anything I can do to manage my condition? Diet, routine, exercise, drugs?
Before	My most worrying symptom is blurred vision - can anything be done about that?
Before	Since getting covid, I have had recurring shingles, 5 times in 7 months. I am left with constant neuropathic pain in my head/scalp. Is this something that others have reported experiencing & how do I get rid of the pain?
Before	Any idea how long the 'flare ups' can go on for. I had COVID in Jan and have just had my first flare up & been diagnosed with long covid but GP saying ride it out. I would like to know if there is any research suggesting how long post covid people re experiencing these flare up occasions- once every few months for the foreseeable for example? Or a year? Anything to help us know what to expect.
Live	Your symptom list excludes things like 'brain fog' and 'tinnitus' - two things experienced a lot by long haulers?

Live	Although anosmia is listed, parosmia isn't. Is this something that you will consider?
Live	As you will be following patients on a journey, hopefully to recovery, they may well attempt to return to work in this time period. So perhaps even more significantly than 'exercise' can you track impacts of returning to work. The employment patient group looking at RTW see a LOT of 'pushing through' and 'relapsing' that can significantly derail recovery. Could you collate and share data with other researchers funded to look into this aspect?
Live	I too have chronic relapsing, and the symptoms during good/bad phases have changed with time, so I agree it's very difficult if your disease is a kind of variable and moving target. People ask if I'm better and I reply different.
Live	Are you looking at patients with LC who had mild disease and then had no ongoing symptoms at first but are now experiencing relapses? My sister and I are in this boat, had covid last March (no tests) and are now experiencing relapses with each one being worse than the one before. It seems to be hard for this set of patients to get diagnosed with LC due to not having symptoms continuously.
After	Will I ever get back to "normal" of how I used to be over a year ago. All my cancer treatments were easier to cope with than what I experience now, having been fit and hyperactive.
After	I am a long covid 13 monther with ongoing fatigue and parosmia with anosimia. I would like parosmia addressed as it's been one of the most difficult aspects of long covid. It affects emotions and the ability to eat a healthy diet to aid fatigue and recovery. I wasn't hospitalised or tested.
RE. LONG COVID AND VACCINATION	
Before	What is the effect and risks of vaccination in those with LongCovid?
Before	<p>I would like to ask the panel about post vaccine (Astra zeneca) severe fatigue enlarged lymph etc.</p> <p>I had Covid 19 March 2020 took 8 weeks to recover enough to work. Had stress episode October took 3 months to recover.</p> <p>My exhaustion fatigue lymph pain returned after my vaccine on 15.3.21 and is still v bad. I thought i had physically recovered ater 6-8 weeks of the same symptoms from 19.3.20 . Can the panel explain. I am unable to function walk more than a few meters return to work even wash.</p>
Live	Lots of people in the patient support groups have had 5 week + relapse post-vaccine but no-one seems to be willing to talk about it, only about positive responses
Live	I also believe that I had early Covid but there was no proper testing. At first I thought it was from my cancer treatments which I had to stop due to restricted access to the cancer centre. I developed tiredness and woozy brain which have not moved for a year now. Will they ever disappear. It does affect my quality of life. Received my two jabs and only developed mild reaction for about a week.

Live	I understand Gez Medinger has found that 2 wks after vax ~1/2 report no change, ~1/3 a bit better, and ~1/6 a bit worse, which fits with a chronic relapsing condition tending to improve with time anyway, i.e. vax makes no difference to LC overall.
After	The positive or negative impact of the vaccine. I had recovered from long covid in July 2020 but my vaccine 6 weeks ago has given me a total relapse.