

To Whom it May Concern:

### **Long-term COVID-19**

It is becoming increasingly clear that a significant number of people are being left with ongoing symptoms of COVID-19.

There are thousands of stories available on social media of people suffering symptoms for 12, 13, 14 weeks and longer. The facebook groups "Covid-19 Support Group (have it/had it)" has 8,435 members at present and "Covid-19 Support Group #covid1in20" has 3,341 members at present. On twitter the hashtags "#LongCovid" and "#COVID1in20" brings up many more stories of prolonged illnesses. Multiple newspaper articles have now been published detailing the personal stories of many patients.<sup>1-10</sup> Dr Tim Spector's COVID-19 symptom tracker app has clarified the extent of the problem, and is suggesting that 10% of patients are having prolonged symptoms<sup>11</sup>. This data is very valuable and should encourage a more in-depth and centralised approach to studying what is happening to these patients. 10% of confirmed cases would represent nearly 30,000 people in the UK having prolonged symptoms, before considering the many cases that have not been confirmed by PCR test.

It is not clear what is causing these prolonged illnesses. The symptoms appear to be indistinguishable in many ways from the symptoms of an acute SARS-CoV-2 infection. Fever, dry cough, tiredness, shortness of breath, gastrointestinal symptoms, rashes, visual problems, headaches etc. Many people report having had improving symptoms before relapsing. Others report the emergence of new symptoms as time goes on.

It is unfortunate that the public health infrastructure in the UK has not been able to scientifically study the natural history of COVID-19 thus far. The number of patients recovered from COVID-19 is not reported in government statistics<sup>12</sup> and this has been identified as a problem by prominent epidemiologists<sup>13</sup>. Understandably the focus has been on the acutely ill but it is now time to get to grips with this hidden catastrophe that has hit many peoples' lives.

What if these symptoms represent a chronic infection with SARS-CoV-2 in a relapsing-remitting fashion? What if these patients are still contagious? A case report from China documents prolonged PCR positive status in a patient who recovered after receiving convalescent plasma<sup>14</sup>. If these studies were replicable, it would surely lend credence to the possibility of persisting infection? It should certainly warrant further investigation and trials. There are papers demonstrating that not everybody makes neutralising antibodies to SARS-CoV-2. In this paper<sup>15</sup>, 10/175 patients that had been confirmed positive cases with PCR (approximately 6% or ~"1 in 20") did not make antibodies. Younger patients had a higher chance of not producing antibodies, to an extent that was statistically significant. The role of antibodies in immunity is not clear at present, but the possibility of persisting infection in some individuals warrants further investigation. The interaction between the immune response and SARS-CoV2, and the role of antibodies, needs to be investigated in this cohort of people suffering long term symptoms in particular. In addition, when combined with PHE's information on the sensitivity and specificity of its antibody tests<sup>16,17</sup>, it is important for employers and healthcare professionals to

recognise that a negative antibody test is an insufficient reason to conclude that someone has not had, or does not have, an infection with SARS-CoV2.

What if these symptoms represent a vasculitis or other autoimmune condition triggered by the virus that would be amenable to medical treatment such as anticoagulation or immune suppression? There are many reports of hypercoagulable states in hospitalised COVID-19 patients<sup>18</sup>. The possibility of complex immunological, vascular and haematological sequelae needs to be evaluated and ruled out, not least as it would offer the possibility for intervention and improving outcome for these patients.

When dealing with a novel pathogen it is safer to investigate this cohort of patients and rule out possibilities of serious but potentially treatable pathology, rather than assuming that this is a “post” viral syndrome. The purpose of my argument is not to claim that any of the above hypotheses represent reality, but that there should be sufficient concern about these possibilities to warrant urgent action and investigation. The risks of inaccurately mis-labelling this situation as “*post*” viral are huge, both from an individual perspective, a public health perspective and an economic perspective.

A centralised approach to following-up patients will be capable of detecting serious complications in this group and potentially saving lives. An app reliant on patients to enter information gives a vital signal that there is an issue, but it is not fit for the purpose of detecting and communicating serious morbidity and mortality data in this group to healthcare professionals, the scientific community and policy makers. How will we study whether people have relapsing infections or can catch the virus twice, for example, if we do not have robust and well co-ordinated studies into patients suffering from long-term symptoms?

Whatever the cause of “Long COVID”, it will be important for policy makers and healthcare professionals to be well informed about the size of the population of people suffering long-term symptoms. Whilst SARS-CoV-1 is different to SARS-CoV-2, it provides an important warning. There is evidence that survivors of SARS in 2003 suffer long-lasting ill health effects. “One year after recovery from SARS, persistent pulmonary function impairment was found in about one third of patients. The health status of SARS survivors was also significantly worse compared with the healthy population.”<sup>19</sup> Another study states “This 2-year study of a selected population of SARS survivors, showed significant impairment of DL<sub>CO</sub> [Diffusing Capacity of Lung for Carbon Monoxide], exercise capacity and health status persisted”<sup>20</sup>. The same study showed that 29.6% of Healthcare workers who had survived SARS had not been able to return to work after 2 years. My intention is not to equate the two conditions, but merely to demonstrate that there is a precedent for long-lasting health issues following infection with novel coronaviruses. These long-term healthcare risks should be anticipated and used to inform decisions about risk when looking at easing lockdown. As the global number of infections with SARS-CoV2 has been so much higher than with SARS, if even a small percentage of patients are left with long-term health issues this will represent a very serious issue indeed. There is already emerging evidence of similar impairments in DL<sub>CO</sub> in COVID-19 survivors- “...impairment of diffusion capacity is the most common abnormality of lung function followed by restrictive ventilatory defect... Pulmonary

function test (not only spirometry, but also diffusion capacity) should be considered to [be] performed in routine clinical follow-up for certain recovered survivors... Subsequent pulmonary rehabilitation might be considered as an optional strategy. Long-term studies are needed to address whether these deficits are persistent.”<sup>21</sup>.

Patients suffering prolonged symptoms would be helped by support and understanding. Patients should be investigated to rule out treatable pathology such as thromboembolic events, secondary bacterial infections, etc. A sample of Long COVID patients should be studied by experts including epidemiologists, infectious diseases and immunology experts to better characterise the condition and pave the way to discussing possible effective treatments. These patients may require financial help and their employers need to have a realistic expectation for the time it will take them to recover. Policy makers need to consider this group, and the risks of increasing its size, when deciding on lockdown easing.

I urge the government to establish a scientific approach to the study of patients undergoing prolonged COVID-19 symptoms (to establish the number of people affected, to investigate the cause of this, and to investigate possible treatments) as a matter of urgency. Awareness needs to be raised amongst health professionals so that treatable pathology is investigated and ruled out. Healthcare professionals have had a high workload and need to be provided with information and guidelines on how to manage long-term COVID19 patients as the situation becomes better characterised. Support should be provided for these patients who are undergoing distressing symptoms and severe impairment of their ability to work and live which at present has an unclear cause but with several concerning features as outlined above. Employers need to be made aware of this phenomenon and additional help may be required for these patients.

Yours sincerely,

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