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The Independent Scientific Advisory Group for Emergencies (SAGE)

The Independent SAGE Report 32

Independent SAGE report on Long COVID

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Submitted to The UK Government and the People of Great Britain & Northern Ireland by Sir David King, former Chief Scientific Adviser, UK Government, Chair of Independent SAGE

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Executive summary

Long COVID – when symptoms of COVID last for many weeks and months – affects people of all ages and even those with mild initial symptoms. Current best estimates are that between 5-10% of people who get COVID will develop Long COVID. We don't yet know how long it takes for lingering symptoms (most commonly fatigue) to resolve, but for some people there will be permanent organ damage. New specialised services are being set up to help those with Long COVID recover. These need to be expanded across the country and existing national guidelines communicated to all clinicians. As this is still a new condition, it is important to set up national databases and research projects to learn more about risk factors, causes, time course and treatments, in partnership with patients.

Introduction

Some people who have COVID-19 experience continuing ill-health long after the initial symptoms of the infection have passed. In some cases this will be for well understood reasons, such as post-ICU (Intensive Care Unit) syndrome, seen in those who have required intensive care, and especially, mechanical ventilation, or the impact of any severe acute illness on people with pre-existing conditions such as frailty, which often leads to a further deterioration in their condition. However, it is now clear that a substantial number of those with persistent symptoms have a condition that was initially labelled post-COVID syndrome but is now most usually referred to as Long COVID. In this brief report, we answer some of the more common questions that we are asked about this condition.

What is Long COVID?

The National Institute for Health and Clinical Excellence (NICE), the Scottish Intercollegiate Guidelines Network, and the Royal College of General Practitioners define Long Covid as *"signs and symptoms that develop during or following an infection consistent with COVID-19 which continue for more than 12 weeks and are not explained by an alternative diagnosis"*.[1] It is important to note that it is not necessary for the patient to have had a positive test for COVID when they were acutely ill to meet this definition. This is because many of those who are now affected didn't access a test; either because they were unavailable, because their initial symptoms did not meet the case definition, or because they chose not to, which is more common among those who cannot afford to self-isolate.[2]

Long COVID is associated with many different symptoms, that can fluctuate over time[1] and have been reported to last an average of 140 days.[3] A majority of patients experience fatigue, headache, feeling unwell after exercise and respiratory symptoms such as shortness of breath, sore throat and persistent cough.[3] Some experience symptoms such as continuing fever, gastrointestinal problems, a fast heart rate or palpitations and neurological problems such as loss of concentration or "brain fog", ringing in the ears or loss of feeling in their extremities.[1,3] Over half of those who experience symptoms for more than 6 months go on to have memory deficits in month 7.[4] A recent large study of patients discharged from hospitals in England showed that 29% of people were re-admitted within 140 days and 12% had died. This study also showed that within this time period, many also developed new diagnoses, including diabetes, heart disease and liver disease.[5]

What causes Long COVID?

The virus that causes COVID-19 attaches to molecular receptors that are found on many different types of cells throughout the human body, but in particular in the lung and the lining of the blood vessels. Other affected organs include the heart, lungs, kidneys, brain, gut lining, and the cells in the pancreas that make insulin.[1] The virus often weakens or kills the cells that it invades, causing direct damage to the organ affected. However, the SARS COV-2 virus can also initiate an aggressive inflammatory response, leading to the production of chemicals designed to kill the virus, but this unintentionally causes more damage to the host cells. [6-8] Worse, this process makes the blood more likely to clot and when blood clots form, they cut-off the blood supply to parts of the organ, doing more damage. As a consequence, COVID-19 does leave some people with heart attacks, strokes,

kidney failure, and even new onset diabetes, although all of these are uncommon. Some of these mechanisms are seen in a number of other viral infections, but they seem especially severe with COVID-19.

How common is Long COVID?

It has been difficult to arrive at a precise figure because the surveys that have been conducted, now in many different countries, often use different ways of counting, different diagnostic criteria and different lengths of follow-up. In addition, some studies are based on reports of symptoms, while others are based on detailed investigations of different body systems including investigations such as x-rays and scans. However, estimates suggest that 5-10% of people will have ongoing symptoms and organ damage beyond 12 weeks. Data from the UK, collected by the Office for National Statistics, suggest that about one in five people experience continued symptoms five weeks after infection.[9,10] The figure is slightly lower, at one in seven, among children aged 2 to 10. However, young children are also at risk from another post-COVID disorder, Kawasaki Syndrome, which can also lead to severe illness. [11] Fortunately, this is a very rare complication. Another study, of people using the Zoe Symptom Tracker App, reported 13% of those who had COVID-19 had persisting symptoms at 28 days. [3]

The largest study to look at clinical outcomes among hospital patients compared clinical outcomes in 47,780 patients discharged alive with COVID-19 compared to similar hospitalised patients who did not have COVID-19. After an average follow-up of 140 days, readmission rates to hospital in COVID-19 patients were 3 times higher than other patients, as were new heart (3 times), respiratory (27 times) and diabetic (1.5 times) events, with the greatest risks observed among those over the age of 70 and in ethnic minorities.[5]

Importantly, people can develop persisting symptoms even if the initial disease is not severe. It can affect people of any age and with initial mild disease. One UK study that carried out blood tests and magnetic resonance imaging (MRI) scans found that long term symptoms and organ damage to the heart, lungs and liver were common even in those not admitted to hospital. [12] This highlights the importance of developing well-functioning surveillance systems. The WHO has created diagnostic codes[13] to be used for COVID-19 and what it refers to as a Post-COVID condition, as well as a multi-system inflammatory syndrome associated with COVID-19, which covers both the severe inflammatory response seen in patients seriously ill with COVID-19 and the specific conditions, such as Kawasaki syndrome in children.

How long does Long COVID last?

By virtue of the fact that we are only now reaching the anniversary of the first cases of COVID-19, it is difficult to say how long Long COVID will last. Some of the complications—especially where there is organ damage due to blood clots—may cause lifelong problems. The more common symptoms of Long COVID, such as fatigue, do seem to resolve in many people, over time, albeit often slowly over several months. However, it is still too early to know what the long term burden beyond 12 weeks of disease due to this condition will be, and a number of studies—that have undertaken detailed investigation of individual organs, such as the heart or lungs—have found a relatively high-frequency of tissue damage that may not have manifested as symptoms,[1] as well as reports of new onset diabetes. [1]

How do we diagnose Long COVID?

There is no simple test for diagnosing Long COVID. It is a clinical diagnosis, based on a history of having had COVID-19 and a failure to fully recover, with development of some of the symptoms already mentioned, and with no obvious alternative cause. There is, however, demand from health workers and patients to develop more specific criteria including investigations that would allow them to move beyond what is, in effect, a diagnosis of exclusion ("it can't be anything else"). [14]

How is Long COVID managed?

The UK National Institute for Health and Care Excellence (NICE), working closely with patient groups and professional associations, has developed guidelines for the management of Long COVID.[1] These highlight the importance of multi-disciplinary assessment services, bringing together health professionals with expertise in different body systems, as well as those with expertise in a range of forms of rehabilitation, including physiotherapy, occupational therapy, clinical psychology, psychiatry and rehabilitation medicine. However, many patients with Long COVID have reported struggling to obtain access to appropriate services, in some cases feeling that they are not being taken seriously by health professionals.[15] Also, when the problems are recognised, patients have often reported that the care they received was fragmented and specialist advice was difficult to obtain. In response, new specialised services tailored for Long COVID are being developed in many parts of the country.

What about self-help groups?

The emergence of Long COVID has been accompanied by a remarkable mobilisation of patients and health professionals, many of whom are themselves affected. [16] These groups have been particularly active in initiating and conducting research on this condition. There are a number of online resources that individuals can draw on, including by some of the existing patient and professional associations, such as an online post-COVID HUB for people with breathing difficulties following COVID-19 infection.[17] The NHS has also developed a website called the NHS Your Covid Online Recovery that has information for patients affected by COVID-19 (https://www.yourcovidrecovery.nhs.uk/).

Is research into Long COVID being undertaken?

The COVID-19 Research Project Tracker[18] is a live database of funded research projects worldwide. The United Kingdom has been particularly active in funding research on Long COVID. Examples include the Post-Hospitalisation COVID-19 study [19], which is following up in-patients with COVID-19 after discharge, documenting their symptoms, markers and results of specialist investigations. This study includes a number of sub-groups looking at particular body systems. In addition, UK research teams are collaborating with colleagues in a number of other countries, for example in the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) global COVID-19 long-term follow-up study. [20]

Key recommendations

- Data should be collected systematically on cases of Long COVID and presented alongside numbers of cases, hospitalisations and deaths from COVID-19.
- Building on the experience of the Post-Hospitalisation study, a national register of patients with Long COVID should be established, including those who have not required hospitalisation, to enable long-term follow-up and thus a better understanding of the natural history of this condition. This should include specific codes for GPs to use so that patients can be followed up and tracked in research studies over the longer term.
- Further efforts should be undertaken to ensure that all health professionals likely to come into contact with patients who have Long COVID are fully aware of the existing NICE guidelines.
- Clinical commissioning groups and their equivalents in the devolved nations should ensure that there are appropriate models of care in place, including multi-disciplinary and multi-specialist teams, with clearly defined pathways through which patients can access them.
- Research studies funded so far will provide invaluable information, but there is a need for continuing review to identify emerging gaps in our knowledge, especially in relation to the impact of Long COVID on people's lives and how they are overcoming the challenges they face.
- Patients with Long COVID should be recognised as an extremely important resource in shaping research and policy in relation to this condition.

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