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# Long Covid: Reviewing the Science and Assessing the Risk

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## Foreword

Since January we have learned a great deal more about Covid-19, particularly how to treat those with the virus. This has resulted in a lower mortality rate and fewer patients ending up in ICU – and more surviving when they do. Most of the research and data has focused on the severe spectrum of disease and those with major respiratory problems. In the first few months of the pandemic, little attention was paid to the infected population who were not sick enough to go to hospital, who made up 99 per cent of cases. It turned out that Covid-19 was not just a bad flu, but in many people it behaved more like an autoimmune disease, affecting multiple systems in the body. In March, my group at King's College London and the health-science company ZOE launched an app that captured the wider range of symptoms people were experiencing and asked them to log these every day. Over 4 million people gave us their data, and this has provided unique insights not available from the routine health statistics. The first insight after a few weeks was that loss of smell was by far the single best predictor of Covid-19, in addition to a positive swab test. This led to many countries adopting this as an official symptom in addition to fever and cough or breathlessness. The other insight was that a great many people didn't get better after two weeks as expected. We kept following them and found out that a significant number still had problems after months. This is the other side of Covid: the long-haulers that could turn out to be a bigger public-health problem than excess deaths from Covid-19, which mainly affect the susceptible elderly.

### **Tim Spector**

*Professor of Genetic Epidemiology, King's College London*

## Overview

There is still much we don't know about the risk of Covid-19. We know people who are poor, elderly or have underlying conditions have higher risks of death. Public understanding of the risks, combined with the style and content of the messaging and the perceived trustworthiness of the source of the information, will all improve the level of compliance with measures such as mask-wearing and social distancing. One part of the debate that has just been emerging is the understanding that survivors may have a chronic debilitating illness for many months – the so-called long Covid.

This term is used to describe individuals who continue to suffer from Covid-19 symptoms outside of the two-week period in which they are believed to be infected. The World Health Organisation (WHO) endorsed this two-week period as enough time for the virus and its symptoms to be able to come and go, yet studies are revealing cases in which symptoms are persisting well outside of this window.<sup>1</sup>

The Covid Symptom Study led by King's College London, underpinned by a self-reporting app from health-science company ZOE, has involved more than 4 million users in the UK and is being used to track and monitor Covid-19 symptoms over time. Researchers have used this data since 24 March to study the patterns and duration of Covid-19 symptoms.<sup>2 3</sup>

In this paper, we combine data from the Covid Symptom Study with emerging evidence from the broader scientific community to understand what we do and – as importantly – don't know about those suffering with long-term symptoms of Covid-19. The Covid Symptom Study is unique as it has one of the largest sample sizes of Covid-19 studies with more than 4 million participants, but it is important to note that the data is collected and analysed based on self-reported symptoms recorded through an app. New findings from the study, which will be published in full by King's College later this month, indicate that around 10 per cent of those taking part in the survey had symptoms of long Covid for a month, with between 1.5 and 2 per cent still experiencing them after three months.

Extrapolating from this, the researchers believe that of those affected by the first wave of the virus in the UK, 300,000 people would have had Covid symptoms for a month and 60,000 for three months or more.

Properly understanding the scope and scale of the issue of long Covid is critical in both communicating and balancing the overall risk of the virus, particularly as governments determine their next steps in containing Covid-19 and avoiding a full lockdown.

As Professor Spector says in his foreword, long Covid is likely a bigger issue than excess deaths as a result of Covid, which are between 0.5 per cent and 1 per cent.<sup>4</sup> But the issue of long Covid, affecting roughly 1.5 per cent of those with Covid after three months, must be considered alongside the economic impact

and other health impacts linked to Covid restrictions – for instance that 1 million women are likely to have missed vital breast cancer screenings this year due to the pandemic. <sup>5</sup>

## What Are the Symptoms of “Long Covid”?

Our understanding of long Covid is still in its early stages, but the most commonly reported symptoms, cited in various studies, include:

- Excessive fatigue/exhaustion
- Breathlessness
- Headache
- Insomnia
- Muscle fatigue/pains
- Chest pain
- Persistent cough
- Loss of taste and smell
- Intermittent fevers
- Skin rashes
- Post-exertional malaise-when overdoing it leads to symptoms coming back

There are additional, less common symptoms that have been reported by long Covid sufferers, which have yet to be confirmed by studies:

- Hearing problems
- Cognitive issues such as “brain fog”
- Mental-health problems
- Hair loss

An analysis of data from symptom-tracking apps has identified six “clusters” of symptoms.<sup>6</sup> These categorisations have proved useful in determining what level of care patients receive when they’re diagnosed with Covid-19 but they also correlate with how likely someone is to have long Covid. The Covid Symptom Study suggested that having a persistent cough, hoarse voice, headache, diarrhoea, loss of appetite and shortness of breath in the first week meant someone was two to three times more likely to get longer-term symptoms. Given the broad spread of these symptoms across the different clusters, it’s likely that long Covid is less predictable in terms of who it may affect, and that anyone could be susceptible.

**Table 1 – Clusters of Covid-19 symptoms identified by the Covid Symptom Study**

Cluster	Symptoms
	(* indicates more likely to get long Covid)
“Flu-like” with no fever	Headache*, loss of smell, muscle pains, cough, sore throat, chest pain, no fever
“Flu-like” with fever	Headache*, loss of smell, cough, sore throat, hoarseness, fever, loss of appetite*
Gastrointestinal	Headache*, loss of smell, loss of appetite*, diarrhoea*, sore throat, chest pain, no cough
Severe level one, fatigue	Headache*, loss of smell, cough*, fever, hoarseness*, chest pain, fatigue
Severe level two, confusion	Headache*, loss of smell, loss of appetite*, cough*, fever, hoarseness*, sore throat, chest pain, fatigue, confusion, muscle pain
Severe level three, abdominal and respiratory	Headache*, loss of smell, loss of appetite*, cough*, fever, hoarseness*, sore throat, chest pain, fatigue, confusion, muscle pain, shortness of breath*, diarrhoea*, abdominal pain

## **Fatigue**

The most common reported symptom has been described by doctors as “profound fatigue”. Data show this to be the most common trait in people who had symptoms beyond three weeks. <sup>7</sup>

## **Brain Fog**

Brain fog can be best understood as a reduced capacity for memory, attention and cognitive ability. It is also another reported symptom of long Covid. The most serious cases of neurological conditions tend to occur in older patients, those with pre-existing conditions, or those who had severe Covid-19 infections and required hospitalisation. <sup>8</sup>

The prevalence of these types of cognitive issues among Covid-19 patients is currently unclear: Early research from the Tongji Medical College in Wuhan suggests that one in three patients will suffer from cognitive issues, though neurobiologist Fernanda De Felice from Rio de Janeiro’s Federal University believes the ratio is more likely to be one in two, especially for individuals who were hospitalised. <sup>9</sup>

## **Long Covid and the Heart**

For a virus that is generally associated with breathing issues and the respiratory system, Covid-19 can also cause notable damage to other vital organs, including the heart. This is especially true with cases of long Covid. According to the Centres for Disease Control in the US, heart conditions associated with Covid-19 include myocarditis (inflammation of the heart muscle itself) or pericarditis (inflammation of the thin membrane surrounding the heart). Heart damage from these conditions may help explain some of the frequently reported long-term symptoms of Covid-19, including shortness of breath, chest pain and heart palpitations. <sup>10</sup>

## Who Is Affected?

Patients who suffered from severe cases of Covid-19 are more likely to report long-term symptoms when compared to those who had mild infections. But there is more to learn as the impact of long Covid on people who had mild cases has not yet been studied in-depth. <sup>11</sup>

Patterns in the Covid Symptom Study suggest that long Covid was about twice as common in women as in men and that the average age of someone presenting with it was about four years older than people who had what might be labelled as “short Covid”. <sup>12</sup>The median age for someone suffering with long Covid is 45.

Young people can be long-haulers too: A study from the US found that in addition to adults and those with chronic conditions reporting long-term symptoms, one in five people aged between 18 and 34 who do not suffer from chronic medical conditions reported cases of long Covid after their initial infection. <sup>13</sup>

One expert we spoke to said their findings indicated that long Covid is very rare in under-18s, rare in over-65s and particularly affects those of working age.

## How Can We Help Those With Long Covid?

Doctors and nurses have come a long way in learning how to treat Covid-19 patients. But treating long Covid is a new challenge as management of Covid-19 after three weeks is currently based on limited evidence. <sup>14</sup>

After addressing serious ongoing complications or comorbidities, and until there are results from long-term studies on long Covid, treatment for long-haulers will need to be managed symptomatically. For example, a fever can be treated with paracetamol, whereas some conditions may require specialist support. <sup>15</sup>

Some doctors are beginning to take non-medication, non-surgical rehabilitation approaches to treat cases of long Covid, according to Doctor Gerard Francisco of McGovern Medical School in the US. These types of approaches include reconditioning programmes for those experiencing chronic fatigue as well as sessions with neuropsychologists for those suffering from cognitive issues. <sup>16</sup>

One expert we spoke to told us that they believe steroid therapy may be useful in treating long Covid. Currently, steroid therapy is being used to treat severe cases of Covid-19 in hospitals, but research has yet to examine steroid therapy's effectiveness in the treatment of long-haulers.

As medical professionals continue to gain a better understanding of long Covid, they will be able to craft more effective treatment plans for individuals or refer them to specialists to help address their lasting symptoms. This information must be collected systematically and internationally.

## How Big of a Problem Is Long Covid?

According to the King's College study, one in ten people from the population, most of whom never visited hospital, are reporting symptoms beyond a generous four-week recovery period and, extrapolating, it is thought that around 300,000 people in the UK could be impacted. Around 1.5 to 2 per cent are still reporting symptoms for longer than three months, which would equate to at least 60,000 people in the UK alone from the first wave (based on estimates that around 3 million people were affected). These figures are based on a subset of King's College/ZOE app users who reported new symptoms, who had logged continuously and also had a positive PCR test for the virus.

The phenomenon of long Covid is not unique in itself; post-viral syndrome can occur after an individual has fought off many types of viral infection, including the common cold, influenza, pneumonia, the Epstein-Barr virus, SARS and HIV.<sup>17</sup> From speaking to the experts, it is clear that the novelty of long Covid is the broad spectrum of symptoms that are being reported and the duration of months not weeks.

For example, similarly to long Covid, symptoms of post-viral syndrome can last for a few days or up to a few months after the initial infection. However, the most commonly reported symptoms for post-viral syndrome tend to be limited to general fatigue, muscle fatigue, trouble concentrating, stiff joints, headaches, and swollen lymph nodes.<sup>18</sup> The list of symptoms for long Covid, however, extends to include those as well as the symptoms and conditions listed earlier in this paper.

### International Evidence on Long Covid

A wide range of studies have now been conducted on long Covid.

A recent study of 110 hospitalised patients found that 74 per cent of respondents had at least one persistent symptom after 12 weeks. The most common symptoms included:

- Excessive fatigue: 39 per cent
- Breathlessness: 39 per cent
- Insomnia: 24 per cent
- Muscle pain: 23 per cent
- Chest pain: 13 per cent
- Cough: 12 per cent
- Loss of smell: 12 per cent
- Headache, fever, joint pain and diarrhoea: Each less than 10 per cent

In Holland, a collaboration between the Long Alliantie Nederland (LAN) and the Longfonds<sup>19</sup> (a lung foundation) conducted a poll of 1,622 people afflicted with Covid-19 and found that nine in ten indicated they had a problem with simple daily activities. Of these, 91 per cent had not been in hospital and just 6 per cent said their health was good after the virus – compared to 85 per cent before being infected.

A recent study published in the Lancet found that 78 of 100 patients in an observational cohort that had recovered from Covid-19 had abnormal findings on cardiovascular MRI and 36 reported dyspnoea (difficulty breathing) and unusual fatigue.<sup>20</sup>

Doctors in a Paris hospital reported that, on average, they saw around 30 long-haulers every week between mid-May and late July. The average age of patients was 40 years, with four times more women than men.<sup>21</sup>

A paper published in the BMJ in August found that around 10 per cent of those who had had Covid-19 experienced prolonged symptoms beyond three weeks, with a smaller proportion experiencing them for months.<sup>22</sup>

The British Medical Association published a press release recently that warned the effects of long Covid would be significant. Almost a third of the 4,000 doctors surveyed had seen or treated people with symptoms they believed were longer-term effects of Covid-19 during the first two weeks of August.<sup>23</sup>

## Long Covid in Context

It's important to understand how likely one is to suffer from long Covid compared to other diseases such as cancer and heart disease. Based on current data, the incidence rate of cancer for a 45-year-old – the median age of those with long Covid – is 410 in 100,000 for women and 213 in 100,000 for men.<sup>24</sup> There are about 367,000 new cases of cancer reported each year, with around 1,000 new cases per day, causing almost 165,000 deaths each year.<sup>25</sup> When it comes to heart disease, almost 11 per cent of those aged between 45 and 54 have a cardiovascular condition. Heart and circulatory diseases cause around 167,000 deaths each year in the UK.<sup>26 27</sup> This is significantly higher than the data for long Covid.

It is currently estimated that around 60,000 people may be suffering from long Covid for longer than three months. According to the British Lung Foundation, around 220,000 people contract pneumonia each year, causing around 30,000 deaths per year.<sup>28</sup> Up to four in ten people with pneumonia require hospitalisation in the UK.<sup>29</sup> During the peak of the 2019 flu season, 1,802 people were admitted to ICU with severe cases of the flu, which can lead to pneumonia.<sup>30</sup>

## Conclusions and Recommendations

While a range of studies have now been conducted on long Covid, many of these draw on only a small sample pool or rely on self-reporting. The King's College London study appears to be the largest in scale and indicates around 10 per cent of those taking part in the survey had symptoms of long Covid for a month, with between 1.5 and 2 per cent still experiencing such symptoms after three months. These appear to be the most reliable statistics on which to base a rough estimate of the scale of long Covid on the population. While we do not have clear evidence about prevalence in asymptomatic cases, it is likely to be lower than these percentages.

Long Covid seems rare in those under 18 and over 65, with higher prevalence among those of working age. The median age of those affected is 45 and it affects women more than men.

As Professor Spector says, long Covid is likely a bigger issue than excess deaths as a result of Covid, but, crucially, the risk must be considered alongside the economic impact and other health impacts linked to Covid restrictions.

Based on the research conducted for this report we recommend the following next steps for government.

### Recommendations:

- **Further Research**

In order to gain a deeper understanding of the scale of long Covid, we recommend further studies are carried out. This should particularly look to draw on international data to give the best possible evidence for the scale of the problem. In particular they should look to build as full a picture of possible on the extent of long Covid, particularly among asymptomatic carriers. This should be built into a publicly available, global database, requiring global coordination. This could be overseen and housed, for instance, by the WHO.

- **Awareness Campaign**

Although the long-term impact of long Covid appears low (with 1.5 per cent suffering after three months), the shorter-term risks are higher. Given these symptoms have affected younger people and those otherwise fit, we recommend this issue be highlighted in government awareness campaigns. We believe doing so would help drive compliance with containment measures such as the use of masks.

- **Diagnosis**

It is important that long Covid cases are correctly identified. This will require mass testing, drawing on both antigen and antibody tests, as well as information on symptom duration, with the information collected centrally. The right case definition is needed alongside this, with certain symptoms, like loss of smell or taste, being highly indicative of Covid. The work King's College London and ZOE are undertaking may help lead to the development of an app that is able to screen for potential cases of long Covid within the first week based on the constellation of symptoms and other risk factors.

- **Specialist Support**

Further work is needed to identify best practice in supporting and treating those suffering from long Covid. This includes building on some of the non-medication approaches being used, as well as identifying therapeutic options. From our conversations with experts, we believe steroid therapy early intervention may be a viable option for supporting those with long Covid and should be properly trialled. This information should similarly be captured using the global database we recommend, ensuring that all approaches are recorded and their effectiveness monitored.

- **Screening Based on The Covid Symptom Study**

The data collected by The Covid Symptom Study is invaluable for informing who is at risk from long Covid. This data should be properly analysed and maintained, before being used to understand how likely one is – based on their age and profile – to suffer from long Covid symptoms. This insight could inform enhanced shielding measures and underpin individual risk profiles.

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## Footnotes

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