

Long covid: Do I have it, how long will it last and can we treat it?

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MORE than a million people in the UK are living with long covid, according to the UK's Office for National Statistics (ONS). And while global figures vary, it is thought that about 14 per cent of people who catch covid-19 end up with lasting symptoms – which is some 25 million people worldwide. This could be a big underestimate, though, because less than 10 per cent of infections are thought to be detected, so the true figure could be nearer 250 million.



Rehab therapy in a long-covid clinic

What is clear is that even after the pandemic is brought under control, millions of people will be left with lingering symptoms that prevent them from working and enjoying life. Here is what we know so far.

What is long covid?

While there is no universally agreed definition, long covid is often taken to include anyone with medical symptoms persisting for several weeks after an infection with the coronavirus. However, the term is being used quite widely. “It’s actually an umbrella term for a whole constellation of different problems,” says David Oliver, a doctor based in Reading, UK, who has been working with covid-19 patients throughout the pandemic.

“There is so much variation in what people are considering long covid to be,” says Nisreen Alwan at the University of Southampton, UK, who has had long covid.

“50-89% - People reporting at least one symptom two months after hospitalisation with covid-19”

According to a report published in March by the UK's National Institute for Health Research (NIHR), of which Oliver was an author, people with long covid can be divided into four groups: those experiencing the after-effects of ventilation in intensive care; those with organ damage caused by the virus; those with post-viral fatigue syndrome; and a miscellaneous group that the authors call those with long-term covid syndrome.

The first two groups are relatively familiar to doctors. People who are put on a ventilator for some time experience muscle wasting. After leaving intensive care, they can need months of rehabilitation, during which they gradually raise their exercise capacity.

There may also be clear reasons for organ damage. Any severe chest infection can cause lung scarring. In some people, the virus can increase blood clotting, boosting the risk of heart attacks and stroke. It can also cause an overreaction of the immune system known as a cytokine storm, which can damage organs such as the heart or kidneys.

The next two groups are harder to define and can include people who weren't admitted to hospital. Post-viral fatigue is long-lasting tiredness, especially in response to only minor exertion, which is sometimes seen after other viral infections, including flu and the Epstein-Barr virus. If it persists for many months, it may be called chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). Fatigue is the most common symptom in people with long covid (see graphs).

“30% – The increased risk of long covid for women compared with men”

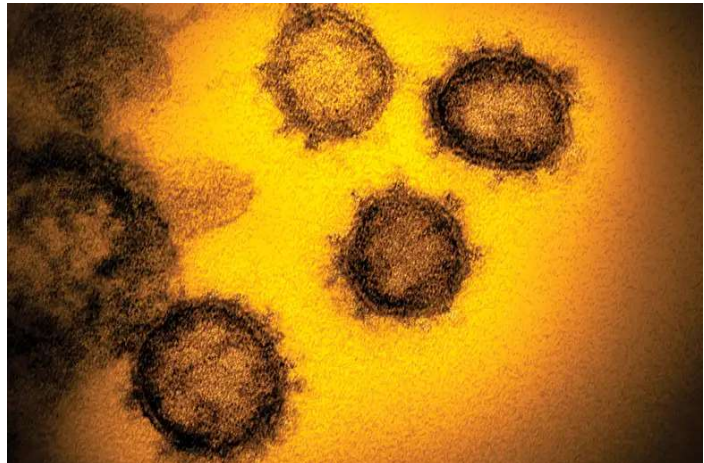
The NIHR authors use the fourth category, long-term covid syndrome, as a catch-all for any other people with ongoing ill health who don't fit the other categories. This is needed because of the wide variety of possible symptoms. As well as fatigue, breathlessness and difficulties concentrating or "brain fog", symptoms can include rashes, heart palpitations or bowel issues.

Using one umbrella term for what could be different conditions means it confuses discussion of prognosis and prevalence. "If you're looking at prevalence, long covid has to be qualified as to what population you're looking at, whether it's people who were hospitalised, not hospitalised or ventilated," says Sarah Tyson at the University of Manchester, UK, who was on the NIHR report's steering group.

Most studies of long covid have focused on people admitted to hospital, who tend to be more likely to have long-lasting ill health. Estimates of the number of people reporting at least one symptom two months after infection range from 50 to 89 per cent. This is to be expected, especially in older people, says Oliver O'Sullivan at the Defence Medical Rehabilitation Centre in Loughborough, UK.

Long covid seems less common in people who aren't admitted to hospital, although estimates vary depending on how much time has passed after infection. In a survey of people using the Zoe Covid Symptom Study App who had tested positive for covid-19, 4.5 per cent reported symptoms lasting more than two months, and this fell to 2.3 per cent by three months.

This study found that people with worse initial illness, experiencing five or more symptoms in the first week of infection, were more than three times as likely to still have symptoms three months later. But it is possible for people who were only mildly affected initially to still be ill months later, says O'Sullivan.



SARS-CoV-2, the virus that causes covid-19

Who is most at risk?

One puzzling feature is that those most prone to long covid aren't those most likely to get sick from the initial infection. The biggest risk factor for death from covid-19 is older age, with men being more likely to be admitted to hospital than women. With long covid, on the other hand, women are 30 per cent more likely to get it than men, and 35 to 69-year-olds are the age group most often affected, according to the ONS. That survey also found a higher prevalence in people from deprived areas and in healthcare staff and social care workers, although more women do those jobs so they might be more likely to catch covid in the first place.

How do I know if I have long covid?

It is hard to know for sure. If you tested positive for SARS-CoV-2 after developing symptoms and some of them have continued for several months, most doctors would agree that you have long covid. If you were never tested, or developed long-lasting symptoms only after the initial infection, matters are less clear. Different doctors may come to different conclusions.

That is because there is still no consensus on what long covid is. There are "nearly as many definitions as studies", according to one recent review. Getting consensus on a definition is essential to diagnose effectively, says Alwan. And for some people, the diagnosis can make the difference between losing their job or not, for instance. "For me, it's about ensuring more justice and equality," she says.

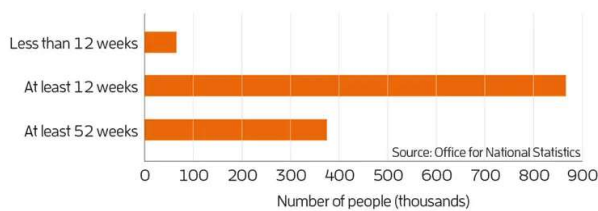
">1 million – People in the UK with long covid"

Janet Diaz at the World Health Organization (WHO) and her colleagues are working with a panel of experts and patients to agree a clinical case definition of “post covid-19 condition”. So far, Diaz told a WHO webinar on long covid on 15 June, there is consensus that people must have been infected with SARS-CoV-2 and have persistent symptoms, such as cognitive impairment, fatigue and shortness of breath, that affect everyday functioning. The symptoms also mustn’t be explainable by an alternative diagnosis.

“It is possible for people who were only mildly affected initially to still be ill months later”

But knowing whether you have had covid-19 can be tricky. Testing was rare early in the pandemic and continues to be infrequent in low-income countries. Even in higher-income countries, most infected people never get tested.

Duration of long covid reported by people in the UK as of 2 May 2021



Then there is the problem that the common symptoms of long covid can have many other causes.

At present, only a small proportion of people with long-lasting symptoms have a condition that can be objectively identified with existing tests, Petter Brodin at the Karolinska Institute in Sweden told the WHO webinar. “I do not mean

the remaining individuals have an imaginary disease or a psychosomatic disorder, that’s not what I’m saying at all,” he said. “It’s just that our tools for diagnosing them are insufficient.”

The WHO is looking into what steps and assessments should be used if long covid is suspected. “You want to pick out anything that could be treated,” says Alwan. “So, for example, damage to the heart or blood clots.”

What causes long covid?

In people who spent time in hospital, there may be a clear cause of persistent symptoms, such as muscle loss. In those who had a milder initial illness yet are sick months later, several other explanations have been suggested.

There are three broad ideas: persistent viral infections; lasting tissue damage caused by the virus; and immune system changes, such as producing autoantibodies that attack your own body.

There is evidence to support all these ideas, said Akiko Iwasaki at Yale School of Medicine, at the WHO webinar. “All of these things could be contributing.”

Persistent infections can be seen with other viruses, such as Ebola, and there is some tentative evidence that fragments of SARS-CoV-2 could linger for months inside people who seem healthy.

The idea that the virus causes changes to the immune system is plausible because of the cytokine storm seen in some people who get severely ill with covid-19. Even in people who don’t get very ill from the initial infection, small studies have shown immune system changes months later, such as a rise in compounds in the blood linked with inflammation and autoantibodies.

Women are more prone to some autoimmune conditions involving such antibodies, says Danny Altmann at Imperial College London, which may be why they seem more likely to get long covid.

Some have proposed that infection may alter how the body triggers the immune responses normally involved in allergic reactions. Paul Glynn at The Physicians’ Clinic in London has found that in a small trial of 25 people with long covid who had an initial mild infection, treatment with antihistamine medicines, usually given for allergies, reduced symptom burden by one month on average, although it wasn’t a placebo-controlled trial.

Other groups are focusing on the disturbances of blood pressure and heart rate. One idea is that covid-19 somehow triggers a condition called orthostatic intolerance, in which people get low blood pressure on standing.

If any of these hypotheses are confirmed, it could lead to specific tests. For instance, blood tests could reveal the presence of autoantibodies. Detecting persistent infections, however, would typically require taking a tissue sample – a biopsy.

What help is available?

There is no proven drug for long covid, but that doesn't mean there is no help for people living with it.

The first port of call is to talk to your doctor. Ideally, the family doctor refers those with the most severe symptoms to a long-covid service. The first dedicated long covid clinic in the UK launched in November 2020 and there are now 83 open in England. To date, there are still no long-covid clinics in Wales, Northern Ireland or Scotland. Mount Sinai Hospital in New York City was the first in the US to open such a clinic, with many others springing up in other states.

“There are a group of people who do very well from the long covid service,” says David Strain at the University of Exeter and the NHS Long Covid Taskforce.

“It's really focused on treating the symptoms, because we don't know the cause. There's a wide range of symptoms and we have some strategies for all of them now,” says Melissa Heightman at University College London Hospitals, who set up one of the UK's first long covid clinics.

Based on data from about 1300 patients, Heightman has found that people with long covid need similar amounts of referral to specialists and rehabilitation, regardless of whether or not they were hospitalised by the initial infection. Persistent symptoms can last for as long as six or 12 months, her research suggests.

Clinics are now much better at identifying what type of long covid a person has, says Strain. “Long covid isn't one disease,” he says. Working out who has what is crucial for the right rehabilitation. For example, graded exercise therapy helps those with pneumonia-like impacts, but can be harmful for those with the CFS/ME-like condition, says Strain.

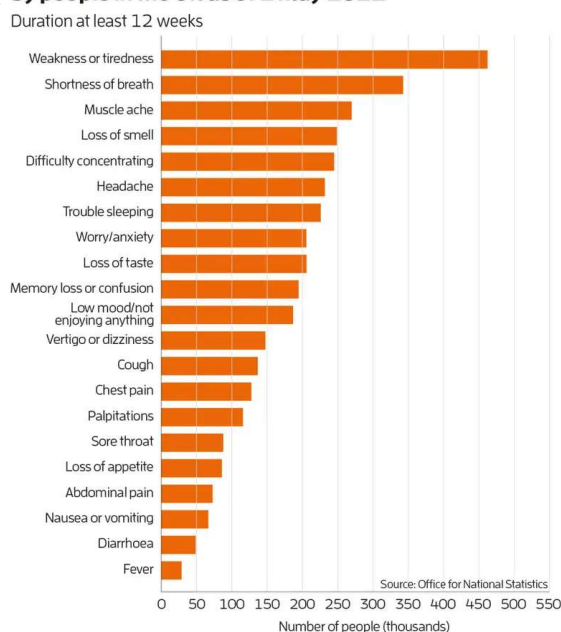
Another vital element of the clinics is psychological support. “People with long covid have almost a post-traumatic stress-type picture. They've gone from fit and healthy people running households, exercising, to all of a sudden they are short of breath walking from the kitchen to the dining room,” says Strain.

England's efforts to tackle long covid compare favourably internationally, but that is partly because it was weak in its response to controlling infections and had a huge load of cases to deal with, says Amitava Banerjee at University College London (UCL).

Unfortunately, there aren't enough clinics or specialists. “We can't refer everyone to a long covid clinic, they'd just be inundated,” says Kamlesh Khunti at the University of Leicester, UK. Family doctors are also still in the process of being trained to better assess long covid.

For people who can't get to a clinic, or who have comparatively mild symptoms, there are apps, social media groups and some community-based care helping with breathlessness and mental health.

Most common symptoms of long covid reported by people in the UK as of 2 May 2021



In the absence of a proven treatment for long covid, there are anecdotal reports from clinics of what patients have found helpful for specific symptoms, including some existing medicines. Lifestyle changes such as increased fluid and salt intake seem to help some people, while others find yoga and swimming beneficial. However, everything is anecdotal for now, says Heightman. “We desperately need trials in this space,” she says.

The effect of vaccinations on people with long covid remains unclear. Khunti and Heightman report that anecdotally some people feel worse and others better post-jab.

Researchers are also looking to test the use of existing drugs. Charlotte Summers at the University of Cambridge is running HEAL-COVID, a randomised control trial of interventions for long covid.

The trial is looking at a statin drug to alleviate ongoing inflammation from long covid, and an oral blood thinner to tackle blood clots.

US biotechnology company PureTech Health has begun a clinical trial of LYT-100, a drug candidate that it believes holds promise for treating inflammation and scarring caused by covid-19, and other conditions. Results are due in late 2021.

More clinical trials will follow. Within the next fortnight, the NIHR is expected to announce where it will allocate £20 million of funding, much of which will go on trials for treatments. “It’s very, very early days,” says Khunti. He doesn’t expect any treatments to be ready for clinical use until next year at the earliest.

What of similarities with chronic fatigue?

Some forms of long covid have parallels with CFS/ME, in which people experience debilitating fatigue and other symptoms such as muscle pains and difficulties concentrating. As with long covid, the mechanism behind it is unclear, there is no consensus on treatment and those affected can face scepticism about there being anything wrong.

Some people hope that because long covid is now being reported by medical professionals, the idea of post-viral fatigue has gained respect. “Clearly, there’s a lot about viruses that we don’t understand,” says Tyson. “Also there’s a lot of funding for research and development of services [for long covid], that has resources spilling over for ME.”

What about children with long covid?

Information on the clinical outcomes for children who catch covid-19 is scarce. The good news is that it is usually asymptomatic or manifests as a short, mild illness. However, some children do seem to experience prolonged symptoms. It is unclear how common this is, and the WHO is working on a separate definition for long covid in young people.

As with adults, estimates of prevalence of long covid in children vary. For instance, results from an ongoing study of children in the US, Costa Rica, Canada and Spain suggest that 6 per cent of children who get covid-19 have ongoing symptoms, rising to about 10 per cent in children who are hospitalised.

A second study of 151 children in Melbourne, Australia, found that about 8 per cent had lingering symptoms, most commonly cough and fatigue, which lasted between three and eight weeks after the initial infection. At the most recent review in March 2021, all 151 children had recovered fully (The Lancet, doi.org/gj9p7b).

In research from the UK, about 4.4 per cent of a group of children who tested positive for covid-19 experienced symptoms more than 28 days later ([medRxiv, doi.org/gjg8](https://medRxiv.org/doi.org/gjg8)).

“The largest published studies worldwide suggest persisting symptoms three months later in approximately 5 per cent of children who have had covid,” says Terence Stephenson at UCL Great Ormond Street Institute of Child Health.

In the UK, the latest figures from the ONS say that as of 2 May, there were about 30,000 children between the ages of 2 and 16 living with long covid. Of these, around 14,000 felt their activity was limited a little, and 3000 said their activity was limited a lot.



Patients in Poland undergo rehabilitation after covid-19 infection

Of all young people, teenagers may be most at risk, says Roz Shafran at UCL. Previous research suggests that they are at increased risk of fatigue and mental health problems after viral infections, such as glandular fever.

More information should be forthcoming. Shafran, Stephenson and their colleagues have been recruiting 30,000 children aged between 11 and 17, half of whom have had confirmed covid-19, in order to follow up on physical and mental health problems. Results are expected by the end of June.

“We can’t refer everyone who needs one to a long covid clinic, they’d just be inundated”

Long covid in children needs more consideration in UK government plans, says Layla Moran, a Liberal Democrat MP who chairs a cross-party group on coronavirus. “The long tail of covid is real and will only get worse if the virus is allowed to let rip among the unvaccinated younger population.”

To deal with long covid in children, “you have to be more serious about preventing children getting the infection in the first place”, says Alwan.

In England at least, parents of children with lasting symptoms who are looking for help received some good news this month, with the announcement of 15 specialist long-covid services for children. The new paediatric hubs will draw together experts on respiratory problems and fatigue, who can treat children directly or refer to family doctors and specialists if needed.