

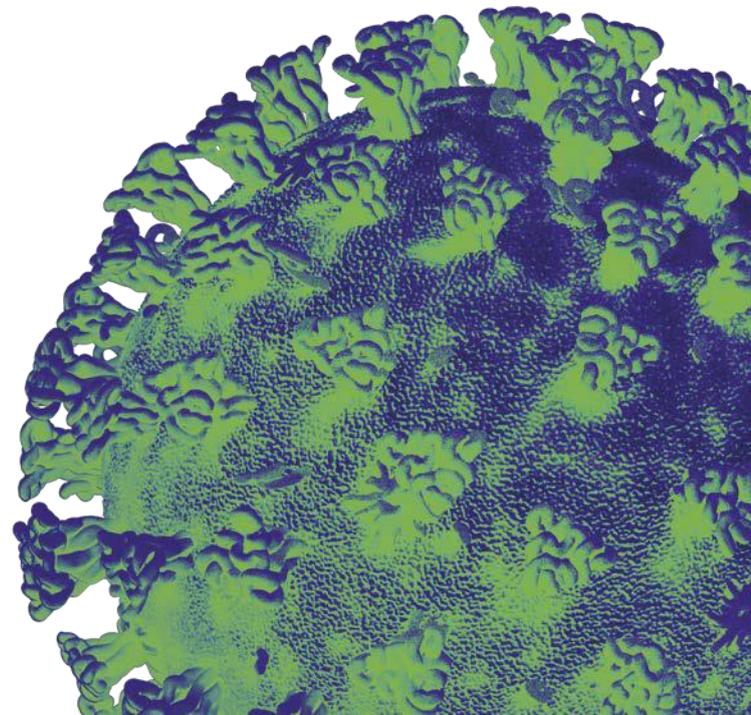
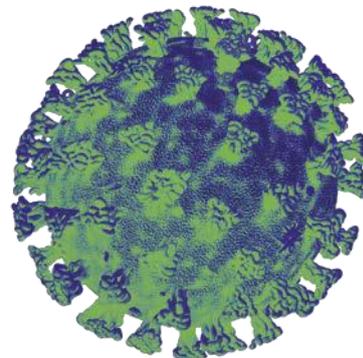
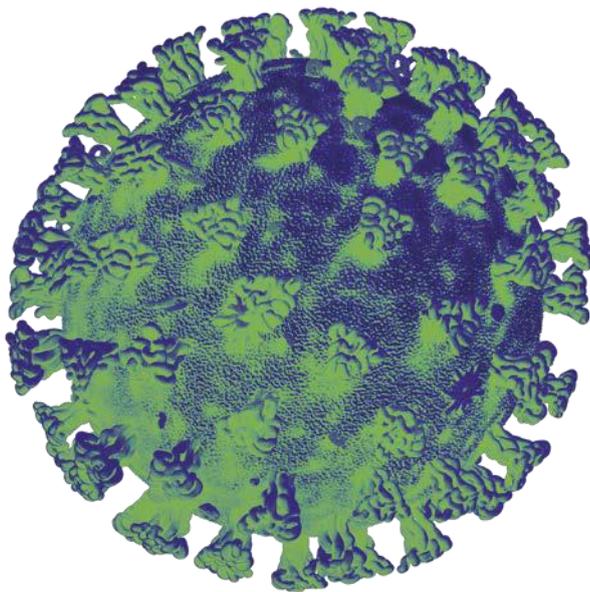


Llywodraeth Cymru
Welsh Government

Technical Advisory Group

“Long-COVID” – what do we know and what do we need to know?

01 February 2021



Technical Advisory Group (TAG)
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Summary

- ‘Long-COVID’ is commonly used to describe signs and symptoms that continue or develop after acute COVID-19. It includes both ‘ongoing symptomatic COVID-19’ (from 4 to 12 weeks) and ‘post-COVID-19 syndrome’ (12 weeks or more).
- ‘Post-COVID-19 syndrome’ has been defined as “Signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis. It usually presents with clusters of symptoms, often overlapping, which can fluctuate and change over time and can affect any system in the body”.
- Symptoms include (but are not limited to) fatigue, muscle weakness, breathlessness, sleep difficulties, anxiety or depression, cognitive blunting or “brain fog”, chest and joint pain.
- Whilst there remains a high degree of uncertainty around Long-COVID, early indications suggest that in people who have previously tested positive for COVID-19, the prevalence of at least one symptom for 12 weeks or more ranges from around 2% to 10% in community samples, to over 70% in people who have been hospitalised. However an unknown number of people have experienced COVID-19 symptoms, have self-cared at home and not accessed a confirmatory test. Symptoms have been reported at 7 months in people with either suspected or confirmed COVID-19.
- Significant health and socioeconomic harms for the individual have been associated with Long-COVID, and an increase in NHS workload is anticipated.
- A [clinical guideline](#) from the National Institute for Health Research has been published and includes relevant [SNOMED](#) terms to facilitate consistent recording. [Welsh Government](#) collaborated in this guideline and a post COVID-19 syndrome group has been established to coordinate the pathways for people with Long-COVID. The rehabilitation framework and guidance has also been updated (publication pending) for Wales.
- As vaccination progresses and the pandemic subsides, the enduring impact of Long-COVID on individuals and services in Wales will become increasingly important to understand, monitor and act upon. There are a range of research questions relevant to Wales, including: measuring and characterising Long-COVID; scenario modelling; estimation of socioeconomic costs; treatment and management; and service delivery.

- Ongoing and future UK research studies focussing on the long-term effects of COVID-19 in hospitalised and non-hospitalised patients will offer important insight. Further evidence needs relevant to scientific advice for Wales will feed into the work of the [Technical Advisory Cell](#), [Wales COVID-19 evidence centre](#), and more widely at a UK-level.

What do we know?

- It is important to note that whilst evolving, the existing evidence base is limited and much uncertainty remains. For context, key findings from existing evidence reviews^{1,2} and additional reports (some of which are not formally peer-reviewed) are highlighted below.
- In people discharged from a Rome hospital following treatment for COVID-19, 87% were still experiencing at least one symptom 60 days following onset and 55% had three or more symptoms, including fatigue (53%), difficulty in breathing (43%), joint pain (27%), and chest pain (22%), with 40% saying it had reduced the quality of their life.³
- 76% of 1176 patients discharged from Jin Yin-tan Hospital (Wuhan, China) experienced lasting effects when assessed 6 months post-acute COVID-19 infection, with fatigue or muscle weakness, sleep difficulties, and anxiety or depression being the most common. Patients who were more severely ill whilst in hospital had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations.⁴
- In a large UK study including 47,780 individuals hospitalised with COVID-19 (mean follow-up time of 140 days), post-discharge multi-organ dysfunction was elevated when compared with matched controls (mean follow-up time of 153 days). People hospitalised with COVID-19 had an increased risk of re-admission and death, with nearly a third of people re-admitted post COVID-19 hospital discharge and more than 1 in 10 died. Post-discharge adverse events were not confined to the elderly population, or uniform across ethnic groups.⁵

¹ Michelen et al, "Characterising long-term covid-19: a rapid living systematic review", Medrxiv (pre-print), December 2020, available at: <https://www.medrxiv.org/content/10.1101/2020.12.08.20246025v1.full.pdf>

² Maxwell, "A dynamic review of the evidence around ongoing Covid19 symptoms (often called Long Covid)", National Institute for Health Research, October 2020, available at: <https://evidence.nihr.ac.uk/themedreview/living-with-covid19/>

³ Carfi et al, "Persistent Symptoms in Patients After Acute COVID-19", Journal of the American Medical Association, July 2020, available at: <https://jamanetwork.com/journals/jama/fullarticle/2768351>

⁴ Huang et al, "6-month consequences of COVID-19 in patients discharged from hospital: a cohort study", The Lancet, January 2021, available at: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32656-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32656-8/fulltext)

⁵ Ayoubkhani et al, "Epidemiology of post-COVID syndrome following hospitalisation with coronavirus: a retrospective cohort study", January 2021, Medrxiv (pre-print), available at: <https://www.medrxiv.org/content/10.1101/2021.01.15.21249885v1.full.pdf>

- In an international web-based survey of suspected and confirmed COVID-19 cases with illness lasting over 28 days, prolonged multisystem involvement and significant disability was reported, with many patients reporting not recovered by 7 months.⁶
- The COVID-19 Infection Survey, which is a nationally-representative sample of the UK community population, has estimated that in respondents testing positive for COVID-19, around 1 in 5 exhibit symptoms for a period of 5 weeks or longer and around 1 in 10 exhibit symptoms for a period of 12 weeks or longer.⁷ Updated estimations confirm this, indicating that the five-week prevalence of any symptom is 22.1%. In the week commencing 27 December 2020, an estimated 9.8% of people still had a COVID-19 symptom 12 weeks after infection, with over 300,000 people estimated to have symptoms lasting 5-12 weeks (England only data).⁸
- Analysis of data from 4182 incident cases of COVID-19 who logged their symptoms via the COVID Symptom Study app, showed that 13.3% had symptoms lasting more than 28 days, 4.5% for more than 8 weeks and 2.3% for more than 12 weeks.⁹
- In a young (mean age, 44 years), low-risk population with ongoing symptoms, almost 70% of 201* individuals had impairment in one or more organs four months after initial symptoms of COVID-19.¹⁰ There are also reports of Long-COVID affecting children, highlighting ongoing concerns about the lack of paediatric services for children with COVID-19.¹¹

⁶ Davis et al, "Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact", Medrxiv (pre-print), December 2020, available at:

<https://www.medrxiv.org/content/10.1101/2020.12.24.20248802v2.full.pdf>

⁷ Office for National Statistics, "The prevalence of long COVID symptoms and COVID-19 complications", December 2020, statement available at:

<https://www.ons.gov.uk/news/statementsandletters/theprevalenceoflongcovidsymptomsandcovid19complications>

⁸ Office for National Statistics, "Updated estimates of the prevalence of long COVID symptoms", January 2021, data available at:

<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/ad-hocs/12788updatedestimatesoftheprevalenceoflongcovidsymptoms>

⁹ Sudre et al, "Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App", Medrxiv (pre-print), October 2020, available at:

https://www.medrxiv.org/content/10.1101/2020.10.19.20214494v1#disqus_thread

¹⁰ Dennis et al, "Multi-organ impairment in low-risk individuals with long COVID", Medrxiv (pre-print), October 2020, available at: <https://www.medrxiv.org/content/10.1101/2020.10.14.20212555v1.full.pdf>.

¹¹ Simpson et al, "Counting long covid in children", The BMJ Opinion, available at:

<https://blogs.bmj.com/bmj/2020/10/16/counting-long-covid-in-children/>

* = typographical error corrected from '67' to '201' on 19.03.21

- The Royal College of GPs¹² anticipates significant primary care will be required to manage significant physical and mental health long-term consequences of COVID-19. Some estimates suggest that up to 50% of people hospitalised would need formal rehabilitation services.¹³
- Emerging findings across organ systems have suggested that the diagnosis, treatment and prevention of post-COVID-19 syndrome will require integrated, multidisciplinary care pathways (potentially drawing from those shown to be effective in other diseases), rather than organ- or disease-specific approaches.¹⁴ A qualitative study¹⁵ including health professionals with long-COVID (thus offering a dual patient-professional perspective), presents a set of co-designed quality standards highlighting the need for equity and ease of access, minimal patient care burden, clinical responsibility, a multidisciplinary and evidence-based approach, and patient involvement.
- Compounded by the healthcare challenges and inequalities that already exist, the long-term impact of COVID-19 is likely to be substantial.¹⁴

What do we need to know?

- There are several research streams which will offer important insight. For example, the [Post-hospitalisation COVID-19 study](#) (PHOSP-COVID), within which Wales is participating, aims to gain a comprehensive picture of the long-term effects on patients hospitalised with COVID-19. Studies from a recently closed [UK-wide funding call](#) will focus on non-hospitalised patients and longer-term effects of COVID-19. An [Office for National Statistics](#) study aims to quantify and characterise post-acute physical and mental health complications of COVID-19.
- There are further important research questions to understand and monitor the impact of long-COVID on individuals and services in Wales, and develop effective care pathways. These will require continual review as evidence needs are fulfilled through ongoing and future research studies, and as new areas of need emerge.

¹² Royal College of General Practitioners (RCGP), “General practice in the post Covid world”, RCGP, July 2020, available at: www.rcgp.org.uk/-/media/Files/News/2020/general-practice-post-covid-rcgp.ashx?la=en

¹³ Murray et al, “We need a Nightingale model for rehab after covid-19”, Health Service Journal, April 2020, available from: www.hsj.co.uk/commissioning/we-need-a-nightingale-model-for-rehab-after-covid-19-7027335.article

¹⁴ Ayoubkhani et al, “Epidemiology of post-COVID syndrome following hospitalisation with coronavirus: a retrospective cohort study”, January 2021, Medrxiv (pre-print), available at: <https://www.medrxiv.org/content/10.1101/2021.01.15.21249885v1.full.pdf>

¹⁵ Ladds et al, “Developing services for long Covid: lessons from a study of wounded healers”, Medrxiv (pre-print), November 2020, <https://www.medrxiv.org/content/10.1101/2020.11.13.20231555v1>

Monitoring long-COVID in Wales

- What is the incidence and prevalence of Long-COVID, by age group, gender, ethnicity, occupation, socioeconomic status, whether they have had a positive COVID-19 test and whether they have been in hospital/intensive care? Can risk factors for Long-COVID be identified?
- What do we know from the lived experiences of people experiencing long-term symptoms of COVID-19? What are the mental health impacts?
- What are the different pathways (e.g. patterns of symptoms, help-seeking) for people with Long-COVID with different characteristics, and what are the associated outcomes?
- What is the extent of multi-organ damage in the population?
- How is Long-COVID characterised in children? What are the needs of children and parents with regards to Long-COVID in children?

The Reasonable Worst Case Scenario (RWC) for Wales and Long-COVID

- What additional effects and demands of Long-COVID on the NHS are identified through RWC analysis for Wales?

Health services for Long-COVID in Wales

- How is Long-COVID currently being managed in Wales and how effective is it? What is the patient experience? What are the recent service innovations?
- How can we avoid over-medicalising people experiencing longer-term symptoms?
- How can [value-based](#), multi-disciplinary, continuous and timely care pathways enabling access close to home be facilitated?
- What are the training and educational needs of the health and social services workforce?
- What is the relative impact of Long-COVID on different health and social services and how will this impact upon responsive planning?

The socioeconomic costs of long-COVID in Wales

- What are the health related quality of life and Quality-Adjusted Life Year (QALY) decrements for Long-COVID, in both hospitalised and non-hospitalised patients?
- What are the productivity losses from Long-COVID (e.g. workplace presenteeism and absenteeism, reduced household production)?

Next steps

- Although there is currently a high degree of uncertainty around Long-COVID, we have started to attempt to include estimates of the costs and QALYs associated with long-COVID as part of epidemiological and economic modelling. This will help to inform scientific advice for decision making around restrictions in Welsh Government and help ensure harms related to COVID-19 are fully accounted for.
- Further evidence needs will feed into the work programme of the [Technical Advisory Cell](#), [Wales COVID-19 evidence centre](#), and UK-wide research programmes where appropriate. Areas benefiting from collaboration across the four UK Nations will be identified.

