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ANMF COVID-19 RESOURCE

What we know about 'Long COVID' or, post COVID-19 condition in 2022

ALERT Evidence regarding COVID-19 is continually evolving, so this article may not include the very latest evidence in real-time.

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Post-COVID condition or 'Long COVID' can be characterised by ongoing symptoms following acute COVID-19 illness. Evidence and understanding of the condition are still emerging, however those who have experienced prior severe COVID-19, are of older age, female sex, and with pre-existing physical and mental health disorders appear most at risk. The most often reported symptoms include fatigue, dyspnoea (breathlessness), coughing, sleep disturbance, anxiety and depression, cognitive impairment, and difficulty concentrating. A full vaccination schedule likely reduces the risk of experiencing prolonged symptoms following COVID-19 illness.

Introduction

COVID-19 has had an unparalleled impact on the health of the global community with millions of cases recorded so far. As has been well reported, the experience of COVID-19 illness varies between individuals and ranges from asymptomatic to severe illness and death. Beyond these acute episodes of disease however, many have reported related symptoms that have either continued or developed after an initial COVID-19 infection with no clear alternative diagnosis. This experience is colloquially referred to as 'long COVID'. Similar post-acute viral syndromes have also been described by those who have experienced illness during other coronavirus epidemics such as the SARS and MERS outbreaks of 2003 and 2012.1

Defining post COVID-19 condition

In the early months of the pandemic, as people began to share their experiences of COVID-19 across social platforms, increasing numbers of reports describing ongoing symptoms following acute periods of COVID-19 infection began to appear.² Although at this time the initial focus of the global effort was to understand the pathology and epidemiology of SARS-CoV-2 and COVID-19, an awareness of the potential long-term effect of COVID-19 was increasingly driven by patient voice and advocacy groups with a number of popular terms for the condition arising, including long COVID, long-haul COVID, post-acute COVID, long term effects of COVID, or chronic COVID. With anecdotal and emerging evidence describing a broad and diverse range of persistent and prolonged symptoms, national health advisory boards progressively adopted and defined 'long COVID' as a condition of continuing or developing symptoms beyond four weeks after an initial SARS-CoV-2 infection.^{3,4} Although there is no globally accepted definition for the condition, the World Health Organization (WHO) formally recognised 'long COVID' in October of 2021 with a standardised clinical case definition.⁵ This definition was developed via a Delphi process and with input from all WHO member countries. The WHO defines, 'post COVID-19 condition' as:

Illness that occurs in people who have a history of probable or confirmed SARS-CoV-2 infection; usually within three months from the onset of COVID-19, with symptoms and effects that last for at least 2 months. The symptoms and effects of post COVID-19 condition cannot be explained by an alternative diagnosis.⁶

This definition is reflective of the general sentiment for what constitutes 'long COVID', and notably does not require that a prior SARS-CoV-2 infection be strictly confirmed via testing for diagnosis (although it does require that prior infection be suspected). Evidence continues to emerge however, and as noted by the WHO, the definition may be updated in the future. Importantly, long COVID does not indicate that someone is still infectious or is a reservoir for the SARS-CoV-2 virus.

Risk factors

Evidence for the prevalence of ongoing symptoms following COVID-19 varies greatly both across and within countries. Across 18 studies Raman and colleagues report prevalence of 1.6 - 71% in the UK, 35 - 77% in Germany, 49 - 76% in China, 68% in Africa, 22% in India, 16 - 46% in Bangladesh, 1% in Denmark, 5 - 51% in Italy, 16 - 53% in USA, and 61% in Norway.⁷ Although the difference in prevalence is suggested to be a result of differences in the study populations, the researchers note that those studies which assessed hospitalised patients typically reported a higher estimate of prevalence.⁷

Published in November of 2021, a rapid review of meta-analysis and large cohort studies by the National Institute for Health and Care Excellence (NICE) also identified prevalence and a number of risk factors for ongoing symptoms.⁸ Within their review, analysis of risk factors from longitudinal study samples (supported by cross analysis with electronic patient health record data) of 6,907 self-reporting adults in the UK found symptoms impacting on normal functioning for more than 12 weeks following SARS-CoV-2 infection occurred in between 1.2% (mean age 20 years old) and 4.8% (mean age 63 years old) of COVID-19 cases. Further, 7.8% (mean age 28 years old) and 17% (mean age 28 years old) reported having any symptoms at more than 12 weeks.

In regard to risk factors associated with ongoing symptoms, the NICE review found being older, of female sex, having poor pre-pandemic health, and poor general health to be associated with a higher risk of experiencing symptoms at more than 12 weeks, as were individuals with asthma, and those who were overweight and obese. Being of a non-white ethnic minority background was found to be a protective factor, and many of the respondents had not been hospitalised.⁹ Similarly, a study of 508,707 participants also reported within the review found being of female sex, and, overweight or obese, increased the risk of experiencing one or more symptoms at more than 12 weeks following acute COVID-19 illness. Severe COVID-19, where severe was defined as requiring hospitalisation, was also found to increase the risk of ongoing symptoms.⁴

Although much of the data presented in these studies was self-reported by patients (and therefore at risk of an inherent level of bias), overall, the findings indicate that factors such as **prior severe COVID-19**, **older age, female sex, and pre-existing physical and mental health disorders** are risk factors for experiencing continuing symptoms at more than 12 weeks following SARS-CoV-2 infection. It is important to note that although these studies have described risk factors for the condition, ongoing symptoms have been described across a broad range of demographics, including those who suffered severe COVID-19 and those who were asymptomatic.¹⁰

Prevalence and symptoms

Ongoing symptoms following COVID-19 manifest in a broad and diverse number of ways. This diversity has been described by sufferers both in the timeframe they have experienced them in, and in the number and type of symptoms experienced. A review of three systematic reviews and three large cohort studies, also undertaken by NICE, reported on the prevalence of symptoms in those with post COVID-19 condition. Their review, ultimately comprising 28 – 45 studies (with some overlap across systematic reviews) categorised symptoms across multiple domains such as cardiopulmonary, upper respiratory, and musculoskeletal, identifying 34 different symptoms across nine domains. The symptoms most prevalent among the commonly reported included **fatigue, dyspnoea** (breathlessness), coughing, sleep disturbance, anxiety and depression, cognitive impairment, and difficulty concentrating. Further, patients receiving a neurological or psychiatric diagnosis was estimated to occur in 33.62% of individuals following a COVID-19 diagnosis, and of those, occur in 12.84% of individuals for the first time. These were most commonly mood, anxiety, or 'any psychotic disorder'.¹¹

Observing trends in the prevalence of symptoms between 4-12 weeks, and greater than 12 weeks, indicated that coughing (28%), sleep disturbance (36%), anxiety and depression (29% and 22%) were more common in the earlier 4 - 12-week period. Conversely, hair loss was reported more often in the later period, after 12 weeks (14 or 22% at 12+ weeks and 10% between 4 - 12 weeks). Other symptoms, including fatigue and concentration difficulties occurred equally across both the 4 - 12-week period, and 'greater than 12 weeks' period (51% and 25% at 4-12, and 47% and 31% at 12+ weeks respectively).¹¹

Overall, this evidence is illustrative of the broad way in which ongoing symptoms following an acute episode of COVID-19 illness can manifest, and while a clear understanding of how and why is still developing, in the very least, the latest ongoing research and hypotheses suggest a complicated explanation, incorporating multiple organ systems.^{1, 7, 12}

Vaccination and post COVID-19 condition

An understanding of how vaccination impacts on risk or severity of post COVID-19 condition is still emerging however some **evidence does suggest vaccines reduce the risk of experiencing ongoing symptoms following infection**. One UK study found that those who received a two-dose vaccine schedule were less at risk of having symptoms that lasted longer than 28 days than those who were unvaccinated, however there was no effect for those who had only received a single dose of a COVID-19 vaccine.¹³ Similarly, an Israeli study of 3,388 people found fully vaccinated participants were less likely to report headaches, fatigue, and muscle pain than those who were unvaccinated.¹⁴ The United States Centers for Disease Control and Prevention (CDC) suggest measures associated with the prevention and reduction of COVID-19 including vaccination are most effective at preventing post COVID-19 conditions,³ and NICE encourage a full course of vaccination to reduce the risk of post COVID-19 conditions, acknowledging the effect of vaccination on the condition is not currently understood.⁸

Conclusion

The evidence regarding long COVID and understandings of the condition are evolving as new reports and analyses emerge. In any case, reports and people's personal experiences following infection clearly suggest that for a large number of people, resolution of an acute COVID-19 infection is not without complications. These ongoing symptoms can severely impact people's health and wellbeing and their ability to return to pre-infection levels of activity, work, and social participation so must be taken seriously. These impacts must be considered carefully in terms of workforce planning and support for health and aged care staff and others including teachers and workers in the wider community. Promisingly, vaccination appears to confer protection against both primary infection and severe symptoms as well as the likelihood of developing long COVID, so vaccination for those who can be, should be recommended. As new evidence emerges and long-term data becomes available, understandings of long COVID-19, how to mitigate against severe impacts, and hopefully how to prevent or limit its duration will develop.

References

- 1. Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nature Medicine*. 2021; 27: 626-631. DOI: 10.1038/s41591-021-01292-y.
- Callard F and Perego E. How and why patients made Long Covid. Soc Sci Med. 2021; 268: 113426. DOI: https://doi. org/10.1016/j.socscimed.2020.113426.
- 3. Centers for Disease Control and Prevention. Post-COVID Conditions. 2021. Available from: <u>https://www.cdc.gov/</u> <u>coronavirus/2019-ncov/long-term-effects/index.html</u>
- 4. National Institute for Health and Care Excellence. COVID-19 Rapid evidence review: risk factors for long-term effects of COVID-19. 2021. Available from: <u>https://www.nice.org.uk/guidance/NG188</u>
- World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021. 2021. Available from: <u>https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1</u> (Oct 2021).
- 6. Soriano JB, Murthy S, Marshall JC, et al. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis.* 2022; 22: e102-e107. 2021/12/21. DOI: 10.1016/S1473-3099(21)00703-9.
- 7. Raman B, Bluemke DA, Lüscher TF, et al. Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus. *Eur Heart J*. 2022; 43: 1157-1172. DOI: 10.1093/eurheartj/ehac031.
- 8. National Institute for Health and care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2021. Available from: <u>https://www.nice.org.uk/guidance/ng188</u>
- 9. Thompson EJ, Williams DM, Walker AJ, et al. Risk factors for long COVID: analyses of 10 longitudinal studies and electronic health records in the UK. *medRxiv* 2021: 2021.2006.2024.21259277. DOI: 10.1101/2021.06.24.21259277.
- 10. Crook H, Raza S, Nowell J, et al. Long covid—mechanisms, risk factors, and management. *BMJ*. 2021; 374: n1648. DOI: 10.1136/bmj.n1648.
- 11. National Institute for Health and Care Excellence. COVID-19 rapid evidence review: signs symptoms and prevalence. 2021. Available from: <u>https://www.nice.org.uk/guidance/NG188</u> (Nov 2021).
- 12. Goudman L, De Smedt A, Noppen M, et al. Is Central sensitisation the missing link of persisting symptoms after COVID-19 Infection? *J Clin Med.* 2021; 10: 5594. DOI: 10.3390/jcm10235594.
- 13. Antonelli M, Penfold RS, Merino J, et al. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. *Lancet Infect Dis.* 2022; 22: 43-55. DOI: https://doi.org/10.1016/S1473-3099(21)00460-6.
- 14. Kuodi P, Gorelik Y, Zayyad H, et al. Association between vaccination status and reported incidence of post-acute COVID-19 symptoms in Israel: a cross-sectional study of patients tested between March 2020 and November 2021. *medRxiv* 2022: 2022.2001.2005.22268800. DOI: 10.1101/2022.01.05.22268800.