

Long COVID and older people

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Long COVID is a poorly understood condition, with a wide spectrum of effects on multiple body systems and variable presentation in different individuals. Long COVID is of particular concern among older people (ie, aged 65 years or older), who are at greater risk than younger people of persisting symptoms associated with COVID-19. In addition, COVID-19 might trigger or exacerbate chronic conditions that occur commonly in older people, such as cardiovascular diseases, respiratory diseases, neurodegenerative conditions, and functional decline. In addition, the disruptive effects of COVID-19 for older people should not be underestimated; lockdowns and other restrictions might have reduced the social interactions of older people, and they are also likely to have lost a spouse or loved one during the pandemic, which can contribute to mental and physical decline. COVID-19 vaccination appears to reduce the effects of long COVID, and older people, especially those living in aged care facilities, should remain up-to-date with their COVID-19 vaccinations. Health-care staff should also consider long COVID in the differential diagnosis of relevant symptoms in older people, rather than assume increasing frailty, and should pursue early multidisciplinary assessment and management of persisting symptoms. Addressing physical, psychological, and functional sequelae will mitigate the effect of long COVID and improve the health and quality of life of older people.

Introduction

Although most individuals make a full recovery from COVID-19, some people have medium-term or long-term wide-ranging effects on multiple body systems. Long COVID is also known as post-COVID-19 condition or post-acute sequelae of COVID-19. Post-COVID-19 condition and long COVID are currently considered to be broadly equivalent designations that encompass illness related to both direct and indirect effects of SARS-CoV-2 infection, whereas the term post-acute sequelae of COVID-19 describes the direct effects of the virus predicated on a confirmed causal relationship.¹ WHO has defined post-COVID-19 condition as occurring in individuals “with a history of probable or confirmed SARS-CoV-2 infection, usually three months from the onset of COVID-19, with symptoms that last for at least two months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others, which generally have an impact on everyday functioning.”² The symptoms can either persist after acute COVID-19 or be of new onset after initial recovery. Symptoms of post-COVID-19 condition can also change or relapse over time.

In this Personal View, we use the term long COVID to denote the effects of this currently unspecified condition across clinical settings. Long COVID can have a wide scope of possible health effects, including on general health and wellbeing, and on cardiovascular, respiratory, neurological, and mental health. These health effects are not necessarily independent, and they can influence each other. Research into long COVID is ongoing, and uncertainties remain regarding its specific causes, the influence of new SARS-CoV-2 variants, and the effect of vaccination.

Although post-acute and long COVID symptoms occur more commonly in patients who had severe infection requiring hospitalisation,³ patients whose initial infection was mild (typically managed in outpatient settings) can also have the condition.⁴ A systematic

review⁵ identified 55 long-term effects (ie, persisting at least 2 weeks after COVID-19 onset and not returning to a healthy baseline) of COVID-19, with 80% of patients infected with SARS-CoV-2 developing one or more of such symptoms. The five most common long-term symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnoea (24%).⁵ Other manifestations were related to lung disease (ie, cough, chest discomfort, sleep apnoea, and pulmonary fibrosis), cardiovascular disease (ie, arrhythmias and myocarditis), neurological disorders (ie, dementia, depression, anxiety, and obsessive-compulsive disorder), and non-specific symptoms, such as tinnitus or night sweats. Study participants were aged 17–87 years, with no stratification of results by age.

A number of studies suggest that the risk of developing long COVID increases with age.^{6–9} A retrospective case study¹⁰ of patients aged 65 years and older hospitalised with acute COVID-19 found that about 25 (9%) of 279 patients had long COVID, with the most common symptoms reported after 90 days being fatigue (25 [8·9%] patients), followed by cough (12 [4·3%] patients) and breathlessness (5 [1·6%] patients). However, research combining datasets from a large longitudinal study and electronic health records found that the risk of long COVID increased with age up to the age of 70 years, and then sharply declined. This finding could be a spurious effect due to “selective competing risk of mortality, nonresponse bias, lower symptom reporting in older adults, misattribution of long COVID to other illness, or a combination of these factors”.¹¹ Some studies^{11,12} indicate that, although being male is a risk factor for severe acute COVID-19, long COVID is more prevalent in women.

Older patients have a greater risk of morbidity and mortality from COVID-19, and are also generally at a higher risk of long COVID than younger patients are.¹³ This Personal View summarises the current knowledge on long COVID in older people and some of the specific challenges in this age cohort. In general, we define

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older people as those aged 65 years or older, although this age cohort is not consistently defined within the literature. We conducted a rapid literature review, examining studies we had already accessed from literature reviews on long COVID, and extracting data for the older population subset. We augmented this with a MEDLINE search using the terms 'post-COVID-19 condition' OR 'post-acute sequelae of COVID-19' OR 'long COVID' AND 'old*' OR 'elder*' OR 'aged*'. We limited results to studies in humans and published in English, with no date restrictions. We grouped papers under the following categories: symptoms and prevalence of long COVID; present or worsening health conditions associated with ageing; mental and social health; relationship between long COVID and persistent physical symptoms, functional somatic disorders, and chronic fatigue syndrome; effect of vaccination and antiviral drugs on long COVID in older people; and other management approaches.

Symptoms and prevalence of long COVID

A scoping review¹⁴ of 50 studies concluded that long COVID is a heterogeneous condition, with a spectrum of over 100 reported symptoms. Study designs and settings vary considerably.¹⁴ The prevalence of long COVID ranges from 10% to 80%, and this rate is influenced by multiple factors, including study design and clinical and demographic characteristics of study participants. Although some symptoms, such as loss of taste and smell, tend to improve over time, other symptoms, such as paraesthesia, can worsen, whereas symptoms such as dyspnoea remain stable.^{15,16}

The prevalence of self-reported long COVID in the UK population is greatest in people aged 35–69 years; women; people living in deprived areas; people working in social care, health care, or teaching and education; and people with another activity-limiting health condition or disability.¹⁷ Older people who have several symptoms (especially fatigue) during their acute COVID-19 infection are at an increased risk of long COVID, which normally manifests with persistent symptoms of fatigue, dyspnoea, joint pain, cough, headache, or loss of sense of smell.

A retrospective cohort study¹⁸ from the USA found an increased risk of one or more new or persistent clinical sequelae after COVID-19 infection in adults older than 65 years, compared with two historical comparison groups. Sequelae included respiratory failure (increased risk difference 7.55, 95% CI 7.18–8.01), fatigue (5.66, 5.03–6.27), hypertension (4.43, 2.27–6.37), memory difficulties (2.63, 2.23–3.13), kidney injury (2.59, 2.03–3.12), mental health diagnoses (2.50, 2.04–3.04), hypercoagulability (1.47, 1.20–1.73), and cardiac arrhythmias (2.19, 1.76–2.57).¹⁸ The risk difference was defined as the difference between the cumulative incidence of the SARS-CoV-2 group and the comparison group.¹⁸

Present or worsening health conditions associated with ageing

The symptoms of long COVID overlap considerably with many of the health conditions that might usually present or worsen with ageing, and there is little clarity about how to distinguish between latent or existing illnesses and the ongoing sequelae of COVID-19.

The prevalence of chronic conditions such as cardiovascular disease, hypertension, diabetes, and prolonged respiratory illness, which are associated with worse outcomes from COVID-19, increases with age.¹⁹ A review²⁰ found that the risk of mortality from COVID-19 increased for patients admitted to intensive care with hypertension, diabetes, respiratory diseases, cardiovascular diseases, and other chronic diseases (eg, cancer), compared with the risk in patients without these conditions. This risk rose significantly with an increasing number of chronic comorbid conditions.

Case-controlled studies indicate that acute COVID-19 infection can precipitate or exacerbate chronic conditions. A UK case-controlled cohort study²¹ of patients with a mean age of 65 years discharged from hospital after acute COVID-19 infection found an increased risk of multiorgan dysfunction (particularly diabetes, cardiovascular disease, and respiratory disease) compared with the expected risk in the general population, and this increase in risk was not confined to older people. Ageing can be a step-wise rather than continuous process, with incremental hits to wellbeing; acute COVID-19 infection might therefore trigger the onset of an incipient chronic condition.

A case-controlled cohort study²² of US veterans aged 60–92 years found that acute COVID-19 infection was associated with an increased risk of negative diabetes outcomes, including anti-hyperglycaemic use across all ages, but the risk and burden were higher in those older than 65 years and with more severe initial infection than in those younger than 65 years and in those with less severe initial infection. Similarly, another case-controlled veteran cohort (with a mean age of 63 years) study²³ found that people who had COVID-19 showed increased risks and 12-month burdens of cardiovascular disease, including cerebrovascular disorders, dysrhythmias, inflammatory heart disease, ischaemic heart disease, heart failure, thromboembolic disease, and other cardiac disorders, with the risks evident independent of age.

A case-controlled study²⁴ from Sweden found that acute COVID-19 infection increased the risk of subsequent deep vein thrombosis, pulmonary embolism, and bleeding, with higher risk in older age groups (older than 50 years) than in younger age groups. A German prospective longitudinal study²⁵ found that the severity of respiratory failure during COVID-19 correlated with the degree of respiratory function impairment and quality of life in the year after acute infection. Conversely, a small prospective cohort study²⁶ of individuals in the USA (with a mean age of 53 years) recovering from COVID-19 with lingering respiratory symptoms of dyspnoea and cough

found that these symptoms did not correlate with COVID-19 severity or pulmonary function.²⁶

Mental and social health

Analyses from a UK self-reported survey and electronic health-care record data found that the risk of long COVID increased with age.¹¹ Poor general and mental health before the pandemic; being overweight or obese; and having asthma were also associated with persistent symptoms, but factors such as cardiometabolic parameters were inconclusive.¹¹ The UK COVID-19 survey also found an increased prevalence of long COVID in people aged 50–69 years.¹⁵ The survey also found that people living in deprived areas and people with another activity-limiting health condition or disability were at greater risk of developing long COVID.¹⁵

In a large study²⁷ of US veterans, an increased risk of mental health disorders (ie, anxiety, depression, stress and adjustment disorders, substance misuse, neurocognitive decline, and sleep disorders) was found in individuals after COVID-19, compared with controls with no history of COVID-19. Risks were higher for those who were hospitalised (with a mean age of 65 years), but new mental health disorders were also evident among those not admitted to hospital (with a mean age of 63 years).²⁷ Furthermore, people with COVID-19 had higher risks of mental health disorders than those with seasonal influenza.²⁷

An Italian study²⁸ observed that many older patients continued to have symptoms such as fatigue, loss of sense of smell, sleep disorders, anxiety, depression, and cognitive dysfunction after their acute SARS-CoV-2 infection was eradicated. Although the continuation of these symptoms might also occur in non-hospitalised patients, the extent of cognitive dysfunction was directly proportional to the severity of the patients' initial respiratory distress.²⁸ Many older people, especially those with mild or moderate dementia, were unable to cope with the disruption in their lives, including lockdown restrictions and inability to use modern technologies, triggering psychological distress and a degree of cognitive and motor dysfunction. The researchers concluded that long COVID is a post-viral condition derived from a complex interaction between biological and psychosocial factors.²⁸

Other studies have also found reduced functional status in some older people after the period of acute infection with SARS-CoV-2. A German study²⁹ of patients (aged 70 years or older) who were hospitalised for COVID-19 found that over a quarter of previously healthy and self-sufficient patients were unable to return home after discharge from hospital. A case-controlled study³⁰ of patients in New York City (NY, USA) aged 55–77 years who survived hospitalisation for COVID-19 found that, 6 months later, over 90% of patients had anxiety, depression, abnormalities in functional outcomes, abnormalities in daily activities, and sleep abnormalities.³⁰

A Chinese cohort study³¹ of COVID-19 survivors aged 60 years or older, which included non-infected spouses as controls, found an increased risk of cognitive decline 1 year after hospital discharge. Retrospective studies of US electronic health records of individuals older than 65 years also indicated an association between COVID-19 and an increased risk of a diagnosis of dementia 6 months after infection with SARS-CoV-2;^{32,33} the effect was greater in patients with more severe manifestations of acute COVID-19. However, a longitudinal imaging study³⁴ of UK participants aged 51–81 years suggested that, even with milder illness, participants who had COVID-19 had, on average, higher cognitive decline and more marked changes in MRI scans of the brain than the control group. Immediate measures are necessary to identify and mitigate the causal mechanisms underlying these effects.

The disruptive effect of COVID-19 on the older population should not be underestimated, particularly during the first waves of the pandemic, at which time the routines and circumstances of older people underwent drastic changes. Lockdowns, other public health restrictions, and self-imposed restrictions might have reduced their social interactions after hospital discharge or resolution of their infection. Older people might also have lost spouses or other loved ones during the pandemic. Not all older people will have the resilience to adapt to adversity, and this could contribute to mental and physical decline.

Relationship between long COVID and persistent physical symptoms, functional somatic disorders, and chronic fatigue syndrome

Functional somatic disorder or persistent physical symptoms, previously known as medically unexplained symptoms, include post-viral syndromes. These syndromes can affect multiple organ systems, single systems, or can present with single symptoms.³⁵ Long COVID fits within this taxonomy, although scarce research data are currently available, especially for older adults. The aetiology of functional somatic disorder is hypothesised to comprise a variety of processes involving both the body (eg, the immune system, the autonomic nervous system, the hypothalamic–pituitary axis, and mitochondrial function) and cognition (eg, processing and perception of bodily signals, central sensitisation, and psychological adaptation).³⁵ An overlap between long COVID and chronic fatigue syndrome, and between long COVID and other functional somatic disorders, is evident, but the matter is still under-researched.³⁶ Fatigue and shortness of breath are common long COVID symptoms, particularly in older people,¹⁷ and are similar to the symptoms of chronic fatigue syndrome. A relatively uniform post-infective fatigue syndrome has previously been documented in a minority of patients for 6 months or more after infection with several different microorganisms, especially Epstein-Barr virus (glandular

fever), *Coxiella burnetii* (Q fever) and Ross River virus (epidemic polyarthritis), and is an established pathophysiological pathway to chronic fatigue syndrome.³⁷

Advocates for people with chronic fatigue syndrome are of the view that chronic fatigue syndrome is a permanent condition, from which few people recover.³⁶ Early evidence suggests that most people recover from long COVID, albeit slowly, although a substantial minority might continue to have symptoms, sometimes episodic, of energy loss, pain, and cognitive limitations after 30 months.³⁸

Controversy persists in the chronic fatigue syndrome community regarding the role of exercise in managing this condition, which can trigger a worsening of symptoms and cause so-called post-exertional malaise. In long COVID, however, a carefully managed increase in exercise appears to be beneficial. A study³⁹ of a supervised rehabilitation programme for long COVID, which combined progressive exercise and education, showed that patients had improvements in their symptoms after rehabilitation.³⁹ Another study⁴⁰ developed quality standards to manage long COVID in primary care. These quality standards included rehabilitation, self-management, and general advice, and this resulted in a reported improvement in symptoms.

The effect of vaccination and antiviral treatments on long COVID in older people

A large prospective case-controlled study⁴¹ of post-vaccination SARS-CoV-2 infection found that vaccination (compared with no vaccination) was associated with reduced odds of hospitalisation, reduced odds of having more than five symptoms in the first week of illness after the first or second dose, and reduced odds of long-duration (≥ 28 days) symptoms after the second dose. However, frailty was associated with an increased risk of post-vaccination (breakthrough) infection in older adults (≥ 60 years) after their first vaccine dose.⁴¹ Adverse determinants of health, such as living in highly deprived areas and having obesity, were also associated with an increased risk of post-vaccination infection in older adults.⁴¹ However, after two vaccine doses, the odds of having symptoms for 28 days or more after breakthrough infection were approximately halved, suggesting that the risk of long COVID is reduced by two doses of vaccination.

A synthesis of 15 observational studies⁴² has found that people who were fully vaccinated against SARS-CoV-2 were less likely to develop long COVID in the medium or long term than those who were unvaccinated, particularly for the symptoms of fatigue, headache, weakness in arms and legs, persistent muscle pain, hair loss, dizziness, shortness of breath, loss of sense of smell, interstitial lung disease, myalgia, and other pain. However, some people in the studies reported worsened symptoms after vaccination.⁴²

An Israeli cross-sectional study⁴³ has found that vaccination with at least two doses is associated with a

substantial decrease in reporting of the most common long COVID symptoms. This effect appears to occur mostly in older age groups (older than 60 years), suggesting that COVID-19 vaccination could have a protective effect against long COVID in older people.⁴³ Another study of US veterans has found that vaccinated people have a lower risk of long COVID after at least 30 days after infection than people who are unvaccinated.⁴⁴ Additionally, a retrospective cohort study⁴⁵ from South Korea showed that fully vaccinated individuals were significantly less likely to have an acute myocardial infarction or ischaemic stroke in the 120 days after a COVID-19 diagnosis.

Scarce evidence currently exists regarding the effect of antiviral treatment during acute COVID-19 on the risk of long COVID. Multivariate analysis from a prospective, single-centre Italian study⁴⁶ of patients hospitalised with COVID-19 (with a median age of 65 years) suggested that treatment with remdesivir during acute illness was associated with lower odds of developing long COVID than no treatment with antiviral medication.⁴⁶ Two case studies^{47,48} have suggested that treatment with nirmatrelvir or ritonavir after the acute infection stage might be associated with mitigation of persisting symptoms associated with COVID-19. However, more robust evidence is required to confirm this benefit.

Other management approaches

For those who had a severe SARS-CoV-2 infection, related factors such as hypoxia, protracted intensive care, immobilisation, and social isolation could result in cardiovascular and neurological complications.²⁸ Furthermore, a post-infective fatigue syndrome might be the pathophysiological pathway for long COVID in some cases. However, the mental and social effects of the COVID-19 pandemic itself should not be underestimated. The results of social deprivation could be profound and lead to cognitive and functional decline, especially for those living in aged care facilities. COVID-19 control measures need to be balanced with compassionate, person-centred care for older people, especially in long-term care settings.^{49,50}

Long COVID will probably pose extra challenges for the older population and for those who provide their care. UK National Institute for Health and Care Excellence guidelines⁵¹ published in 2020 (and updated in 2021) recommend the use of a multidisciplinary approach to guide rehabilitation, including physical, psychological, and psychiatric aspects of management, after any symptoms or factors that could affect a person's ability to start rehabilitation safely have been thoroughly investigated. Similarly, the focus in Dutch guidance⁵² for the management of long COVID is geriatric rehabilitation. The general aim of geriatric rehabilitation is to improve the complete health status and functional status (or both) of older patients, and to prevent and treat the physical, functional, and psychological impairments resulting from COVID-19.⁵²

Conclusion

Accumulated evidence indicates that the aetiology of long COVID is multifactorial, especially in older people. Long COVID can consist of a spectrum of health-related symptoms that present differently across individuals, and these symptoms can have different rates of onset. COVID-19 might lead to an increased health burden, both directly from specific long COVID-associated symptoms and from the exacerbation of pre-existing health issues.

In addition to its many associated symptoms, COVID-19 might also trigger or exacerbate existing chronic conditions, such as diabetes and cardiovascular disease. Symptoms of long COVID might be difficult to distinguish from those perceived to be due to ageing, particularly in older people with comorbidities and potential side-effects from polypharmacy.

COVID-19 vaccination can decrease the effects of long COVID, and ensuring that older people (especially those living in aged care facilities) remain up-to-date with their vaccinations is an important measure. Post-infection sequelae require early multidisciplinary assessment and management to mitigate the effects of COVID-19 on older people.

Older people, especially those living in long-term care facilities and aged care facilities within otherwise prosperous nations, are the most affected when it comes to the effects of COVID-19.⁵³ Further research focusing on long COVID in this vulnerable group is necessary. Long COVID must be considered in the differential diagnosis of symptoms that might otherwise be ascribed to frailty in older patients, so as to ensure that this population is not deprived of the benefits of multidisciplinary care that can improve their functioning and quality of life.

Contributors

VM conducted the initial literature review. All authors provided additional references and assisted in analysis. FG-S wrote the first draft of the document. All authors contributed to the writing and revision and approved the final version of this Personal View.

Declaration of interests

We declare no competing interests.

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