Outcomes of COVID-19 in the community

A prospective cohort study

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Background and objective
The literature indicates that patients who had previously had COVID-19 are reporting ongoing symptoms. The objective of this study was to examine ongoing symptoms, functional limitations and quality of life over time in a cohort of individuals who were deemed to have recovered.

Methods
This was a prospective observational study on biopsychosocial outcomes at enrolment and again one month later.

Results
In a cohort of 59 participants, ongoing symptoms were reported by 73% at 4.5 months (standard deviation = 1.4) post diagnosis, with 45% reporting difficulty with pre-illness activities of daily living. Of the 52 participants who completed the follow-up survey (mean 5.6 months post diagnosis), 42% reported ongoing symptoms, lower physical quality of life (12-Item Short Form Health Survey) and higher levels of anxiety, depression and stress (Depression, Anxiety and Stress Scale).

Discussion
Ongoing symptoms such as fatigue, pain and limb weakness as well as functional impairment post initial diagnosis were common. Improved understanding of this cohort can assist general practitioners in providing care.

COVID-19 is a viral infection that emerged from Wuhan, China, in December 2019. This disease has spread throughout the world (221 countries) and was declared a pandemic by the World Health Organization on 11 March 2020.[1,2] Globally, by 21 June 2021, there were 178,433,377 confirmed cases, including 3,864,702 deaths (https://covid19.who.int). Of these reported cases, 163,827,935 were deemed to have recovered by various public health authorities (www.worldometers.info/coronavirus). In Australia, there had been 30,331 cases with 910 deaths at 21 June 2021, with 27,021 of these cases classified as recovered. Despite this, there have been many reports of individuals with COVID-19 experiencing debilitating symptoms long after being cleared of the acute infection.[3] The term 'long COVID' has been used in the literature to describe the condition,[4] and further studies are emerging to investigate the effects of this condition on the human body.[5]

Various studies from other countries report ongoing morbidities of patients with COVID-19. These morbidities relate to severe pulmonary limitation,[6] hepatic impairment,[7] hemostatic changes[8] and neurological complications.[9] Carfi et al reported that in a cohort of 143 hospitalised patients who had recovered from COVID-19, 87.4% reported persistence of one symptom at a mean of 60.3 days (standard deviation [SD] = 13.6) after the onset of their first COVID-19 symptom.[10] Similarly, Huang et al reported that 76% of patients hospitalised with COVID-19 (n = 1655) were symptomatic at follow-up.[11] In a systematic literature review, Nasserie et al found that 72.5% of patients reported at least one symptom at 60 days or more after diagnosis, symptom onset or hospitalisation or at 30 days or more after recovery from acute illness or hospital discharge.[12]

The speed and ferocity of transmission of COVID-19 throughout the world has resulted in a scarcity of data on biopsychosocial and functional outcomes of survivors of COVID-19 in the community. An analysis of the clinical progress, ongoing morbidities, functional outcomes and demand on current services after a positive COVID-19 diagnosis would facilitate appropriate future resource allocation required to address these concerns and prevent their escalation before they put additional strain on the healthcare system.[13] Based on Communicable Diseases Network Australia (CDNA) guidelines (version 5.1),[14] an individual in the community who tested positive for COVID-19 is deemed to have recovered sufficiently to be discharged from virtual care under the following criteria: 1) 14 days after a positive polymerase chain reaction (PCR) test if asymptomatic, 2) if the patient has been afebrile for the preceding 72 hours with substantial improvement of respiratory symptoms or 3) 20 days after a positive PCR test even if still symptomatic. In April 2020, the criterion (version 2.7) was the patient being afebrile for three consecutive days in the preceding 10 days.

It is hypothesised that individuals with a positive COVID-19 diagnosis will have ongoing health issues and needs after being classified as 'recovered' under current guidelines. The aim of this study was to investigate the biopsychosocial status of a cohort of individuals who had been diagnosed with COVID-19 and deemed to have recovered by health authorities, and to describe any ongoing symptoms and functional and/or mental health outcomes on enrolment to the study and one month later.

Methods

Study design

This was a prospective observational study to investigate the longer-term health impact over a period of seven months on a cohort of individuals who had previously tested positive to COVID-19 in Australia. Participants were recruited via local public health units and media exposure. Interested participants then contacted the investigators of the study via email or telephone. This study was approved by the Joint University of Wollongong and Illawarra Shoalhaven Local Health District Health Medical Human Research Ethics Committee (2020/ETH01025). Informed written consent was obtained prior to the participants being enrolled into the study.

Participants

All individuals with a positive diagnosis of COVID-19 who had the capacity to respond to questions either online or over the telephone were eligible for inclusion in the study. Participants were also required to be older than 18 years of age and able to give consent. Participants in this study had been diagnosed with the original Wuhan strain and the Alpha (UK) variant of COVID-19 from March 2020.

Data collection procedures

Participants were asked to complete an online enrolment survey with questions on demographic information (age, sex, level of education, employment status), current medical conditions, current prescribed medications or health supplements, smoking status, date of positive COVID-19 test result, symptoms experienced during acute COVID-19 illness, current COVID-19 symptoms, medical treatments for new conditions since their positive COVID-19 test result, ability to complete daily activities and any other comments regarding their experience with COVID-19.

At one month after enrolment into the study, participants were asked to complete an additional online survey with questions regarding current symptoms of COVID-19, symptoms they experienced during acute illness, additional positive COVID-19 test results, new symptoms, new medications, new medical complications, 12-Item Short Form Health Survey (SF-12),[15] Depression, Anxiety and Stress Scale (DASS),[16,17] current self-isolation requirements, the effect of isolation on their mental health, difficulty performing activities they were able to complete prior to COVID-19 and any additional information regarding their experience with COVID-19. The surveys included multiple-choice questions (with 'other' options to allow participants to write additional information), rating scales and text boxes for open comments.

The SF-12 is a 12-item self-report measure of physical and mental health status. Higher scores indicate better physical or mental health. The items were recoded, scored and compared with Australian normative data.[15] The DASS-21 is a 21-item self-report measure of symptoms of depression (eg sadness or worthlessness), anxiety (eg trembling or faintness) and stress (eg difficulty relaxing, tension or irritability).[18] Higher scores indicate higher anxiety, depression or stress. The scores of the DASS-21 were scored and compared with Australian normative data.[19]

Statistical analysis

Continuous variables were presented as mean (SD) or median (range), while categorical variables were presented as counts and percentages. The statistics were reported on the basis of the number of answers to each survey question and without imputing missing data. The statistical analysis was completed using R 3.6.[20] Text data were analysed using inductive content analysis, which allowed grouping responses into fewer and meaningful categories.

Results

Enrolment survey

On 21 June 2021, a total of 59 participants, of whom 51% were men, had completed the enrolment survey. The enrolment survey was completed an average of 4.5 months (SD = 1.4) after receiving a positive COVID-19 test result. Approximately 50% of participants had returned to work, 42% were retired and 7% had not been able to return to work. All participants had recovered from the acute phase of COVID-19 and were living in the community at the time of the study (Table 1).

Of the 59 participants who answered the enrolment survey, 46% had one or more comorbidities other than COVID-19 including cardiovascular illness (20%), cancer (12%) mental illness (9%), diabetes (7%) and stroke (5%). In addition, 76% of participants were taking medications, resulting in a total of 140 medications that were grouped into the following categories: 11% cholesterol-lowering medications, 8% angiotensin converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs), 8% antidepressants, 7% cardiovascular agents, 7% anticoagulants, 4% pain medications, 2% respiratory medications and 1% immunosuppressants. An additional 20% of the medications were supplements and 30% were other types of medications. Thirty-two per cent of participants reported seeking medical treatment for physical conditions that were not present prior to their COVID-19 diagnosis, while 14% of participants had sought treatment for mental health conditions.

Currently experienced symptoms were reported by 73% of the participants, with a median number of two symptoms per participant (range = 0–20 symptoms). The most common symptoms were fatigue (59%), musculoskeletal pain (31%), arm or leg weakness (22%), loss of appetite (22%) and shortness of breath (22%). Gastrointestinal symptoms such as nausea and vomiting (7%) and diarrhoea (5%) were reported by a small number of patients (Table 2). Participants (45%) also reported difficulty carrying out activities that they were able to do before having COVID-19. Of these participants,

Table 1. Characteristics of participants at enrolment and one-month follow-up

Characteristic	Overall percentage distribution		Percentage yes: COVID-19 symptoms		Percentage yes: Difficulty doing pre-COVID-19 activities	
	Enrolment (n = 59)	One-month follow-up (n = 52)	Enrolment (n = 52)*	One-month follow-up (n = 52)	Enrolment (n = 52)*	One-month follow-up (n = 52)
Age in years						
25–49	23%	22%	24%	18%	29%	29%
50–70	53%	52%	49%	50%	43%	35%
≥71	25%	26%	27%	32%	29%	35%
Sex						
Male	51%	50%	50%	50%	50%	59%
Female	49%	50%	50%	50%	50%	41%
Highest education						
Secondary	24%	25%	29%	27%	36%	41%
Tertiary	76%	75%	71%	73%	64%	59%
Employment status						
Employed	56%	54%	45%	50%	45%	53%
Retired	42%	44%	53%	50%	55%	47%
Unemployed/Not stated	2%	2%	3%	0%	0%	0%
Taking medication						
Yes	76%	76%	78%	90%	86%	94%
No	24%	24%	22%	10%	14%	6%
Other self-reported comorbidities						
0	54%	56%	45%	36%	45%	35%
1	29%	29%	34%	32%	27%	29%
≥2	17%	15%	21%	32%	27%	35%
Weeks since COVID-19 diagnosis						
<12 weeks	7%	6%	8%	5%	9%	6%
≥12 weeks	93%	94%	92%	95%	91%	94%
Ever hospitalised because of COVID-19						
Yes	–	12%	17%	29%	25%	35%
No	–	88%	83%	71%	75%	65%
Total	100%	100%	73%	42%	43%	35%

**Includes participants who completed both enrolment and one-month follow-up*

65% attributed this difficulty to lack of energy, 50% to shortness of breath, 39% to arm or leg weakness, 31% to lack of motivation, 15% to chest pain, 15% to dizziness and 12% to other types of pain. Males reported more symptoms (median = 4) than females (median = 1), as indicated by the Wilcoxon test ($P = 0.0344$; Figure 1). A Kruskal–Wallis test showed no significant association between age group and number of symptoms ($P = 0.9419$; Figure 1).

The enrolment survey included an open-ended question that asked participants to further comment on their experience of COVID-19. Forty-nine participants answered this question, and their comments were grouped into categories on the basis of identified similarities. Of these participants, 59% reported having experienced a variety of symptoms while infected with COVID-19, 16% reported mild symptoms and 14% experienced fatigue post infection.

Examples of what participants reported about their experience of COVID-19 are shown in Table 3.

One-month follow-up survey

The follow-up survey was completed by 52 participants on an average of 5.6 months (SD = 1.4) after their positive COVID-19 test result, with seven participants lost to follow-up (Table 2). Of the participants who responded, 42% had one or more current symptoms, and the number of symptoms per patient ranged from 0 to 8 (median = 0). Forty-seven per cent reported having experienced unusual symptoms since their diagnosis of COVID-19 such as hair loss, blurred vision, mental fogginess, forgetfulness, tingling in arms and feet, numbness in fingers, foot cramps and constipation.

Table 2. Percentage distribution of COVID-19 symptoms reported at enrolment and one-month follow-up

	All enrolled participants	Participants who completed both enrolment and one-month follow-up (n = 52)	
Current symptoms	Enrolment (n = 59)	Enrolment (n = 52)	One-month follow-up (n = 52)
Number of symptoms			
0	27%	27%	58%
1–2	29%	31%	23%
3–4	17%	19%	10%
≥5	27%	23%	10%
Type of symptom			
Fatigue (feeling tired)	59%	60%	38%
Musculoskeletal (muscle/joint) pain	31%	29%	12%
Arm or leg weakness	22%	19%	8%
Loss of appetite	22%	17%	2%
Shortness of breath	22%	15%	15%
Malaise (general feeling of discomfort)	17%	15%	2%
Loss of sense of smell	17%	13%	10%
Cough	17%	12%	4%
Dizziness on standing	15%	10%	6%
Headache	14%	10%	4%
Rhinorrhoea (runny nose)	14%	12%	4%
Sore throat	12%	12%	4%
Chest pain	12%	8%	4%
New onset of pain	8%	8%	4%
Tendency to bruise easily	8%	8%	2%
Fever and chills	8%	6%	0%
Nausea and vomiting	7%	2%	0%
Diarrhoea	5%	6%	0%
Conjunctivitis (sore eyes)	3%	2%	2%
Pneumonia	2%	0%	0%

Six participants (12%) were admitted to hospital while sick with COVID-19, with length of stay ranging from one to 86 days, and three were treated in an intensive care unit. Ten per cent of participants had been told by their doctors that they had one or more complications due to COVID-19. Three participants reported cardiac complication plus another complication, namely epilepsy (n = 1), gastrointestinal complication (n = 1) and kidney disease (n = 1); another participant reported loss of vision and stroke; and one more participant reported having blood clots. Fourteen participants (28%) were prescribed medication after their diagnosis of COVID-19. Medications included antidepressants (n = 3), antihypertensives (n = 4), anticoagulants (n = 2), neuropathic pain medication (n = 1), anti-epileptic medication (n = 1) and appetite suppressants (n = 1).

The scores of the SF-12 and DASS-21 are shown in Table 4. When compared with the Australian normative values, study participants had considerably lower scores on the physical component scale of the SF-12, indicating pain or role limitations due to physical problems. Their scores on the mental health scale, however, were above the Australian average values. Participants who at enrolment reported one or more comorbidities (n = 23) had lower scores on the physical component scale (mean = 29.7) than participants with no comorbidity (mean = 36.1; $P = 0.0157$).

Scores of the DASS-21 showed that study participants had slightly more symptoms of depression, anxiety and stress than the Australian population. Stress scores, such as irritability and tension, were higher than Australian average values. Participants who at enrolment reported one or more comorbidities had higher anxiety scores (median = 2) than participants with no other comorbidity (median = 1; $P = 0.008$). Women had higher depression scores (median = 3) than men (median = 1; $P = 0.032$).

Comparison of baseline and one-month follow-up data

Overall, the percentage of participants with symptoms at follow-up was smaller than the percentage of symptomatic

participants at enrolment (Table 2). An exception was shortness of breath, which remained the same over time. Fatigue was the most common symptom both at enrolment (60%) and at one-month follow-up (39%). In addition, 31% of participants reported difficulties performing activities as a result of COVID-19 both at enrolment and at one-month follow-up.

Discussion

This study investigated the ongoing effects of COVID-19 on a convenience sample of 'recovered' participants who were diagnosed with COVID-19 from March 2020. Seventy-three per cent of participants reported that they were still experiencing symptoms 4.5 months post diagnosis. This is comparable to the prevalence of 72.5% reported by Nasserie et al,[12] 76% by Huang et al[11] and 87.5% by Carfi et al[10] in hospitalised patients.

The most common symptoms in this cohort were fatigue, musculoskeletal pain, limb weakness, loss of appetite and shortness of breath. This is in comparison to fatigue, dyspnoea, joint pain and chest pain reported by Carfi et al,[10] and fatigue, muscle weakness, sleep difficulties and depression/anxiety reported by Huang et al.[11]

At one-month follow-up (5.6 months after their COVID-19 diagnosis), 42% of respondents continued to report health issues from COVID-19.

Some symptoms reported in this study may be permanent impairments, such as visual loss, peripheral neuropathy, susceptibility to epileptic seizures, liver cyst and pain. It was found that symptoms such as constipation, forgetfulness and loss of taste only became evident to the individuals concerned after recovery from their initial illness. In addition, 45% of participants were unable to perform activities that they performed prior to COVID-19. This limitation of activities persisted in the majority of these participants at one-month follow-up.

Carfi et al[10] found that 44.1% of patients hospitalised with COVID-19 reported a 'worsened' quality of life (>10 points reduction in the EuroQol visual analogue scale).[10] Gonzalez et al[21] reported a median of 45.9 points (interquartile range [IQR]: 36.1–54.4) for physical health and 55.5 points (IQR: 40.6–58.0) for mental health on SF-12. Similarly, Arnold et al[22] and Chen et al[23] reported SF-36 scores of 40.2 and 55.9 for physical health and 44.8 and 48.9 for mental health, respectively. This study found a considerable reduction in the physical component of SF-12 (33.5) but no reduction in the mental component of the SF-12 (59.3) when compared with Australian population normative values of 50.5 and 51, respectively. The physical component score of the present study is also lower than the average physical component score of 36.0 that has been found among Australians who take medications for physical and mental ailments[15] other than COVID-19. This suggests that COVID-19 can have a strong negative effect on the physical functioning of non-clinical populations.

The DASS-21 revealed increased depression, anxiety and stress in participants in this study. This is similar to the findings of Huang et al, who also reported anxiety/depression in 23% of their study cohort using the EuroQol 5 Dimension 5 Level (EQ-5D-5L) assessment.[11] Given that the general population may experience negative emotions during the COVID-19 pandemic,[24] further research is required to better understand the relationship between psychological distress and COVID-19 among non-clinical populations.

It was reported by Richardson et al that hospital readmission rates and discharge to nursing home are progressively higher with increasing age.[25] The present study found no significant association between age group and number of symptoms. Mortality rates have been reported in the literature to be higher for males when compared with females in every age group older than 20 years.[25] This study found that males reported more symptoms than females.

Richardson et al identified hypertension, obesity and diabetes as the most common comorbidities.[25] It is not clear if pre-existing health issues increase susceptibility to COVID-19 and complications. However, Shang et al reported that 80% of mortalities and 50% of participants classified as the 'severe/critical survivors' group had 'concomitant diseases' such as hypertension, diabetes, stroke, renal impairment and hepatic dysfunction, compared with only 29% in the 'common survivors' group.[26] In the present study, 46% of participants had pre-existing medical conditions, with 76% taking some form of regular medication or supplements, which included 8% taking

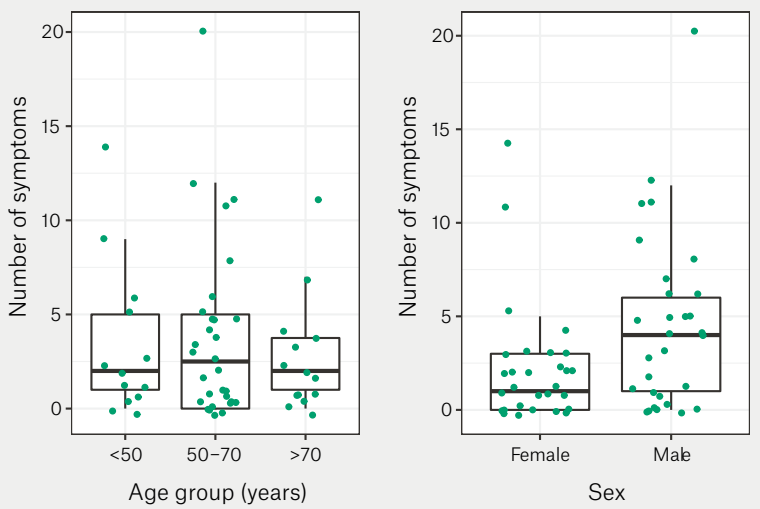

Figure 1. Distribution of currently experienced symptoms by age and sex

ACE inhibitors or ARBs. Participants with pre-existing comorbidities reported a higher anxiety level at follow-up, as measured with the DASS-21. Based on participant comments, COVID-19 appeared to exacerbate pre-existing comorbidities such as hypertension, diabetes and leukaemia.

The findings from this study appear to support the hypothesis that individuals with a positive COVID-19 diagnosis will have ongoing health issues and needs after being classified as 'recovered' under current guidelines.

One of the limitations of this study is that the study was designed at the beginning of the COVID-19 pandemic when the presentation, symptomatology, natural progression and longer-term complications of COVID-19 were largely unknown. The study was structured as a contact-free study to enable implementation during the COVID-19 lockdown. Further studies using direct interviewing techniques or individual medical appointments may be beneficial. Another limitation is the small sample size, which is a reflection of the relatively low number of COVID-19 cases in Australia when compared with the rest of the world.

There is a potential for selection bias in that people with more severe symptoms may be more likely to participate. However, the lack of need for hospitalisation and ongoing medical care in this study would suggest otherwise. The proportion of hospitalisation in this cohort was 12%, compared with the national figure that ranged from 3.18% in June 2020 to 16.33% in September 2020.[27] From October 2020, the rate of hospitalisation is no longer an accurate indication of severity, as Queensland and the Northern Territory started to hospitalise all acute cases irrespective of severity.[27]

A major strength of this study is that it was based on a community-recruited cohort rather than predominately hospitalised patients who have participated other studies. It is interesting to note that the number of non-hospitalised individuals with COVID-19 with ongoing symptoms is comparable with that of patients hospitalised with COVID-19 from other research.[10–12] Being a prospective longitudinal study, it was possible to follow the progress of participants through their recovery journeys. This study is ongoing, with further data from three months' and six months' follow-up to be released when available. The study is currently open to individuals with the Delta variant.

Table 3. Content analysis of comments given by participants (n = 49) who answered enrolment survey question about the experience of COVID-19

Category	%	Example comments
Experienced varied symptoms ranging from moderate to severe	59	'Pretty horrible, never been that sick … Constipation, loss of sense of smell, episode of confusion in acute stages, mild cognitive impairment, lethargy …'
		'I thought I could not survive the pain hitting my left side and right side at least 10 times on each side. Then on my ears left and right like inserting a long pin through my head.'
		'I experienced strange dreams that went away after the fever went away. Short-term memory, such as remembering names of people, was poor for about four weeks. Has now returned to normal. Had a mild cough that took about eight weeks to go away.'
Experienced mild symptoms	16	'I would have not known that I had COVID-19 … The only light symptom I had was a runny nose and a very mild sore throat. At present, my health is the same as before the COVID-19.'
		'I had a runny nose and a slight cough similar to normal flu-like symptoms which only lasted a few days.'
		'Fortunately I didn't get it as bad as other people. Did lose taste and smell but they have now returned.'
Persistent fatigue post COVID-19	14	'I consider that I was fit and active … I feel at this stage I won't get back to how I felt before … I feel fatigued and lack motivation.'
		'The fatigue has persisted. Although I returned to work after testing positive, I could not safely complete my duties due to fatigue and I had to take more sick leave.'
		'I consider I was more active and motivated before I contracted the virus … I tire easily and sleep longer.'
Other	10	

Conclusion

Many survivors of COVID-19 living in the community report ongoing symptoms 4.5 months and 5.6 months post initial diagnosis. The aim of this study was to fill the gap in understanding of longer-term complications and health issues from COVID-19. This study highlights the need for ongoing care and support for this cohort and can assist healthcare workers to care for patients who have 'recovered' from COVID-19 in the community. Improved understanding of the health needs of patients with 'long COVID' will become more crucial as cases surge with emergence of new variants and mortality decreases with increased rates of vaccination.

Implications for general practice

- After a COVID-19 diagnosis, 73% and 42% of individuals in the community reported ongoing symptoms at 4.5 months and 5.6 months, respectively.
- The most common reported symptoms were fatigue, musculoskeletal pain, limb weakness, loss of appetite and shortness of breath.
- Individuals reported a reduced quality of life (physical component) and increased depression, anxiety and stress post COVID-19.

Table 4. 12-Item Short Form Health Survey (SF-12) and Depression, Anxiety and Stress Scale 21 (DASS-21) scores of participants who completed both enrolment and one-month follow-up survey (n = 52)

Characteristic	Study population	Australian normative population*
SF-12, mean		
Physical component score	33.3	50.5
Mental component score	59.3	51.0
DASS-21, mean (standard deviation)		
Depression	2.72 (2.62)	2.21 (3.60)
Anxiety	1.67 (1.86)	1.48 (2.60)
Stress	4.18 (3.93)	3.79 (4.10)

**SF-12 Australian population as reported by Tucker et al (2010);[15] DASS-21 Australian population 25–90 years of age as reported by Crawford et al (2011)[19]*

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