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COVID-19 infection associated with poorer mental health in a representative population sample

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ABSTRACT

Objective: There is limited evidence of the direct effects of COVID-19 infection on mental health, and whether these are influenced by vaccination or physical health symptoms. We aimed to investigate the relationships of COVID-19 infection, current symptom presentation, and vaccination status with mental health symptoms in adults.

Study design and setting: A cross-sectional sample of the Australian adult population that was representative by age, gender, and location was recruited through market research panels ($N = 1407$, 51.3% female, mean age 47.9 years). Hierarchical regression analyses were used to examine the associations of COVID-19 infection history and current COVID-19 symptoms with symptoms of depression (Patient Health Questionnaire-9), generalized anxiety (Generalized Anxiety Disorder-7) and social anxiety (Mini-Social Phobia Inventory).

Results: COVID-19 infection was associated with significantly higher depression and anxiety symptoms, but only in those who were not fully vaccinated. Current experience of COVID-related symptoms was associated with significantly higher depression and anxiety symptoms, and attenuated the direct effect of infection on mental health outcomes to non-significance.

Conclusion: COVID-19 infection may be associated with increased mental health symptoms. However, the effects of infection on mental health were primarily evident in those who were not fully vaccinated and were explained by greater physical health problems associated with COVID-19 infection. The findings reinforce the efficacy of vaccination for reducing physical and mental health symptoms following infection.

The coronavirus disease (COVID-19) pandemic has led to concerns of rising mental ill health in the population [1–4]. Although preliminary data indicated an increase in the population prevalence of depression and anxiety [1], longitudinal data suggest much of this increase is likely to be transient [5,6]. Nevertheless, public health protections such as stay-at-home orders may have increased social isolation and loneliness [7–10] and impaired the employment and financial security of many in the community [11–13]. There is longitudinal evidence these indirect impacts of the pandemic have had negative effects on mental health for many people [5,6,11].

However, there is less evidence regarding the direct effects of COVID-19 infection on mental health. Existing studies have indicated

that people who have experienced a COVID-19 infection have higher rates of mental ill health than the general population [2,14], particularly in the six months following infection [15]. COVID-19 is a multi-organ disease with clear effects on the brain [16], although the specific mechanisms that may precipitate neuropsychiatric problems following infection remain unclear [17,18]. It has been proposed that COVID-19 may have direct effects on mental health through a range of processes such as infection of the nervous system, ongoing viral reservoirs, or persistent inflammation, which may directly lead to increased symptoms of depression and anxiety, along with other sequelae such as psychotic symptoms [18–21]. Furthermore, the possible consequences of the COVID-19 illness, such as the trauma associated with the experience of

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major illness and invasive medical procedures, may also contribute to ongoing symptoms of anxiety, depression, and post-traumatic stress disorder [22]. Indeed, the severity of physical symptoms in COVID-19 shows a strong relationship with individual's severity of mental health symptoms [23].

Long-COVID, also termed Post-Acute Sequelae of COVID (PASC) [24], is characterised as a condition occurring in those with history of SARS-CoV-2 infection who experience ongoing symptoms persisting at least 3 months beyond the initial infection [25]. Long-COVID is associated with a range of physical dysfunctions reflecting the multi-systemic nature of COVID-19 infections [16]. Specifically, persistent COVID-related symptoms may affect the cardiopulmonary (e.g., fatigue, shortness of breath, palpitations), nervous (e.g., memory problems/inability to concentrate or "brain fog"), naso-opharyngeal (e.g., loss of taste/smell, cough), gastrointestinal (e.g., nausea, diarrhoea), and musculoskeletal (e.g., muscle and joint pain) systems [26,27]. Some of these symptoms are also characteristic of depression or anxiety, including fatigue, reduced concentration, and sleep disturbance. Therefore, long-COVID may trigger or exacerbate mental ill health [14,18]. Initial evidence suggests mental health symptoms are higher at two years following COVID-19 infection in people who have persistent COVID-19 symptoms than those who do not [15].

A shortcoming of the research on the mental health effects of COVID-19 infection is that the majority of studies examining this relationship have used clinical rather than population samples, with few studies incorporating uninfected controls [28], unlike research on the physical health sequelae of COVID-19 [29]. There is evidence that people with mental illness, particularly severe mental illness, are at significantly increased risk of COVID-19 infection and COVID-related death [30]. Thus, elevated symptoms among people who have had a COVID-19 infection may be related to the profile of the infected population, rather than a result of the infection itself. Population-based studies that incorporate representative samples may therefore be beneficial in assessing whether greater mental health symptoms can be attributed to the infection or extraneous factors that are associated with infection.

The role of vaccinations on mental health outcomes has also received limited attention. There is evidence that vaccination reduces the prevalence and duration of COVID-19 symptoms [31,32], with benefits increasing with more doses [33], which may therefore reduce the fatigue and other somatic symptoms that may influence mental health. Vaccination also reduces rates of serious illness [32,34,35], which may lead to reduced trauma responses and related mental health problems [34,36]. However, the effects of vaccination on mental health may be complicated by interactions between mental health and vaccine efficacy, with poorer vaccine response among people with mental illness [37]. Given the benefits of vaccination for health outcomes, it may be important to also quantify how much vaccination protects against poor mental health outcomes among people who have had a COVID-19 infection.

The current study aimed to examine the association between COVID-19 infection and mental health outcomes, including symptoms of depression, generalized anxiety, and social anxiety, in a cross-sectional cohort representative sample of the Australian adult population on the basis of age, gender and location (State/Territory of residence). We tested whether vaccine dosage was associated with reduced symptoms among those who reported an infection. We also tested whether greater mental health symptoms were independent of physical health symptoms that are characteristic of COVID-19, adjusting for long-COVID diagnosis. We hypothesized that mental health symptoms would be elevated among people who reported a COVID-19 infection, although this association would be mitigated by full vaccination and partially explained by presence of COVID-related physical symptoms.

1. Method

1.1. Participants and procedure

A representative sample of Australian adults aged 18 years and over were recruited in May 2022 to participate in the current study via the online market research panel Qualtrics Research Services. Quota sampling was used to obtain a sample that was representative on the basis of age group, gender, and State/Territory of residence. Participants were emailed an invitation to complete the online survey via Qualtrics. From the quota sampling, $n = 1407$ survey completers were recruited to enable detection of small effects associated with mental health outcomes. Written informed consent was obtained online from all participants prior to participation in the study, which was approved by The Australian National University Human Research Ethics Committee (protocol 2020/152).

1.2. Measures

Demographic variables included gender (Male/Female/Other/Prefer not to say), age (in years), education (measured in 10 common education attainment categories converted into years), country of birth (Australia/Other countries), and language spoken at home (only English/other language). These demographic factors have been shown to be associated with mental health previously [6,11]. We also asked participants to report if they had previously been diagnosed with a range of common mental health disorders by a medical professional in their lifetime (anxiety, depression, bipolar disorder, schizophrenia, post-traumatic stress disorder, autism spectrum disorder, alcohol or substance use disorder, eating disorder, other).

Depression symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9; [38]), which consists of nine items assessing symptoms of depression based on the past two weeks, with high criterion validity for depression diagnosis. *Anxiety symptoms* were measured by the Generalized Anxiety Disorder-7 (GAD-7; [39]) that contains seven anxiety symptoms assessed based on the past two weeks. For both the PHQ-9 and GAD-7, participants were asked to evaluate the frequency of experiencing each of the symptoms over the last two weeks on a response scale ranging from not at all (0) to nearly every day (3). Higher total scale scores on the PHQ-9 (Cronbach's $\alpha = 0.93$) and GAD-7 ($\alpha = 0.95$) reflect higher levels of depression and anxiety respectively. Scores ≥ 10 for the PHQ-9 and GAD-7 are indicative of possible clinical caseness. *Social anxiety* was measured by the Mini-Social Phobia Inventory (MINI-SPIN; [40]). The MINI-SPIN has three items that describe social phobia symptoms and participants are asked to evaluate their experience in the past week on a 5-point scale ranging from not at all (1) to extremely (5). Higher total scale scores are indicative of higher levels of social phobia ($\alpha = 0.90$). Scores ≥ 6 on the Mini-SPIN are indicative of possible clinical caseness.

COVID-19 infection was based on a series of questions asking respondents whether they ever had a diagnosed COVID-19 infection (based on either polymerase chain reaction or rapid antigen test), and if so, how many vaccinations they had at the time of infection (0, 1, 2, 3 or more), with a minimum of two doses considered fully vaccinated in Australia at the time of this study. This information was collapsed into a single variable with three categories: no known infection, infection after 0–1 vaccinations, and infection after 2 or more vaccinations. Further breakdown was not appropriate due to small cell sizes.

COVID-related symptoms were assessed using a series of items capturing eight core symptoms of COVID-19, reflecting the most common and persistent symptoms [29]: fatigue, muscle aches, dizziness, difficulties concentrating, breathlessness, persistent cough, and loss of smell or taste. Each was rated on a 5-point scale ranging from never (0) to always (4). A total score reflecting the severity of COVID-related symptoms was calculated as the sum of item responses, ranging from 0 to 32, with high internal consistency (Cronbach $\alpha = 0.89$).

Presence of Long-COVID diagnosis was based on a single item, “Are you currently, or have you ever been, diagnosed by an appropriate clinician with any of the following medical conditions?”, with participants responding to a list of 21 medical conditions including Long-COVID.

1.3. Analysis

Participant characteristics were summarised based on COVID-19 infection and vaccination status. For categorical and continuous characteristics, χ^2/F tests respectively were used to assess differential associations with the three COVID-19 infection groups (no infection, infection with 0–1 vaccinations, infection with 2+ vaccinations). Linear regression models were estimated to examine the association of COVID-19 infection with the three mental health outcomes, controlling for gender, age, and lifetime mental health diagnosis. Additional potential confounders that were measured in the study, including education, employment, country of birth and language, had no significant impact on the three models so were excluded for parsimony. A subsequent model added the effects of long-COVID diagnosis and COVID-related symptom severity to adjust for the role of physical comorbidities. The Type I error rate was set at 0.01 for all analyses to account for multiple comparisons and the large sample size. All analyses were conducted in SPSS v28 (IBM Corp, Chicago IL USA).

2. Results

Overall, 51.3% of participants were women ($n = 722$) and the mean age was 47.9 ($SD = 17.6$) years, with 378 (27%) reporting a previous COVID-19 infection and 81 (5.8%) reporting a diagnosis of long-COVID. All included participants ($n = 1407$) had complete data. The characteristics of the sample across the three COVID-19 infection groups are shown in Table 1. The two groups with COVID-19 infection were younger, had greater education and a greater proportion of life-time mental health diagnosis compared to the group without COVID-19 infection. The proportion of native English speakers was highest in the group that had COVID-19 with 0–1 vaccines. All physical symptoms associated with long-COVID were more prevalent in the groups that

experienced COVID-19 infection, with highest levels of dizziness, difficulties concentrating, breathlessness, persistent cough, and loss of smell or taste observed in the group that had COVID-19 infection with 0–1 vaccinations. For most participants, mental health indices were in the healthy range below clinical cutoffs. However, the bivariate associations suggested symptoms were higher in the COVID-19 infected groups, particularly those with 0–1 vaccinations.

The regression models on depression, generalized anxiety, and social anxiety symptoms are presented in Tables 2–4, respectively. All three models showed highly consistent relationships with the exposures of interest, which may reflect the strong correlations between the three outcomes (0.89 for PHQ-9 and GAD-7, 0.70 for PHQ-9 and Mini-SPIN and 0.69 for GAD-7 and Mini-SPIN). Specifically, people who had experienced COVID-19 infection with 0–1 vaccinations had higher depression, anxiety, and social anxiety symptoms than those with no known infection. These associations remained significant after adjusting for age, gender, or existing mental health diagnosis. However, after including self-reported long-COVID diagnosis and COVID-related symptom severity scores in the models, the effects of COVID-19 on mental health outcomes were attenuated to non-significance. When age and gender were omitted from the final models, these outcomes remained consistent.

Other significant associations in the models indicated that women, younger adults, and those with a lifetime mental health diagnosis had significantly higher symptom severity (although the effect of gender on generalized anxiety was non-significant in Model 2). In addition, although long-COVID diagnosis had no significant relationship with mental health, greater severity of COVID-related physical symptoms was significantly associated with higher severity of depression, generalized anxiety, and social anxiety symptoms.

3. Discussion

In an Australian adult sample that was representative of the general population based on age group, gender and location, mental health symptoms were significantly more severe among people who had been infected with COVID-19. Symptom scores were highest among those who had experienced a COVID-19 infection before being fully

Table 1

Descriptive characteristics for the sample based on presence/absence of COVID-19 infection and vaccination status ($N = 1407$).

	No known COVID-19 infection ($n = 1029$)		COVID-19 infection with 0–1 vaccinations ($n = 146$)		COVID-19 infection with 2+ vaccinations ($n = 232$)		χ^2 / F	p
	n (%) or M (SD)		n (%) or M (SD)		n (%) or M (SD)			
Gender							8.11	0.088
Women	512 (49.8%)		74 (50.7%)		136 (58.6%)			
Men	514 (50.0%)		71 (48.6%)		94 (40.5%)			
Non-binary/Unspecified	3 (0.3%)		1 (0.7%)		2 (0.9%)			
Age in years (M/SD)	51.33 (17.35)		37.05 (12.99)		39.63 (15.68)		81.10	<0.001
Years of education (M/SD)	14.14 (2.06)		14.62 (1.91)		14.63 (1.80)		7.99	<0.001
Born in Australia	791 (76.9%)		115 (78.8%)		196 (84.5%)		6.48	0.039
Only English spoken at home	901 (87.6%)		103 (70.5%)		198 (85.3%)		30.24	<0.001
Lifetime mental health diagnosis	316 (30.7%)		64 (43.8%)		90 (38.8%)		13.53	0.001
Long-COVID diagnosis	0 (0.0%)		39 (26.7%)		40 (17.2%)		233.25	<0.001
COVID-related symptom score (M/SD)	7.23 (6.42)		12.21 (7.52)		10.16 (7.26)		47.15	<0.001
Fatigue	544 (52.9%)		98 (67.1%)		157 (67.7%)		24.00	<0.001
Muscle aches	498 (48.4%)		86 (58.9%)		135 (58.2%)		11.24	0.004
Dizziness	252 (24.5%)		70 (47.9%)		91 (39.2%)		47.66	<0.001
Difficulties concentrating	345 (33.5%)		84 (57.5%)		112 (48.3%)		43.24	<0.001
Breathlessness	241 (23.4%)		71 (48.6%)		74 (31.9%)		43.59	<0.001
Persistent cough	161 (15.6%)		71 (48.6%)		69 (29.7%)		94.44	<0.001
Forgetfulness	307 (29.8%)		71 (48.6%)		98 (42.2%)		29.11	<0.001
Loss of smell or taste	73 (7.1%)		48 (32.9%)		44 (19.0%)		96.18	<0.001
PHQ-9 depression score (M/SD)	6.13 (6.80)		10.44 (6.86)		8.43 (7.27)		31.41	<0.001
GAD-7 anxiety score (M/SD)	4.60 (5.78)		8.58 (5.92)		6.72 (6.58)		36.01	<0.001
Mini-SPIN social anxiety score (M/SD)	2.94 (3.54)		5.21 (3.63)		4.04 (3.85)		30.32	<0.001

Note: **bold** figures indicate $p < 0.01$. COVID: coronavirus disease; PHQ-9: Patient Health Questionnaire-9; GAD-7: Generalized Anxiety Disorder-7; Mini-SPIN: Mini Social Phobia Inventory

Table 2
Linear regression models of depression symptoms (N = 1407).

	Model 1 (excluding COVID-19 symptoms)			Model 2 (including COVID-19 symptoms)		
	B	SE	p	B	SE	p
Intercept	7.353	0.636	<0.001	2.684	0.493	<0.001
Gender						
Women	1.496	0.334	<0.001	0.870	0.250	<0.001
Non-binary/Unspecified	-0.646	2.471	0.794	-1.474	1.840	0.423
Men (reference)	0.000			0.000		
COVID-19 infection status						
Infected with 0–1 vaccinations	2.505	0.549	<0.001	-0.082	0.435	0.851
Infected with 2+ vaccinations	0.853	0.450	0.058	-0.526	0.348	0.131
No known infection (reference)	0.000			0.000		
Mental health diagnosis (yes vs no)	5.763	0.348	<0.001	2.267	0.280	<0.001
Age in years	-0.073	0.010	<0.001	-0.047	0.008	<0.001
Long-COVID diagnosis (yes vs no)				0.556	0.575	0.334
COVID-related symptom score				0.656	0.020	<0.001

Notes: depression symptoms were assessed using the Patient Health Questionnaire-9, ranging 0–27; COVID-related symptoms were assessed based on reported frequency of fatigue, muscle aches, dizziness, difficulties concentrating, breathlessness, persistent cough, forgetfulness, loss of smell or taste; categorical variables are dummy coded; bold values represent $p < .01$.

Table 3
Linear regression models of generalized anxiety symptoms (N = 1407).

	Model 1 (excluding COVID-19 symptoms)			Model 2 (including COVID-19 symptoms)		
	B	SE	p	B	SE	p
Intercept	6.247	0.545	<0.001	2.589	0.451	<0.001
Gender						
Women	1.002	0.287	<0.001	0.502	0.229	0.028
Non-binary/Unspecified	0.347	2.120	0.870	-0.344	1.684	0.838
Men (reference)	0.000			0.000		
COVID-19 infection status						
Infected with 0–1 vaccinations	2.292	0.471	<0.001	0.329	0.398	0.409
Infected with 2+ vaccinations	0.791	0.386	0.041	-0.246	0.318	0.440
No known infection (reference)	0.000			0.000		
Mental health diagnosis (yes vs no)	4.967	0.299	<0.001	2.242	0.256	<0.001
Age in years	-0.072	0.009	<0.001	-0.052	0.007	<0.001
Long-COVID diagnosis (yes vs no)				0.164	0.526	0.755
COVID-related symptom score				0.515	0.018	<0.001

Notes: generalized anxiety symptoms were assessed using the Generalized Anxiety Disorder-7, ranging 0–21; COVID-related symptoms were assessed based on reported frequency of fatigue, muscle aches, dizziness, difficulties concentrating, breathlessness, persistent cough, forgetfulness, loss of smell or taste; categorical variables are dummy coded; bold values represent $p < .01$.

Table 4
Linear regression models of social anxiety symptoms (N = 1407).

	Model 1 (excluding COVID-19 symptoms)			Model 2 (including COVID-19 symptoms)		
	B	SE	p	B	SE	p
Intercept	4.474	0.342	<0.001	2.350	0.294	<0.001
Gender						
Women	0.684	0.180	<0.001	0.391	0.149	<0.001
Non-binary/Unspecified	2.318	1.329	0.081	1.908	1.099	0.083
Men (reference)	0.000			0.000		
COVID-19 infection status						
Infected with 0–1 vaccinations	1.230	0.295	<0.001	0.104	0.260	0.690
Infected with 2+ vaccinations	0.255	0.242	0.292	-0.339	0.208	0.103
No known infection (reference)	0.000			0.000		
Mental health diagnosis (yes vs no)	2.292	0.187	<0.001	0.711	0.167	<0.001
Age in years	-0.050	0.005	<0.001	-0.039	0.005	<0.001
Long-COVID diagnosis (yes vs no)				0.039	0.343	0.910
COVID-related symptom score				0.299	0.012	<0.001

Notes: social anxiety symptoms were assessed using the Mini-Social Phobia Inventory, ranging 0–15; COVID-related symptoms were assessed based on reported frequency of fatigue, muscle aches, dizziness, difficulties concentrating, breathlessness, persistent cough, forgetfulness, loss of smell or taste; categorical variables are dummy coded; bold values represent $p < .01$.

vaccinated, with mean depression scores exceeding clinical cut-points in this group. The significant difference in symptom scores for this group remained even after adjusting for lifetime mental health diagnosis, which suggests the association is not simply due to higher prevalence of COVID-19 among people with existing mental illness. This finding is consistent with research suggesting higher rates of mental ill health among those who have experienced COVID-19 infection [2,14]. Full vaccination reduced the impact of infection on mental health outcomes to non-significance, particularly after adjusting for demographic factors and existing mental ill health in the multivariate model. This finding is consistent with rigorous population-based research on the physical health sequelae of COVID-19 infection [32]. Our findings that women, younger people, and those with a pre-existing mental health condition had higher mental health symptom severity align with evidence obtained from a scoping review conducted earlier in the pandemic [4].

Further adjustment for the core physical symptoms associated with COVID-19 infection resulted in the effects of infection being attenuated to non-significance. These findings suggest that the physical morbidity associated with COVID-19 infections, including impairment to respiratory, cognitive and musculoskeletal functioning, may lead to a deterioration in mental health for many people. Our work is consistent with previous qualitative work [41], which has indicated that people with long-COVID report their experience of poor mental health was exacerbated by persistent physical or neurological symptoms. This exacerbation of physical symptoms may have other compounding impacts such as preventing engagement in usual coping strategies [42] such as exercise or breathing exercises, or reducing the ability to socialise, potentially increasing loneliness and isolation [9]. Symptoms of depression and anxiety may also be increased by the lack of available and effective treatment options, and by uncertainty around how long the condition may last [41].

As the population prevalence of long-COVID increases, we may see a concomitant rise in mental ill health. However, this rise may be most acute in the months following infection, with substantial subsequent

improvements in mental health expected for most people [15]. Nevertheless, a minority of individuals may experience chronic mental health outcomes following COVID-19 infection, given the tight coupling between the physical and mental features of the illness [23] and long-term relationships between chronic physical illness and mental ill health [43]. It is critical that longitudinal data continue to monitor symptom patterns, to identify characteristics of those who are most at risk of long-term poor mental health outcomes. Clinicians should closely monitor the mental health of patients experiencing persistent COVID-19 symptoms, particularly among patients who had a COVID-19 infection before they were fully vaccinated.

While this study is one of the first to examine population representative data on the effects of COVID-19 infection on mental health symptoms, there are several limitations that should be considered. The data were cross-sectional and reliant on retrospective reporting. Therefore, there may be reverse causation or effects due to confounding, although we adjusted for existing mental health diagnoses. Limited data regarding COVID-19 infection were collected – we only asked about history of COVID-19 infection and current symptoms, without assessing time since infection, duration of symptoms, or severity of symptoms. Consequently, we were unable to adjust for time since infection in our models. Further research may benefit from exploring whether there are differential effects of acute and prolonged physical symptoms on mental health. Mental health symptoms associated with COVID-19 are likely to be highest shortly after infection, decreasing over time [15]. Similarly, limited data on vaccination was collected, with no information on the type of vaccine (or mix of vaccines) received. Within an epidemiological sample recruited from the community, it was not possible to obtain clinical ascertainment of COVID-19 status, nor verifiable information about the testing protocol. Nevertheless, results are likely to be conservative given false negatives (i.e., unreported or asymptomatic COVID-19 infections) are likely to be more common than false positive infections. Similarly, validated mental health measures were used to ascertain outcomes, as clinical interviews were not feasible within this setting. We did not examine the effects of specific physical symptoms such as fatigue, as we did not have a priori hypotheses about which symptoms would most impact on mental health. Finally, while the sample reflected the national population on the basis of age, gender and location, it comprised people who engage in market research panels, which may have led to under-representation of some groups.

In conclusion, in a large representative population sample, COVID-19 infection was associated with significantly higher symptoms of depression and anxiety among adults who were not fully vaccinated. These effects were explained by the higher severity of physical health symptoms in this group, suggesting that people experiencing ongoing physical symptoms associated with COVID-19 may also experience reductions in mental health. These associations were not explained by pre-existing mental health conditions. The present findings reinforce the efficacy of vaccination for reducing both the physical and mental health impacts of COVID-19 infection.

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Ethical standards

Written informed consent was obtained online from all participants prior to participation in the study, which was approved by The Australian National University Human Research Ethics Committee

(protocol 2020/152).

CRediT authorship contribution statement

Philip J. Batterham: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Amy Dawel:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Yiyun Shou:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Amelia Gulliver:** Writing – review & editing, Methodology, Investigation. **Nicolas Cherbuin:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Alison L. Calear:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Louise M. Farrer:** Writing – review & editing, Methodology, Investigation. **Conal Monaghan:** Writing – review & editing, Methodology, Investigation.

Declaration of competing interest

The authors have no competing interests to report.

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References

- [1] D.F. Santomauro, A.M. Mantilla Herrera, J. Shadid, P. Zheng, C. Ashbaugh, D. M. Pigott, C. Abbafati, C. Adolph, J.O. Amlag, A.Y. Aravkin, B.L. Bang-Jensen, G. J. Bertolacci, S.S. Bloom, R. Castellano, E. Castro, S. Chakrabarti, J. Chattopadhyay, R.M. Cogen, J.K. Collins, X. Dai, W.J. Dangel, C. Dapper, A. Deen, M. Erickson, S.B. Ewald, A.D. Flaxman, J.J. Frostad, N. Fullman, J. R. Giles, A.Z. Giref, G. Guo, J. He, M. Helak, E.N. Hulland, B. Idrisov, A. Lindstrom, E. Linebarger, P.A. Lotufo, R. Lozano, B. Magistro, D.C. Malta, J.C. Månsson, F. Marinho, A.H. Mokdad, L. Monasta, P. Naik, S. Nomura, J.K. O'Halloran, S. M. Ostroff, M. Pasovic, L. Penberthy, R.C. Reiner Jr., G. Reinke, A.L.P. Ribeiro, A. Sholokhov, R.J.D. Sorensen, E. Varavikova, A.T. Vo, R. Walcott, S. Watson, C. S. Wiysonge, B. Zigler, S.I. Hay, T. Vos, C.J.L. Murray, H.A. Whiteford, A.J. Ferrari, Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic, *Lancet* 398 (10312) (2021) 1700–1712.
- [2] N. Vindegaard, M.E. Benros, COVID-19 pandemic and mental health consequences: systematic review of the current evidence, *Brain Behav. Immun.* 89 (2020) 531–542.
- [3] J. Xiong, O. Lipsitz, F. Nasri, L.M.W. Lui, H. Gill, L. Phan, D. Chen-Li, M. Iacobucci, R. Ho, A. Majeed, R.S. McIntyre, Impact of COVID-19 pandemic on mental health in the general population: a systematic review, *J. Affect. Disord.* 277 (2020) 55–64.
- [4] Y. Zhao, L.S. Leach, E. Walsh, P.J. Batterham, A.L. Calear, C. Phillips, A. Olsen, T. Doan, C. LaBond, C. Banwell, COVID-19 and mental health in Australia – a scoping review, *BMC Public Health* 22 (1) (2022) 1200.
- [5] E. Robinson, A.R. Sutin, M. Daly, A. Jones, A systematic review and meta-analysis of longitudinal cohort studies comparing mental health before versus during the COVID-19 pandemic in 2020, *J. Affect. Disord.* 296 (2022) 567–576.
- [6] P.J. Batterham, A.L. Calear, S.M. McCallum, A.R. Morse, M. Banfield, L.M. Farrer, A. Gulliver, N. Cherbuin, R.M. Rodney Harris, Y. Shou, A. Dawel, Trajectories of depression and anxiety symptoms during the COVID-19 pandemic in a representative Australian adult cohort, *Med. J. Aust.* 214 (10) (2021) 462–468.
- [7] A.C. Tonon, A. Abreu, M.M.D. Silva, P.S. Tavares, F. Nishino, P. Versignassi, G. R. Amado, D.B. Constantino, L.K. Pilz, E. Steibel, D. Suchecki, F.G.D. Amaral, M. P. Hidalgo, Human social isolation and stress: a systematic review of different contexts and recommendations for future studies, *Trends Psychiatry Psychother.* (2022), <https://doi.org/10.47626/2237-6089-2021-0452> ahead of print.
- [8] C. Lazzari, M. Rabottini, COVID-19, loneliness, social isolation and risk of dementia in older people: a systematic review and meta-analysis of the relevant literature, *Int. J. Psychiatry Clin. Pract.* 26 (2) (2022) 196–207.
- [9] S.M. McCallum, A.L. Calear, N. Cherbuin, L.M. Farrer, A. Gulliver, Y. Shou, A. Dawel, P.J. Batterham, Associations of loneliness, belongingness and health behaviors with psychological distress and wellbeing during COVID-19, *J. Affect. Disord. Rep.* 6 (2021) 100214.
- [10] S. Lin, The “loneliness epidemic”, intersecting risk factors and relations to mental health help-seeking: a population-based study during COVID-19 lockdown in Canada, *J. Affect. Disord.* 320 (2022) 7–17.
- [11] A. Dawel, Y. Shou, M. Smithson, N. Cherbuin, M. Banfield, A.L. Calear, L.M. Farrer, D. Gray, A. Gulliver, T. Housen, S.M. McCallum, A.R. Morse, K. Murray, E. Newman, R.M. Rodney Harris, P.J. Batterham, The effect of COVID-19 on mental

- health and wellbeing in a representative sample of Australian adults, *Front. Psychol.* 11 (2020) 579985.
- [12] B.d.A. Vitória, M.T. Ribeiro, V.S. Carvalho, The work-family interface and the COVID-19 pandemic: a systematic review, *Front. Psychol.* 13 (2022).
- [13] E.P.X. Lee, R.E.K. Man, T.L.A. Gan, E.K. Fenwick, A. Aravindhan, K.C. Ho, S. C. Sung, T.Y. Wong, C.S.H. Ho, P. Gupta, E.L. Lamoureux, The longitudinal psychological, physical activity, and financial impact of a COVID-19 lockdown on older adults in Singapore: the PIONEER-COVID population-based study, *Int. J. Geriatr. Psychiatry* 37 (1) (2021).
- [14] M.M. Hossain, S. Tasnim, A. Sultana, F. Faizah, H. Mazumder, L. Zou, E.L. J. McKyer, H.U. Ahmed, P. Ma, Epidemiology of mental health problems in COVID-19: a review, *F1000Res* 9 (2020) 636.
- [15] L. Huang, X. Li, X. Gu, H. Zhang, L. Ren, L. Guo, M. Liu, Y. Wang, D. Cui, Y. Wang, X. Zhang, L. Shang, J. Zhong, X. Wang, J. Wang, B. Cao, Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study, *Lancet Respir. Med.* 10 (9) (2022) 863–876.
- [16] M. Gavriatopoulou, E. Korompoki, D. Fotiou, I. Ntanasis-Stathopoulos, T. Psaltopoulou, E. Kastritis, E. Terpos, M.A. Dimopoulos, Organ-specific manifestations of COVID-19 infection, *Clin. Exp. Med.* 20 (4) (2020) 493–506.
- [17] J.A. Frontera, N.M. Simon, Bridging knowledge gaps in the diagnosis and management of neuropsychiatric sequelae of COVID-19, *JAMA Psychiatry* 79 (8) (2022) 811–817.
- [18] M. Taquet, R. Sillett, L. Zhu, J. Mendel, I. Camplisson, Q. Dercon, P.J. Harrison, Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients, *Lancet Psychiatry* 9 (10) (2022) 815–827.
- [19] F. Khatoun, K. Prasad, V. Kumar, COVID-19 associated nervous system manifestations, *Sleep Med.* 91 (2022) 231–236.
- [20] S. Spudich, A. Nath, Nervous system consequences of COVID-19, *Science* 375 (6578) (2022) 267–269.
- [21] A. Varatharaj, N. Thomas, M.A. Ellul, N.W.S. Davies, T.A. Pollak, E.L. Tenorio, M. Sultan, A. Easton, G. Breen, M. Zandi, J.P. Coles, H. Manji, R. Al-Shahi Salman, D.K. Menon, T.R. Nicholson, L.A. Benjamin, A. Carson, C. Smith, M.R. Turner, T. Solomon, R. Kneen, S.L. Pett, I. Galea, R.H. Thomas, B.D. Michael, G. CoroNerve Study, Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study, *Lancet Psychiatry* 7 (10) (2020) 875–882.
- [22] S. Houben-Wilke, Y.M. Goertz, J.M. Delbressine, A.W. Vaes, R. Meys, F. V. Machado, M. van Herck, C. Burtin, R. Posthuma, F.M. Franssen, H. Vijlbrief, Y. Spies, A.J. van't Hul, M.A. Spruit, D.J. Janssen, The impact of long COVID-19 on mental health: observational 6-month follow-up study, *JMIR Ment. Health* 9 (2) (2022) e33704.
- [23] R.A. Evans, H. McAuley, E.M. Harrison, A. Shikotra, A. Singapur, M. Sereno, O. Elneima, A.B. Docherty, N.I. Lone, O.C. Leavy, L. Daines, J.K. Baillie, J.S. Brown, T. Chalder, A. De Soya, N. Diar Bakerly, N. Easom, J.R. Geddes, N.J. Greening, N. Hart, L.G. Heaney, S. Heller, L. Howard, J.R. Hurst, J. Jacob, R.G. Jenkins, C. Jolley, S. Kerr, O.M. Kon, K. Lewis, J.M. Lord, G.P. McCann, S. Neubauer, P.J. M. Openshaw, D. Parekh, P. Pfeffer, N.M. Rahman, B. Raman, M. Richardson, M. Rowland, M.G. Semple, A.M. Shah, S.J. Singh, A. Sheikh, D. Thomas, M. Toshner, J.D. Chalmers, L.P. Ho, A. Horsley, M. Marks, K. Poinasamy, L. V. Wain, C.E. Brightling, P.-C.C. Group, Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study, *Lancet Respir. Med.* 9 (11) (2021) 1275–1287.
- [24] A.D. Proal, M.B. VanElzakker, Long COVID or post-acute sequelae of COVID-19 (PASC): an overview of biological factors that may contribute to persistent symptoms, *Front. Microbiol.* 12 (2021) 698169.
- [25] World Health Organization, A clinical case Definition of Post COVID-19 Condition by a Delphi consensus, 6 October 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1,2021 (Accessed 14/09/2022).
- [26] O.L. Aiyegbusi, S.E. Hughes, G. Turner, S.C. Rivera, C. McMullan, J.S. Chandan, S. Haroon, G. Price, E.H. Davies, K. Nirantharakumar, E. Sapey, M.J. Calvert, Symptoms, complications and management of long COVID: a review, *J. R. Soc. Med.* 114 (9) (2021) 428–442.
- [27] M.S. Alkodaymi, O.A. Omrani, N.A. Fawzy, B.A. Shaar, R. Almamlouk, M. Riaz, M. Obeidat, Y. Obeidat, D. Gerberi, R.M. Taha, Z. Kashour, T. Kashour, E. F. Berbari, K. Alkattan, I.M. Tleyjeh, Prevalence of post-acute COVID-19 syndrome symptoms at different follow-up periods: a systematic review and meta-analysis, *Clin. Microbiol. Infect.* 28 (5) (2022) 657–666.
- [28] Z. Amin-Chowdhury, S. Ladhani, Causation or confounding: why controls are critical for characterizing long COVID, *Nat. Med.* 27 (2021) 1–2.
- [29] A.V. Ballering, S.K.R. van Zon, T.C. Olde Hartman, J.G.M. Rosmalen, I. Lifelines Corona Research, Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study, *Lancet* 400 (10350) (2022) 452–461.
- [30] J.-Y. Seon, S. Kim, M. Hong, M.K. Lim, I.-H. Oh, Risk of COVID-19 diagnosis and death in patients with mental illness: a cohort study, *Epidemiol. Psychiatr. Sci.* 30 (2021) e68.
- [31] M. Taquet, Q. Dercon, P.J. Harrison, Six-month sequelae of post-vaccination SARS-CoV-2 infection: a retrospective cohort study of 10,024 breakthrough infections, *Brain Behav. Immun.* 103 (2022) 154–162.
- [32] M. Antonelli, R.S. Penfold, J. Merino, C.H. Sudre, E. Molteni, S. Berry, L.S. Canas, M.S. Graham, K. Klaser, M. Modat, B. Murray, E. Kerfoot, L. Chen, J. Deng, M. F. Österdahl, N.J. Cheetham, D.A. Drew, L.H. Nguyen, J.C. Pujol, C. Hu, S. Selvaichandran, L. Polidori, A. May, J. Wolf, A.T. Chan, A. Hammers, E. L. Duncan, T.D. Spector, S. Ourselin, C.J. Steves, 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.* 22 (1) (2022) 43–55.
- [33] D. Ayoubkhani, C. Bermingham, K.B. Pouwels, M. Glickman, V. Nafilyan, F. Zaccardi, K. Khunti, N.A. Alwan, A.S. Walker, Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study, *BMJ* 377 (2022) e069676.
- [34] U. Agrawal, S.V. Katikireddi, C. McCowan, R.H. Mulholland, A. Azcoaga-Lorenzo, S. Amele, A.F. Fagbamigbe, E. Vasileiou, Z. Grange, T. Shi, S. Kerr, E. Moore, J.L. K. Murray, S.A. Shah, L. Ritchie, D. O'Reilly, S.J. Stock, J. Beggs, A. Chuter, F. Torabi, A. Akbari, S. Bedston, J. McMenamin, R. Wood, R.S.M. Tang, S. de Lusignan, F.D.R. Hobbs, M. Woolhouse, C.R. Simpson, C. Robertson, A. Sheikh, COVID-19 hospital admissions and deaths after BNT162b2 and ChAdOx1 nCoV-19 vaccinations in 2.57 million people in Scotland (EAVE II): a prospective cohort study, *Lancet Respir. Med.* 9 (12) (2021) 1439–1449.
- [35] E.J. Haas, F.J. Angulo, J.M. McLaughlin, E. Anis, S.R. Singer, F. Khan, N. Brooks, M. Smaja, G. Mircus, K. Pan, J. Southern, D.L. Swerdlow, L. Jodar, Y. Levy, S. Alroy-Preis, Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data, *Lancet* 397 (10287) (2021) 1819–1829.
- [36] S.B. Naidu, A.J. Shah, A. Saigal, C. Smith, S.E. Brill, J. Goldring, J.R. Hurst, H. Jarvis, M. Lipman, S. Mandal, The high mental health burden of “Long COVID” and its association with on-going physical and respiratory symptoms in all adults discharged from hospital, *Eur. Respir. J.* 57 (6) (2021).
- [37] A.A. Madison, M.R. Shrout, M.E. Renna, J.K. Kiecolt-Glaser, Psychological and behavioral predictors of vaccine efficacy: considerations for COVID-19, *Perspect. Psychol. Sci.* 16 (2) (2021) 191–203.
- [38] R.L. Spitzer, K. Kroenke, J.B. Williams, Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire, *JAMA* 282 (18) (1999) 1737–1744.
- [39] R.L. Spitzer, K. Kroenke, J.B. Williams, B. Lowe, A brief measure for assessing generalized anxiety disorder: the GAD-7, *Arch. Intern. Med.* 166 (10) (2006) 1092–1097.
- [40] K.M. Connor, K.A. Kobak, L.E. Churchill, D. Katzelnick, J.R. Davidson, Mini-SPIN: a brief screening assessment for generalized social anxiety disorder, *Depress. Anxiety* 14 (2) (2001) 137–140.
- [41] A. Burton, H. Aughterson, D. Fancourt, K.E.J. Philip, Factors shaping the mental health and well-being of people experiencing persistent COVID-19 symptoms or ‘long COVID’: qualitative study, *BJPsych. Open* 8 (2) (2022) e72.
- [42] A. Gulliver, M. Banfield, P.J. Batterham, A.L. Calear, L.M. Farrer, A. Dawel, S. McCallum, K. Murray, A.R. Morse, Effects of previous exposure to psychotherapeutic strategies on depression and anxiety symptoms during the COVID-19 pandemic, *BJPsych. Open* 7 (1) (2021) e38.
- [43] M. Prince, V. Patel, S. Saxena, M. Maj, J. Maselko, M.R. Phillips, A. Rahman, No health without mental health, *Lancet* 370 (9590) (2007) 859–877.