



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



ELSEVIER

JOURNAL OF
ADOLESCENT
HEALTH

www.jahonline.org

Original article

A Cross-Sectional Study of the Health of Emerging Young Adults in England Following a COVID-19 Infection

Fiona Newlands, M.Sc.^{a,*}, Natalia K. Rojas^a, Manjula Nugawela, Ph.D.^a, Snehal M. Pinto Pereira, Ph.D.^b, Marta Buszewicz, Ph.D.^c, Trudie Chalder, Ph.D.^f, Emily Y. Cheung^a, Emma Dalrymple, M.Sc.^a, Tamsin Ford, Ph.D.^g, Isobel Heyman, Ph.D., M.D.^a, Shamez N. Ladhani, Ph.D.^e, Kelsey McOwat, M.Sc.^d, Ruth Simmons, Ph.D.^d, Terence Stephenson, Ph.D.^{a,1}, and Roz Shafran, Ph.D.^{a,1}

^aUCL Great Ormond Street Institute of Child Health, London, United Kingdom

^bDivision of Surgery & Interventional Science, Faculty of Medical Sciences, University College London, United Kingdom

^cResearch Department of Primary Care & Population Health, Faculty of Population and Health Sciences, University College London, Royal Free Campus, London, United Kingdom

^dImmunisation Department, Public Health England, London, United Kingdom

^ePaediatric Infectious Diseases Research Group, St. George's University of London, Cranmer Terrace, London, United Kingdom

^fDepartment of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

^gDepartment of Psychiatry, University of Cambridge, Hershel Smith Building Cambridge Biomedical Campus, United Kingdom

Article history: Received July 26, 2022; Accepted January 25, 2023

Keywords: Long COVID; Symptoms; Emerging adults

ABSTRACT

Purpose: This study describes long COVID symptomatology in a national sample of 18- to 20-year-olds with Polymerase Chain Reaction (PCR)-confirmed Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and matched test-negative controls in England. Symptoms in 18- to 20-year-olds were compared to symptoms in younger adolescents (aged 11–17 years) and all adults (18+).

Methods: A national database was used to identify SARS-CoV-2 PCR-positive 18- to 20-year-olds and test-negative controls matched by time of test, age, gender, and geographical region. Participants were invited to complete a questionnaire about their health retrospectively at time of test and also when completing the questionnaire. Comparison cohorts included children and young people with long COVID and REal-time Assessment of Community Transmission studies.

Results: Of 14,986 people invited, 1,001 were included in the analysis (562 test-positive; 440 test-negative). At testing, 46.5% of test-positives and 16.4% of test-negatives reported at least one symptom. At the time of questionnaire completion (median 7 months post-testing), 61.5% of test-positives and 47.5% of test-negatives reported one or more symptoms. The most common symptoms were similar amongst test-positives and test-negatives and included tiredness (44.0%; 35.7%), shortness of breath (28.8%; 16.3%), and headaches (13.7%; 12.0%). Prevalence rates were similar to those reported by 11–17-year-olds (66.5%) and higher than those reported in all adults (37.7%).

IMPLICATIONS AND CONTRIBUTION

This study describes the long-term symptoms experienced by emerging adults (18- to 20-year-olds) after a COVID-19 infection. The emerging adult population is currently neglected in the literature and knowledge of how they are impacted by long COVID is important to help establish appropriate treatments for those living with the condition.

Conflicts of interest: Terence Stephenson is Chair of the Health Research Authority and therefore recused himself from the Research Ethics Application. Trudie Chalder is a member of the National Institute for Health and Care Excellence committee for long COVID. She has written self-help books on chronic fatigue and has done workshops on chronic fatigue and post infectious syndromes. All remaining authors have no conflict of interest.

Ethics Approval: Yorkshire & The Humber - South Yorkshire Research Ethics Committee (REC reference: 21/YH/0060; IRAS project ID:293495).

* Address correspondence to: Fiona Newlands, UCL Great Ormond Street Institute of Child Health, 30 Guilford Street, London, WC1N 1EH.

E-mail address: fiona.newlands.18@ucl.ac.uk (F. Newlands).

¹ Joint senior authors.

For 18- to 20-year-olds, there was no significant difference in health-related quality of life and well-being ($p > .05$). However, test-positives reported being significantly more tired than test-negatives ($p = .04$).

Discussion: Seven months after PCR test, a high proportion of test-positive and test-negative 18- to 20-year-olds reported similar symptoms to each other and to those experienced by younger and older counterparts.

© 2023 Society for Adolescent Health and Medicine. All rights reserved.

The acute symptoms of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the virus responsible for COVID-19, are increasingly clearly defined [1,2]. While many people go on to recover from the infection, some continue to experience persistent and on-going symptoms, which has been termed 'long COVID'. Long COVID is defined as a post-COVID-19 condition that occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually commencing within 3 months from the onset of COVID-19 with symptoms that last for at least 2 months that cannot be explained by an alternative diagnosis [3]. Currently, long COVID is poorly understood. Little is known about its prevalence, mechanisms, duration, and treatment. In the UK, the Office of National Statistics (ONS) estimates that 3% of the population is living with self-reported long COVID, with common symptoms including fatigue, shortness of breath, loss of smell, and muscle ache [4]. Prevalence estimates for long COVID are highly variable, ranging from 10%–90% [5]. However, these studies typically include adults with a broad age range (18 + years), making it difficult to draw conclusions about prevalence and symptoms in younger adults. Studies in adult populations have also produced contradictory findings regarding who is most at risk of developing long COVID. While some report the prevalence increases with age [6,7], a recent matched cohort study in the UK found that the risk of developing long COVID decreased with age; younger adults were at higher risk [8].

While children and young people (CYP) typically experience less severe acute COVID-19 than adults, the high rates of infection mean that some CYP will also be affected by long COVID [9]. In a national matched cohort study of SARS-CoV-2 Polymerase Chain Reaction (PCR)-positive and test-negative 11- to 17-year-olds, 66.5% of CYP had one or more symptoms 3 months after a positive PCR test compared to 53.3% among test-negatives [10]. Reported symptoms were similar to those experienced by adults, including unusual tiredness, shortness of breath, and headache. This is consistent with findings from the wider literature indicating that some CYP continue to experience continued symptoms after a COVID-19 infection [9,11–14]. Additionally, the study reported a higher prevalence of symptoms among older (15- to 17-year-olds) than younger (11- to 14-year-olds) adolescents replicating international data reported in a systematic review and meta-analysis of persistent symptoms reported by CYP after COVID-19 which also found increasing risk of long COVID with increasing age [15].

The existing literature focuses primarily on young people up to the age of 18 or adults from age 18. The latter includes a very wide range of ages with little information about young adults in the 18–20 age range. There is, therefore, a need to identify the prevalence and symptoms of long COVID in emerging adults (defined as 18- to 20-year-olds) as this is a particularly

vulnerable group. Prepandemic, older adolescents were more likely to have a mental disorder than children and younger adolescents [16], while during the pandemic, younger adults (those under 25) reported significantly greater loneliness than older age groups [17]. Most recently, in young people aged 17–19 years, rates of a probable mental disorder rose from 10.1% in 2017, to 17.7% in 2020, and to 25.7% in 2022 [18]. Studies of CYP have found mental health prior to the pandemic and loneliness to be predictors of experiencing at least one impairing physical symptom after a COVID-19 infection [19], indicating this group may be more at risk of long COVID and making it imperative to focus on understanding the prevalence and symptom profile of long COVID in emerging adults.

Objectives

The primary objective of this study was to describe and estimate the prevalence of on-going symptoms in a national sample of non-hospitalised 18- to 20-year-olds at least 3 months after a SARS-CoV-2 PCR-positive test compared with matched PCR-negative 18- to 20-year-olds. Our secondary objective was to compare on-going symptoms in emerging adults with CYP with adults across the age range (18 years+). Based on the literature, we hypothesised that symptoms experienced by emerging adults aged 18–20 would be similar to those reported by their younger and older counterparts, and that the prevalence of reported symptoms would be higher than in CYP but lower than in adults.

Methods

The study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines [20] (see supplementary materials for the STROBE checklist).

Study design

This study draws on cross-sectional questionnaire data of SARS-CoV-2 PCR-positive emerging adults, matched at study invitation, by month of test, age, sex, and geographical area to SARS-CoV-2 test-negative emerging adults. Participants were matched using the national SARS-CoV-2 testing dataset held by the United Kingdom Health Security Agency (UKHSA; formally Public Health England) [21]. UKHSA received results of all SARS-CoV-2 PCR tests in England. The database recorded UK National Health Service (NHS) number, name, age, sex, postcode, and PCR test result. UKHSA can access the electronic patient demographic service which allowed potential participants to be approached by post for them to consent and complete an online questionnaire.

Setting

Emerging adults who took a PCR test between September 2020 and March 2021 were contacted in July 2021 and invited to take part in the study. A letter was posted to potential participants informing them about the study and inviting them to take part using an online link. The link contained information about the study and details of how to consent. The online questionnaire closed in January 2022, and therefore participants completed the questionnaire between 3 and 16 months after their PCR test (Figure S1 in supplementary materials).

Participants

The study collected data on participants who were emerging adults aged 18–20 years old, who took a PCR test between September 2020 and March 2021 which was submitted the test result to the UKHSA testing database. Participants were either SARS-CoV-2 PCR-positive or SARS-CoV-2 PCR-negative at initial testing.

The study was approved by Yorkshire and The Humber—South Yorkshire Research Ethics Committee (REC reference: 21/YH/0060; IRAS project ID:293,495).

Variables

Participants completed a questionnaire which was also used in the CYP with long COVID study [10]. The questionnaire was based on the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) working group [22] and contained demographic information including age, gender and ethnicity. It included an assessment of 21 symptoms as well as standardised well-being measures.

Symptoms. Participants were asked to indicate the presence/absence of 21 different symptoms frequently associated with long COVID at two time points; the time of their PCR test (retrospective) and at the time of completing the questionnaire (current).

Standardised well-being measures. Health related quality of life/functioning was measured using the EQ-5D-5L (comprising five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression) [23]. The EQ Visual Analogue Scale (EQ VAS) was also included where participants rated their health from 0% (worst health you can imagine) to 100% (best health you can imagine). Mental health symptoms were measured using the Short seven-item version of the Warwick Edinburgh Mental Well-being Scale (SWEMWBS) [24], the Patient Health Questionnaire for depression (PHQ-9) [25], and the Generalised Anxiety Disorder questionnaire (GAD-7) [26]. Loneliness was measured using the three-item UCLA (University of California, Los Angeles) loneliness scale (UCLA-3) [27] and fatigue was measured using the 11-item Chalder Fatigue Questionnaire (CFQ) [28]. Higher scores on the SWEMWBS indicate better mental well-being. Higher scores on the remaining measures indicate a greater degree of symptom severity (further details on calculating scores and cut-off points are presented in Table S1 in the supplementary materials). These measures are all validated and have been shown to have good psychometric properties [25,27,29–34].

Long COVID. A research definition of long COVID in CYP has been developed using the Delphi process which defines the condition as occurring 'in young people with a history of confirmed SARS-CoV-2 infection, with at least one physical symptom for a minimum duration of 12 weeks after initial testing that cannot be explained by an alternative diagnosis. The symptoms have an impact on everyday functioning, may continue or develop after COVID infection, and may fluctuate or relapse over time.' [35]. The definition was operationalised using participant responses to the EQ-5D-5L domains as an indication of impairment.

Socio-economic status. The Index of Multiple Deprivation (IMD) was used as a proxy for socio-economic status and was derived from the participants' lower super output area (a small local area level based geographic hierarchy) [36]. IMD quintiles were calculated from most (quintile 1) to least (quintile 5) deprived.

Data source/measurement

Data were also drawn from two additional sources to allow comparison across age groups. For CYP, data were drawn from the CLoCk study. CLoCk is a matched cohort study of approximately 30,000 SARS-CoV-2 positive and negative CYP aged 11–17 years old in England [21]. Participants were invited to complete an online questionnaire 3, 6, 12, and 24 months after a PCR. Participants in the CLoCk study completed a questionnaire with the same demographic and symptom questions outlined above with standardised well-being measures replaced by those appropriate for use by CYP. This study draws on findings 3 months after a PCR test [10].

Data were also drawn from a random community sample of adults (older than 18 years old) in England who were involved in the REal-time Assessment of Community Transmission-2 (REACT-2) study [6]. Data captures participants who took part in rounds 3–5 of the study ($n = 508,707$; September 2020 to February 2021). As part of their involvement, participants were asked to complete an online questionnaire including questions about the presence of 29 different symptoms associated with long COVID. The study included data on participants who reported symptoms lasting 12 weeks or more following suspected or PCR-confirmed COVID-19.

Bias

The study was matched to incorporate a comparator cohort of emerging adults who had experienced the pandemic, lockdown measures and social isolation but who had a negative PCR test. The test-negative comparison group was included to distinguish the symptoms associated with long COVID from symptoms attributable to the pandemic more broadly [21]. To reduce selection bias, test-positive and test-negative participants were invited to participate at a rate of 1:2 as it was anticipated test-negative participants would be less likely to respond to the questionnaire. A comparison of the study participants to the entire target population (i.e., all those people invited) and the general population (UK census data) is presented in Table S2 in the supplementary materials.

Study size

Total population sampling was employed where all participants who submitted a positive PCR test result to the UKHSA

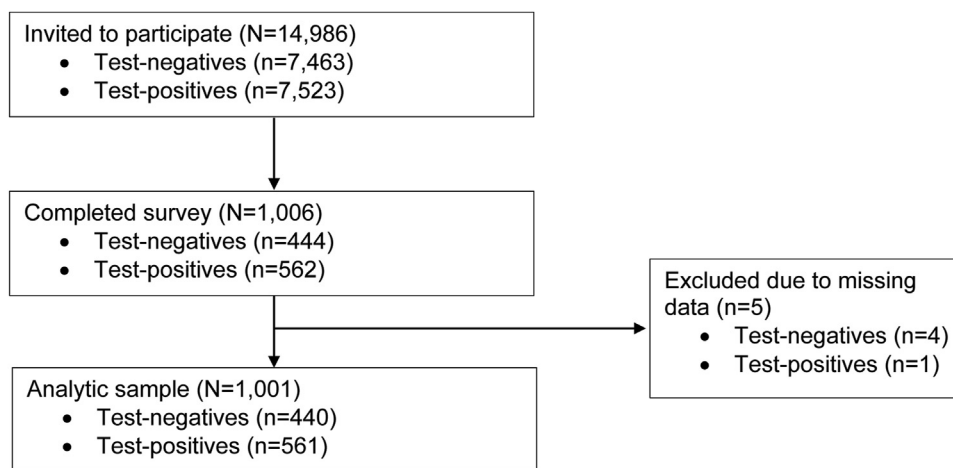


Figure 1. Flow chart of participants in the study.

testing database were invited to take part in the study. Test-negatives were matched by age, sex, and postcode, and randomly sampled and invited at a rate of 1:2 (test-positives: test-negatives).

Statistical methods

Analysis was conducted using STATA v17. Descriptive statistics were used to describe participants' characteristics (sex, age, ethnicity and region of residence) which were compared both to the general population using census data and also those in the target population (all invited participants; Table S2 in supplementary materials). Descriptive statistics were also used to describe the total number of symptoms experienced, the presence of specific symptoms and the frequency (percentage) of participants meeting the Delphi definition of long COVID in CYP [35]. A sensitivity analysis was conducted on the frequency of participants meeting the Delphi definition of long COVID and symptoms at time of questionnaire by removing test-positive-participants who were reinfected with SARS-CoV-2 and test-negative participants who were subsequently infected before completing the questionnaire.

When appropriate, data were summarised using means and standard deviations. Where data were non-normally distributed, the median and interquartile range (IQR) was presented. Chi-squared and Mann-Whitney U tests were used to determine any differences between test-positives and test-negative groups. *p* values less than 0.05 were considered significant. A scatter plot was used to display the mean number of symptoms in test-positives and test-negatives at different time-points after their PCR test. The mean number of symptoms for months 3–4 and 10–16 were grouped to account for small sample sizes at these time points.

Findings

Of the 14,986 participants tested and invited to participate in the study between September 2020 and March 2021, 1,006 returned the questionnaire, including 562 test-positives and 444 PCR test-negatives (response rate 6.7%). Four test-negative participants and one test-positive were excluded because the date of

their PCR test was missing or there were missing data in their questionnaire. Figure 1 shows participant flow.

Most of the final analytic sample were female (62.7%) and white (81.9%), while age, region and IMD quintile were more equally distributed between test-positives and test-negatives (Table 1). A comparison of the analytic sample to the target population and UK census data reflected an overrepresentation of females in the study (analytic sample: 62.7%; general population: 49.1%; target population: 50.2%) (Table S2 in supplementary materials). No other major differences in demographic characteristics were noted.

Participants completed the questionnaires between July 2021 and January 2022. The median (IQR) duration between PCR test and completing the questionnaire was 7 (5–9) months. Table 2 provides details on the time between PCR test and completing the questionnaire.

Symptoms at time of PCR test (retrospective)

At testing, 261 test-positive participants (46.5%) and 72 test-negative participants (16.4%) retrospectively reported having had at least one symptom; 239 (42.6%) of test-positives had 3 + symptoms and 188 (33.5%) had 5 + symptoms compared to 66 (15.0%) and 47 (10.7%) of test-negatives, respectively (Table S3, supplementary materials).

The five most common symptoms amongst test-positives were headaches (34.2%), tiredness (33.0%), loss of taste/smell (32.8%), fever (27.1%), and sore throat (24.4%). The five most common symptoms amongst test-negatives were similar: headaches (11.4%), sore throat (11.4%), tiredness (8.9%), persistent cough (8.6%), and fever (8.4%).

Symptoms at time of completing questionnaire (current)

At the time of completing the questionnaire (on average 7 months post-testing), 61.5% of test-positive participants reported at least one symptom, 28.5% had 3 + symptoms and 10.5% had 5 + symptoms, which compared with 47.5%, 21.4%, and 10.2%, respectively for test-negatives (Table 3).

Table 1
Characteristics of study participants

	All participants (n = 1,001)	Positive for SARS-CoV-2 (n = 561)	Negative for SARS-CoV-2 (n = 440)
Sex			
Female	628 (62.7%)	359 (64.0%)	269 (61.1%)
Male	373 (37.3%)	202 (36.0%)	171 (38.9%)
Age at time of test			
18	296 (29.6%)	175 (31.2%)	121 (27.5%)
19	357 (35.7%)	204 (36.4%)	153 (34.8%)
20	348 (34.7%)	182 (32.4%)	166 (37.7%)
Ethnicity			
White	820 (81.9%)	457 (81.4%)	363 (82.5%)
Asian or Asian British	108 (10.8%)	65 (11.5%)	43 (9.8%)
Mixed	42 (4.2%)	24 (4.3%)	18 (4.1%)
Black, African, or Caribbean	14 (1.4%)	6 (1.1%)	8 (1.8%)
Other	13 (1.3%)	7 (1.3%)	6 (1.4%)
Unknown	4 (0.4%)	2 (0.4%)	2 (0.4%)
Region			
East Midlands	123 (12.3%)	72 (12.8%)	51 (11.6%)
East of England	114 (11.4%)	65 (11.5%)	49 (11.1%)
London	81 (8.0%)	52 (9.3%)	29 (6.6%)
North East England	119 (11.9%)	64 (11.4%)	55 (12.5%)
North West England	109 (10.9%)	53 (9.5%)	56 (12.7%)
South East England	120 (12.00%)	73 (13.0%)	47 (10.7%)
South West England	125 (12.5%)	76 (13.6%)	49 (11.1%)
West Midland	99 (9.9%)	48 (8.6%)	51 (11.6%)
Yorkshire and the Humber	111 (11.1%)	58 (10.3%)	53 (12.1%)
IMD quintile			
1 (most deprived)	197 (19.7%)	106 (18.9%)	91 (20.7%)
2	229 (22.9%)	125 (22.3%)	104 (23.6%)
3	183 (18.2%)	99 (17.6%)	84 (19.1%)
4	204 (20.4%)	122 (21.8%)	82 (18.6%)
5 (least deprived)	188 (18.8%)	109 (19.4%)	79 (18.0%)

IMD, Index of Multiple Deprivation.

Figure 2 shows the mean number of symptoms reported by participants in the months after their PCR test. The mean number of symptoms reported by test-positives and test-negatives is relatively consistent at each timepoint.

Overall, 31.4% (95% CI 27.6%–35.4%) of test-positives met the Delphi definition of impairing symptoms at the time of completing the questionnaire. The five most common symptoms amongst test-positives were tiredness (44.0%), shortness of breath (28.9%), headaches (13.7%), loss of smell/taste (12.1%), and unusual chest pain (9.3%). There were similar reports from the

test-negatives, for whom the five most common symptoms were tiredness (35.5%), shortness of breath (16.1%), headaches (11.6%), dizziness/light headedness (8.6%), and unusual chest pain (6.6%; Table 3). The frequency of participants meeting the Delphi definition of long COVID and the number and type of symptoms reported at the time of completing the questionnaire remained largely similar even after excluding test-negatives who were subsequently infected and test-positives who were reinfected in the time between their PCR test and questionnaire completion (Table S4 in supplementary materials).

Table 2
Months between PCR test and completing questionnaire^a

Duration between test and questionnaire	All participants (%)	SARS-CoV-2 positive participant (%)	SARS-CoV-2 negative participants (%)
16 months	1 (0.1%)	1 (0.2%)	0 (0.0%)
15 months	1 (0.1%)	1 (0.2%)	0 (0.0%)
14 months	0 (0.0%)	0 (0.0%)	0 (0.0%)
13 months	3 (0.3%)	2 (0.4%)	1 (0.2%)
12 months	2 (0.2%)	1 (0.2%)	1 (0.2%)
11 months	12 (1.2%)	6 (1.1%)	6 (1.4%)
10 months	119 (11.9%)	57 (10.2%)	62 (14.1%)
9 months	137 (13.7%)	81 (14.4%)	56 (12.7%)
8 months	151 (15.1%)	86 (15.3%)	65 (14.8%)
7 months	143 (14.3%)	83 (14.8%)	60 (13.6%)
6 months	157 (15.7%)	90 (16.0%)	67 (15.2%)
5 months	159 (15.9%)	83 (14.8%)	76 (17.3%)
4 months	111 (11.1%)	66 (11.8%)	45 (10.2%)
3 months	5 (0.5%)	4 (0.7%)	1 (0.2%)
Total participants	1,001	561	440

^a months calculated under assumption average of 30 days per month.

Table 3
Reported symptoms at the time of completing the questionnaire

	CLoCk (11- to 17-year-old) [11]		Emerging adults (18- to 20-year-olds)		Adults REACT-2 (18+) [6] ^a
	Tested positive for SARS-CoV-2 (n = 3,065)	Tested negative for SARS-CoV-2 (n = 3,739)	Tested positive for SARS-CoV-2 (n = 561)	Testeds negative for SARS-CoV-2 (n = 440)	Probable or confirmed SARS-CoV-2 rounds 3–5 (n = 508,707)
Time of questionnaire: CLoCk median of 14 9 weeks (IQR 13·1–18 9)/18- to 20-year-olds median 7 months (3–16)/REACT-2 12 weeks or more					
Number of symptoms					
No reported symptom	1,027 (33 5%)	1,746 (46 7%)	216 (38.5%)	231 (52.5%)	
1 symptom (<i>at least one symptom</i>) ^b	671 (21 9%)	1,019 (27 3%)	109 (19.4%)	70 (15.9%)	37.7%
2 symptoms	439 (14 3%)	371 (9 9%)	76 (13.6%)	45 (10.2%)	
3 symptoms	300 (9 8%)	228 (6 1%)	61 (10.9%)	34 (7.7%)	
4 symptoms	217 (7 1%)	137 (3 7%)	40 (7.1%)	15 (3.4%)	
5 + symptoms	411 (13 4%)	238 (6 4%)	59 (10.5%)	46 (10.2%)	
Specific symptoms					
Fever	50 (1.6%)	55 (1.5%)	13 (2.3%)	12 (2.7%)	897 (1.2%)
Chills	269 (8 8%)	192 (5 1%)	25 (4.5%)	7 (1.6%)	906 (1.2%)
Persistent cough (<i>new persistent cough</i>) ^b	98 (3 2%)	98 (2 6%)	22 (3.9%)	27 (6.1%)	3,073 (4.2%)
Tiredness	1,196 (39 0%)	911 (24 4%)	247 (44.0%)	156 (35.5%)	12,214 (16.8%)
Shortness of breath	717 (23 4%)	388 (10 4%)	162 (28.9%)	71 (16.1%)	7,166 (9.8%)
Loss of smell/taste	414 (13 5%)	51 (1 4%)	68 (12.1%)	19 (4.3%)	
Unusually hoarse voice (<i>hoarse voice</i>) ^b	56 (1 8%)	46 (1 2%)	4 (0.7%)	14 (3.2%)	1,572 (2.2%)
Unusual chest pain (<i>chest pain</i>) ^b	216 (7 0%)	129 (3 5%)	52 (9.3%)	29 (6.6%)	1,854 (2.5%)
Unusual abdominal pain (<i>abdominal pain/belly ache</i>) ^b	119 (3 9%)	107 (2 9%)	20 (3.6%)	11 (2.5%)	1,175 (1.6%)
Diarrhoea	92 (3 0%)	80 (2 1%)	30 (5.4%)	11 (2.5%)	983 (1.4%)
Headaches	710 (23 2%)	530 (14 2%)	77 (13.7%)	51 (11.6%)	3,792 (5.2%)
Confusion, disorientation or downiness	198 (6 5%)	123 (3 3%)	29 (5.8%)	24 (5.5%)	
Unusual eye-soreness (<i>sore eyes</i>) ^b	182 (5 9%)	134 (3 6%)	31 (5.5%)	23 (5.2%)	2,154 (3.0%)
Skipping meals	296 (9 7%)	275 (7 4%)	41 (7.3%)	27 (6.1%)	
Dizziness, or light-headedness (<i>dizziness</i>) ^b	419 (13 7%)	314 (8 4%)	50 (8.9%)	38 (8.6%)	2,224 (3.1%)
Sore throat	291 (9 5%)	281 (7 5%)	36 (6.4%)	27 (6.1%)	2,212 (3.0%)
Unusually sore muscle pains (<i>muscle aches</i>) ^b	165 (5 4%)	83 (2 2%)	30 (5.4%)	9 (2.1%)	5,264 (7.2%)
Earache or ringing in the ears	191 (6 2%)	165 (4 4%)	22 (3.9%)	15 (3.4%)	
Raised welts on skin or swelling (<i>red, itchy areas on the skin</i>) ^b	48 (1 6%)	32 (0 9%)	4 (0.7%)	0 (0.0%)	794 (1.1%)
Red or purple sores or blisters on feet (<i>purple sores/blisters on the feet</i>) ^b	35 (1 1%)	40 (1 1%)	3 (0.5%)	3 (0.7%)	221 (0.3%)
Loss or change to sense of smell					3,510 (4.8%)
Loss or change to sense of taste					2,927 (4.0%)
Tight chest					4,234 (5.8%)
Appetite loss					1,942 (2.7%)
Nausea/vomiting					600 (0.8%)
Runny nose					1,882 (2.6%)
Sneezing					1,512 (2.1%)
Blocked nose					2,102 (2.9%)
Difficulty sleeping					5,427 (7.5%)
Severe fatigue					2,098 (2.9%)
Numbness/tingling					1,511 (2.1%)
Heavy arms/legs					2,331 (3.2%)
Sudden swelling to face or lips					67 (0.1%)
Other	335 (10 9%)	590 (15 8%)	48 (8.6%)	19 (4.3%)	

^a Data for REACT-2 was drawn from Table 1 in the main manuscript and Table S2 in supplementary information.

^b The comparable symptom terminology used in the REACT-2 study.

Comparison with CYP (aged 11–17) and adults (aged 18+)

The proportion of CYP (aged 11–17) in the CLoCk study reporting symptoms 3 months post-test was 66.5% for test-positives and 53.3% for test-negatives. The five most common symptoms reported by test-positive CYP in CLoCk were tiredness (39.0%), shortness of breath (23.4%), headaches (23.2%), dizziness (13.7%), and loss of smell/taste (13.5%), whilst the five most common symptoms reported by test-negative CYP in CLoCk were tiredness (24.0%), other unspecified symptom (15.8%), headaches (14.2%), shortness of breath (10.4%), and dizziness (8.4%).

For adults in REACT-2, 37.7% had at least one symptom at 12 or more weeks. The five most common symptoms were tiredness (16.8%), shortness of breath (9.8%), difficulty sleep (7.5%), muscle aches (7.2%), and tight chest (5.8%).

Standardised well-being measures at time of questionnaire

For the 18- to 20-year-olds, there were no significant differences between test-positives and test-negatives on any of the EQ-5D-5L quality of life domains (all *p* values > 0.05). However, over half (54.9%) of all participants reported feeling anxious or

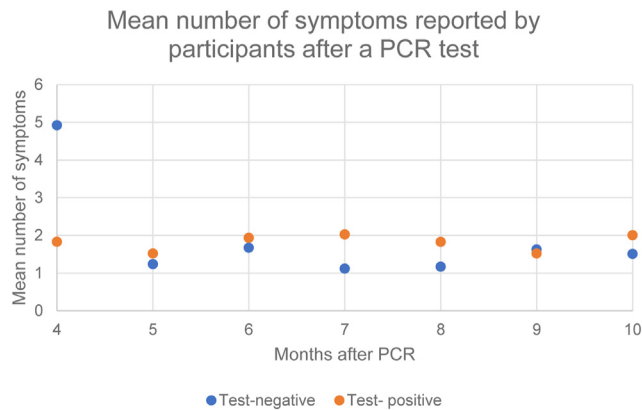


Figure 2. Mean number of symptoms reported by participants after a PCR test. Month 4 represents participants who completed the questionnaire 3–4 months after their PCR and month 10 represent those who completed the questionnaire 10–16 months after their PCR.

depressed to some extent as indicated by a single item on the EQ-5D-5L. The median score on the EQ-VAS for both test-positives and test-negatives was 85 (IQR 75–95; p value for differences between the groups = 0.31).

Test-positives and test-negatives were similar with respect to symptoms of mental distress as measured by the PHQ-9 ($p = .94$), GAD-7 ($p = .46$) and SWEMWBS ($p = .75$). Median PHQ-9 scores were 4 (IQR 1–9) for test-positives and test-negatives. Median GAD-7 scores were 3 (IQR test-positives: 0–7; IQR test-negatives: 0–8). Around a quarter of participants suffered mild depression (25.1%) or anxiety (23.9%) as categorised by the PHQ-9 and GAD-7. The proportion of participants reporting moderate to severe depression and anxiety was 22.9% and 16.4% respectively. Scores on the SWEMWBS were similar among those who tested positive (Median = 20.7, IQR 18.0–23.2) and those who tested negative (Median = 20.7, IQR 18.0–24.1).

In terms of fatigue, test-positives scored significantly higher (i.e., were more tired) than test-negatives ($p = .04$; positives: Mean (SD) = 13.5 (5.6); negatives: Mean = 12.9 (5.3)). Median UCLA-3 scores were 4 (IQR 1–3) for both groups. A Mann Whitney U test indicated no difference between the groups ($p = .09$). Overall, 29.7% of participants scored as lonely on the UCLA-3 (27.3% of test-positives and 32.7% of test-negatives).

Discussion

This study describes post-COVID symptomatology in a national sample of non-hospitalised 18- to 20-year-olds following a SARS-CoV-2 PCR-positive test compared with matched 18- to 20-year-olds with a negative PCR test. At the time of completing the questionnaire at a median of seven months after their test, 61.5% of test-positives and 47.5% of test negatives reported experiencing symptoms. Common symptoms experienced by the test-positive and test-negative participants at the time of the questionnaire were similar and included tiredness, shortness of breath, headaches, and unusual chest pain. Loss of smell/taste was a common symptom reported by test-positives and dizziness/light headedness was a common symptom reported by the test-negatives.

Our analysis found the prevalence of symptoms for both the test-positives and the test-negative control group was higher at the time of completing the questionnaire (61.5% and 47.5% respectively) than recollected at the time of testing for both the

test-positives (46.5% and 16.4%, respectively). A likely explanation is self-selection among the responders. It is also possible that retrospectively describing symptoms several months after a PCR test may have led to some recall bias. It is also possible that some participants among test-positives and test-negatives may have been exposed to SARS-CoV-2, or potentially other viral illnesses, in the intervening period between PCR testing and completing the questionnaire. However, after excluding test-negatives who were subsequently infected and test-positives who were reinfected in the time between their PCR test and questionnaire completion, the prevalence of symptoms remained largely similar. Additionally, these findings are consistent with the CLoCk study where younger adolescents also reported a higher prevalence of symptoms at 3 months after their PCR-test [10], and with published reports of symptoms emerging weeks to months after infection [37].

The prevalence of symptoms reported by the test-negative group at the time of the questionnaire was high: 47.5% reported at least one symptom, 32.6% reported 3 + symptoms, and 10.2% reported 5 + symptoms. This highlights the importance of including a control group and potentially indicates that the burden of living through a pandemic has been considerable. However, these findings need to be considered in the context of the wider literature, particularly in relation to common symptoms such as fatigue which were prevalent in this age group even before the pandemic [38].

For 18- to 20-year-olds, there was no significant difference between the test-positive and test-negative groups on the standardised well-being measures except for fatigue reported using the Chalder Fatigue Scale. Similarly, there were no differences between test-positive and test-negative groups on validated measures of anxiety, depression and well-being (measured by GAD-7, PHQ-9, and SWEMWBS), with participants in both groups reporting similar scores to population norms [24,39]. On the other hand, 54.7% of test-positive and 55.0% of test-negatives participants reported feeling anxious or depressed to some extent as indicated by a single item on the EQ-5D-5L which is consistent with reports from the wider literature indicating poor mental health amongst emerging adults [18]. It is important to differentiate between long COVID symptoms and the mental health toll that the COVID-19 pandemic has had on the population. Arguably the latter particularly affected emerging adults as their psychosocial milieu and environment was significantly limited during a key developmental transition.

A secondary aim of the study was to compare the symptomatology of 18- to 20-year-olds with CYP and adults across the age range. We hypothesised that symptom prevalence would increase with age. However, findings indicated that the prevalence of one or more symptoms was similar across CYP and emerging adults in the test-positive (CYP: 66.5%; 18- to 20-year-olds: 61.50%) and test-negative groups (CYP: 53.3%; 18- to 20-year-olds: 47.50%) but lower than the adult cohort in REACT-2 (37.7%). The variation in symptom prevalence, however, could be due to differences in study design and data collection methodology. For example, REACT-2 authors reported the prevalence of symptoms lasting 12 weeks or more, while in CLoCk there was a median of 14.9 weeks (IQR: 13.1–18.9) between PCR testing and completing the questionnaire. The current study reported prevalence at a median of 7 months after their PCR test.

There was some overlap in the five most common symptoms experienced by the three age groups. Tiredness and shortness of

breath were reported in the top five common symptoms in all three cohorts. CYP in CLoCk and the 18- to 20-year-olds also reported headaches with test-positives reporting loss of smell and test-negatives reporting dizziness as one of the top five common symptoms, while the emerging adults in the present study and adults in the REACT-2 study reported unusual chest pain or tight chest as one of the top five common symptoms. Loss of smell was one of the most common symptoms experienced by test-positives in CLoCk and by emerging adults but not by test-negatives indicating this symptom may be a differentiating symptom for test-positives.

There are several strengths to this study. Firstly, participants were recruited nationally, not from a single site, increasing the generalisability of findings. Secondly, the assessment of SARS-CoV2 infection status was based on PCR testing and not self-reported as used in many other studies. Finally, the test-negative comparison group helped establish the impact of SARS-CoV-2 infection compared to living through a pandemic.

The study has some limitations. The response rate for the study was low (6.7%) and below that of the comparator studies (REACT-2: 30%, CLoCk: 13.4%). This may be due to the population of interest as previous research has identified low response rates amongst younger adults [40]. Additionally, it could be due to differences in study design and procedures, for example participants in CLoCk received two reminders inviting them to participate whereas 18- to 20-year-olds only received one invitation letter. Self-selection bias raises challenges with the generalisability of findings as it may be that those with symptoms were more likely to participate, which may explain the high prevalence of symptoms amongst the test-negative group. There may also be recall bias introduced because of the interval between testing and completing the questionnaire. Further differences in study design and methods employed in the comparison studies mean that our comparisons are exploratory and should be interpreted cautiously. In addition to these, the cross-sectional design provides a snapshot of symptoms experienced by this group and it was not possible to follow the trajectory of symptoms over time for individuals. This may be particularly important given that some of the symptoms have been reported to be intermittent, waxing and waning or appearing weeks to months after infection [37].

We found that, like their older and younger counterparts, a high proportion of emerging adults continue to experience symptoms in the months after a SARS-CoV-2 PCR test. Symptoms reported by emerging adults were similar to those experienced by CYP and adults in the wider literature. The high proportion of test-negative participants experiencing symptoms in the months after their PCR-test suggests there may be a considerable burden of living through a pandemic. A greater understanding of the symptoms that are specific to long COVID is required to better support those living with the condition.

Acknowledgments

Michael Lattimore, UKHSA, as Project Officer for the CLoCk study. Olivia Swann and Elizabeth Whittaker designed the elements of the ISARIC Paediatric COVID-19 follow-up questionnaire which were incorporated into the online questionnaire used in this study to which all the CLoCk Consortium members contributed.

Fiona Newlands (fiona.newlands.18@ucl.ac.uk) drafted the manuscript, conducted the statistical analyses for the manuscript,

accessed and verified the data and reviewed and edited the manuscript. Natalia K Rojas (n.rojas@ucl.ac.uk) conducted statistical analyses for the manuscript, accessed and verified the data and reviewed the manuscript. Manjula D Nugawela (manjula.nugawela@ucl.ac.uk) assisted the statistical analysis for the manuscript, accessed and verified the data, and reviewed the manuscript. Snehal M Pinto Pereira (snehal.pereira@ucl.ac.uk) designed and assisted the statistical analyses for the manuscript, accessed and verified the data and reviewed the manuscript. Marta Buszewicz (m.buszewicz@ucl.ac.uk) contributed to the design of the study and reviewed the manuscript. Trudie Chalder (trudie.chalder@kcl.ac.uk) contributed to the design of the study, reviewed the manuscript, and supervised the study. Emily Y Cheung (emily.cheung@kcl.ac.uk) contributed to the literature review and reviewed the manuscript. Emma Dalrymple (e.dalrymple@ucl.ac.uk) contributed to the design and reviewed the manuscript. Tamsin Ford (tjf52@medschl.cam.ac.uk) contributed to the design and reviewed the manuscript. Isobel Heyman (i.heyman@ucl.ac.uk) contributed to the design, reviewed the manuscript, and supervised the study. Shamez Ladhani (shamez.ladhani@phe.gov.uk) developed the study methodology and reviewed the manuscript. Kelsey McOwat (Kelsey.Mcowat@phe.gov.uk) accessed and verified the data and reviewed the manuscript. Ruth Simmons (Ruth.Simmons@phe.gov.uk) accessed and verified the data. Terence Stephenson (t.stephenson@ucl.ac.uk) conceived the idea for the study, submitted the successful grant application, and reviewed the manuscript and supervised the study. Roz Shafran (r.shafran@ucl.ac.uk) contributed to the design of the study, supervised the study, submitted the ethics and R&D applications, and reviewed the manuscript.

Funding sources

Funded by The Department of Health and Social Care, in their capacity as the National Institute for Health Research (NIHR), and by UK Research & Innovation who have awarded funding grant number COVLT0022. The Department of Health and Social Care, as the NIHR, and UKRI were not involved in study design, data collection, analysis or interpretation of the data, nor the writing of the present study or the decision to submit the article for publication. All research at Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health is made possible by the NIHR Great Ormond Street Hospital Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, UKRI or the Department of Health. SMPP is supported by a UK Medical Research Council Career Development Award (ref: MR/P020372/1). FN is funded by a Beryl Alexander Charity PhD studentship (Sponsor reference: W1168; Award number: 183885).

Supplementary Data

Supplementary data related to this article can be found at [10.1016/j.jadohealth.2023.01.026](https://doi.org/10.1016/j.jadohealth.2023.01.026).

References

- [1] Esakandari H, Nabi-Afjadi M, Fakkari-Afjadi J, et al. A comprehensive review of COVID-19 characteristics. *Biol Proced Online* 2020;22:19.
- [2] Viner RM, Ward JL, Hudson LD, et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. *Arch Dis Child* 2021;106:802–7.

- [3] World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1. Accessed July 18, 2022.
- [4] Ayoubkhani D, King S, Pawelek P. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 7 July 2022. 2022. Available at: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/7july2022>. Accessed July 26, 2022.
- [5] Wu Q, Ailshire J, Crimmins E. Long COVID and symptom trajectory in a representative sample of Americans. *Res Sq* 2022;12:11647.
- [6] Whitaker M, Elliott J, Chadeau-Hyam M, et al. Persistent COVID-19 symptoms in a community study of 606,434 people in England. *Nat Commun* 2022;31:1957.
- [7] Thompson EJ, Williams DM, Walker AJ, et al. Long COVID burden and risk factors in 10 UK longitudinal studies and electronic health records. *Nat Commun* 2022;13:3528.
- [8] Subramanian A, Nirantharakumar K, Hughes S, et al. Symptoms and risk factors for long COVID in non-hospitalized adults. *Nat Med* 2022;28:1706–14.
- [9] Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Arch Dis Child* 2020;106:429–39.
- [10] Stephenson T, Pinto Pereira SM, Shafran R, et al. Physical and mental health 3 months after SARS-CoV-2 infection (long COVID) among adolescents in England (LoCk): A national matched cohort study. *The Lancet Child Adolesc Health* 2022;6:230–9.
- [11] Asadi-Pooya AA, Nemati H, Shahsavandi M, et al. Long COVID in children and adolescents. *World J Pediatr* 2021;17:495–9.
- [12] Kikkenborg Berg S, Dam Nielsen S, Nygaard U, et al. Long COVID symptoms in SARS-CoV-2-positive adolescents and matched controls (Long-COVIDKidsDK): A national, cross-sectional study. *Lancet Child Adolesc Health* 2022;6:240–8.
- [13] Lopez-Leon S, Wegman-Ostrosky T, Ayuzo Del Valle NC, et al. Long-COVID in children and adolescents: A systematic review and meta-analyses. *Sci Rep* 2022;12:9950.
- [14] Maddux AB, Berbert L, Young CC, et al. Health impairments in children and adolescents after hospitalization for acute COVID-19 or MIS-C. *Pediatrics* 2022;150:e2022057798.
- [15] Behnood SA, Shafran R, Bennett SD, et al. Persistent symptoms following SARS-CoV-2 infection amongst children and young people: A meta-analysis of controlled and uncontrolled studies. *J Infect* 2022;84:158–70.
- [16] Sadler K, Vizard T, Ford T, et al. Mental Health of Children and Young People in England, 2017, Summary of key findings. Available at: <https://dera.ioe.ac.uk/32622/1/MHCYP%202017%20Summary.pdf>. Accessed November 10, 2021.
- [17] Groarke JM, Bery E, Graham-Wisener L, et al. Loneliness in the UK during the COVID-19 pandemic: Cross-sectional results from the COVID-19 Psychological wellbeing study. *PLoS One* 2020;15:e0239698.
- [18] Newlove-Delgado TMF, Williams T, Mandalia D, et al. Mental health of children and young people in England, 2022. Leeds: NHS Digital; 2022.
- [19] Nugawela MD, Stephenson T, Shafran R, et al. Predictive model for long COVID in children 3 months after a SARS-CoV-2 PCR test. *BMC Med* 2022;20:465.
- [20] von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Int J Surg* 2014;12:1495–9.
- [21] Stephenson T, Shafran R, De Stavola B, et al. Long COVID and the mental and physical health of children and young people: National matched cohort study protocol (the LoCk study). *BMJ Open* 2021;11:e052838.
- [22] Sigfrid L, Maskell K, Bannister PG, et al. Addressing challenges for clinical research responses to emerging epidemics and pandemics: A scoping review. *BMC Med* 2020;18:190.
- [23] Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–36.
- [24] Ng Fat L, Scholes S, Boniface S, et al. Evaluating and establishing national norms for mental wellbeing using the short Warwick-Edinburgh mental well-being scale (SWEMWBS): Findings from the health survey for England. *Qual Life Res* 2017;26:1129–44.
- [25] Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
- [26] Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med* 2006;166:1092–7.
- [27] Russell DW. UCLA loneliness scale (version 3): Reliability, validity, and factor structure. *J Pers Assess* 1996;66:20–40.
- [28] Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. *J Psychosom Res* 1993;37:147–53.
- [29] Plummer F, Manea L, Trepel D, et al. Screening for anxiety disorders with the GAD-7 and GAD-2: A systematic review and diagnostic metaanalysis. *Gen Hosp Psychiatry* 2016;39:24–31.
- [30] Hinz A, Klein AM, Brähler E, et al. Psychometric evaluation of the generalized anxiety disorder screener GAD-7, based on a large German general population sample. *J Affect Disord* 2017;210:338–44.
- [31] Fong TCT, Chan JSM, Chan CLW, et al. Psychometric properties of the Chalder fatigue scale revisited: An exploratory structural equation modeling approach. *Qual Life Res* 2015;24:2273–8.
- [32] Clarke A, Friede T, Putz R, et al. Warwick-Edinburgh mental well-being scale (WEMWBS): Validated for teenage school students in England and Scotland. A mixed methods assessment. *BMC Public Health* 2011;11:487.
- [33] Koushede V, Lasgaard M, Hinrichsen C, et al. Measuring mental well-being in Denmark: Validation of the original and short version of the Warwick-Edinburgh mental well-being scale (WEMWBS and SWEMWBS) and cross-cultural comparison across four European settings. *Psychiatry Res* 2019;271:502–9.
- [34] Feng Y-S, Kohlmann T, Janssen MF, et al. Psychometric properties of the EQ-5D-5L: A systematic review of the literature. *Qual Life Res* 2021;30:647–73.
- [35] Stephenson T, Allin B, Nugawela MD, et al. Long COVID (post-COVID-19 condition) in children: A modified Delphi process. *Arch Dis Child* 2022;107:674–80.
- [36] Ministry of Housing CLG. The english indices of deprivation. Available at: <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015>. Accessed December 1, 2022.
- [37] Amin-Chowdhury Z, Ladhani SN. Causation or confounding: Why controls are critical for characterizing long COVID. *Nat Med* 2021;27:1129–30.
- [38] Findlay SM. The tired teen: A review of the assessment and management of the adolescent with sleepiness and fatigue. *Paediatr Child Health* 2008;13:37–42.
- [39] Shevlin M, Butter S, McBride O, et al. Measurement invariance of the Patient health questionnaire (PHQ-9) and generalized anxiety disorder scale (GAD-7) across four European countries during the COVID-19 pandemic. *BMC Psychiatry* 2022;22:154.
- [40] Lallukka T, Pietiläinen O, Jäppinen S, et al. Factors associated with health survey response among young employees: A register-based study using online, mailed and telephone interview data collection methods. *BMC Public Health* 2020;20:184.