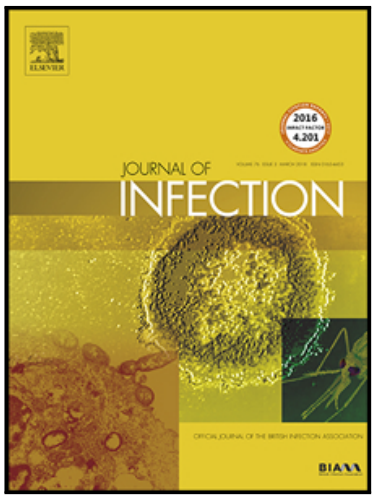

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Letter to the Editor | Letter to the Editor

The relationship between Post COVID symptoms in young people and their parents

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Dear Editor

We read with interest the recent study on risk factors for long COVID. (1) Similar risk factors, including female gender, older age and higher number of symptoms, have been reported in children and young people (CYP).(2) In England, the CLoCk study was established to investigate long COVID in a cohort of >30,000 CYP aged 11-17 years with PCR-confirmed SARS-CoV-2 infection and a contemporaneous PCR-negative group, matched by age, sex, geography and time.(3) Outcomes at 3 months follow-up have been published.(4) Anecdotal information suggested many CYP with ongoing symptoms had other household members symptoms after COVID-19. We hypothesised that CYP reporting long COVID were more likely to have a parent with ongoing symptoms.

We examined this in a subset of CLoCk participants who completed their six-month questionnaire after a positive or negative SARS-CoV-2 PCR-test between October 2020 and March 2021 (n=14,377). We excluded CYP with subsequent SARS-CoV-2 infections (48/6,878 PCR-positive at baseline, 317/7,499 PCR-negative at baseline), those who returned the questionnaire after 34 weeks (n=1,063) and those who did not answer the question of interest (n=161). The final sample included 12,788 CYP (6,334 PCR-positives, 6,454 PCR negatives).

The questionnaire included demographics, elements of the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) questionnaire,(4) 21 symptoms as well as the Strengths and Difficulties questionnaire (SDQ) (6) embedded within it, the EQ5D-

Y scale,(5) Short Warwick Edinburgh Mental Health Wellbeing scale (SWEMBS),(6) Chalder Fatigue Scale,(7) and the following question: "*Has COVID-19 affected family members (in your house): Does anyone have ongoing problems from Covid-19? If so, can you tell us who?*". We grouped responses as 'no', 'ongoing problems in parents', or 'other' if ongoing symptoms were reported in other family members or if the relationship was unclear (e.g., specific names given). The Delphi consensus research definition of long COVID adapted to CYP was used: experiencing ≥1 symptom AND problems with mobility, self-care, doing usual activities or having pain/discomfort or feeling very worried/sad, based on the EQ-5D-Y scale, at the time of questionnaire completion around 6 months after their PCR-test.(8) We assessed the association between on-going symptoms in CYP and their parents having on-going symptoms using a logistic regression model that adjusted for age, sex, deprivation (index of multiple deprivation [IMD] quintiles) and SARS-CoV-2 PCR-test status. All analyses were done in Stata v17.

Among test-positive CYP, 19.1% (1,207/6,334) reported having a parent with ongoing problems after COVID-19. In this group, the prevalence of long COVID six months post-test in CYP reporting a parent with ongoing problems was 33.3% (402/1,207) compared to 22.6% (1,156/5,127) in CYP who did not report parents having ongoing problems after COVID-19 (**Table**).

The same pattern, albeit with lower prevalence, was observed among SARS-CoV-2 PCR-negative CYP, where 5.5% (354/6,454) reported having parents with ongoing COVID-19 related symptoms. In this group, the prevalence of long COVID six months post-test in CYP reporting a parent with symptoms was 28.0% (99/354) compared to 17.3% (1,052/6,100) in CYP not reporting parents having ongoing symptoms (**Table**).

In the logistic regression model including age, sex and deprivation and SARS-CoV-2 status, CYP reporting parents with ongoing symptoms were 1.79-times (95% CI, 1.58-2.02) more likely to have long COVID at 6 months than CYP who did not report parents having ongoing symptoms, independently of age, sex, deprivation and SARS-CoV-2 PCR-test results. Notably, Chalder Fatigue Scale, SWEMBS and SDQ scores (for total difficulties as well as subscales) were broadly similar, irrespective of the CYP' SARS-CoV-2 PCR-status or parental ongoing symptom status (**Table**).

In summary, this association between having a parent with ongoing symptoms after COVID-19 and CYP experiencing long COVID 6 months after their SARS-CoV-2 test was present in test-positive and test-negatives CYP *albeit* at a lower prevalence among the latter. Possible explanations for the increased risk of long COVID in CYP with PCR-confirmed SARS-CoV-2 infection who reported parents with ongoing symptoms include exposure to an increased viral load when infected and shared genetic vulnerability to post-COVID syndrome, such as viral persistence. There could also be shared environmental and genetic factors related to pre-existing poor physical and mental health among both test positive and test negative participants, such as those arising from socioeconomic status, including higher living density which may increase exposure to viral shedding even in those testing negative.(9) Another explanation relevant to both groups might be an increased focus on symptoms among families with ongoing symptoms, potentially resulting in increased symptoms or reporting by their children. Additionally, this could result in proxy selection bias: parents with ongoing COVID-19 problems may have encouraged their children to participate in the study. The lack of substantial differences in mental health and wellbeing symptoms suggests that the increased risk of long COVID in CYP of parents with ongoing symptoms is not associated with the child's current mental wellbeing.

Strengths and limitations of the study methodology have been discussed previously.(4) Using a national dataset with PCR-confirmed test-positives and matched test-negatives is a strength of this analysis, highlighting the higher prevalence of symptoms in children of parents with ongoing problems independently of the children's own SARS-CoV-2 infection status. We excluded CYP who were (re)infected between their original PCR-test and questionnaire completion but acknowledge misclassification may still exist. Although CYP reported their own symptoms, there is a risk of selection bias as described above. Reporting bias might occur if children of parents with ongoing problems were hypervigilant regarding the same symptoms. Finally, we also have no information about the symptoms, duration or severity of on-going problems in parents.

In conclusion, we have identified an association between having a parent with ongoing problems after COVID-19 problems and long COVID at six months post-test in CYP, irrespective of their SARS-CoV-2 positivity status. At present, services for post-COVID syndromes are separate for adults and children. The importance of working with the family in CYP clinics is highlighted. There may be some benefit for integrated joint services focussing on holistic strategies and interventions for the whole family unit, as is currently in place for other infections such as viral hepatitis and HIV.

Ethical approval

The study was approved by Yorkshire and the Humber–South Yorkshire Research Ethics Committee (REC reference: 21/YH/0060; IRAS project ID: 293495). UKHSA has legal permission, provided by Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002, to process patient confidential information for national surveillance of communicable diseases. Individual patient consent is not required for initial invitation to the study.

Data availability

Data are sensitive and not publicly available. All requests for data will be reviewed by the Children & young people with LONG-COVID (CLoCk) study team, to verify whether the request is subject to any intellectual property or confidentiality obligations. Requests for access to the participant-level data from this study can be submitted via email to clock@ukhsa.gov.uk with detailed proposals for approval. A signed data access agreement with the CLoCK team is required before accessing shared data. Code is not made available as we have not used custom code or algorithms central to our conclusions.

Declaration of Competing Interest

TS is Chair of the Health Research Authority and therefore recused himself from the research ethics application. All other authors declare no competing interests.

Table 1. Number of CYP with LONG-COVID, number of symptoms and scores from the SDQ questionnaire, SWEMBS and Chalder fatigue scale six months post-test stratified by SARS-CoV-2 status and ongoing COVID-19 problmes in parents (number and percentages)

	CYP SARS-CoV-2 positive at baseline only (n=6,334)		**CYP SARS-CoV-2 negative since baseline (n=6,454)**	
	Parents with ongoing COVID-19 problems		**Parents with ongoing COVID-19 problems**	
	Yes	No	Yes	No
	1,207 (19.1%)	5,127 (80.9%)	354 (5.5%)	6,100 (94.5%)
LONG-COVID* in CYP				
Yes	402 (33.3%)	1,156 (22.6%)	99 (28.0%)	1,052 (17.3%)

No	805 (66.7%)	3,3971 (77.5%)	255 (72.0%)	5,048 (82.8%)
No of symptoms (CYP)				
0	363 (30.1%)	2,111 (41.2%)	163 (46.1%)	3,505 (57.5%)
1	221 (18.3%)	1,120 (21.9%)	56 (15.8%)	1,151 (18.9%)
2	179 (14.8%)	594 (11.6%)	30 (8.5%)	523 (8.6%)
3	130 (10.8%)	437 (8.5%)	25 (7.1%)	290 (4.8%)
4	95 (7.9%)	291 (5.7%)	20 (5.7%)	195 (3.2%)
5+	219 (18.1%)	574 (11.2%)	60 (17.0%)	436 (7.2%)
SDQ				
SDQ Total Difficulties				
Median	11	10	12	11
(25^{th}, 75^{th})	(7,16)	(6,15)	(2,18)	(6,16)
SDQ Emotional symptoms				
Median	4	3	4	3
(25^{th}, 75^{th})	(2,6)	(1,5)	(2,6)	(1,5)
SDQ Conduct problems				
Median	1	1	2	1
(25^{th}, 75^{th})	(0,2)	(0,2)	(1,3)	(0,2)
SDQ Hyperactivity/inattention				
Median (25^{th}, 75^{th})	4	4	4	4
	(2,6)	(2,6)	(2,6)	(3,6)
SDQ peer relationship problem				

Median	2	2	2	2
(25^{th}, 75^{th})	(1,3)	(1,3)	(1,3)	(1,3)
SWEMBS				
Median	21.5	21.5	20.0	20.7
(25^{th}, 75^{th})	(18.5,24.1)	(18.5,24.1)	(18.0,23.2)	(18.6,24.1)
Chalder fatigue scale				
Median	13	12	13	11
(25^{th}, 75^{th})	(11,15)	(11,18)	(11,17)	(11,15)

**Using data from the questionnaire on symptoms and the EQ-5D-Y scale at the time of the questionnaire (i.e., approximately 6 months after the PCR-test), LONG-COVID was operationalized as having at least 1 symptom and experiencing some/a lot of problems with respect to mobility, self-care, doing usual activities or having pain/discomfort or feeling very worried/sad.*

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