

Long COVID - the physical and mental health of children and non-hospitalised young people 3 months after SARS-CoV-2 infection; a national matched cohort study (The CLoCk) Study.

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Abstract

Introduction: We describe post-COVID symptomatology in a national sample of 11-17-year-old children and young people (CYP) with PCR-confirmed SARS-CoV-2 infection compared to test-negative controls.

Methods and analysis: A cohort study of test-positive (n=3,065) and age-, sex- and geographically-matched test-negative CYP (n=3,739) completed detailed questionnaires 3 months post-test.

Results: At PCR-testing, 35.4% of test-positives and 8.3% of test-negatives had any symptoms whilst 30.6% and 6.2%, respectively, had 3+ symptoms. At 3 months post-testing, 66.5% of test-positives and 53.3% of test-negatives had any symptoms, whilst 30.3% and 16.2%, respectively, had 3+ symptoms. Latent class analysis identified two classes, characterised by “few” or “multiple” symptoms. This latter class was more frequent among test-positives, females, older CYP and those with worse pre-test physical and mental health.

Discussion: Test-positive CYP had a similar symptom profile to test-negative CYP but with higher prevalence of single and, particularly, multiple symptoms at PCR-testing and 3 months later.

Introduction

Children and young people (CYP) are more likely to have a mild illness and less likely to be hospitalised following SARS-CoV-2 exposure compared to adults. More children¹ recover without sequelae compared to adults². However, we know little about the diagnosis, prevalence, phenotype or duration of Long COVID (also called long haulers and post-acute COVID syndrome) in CYP. More than 200 different symptoms have been associated with Long COVID^{3,4}, with an adult prevalence up to 80%⁵. Long COVID has been reported in those symptomatic or asymptomatic at time of SARS-CoV-2 testing, and in laboratory-confirmed or unconfirmed cases, with symptoms beginning at or after acute infection, which may be persistent, intermittent or relapsing in nature^{3,5}. Adolescents may have a higher risk than younger children^{1,6} but it is unclear whether the features associated with Long COVID are related to the viral infection or the effects of the pandemic, lockdown and school closures with consequent social isolation.

A literature review of Long Covid in CYP identified 17 relevant publications with sample size ≥ 10 (Supplementary Table 1). Existing studies were all observational, including cohort (n=9), matched cohort (n=2), and cross-sectional (n=6) designs. Clinical diagnosis of COVID-19 infection was confirmed by either a positive reverse transcription polymerase chain reaction (PCR) result or serological testing in 13 studies; the remaining studies included COVID-19 cases that were diagnosed clinically, were self-reported COVID-19, using rapid antigen tests or through an unspecified method of confirmation. These studies included 15,250 CYP up to 20 years with follow-up of 28 to 324 days. The most common persistent symptoms across studies were fatigue, insomnia, anosmia and headaches. The prevalence of Long

COVID in CYP with laboratory-confirmed or suspected COVID-19 ranged from 1%-51%, with smaller studies reporting higher prevalence rates.

An online, nationally-representative survey of 313,216 people asking about self-reported Long COVID (unexplained symptoms persisting for more than four weeks after suspected COVID-19) estimated the UK population Long COVID prevalence to be 0.14% for 2-11 years, 0.50% for 12-16 years, and 1.51% for 17-24 years⁶.

The mental health of CYP have received less attention than the physical symptoms of COVID-19, despite the significant negative impact of the pandemic on their wellbeing⁷. Miller, et al. ⁸ found 10% of children with Long COVID reported unspecified persistent psychological/psychiatric symptoms. However, no significant differences between depression, anxiety, and perceived stress were found comparing CYP with Long COVID to COVID negative controls⁹. Similarly, a study of 1,560 CYP (median age 15 years) found a high rate of neurocognitive, pain and mood symptoms but no difference between seronegative and seropositive participants, highlighting the importance of including a negative control group in longitudinal studies of Long COVID¹⁰.

The CLoCk study is a national, longitudinal cohort study of CYP in England¹¹ with the primary aim of describing the clinical phenotype and prevalence of post-COVID physical symptoms and mental health problems among CYP with laboratory-confirmed SARS-CoV-2 infection compared to test-negative controls, to identify those most at risk and their illness trajectory. This paper presents the results of the study 3 months after PCR-testing in CYP across England.

Methods

Design

A cohort study of SARS-CoV-2 PCR-positive CYP aged 11–17 years matched on month of test, age, sex and geographical area to SARS-CoV-2 test-negative controls selected from the database of test results held by Public Health England (PHE). Since the start of the pandemic in England, PHE receives daily electronic notifications of all SARS-CoV-2 PCR tests performed in healthcare settings (Pillar 1 tests) and in the community (Pillar 2 tests) reported through the Second Generation Surveillance System (SGSS). Information within the SGSS includes National Health Service (NHS) number, name, age, sex, postcode, date of sample, reporting laboratory and test result. PHE also has access to the electronic Patient Demographic Service (PDS), which contains the names, postal addresses and vital status (alive/dead) of all patients registered with the NHS.

Participants

Between September 2020 and March 2021, 234,803 young people aged between 11 and 17 years tested positive for SARS-CoV-2 in England. During the same period, there were 1,481,154 negative tests among this age-group from 1,203,996 CYP (some CYP had more than one negative test). Among those who tested negative, 76,689 individuals (100,154 tests) were excluded as they had a positive result before or (up to 31 March 2021) after their negative test. The 234,803 test-positive CYP were matched with some oversampling to negative CYP according to their age at test, gender, month of test, and lower super output area (geographical area of ~ 1500 people), resulting in 102,402 test-positive individuals and 147,561 matched, negative individuals. Using secure procedures, matched individuals were checked against the NHS PDS to exclude individuals who had died and to extract participants' postal addresses. 37 individuals were excluded because they had died since their COVID-19 test (6 test-positives, 31 test-negatives), while 11,193 test-positive individuals and 19,251 test-negative individuals were excluded because a residential address was not available. Finally, 246 young people were excluded because they were included in a previous pilot study. Following these exclusions, 91,016 test-positive CYP and 128,220 negative CYP were contacted. A letter was posted to all those selected, inviting them to take part in this study using an online link which provided them with details of the study, an option to consent online and complete a short recruitment questionnaire.

We began contacting individuals from April 2021 onwards. In this paper, we focus on those who were tested in January-March 2021 because only they could report symptoms 3 months post-test with minimal recall bias of symptoms at time of testing. For this group, a total of 50,846 individuals (23,048 test-positives, 27,798 test-negatives) were invited to participate (Fig. 1).

Sample size calculations

The original study design was based on the calculation that 5,000 participants (2,500 test-positives, 2,500 test-negatives) would have 80% power to detect at least a 4% difference in symptom frequency at 5% significance, if test-negative participants had a 34% prevalence (based on available data at the time from the sKIDs study¹²), accounting for attrition and possible lower baseline symptom prevalence. However, studying multiple symptoms and identifying risk factors for Long COVID requires a larger sample size. For this reason, we amended our calculations to invite all available participants in England (except those tested in December 2020 due to funding constraints at present)¹¹.

Data collection

Participants who were tested between January-March 2021 were contacted 3 months after testing. Following online informed consent, the CYP self-completed an online (or paper) questionnaire about their physical and mental health at the time of the original test ("baseline") and at the time of completing the questionnaire; younger CYP and CYP with special educational needs or disability could request the help of their carer. The completed questionnaires were returned at a median time of 14.9 weeks after testing

[25th ,75th centiles: 13.1, 18.9]. A total of 63 test-negative CYP reported having had a previous positive SARS-CoV-2 test and were excluded from analysis.

Measures

The first questionnaire sent to CYP included demographic characteristics, elements of the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) Paediatric COVID-19 follow-up questionnaire¹³ and the recent Mental Health of Children and Young people in England surveys (<https://tinyurl.com/NHSWave1FU>). The follow-up questionnaires were identical but did not include questions on demographic characteristics. They were designed together with ISARIC Paediatric Working Group to produce a harmonised data collection tool, to facilitate international comparisons regarding the risk factors and profile of Long COVID in CYP.

The elements taken from the ISARIC Paediatric COVID-19 follow-up questionnaire¹³ included questions about physical symptoms, particularly cough and fever (the main acute symptoms in non-hospitalised CYP)¹⁴ and gastrointestinal symptoms which were commonly reported in seropositive CYP¹⁵. Other symptoms which might manifest later in Long COVID (e.g., tiredness, headaches, myalgia etc.) were also included.

We asked CYP to rate their general physical and mental health before their SARS-CoV-2 test, in two separate questions using a 5 category Likert scale; in analyses we recoded these variables into two categories (very poor/poor/ok versus good/very good). To measure mental health and wellbeing, the Strengths and Difficulties Questionnaire (SDQ)¹⁶ was summarised into the total difficulties score that excluded the prosocial dimension, along with the short 7-item version of the Warwick Edinburgh Mental Wellbeing Scale (SWEMWBS)¹⁷. A higher SDQ total difficulties score is indicative of more problems, whereas a higher SWEMWBS score indicates a higher level of mental well-being. Quality of life/functioning was measured via the EQ-5D-Y¹⁸ and fatigue was measured by the 11-item Chalder Fatigue Questionnaire (CFQ)¹⁹.

Statistical methods

To assess the representativeness of our study participants we compared their demographic characteristics (sex, age, region of residence) to those of the target population. The participants' demographic characteristics, physical symptoms at "baseline", and physical symptoms, mental health status, well-being, quality of life/functioning, and fatigue 3-months post-test were compared by SARS-CoV-2 test status. We carried out comparisons separately by age-groups (11-15y vs. 16-17y) as the prevalence of Long COVID may vary by age (<https://tinyurl.com/ONSPrevalence0721>).

We used latent class analysis²⁰ to assess whether and how baseline and 3-month physical symptoms clustered among CYP, allowing for differential model parametrization by SARS-CoV-2 test status (while analysing the data jointly by test status but separately by time). The number of classes was selected by comparing the Bayesian Information Criteria. Predicted class membership was estimated and used to

assign CYP to their most likely class; this classification was then used to describe the characteristics of the latent classes.

As this is mainly a descriptive study, we do not report p-values for comparisons by SARS-CoV-2 test status. We do report estimates of latent class prevalence by SARS-CoV-2 test status, as well as their ratio, with confidence intervals computed using the delta method²¹. To assess the impact of potential response bias, we reweighted all symptom frequencies according to the age, sex, region and SARS-CoV-2 test status of the responders.

Results

Study representativeness

A total of 6,804 CYP who had been tested between January and March 2021 participated in the study by completing the 3-month questionnaire. The overall response rate was 13.4%, with a similar proportion of test-positives (13.3%) and test-negatives (13.5%) contributing (Table 1). More females and older CYP (16-17-year-olds) responded. Response rates also varied by region of England. Overall, there was little difference in demographic characteristics between test-positive and test-negative participants, reflecting the matched study design (Table 2).

Physical symptoms and profile: baseline and 3-month post-test

At the time of testing, test-positive CYP had higher percentages of physical symptoms compared to test-negative CYP (Table 3); 35.4% of test-positives and 8.3% of test-negatives had any symptoms whilst 30.6% of test-positives and 6.2% of test-negatives had 3+ symptoms. The types of symptoms reported by test-positives and negatives were the same in the two age-groups: the most common symptoms among test-positives were sore throat, headache, tiredness and loss of smell while test-negatives had sore throat, headache, fever and persistent cough. The prevalence of these symptoms, however, varied by SARS-CoV-2 test result (e.g. 26.3% of positives compared to 4.8% of negatives reported headaches).

Three months after the SARS-CoV-2 test, the presence of physical symptoms was higher than at baseline in both groups; 66.5% of test-positives and 53.4% of test-negatives had any symptoms whilst 30.3% of test-positives and 16.2% of test-negatives had 3+ symptoms. The symptom profile did not vary by age: for both 11-15y and 16-17y the most common symptoms among test-positives were tiredness, headache and shortness of breath and, among test-negatives, tiredness, headache and the unspecified category of "other". Again, the prevalence of tiredness and headache was consistently higher in the test positives, 39.0% and 23.2% versus 24.4% and 14.2% in negatives, respectively. Prevalence was higher for 16-17-

year-olds; for example, 46.4% of test-positives reported being tired compared to 29.6% of test-negatives. When we reweighted the percentage of reported symptoms at baseline and at 3 months post-test, broadly similar patterns were observed to those reported above (Supplementary Table 2).

Mental health, well-being, quality of life/functioning and fatigue 3-month post-test

There was no difference in the distribution of mental health scores (assessed by the SDQ total difficulties scores) and well-being (assessed by SWEMBS) between test positives and negatives, overall or in either age-group. The SDQ median (25th,75th centile) was 10 (6,15) for both test-positive and test-negative CYP aged 11-15y. For CYP aged 16-17y, the corresponding values were 11 (7,16) for test-positives and 12 (8,16) for test-negatives. Likewise, SWEMBS scores were similar among test-positives (Mean=21.5, SD=4.3) and test-negatives (Mean=21.4, SD=4.3). Similarly, fatigue (assessed by CFQ) showed no substantial differences between positives (Mean=13.3, SD=5.2) and negatives (Mean=12.5, SD=5.1). However, older CYP (16-17y) did report slightly higher values: test-positives (Mean=14.0, SD=5.5) and test-negatives (Mean=13.4, SD=5.2). In terms of Health-Related Quality of Life (EQ-5D-Y) test positives in both age groups were more likely to report problems with mobility, doing usual activities, and pain/discomfort (Supplementary Figure 1). Strikingly, while 40.8% of positives felt worried, sad or unhappy on the single item of the EQ-5D-Y, 39.2% of the negatives also reported feeling this way (Supplementary Figure 1).

Physical symptom clustering at baseline and 3-months post-test

No evidence of clustering of baseline symptoms was found for either test-positive or test-negative participants. There was, however, evidence of clustering in symptoms reported at 3 months, with two subgroups emerging for both test-positive and test-negative CYP (Figure 2). In each, the largest subgroup (class 1) had very low prevalence of most symptoms, while the second subgroup (class 2) was characterised in both positives and negatives by multiple symptoms dominated by tiredness, headache, shortness of breath and dizziness. We refer to these classes as “few” and “multiple” symptoms classes. The estimated probability (risk) of being in the multiple symptom class (class 2) was 29.6% (95% confidence interval, 27.4%, 31.7%) for test-positives and 19.3% (17.7%, 21.0%) for test-negatives and the risk ratio of being in class 2 versus class 1 comparing test-positives to test-negatives was 1.53 (1.35, 1.70).

For both test-positive and test-negative CYP, those assigned to class 2 were more likely to be female, older, to have poorer baseline physical and mental health (relative to the overall percentages of 19% and 30%) and, at 3-months, to be more likely to have problems with mobility, self-care, usual activities and pain/discomfort. They also have higher SDQ total difficulties and CFS scores, and lower SWEMBS scores (Table 4).

Discussion

Given that there is no universally agreed definition of Long COVID, we elected not to start with an arbitrary definition of a new condition but to seek the descriptions from almost 7,000 CYP of their physical and mental experiences in the months following a SARS-CoV-2 test. This is the largest study on symptoms post-COVID in children to date and, uniquely, uses child-reported symptoms, is confined to PCR-proven SARS-CoV-2 status, has a PCR-negative control group, and uses standardised measures to assess mental health, well-being, and fatigue.

Several important findings contribute to the current knowledge of Long COVID in CYP. First, three months after the SARS-CoV-2 test, the presence of physical symptoms was higher than at the time of testing. This finding emphasises the importance of having a comparison group to objectively interpret the findings and derive prevalence estimates. Although 64.6% of test-positives reported no symptoms at time of testing (compared to 91.7% of test-negatives), they did not continue to remain asymptomatic, with only 33.5% of test-positives (and 46.7% of test-negatives) reporting no symptoms at 3 months. This finding warrants further exploration and could be due to self-selection into the study because they were experiencing ongoing symptoms, recall bias, external factors relating to the pandemic such as returning to school and exposure to other sources of infection, and the actual trajectory of the illness, although this wouldn't explain the high prevalence among test-negative CYP.

Second, symptoms reported at time of testing among test-positives were sore throat, headache, tiredness and loss of smell while test-negatives had sore throat, headache, fever and persistent cough. The symptom profile does not distinguish test-negatives and test-positives. However, the two groups could be separated according to the number of symptoms at three months, when 30.3% of test-positives and 16.2% of test-negatives had 3+ symptoms, with tiredness and headache being common in both groups, but higher in the test-positives. Consideration of number of symptoms, rather than profile, is particularly important given that 53.3% of the test-negatives had at least one symptom 3 months post-test. These figures should be seen in the context of published norms. For example, high levels of fatigue have been reported in the general adolescent population with an estimated incidence of 30% in CYP aged 11–15 over a 4-6-month pre-pandemic period²².

Third, our findings showed that, for both test-positives and test-negatives, those assigned to the latent class with “multiple symptoms” at three months were more likely to be female, older and have poorer physical and mental health before COVID-19, suggesting that pre-existing physical and mental health difficulties may influence symptoms at three months. Unsurprisingly, those with multiple physical

symptoms had poorer mental health, reflecting the close relationship between physical and mental health.

Fourth, whilst the prevalence of physical symptoms differed between test-positives and test-negatives, no differences were found in mental health, wellbeing and fatigue scores. The scores on the measures are broadly comparable to pre-pandemic published norms on the standardised measures^{23,24}(<https://sdqinfo.org/norms/UKNorm1.pdf>). However, a large proportion (~ 40%) in both groups reported feeling worried, sad or unhappy. This is consistent with parent-reported surveys of mental health of CYP during the pandemic²⁵ and highlights the need for mental health interventions²⁶ for parents and CYP regardless of COVID status. The findings emphasise the importance of incorporating a comparator matched cohort of test-negative CYP who have contemporaneously experienced a pandemic, school closure and social isolation.

Despite a need to estimate Long COVID prevalence in CYP, this first requires an evidence-based case definition²⁷. Our findings indicate that any definition of Long COVID should consider multiple symptoms and, as in adult studies on Long COVID, there may be different clusters of symptoms²⁸. Given our findings of multiple, varied symptoms three months after infection, it seems a multi-component intervention will be required, building on existing interventions for management of problems such as headache and fatigue.

Our findings should be seen alongside the CYP literature. The commonest symptoms reported at three months in test-positives of tiredness, headache, shortness of breath, dizziness and anosmia are consistent with Molteni, et al.¹ where parents reported symptoms ≥ 28 days (fatigue 84%, headache 80% and anosmia 80%). They also reported that persistent symptom prevalence was higher in girls, teenagers and children with long-term conditions. The ONS survey⁶ describes population prevalence rates of persisting 'symptoms more than 4 weeks after COVID-19' whereas the present study gives rates in a test-positive population; hence apparent differences may be attributable to differences in definitions and methodology.

Taking the studies together, there is consistent evidence that some teenagers will have persisting symptoms after testing positive for SARS-CoV-2 and that mental and physical health symptoms are closely related. Avoiding false dichotomies between mind and body is likely to be helpful as, for example, stressed individuals may present with somatic symptoms or conversely persisting physical symptoms may be associated with depression and anxiety. Some individuals may develop somatic symptoms disorders²⁹ and the existing evidence for effective management of conditions such as pain, headache and fatigue³⁰ might be usefully evaluated in CYP presenting with persistent physical symptoms post-COVID. CYP with clinically impaired mental health should receive the appropriate evidence-based treatments whether or not they have physical symptoms. Family approaches and understanding of persistent symptoms is key³¹. Investigation of persisting symptoms may be needed or requested, with

consideration of the potentially negative impact of protracted medical treatments or investigations if no abnormalities are found²⁹.

This study has limitations. PCR-testing can result in some false negative and false positive results and we were unable to independently determine whether the test-negatives had previously had COVID unless they had been tested although this is likely to account for only a minority of cases. We could not recruit based on ethnicity as this was not recorded at time of test but ethnicity was very similar in test-positives and negatives (Table 2) and geographical region served as a proxy for socio-economic status; both these variables are thought to influence COVID in adults and could be important in Long COVID³². As in any self-selected online study, we need to acknowledge our response rate of 13.5%. It is possible that there is a response bias for example, towards those continuing to experience symptoms at 3 months being more motivated to participate, resulting in an over-representation of symptom prevalence. It is also possible that recall bias influenced the reporting of symptoms at the time of testing as well as physical and mental health prior to testing, in particular, if tested positive. However, we tried to minimize the impact of this bias by only considering CYP that reported on baseline ~ 3m later. We did not assess whether symptoms were continuous for the entire 3 months, or whether they waxed and waned. Finally, the experiences of the CYP in January, February and March were likely to be highly varied with regard to school closure. At the time of testing, schools were closed, while, at 3 months after testing, schools had reopened albeit with social distancing, repeated testing and restriction of activities. Schools can be a source of both stress and support, and the return to school may partly explain some of the findings, in particular, the higher prevalence of symptoms at 3 months compared to baseline. The responders are largely representative of our target population though we have over-representation of girls and older CYP, with under-representation from North-West England and London. Inclusion of the comparator group was essential to place the findings within the wider context of the pandemic.

These data also reflect symptomatology at a time when the Alpha variant was predominant in the UK. Whilst these findings may change with different variants, the prospective nature of this study makes it uniquely placed to detect such changes across the pandemic waves.

In summary, post-COVID is different in CYP to adults and one should not extrapolate from the adult literature to decide policy and services for CYP. Our research demonstrates (1) the importance of having a control, test-negative group to interpret findings and prevalence estimates, (2) that it is essential to consider multiple symptoms in any clinical phenotype of Long COVID, (3) that mental and physical health symptoms should both be considered, (4) PCR-proven SARS-CoV-2 positive CYP had a higher frequency of any symptoms and multiple symptoms three months post-test than test-negatives. These results would have been very difficult to interpret without a control group and laboratory-confirmed SARS-COV-2 status. Hence, prevalence estimates and definitions of Long COVID should consider the presence of multiple symptoms, proven SARS-COV-2 status and include control groups. We will use these data and a Delphi consensus process to formulate a research definition of long COVID in CYP and will follow up the CYP over time to understand the long-term course in SARS-CoV-2 positive CYP.

This paper does not provide an evidence base for management of Long COVID or for any infective/immunological mechanisms underlying it. More research is needed.

Declarations

Acknowledgement: Michael Lattimore, Public Health England, as Project Officer for the CLoCk study

Author contributions:

Terence Stephenson t.stephenson@ucl.ac.uk conceived the idea for the study, submitted the successful grant application and drafted the manuscript.

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Lauren O'Mahoney lom1@leicester.ac.uk contributed to the scoping review of the literature.

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Shamez Ladhani shamez.ladhani@phe.gov.uk developed the study methodology, operationalised the regulatory and recruitment ideas for the study and revised the manuscript.

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.

All members of the CLoCk Consortium made contributions to the conception or design of the work; were involved in drafting both the funding application and this manuscript; approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests statement: 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 NICE committee for Long COVID. She has written self-help books on chronic fatigue and has conducted workshops on chronic fatigue and post infectious syndromes.

Data availability statement: 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@phe.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.

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

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Tables

Table 1. Response rate of participants who completed the 3-month questionnaire by sex, age and area of residence at time of testing, overall and stratified by SARS-CoV-2 status.

SARS-CoV-2 Status		Target Population	Study Participants
		N	N % of Target Population
Overall		50,846	6,804 13.4
Negative	All	27,798	3,739 13.5
	Sex		
	Female	15,120	2,352 15.6
	Male	12,678	1,387 10.9
	Age (y)		
	11-15	16,341	2,147 13.1
	16-17	11,457	1,592 13.9
	Region		
	East Midlands	2,132	340 15.9
	East of England	4,278	630 14.7
	London	5,356	629 11.7
	North East	925	122 13.2
	North West	3,816	426 11.2
	South East	4,262	620 14.5
	South West	1,554	293 18.9
	West Midlands	3,414	431 12.6
	Yorkshire and the Humber	2,061	248 12.0
Positive	All	23,048	3,065 13.3
	Sex		
	Female	12,412	1,945 15.7
	Male	10,636	1,120 10.5
	Age (y)		
	11-15	13,630	1,721 26.0
	16-17	9,418	1,344 14.3
	Region		
	East Midlands	1,815	297 16.4
	East of England	3,392	466 13.7
	London	4,412	510 11.6
	North East	819	111 13.6
	North West	3,235	371 11.5
	South East	3,496	483 13.8
	South West	1,238	238 19.2
	West Midlands	2,854	373 13.1
	Yorkshire and the Humber	1,787	216 12.1

Table 2. Frequencies (and percentages) of participants who completed the 3-month questionnaire by sex, age, ethnicity and area of residence at time of testing, overall and stratified by SARS-CoV-2 status.

	All participants		SARS-CoV-2 Negative		SARS-CoV-2 Positive	
	N	%	N	%	N	%
All	6,804	100.0	3,739	100.0	3,065	100.0
Female	4,297	63.2	2,352	62.9	1,945	63.5
Age (years)						
11-15	3,868	56.8	2,147	57.5	1,721	56.1
16-17	2,936	43.2	1,592	42.6	1,344	43.9
Ethnicity						
White	5,035	74.0	2,804	75.0	2,231	72.8
Asian/Asian British	1,011	14.9	520	13.9	491	16.0
Mixed	342	5.0	195	5.2	147	4.8
Black/African/Caribbean	249	3.7	140	3.7	109	3.6
Other	115	1.7	55	1.5	60	2.0
Unknown	52	0.8	25	0.7	27	0.9
Region						
East Midlands	637	9.4	340	9.1	297	9.7
East of England	1,096	16.1	630	16.9	466	15.2
London	1,139	16.7	629	16.8	510	16.6
North East	233	3.4	122	3.3	111	3.6
North West	797	11.7	426	11.4	371	12.1
South East	1,103	16.2	620	16.6	483	15.8
South West	531	7.8	293	7.8	238	7.8
West Midlands	804	11.8	431	11.5	373	12.2
Yorkshire and the Humber	464	6.8	248	6.6	216	7.1

Table 3. Number and percentage of reported symptom(s) at the time of test and at the 3 months questionnaire by SARS-CoV-2 status, overall and stratified by age-group.

	All participants				Age: 11-15				Age: 16-17			
	SARS-CoV-2 Negative		SARS-CoV-2 Positive		SARS-CoV-2 Negative		SARS-CoV-2 Positive		SARS-CoV-2 Negative		SARS-CoV-2 Positive	
	N	%	N	%	N	%	N	%	N	%	N	%
ii	3,739	100.0	3,065	100.0	2,147	100.0	1,721	100.0	1,592	100.0	1,344	100.0
Time of test												
no reported symptoms	3,430	91.7			1,954	91.0	1,157	67.2	1,476	92.7	824	61.3
1-2 symptoms	78	2.1	1,981	64.6	59	2.8			19	1.2	55	4.1
			148	4.8			93	5.4				
3-4 symptoms	88	2.4			55	2.6			33	2.1	81	6.0
			210	6.9			129	7.5				
5+ symptoms	143	3.8			79	3.7			64	4.0	384	28.6
			726	23.7			342	19.9				
Specific symptoms												
Fever	148	4.0	548	17.9	91	4.2	271	15.8	57	3.6	277	20.6
Chills	91	2.4	461	15.0	49	2.3	224	13.0	42	2.6	237	17.6
Persistent cough	143	3.8	476	15.5	82	3.8	224	13.0	61	3.8	252	18.8
Tiredness	125	3.3	696	22.7	71	3.3	331	19.2	54	3.4	365	27.2
Shortness of breath	56	1.5	354	11.6	25	1.2	150	8.7	31	2.0	204	15.2
Loss of smell	55	1.5	631	20.6	29	1.4	301	17.5	26	1.6	330	24.6
Unusually hoarse voice	41	1.1	145	4.7	22	1.0	69	4.0	19	1.2	76	5.7
Unusual chest pain	57	1.5	280	9.1	25	1.2	119	6.9	32	2.0	161	12.0
Unusual abdominal pain	44	1.2	138	4.5	27	1.3	71	4.1	17	1.1	67	5.0
Diarrhoea	41	1.1	166	5.4	24	1.1	71	4.1	17	1.1	95	7.1
Headaches	178	4.8	806	26.3	108	5.0	417	24.2	70	4.4	389	28.9
Confusion, disorientation or drowsiness	29	0.8	225	7.3	11	0.5	91	5.3	18	1.1	134	10.0
Unusual eye-soreness	30	0.8	185	6.0	16	0.8	83	4.8	14	0.9	102	7.6
Skipping meals	67	1.8	360	11.8	32	1.5	159	9.2	35	2.2	201	15.0
Dizziness or light-headedness	86	2.3	462	15.1	43	2.0	206	12.0	43	2.7	256	19.1
Sore throat	200	5.4	687	22.4	122	5.7	351	20.4	78	4.9	336	25.0
Unusual strong muscle pains	45	1.2	338	11.0	22	1.0	154	9.0	23	1.4	184	13.7

Earache or ringing in ears	41	1.1	155	5.1	16	0.8	69	4.0	25	1.6	86	6.4
Raised welts on skin or swelling	7	0.2	35	1.1	5	0.2	19	1.1	2	0.1	16	1.2
Red/purple sores/blisters on feet	9	0.2	21	0.7	8	0.4	12	0.7	1	0.1	9	0.7
Other	17	0.5	73	2.4	13	0.6	38	2.2	4	0.3	35	2.6

	All participants				Age: 11-15				Age: 16-17			
	SARS-CoV-2 Negative		SARS-CoV-2 Positive		SARS-CoV-2 Negative		SARS-CoV-2 Positive		SARS-CoV-2 Negative		SARS-CoV-2 Positive	
	N	%	N	%	N	%	N	%	N	%	N	%

At time of 3-month questionnaire	N	%	N	%	N	%	N	%	N	%	N	%
0 reported symptoms	1,746	46.7	1,027	33.5	1,056	49.2	645	37.5	690	43.3	382	28.4
1-2 symptoms	1,390	37.2	1,110	36.2	779	36.3	618	35.9	611	38.4	492	36.6
3-4 symptoms	365	9.8	517	16.9	184	8.6	257	14.9	181	11.4	260	19.4
5+ symptoms	238	6.4	411	13.4	128	6.0	201	11.7	110	6.9	210	15.6

Specific symptoms	N	%	N	%	N	%	N	%	N	%	N	%
Fever	55	1.5	50	1.6	29	1.4	21	1.2	26	1.6	29	2.2
Chills	192	5.1	269	8.8	119	5.5	154	9.0	73	4.6	115	8.6
Persistent cough	98	2.6	98	3.2	57	2.7	56	3.3	41	2.6	42	3.1
Tiredness	911	24.4	1,196	39.0	440	20.5	572	33.2	471	29.6	624	46.4
Shortness of breath	388	10.4	717	23.4	198	9.2	321	18.7	190	11.9	396	29.5
Loss of smell	51	1.4	414	13.5	23	1.1	205	11.9	28	1.8	209	15.6
Unusually hoarse voice	46	1.2	56	1.8	25	1.2	30	1.7	21	1.3	26	1.9
Unusual chest pain	129	3.5	216	7.1	70	3.3	101	5.9	59	3.7	115	8.6
Unusual abdominal pain	107	2.9	119	3.9	54	2.5	64	3.7	53	3.3	55	4.1
Diarrhoea	80	2.1	92	3.0	45	2.1	53	3.1	35	2.2	39	2.9
Headaches	530	14.2	710	23.2	281	13.1	376	21.9	249	15.6	334	24.9
Confusion, disorientation or drowsiness	123	3.3	198	6.5	66	3.1	101	5.9	57	3.6	97	7.2
Unusual eye-soreness	134	3.6	182	5.9	69	3.2	88	5.1	65	4.1	94	7.0

Skipping meals	275	7.4	296	9.7	132	6.2	135	7.8	143	9.0	161	12.0
Dizziness or light-headedness	314	8.4	419	13.7	169	7.9	202	11.7	145	9.1	217	16.2
Sore throat	281	7.5	291	9.5	147	6.9	181	10.5	134	8.4	110	8.2
Unusual strong muscle pains	83	2.2	165	5.4	45	2.1	77	4.5	38	2.4	88	6.6
Earache or ringing in ears	165	4.4	191	6.2	96	4.5	108	6.3	69	4.3	83	6.2
Raised welts on skin or swelling	32	0.9	48	1.6	16	0.8	28	1.6	16	1.0	20	1.5
Red/purple sores/blisters on feet	40	1.1	35	1.1	23	1.1	21	1.2	17	1.1	14	1.0
Other	590	15.8	335	10.9	369	17.2	199	11.6	221	13.9	136	10.1

Table 4. Characteristics of CYP assigned to each latent class, by SARS-CoV-2 status

	SARS-CoV-2 test Negatives (N=3,739)		SARS-CoV-2 test Positives (N=3,065)	
	Class 1	Class 2	Class 1	Class 2
	%	%	%	%
All	80.7	19.3	70.4	29.6
Baseline				
Sex				
Male	88.5	11.5	82.4	17.6
Female	79.0	21.0	65.9	34.1
Age (years)				
11-15	84.0	16.0	75.3	24.7
16-17	80.6	19.4	67.7	32.3
Previous physical health				
Very poor/poor/OK	71.9	28.1	62.8	37.2
Good/v Good	85.8	14.2	74.8	25.2
Previous mental health				
Very poor/poor/OK	72.3	27.7	60.4	39.6
Good/v Good	88.8	11.2	79.2	20.8
At 3 months				
EQ5DY*:				
Mobility	62.0	38.0	37.5	62.5
Self-care	62.2	37.9	40.3	59.7
Usual activities	59.2	40.8	40.3	59.7
Pain/discomfort	50.2	49.8	35.4	64.6
Feeling worried	69	31	55.4	44.6
SDQ total difficulties				
Median (25 th , 75 th)	10 (6,14)	16 (11,20)	9 (6, 14)	15 (10, 19)
SWEMBS				
Median (25 th , 75 th)	21.5 (19.3,24.1)	18.6 (16.9,21.5)	21.5 (19.3,25.0)	19.3 (17.4,22.4)
Mean (SD)	21.9 (4.4)	19.1 (3.7)	22.1 (4.3)	20.0 (3.9)
Chalder fatigue scale				
Median (25 th , 75 th)	11 (10,14)	16 (12,20)	11 (11,14)	17 (13,21)
Mean (SD)	11.6 (4.5)	16.4 (6.0)	11.8 (4.2)	17.0 (5.7)

*Some/a lot of problems with mobility (e.g. walking about), self-care (e.g. washing/dressing) or doing usual activities (e.g. going to school); some/a lot of pain/discomfort or a bit/very worried, sad or unhappy.

SD: standard deviation

Figures

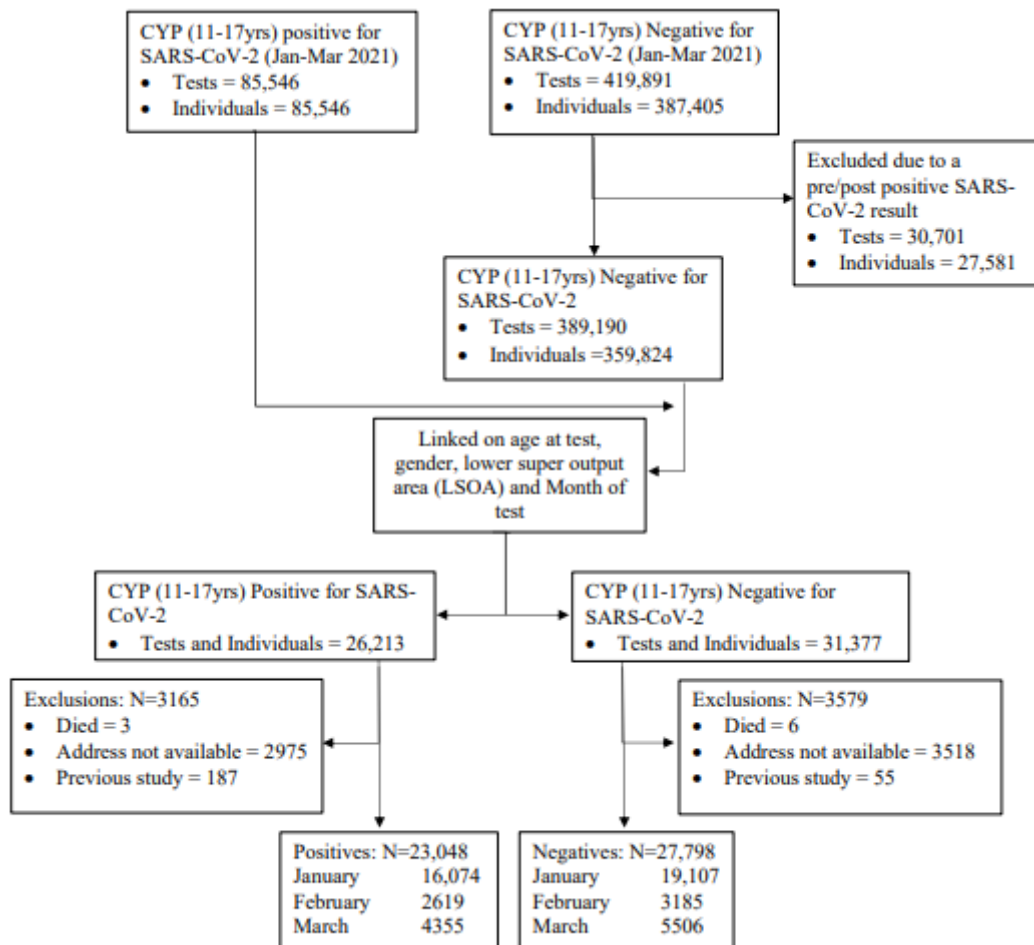
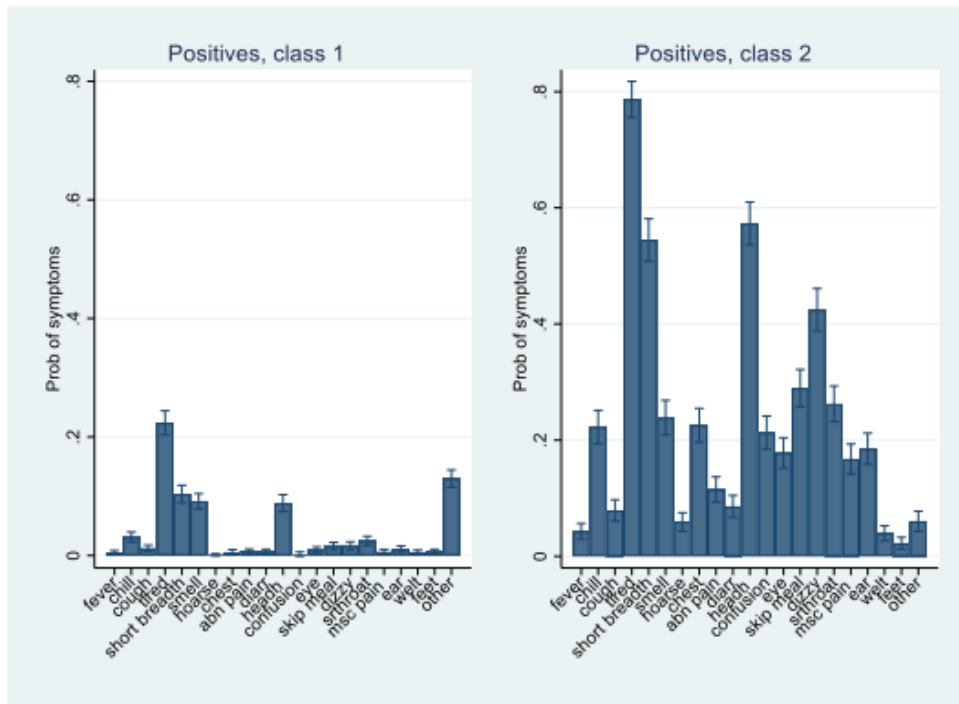


Figure 1

Flowchart of young people invited to participate in the Study.

(a) Positives



(b) Negatives

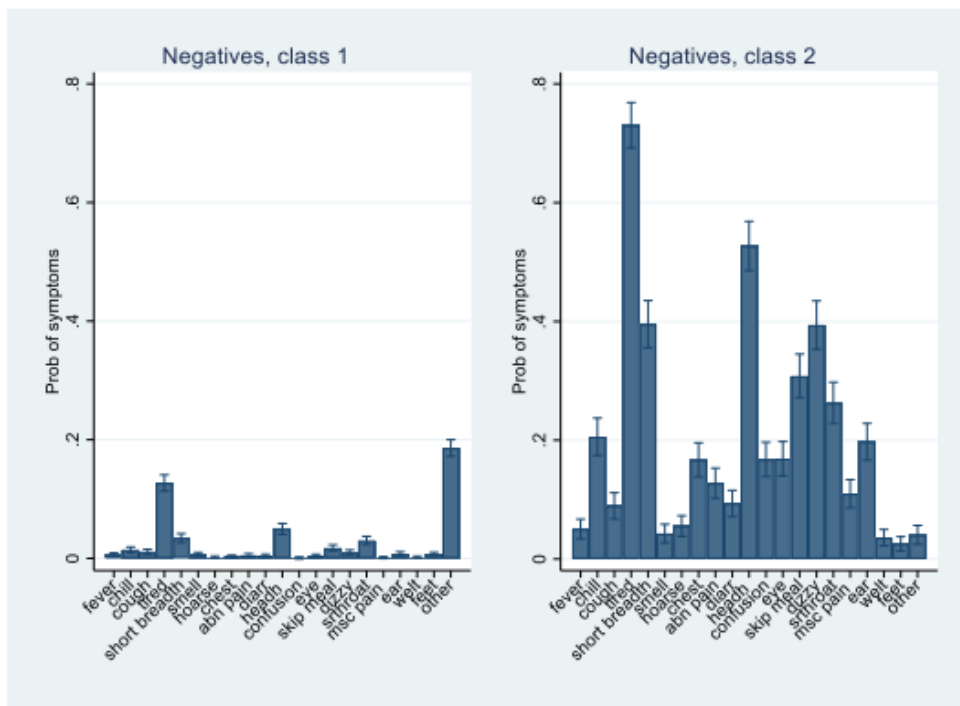


Figure 2

(a) Latent classes of symptoms at 3 months in SARS-CoV-2 test positive CYP; (b) Latent classes of symptoms at 3 months in SARS-CoV-2 test negative CYP. BIC for 1-class solution for the two test groups: 66,743.600; BIC for 2-class solution for the two test groups: 58,991.627 ; no convergence for the 3-class model

Supplementary Files

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