Characteristics and predictors of persistent symptoms post-COVID-19 in children and young people: a large community cross-sectional study in England

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ABSTRACT
Objective To estimate the prevalence of, and associated risk factors for, persistent symptoms post-COVID-19 among children aged 5–17 years in England.

Design Serial cross-sectional study.

Setting Rounds 10–19 (March 2021 to March 2022) of the REal-time Assessment of Community Transmission-1 study (monthly cross-sectional surveys of random samples of the population in England).

Study population Children aged 5–17 years in the community.

Predictors Age, sex, ethnicity, presence of a pre-existing health condition, index of multiple deprivation, COVID-19 vaccination status and dominant UK circulating SARS-CoV-2 variant at time of symptom onset.

Main outcome measures Prevalence of persistent symptoms, reported as those lasting ≥3 months post-COVID-19.

Results Overall, 4.4% (95% CI 3.7 to 5.1) of 3173 5–11-year-olds and 13.3% (95% CI 12.5 to 14.1) of 6886 12–17-year-olds with prior symptomatic infection reported at least one symptom lasting ≥3 months post-COVID-19, of whom 13.5% (95% CI 8.4 to 20.9) and 10.9% (95% CI 9.0 to 13.2), respectively, reported their ability to carry out day-to-day activities was reduced ‘a lot’ due to their symptoms. The most common symptoms among participants with persistent symptoms were persistent coughing (27.4%) and headaches (25.4%) in children aged 5–11 years and loss or change of sense of smell (52.2%) and taste (40.7%) in participants aged 12–17 years. Higher age and having a pre-existing health condition were associated with higher odds of reporting persistent symptoms.

Conclusions One in 23 5–11-year-olds and one in eight 12–17-year-olds post-COVID-19 report persistent symptoms lasting ≥3 months, of which one in nine report a large impact on performing day-to-day activities.

INTRODUCTION
Compared with adults, children and young people (CYP) are more likely to be asymptomatic or develop mild, transient symptoms following SARS-CoV-2 infection,1 and life-threatening illness and death from COVID-19 are rare.2 However, like adults, CYP who have been infected with SARS-CoV-2 may experience persistent, postacute symptoms, which may last for many months.2,3 Frequently termed ‘long COVID’ or ‘post-COVID-19 condition’, recently published systematic reviews indicate that most studies have been conducted in adults.4–7

The most common persistent symptoms post-COVID-19 reported across existing studies in CYP are headaches, fatigue, insomnia and anosmia.8–11 However, estimates of symptom persistence vary substantially ranging from 1% to 51%, arguably due to heterogeneous study designs, follow-up periods and definitions.8–17 A recent meta-analysis of five controlled studies in CYP found that the frequency of the majority of reported persistent symptoms was similar in SARS-CoV-2 positive cases and SARS-CoV-2 negative controls. Small but significant increases in the pooled risk difference

WHAT IS ALREADY KNOWN ON THIS TOPIC
The most common persistent symptoms post-COVID-19 reported across existing studies in children are headaches, fatigue, insomnia and anosmia. However, symptom persistence estimates in children post-COVID-19 vary substantially from 1% to 51% due to heterogeneous study designs, variable follow-up periods and differing definitions.

WHAT THIS STUDY ADDS
In England at some point since the start of the pandemic until the end of March 2022, 4.4% of 5–11-year-olds and 13.3% of 12–17-year-olds with prior symptomatic infection had persistent symptoms for 3 months or more following COVID-19. Approximately one in nine of these children reported a large impact in their ability to carry out day-to-day activities due to their symptoms. The most common persistent symptoms were coughing, headaches and loss or change of sense of smell or taste.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
This study shows that persistent symptoms post-COVID-19 are multiple and varied. These findings have implications for researchers, clinicians and affected families in understanding the prevalence and manifestation of long COVID in children and young people.

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were observed for loss of smell (8%), headaches (5%), cognitive difficulties (3%) and sore throat and eyes (2% each). Here, we use data from the REAct-time Assessment of Community Transmission-1 (REACT-1) study to estimate the prevalence of, and associated risk factors for, persistent symptoms post-COVID-19 among CYP aged 5–17 years in England.

METHODS

Study design and participants

During each round of the REACT-1 study, a random subset of the population (over 5 years old) of England was chosen from the National Health Service (NHS) general practitioner’s list and invited to participate in the study. There was a round of the study approximately monthly from May 2020 to March 2022, with each round of data collection including between 15 000 and 35 000 participants aged 5–17 years. The study protocol aimed to achieve approximately equal sample sizes from each lower tier local authority (n=315). Individuals who agreed to participate provided a self-administered throat and nose swab (parent/guardian administered for those aged 5–12 years old) which included information on demographic variables, recent symptoms, whether or not they thought that they had had COVID-19 and whether or not they had had a previous PCR test. From round 10, participants were asked about persistent symptoms related to previous COVID-19 and severity and duration of these symptoms. These included a set of 30 clinically relevant symptoms potentially related to COVID-19. The questionnaires used and a table showing the sampling dates and response rates for REACT-1 are available on the study website.

Data analysis

We estimated the prevalence of persistent symptoms at 3 months post-symptom onset in individuals with a history of COVID-19. We included all self-reported prior COVID-19 episodes including test confirmed and suspected but not confirmed. We only included those who reported onset of COVID-19 ≥3 months prior to the date of the survey and for whom we had complete data. We reported persistent symptoms by age, sex, ethnicity, presence of a pre-existing health condition, index of multiple deprivation (IMD), COVID-19 vaccination status and dominant UK circulating SARS-CoV-2 variant at time of symptom onset. A valid COVID-19 vaccine dose was defined as a date of vaccination 14 days or more prior to COVID-19. The wild-type strain was dominant in the UK prior to December 2020. Alpha dominated between December 2020 and April 2021 followed by delta (May 2021 to mid-December 2021) and omicron (late December 2021 onwards). To estimate background prevalence of symptoms, we used data on history of any of 26 symptoms lasting 11 or more days (that were present within the 7 days prior to questionnaire completion) for children aged 5–17 years who had a negative PCR test in the REACT-1 study. The data were weighted by sex, age, ethnicity, lower tier local authority population and IMD to take account of the sampling design and differential response rates to obtain prevalence estimates that were representative of the 5–17 year-old population of England.

We used logistic regression to quantify the associations of age, sex, ethnicity, presence of a pre-existing health condition, IMD, COVID-19 vaccination status and dominant UK circulating SARS-CoV-2 variant at time of symptom onset with persistence of symptoms at 3 months or more. ORs and 95% CIs were estimated.

Results

Of 191 593 REACT-1 participants aged 5–17 years, 78 948 (41.2%) did not attempt the questionnaire. Of those (or parent/guardian) who completed the questionnaire, 111 444/112 645 (98.9%) reported whether the individual had previously had COVID-19 or not (online supplemental figure S1). Differential non-response was observed by age, sex, ethnicity and deprivation (online supplemental table S1), similar to non-response characteristics of REACT-1 overall. Of participants reporting a COVID-19 episode, 10 059/22 169 (45.4%) reported a valid date of symptom onset ≥3 months before their survey date, providing our denominator population for estimates of persistent symptoms. Table 1 shows the key characteristics of these participants.

The cumulative prevalence of reported COVID-19 increased from 11.4% (5–11 years: 9.7% and 12–17 years: 13.2%) in Round 10 (March 2021) to 48.2% (5–11 years: 51.6% and 12–17 years: 46.9%) in Round 19 (March 2022). Figure 1 shows how the epidemic in CYP evolved between January 2020 and March 2022.

Prevalence of persistent symptoms

Overall, 4.4% (95% CI 3.7 to 5.1; 138/3173) of 5–11-year-olds and 13.3% (95% CI 12.5 to 14.1; 913/6886) of 12–17-year-olds symptomatic at infection had one or more persistent symptoms (from a list of 30 surveyed symptoms) for ≥3 months (table 1, online supplemental figure S2). Of which, 11.2% (95% CI 9.4 to 13.3) reported their ability to carry out day-to-day activities was reduced “a lot” due to their symptoms (table 2). Among 123 468 REACT-1 PCR-negative individuals, average weighted prevalence of any of 26 symptoms lasting 11 or more days was 2.2% (95% CI 2.1 to 2.3) and 2.6% (95% CI 2.5 to 2.7) in those aged 5–11 and 12–17 years, respectively (online supplemental figure S3).

Factors associated with persistent symptoms

Older children with prior symptomatic infection were three times more likely to report persistent symptoms compared with 5–11-year-olds with prior symptomatic infection, adjusted OR 3.4 (95% CI 2.8 to 4.0) (figure 2). Persistent symptoms post-COVID-19 were higher in those with pre-existing health conditions compared with those without (5–11 years: OR 2.6 (95% CI 1.8 to 3.9); 12–17 years: OR 2.0 (95% CI 1.7 to 2.3)) (figure 2). In 12–17-year-olds, being male, Asian ethnicity and living in more affluent areas were associated with lower odds of persistent symptoms (figure 2). Persistent symptoms in children aged 12–17 years were higher in those infected when delta (OR 1.6; 1.3–1.8) was the dominant SARS-CoV-2 variant circulating in the UK population compared with when the original wild-type strain was dominant earlier in the pandemic (figure 2). With regards to COVID-19 vaccination, persistent symptoms post-COVID-19 were lower in 12–17-year olds with at least one valid vaccine dose compared with those without (OR 0.74 (95% CI 0.52 to 1.04)) (figure 2, online supplemental table S2). However, this was not statistically significant at the 5% level.

Symptom profiles

The most common symptoms among participants with persistent symptoms were persistent coughing (27.4%; 95% CI 20.5 to
35.6) and headaches (25.4%; 95%CI 18.6 to 33.6) in children aged 5–11 years and loss or change of sense of smell (52.2%; 95%CI 48.9 to 55.5) and taste (40.7%; 95%CI 37.5 to 44.0) in participants aged 12–17 years (figure 3, online supplemental table S3).

**DISCUSSION**

In this community-based study in England among children aged 5–17 years with prior COVID-19 and 3 months’ observation time, the prevalence of persistent symptoms for ≥3 months (from a list of 30 clinically relevant symptoms potentially related to COVID-19) was 4.4% and 13.3% in children aged 5–11 years and 12–17 years, respectively. This compares with a background prevalence of symptoms in PCR test negative participants in REACT-1 of 2.2% and 2.6% in 5–11 and 12–17-year-olds, respectively. Our prevalence estimates of persistent symptoms in children post-COVID-19 are therefore approximately twofold and fivefold the background prevalence in children aged 5–11 and 12–17 years, respectively.

This is one of the few studies to provide prevalence estimates of persistent symptoms post-COVID-19 in 5–11-year-olds lasting ≥3 months and to report on how symptoms reduce ability to carry out day-to-day activities and what level of medical care is being accessed for these symptoms. Previous studies in England have focused on older children (CLoCk study: 11–17 years old\(^9\)\(^{24}\)) or on persistent symptoms lasting >28 days (COVID Symptom Study\(^8\)). The COVID Symptom Study found that 4.4% of UK school-aged children (aged 5–17 years) with COVID-19 still reported symptoms at 28 days.\(^5\) The UK Office for National Statistics (ONS) estimated 7.4% of those aged 2–11 years and 8.2% of those aged 12–16 years still reported symptoms at 12 weeks.\(^6\) The CLoCk study reported 66.5% of 11–17-year-olds who tested SARS-CoV-2 positive had symptoms at 3 months, compared with 53.3% in negative controls.\(^9\)\(^{24}\) These estimates are much higher than our study. There are several potential explanations for this. First, they limited their study to 11–17-year-olds, among whom persistent symptoms are higher.\(^6\) Second, participation bias if more CLoCk non-responders had no symptoms compared with the study population. This is possible as participants recruited to REACT-1 were not approached with the specific aim of studying persistent symptoms and were offered PCR testing that could have incentivised participation more universally. Third, CLoCk is a prospective longitudinal study, therefore subject to less recall bias. Finally, differences in study period. Our study looked across a longer timeframe during the pandemic with a mixture of the wild-type alpha and delta variants, whereas CLoCk focused on infections during a period when alpha predominated in the UK.\(^5\) There are differences in the nature of the virus, for example, we know that alpha is more infectious and more likely to be associated with hospitalisations.
than the original wild-type variant. This may translate into more cases of long COVID. In addition, the rate of continuing post-COVID-19 symptoms might vary between variants.

Recently, a Delphi research definition for post-COVID-19 condition in CYP has been developed, ‘Post-COVID-19 condition occurs in young people with a history of confirmed SARS-CoV-2 infection, with one or more persisting physical symptoms 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-19 infection, and may fluctuate or relapse over time.’ Despite collecting information on how persistent symptoms

Figure 1  Reconstruction of epidemic curve from study participants with valid date of symptom onset alongside cumulative prevalence of reported COVID-19 and official case numbers for England reported by the UK Government. (A) Number of reported COVID-19 episodes by month in REACT-1 (solid black line: 5–11 year-olds/solid grey line: 12–17 year-olds) (left y-axis) alongside cumulative prevalence of reported COVID-19 by month in which REACT-1 study round was completed (dotted black line: 5–11 year-olds/dotted grey line: 12–17 year-olds) (right y-axis). (B) Number of test positive COVID-19 cases by month in England (solid dark grey line). Data from UK Government website. Shading (dominant SARS-CoV-2 variant): yellow: wild type; green: alpha; blue: delta; white: omicron. a=17 585: asymptomatic individuals and symptomatic participants whose date of COVID-19 was unknown are excluded; b=27 035: individuals reporting a history of COVID-19; c widespread testing for SARS-CoV-2 only became available in the UK from April 2020. REACT-1, Real-time Assessment of Community Transmission-1.
Impact day-to-day activities, we only had information on symptomatic SARS-CoV-2 infections. The research definition of long COVID in CYP includes all confirmed SARS-CoV-2 infection (symptomatic and asymptomatic). Therefore, our estimates are likely higher and not directly comparable with studies applying this definition.

Few studies have reported on measures of association between key characteristics and persistent symptoms lasting ≥3 months in CYP. We show that increasing age and reporting a pre-existing health condition were associated with higher odds of persistent symptoms following COVID-19, consistent with other studies in children. Persistent symptoms in children aged 12–17 years were higher in those infected during the Delta period compared with the original wild-type period earlier in the pandemic. This association is temporal to a large extent as delta was circulating later in the pandemic and therefore may be confounded by the number of previous infections, information on which was not collected as part of our study. A recent case–control study conducted in the UK found a lower odds of long COVID with the omicron versus the delta variant, ranging from OR 0.2 (95% CI 0.2 to 0.3) to 0.5 (95% CI 0.4 to 0.6), suggesting that the risk of long COVID may vary by variant.

Strengths and limitations
This study included data from a large random community sample, thus providing representative information on persistent COVID-19 symptoms in children with prior symptomatic infection in the community. The REACT-1 response rate in 5–17-year-olds was low (14.9%), with questionnaire response rate at 6.0%. This was lower than questionnaire response rates of the CloCK and ONs studies, with 11.2% and 12%, respectively. Similar to these studies, our participants were more likely to be female, older teenagers, white ethnicity, from the southeast (less likely to be from London or the North West) and were more likely to be from the least deprived areas. In contrast to the CloCK study, our participants were broadly more similar to the England population aged 5–17 years, reflecting the random population sampling design on supplemental table S4.

We used information regarding presence of symptoms rather than whether participants described themselves as having ‘long COVID’ to reduce potential reporting bias. However, the retrospective study design introduces the possibility of recall bias. In addition, we included all self-reported prior COVID-19 episodes including test confirmed and suspected but not confirmed, which introduces the possibility of misclassification bias. When we limited the analysis to test confirmed COVID-19 episodes, the prevalence of persistent symptoms for ≥3 months was higher compared with the prevalence in suspected COVID-19 episodes (5–11 year-olds: 5.1% vs 3.7%, 12–17 year-olds: 16.0% vs 8.6%), and the magnitude and direction of associations between sociodemographic factors and persistent symptoms were similar (online supplemental tables S5 and S6). However, given the limited availability of testing early in the pandemic, it was necessary to include suspected cases. Reassuringly, our epidemic curve produced from participant reported symptom onset date closely tracked the epidemic (figure 1).

A major limitation is the lack of a SARS-CoV-2 negative control group which makes it hard to separate symptoms due to SARS-CoV-2 infection from those caused by normal life, other infections, or the pressures of a pandemic. REACT-1 was originally designed as a surveillance study to provide reliable and timely prevalence estimates of SARS-CoV-2 infection in the community to inform the immediate public health response and so we did not collect baseline information on symptom profiles at the time of symptom onset in those with a history of COVID-19, nor did we collect comparable data on participants with no history of COVID-19. Therefore, our estimates may partly reflect the large list of symptoms we surveyed, many of which are common and not specific to COVID-19. We estimated background prevalence of persistent symptoms to be 2.2% and 2.6% in 5–11 and 12–17 year-olds, respectively. These provide upper bounds for non-COVID-19 related prevalence of persistent symptoms at 3 months or more.
CONCLUSION

One in 23 children aged 5–11 years and 1 in 8 individuals aged 12–17 years have persistent symptoms lasting ≥3 months post-COVID-19. Persistent symptoms were multiple and varied with approximately one in nine children reporting a large impact in ability to carry out day-to-day activities due to their symptoms. Our study contributes to a growing evidence base regarding the

Figure 2

Logistic regression models with one or more symptoms at 3 months (y/n) as the binary outcome variable, adjusted odds ratios (dot) and 95% CIs (line) presented separately for participants aged 5–11 years (black) and 12–17 years (grey), n=10059. *Mutually adjusted for age, sex, ethnicity, IMD, comorbidities, vaccination status (over 12 year-olds only) and dominant variant at time of infection. No vaccination status estimate provided for children aged 5–11 years because only 5–11 year-olds with certain health conditions, or those with a weakened immune system were being offered vaccination during the study period and no participant aged 5–11 years in our study cohort reported having been vaccinated.

Figure 3

Percentage of individual symptoms among participants with persistent symptoms at 3 months or more post-COVID-19 onset for whom we have 3-month follow-up and complete data, n=1051.
prevalence, risk factors and characteristics of long COVID in children.

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Contributors
CJA, HW, GSC and PE conceptualised and designed the study, coordinated and supervised data collection, drafted the initial manuscript and critically reviewed and revised the manuscript. MW, CA and MC-H carried out the initial analyses, and critically reviewed and revised the manuscript. SR, WB, AD and DA conceptualised and designed the study and critically reviewed and revised the manuscript for important intellectual content. HW is guarantor.

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Competing interests
None declared.

Patient consent for publication
Not applicable.

Ethics approval
Research ethics approval was obtained from the South Central-Berkshire B Research Ethics Committee (IRAS ID: 283787). Participants gave informed consent to participate in the study before taking part.

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Data availability statement
Data are available on reasonable request. Deidentified individual participant data (including data dictionaries) will be made available, in addition to study protocols, the statistical analysis plan and the informed consent form. The data will be made available on publication to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to: react.lc.study@imperial.ac.uk.

Supplemental material
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REFERENCES