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Long COVID in children

Authors' reply

We thank Sammi Mcfarland and colleagues and Deepti Gurdasani and colleagues for their interest in our Article.

The Office for National Statistics (ONS) have now updated and corrected their earlier estimates reporting symptom prevalence 4–8 weeks post-infection, and they are consistent with ours: 3.3% in primary-school aged children and 4.6% in secondary-school aged children, with a matched control group symptom prevalence of 3.6% in primary-school aged children and 2.9% in secondary-school aged children.^{1,2}

We openly acknowledged that our cohort is not fully representative of the UK population; hence we compared demographic data with the UK population (presented in the appendix of the Article).³ Gurdasani's statement of "only 25% of cases had data logged" is not strictly correct—these were cases fulfilling pre-hoc defined inclusion and exclusion criteria, which allowed accurate duration calculation.

Both Correspondence pieces suggested our symptom assessment was limited. Our 19 symptoms encompassed all commonly reported, and some rarer, COVID-19 symptoms (including the most commonly reported symptoms in the ONS and CLOCK studies⁴). Although some symptoms (brain fog, low mood) were not explicitly asked in all 1734 children, the median durations in the 1439 (83%) children who were explicitly asked were extremely short (1–2 days each) and are therefore unlikely to change our overall results. Free text provided an opportunity to detect symptoms unique to children; no such symptoms emerged. We are mindful of Bradford-Hill criteria 3 (specificity); considering the approximately 200 symptoms reported with COVID-19 or Long-COVID:⁵ suggesting that not all of these symptoms are causally related.⁶

We disagree that proxy-logging via smartphone is laborious, noting here the high assiduousness (mostly

daily) and persistence (>90%) of proxy-reporting. We share concern that proxy-logging cessation before a healthy report might affect results, hence our sensitivity analyses, which included counting all children who had symptoms for at least 4 weeks (LC28) even if logging subsequently ceased, and estimates remained within confidence intervals. When discontinuation occurred, it was mostly at a time concomitant with median illness duration. If all 161 early-cessation children ultimately had LC28, our estimates would increase. However, if LC28 rates were proportionate to the more than 90% of children logged until healthy, seven extra LC28 cases would result, giving LC28 rates of 84 (4.8%) of 1734 children, which is still within our confidence intervals.

We allowed for up to a week of logging as asymptomatic (or healthy) within a child's total illness duration, a choice which was informed by the following: (1) this threshold was as previously published;⁷ (2) the median duration of illness in children with COVID-19 is less than 7 days; and (3) as wellness periods lengthen between illness episodes it becomes increasingly difficult to attribute with clinical confidence later episodes of illness to initial infection. Here, standardising post-COVID syndromes definitions in children will help future research.

We disagree with Gurdasani and colleagues that our estimates are seven-fold lower than the CLOCK study. The CLOCK study⁴ reported 66.5% positively tested and 53.4% negatively tested children had at least one symptom for 3 months post-infection, a risk ratio of 1.25, an extremely modest risk. If we use the same criteria, at 4 weeks our risk ratio was 5.1. Importantly, both CLOCK⁴ and the ONS⁵ showed high symptom prevalence in children testing negative, presumably capturing both effects of other illnesses and the pandemic.

We reiterate our conclusion that "a holistic approach for all children with persistent illness during the pandemic

is appropriate", irrespective of whether the illness is caused by SARS-CoV-2.³

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- Office for National Statistics. Technical article: Updated estimates of the prevalence of post-acute symptoms among people with coronavirus (COVID-19) in the UK: 26 April 2020 to 1 August 2021. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/technicalarticleupdatedestimatesoftheprevalenceofpostacute symptomsamongpeoplewithcoronaviruscovid19intheuk/26april2020to1august2021> (accessed Nov 1, 2021).
- Ayoubkhani D. How common is long COVID? That depends on how you measure it. <https://blog.ons.gov.uk/2021/09/16/how-common-is-long-covid-that-depends-on-how-you-measure-it/> (accessed Oct 4, 2021).
- Molteni E, Sudre CH, Canas LS, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. *Lancet Child Adolesc Health* 2021; **5**: 708–18.
- Public Health England, UCL. Children and young people with long COVID. 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/977177/Children_and_young_people_with_Long_Covid_CLoCK_.pdf (accessed Nov 4, 2021).
- Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine* 2021; **3**: 101019.
- Hill AB. The environment and disease: association or causation? *Proc R Soc Med* 1965; **58**: 295–300.
- Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nat Med* 2021; **27**: 626–31.