Letter in response to Molteni *et al*. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2, The Lancet Child & Adolescent Health, 2021.

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In their article,[1] Molteni et al. reported that 1.8% of children testing positive for SARS-CoV-2 have symptoms beyond 56 days. Given important methodological limitations, we believe their results are likely a significant underestimate. In addition to limitations already highlighted by the authors, including the lack of representativeness of Zoe app users[1], and the impact of response biases, (only 25% of cases had data logged) [1,2] we discuss three other key limitations here.

First, only a limited number of symptoms reported in long COVID were assessed[1], with other Molsymptoms only captured if parents entered them as free text. Given that logging of symptoms regularly is laborious, this is likely to underestimate persisting symptoms for longer periods of time. Some important symptoms, such as 'brain fog' and low mood, were added to the list only later in the study, and not included in the main illness profile analysis, despite being reported in 11%, and 15% of older children, respectively.[1]

Second, the study did not account adequately for the well-known relapsing and remitting nature of long COVID.[3] Children with any gap in symptoms longer than one week were excluded,[1] so children whose symptoms temporarily resolved for more than a week and then recurred, were not counted.[1]

Third, the duration estimates for long COVID are based on parents either reporting their child as asymptomatic with no symptoms for a week, or the last symptomatic report if parents stopped using the app.[1] Using cessation of proxy-logged symptom data to signal resolution is unlikely to be valid. The drop off in reporting for many parents could instead be related to ongoing illness in children and the demands of managing it. Indeed, incomplete reporting was higher for children with confirmed infection (10.6%) compared to children who had tested negative (3.5%).[1] A much higher proportion ceased logging symptoms while still having ongoing symptoms (28.6% among those reporting symptoms for >28 days compared to 9.7% for those reporting <28 days). This affects both the duration and prevalence estimates of long COVID. Given these data are likely missing not at random, excluding them (as in the authors' sensitivity analysis) is also biased, underestimating the symptom duration.

Collectively, these factors all introduce bias in a single direction, namely to underestimate the incidence and duration of long COVID. Given all factors, this underestimation might be substantial, which could partly explain why Molteni et al.'s estimates are at least 7 times lower than those of the than in a recently published prospective large-scale study that allowed for remitting and relapsing symptoms, with follow up at 3 months (**Table 1**), [4] but similar to other studies that were limited in systematic assessment of common symptoms of long COVID.[5,6,7]

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Table 1: Summary of long COVID prevalence studies in children

	CLoCk study[4]	**ONS study[5]**	**Buonsenso et al.[8]**	**Miller et al. [7]**	**Radke et al. [6]**	**Molteni et al. [1]**
Study design	Case-control study, England	Community-based sampling from the UK	Community-based, Italy.	Household cohort, England and Wales,	55 randomly selected schools, Switzerland	Symptom based survey using Zoe symptom tracker app
Representativeness	More females and older children (16-17-yr-olds) responded	Sampled, and weighted to be representative of UK population	Convenience sample. Children with severe neuro-cognitive impairment excluded	Non-representative, higher socio-economic status	Randomly sampled schools	Poor representation of ethnic minorities. Higher SES
Case ascertainment	SARS-CoV-2 test positive between Jan 2021 and March 2021 and test-negative controls	Asymptomatic and symptomatic PCR positivity	PCR positivity	PCR positivity and serology	Positive serology	Symptom based, PCR positivity
Sample size	23,048 cases, and 27,798 controls	3,403 2-16 yr old with positive PCR test)	129 <=18 years PCR positive > 30 days prior	4,678 (175 with confirmed infection)	1,355 (109 seropositive)	1,734 (PCR or LFD positive) and 1,734 controls
Response rate	13.4%	Unclear	Unclear, convenience sample	Unclear	54%	25%
Symptoms assessed directly	20 symptoms	(1)12 symptoms, and (2) self-reported persistent symptoms	41 (Assessment by paediatricians)	Open ended only	?8 (unclear)	19 symptoms + free text
Prevalence among infected	At 3 months: 66.5 (any symptoms) 30.3% (3+ symptoms)	One or more of 12 symptoms At 5 weeks: 3.8% (2-11 yrs) 4.8% (12-16 yrs) At 12 weeks: 0.7% (2-11 yrs) 1.2% (12-16 yrs)	<=18 years 42.6% at >60 days	<=17 year olds 4.6% at 4 weeks	In 6-16 year olds: 9.4% at 4 weeks 3.7% at 12 weeks	In 5-17 year olds: 4% at 4 weeks, 1.8% at 12 weeks

		Self-reported long COVID At 4 weeks: 1.9% (2-11 yrs) 4.7% (12-16 yr) At 12 weeks: 1.7% (2-11 yrs) 5.7% (12-16 yr)				
Prevalence in controls	53.3% (any symptoms) 16.2% (3+ symptoms)	At 5 weeks: 2.1% (2-11 yrs) 1.1% (12-16 yrs)	No control group	<=17 year olds 1.7% at 4 weeks	In 6-16 year olds: 9.7% at 4 weeks 2.2% at 12 weeks	In 5-17 year olds: 0.9% at 4 weeks
Gaps allowed	Waxing and waning allowed. No criteria for gaps.	2 consecutive follow ups without symptoms	Unspecified	Unspecified- relapsing and remitting symptoms considered	Unclear in reported methodology	1 week
Follow up	Retrospective: 3 months after positive or negative test	Weekly up to 4 weeks, and monthly up to a year.	Assessed on average 5.4 months later.	Retrospective – recall from February 2020.	Retrospective: 5-7 months previously.	Up to 5 months, Last report considered symptom resolution.
Comments on biases	Test negatives may have had other viral illnesses, recall bias, poor response rate (direction of bias depends on whether healthy individuals more or less likely to have participated)	Limited number of symptoms assessed, recall bias, asymptomatic acute infections assessed. Likely underestimate	Possible overestimation, retrospective, lack of controls, ascertainment of cohort unclear, possible selection bias and recall bias.	Likely underestimate Non-representative, retrospective, misclassification bias, no direct assessment of symptoms.	Likely underestimate Misclassification due to serological testing, retrospective nature, recall bias, and limited symptoms reporting.	Likely underestimate Non-representative, poor response, common symptoms not assessed, relapsing and remitting nature not considered.