



Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year

Clare Smith ^{1,2}✉, David Odd ^{3,4}, Rachel Harwood ^{5,6}, Joseph Ward ⁷, Mike Linney^{8,9}, Matthew Clark ¹, Dougal Hargreaves ¹⁰, Shamez N. Ladhani^{11,12}, Elizabeth Draper¹³, Peter J. Davis ^{1,2}, Simon E. Kenny ^{1,5,6}, Elizabeth Whittaker ^{14,15}, Karen Luyt ⁴, Russell Viner ⁷ and Lorna K. Fraser ¹⁶

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is rarely fatal in children and young people (CYP, <18 years old), but quantifying the risk of death is challenging because CYP are often infected with SARS-CoV-2 exhibiting no or minimal symptoms. To distinguish between CYP who died as a result of SARS-CoV-2 infection and those who died of another cause but were coincidentally infected with the virus, we undertook a clinical review of all CYP deaths with a positive SARS-CoV-2 test from March 2020 to February 2021. The predominant SARS-CoV-2 variants were wild-type and Alpha. Here we show that, of 12,023,568 CYP living in England, 3,105 died, including 61 who were positive for SARS-CoV-2. Of these deaths, 25 were due to SARS-CoV-2 infection (mortality rate, two per million), including 22 due to coronavirus disease 2019—the clinical disease associated with SARS-CoV-2 infection—and 3 were due to pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. In total, 99.995% of CYP with a positive SARS-CoV-2 test survived. CYP older than 10 years, Asian and Black ethnic backgrounds and comorbidities were over-represented in SARS-CoV-2-related deaths compared with other CYP deaths. These results are important for guiding decisions on shielding and vaccinating children. New variants might have different mortality risks and should be evaluated in a similar way.

Identifying CYP at risk of severe illness and death after SARS-CoV-2 infection is essential to guide families, clinicians and policymakers about future shielding policies, school attendance, novel therapeutic agents and vaccine prioritization.

SARS-CoV-2 infection is usually mild and asymptomatic in CYP^{1–3}. Therefore, CYP have comprised a very low proportion of all hospitalizations and deaths from coronavirus disease 2019 (COVID-19) globally⁴. The clinical manifestations of COVID-19 in CYP are different than those in adults¹. Although many CYP present with the typical fever, cough and shortness of breath, they also present with broader non-specific symptoms, including abdominal pain, nausea, headache and sore throat^{1,3}. This, in combination with a mild or asymptomatic phenotype², provides a challenge for describing how SARS-CoV-2 directly affects CYP.

Severe illness and death associated with SARS-CoV-2 in CYP is rare and can be due to either acute COVID-19 or pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS)^{2,5}. PIMS-TS, also called multisystem inflammatory syndrome in children, is a rare syndrome characterized by persistent fever, inflammation (neutrophilia, lymphopenia

and raised C-reactive protein) and evidence of single- or multi-organ dysfunction that might occur concurrently or after infection⁶. As death from acute COVID-19 or PIMS-TS in CYP is extremely rare^{4,7,8}, those who have died have been poorly characterized⁹. Furthermore, it remains unclear to what extent these rare deaths relate directly to the pathological processes of COVID-19 or whether CYP who died from alternative causes were coincidentally positive for SARS-CoV-2 around the time of death. This issue is made more difficult by the very high prevalence of asymptomatic infection at times of high prevalence, with reported prevalence up to 4–6% of United Kingdom CYP during December 2020 (ref. ¹⁰). The distinction between those who died of SARS-CoV-2 infection and those who died of an alternative cause with a coincidental positive SARS-CoV-2 test is important for understanding which CYP are truly at higher risk for severe disease or death.

Answering this important question required detailed examination of all deaths in a large population, going beyond simple cause of death registration, to review the contribution of SARS-CoV-2 to death. We used detailed clinical data in the National Child Mortality Database (NCMD)¹¹, which is a comprehensive and unique mandatory

¹NHS England and NHS Improvement, London, UK. ²Paediatric Intensive Care Unit, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK. ³Division of Population Medicine, Cardiff University, Cardiff, Wales, UK. ⁴National Child Mortality Database, University of Bristol, Bristol, UK. ⁵Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, UK. ⁶Department of Paediatric Surgery, Alder Hey in the Park, Liverpool, UK. ⁷Population, Policy and Practice Department, UCL Great Ormond St. Institute of Child Health, London, UK. ⁸Royal College of Paediatrics and Child Health, London, UK. ⁹Department of Paediatrics, University Hospitals Sussex NHS Foundation Trust, Brighton, UK. ¹⁰School of Public Health, Imperial College London, London, UK. ¹¹Immunisation and Countermeasures, Public Health England, London, UK. ¹²Paediatric Infectious Diseases Research Group, St. George's University of London, London, UK. ¹³Paediatric Intensive Care Audit Network (PICANet), Department of Health Sciences, University of Leicester, Leicester, UK. ¹⁴Department of Paediatric Infectious Diseases, Imperial College Healthcare NHS Trust, London, UK. ¹⁵Section of Paediatric Infectious Diseases, Faculty of Medicine, Imperial College London, London, UK. ¹⁶Martin House Research Centre, University of York, York, UK. ✉e-mail: clare.smith107@nhs.net

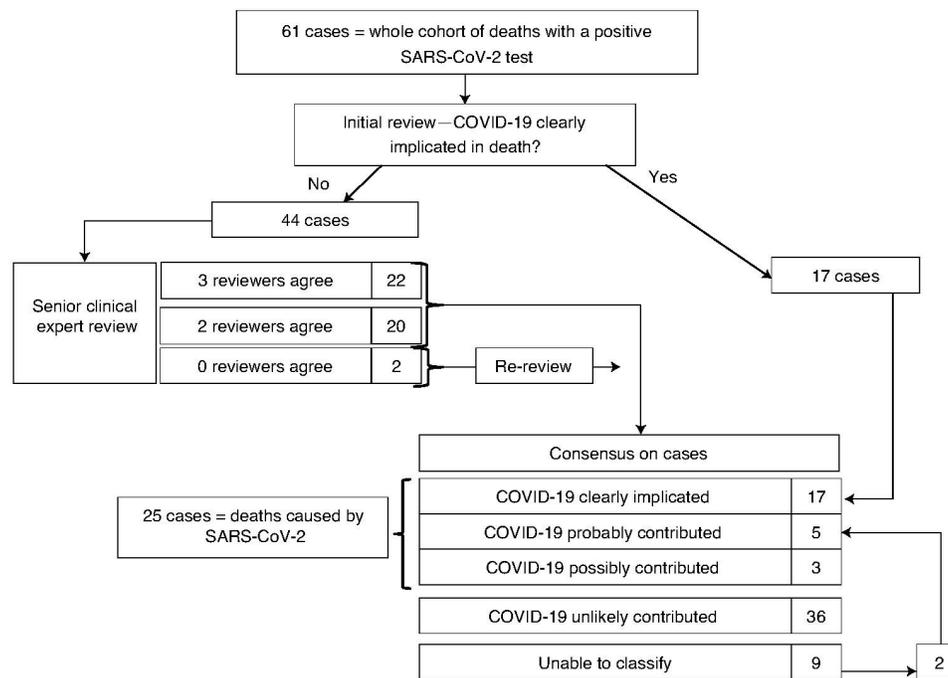


Fig. 1 | Flow diagram of the approach used to determine if SARS-CoV-2 contributed to death or if it was a coincidental finding. This approach was applied to all CYP who died and had a positive SARS-CoV-2 test. The numbers are included at each representative stage.

national dataset of deaths of individuals younger than 18 years of age, to review the contribution of SARS-CoV-2 to death.

If higher-risk groups are identified, they might benefit from vaccination and/or protective ‘shielding’ at times of high prevalence, whereas ‘shielding’ based upon erroneous assumptions of vulnerability is likely to cause significant secondary harms—for example, the effects of not attending school and restrictive or reduced socializing, affecting both development and mental health. Similarly, risks from the disease need to be weighed against potential risks of vaccination in informing vaccination policy. Therefore, this study aimed to:

1. Quantify the number of CYP who died of SARS-CoV-2 by differentiating between CYP who died of SARS-CoV-2 and those who died of an alternative cause with a coincidental positive SARS-CoV-2 test.
2. Assess the clinical and demographic characteristics of the CYP who died of SARS-CoV-2 compared to CYP deaths from all other causes during the first pandemic year.

Results

Between March 2020 and February 2021, 3,105 CYP in England died of all causes. Of these, 61 CYP had a positive SARS-CoV-2 test, and 3,044 died of all other causes.

Clinical records of the 61 CYP who died with a positive SARS-CoV-2 test were reviewed to identify if SARS-CoV-2 contributed to death. This process initially included identifying whether SARS-CoV-2 was listed as 1a (the direct cause of death) on the Certificate of Cause of Death and whether the clinical course described was typical of SARS-CoV-2 infection. In these circumstances, the classification ‘SARS-CoV-2 clearly contributed to death’ was applied. In England, the Certificate of Cause of Death is set out in two parts¹². Part 1a is the immediate, direct cause of death. The sequence of events or conditions that led to the death are then listed as 1b and 1c (if necessary)¹².

If the role of SARS-CoV-2 in contributing to death was not clearly apparent, each case underwent review by three independent senior clinical experts in relevant fields (General Pediatrics, Neonatology

and Pediatric Intensive Care) who were asked to classify each case. Definitions for each category and the details behind the process are outlined in the Supplementary Information and in Fig. 1.

In total, 25 (41%) of the 61 CYP died of SARS-CoV-2, including 22 with acute COVID-19 and three with PIMS-TS. In the other 36 (59%) of the 61 test-positive CYP, SARS-CoV-2 did not contribute to death (Table 1 and Figs. 1 and 2).

An estimated 469,982 CYP were infected with SARS-CoV-2 in England from March 2020 to February 2021, giving an infection fatality rate of five per 100,000 CYP (0.005%) and, based on a population of 12,023,568, a mortality rate of two per million CYP (0.0002%)¹³.

Demographics. There were small amounts of missing demographic data for the reference population (2.3% sex, 10.6% ethnicity and 0.6% deprivation (Table 1), but there were no missing demographic data for the 25 CYP who died of SARS-CoV-2.

CYP who died of SARS-CoV-2 ($n=25$) were older than those who died from all other causes ($n=3,080$) in the same time period. Eighteen of 25 (72%) young people who died of SARS-CoV-2 were aged 10 years or older compared to 19% in the deaths from all other causes (chi-squared 59.7, $P<0.001$). All three deaths in CYP who died of PIMS-TS were aged 10–14 years. Of interest, specific to vaccination policy in the United Kingdom, there were eight deaths in young people aged 12–15 years. The sex distribution was equally split between males and females (12 (48%) and 13 (52%), respectively) and did not differ from the deaths from all other causes (chi-squared 0.64, $P=0.28$). A greater proportion of CYP from Asian (36% compared to 16%) and Black (20% compared to 8%) ethnicity died of SARS-CoV-2 compared to deaths from all other causes (chi-squared 17.9, $P<0.001$). The three CYP who died of PIMS-TS were from different ethnic groups. No significant difference was observed in the deprivation categories between CYP who died of SARS-CoV-2 and deaths from all other causes (chi-squared 0.35, $P=0.99$), although more CYP from more deprived areas died in both groups.

The mortality rate in CYP who died of SARS-CoV-2 was 0.2 per 100,000 (95% confidence interval (CI), 0.1–0.3) compared to

Table 1 | Demographic details for CYP who died between March 2020 and February 2021 from all causes and the 61 CYP who died with a positive SARS-CoV-2 test, split by the likely cause of death

All deaths	All deaths, March 2020–February 2021 (n = 3,105)								Comparison of frequencies ^a
	Reference population (n = 3,080), all other causes of death					Died of COVID-19/PIMS-TS (n = 25)			
	Died without positive test for SARS-CoV-2 (n = 3,044)		Incidental positive SARS-CoV-2 test at death (n = 36)		Est. rate per 100,000 person years (95% Poisson CI)	Number	Percentage	Est. rate per 100,000 person years (95% Poisson CI)	
	Number	Percentage	Number	Percentage					
	3,044	100%	36	100%	25.5 (24.7–26.5)	25	100%	0.2 (0.1–0.3)	
Age									
0–27 d	1,388	45.6%	3	8.3%	289.3 (276.8–302.1)	0	0.0%	0.3 (0.0–11.0)	<0.001
28–364 d	616	20.2%	11	30.6%		2	8.0%		
1–4 years	281	9.2%	4	11.1%	10.4 (9.2–11.6)	0	0.0%	0.00 (-)	
5–9 years	191	6.3%	4	11.1%	5.7 (4.9–6.6)	5	20.0%	0.1 (0.0–0.3)	
10–14 years	252	8.3%	6	16.7%	7.6 (6.7–8.6)	9	36.0%	0.3 (0.1–0.5)	
15–17 years	316	10.4%	8	22.2%	17.3 (15.5–19.3)	9	36.0%	0.5 (0.2–0.9)	
Sex									
Female	1,667	54.8%	18	50.0%	22.4 (21.2–23.7)	12	48.0%	0.2 (0.1–0.4)	0.28
Male	1,308	43.0%	18	50.0%	27.1 (25.9–28.5)	13	52.0%	0.2 (0.1–0.3)	
Missing	69	2.3%	-	-	-	-	-	-	
Ethnicity									
Asian or Asian British	471	15.5%	10	27.8%	31.3 (28.6–34.2)	9	36.0%	0.6 (0.3–1.1)	<0.001
Black or Black British	241	7.9%	4	11.1%	37.8 (33.2–42.9)	5	20.0%	0.8 (0.3–1.8)	
Mixed	169	5.6%	1	2.8%	23.3 (19.9–27.1)	4	16.0%	0.5 (0.1–1.4)	
Other	74	2.4%	0	0.0%	49.8 (39.1–62.5)	0	0.0%	0.00 (-)	
White	1,764	58.0%	20	55.6%	19.7 (18.8–20.6)	7	28.0%	0.1 (0.0–0.2)	
Missing	325	10.7%	1	2.8%	-	-	-	-	
Deprivation category									
1	985	32.4%	15	41.7%	34.8 (32.7–37.0)	9	36.0%	0.3 (0.1–0.6)	0.99
2	687	22.6%	8	22.2%	27.9 (25.9–30.1)	6	24.0%	0.2 (0.1–0.5)	
3	615	20.2%	6	16.7%	27.4 (25.3–29.6)	5	20.0%	0.2 (0.1–0.5)	
4	402	13.2%	3	8.3%	18.7 (16.9–20.6)	3	12.0%	0.1 (0.0–0.4)	
5	337	11.1%	4	11.1%	15.3 (13.8–17.1)	2	8.0%	0.1 (0.0–0.3)	
Missing	18	0.6%	-	-	-	-	-	-	

Table 1 shows the demographic details for the CYP who died of all causes and the CYP who died of SARS-CoV-2. ^aThe CYP who died of SARS-CoV-2 were compared to CYP who died from all other causes using summary statistics, and differences between groups were compared using the two-sided chi-squared test or Fisher's exact test if small numbers. No adjustment for multiple testing was undertaken. Values are n (%) or median (interquartile range) as appropriate.

25.5 per 100,000 (95% CI, 24.7–26.5) for all other causes of death. Although the proportion of CYP from Asian and Black ethnic groups who died of SARS-CoV-2 was higher, their absolute risk of death from SARS-CoV-2 was still extremely low at 0.6 per 100,000 (95% CI, 0.3–1.1) and 0.8 per 100,000 (95% CI, 0.3–1.8), respectively. Similarly, the proportion of CYP aged 10–14 years and 15–17 years who died of SARS-CoV-2 was higher than the proportion of CYP in the same age categories who died of all other causes. However, their absolute risk of death from SARS-CoV-2 was still extremely low at 0.3 per 100,000 (95% CI, 0.1–0.5) and 0.5 (95% CI, 0.2–0.9) per 100,000, respectively.

Comorbidities. A similar proportion of the 25 CYP who died of SARS-CoV-2 (n = 19, 76%) and the 3,080 deaths from all other

causes (n = 2,267, 74%) (chi-squared 0.004, P = 0.60) had a chronic underlying health condition (Tables 2 and 3). Significantly more CYP who died of SARS-CoV-2 had a life-limiting condition (n = 15, 60%) compared to deaths from all other causes (n = 988, 32%) (chi-squared 8.5, P = 0.005). Of the 25 CYP who died of SARS-CoV-2, 64% (n = 16) had comorbidities in two or more body systems compared to 45% (n = 1,373) of the CYP who died from all other causes (chi-squared 5.5, P = 0.14).

Six (24%) of the 25 CYP who died of SARS-CoV-2 appeared to have no underlying health conditions, similar to 24% (729 of the 3,080 CYP) who died of all other causes. These six deaths included two CYP who died of PIMS-TS.

Neurological conditions were the most common comorbidity in both the CYP who died of SARS-CoV-2 (n = 13/25, 52%)