

Seroprevalence of SARS-CoV-2 antibodies in children: a prospective multicentre cohort study

Thomas Waterfield ^{1,2}, Chris Watson,¹ Rebecca Moore ³, Kathryn Ferris ⁴, Claire Tonry,¹ Alison Watt,⁵ Claire McGinn,³ Steven Foster,⁶ Jennifer Evans,⁷ Mark David Lyttle,^{8,9} Shazaad Ahmad,^{10,11} Shamez Ladhani,¹² Michael Corr ⁴, Lisa McFetridge,¹³ Hannah Mitchell,¹³ Kevin Brown,¹⁴ Gayatri Amirthalingam,¹⁵ Julie-Ann Maney,¹⁶ Sharon Christie¹⁷

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/archdischild-2020-320558>).

For numbered affiliations see end of article.

Correspondence to

Dr Thomas Waterfield, Emergency Department, Children's Health Ireland at Temple Street, Dublin D01 YC67, Ireland; thomas.waterfield@googlemail.com

Received 27 August 2020
Accepted 12 October 2020

ABSTRACT

Background Studies based on molecular testing of oral/nasal swabs underestimate SARS-CoV-2 infection due to issues with test sensitivity, test timing and selection bias. The objective of this study was to report the presence of SARS-CoV-2 antibodies, consistent with previous infection.

Design This multicentre observational cohort study, conducted between 16 April to 3 July 2020 at 5 UK sites, recruited children of healthcare workers, aged 2–15 years. Participants provided blood samples for SARS-CoV-2 antibody testing and data were gathered regarding unwell contacts and symptoms.

Results 1007 participants were enrolled, and 992 were included in the final analysis. The median age of participants was 10.1 years. There were 68 (6.9%) participants with positive SARS-CoV-2 antibody tests indicative of previous SARS-CoV-2 infection. Of these, 34/68 (50%) reported no symptoms prior to testing. The presence of antibodies and the mean antibody titre was not influenced by age. Following multivariable analysis four independent variables were identified as significantly associated with SARS-CoV-2 seropositivity: known infected household contact OR=10.9 (95% CI 6.1 to 19.6); fatigue OR=16.8 (95% CI 5.5 to 51.9); gastrointestinal symptoms OR=6.6 (95% CI 3.0 to 13.8); and changes in sense of smell or taste OR=10.0 (95% CI 2.4 to 11.4).

Discussion Children demonstrated similar antibody titres in response to SARS-CoV-2 irrespective of age. Fatigue, gastrointestinal symptoms and changes in sense of smell or taste were the symptoms most strongly associated with SARS-CoV-2 antibody positivity.

Trial registration number NCT0434740.

INTRODUCTION

During the first wave of the SARS-CoV-2 pandemic in England, children accounted for just 1% of confirmed infections,¹ had a milder clinical course and had much lower mortality than adults,^{1–4} a pattern similar to other international settings.^{3,4} The reasons for this are unknown, but various hypotheses exist. Public health measures, such as school closures, may have minimised children's exposure to SARS-CoV-2. It is also possible that children have a different immune response to the virus, for example, reduced expression of the ACE2 gene,

What is already known on this topic?

- Children are relatively unaffected by the SARS-CoV-2 infection with very few requiring hospitalisation.
- A large, but unknown proportion of children with SARS-CoV-2 infection are asymptomatic.
- Molecular testing of oral/nasal swabs underestimates SARS-CoV-2 infection.

What this study adds?

- Gastrointestinal upset is a relatively common symptom of COVID-19 in children. Adding gastrointestinal upset to the list of symptoms triggering a test in children would improve case-finding.
- Asymptomatic and mildly symptomatic children are capable of developing an antibody response to SARS-CoV-2.
- This study did not find a difference in rates of seropositivity or antibody responses according to age in the children of healthcare workers.

the host receptor for SARS-CoV-2 virus in airway cells.^{5–7}

Despite existing data, it is impossible to state accurately what proportion of children were infected with SARS-CoV-2 in the UK. Studies based on molecular testing of oral/nasal swabs with real-time reverse transcription PCR (RT-qPCR) underestimate infection due to issues with test sensitivity, timing of testing and selection bias due to only symptomatic individuals undergoing testing.⁸ A potentially more reliable method is to test for specific antibodies. Existing antibody tests typically detect IgG or total antibody to either the nucleocapsid or spike proteins of the virus.⁹ Antibody testing has greater potential than RT-qPCR to detect previous asymptomatic/mildly symptomatic infection, and is not dependent on coinciding with active infection. Current best seroprevalence estimates from adults in the UK indicate that approximately 6.2% have antibodies consistent with previous SARS-CoV-2



© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Waterfield T, Watson C, Moore R, et al. *Arch Dis Child* Epub ahead of print: [please include Day Month Year]. doi:10.1136/archdischild-2020-320558

infection.¹⁰ These findings are similar to other domestic and international seroprevalence studies.^{11–14}

It is unclear what proportion of children are asymptomatic and which symptoms are most associated with paediatric SARS-CoV-2 infection. Estimates based on RT-qPCR testing of oral/nasal swabs suggest that cough or fever are the most common symptoms.^{15–20} However, these studies focus on symptomatic cohorts, introducing selection bias,^{15–20} which leads to underestimation of the asymptomatic proportion.

The objective of this study was to report the presence, and titres, of SARS-CoV-2 antibodies in healthy children of healthcare workers across the UK and to report the symptomatology of infection including the asymptomatic rate.

METHODS

Study design

This multicentre observational prospective cohort study was designed to determine the seroprevalence of SARS-CoV-2 antibodies in healthy children, and report the symptomatology of infection. This study has been written in conjunction with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.²¹ The study protocol has undergone external peer review and is available as an open access publication.²²

Setting

Participants were recruited from five UK centres, in the four regions of the UK, between 16 April 2020 and 3 July 2020. The sites included tertiary National Health Service (NHS) hospitals (Belfast, Cardiff, Manchester and Glasgow) and a Public Health England site (London).

Participants

Children of healthcare workers, aged between 2 years and 15 years at the time of recruitment, were eligible to participate. A 'healthcare worker' was defined as an NHS employee. Healthcare workers were categorised according to role, including whether that role involved patient facing activities. Approximately 150 non-patient facing staff were included to provide a comparison group, and to improve the generalisability of the results. Participants were identified at each participating NHS organisation using internal intranet advertisements and email circulars. Children were excluded if they were receiving antibiotics, had been admitted to hospital within the last 7 days, were receiving oral immunosuppressive treatment or if ever diagnosed with a malignancy.

Informed consent

Informed consent was obtained, and assent given by children where possible. Participants were free to decline/withdraw consent at any time without providing a reason and without being subject to any resulting detriment.

Assessments and procedures

All children underwent phlebotomy performed by experienced paediatric medical and nursing professionals. Serum and/or plasma were tested for antibodies to SARS-CoV-2, in United Kingdom Accreditation Service accredited laboratories using the following assays, which have been validated for use in adults:^{23–25}

- ▶ Nucleocapsid assays (Abbott Architect SARS-CoV-2 IgG and Roche Elecsys anti-SARS-CoV-2 total antibody)
- ▶ Spike protein assays (DiaSorin LIAISON SARS CoV-2 S1/S2 IgG assay)

Table 1 Summary of antibody tests used

Name of assay	Target	Units	Cut-off
Abbott Architect SARS-CoV-2 IgG	Nucleocapsid	Calculated index S/C	1.45/C
Roche Elecsys anti-SARS-CoV-2	Nucleocapsid	Cut-off index COI	1.0 COI
DiaSorin LIAISON SARS CoV-2 S1/S2 IgG assay	Spike protein	Arbitrary units (AU)/ml	15.0 AU/ml

COI, Cut-off Index.

The Abbott, Roche and DiaSorin assays are highly specific for SARS-CoV-2 antibodies, using the manufacturer's suggested cut-offs, with specificities of 1.00 (95% CI 0.98 to 1.00), 1.00 (95% CI 0.99 to 1.00) and 0.98 (95% CI 0.96 to 0.99), respectively.^{23–25} They do, however, have lower sensitivities at 0.94 (95% CI 0.86 to 0.98), 0.84 (95% CI 0.75 to 0.91) and 0.64 (95% CI 0.54 to 0.73), respectively.^{23–25} A summary of the tests used is provided in table 1.

Study data were collected on a case report form (CRF) using REDCap (Research Electronic Data Capture) electronic data capture tools.²⁶ Participants and their parents provided information at enrolment relating to age, sex, previous health and potential predictors of SARS-CoV-2 seropositivity including; known contact with individuals with COVID-19, contact with individuals who have been symptomatic and/or self-isolating and results of any diagnostic testing such as RT-qPCR testing/antibody testing. Participants and their parents also reported any symptoms and illness episodes since the onset of the pandemic in March but prior to the first clinic appointment. Data were collected relating to symptoms but not relating to time of onset or duration of illness. To minimise recall bias, data relating to exposures and illness episodes were collected blinded to antibody testing results. Copies of the CRFs used at enrolment can be found in the online supplemental material.

Primary outcome measures

- ▶ Presence of antibodies (IgG/total antibody) to SARS-CoV-2 in serum or plasma reported as titres.
- ▶ SARS-CoV-2 seropositivity defined as a positive antibody test using the manufacturer's advised positivity cut-off.

Secondary outcome measure

- ▶ Predictors of SARS-CoV-2 positivity including reported symptoms.

Sample size justification

The study was powered to detect a change in seroprevalence of SARS-CoV-2 antibodies at three time points (enrolment, and 2 months and 6 months following enrolment). To achieve this, 675 participants were required (assuming alpha of 0.05 and beta of 0.2). Allowing for a 30% dropout rate, we aimed to recruit 900 participants from five sites. The data presented in this study reflect only the data collected at enrolment and the study is ongoing.

Statistical analysis plan

Variables including sex, age, parent role, symptomatology, household contacts and SARS-CoV-2 antibody prevalence were analysed using descriptive statistics (number and proportion for discrete variables, median and IQR for continuous variables). Seroprevalence rates between sites were compared using Fisher's exact test and antibody titres were correlated with age using the Kendall's rank correlation test and mean titres were compared

between symptomatic and asymptomatic participants using the Wilcoxon rank sum test.

Variables associated with SARS-CoV-2 positivity were analysed using univariate and multivariable analyses to identify predictors of SARS-CoV-2 seropositivity. Initially all possible variables were assessed using univariate analysis with Fisher's exact testing of categorical data, and the Mann-Whitney U test for continuous data (continuous data were skewed). All variables were then included in a weighted binary multivariable logistic regression model. Participants with incomplete CRFs were excluded from univariate and multivariable analyses. Analysis was conducted in R (R Core Team, 2014).

Patient and public involvement

A patient and public involvement (PPI) group comprising parents and children was convened. The PPI group met virtually and via socially distanced meetings. The group contributed to the design of the study through online surveys and video discussions. They have also contributed to media interviews on national television and the lead young person has coauthored a manuscript outlining their experience of taking part in the study.²⁷

Study registration

This study was registered at <https://www.clinicaltrials.gov> (trial registration: NCT0434740) on 15 April 2020 (last updated 27 May 2020). At the time of registration no patients had been recruited to the study which opened on 16 April 2020. The end of the study will be the last study visit.

FINDINGS

In total, 1042 potential participants were screened for inclusion, of whom 35 were excluded; 18 were outside the specified age range, 1 met specific exclusion criteria and 16 declined consent. The remaining 1007 children were enrolled, of which 15 were excluded from analysis due to unsuccessful phlebotomy; 992 were included in the final analysis (figure 1). The recruitment by site is shown in table 2. In the analysis cohort 962/992 (97%) had complete CRFs and 30/992 (3%) had partially complete CRFs.

The median age of participants was 10.1 years (range 2.03 to 15.99 years), with 484 (49%) aged under 10 years; 509

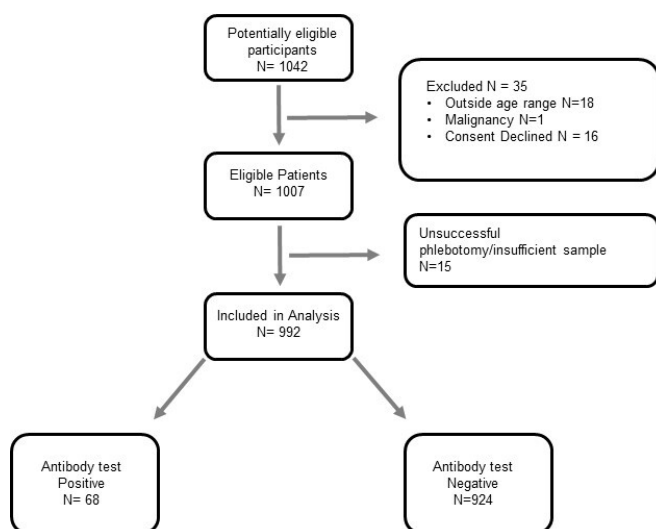


Figure 1 Flow chart of children of healthcare workers through the study.

Table 2 Recruitment summary of children of healthcare workers and seroprevalence by site (N and (%) unless otherwise stated)

Site	Screened	Included participants	Antibody positive	95% CI
Belfast	217	215	2	0.9 (0.2 to 3.3)
Cardiff	192	178	10	5.6 (3.1 to 10.0)
Glasgow	229	224	20	8.9 (5.9 to 13.4)
London	215	199	23	11.6 (7.8 to 16.8)
Manchester	189	176	13	7.4 (4.4 to 12.2)
Total	1042	992	68	6.9 (5.4 to 8.6)

(51%) were male. The roles of participants' parents are shown in figure 2. There were 359/992 (36.2%) children of hospital medical staff, 191/992 (19.3%) children of hospital nursing/midwifery staff, 95/992 (9.6%) children of community medical staff, 36/992 (3.6%) children of community nursing staff and 160/992 (16.1%) children of other patient facing staff such as radiographers, physiotherapists and other allied healthcare professionals. There were 151/992 (15.2%) children of non-patient facing staff such as managerial and administrative staff.

There were 68/992 participants with positive SARS-CoV-2 antibodies, giving a seroprevalence of 6.9% (95% CI 5.4% to 8.6%, n=992). Of those with positive SARS-CoV-2 antibody tests, 34/68 (50%) reported no symptoms. The most commonly reported symptoms associated with SARS-CoV-2 seropositivity were fever 21/68 (31%), gastrointestinal symptoms (diarrhoea, vomiting and abdominal cramps) 13/68 (19%) and headache 12/68 (18%). The presence of fever, cough or changes in a sense of smell/taste were recorded in 26/68 (38%) of participants. No children within this cohort had severe disease requiring hospital admission. A summary of reported symptoms and their frequency can be seen in table 3.

Seroprevalence of SARS-CoV-2 antibodies varied between sites. Belfast had significantly lower seroprevalence than all other sites at 0.9% (95% CI 0.2% to 3.3%, n=215); $p < 0.0001$, and in London seroprevalence was significantly higher than all other sites at 11.6% (95% CI 7.8% to 16.8% n=199); $p = 0.0069$. The remaining three sites reported seroprevalence rates between 5.6% and 8.9%. The differences between these three sites were not statistically significant (table 2).

The mean antibody titres, for those testing positive, were;

- ▶ 4.86 *Calculated Index S/C* (95% CI 4.28 to 5.45, n=58) for the Abbott Architect SARS-CoV-2 IgG assay.
- ▶ 65.32 *Cut-off Index COI* (95% CI 43.24 to 87.40, n=31) for the Roche Elecsys anti-SARS-CoV-2 total antibody assay.
- ▶ 64.17 AU/ml (95% CI 37.99 to 90.36, n=31) for the DiaSorin LIAISON SARS CoV-2 S1/S2 IgG assay.

There was no correlation between age and antibody titres (figure 3). The results from the Abbott Architect SARS-CoV-2 IgG assay indicated a small but significant difference in mean antibody titres between asymptomatic 4.3 S/C (95% CI 3.4 to 5.2) and symptomatic participants 5.5 S/C (95% CI 4.7 to 6.2); $p = 0.04$. There was no significant difference in mean antibody titres for the Roche Elecsys or DiaSorin LIAISON assays when comparing symptomatic and asymptomatic participants ($p = 0.23$ and 0.58 , respectively) (figure 3). A table of concordance between the three assays used is available in the online supplemental material.

The univariate analysis of individual variables associated with SARS-CoV-2 seropositivity is shown in table 3. In addition to clinical features, variables such as age, gender, the role of the parent (patient facing or not) and known household contacts

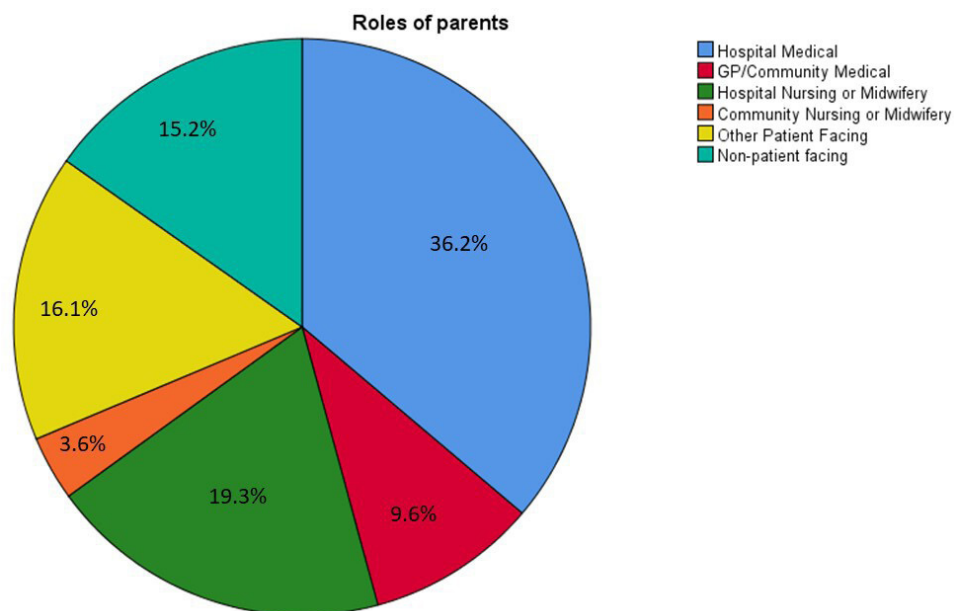


Figure 2 Summary of participants' parents' roles. GP, general practitioner.

were included. Age and gender were not significantly associated with SARS-CoV-2 seropositivity (table 3). Parental role showed significant association in the univariate analysis, but this was no longer significant once corrected for site and other variables in the multivariable analysis. Contact with a household member with confirmed SARS-CoV-2 infection was significantly associated with SARS-CoV-2 seropositivity in the participant in both the univariate and multivariable analyses (table 3). The multivariable analysis identified four variables independently associated with SARS-CoV-2 seropositivity: (1) Known household contact with confirmed SARS-CoV-2 ($p < 0.0001$), (2) Fatigue ($p = 0.001$), (3) Gastrointestinal symptoms ($p = 0.0001$), and (4) Changes in sense of smell or taste ($p < 0.0012$).

INTERPRETATION

This observational study is one of the largest UK studies of paediatric SARS-CoV-2 antibody seroprevalence, and the only study to recruit from all regions of the UK. Following the first pandemic wave in the UK, 68/992 (6.9%) children of health-care workers had evidence of prior infection with SARS-CoV-2. While this is likely to be higher than the general population it is surprisingly similar to the seroprevalence reported by the Office for National Statistics study of adults from England and Wales (6.2%),¹⁰ and similar to international estimates.¹¹⁻¹³ As expected, there was marked geographical variation, with London reporting the highest seropositivity rates (11.6%) and Belfast the lowest

Table 3 Univariate analysis of variables for SARS-CoV-2 antibodies in children of healthcare workers (Fisher's exact test for categorical variables, Mann-Whitney U test for continuous variables). Number and per cent (%) with feature shown for categorical variables and median for continuous variables unless otherwise stated

Variable	Complete data N (%)	Without SARS-CoV-2 antibodies N (%)	With SARS-CoV-2 antibodies N (%)	OR (95% CI)	P value
Median age (years)	992 (100)	10.1 (5.8)	10.2 (6.9)	–	0.481
Aged 10 years and over	992 (100)	472 (51)	36 (53)	1.1 (0.6 to 1.8)	0.802
Male gender	991 (99.9)	468 (51)	41 (60)	1.5 (0.9 to 2.5)	0.133
Parents (patient contact)	992 (100)	789 (85)	52 (76)	0.6 (0.3 to 1.1)	0.055
Confirmed household contact	960 (97)	63 (7)	30 (44)	10.9 (6.1 to 19.6)	<0.0001
Fever	962 (97)	102 (11)	21 (31)	3.5 (1.9 to 6.2)	<0.0001
Gastrointestinal symptoms	962 (97)	31 (3)	13 (19)	6.6 (3.0 to 13.8)	<0.0001
Headache	962 (97)	34 (4)	12 (18)	5.4 (2.4 to 11.4)	<0.0001
Lethargy/fatigue	962 (97)	8 (1)	9 (13)	16.8 (5.5 to 51.9)	<0.0001
Cough	962 (97)	90 (10)	7 (10)	1.03 (0.38 to 2.3)	1.000
Change in sense of smell/taste	962 (97)	7 (1)	5 (7)	10.0 (2.4 to 37.8)	<0.0008
Myalgia/arthralgia	962 (97)	21 (2)	5 (7)	3.3 (0.94 to 9.4)	0.031
Sore throat	962 (97)	41 (5)	5 (7)	1.7 (0.5 to 4.4)	0.367
Shortness of breath	962 (97)	13 (1)	3 (4)	3.1 (0.6 to 11.8)	0.098
Coryza	962 (97)	27 (3)	1 (1)	0.5 (0.0 to 3.0)	0.715
Rash	962 (97)	10 (1)	1 (1)	1.3 (0.0 to 9.5)	0.556
Conjunctivitis	962 (97)	1 (0)	0 (0)	0.0 (0.0 to 508.7)	1.000

Red type denotes those values that are statistically significant.

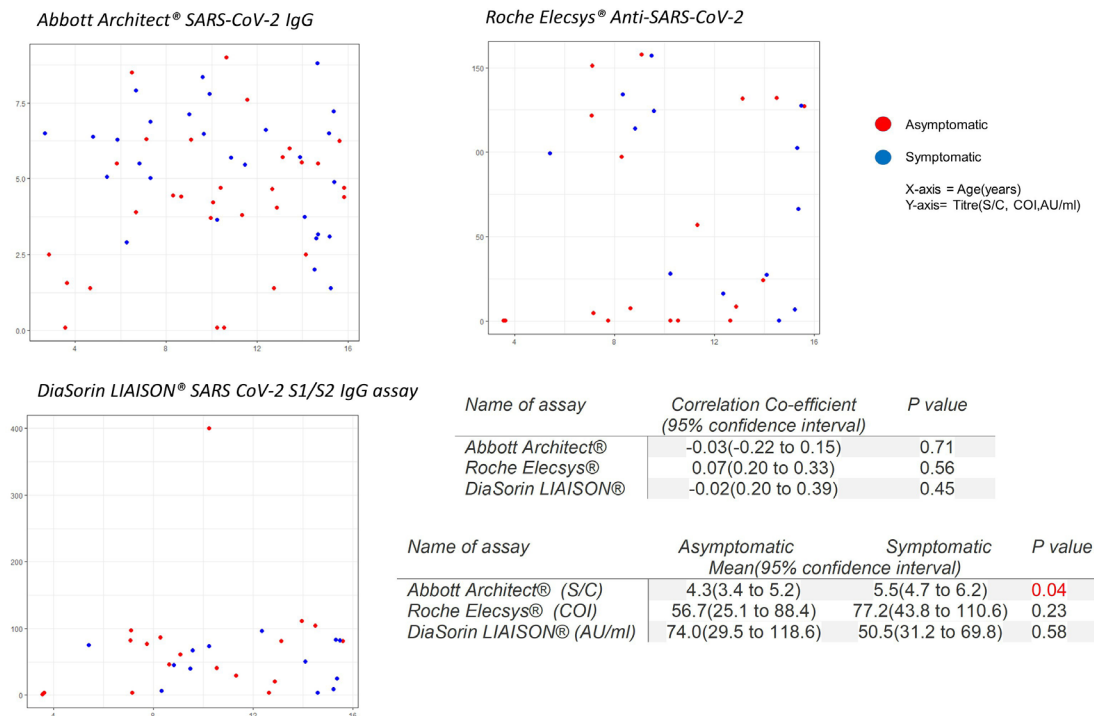


Figure 3 Scatter diagrams of age/symptoms in children of healthcare workers and SARS-CoV-2 assay titre. Abbott architect reported in S/C, Roche Elecsys reported in COI, DiaSorin liaison reported in AU/ml. COI, Cut-off Index.

(0.9%) $p < 0.0001$. These regional variations are consistent with published adult estimates of seroprevalence from the same time period.¹⁰

In this study there was a near equal number of children under 10 years of age 32/68 (47%) and children over 10 years of age 36/68 (53%) developing antibodies consistent with previous SARS-CoV-2 infection. Age, as a categorical or continuous variable, was not a statistically significant factor in predicting the presence of antibodies, or the overall titres in children irrespective of the assay used (figure 3).

Of the 68 participants with positive antibody tests, 34/68 (50%) reported no symptoms. The most commonly reported symptoms associated with SARS-CoV-2 seropositivity were fever (21/68, 30%) and gastrointestinal symptoms (13/68, 19%). These symptoms, in addition to fatigue, and changes in sense of smell or taste, were independently associated with previous SARS-CoV-2 seropositivity based on the weighted binary multivariable regression modelling. These findings reflect a number of international studies.¹⁵⁻²⁰ Current UK testing strategies directing testing only for those with fever, cough or changes in smell/taste would have identified 26/34 (76%) of symptomatic participants in this study (assuming 100% sensitivity and specificity of RT-qPCR swab testing). Adding gastrointestinal symptoms would have identified nearly all symptomatic cases in this cohort (33/34, 97%). It is, however, important to note that the predictive value of individual symptoms is context-dependent and their utility will vary depending on the season and the symptomatology of other circulating infections. These findings may be useful to policy makers when considering the best approach to screening paediatric populations for SARS-CoV-2.

There is evidence from adult serological studies that those with severe illness develop a significantly greater antibody response than those with mild or asymptomatic disease.²⁸⁻³⁰ This has raised concerns that children, who typically have mild disease, may fail to develop a meaningful antibody response

to SARS-CoV-2 infection. More recently, emerging adult data suggest that even asymptomatic adults are capable of mounting a potentially lasting and protective immune response.^{31 32} In our study antibody titres measured using the Abbott Architect SARS-CoV-2 IgG assay were significantly higher in symptomatic children compared with asymptomatic children ($p = 0.04$). These findings were not replicated with either the Roche Elecsys anti-SARS-CoV-2 or DiaSorin LIAISON SARS CoV-2 S1/S2 IgG assays. It therefore remains unclear to what extent the severity of symptoms in children influences the antibody response.

STRENGTHS/LIMITATIONS

The strengths of this study are that it is a large multicentre study including children from across the four nations of the UK. The findings are based on systematically screening children for SARS-CoV-2 antibodies and this removes selection bias from assessment of the asymptomatic proportion and determination of symptomatology.

The limitations of this study are:

- ▶ The SARS-CoV-2 antibody tests have not been validated for use in children.
- ▶ The absolute sample size of seropositive participants is relatively small.
- ▶ There was selection bias towards children of hospital staff and children with only mild disease.
- ▶ There is a risk of recall bias due to the retrospective nature of data collection relating to symptomatology.

SUMMARY

This study demonstrates that approximately half of children with positive antibody tests for SARS-CoV-2 reported no symptoms. This study also demonstrates that younger children were just as likely to have SARS-CoV-2 antibodies as older children and that they are capable of mounting a similar antibody response.

Author affiliations

- ¹Queen's University Belfast Wellcome-Wolfson Institute for Experimental Medicine, Belfast, UK
- ²Emergency Department, Children's Health Ireland at Temple Street, Dublin D01 YC67, Ireland
- ³General Paediatrics, Royal Belfast Hospital for Sick Children, Belfast, UK
- ⁴Belfast Health and Social Care Trust, Belfast, UK
- ⁵Regional Virus Laboratory, Belfast Health and Social Care Trust, Belfast, UK
- ⁶Emergency Department, Royal Hospital for Children, Glasgow, UK
- ⁷Cardiff and Vale University Health Board, Cardiff, UK
- ⁸Emergency Department, University Hospitals Bristol NHS Foundation Trust, Bristol, UK
- ⁹Health and Applied Sciences, University of the West of England, Bristol, UK
- ¹⁰Department of Virology, Manchester Medical Microbiology Partnership, Manchester University NHS Foundation Trust, Manchester, UK
- ¹¹Manchester Academic Health Science Centre, Manchester, UK
- ¹²Immunisation and Countermeasures Division, Public Health England, London, UK
- ¹³Mathematical Sciences Research Centre, Queen's University Belfast, Belfast, UK
- ¹⁴Virus Reference Department, Public Health England, Colindale, UK
- ¹⁵Immunisation, Hepatitis & Blood Safety Department, Public Health England Immunisation and Countermeasures Division, London, UK
- ¹⁶Emergency Department, Royal Belfast Hospital for Sick Children, Belfast, UK
- ¹⁷Paediatric Infectious Diseases, Royal Belfast Hospital for Sick Children, Belfast, UK

Correction notice This paper has been amended since it was published online. The end of the abstract originally referred to SARS-CoV-1 instead of SARS-CoV-2.

Twitter Mark David Lyttle @mdlyttle, Shamez Ladhani @shamezladhani and Julie-Ann Maney @julieannmaney

Acknowledgements The authors thank all of the children and their families who participated in this study. The authors also thank all of the sites (Belfast Health and Social Care Trust, The Ulster Independent Clinic, Cardiff and Vale University Health Board, NHS Greater Glasgow and Clyde, Public Health England, London, Manchester University NHS Foundation Trust, NIHR Manchester Clinical Research Facility) and staff who participated in screening and enrolment. The authors also thank St Jude's Children's Cancer Aid and Research Institute for providing artwork for the participant information sheet. The authors individually thank Elizabeth Waxman, Derek Fairley, Gala Roew-Setz, James McKenna, Peter Mallet, Ryan Chrisite, Katherine Christie, Emma McManus, Christian Bennison, Kate Mullan, Diarmuid McLaughlin, Christine Sloane, Rhiannon McBay, Ben Moore, Aleksandra Metryka, Julie Aitken, Hayley-Isabella Cawley, Peter Cawley, Kirsty Gray, Jaclyn Keightley, Sean Kelly, Stephanie McCallion, Marc McNulty, Nicholas Roe, Fiona Russell, Aoife Ryan, Kathryn Smith, Jenna Stewart, Andrew Tester, Z.Morrison, D.Kelly, H.Davies, A.Moore, S.Goyal, B.Saunders, L.Price, P.Robb, S.Richards, H.Davies, T.Cromarty, J.Davies, C.Rees, C.Crosland, L.PowerC.Kruppa

Contributors TW, CW, SL and SC conceived the study idea. TW, CW, SL, SC, RM, KF, CM, SF, JE, MDL, SA, MC, LM, HM and J-AM contributed to the design of the study. TW coordinated the running of the study including data management and site training. MC wrote the study protocol. MDL designed the electronic CRFs. RM coordinated and led the PPI group. SC, KF, SF, JE, SA and SL were site leads. CT, CW, GA, KB and AW were responsible for performing laboratory testing. LM and HM provided statistical expertise and performed the statistical analysis. All authors contributed to the writing of the manuscript.

Funding This work was supported by HSC R&D Division, Public Health Agency Ref: COM/5596/20. This funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data or decision to submit the result.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from the London - Chelsea Research Ethics Committee (REC Reference - 20/HRA/1731) and the Belfast Health & Social Care Trust Research Governance (Reference 19147TW-SW).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. All of the individual participant data collected during this study will be available (including data dictionaries) on the Queen's University Belfast database within 3 months of completion of the study.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines,

terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

ORCID iDs

Thomas Waterfield <http://orcid.org/0000-0001-9452-7716>
 Rebecca Moore <http://orcid.org/0000-0002-1585-5867>
 Kathryn Ferris <http://orcid.org/0000-0001-9452-7716>
 Michael Corr <http://orcid.org/0000-0001-9272-2323>

REFERENCES

- Ladhani SN, Amin-Chowdhury Z, Davies HG, *et al.* COVID-19 in children: analysis of the first pandemic peak in England. *Arch Dis Child* 2020. doi:10.2139/ssrn.3622390. [Epub ahead of print: 12 Aug 2020].
- Lipsitch M, Swerdlow DL, Finelli L. Defining the Epidemiology of Covid-19 - Studies Needed. *N Engl J Med* 2020;382:1194-6.
- CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:422-6.
- Children and COVID-19. Amsterdam: National Institute for public health and the environment (RIVM), 2020. Available: <https://www.rivm.nl/en/novelcoronavirus-covid-19/children-and-covid-19>
- Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. *JAMA* 2020;323:2427.
- Li Y, Zhou W, Yang L, *et al.* Physiological and pathological regulation of ACE2, the SARS-CoV-2 receptor. *Pharmacol Res* 2020;157:104833.
- Bourgonje AR, Abdulle AE, Timens W, *et al.* Angiotensin-Converting enzyme 2 (ACE2), SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19). *J Pathol* 2020;251:228-48.
- Bullis SSM, Crothers JW, Wayne S, *et al.* A cautionary tale of false-negative nasopharyngeal COVID-19 testing. *IDCases* 2020;20:e00791.
- Public Health England. COVID-19: Phe laboratory assessments of molecular tests. Available: <https://www.gov.uk/government/publications/covid-19-phe-laboratory-assessments-of-molecular-tests>
- Latest data and analysis on coronavirus (COVID-19) in the UK and its effect on the economy and society. Available: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases>
- Pollán M, Pérez-Gómez B, Pastor-Barriuso R, *et al.* Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet* 2020;396:535-44.
- Stringhini S, Wisniak A, Piumatti G, *et al.* Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. *Lancet* 2020;396:313-9.
- Pagani G, Conti F, Giacomelli A, *et al.* Seroprevalence of SARS-CoV-2 IgG significantly varies with age: results from a mass population screening (SARS-2-SCREEN-CdA). *MedRxiv* 2020.
- What's the Story - PHE England. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/916993/Weekly_COVID19_Surveillance_Report_week_37_FINAL.pdf
- Dong Y, Mo X, Hu Y, *et al.* Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;145:e20200702.
- Liu W, Zhang Q, Chen J, *et al.* Detection of Covid-19 in children in early January 2020 in Wuhan, China. *N Engl J Med* 2020;382:1370-1.
- Lu X, Zhang L, Du H, *et al.* SARS-CoV-2 infection in children. *N Engl J Med* 2020;382:1663-5.
- Parri N, Lenge M, Buonsenso D, *et al.* Children with Covid-19 in pediatric emergency departments in Italy. *N Engl J Med* 2020;383:187-90.
- Qiu H, Wu J, Hong L, *et al.* Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis* 2020;20:689-96.
- Tagarro A, Epalza C, Santos M, *et al.* Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. *JAMA Pediatr* 2020. doi:10.1001/jamapediatrics.2020.1346. [Epub ahead of print: 08 Apr 2020].
- von Elm E, Altman DG, Egger M, *et al.* The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453-7.
- Waterfield T *et al.* Seroprevalence of SARS-CoV-2 antibodies in children of healthcare workers - a prospective multicentre cohort study protocol, 2020.
- Public Health England. Evaluation of the Abbott SARS-CoV-2 IgG for the detection of anti-SARSCoV-2 antibodies. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/890566/Evaluation_of_Abbott_SARS_CoV_2_IgG_PHE.pdf
- Public Health England. Evaluation of Roche Elecsys AntiSARS-CoV-2 serology assay for the detection of anti-SARS-CoV-2 antibodies. Available: <https://assets.publishing>

- service.gov.uk/government/uploads/system/uploads/attachment_data/file/891598/Evaluation_of_Roche_Elecsys_anti_SARS_CoV_2_PHE_200610_v8.1_FINAL.pdf
- 25 Public Health England. Evaluation of DiaSorin liaison SARS-CoV-2 S1/S2 IgG serology assay for the detection of anti-SARS-CoV-2 antibodies. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/893435/Evaluation_of_Diasorin_Liaison_anti_SARS_CoV_2.pdf
- 26 Harris PA, Taylor R, Thielke R, *et al.* Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
- 27 Moore R *et al.* *Listening to the voices of children and young people involved in medical research*, 2020.
- 28 Choe PG, Kang CK, Suh HJ, *et al.* Antibody responses to SARS-CoV-2 at 8 weeks postinfection in asymptomatic patients. *Emerg Infect Dis* 2020;26:2484–7.
- 29 Long Q-X, Liu B-Z, Deng H-J, *et al.* Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med* 2020b;26:845–8.
- 30 Qu J, Wu C, Li X, *et al.* Profile of immunoglobulin G and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clin Infect Dis* 2020;395.
- 31 Sekine T, Perez-Potti A, Rivera-Ballesteros O, *et al.* Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19. *Cell* 2020;183:158–68.
- 32 Ripberger TJ, Uhrlaub JL, Watanabe M, *et al.* Detection, prevalence, and duration of humoral responses to SARS-CoV-2 under conditions of limited population exposure. *medRxiv* 2020. doi:10.1101/2020.08.14.20174490. [Epub ahead of print: 15 Aug 2020].