What's the STORY (Seroprevalence of representative youngsters)

Summary of results to end July 2020

Version 1.0

August 15th 2020

1. Introduction

This is an interim report of results for the 'What's the STORY' seroprevalence study, providing results of testing for antibodies specific to SARS-CoV-2 from October 2019 to end July 2020

Study Title : Sero-epidemiological survey of England in 2019/2020

Short title: What's the STORY? (Serum Testing Of Representative Youngsters)

IRAS Project ID: 263097, **Ethics reference:** 19/LO/1040, **Sponsor code:** OVG2019/01
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Sponsor: University of Oxford

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This study is conducted as a collaboration between the Oxford Vaccine Group, University of Oxford and Public Health England, across the National Immunisation Schedule Evaluation Consortium (NISEC) network of NIHR supported study sites.

This report has been prepared by Dr Helen Ratcliffe (DPhil student, University of Oxford), Professor Matthew Snape, Dr Gayatri Amirthalingam and Professor Nick Andrews (Public Health England).

A full list of study Collaborators and Investigators is included in Appendix A

2. Summary

To the end of July 2020, 1032 children, teenagers and young adults have been recruited to the 'What's the STORY (Serum Testing of Representative Youngsters) study across 10 sites in England.

Results from analysis with the ABBOTT assay (testing for IgG specific to the SARS-CoV-2 nucleocapsid protein) are available for 900 participants, 766 of whom are children and teenagers aged 0-19 years. Seroprevalence estimates from the Abbott assay were adjusted for sensitivity of 93.8% and specificity of 99.1% at a cut off of 0.8 (equivocal cut off).

From these children and teenagers:

- 119 of the 120 samples collected from October 2019 to March 2020, were negative (defined as <0.8 units) and 1 was equivocal (range 0.8 < 1.4, which was considered positive). Of note is that these samples were predominantly collected in the Thames Valley; the one 'positive' sample was collected on 20th February 2020 from a 10 – 14 year old Thames Valley participant
- In April and May 2020, 13 out of 352 (3.7%) participants were positive or equivocal (counted as positive). Adjusting for the sensitivity and specificity of the assay this gives an adjusted seroprevalence of 2.9% (95% C.I. 0.9 – 5.4%).
- Results during this period were very variable by region, ranging from between
    - 7/57 in South London (12.3%, corrected seroprevalence 11.7%, 95% C.I. 4.6 to 22.2%)
    - 0/41 in Bristol (0%, corrected seroprevalence 0.4%, 95% C.I. 0- 5.3%)
- In June and Jul 2020, 15 out of 294 (5.1%) were considered positive, giving an adjusted seroprevalence of 4.4% (2 – 7.5%)
    - In this period adjusted seroprevalence rates were highest in South London (10.4%, 95% C.I. 0.1 to 40.5) and Bristol (7.9%, 95% C.I. 2.1 – 7.3%
    - Adjusted seroprevalence rates were lowest in the Yorkshire and Humber sites (Leeds, Sheffield, Bradford), all of which were 1.2% or below.

Adjusted seroprevalence numbers with SARS-COV2 IgG and symptoms by age group are below

Table 1:

Age band (years)	April/May		June/July		Number of seropositive results	COVID-19 Symptoms
	Number	Adjusted seroprevalence	Number	Adjusted seroprevalence		
0 – 4	63	0.7% (0-5.8)	33	1.8% (0-11.5)	2	0
5 – 9	83	3.8% (0.2-10.1)	81	4% (0.3-10.4)	8	4
10-14	107	2.7% (0-7.7)	93	3.3% (0.1-9)	9	1
15 – 19	99	3% (0.1-8.4)	87	6.2% (1.7-13.1)	10	3
20-24	72	7.7% (2.4-15.9)	59	16.6% (8.2-27.9)	16	11
Total	**424**	**3.7% (1.8-6.2))**	**353**	**6.5% (3.9-9.7)**	**45**	**19**

Therefore only 8 of 29 (28%) of children and adolescents with antibodies against SARS-CoV-2 had any symptoms possibly related to COVID-19, suggesting most infections in this age group are asymptomatic. The 20 to 24 year olds enrolled in this study were more likely to have been infected with SARS-CoV-2 than younger cohorts, and more likely to have been symptomatic.

3. Study Design

This is an ongoing sero-epidemiology study that commenced in October 2019. The initial purpose of this study was to determine antibody levels against vaccine preventable diseases in children, adolescents and young adults. This was a pilot, feasibility study to obtain sera from a representative cross section of the paediatric population, enabling comparisons with existing methods of seroprevalence studies (analysing residual sera from clinical collections).

Following the onset of the COVID-19 pandemic the study was adapted to become a repeat cross-sectional sero-prevalence study evaluating the proportion of < 25 year olds with antibodies against SARS-CoV-2 across England throughout 2020/21, and was classified as an NIHR Urgent Public Health priority study.

The study is recruiting at 10 sites as outlined in Table 2. For all sites except Nottingham and Plymouth recruitment is primarily of participants living in postcode districts selected as being representative (in terms of Index of Multiple deprivation (IMD) scores) of their region. Recruitment at these sites has primarily been by direct mail out to households of children at the appropriate age living at the selected post-codes. Nottingham and Plymouth were added as sites following an expansion of the study in response to the COVID-19 pandemic, and recruit through community advertising. Potential participants and their families are invited to visit the study website (https://whatsthestory.web.ox.ac.uk/) for more information about the study, including translation of documents in 11 languages, and to contact the regional study site if they wished to participate.

Table 2. Study sites, recruiting methods and areas.

Site	Recruitment method	Postcodes
Bradford	Mail out, social media	BD6, BD15
Bristol	Mail out, social media	BS2, BS20, BS3, BS37, BS41, BS8
Leeds	Mail out, social media	LS25, WF2
Manchester	Mail out, social media	M1, M12, M20, M23, M25, M6
Oxford (Thames Valley)	Mail out, social media	HP17, HP22, HP23, MK13, OX1, OX11, OX28
Sheffield	Mail out, social media	S14, S43
Southampton	Mail out, social media	SO16, SO23, SO24, SO50, SO51, SO52
St Georges (London)	Mail out, social media	CR4, KT18, KT6, SM3, SW11, SW20
Nottingham	Social media	
Plymouth	Social media	

The majority of participants in this study are providing a single blood sample and completing a questionnaire to determine:

- COVID-19 symptoms/diagnoses in participants and their contacts
- Demographic data – gender, age, ethnicity, religion, educational institution and whether they are attending school at the time of the visit.

A subset of up to 20% of participants are being recruited to a longitudinal cohort providing up to 3 additional blood samples at 2 to 4 monthly intervals, along with saliva samples as an alternative method of measuring anti-SARS-Cov_2 antibodies.

Results from this study will be reported following the first wave of the pandemic, and up to monthly thereafter, with the frequency determined by events such as subsequent waves of COVID-19 infections and further 'lockdowns'.

The results of the 'first wave' are categorised according to the timing of the blood sample, allowing for the at least 2 to 4-week lag in development of SARS-CoV-2 specific antibodies, i.e.:

- Pre/early pandemic (pre - March 2020)
- Peri-'first wave' pandemic (April/May 2020)
- Post 'first wave' pandemic (June/July 2020)

Subsequent categorisation of participants will be determined according to significant milestones in the COVID-19 outbreak (e.g. school re-openings, second and subsequent waves of infection and/or subsequent restrictions in social movement).

Within these categories results are being presented according to:

- study site
- age band (0-4,5-9,10-14,15-19, 20-24) years of age

For each participant with evidence of an immune response to SARS-CoV-2 the presence of symptoms consistent with COVID-19 and likely household contacts is being collected.

4. Immunological assessment

Blood samples are being analysed for SARS-CoV-2 specific antibody responses using the ABBOTT assay, detecting IgG specific to SARS-CoV-2 nucleocapsid antigen. In independent analysis by Public Health England this has been found to be 93.8% sensitive and 99.1% specific for SARS-CoV-2 infections using the positivity threshold of >0.8 S/C (adapted from manufacturer's threshold of 1.4). Participants with results between 0.8 and 1.4 S/C will be reported as equivocal and considered positive for the purposes of estimating prevalence.

5. Objectives

The study protocol objectives relevant to COVID-19 are as follows:

5.1 Primary

To evaluate the feasibility and added public health benefit of an England, population based sero-epidemiological programme in 0 to 24 year olds

5.2 Secondary

- To evaluate the effectiveness of recruitment methods employed
- To assess, in relevant age groups, antibody concentrations against infections and vaccine preventable diseases including, but not limited to diphtheria, group C meningococcus and novel coronavirus (COVID-19)
- To determine the prevalence of SARS-CoV-2 infections in 0 – 24 year olds, and variation in prevalence in time, age and geography (cross-sectional sero-epidemiological study)
- To determine the kinetics of antibodies specific to SARS-CoV-2 following infection in a paediatric population (serial blood sampling in population sub-group)
- To determine relationship between serum and salivary antibodies against SARS-CoV-2

6. Statistical methods

The unweighted observed prevalence, $prev_{obs}$, is calculated as n^+/N, where n^+ is the number of individuals who tested positive and N is the total number of individuals tested with an available result. 95% exact confidence intervals were calculated for $prev_{obs}$ in STATA (version 14).

The results for each assay are analysed separately, and the alignment/nonalignment of results according to the two assays reported descriptively.

Adjusted prevalence for positive rates are calculated to take into account the sensitivity and specificity of each assay as described in Appendix B.

Population weighted observed prevalence data will be calculated using svy commands with the poststrata() option in STATA (version 14) and included in subsequent reports.

7. Results

7.1 Participants and demographics

As of 30th July 2020, 1032 participants have been recruited, as per Table 3.

Table 3: Participant details

Site	Age Band	Number up until 30/7/2020	Number of results available	Total per site up until 30/7/2020	Total number of results available
Bradford	0-4	14	9	92	80
	5-9	18	15		
	10-14	25	23		
	15-19	24	23		
	20-24	11	10		
Bristol	0-4	18	16	140	136
	5-9	28	27		
	10-14	35	34		
	15-19	22	22		
	20-24	37	37		
Leeds	0-4	7	1	39	13
	5-9	9	4		
	10-14	10	5		
	15-19	10	3		
	20-24	3	0		
Manchester	0-4	11	10	106	103
	5-9	30	28		
	10-14	25	25		
	15-19	20	20		
	20-24	20	20		
Nottingham	0-4	2	2	25	25
	5-9	7	7		
	10-14	7	7		
	15-19	9	9		
Oxford	0-4	48	31	279	247
	5-9	61	54		
	10-14	72	67		
	15-19	62	61		

	20-24	36	34		
Plymouth	0-4	8	3	49	35
	5-9	15	11		
	10-14	13	10		
	15-19	13	11		
Sheffield	0-4	12	11	66	61
	5-9	12	10		
	10-14	18	18		
	15-19	15	14		
	20-24	9	8		
Southampton	0-4	20	17	138	114
	5-9	30	22		
	10-14	40	34		
	15-19	31	27		
	20-24	17	14		
St Georges	0-4	18	16	98	86
	5-9	20	17		
	10-14	18	17		
	15-19	30	25		
	20-24	12	11		
All sites	Total no. participants	1032	900	1032	900
	0-4	158	115		
	5-9	230	195		
	10-14	263	240		
	15-19	236	215		
	20-24	145	134		

The demographic aspects of study participants are shown in Tables 4 to 6.

Table 4: Gender of study participants

	Brad.	Bristol	Leeds	Manch.	Nott.	Thames Valley	Plymouth	Sheff.	Southamp.	London	All sites
Male	41	69	17	46	12	149	23	29	78	48	512
Female	50	71	20	59	13	130	25	37	53	50	508
Missing data	1	0	2	1	0	0	1	0	7	0	12
Total	92	140	39	106	25	279	49	66	138	98	1032

Table 5: Ethnicity of Study participants

	Brad.	Bristol	Leeds	Manch.	Nott.	Thames Valley	Plymouth	Sheff.	Southamp.	London	All sites
White	75	128	36	74	22	232	45	60	117	80	869
Mixed/multiple ethnic groups	6	7	1	10	1	18	1	4	9	10	67
Asian/ Asian British	7	0	0	15	1	6	1	0	2	3	35
Black/ African/ Caribbean/ Black British	0	0	0	2	0	3	1	2	0	3	11
Other ethnic group	1	0	1	3	0	0	0	0	0	0	5
Missing data	3	5	1	2	1	21	1	0	10	2	46
Total	92	140	39	106	25	279	49	66	138	98	1032

Table 6. Participants and Index of Material Deprivation quintile

Quintiles/Site	**1 (most deprived)**	**2**	**3**	**4**	**5 (Least deprived)**	**Total by site**
Bradford	24	24	13	12	7	80
Bristol	8	13	22	40	60	143
Leeds	4	0	7	4	20	35
London	1	12	15	20	48	96
Manchester	36	8	19	21	0	84
Nottingham	3	2	7	6	7	25
Thames Valley	11	24	28	54	158	275
Plymouth	7	8	7	16	8	46
Sheffield	32	19	8	6	3	68
Southampton	8	8	23	36	56	131
Total	**134**	**118**	**149**	**215**	**367**	**983***

* IMD data not available for the postcode of 49 participants

7.2 Immunology

The results of serological testing by both assays are summarised in Tables 7 to 9 below. Of note is that for the ABBOTT assay equivocal results are counted as positive for seroprevalence calculations

Table 7: Summary of Abbott assays across three study periods

Table 7.1: all ages

Time period	+ve result	Equivocal	-ve result	Number of participants	Proportion +ve (95% C.I.)	Adjusted prevalence (95% C.I.)
October 2019-March 2020	0	1	122	123	0.8% (0-4.4)	0.3% (0-2.8)
April – May 2020	17	2	405	424	4.5% (2.7-6.9)	3.7% (1.8-6.2)
Jun-July 2020	17	8	328	353	7.1% (4.6-10.3)	6.5% (3.9-9.7)

Table 7.2: 0 – 19 year olds

Time period	+ve result	Equivocal	-ve result	Number of participants	Proportion +ve	Adjusted prevalence (95% C.I.)
October 2019-March 2020	0	1	119	120	0.8% (0-4.6)	0.3% (0-2.9)
April – May 2020	11	2	339	352	3.7% (2-6.2)	2.9% (0.9-5.4)
Jun-July 2020	10	5	279	294	5.1% (2.9-8.3)	4.4% (2-7.5)

Table 8: Proportion of participants with detectable IgG specific to SARS-CoV-2 on Abbott assay by site and study period

Table 8.1 – November 2019 to March 2020 all ages

Site	+ve result	Equivocal	-ve result	Number of samples analysed	Proportion +ve	Adjusted prevalence (95% C.I.)
Bradford	0	0	2	2	0% (0-84.2)	NA
Thames Valley	0	1	109	110	0.9% (0-5)	0.3% (0-3.2)
St Georges	0	0	11	11	0% (0-28.5)	1.2% (0-17.2)
Total	0	1	122	123	0.8% (0-4.4)	0.2% (0-2.8)

Table 8.2– November 2019 to March 2020, 0 – 19 years

Site	+ve result	Equivocal	-ve result	Number of samples analysed	Proportion +ve	Adjusted prevalence (95% C.I.)
Bradford	0	0	2	2	0% (0-84.2)	NA
Thames Valley	0	1	107	108	0.9% (0-5.1)	0.3% (0-3.2)
St Georges	0	0	10	10	0% (0-30.8)	1.3% (0-18.6)
Total	0	1	119	120	0.8% (0-4.6)	0.3% (0-2.8)

Table 8.3 – April to May 2020, all ages

Site	+ve result	Equivocal	-ve result	Number of participants	Proportion +ve	Adjusted prevalence (95% C.I.)
Bradford	1	1	62	64	3.1% (0.4-10.8)	1.9% (0-8.4)
Bristol	1	0	53	54	1.9% (0-9.9)	0.9% (0-6.8)
Leeds						
Manchester						
Nottingham						
Thames Valley	3	1	108	112	3.6% (1-8.9)	2.5% (0-7.4)
Plymouth						
Sheffield	2	0	45	47	4.3% (0.5-14.5)	3.1% (0-11.7)
Southampton	2	0	83	85	2.4% (0.3-8.2)	1.2% (0-6.1)
St Georges	8	0	54	62	12.9% (5.7-23.9)	12.4% (5.3-22.6)
Total	17	2	405	424	4.5% (2.7-6.9)	3.7% (1.8-6.2)

Table 8.4 – April to May 2020, 0 – 19 years

Site	+ve result	Equivocal	-ve result	Number of participants	Proportion +ve	Adjusted prevalence (95% C.I.)
Bradford	1	1	53	55	3.6% (0.4-12.5)	2.4% (0-9.9)
Bristol	0	0	41	41	0% (0-8.6)	0.4% (0-5.3)
Leeds						
Manchester						
Nottingham						
Thames Valley	1	0	82	83	1.2% (0-6.5)	0.5% (0-4.4)
Plymouth						
Sheffield	1	0	42	43	2.3% (0.1-12.3)	1.2% (0-8.7)
Southampton	2	0	72	74	2.7% (0.3-9.4)	1.5% (0-7.1)
St Georges	7	0	50	57	12.3% (5.1-23.7)	11.7% (4.6-22.2)
Total	11	2	339	352	3.7% (2-6.2)	2.9% (0.9-5.4)

Table 8.5 - June – July 2020, all ages

Site	+ve result	Equivocal	-ve result	Number of samples analysed	Proportion +ve	Adjusted prevalence (95% C.I.)
Bradford	1	0	13	14	7.1% (0.2-33.9)	5.7% (0-26)
Bristol	7	0	75	82	8.5% (3.5-16.8)	7.9% (2.8-15.6)
Leeds	0	0	13	13	0% (0-24.7)	1.1% (0-15)
Manchester	6	4	93	103	9.7% (4.8-17.1)	9.2% (4.2-16.3)
Nottingham	0	1	24	25	4% (0.1-20.4)	2.7% (0-15.1)
Thames Valley	0	1	24	25	4% (0.1-20.4)	2.7% (0-15.2)
Plymouth	1	0	34	35	2.9% (0.1-14.9)	1.7% (0-10.9)
Sheffield	1	0	13	14	7.1% (0.2-33.9)	5.6% (0-25.8)
Southampton	0	2	27	29	6.9% (0.8-22.8)	5.7% (0.1-18.9)
St Georges	1	0	12	13	7.7% (0.2-36)	6.1% (0-27.8)
Total	17	8	328	353	7.1% (4.6-10.3)	6.5% (3.9-9.7)

Table 8.6 June – July 2020, 0 – 19 years

Site	+ve result	Equivocal	-ve result	Number of samples analysed	Proportion +ve	Adjusted prevalence (95% C.I.)
Bradford	0	0	13	13	0% (0-24.7)	1.1% (0-14.9)
Bristol	5	0	53	58	8.6% (2.9-19)	7.9% (2.1-17.3)
Leeds	0	0	13	13	0% (0-24.7)	1.1% (0-15.1)
Manchester	3	2	78	83	6% (2-13.5)	5.2% (1-12)
Nottingham	0	1	24	25	4% (0.1-20.4)	2.7% (0-15.2)
Thames Valley	0	1	21	22	4.5% (0.1-22.8)	3.2% (0-17.4)
Plymouth	1	0	34	35	2.9% (0.1-14.9)	1.7% (0-10.8)
Sheffield	0	0	11	11	0% (0-28.5)	1.2% (0-17.3)
Southampton	0	1	24	25	4% (0.1-20.4)	2.6% (0-14.7)
St Georges	1	0	7	8	12.5% (0.3-52.7)	10.4% (0.1-40.5)
Total	10	5	279	294	5.1% (2.9-8.3)	4.4% (2-7.5)

Table 9: Proportion of participants with detectable IgG specific to SARS-CoV-2 on Abbott assay by age band

Table 9.1– November 2019 to March 2020

Age band	+ve result	Equivocal result	-ve result	Number of participants	Proportion +ve	Adjusted prevalence (95% C.I.)
0-4	0	0	20	20	0% (0-16.8)	0.7% (0-10.1)
5-10	0	0	31	31	0% (0-11.2)	0.5% (0-6.9)
11-14	0	1	39	40	2.5% (0.1-13.2)	1.4% (0-9.4)
15- 19	0	0	29	29	0% (0-11.9)	0.5% (0-7.2)
20 – 24	0	0	3	3	0% (0-70.8)	NA

Table 9.2 – April to May 2020

Age band	+ve result	Equivocal results	-ve result	Number of participants	Proportion +ve	Adjusted prevalence (95% C.I.)
0-4	1	0	62	63	1.6% (0-8.5)	0.7% (0-5.8)
5-10	3	1	79	83	4.8% (1.3-11.9)	3.8% (0.2-10.1)
11-14	3	1	103	107	3.7% (1-9.3)	2.7% (0-7.7)
15- 19	4	0	95	99	4% (1.1-10)	3% (0.1-8.4)
20 – 24	6	0	66	72	8.3% (3.1-17.3)	7.7% (2.4-15.9)

Table 9.3 – June to July 2020

Age band	+ve result	Equivocal results	-ve result	Number of participants	Proportion +ve	Adjusted prevalence (95% C.I.)
0-4	1	0	32	33	3% (0.1-15.8)	1.8% (0-11.5)
5-9	4	0	77	81	4.9% (1.4-12.2)	4% (0.3-10.4)
10-14	2	2	89	93	4.3% (1.2-10.6)	3.3% (0.1-9)
15- 19	3	3	81	87	6.9% (2.6-14.4)	6.2% (1.7-13.1)
20 – 24	7	3	49	59	16.9% (8.4-29)	16.6% (8.2-27.9)

8. Characteristics of participants with IgG against SARS-CoV-2 nucleocapsid protein

The participants classified as being positive for SARS-CoV-2 IgG are summarised in Table 10. Of these 45 participants, 29 were children and teenagers and 16 were aged 20 – 24 years.

Amongst the 29 children and teenagers 14 were female, 23 (79%) were of 'White' ethnicity and 8/29 (27%) had possible COVID-19 symptoms.

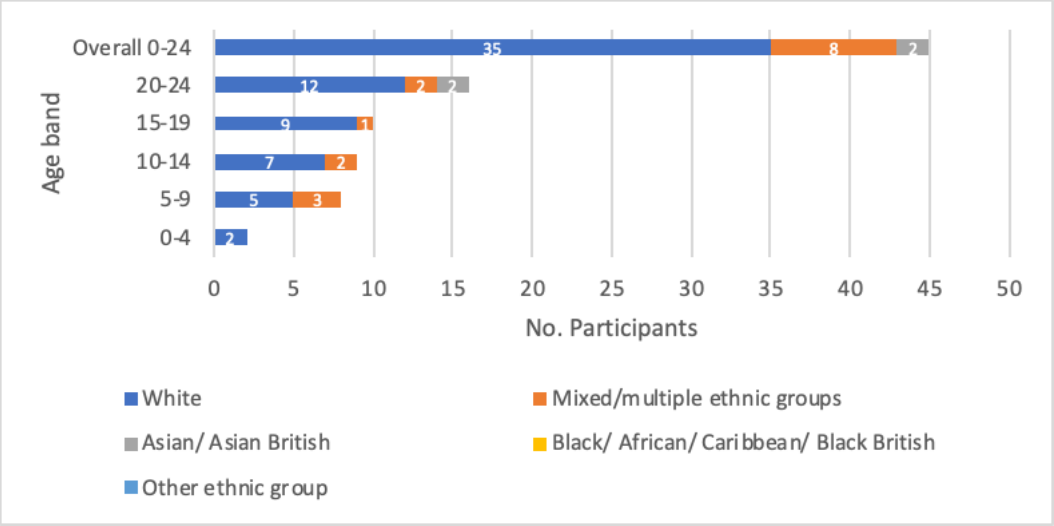
Amongst the 16 participants aged 20 – 24 year olds with positive antibodies, 10 were female, 12 (75%) were of 'White' ethnicity and 11 (68%) had symptoms possibly related to COVID-19.

Table 10: Summary of participants with detectable IgG to SARS-Cov-2 by ABBOTT assay

Age	Gender	Site	Date of test	ABBOTT IgG	Symptoms COVID-19?
13	M	Bradford	04/2020	0.98	N
5	F	Bradford	05/2020	4.41	Y
20	M	Bradford	06/2020	2.23	Y
21	F	Bristol	04/2020	3.2	y
9	F	Bristol	06/2020	4.62	Y
15	M	Bristol	06/2020	2.72	n
22	F	Bristol	07/2020	2.94	y
9	M	Bristol	07/2020	2.48	n
14	F	Bristol	07/2020	2.01	y
22	M	Bristol	07/2020	2.44	Y
3	M	Bristol	07/2020	5.23	N
7	M	Manchester	06/2020	5.56	N
22	F	Manchester	06/2020	4.94	Y
22	F	Manchester	06/2020	7.51	Y
7	F	Manchester	07/2020	3.45	Y
21	F	Manchester	07/2020	3.14	N
24	F	Manchester	07/2020	1.21	Y
16	F	Manchester	07/2020	1.02	N
13	F	Manchester	07/2020	3.39	N
20	F	Manchester	07/2020	1.36	Y
13	F	Manchester	07/2020	1.25	N
13	F	Oxford	02/2020	1.03	n
21	M	Oxford	04/2020	4.31	n
9	M	Oxford	04/2020	1.3	y
23	M	Oxford	04/2020	7.65	n
24	F	Oxford	05/2020	3.03	Y
19	F	Oxford	06/2020	1.34	y
9	F	Sheffield	04/2020	4.70	n
21	F	Sheffield	04/2020	6.02	y
21	F	Sheffield	06/2020	2.32	n
17	M	Southampton	06/2020	1.1	n

20	M	Southampton	06/2020	1.1	n
14	M	Southampton	05/2020	4.85	n
17	M	Southampton	05/2020	3.59	n
16	F	London	04/2020	6.93	y
2	M	London	04/2020	3.78	n
10	M	London	04/2020	3.35	n
15	M	London	04/2020	4.34	n
9	F	London	04/2020	4.43	n
11	M	London	04/2020	3.34	n
16	F	London	05/2020	2.35	n
24	M	London	05/2020	2.31	y
18	M	London	07/2020	1.78	y
14	F	Nottingham	07/2020	0.97	N
16	M	Plymouth	06/2020	5.05	N

Figure 1: Summary of seropositive participants per age band by ethnicity



9 Conclusions

In this report we have shown that, up until the end of July 2020, the vast majority of children and teenagers in England have no evidence of having been infected with SARS-C0V-2. Of those with infection, the majority have been asymptomatic.

The first sample with an (equivocal) positive result was taken on the 20th February, with the next positive sample being collected on the 3rd of April raising the possibility that the February result was a false positive.

It is important to note that the validation of the ABBOTT assay, and calculation about sensitivity and specificity, have primarily been performed in the adult, rather than paediatric, population and there is the possibility that the SARS-CoV-2 nucleocapsid-specific IgG response to infection, and the longevity of that response, may differ in younger age groups. Nevertheless the low rates of seropositivity in 0 – 4 year olds is striking, with an adjusted seroprevalence of less than 2% for both post-baseline study periods. While adjusted seroprevalence rates for the 5 to 14 year olds were relatively consistent, both within age bands and between post-baseline time periods (2.7% to 4%), by June/July an apparent age based increment was apparent, with an adjusted seroprevalence for 15 to 19 year olds of 6.2%, and for 20 – 24 of 16.6%. The later figure is higher than the 6.9% adjusted seroprevalence observed in 18 to 24 year olds during the same period in the REACT2 seroprevalence study using a self-administered lateral flow test kit (6.9%)(1).

The regional differences observed in reports of disease incidence were reflected in this paediatric sero-epidemiology study, with seroprevalence rates in London in 0 to 19 year olds in April/May (11.7%) apparently higher than all other sites in this period (maximum 2.4%, although no samples from Manchester, Leeds, Nottingham or Plymouth were available for April/May).

Also notable were low paediatric and teenage seropositivity rates in the three Yorkshire and Humber sites (Bradford, Leeds, Sheffield), with only 3 out of 132 (2.2%) post-baseline samples being positive or equivocal, and adjusted seroprevalence rates of 1.1% to 1.2% in June/July. Only 4 samples from 20 – 24 year olds from this region were taken in June/July, 2 of which were positive, which appears to be more in keeping with local emergence of disease in this are in July.

The increased risk of COVID-19 disease in Black and Minority Ethnic (BAME) communities is well recognised, and recent reports in the adult population have also shown higher rates of SARS-CoV-2 sero-positivity in BAME participants. In this study 863/981 (87.9%) of participants with data available described themselves as being of white, with only 11 (1.1%) describing themselves as being of Black/ African/ Caribbean/Black British ethnicity. The proportions of participants with detectable antibodies who described themselves as being of English/Welsh/Scottish/Northern Irish/ British ethnicity (78%) was only slightly lower than the general study population, however formal comparisons of infection rates across different ethnicities are limited by the lower numbers in the BAME cohorts, and models for an additional study group with enhanced recruitment in the BAME community are currently under consideration.

Across the study, 275 out of 983 (37%) of participants with IMD data available came from the 5th (least deprived) quintile, however this figure was heavily skewed by the demographics of the Thames Valley participants, where 158 out of 275 (57%) came from this quintile. Across the remainder of the sites

this proportion was 29%, and further analysis will be undertaken to account for this potential bias in seroprevalence data.

The understanding of the frequency of paediatric SARS-CoV-2 infections will be enhanced by ongoing work in this study, including:

- further analysis of the samples taken using the RBD assay
- assessment of the kinetics of the antibody response
- assessment of the T cell response
- undertaking logistical regression to formally asses impact of age, region, socio-economic status and ethnicity on seroprevalence, and to determine population prevalence weighted for these factors

Sample collection in the study is ongoing, and will continue to collect samples after re-opening of schools in September 2020, and through the coming autumn and winter, providing an ongoing evidence base to inform the understanding of the prevalence and nature of infections in English children, teenagers and young adults.

1. Ward H, Atchison C, al e. Antibody prevalence for SARS-CoV-2 following the peak of the pandemic in England: REACT 2 study in 100,000 adults 2020 [Available from: https://www.imperial.ac.uk/media/imperial-college/institute-of-global-health-innovation/Ward-et-al-120820-REACT-2.pdf.

Appendix A:

Collaborators, Investigators and Acknowledgments

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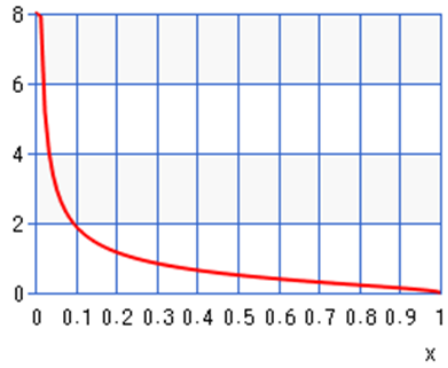
Appendix B: Statistical methods: calculation of estimated seroprevelence

It is understood that all assays are imperfect and can sometimes give false positive and false negative results, with probability (1-*Sp*) and (1-*Se*) respectively, where *Sp* denotes the Specificity or the probability that the test gives a negative result in individuals who have not experienced the disease, and *Se* denotes the Sensitivity or the probability that the test gives a positive result in individuals who have experienced the disease. The adjusted prevalence, denoted $prev_{adj}$, should better reflect the proportion of the population that have experienced the disease; this is related to the observed prevalence as follows:

$$prev_{obs} = Se \times prev_{adj} + (1 - Sp) \times \left(1 - prev_{adj}\right)$$

(see Diggle 2011, Lewis & Torgerson 2012). This relation was incorporated in a Bayesian model, along with the sampling distribution for positive tests n^{+}~Binomial(N, $prev_{obs}$). The sensitivity and specificity are not known exactly, but are informed by data. Counts of true positives and false negatives in convalescent sera were used to estimate the sensitivity, and similarly counts of true negatives and false positives in pre-covid19 baseline sera were used to estimate the specificity. The sensitivity, *Se*, and specificity, *Sp*, were included in our Bayesian model each by way of a conjugate Beta-Binomial model with a Beta(0.5,0.5) reference prior, thus uncertainty in their true value was taken into account.

In unweighted adjustment models, we use a Beta(0.4,1.6) prior for the adjusted prevalence $prev_{adj}$. This is distributed as below and has a mean of 0.2 (see below for probability density). In other PHE seroprevalence estimates a Beta(0.5,0.5) (Jeffrey's prior - mean of 0.5) has been used. These priors will only make a meaningful difference if the sample size is very small.



MCMC models were run using the NIMBLE package in R, default sampler, 500,000 iterations with a burn-in of 1,000 iterations and a thinning interval of 5.

Models to estimate population weighted $prev_{adj}$ (which have not as yet been fitted) will be further extended to a multilevel logistic regression model, including a random effect for age and region specific seroprevalences (plus a fixed effect for gender when modelling the NHSBT data), following Park et al

(2004)'s multilevel regression and poststratification (MRP) models. If each `cell' combination of age and region (and gender, if included) is denoted *j*, then the weighted or poststratified prevalence is given by

$$prev_{weighted} = \frac{\sum_j N_j prev\_adj_j}{\sum_j N_j}$$

Where N_j denotes the population of each cell taken from ONS data. MCMC models were run using STAN and the rstan package in R, 4 chains of length 25,000, with a burn-in of 1,000 iterations.