A Prospective Study on the Prevalence of SARS-CoV-2 Antibodies among Children in Ireland, 2024

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20 January 2025

Key Points

Anonymised residual sera collected between 01 February and 19 June 2024, from 2,709 children aged 3-17 years were tested for SARS-CoV-2 antibodies. Results presented are based on serology testing with nucleocapsid (N) and spike (S) antibody assays. Spike protein antibodies are detected after COVID-19 vaccination and are also detected after SARS-CoV-2 infection. Nucleocapsid protein antibodies develop only after natural infection. Seroprevalence refers to those who tested positive on either assay.

1. **High seroprevalence of SARS-CoV-2 antibodies in children, 2024:**
    - Overall, 97.6% (95% CI:97.0-98.1) of children aged 3-17 years had detectable antibodies to either the spike or nucleocapsid protein.
    - Seroprevalence was high among both females 97.9% (95% CI: 97.0-98.5) and males 97.3% (96.3-98.1) and was not significantly different by sex.
    - Seroprevalence was high in all age groups overall and increased with age-group. It was 93.0% (95% CI:89.5-95.4) in the 3-4 year age-group, 96.7% (95% CI:95.3-97.7) in the 5-11 year age-group, and it was particularly high in the 12-17 year age-group at 99.0% (95% CI:98.4-99.4), $p<0.001$).

2. **High seroprevalence of SARS-CoV-2 in children throughout the study period:**
    - Seroprevalence was consistently high between February and June 2024, and when stratified by sex and age-group.

3. **Increased SARS-CoV-2 seroprevalence among children since 2022:**
    - As expected, due to increased exposure from natural infection and due to vaccine eligibility among children in Ireland from December 2021 onwards, seropositivity among children has increased over time, from 39.4% (95% CI:32.4-46.9) in January 2022, to 88.5% (95% CI:84.3-91.8) in July 2022 and and 97.6% (95% CI:97-98.1) between February and June 2024.

4. **Similar seroprevalence among adults in Ireland in 2024:**
    - Seroprevalence among adults for the same period in 2024 (99.5% (95% CI: 99.2-99.7) was comparable to the seroprevalence among children in this study. This is in contrast with differences in seroprevalence reported for adults and children in 2022.

5. **Seroprevalence data supported the development of primary vaccine recommendations for children in Ireland.**
    - Data from this study contributed to the changes made to the most recent recommendations by the National Immunisation Advisory Committee on the SARS-CoV-2 primary schedule for children published in August 2024.

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Background

The National Serosurveillance Programme (NSP) is the national programme for serosurveillance of notifiable communicable diseases in Ireland. The NSP was established in 2021 as part of the emergency response to the COVID-19 pandemic to monitor SARS-CoV-2 antibody seroprevalence. Since then, it has evolved to monitor other notifiable infectious diseases of public health importance in both adult and paediatric populations. The NSP is managed by the Sero-epidemiological Unit (SEU) in the Health Protection Surveillance Centre (HPSC) and is governed by a multidisciplinary and multisectoral steering committee.

Seroepidemiological data has an important role in comprehensive infectious disease and vaccine surveillance, complementing other types of surveillance data. During the COVID-19 pandemic, SARS-CoV-2 seroprevalence data were used to aid an evidence-based public health response (1).

In 2020, the World Health Organization (WHO) developed a protocol for population-based SARS-CoV-2 serosurveillance studies (2), which were implemented globally, including in Ireland (1, 3). In July 2020, a population-based study led by the HPSC estimated that SARS-CoV-2 seroprevalence among individuals aged 12-69 years in Ireland was 1.69% (3). Routine ongoing national surveillance of SARS-CoV-2 seroprevalence in adults was initiated by the NSP in 2021 (4) and since then, the NSP has conducted two national studies on SARS-CoV-2 seroprevalence in children, in 2022 (5, 6).

In 2024, the third national SARS-CoV-2 serosurvey in children was conducted to provide updated estimates of SARS-CoV-2 antibody seroprevalence in the paediatric population to support and inform vaccine recommendations for children in Ireland by the National Immunisation Advisory Committee (NIAC). This report details the findings of that study.

Study objectives

1. To measure overall, age group- and sex-specific prevalence of SARS-CoV-2 immunoglobulin G (IgG) antibodies to the spike or nucleocapsid proteins (S/N) in residual sera from children in Ireland aged 3-17 years.
2. To provide data to NIAC to support the development of primary vaccine recommendations for children in Ireland.
3. To report on and use data from the study to add to expand the knowledge and understanding of SARS-CoV-2 seroprevalence in children in Ireland.

Methods

Study design

This was a cross-sectional study using residual serum collected between 01 February 2024 and 19 June 2024, from children aged 3-17 years. Anonymised residual sera were collected primarily as part of a different study to estimate the seroprevalence of measles IgG antibodies in children. For the current study, residual sera with sufficient volume after measles testing were tested for antibodies to the SARS-CoV-2 spike and nucleocapsid proteins. Based on recommendations from NIAC, three age groups were analysed: 3-4, 5-11, and 12-17 years, which best aligned with the age-groups used for the Pfizer COVID-19 vaccination guidelines in Ireland; 6 months-4 years, 5-11 years and 12+ years (7).

Sample and data collection

Convenience sampling was conducted, and samples were chosen randomly. The minimum sample required was estimated to be approximately 2,400 samples, the final sample count was 2,709 samples, from which we can report estimates by sex and age-group with +/-3% precision. Existing residual serum samples were collected by the Laboratory Surveillance Network (LSN) in four hospital clinical laboratories: Letterkenny University Hospital (LUH), St Vincent's University Hospital Dublin (SVUH), Tallaght University Hospital Dublin (TUH), and University Hospital Limerick (UHL). Samples were sourced from general practitioners (GPs), emergency departments, urgent care centres, and outpatient departments. Urgent care samples came from the urgent care centres at TUH and SVUH, and clinics set up for incoming foreign nationals without GP care, collected via LUH. Anonymised samples were sent directly from laboratories to the National Virus Reference Laboratory (NVRL) serosurveillance unit for testing, and anonymised demographic data for each sample were sent to the SEU. The SEU received test results directly from the NVRL and linked the demographic dataset using a unique anonymised SEU ID. A minimum demographic dataset was collected for each sample, comprising sex, date of birth, and county of residence. Sample collection date, sample source, test result date, as well as quantitative and qualitative results from laboratory testing were also included in the dataset.

Exclusion criteria

Samples found to be of insufficient volume, or samples that were haemolysed, icteric or lipaemic were excluded from the analysis. The age range for sample collection started at 3 years and excluded younger children due to the challenge of obtaining sufficient volumes of sera in that group. Samples from hospitalised patients were excluded as being particularly unrepresentative of the general population. Samples that were missing data on source were also excluded from this study to ensure that hospitalised patients were not inadvertently included.

SARS-CoV-2 serology

Serology testing was carried out by the NVRL using the testing platforms listed in Table 1. A parallel testing algorithm was employed, with all samples tested for antibodies to both the SARS-CoV-2 spike (S) protein and the nucleocapsid (N) protein. This approach differs from prior SARS-CoV-2 seroprevalence studies conducted by the NSP, where sequential testing algorithms were employed, testing first for antibodies the spike protein and then only testing spike positive samples for antibodies to the nucleocapsid protein.

Testing and interpretation of results are outlined in **Figure 1**. Antibodies to the SARS-CoV-2 spike protein were detected using the Abbott SARS-CoV-2 IgG II Quantitative Assay, which provides results in arbitrary units (AU) per mL. These were converted to the WHO international standard Binding Antibody Units (BAU) with the formula: AU/mL * 0.142.

Table 1. The testing platforms used to determine SARS-CoV-2 seroprevalence:

Assay name	Sensitivity	Specificity	Quantitative result	Qualitative result
Abbott Architect SARS-CoV-2 IgG II	98.75% (95% CI: 93.25-99.94)	99.5% (95% CI: 99.15- 99.76)	Arbitrary units per millilitre (AU/ml), range 21 - 40,000	A result of at least 50.0 AU/mL is considered positive (**S+**)
Roche Elecsys Anti-SARS-CoV-2 Q	99.5% (95% CI: 97.0-100)	99.8% (95% CI: (99.69-99.88)	Cut-off index	A result of at least 1.0 is considered positive (**N+**)

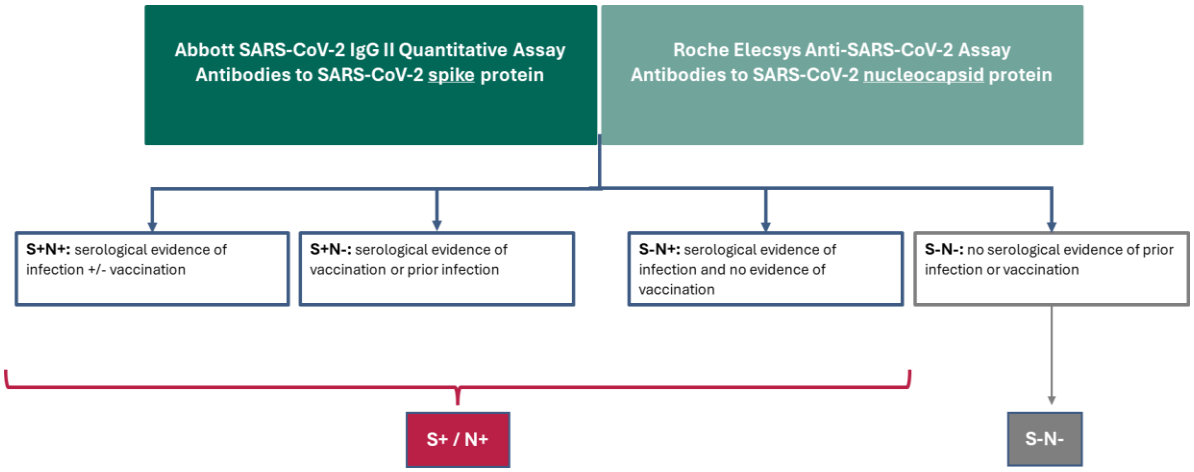

Figure 1. SARS-CoV-2 laboratory testing algorithm and interpretation. All samples were tested for antibodies to the SARS-CoV-2 spike and nucleocapsid proteins. Samples with detectable antibodies (IgG) to the spike protein (S+N-) or the nucleocapsid protein (S-N+) or to both (S+N+) were defined as '**S+/N+**'.

Interpretation of serology results

Spike protein antibodies are detected after COVID-19 vaccination and are also detected after SARS-CoV-2 infection. Nucleocapsid protein antibodies develop only after natural infection. Any sample that tested positive for spike protein-specific IgG antibodies was defined as '**S+**', suggestive of response to vaccination or prior infection. Any sample that tested positive for nucleocapsid protein-specific IgG antibodies was defined as '**N+**', suggestive of previous SARS-CoV-2 infection. To capture the varied responses seen from individual to individual, seroprevalence in this study is defined as the proportion of samples that tested positive for either spike protein-specific IgG or nucleocapsid protein-specific IgG or both: '**S+/N+**'.

Data analysis

All data validation and statistical analysis was performed using R version 4.4.0 (https://www.R-project.org/). To explore the possibility of sampling bias, proportions by sex and age-group were compared to the national census of Ireland in 2022 (8) using a binomial exact test. Seroprevalence was calculated by dividing the number of specimens that tested positive for spike or nucleocapsid IgG antibodies by the total number of specimens with a valid test result.

Seroprevalence estimates were adjusted for assay sensitivity and specificity using the Rogan-Gladen estimator (9) and include a 95% confidence interval (CI). See technical notes for details. A logistic regression model was used to explore the association between seropositivity and demographic variables; sex and age-group.

Results

Demographic characteristics

In total, 2,709 residual serum samples were tested for SARS-CoV-2 antibodies: 1,462 (54.0%) females and 1,247 (46.0%) males. The median age of those included in the study was 13 years. Age was grouped for analysis as 3-4 years (n = 287; 10.6%), 5-11 years (n = 872; 32.2%), and 12-17 years (n = 1,550; 57.2%); Table 2. Most samples were from children residing in Dublin (n = 1,390; 51.3%) or Donegal (n = 545; 20.1%), with the largest percentage of samples collected by hospitals in Dublin: TUH (n = 1,308; 48.3%), SVUH (n = 705; 26.0%). The remaining samples were collected by LUH (n = 544; 20.1%) and UHL (n = 152; 5.6%). Samples were primarily sourced from GPs (n = 1512; 55.8%) or emergency departments (n = 642; 23.7%), followed by outpatient clinics (n= 403; 14.9%) and urgent care centres (n = 152; 5.6%).

Representativeness by sex and age-group

The proportion by sex and age group in this study differed significantly to the Irish population (appendix table A1), however when the data were weighted to the national population structure, there was no significant difference in seroprevalence between weighted and unweighted estimates, (97.2% (95% CI: 96.4-97.8) and 97.6% (95% CI:97.0-98.1) respectively). Therefore, the seroprevalence estimates calculated as part of this study are applicable to the general population. Representativeness by other variables (e.g. ethnic group) could not be explored as those variables were not included in this study.

Seroprevalence of SARS-CoV-2 by sex and age-group

Seroprevalence was 97.6% (95% CI:97.0-98.1) overall, 97.9% (95% CI:97.0-98.5) in females and 97.3% (95% CI:96.3-98.1) in males, **Table 2**. S+/N+ seroprevalence was 93.0% (95% CI:89.5-95.4) in the 3-4 year age-group, 96.7% (95% CI:95.2-97.7) in the 5-11 year age-group, and 99% (95% CI:98.4-99.4) in the 12-17 year age-group (Table 2, appendix Figure A1). A similar pattern was observed across age-groups stratified by sex, with the highest estimates in the 12-17 year age-group and the lowest estimates in the 3-4 year age-group (Table 2 and appendix Figure A2). For unadjusted seroprevalence estimates, see appendix Table A2.

Table 2. SARS-CoV-2 seroprevalence estimates in children, adjusted for assay sensitivity and specificity: 01 February 2024 to 19 June 2024

Sample	Age-group (years)	Count	%	S+ / N+ count	S+ / N+ (%)	S+ / N+ 95% CI
All		2709	100	2645	97.6	97.0, 98.1
Female		1462	54.0	1431	97.9	97.0, 98.5
Male		1247	46.0	1214	97.3	96.3, 98.1
3-4		287	10.6	267	93.0	89.4, 95.4
5-11		872	32.2	843	96.7	95.2, 97.7
12-17		1550	57.2	1535	99.0	98.4, 99.4
Female	3-4	128	4.72	118	92.1	86.1, 95.7
	5-11	433	16.0	421	97.2	95.2, 98.4
	12-17	901	33.3	892	99.0	98.1, 99.5
Male	3-4	159	5.87	149	93.7	88.7, 96.5
	5-11	439	16.2	422	96.1	93.9, 97.6
	12-17	649	24.0	643	99.1	98.0, 99.6

Seropositivity to the spike protein (S+), indicating prior infection or vaccination, was 95.8% (95% CI:94.9-96.6). Seropositivity to the nucleocapsid protein (N+), indicating prior SARS-CoV-2 infection, was 93.5% (95%CI: 92.4-94.4). The breakdown by sex and age-group is shown in Table A3.

Overall, 2,645 samples tested positive for either spike or nucleocapsid protein IgG, of which, 2,438 (92.2%) tested positive for both. Of the remaining 207 samples: 125 (4.6%) tested positive for spike IgG and negative for nucleocapsid IgG (S+N-), and 82 (3.2%) tested negative for spike IgG and positive for nucleocapsid IgG (S-N+). Of the 82 samples that tested positive for nucleocapsid IgG only (S-N+), 20 (7%) were aged 3-4 years, 43 (5%) were aged 5-11 years, and 19 (1%) were aged 12-17 years. A total of 2.4% (n = 64) of all samples did not test positive for spike protein or nucleocapsid protein IgG, indicating no serological evidence of past exposure to or vaccination against SARS-CoV-2.

Quantitative SARS-CoV-2 antibody levels

Median spike and nucleocapsid antibody levels were higher in the 12-17 year age-group (550.5 BAU/ml, 93.2 AU/ml) compared with the 5-11 year old age-group (87.9 BAU/ml, 44.8 AU/ml) and the 3-4 year age-group (45.4 BAU/ml, 27.3 AU/ml; appendix Table A4), and this difference was largely consistent over time (appendix Figure A3). Median antibody levels for both spike and nucleocapsid were higher in females (252.0 BAU/ml, 76.0 AU/ml) compared with males (165.3 BAU/ml, 56.9 AU/ml) and this difference was consistent over time (appendix Table A4, Figure A4). For the distribution of spike and nucleocapsid IgG levels by sex and age-group see Figure A5 – A8 in the Appendix.

SARS-CoV-2 seroprevalence over time

Seroprevalence estimates were calculated by month from February to May 2024. Seroprevalence was consistently high (>90%) over time (Table 3), and when stratified by sex and age-group, with marginally lower estimates observed in May for all groups (appendix Table A5). Data from June were excluded from all graphs due to the low number of samples tested (appendix Table A6 n=7). The variability by month observed in the 3-4 year old age group should be interpreted with caution due to low numbers tested. There was no evidence of an increasing or decreasing trend over time.

Table 3. Seroprevalence by month from February to May 2024, adjusted for assay sensitivity and specificity:

Month	Count	S+/N+ count	S+/N+ (%)	S+/N+ 95% CI
Feb	469	464	98.9	97.5, 99.5
Mar	609	592	97.2	95.6, 98.2
Apr	1116	1096	98.2	97.2, 98.8
May	508	486	95.6	93.5, 97.1

Regression analysis by sex and age-group

When compared to children aged 3-4 years, children aged 5-11 years had two-fold odds of seropositivity ($p \leq 0.05$) and children aged 12-17 years had over seven-fold odds of seropositivity ($p \leq 0.05$). There was no significant difference by sex ($P = 0.79$). Table 4.

Table 4. Logistic regression results: association between S+/N+ seropositivity, sex and age-group

Category	Independent Variable	Odds Ratio	95% CI	P-value
Sex	Male	*reference*	--	--
	Female	1.07	0.65, 1.78	0.79
Age-group (years)	3-4	*reference*	--	--
	5-11	2.17	1.19, 3.88	<0.05
	12-17	7.60	3.84, 15.3	<0.05

Comparison of SARS-CoV-2 seroprevalence with previous studies and estimates in the adult population

SARS-CoV-2 seroprevalence estimates in this study were compared to previous paediatric serosurveillance studies carried out in January 2022 and October 2022, and to estimates in the adult population during the same period in 2024.

Sample collection, testing and analysis

Paediatric studies: 2022

Residual sera from children attending GPs, outpatient clinics, phlebotomy clinics and urgent care centres were collected over three time periods in 2021-2022. In the first study, samples from children aged 1-12 years were collected between 19 December 2021 and 22 January 2022 from clinical laboratories in Children's Health Ireland (CHI), Temple Street (5). In the second study, samples from children aged 0-17 years were collected between 30 May 2022 and 10 June 2022, and between 04 July 2022 and 16 July 2022, from clinical laboratories in CHI, Temple Street and Connolly Hospital (6). A small number of samples from children aged 17 years were collected from Cork University Hospital, LUH, SVUH and TUH. Samples were tested at the NVRL using the same testing platforms listed in Table 1 and adjusted for assay sensitivity and specificity as per the methods used in this study. For comparison purposes, seroprevalence was re-calculated using the parallel testing algorithm (S+/N+) and in the age groupings used in this study. The maximum age in the 2022 study was 12 years, therefore, comparisons in the 13–17-year age-group cannot be made for that period. Seroprevalence estimates among children tested in 2024 were significantly higher than those tested in January 2022 and in July 2022, and this difference was consistent across sex and age-groups (Table 5).

Table 5. SARS-CoV-2 seroprevalence estimates in children adjusted for assay sensitivity and specificity: February to June 2024, December 2021 to January 2022, and May to July 2022.

Sample	Collection Period	Year	Count	S+/N+ count	S+/N+ (%)	95% CI
All	01 February – 19 June	2024	2709	2645	**97.6**	97.0, 98.1
	30 May – 16 July	2022	279	247	**88.5**	84.3, 91.8
	19 December – 22 January	2021-2022	170	67	**39.4**	32.4, 46.9
Female	01 February – 19 June	2024	1462	1431	**97.9**	97.0, 98.5
	30 May – 16 July	2022	138	121	**87.7**	81.2, 92.2
	19 December – 22 January	2021-2022	84	36	**42.9**	32.8, 53.5
Male	01 February – 19 June	2024	1247	1214	**97.3**	96.3, 98.1
	30 May – 16 July	2022	141	126	**89.4**	83.2, 93.4

Sample	Collection Period	Year	Count	S+/N+ count	S+/N+ (%)	95% CI
	19 December – 22 January	2021-2022	86	31	**36.0**	26.7, 46.6
5-12 years	01 February – 19 June	2024	1033	1003	**97.1**	95.9, 98.0
	30 May – 16 July	2022	127	120	**94.5**	89.1, 97.3
	19 December – 22 January	2021-2022	97	44	**45.4**	35.8, 55.3
13-17 years	01 February – 19 June	2024	1389	1375	**99.0**	98.3, 99.4
	30 May – 16 July	2022	54	52	**96.3**	87.5, 99.0

Adult study: 2024

Residual serum samples from adults aged ≥18 years were sourced from six hospital clinical laboratories participating in routine collections for the NSP to monitor the seroepidemiology of COVID-19 in Ireland (4). These included Beaumont Hospital, Galway University Hospital, LUH, SVUH, TUH, and UHL. Samples were tested at the NVRL using the same testing platforms listed in Table 1. Adults aged ≥70 years were oversampled from April 2023 onwards. The median age for the adult study was 72 years. Seroprevalence estimates in children were compared with estimates calculated for adults aged ≥18 years for the same period. For comparison purposes, seroprevalence in the adult study was re-calculated using the parallel testing algorithm (S+/N+). Seroprevalence estimates in adults and children were comparable but marginally lower (<2%) in children overall, and in males and females (Table 6).

Table 6. Adjusted SARS-CoV-2 seroprevalence estimates in adults aged ≥18 years and children aged 3-17 years in Ireland, 01 February 2024 to 19 June 2024.

Sample	Population	Count	S+/N+ count	S+/N+ (%)	S+/N+ 95% CI
All	paediatric	2709	2645	**97.6**	97.0, 98.1
	adult	3460	3443	**99.5**	99.2, 99.7
Male	paediatric	1247	1214	**97.3**	96.3, 98.1
	adult	1719	1706	**99.2**	98.7, 99.6
Female	paediatric	1462	1431	**97.9**	97.0, 98.5
	adult	1741	1737	**99.8**	99.4, 99.9

Discussion

SARS-CoV-2 IgG seroprevalence estimates were high (>90%) among children in this study, particularly among older children aged 12-17 years (99.0%), and likely suggest a high degree of protection against severe disease. These results are generally applicable to the paediatric population in Ireland in terms of sex and age-group. Age-related differences in paediatric SARS-CoV-2 seroprevalence were reported in other European countries early in the COVID-19 pandemic (10-13), with findings that are consistent with this study. However, there is a lack of serosurveillance studies carried out more recently to allow for robust comparison.

As expected, due to ongoing transmission of SARS-CoV-2, SARS-CoV-2 seroprevalence among children in Ireland was significantly higher in 2024 (97.6%, 95% CI:97.0-98.1) compared with January 2022 (39.4%, 95%CI: 32.4-46.9) and July 2022 (88.5%, 95% CI:84.3-91.8) (6). The increase of 49.1% seen in SARS-CoV-2 antibody seropositivity between January and July 2022 studies is likely multi-factorial. Firstly, there was a marked increase in community transmission in late 2021 and the first half of 2022 (see Epidemiology of COVID-19 in Ireland hub) due to the newly circulating omicron variant and subsequent wave of COVID-19 infections. It is likely that the increase in cases was not captured in the serosurveillance data in December 2021 and January 2022 as IgG antibody levels tend to peak ~30 days after symptom onset (15). In addition to this, the January serosurvey included children aged 1-12 years only which may account for some of the difference. Previous studies had considerably smaller sample sizes and were carried out earlier in the COVID-19 pandemic when circumstances differed. For example, there may have been a higher proportion of vulnerable or 'cocooned' children, particularly in December 2021 and January 2022 when public health social distancing measures such as the use of 'pods' in schools were still in place in Ireland. Samples collected in 2022 were sourced from CHI and were therefore likely to come from a more vulnerable or cocooning cohort. In January 2022, S+ seropositivity reported in adults was 96.5% (95% CI 95.2-97.5), highlighting a significant gap in SARS-CoV-2 seroprevalence between adults and children at that time (5). We retrospectively calculated the S+/N+ seropositivity estimate for adults between 30 January 2022 and 19 February 2022, which was 95.9% (95% CI: 94.7-96.8). By July 2022, SARS-CoV-2 seroprevalence in children had risen to 88.5% (95% CI:84.3-91.8) (6), but remained lower than seroprevalence in adults at that time: 98.8% (95% CI:98.4-99.1) (4). In the current study, the seroprevalence gap between adults and children has closed, with seroprevalence only marginally higher in adults (~1.9%) compared to children. The high proportion of children in this study that were detected with antibodies to the nucleocapsid protein (93.5% (95% CI: 92.4-94.4) overall), reflects the extent of natural SARS-CoV-2 infection that has occurred among children in Ireland. As of June 2024, over 90% of people in Ireland aged ≥3 years were estimated to have detectable IgG antibodies to SARS-CoV-2, demonstrating some level of protection against severe disease. Since 2020, the rapid evolution of SARS-CoV-2 variants associated with increased transmissibility and lower rates of hospitalisations (16, 17), in combination with wide access to COVID-19 vaccination, has likely contributed to high prevalence estimates in the general population.

The Irish Health (Preservation and Protection and other Emergency Measures in the Public Interest) Act 2020 ceased in March 2022, ending all COVID-19 related measures and restrictions in Ireland, and in May 2023 the WHO declared that COVID-19 was no longer a global health emergency. Given these changes and the ongoing transmission of SARS-CoV-2 and emergence of new variants since, it is not surprising to see very high SARS-CoV-2 seroprevalence estimates among children and adults in Ireland in 2024.

Limitations

Samples were sourced from GPs, emergency departments, urgent care centres, and outpatient departments only, and this selection bias may limit the generalisation of our findings as most children in the general population do not require blood tests. However, sample source was consistent across all studies reported. Unintended testing bias may have occurred due to the omission of samples with insufficient volume for testing (n = 239). To explore this potential bias, we compared the demographics of samples tested with those not tested. The proportion of females (n=131; 55%) and males (n=108; 45%) that were not tested was not significantly different to the proportion that were tested: 1,462 (54%) females and 1,247 (46%) males, suggesting that there was no testing bias in terms of sex. Age-group proportions differed between samples tested and not tested, with the 5-11 year olds making up the largest proportion of untested samples (n=108;45.2%). The 3-4 year old age-group made up 20.1% of untested samples compared to 10.6% of samples tested, and the 12-17 year old age-group made up 34.7% of untested samples compared to 57.2% of samples tested. However, it is likely that these differences can be explained by the higher sample volume availability from older children compared with younger children, rather than a testing bias. A total of 113 samples were excluded from the study due to inpatient status (n=15) or unknown sample source (n=98) resulting from an administrative error. Seroprevalence was 99.1% in the excluded samples compared to 97.6% in the study sample. This difference may have been driven by the marginally higher proportion of 12-17 year olds in the excluded samples (59.3%) compared to the samples analysed in this study (57.2%).

Due to the nature of this serosurveillance study and the use of anonymised residual sera, data collection was limited to a minimal number of variables. Collection of supplementary information on vaccination status, infection history, or underlying conditions were not collected as part of this dataset. Other variables of interest for SARS-CoV-2 in children, such as indicators of severity (e.g., clinical symptoms, hospitalisation, and outcome), were also not available in this study, as they were not collected. Furthermore, children <3 years of age were not included.

Sample collection was limited to laboratories that routinely test paediatric samples, and to those with capacity to collect samples. The representativeness of our sample was likely impacted by the catchment areas associated with those hospitals. Over 50% of samples came from children residing in Dublin and >20% from children residing in Donegal, with the remaining sample coming from the South, South-East and the Midlands. Despite the small number of collection sites, the broad geographical distribution of samples overall grants a reasonable level of representativeness.

Finally, a general limitation of serosurveillance studies is the uncertainty around the detection of antibodies and immunity. Serosurveys do not capture all aspects of the immune response, such as cell-mediated immunity, and may underestimate the true level of immunity within a population. A study carried out by the SEU in 2023 addressed this limitation and demonstrated that that anti-spike IgG levels correlated well with levels of functional antibodies which are more indicative of protection, in an Irish population (18).

Application of these results and recommendations for future surveillance

Data from this study contributed to the changes made to the most recent NIAC recommendations on the SARS-CoV-2 primary schedule for children published in August 2024 (19). A primary schedule vaccine is now recommended only for those aged 6 months to 59 years with immunocompromise associated with a suboptimal response to vaccination or medical conditions associated with a higher risk of SARS-CoV-2 severity, hospitalisation, or death. Prior guidance from December 2023 recommended a single dose of COVID-19 mRNA vaccine for all children aged 6 months or more regardless of immunocompromise (20).

As the current epidemiological setting (incidence and hospitalisation rates) for SARS-CoV-2 in children has remained relatively constant, it is unlikely that an additional study on SARS-CoV-2 seroprevalence between now and the spring 2025 booster campaign would add significant value to the review of immunisation recommendations, therefore a repeat study is not planned at present. A decision to repeat this study will depend on epidemiological factors such as the emergence of new variants or a meaningful change in the clinical impact of SARS-CoV-2 infection, particularly in children, and will require consultation with stakeholder groups such as NIAC.

SARS-CoV-2 data generated by the NSP in collaboration with the LSN and the NVRL, have helped identify the true extent of prior exposure to SARS-CoV-2 and potential immunity in the population, which can be largely underestimated based on COVID-19 case notifications alone if testing and diagnosis of cases is not comprehensive, and highlights the value of serosurveillance data to inform public health decision making.

References

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Technical Notes

Parallel serology testing

Laboratory testing carried out by the NVRL, used two tests in parallel: an anti-spike IgG antibody assay (Abbott) and an anti-nucleocapsid IgG antibody assay (Roche). When two tests are combined in an "or" manner (A or B), i.e., anti-spike or anti-nucleocapsid, the overall sensitivity is stronger than for either alone, and the overall specificity is weaker than for either alone. A positive result for either or both tests indicates some level of protection against SARS-CoV-2. This includes samples with detectable antibodies to one protein and not the other (**S+N-** or **S-N+**), as well as samples with detectable antibodies to both proteins (**S+N+**). Sensitivity and specificity values for both testing platforms were combined and applied to the Rogan-Gladen estimator to adjust seroprevalence values for the pooled estimate grouping (**S+/N+**). The following formula was used to combine the sensitivity of the Abbott (0.9875) and Roche (0.995) tests: $(A)_{sensitivity} + (B)_{sensitivity} - [(A)_{sensitivity} \times (B)_{sensitivity}]$. The following formula was used to combine the specificity of the Abbott (0.9955) and Roche (0.998) tests: $(A)_{specificity} \times (B)_{specificity}$ (21).

Acknowledgements

1. The Laboratory Serosurveillance Network (LSN).
   Letterkenny University Hospital, St. Vincent's University Hospital, Tallaght University Hospital, University Hospital Limerick.
2. UCD National Virus Reference Laboratory Serosurveillance Unit (NVRL SSU).
   Kate Browne, Deridre Burke, Cillian F. De Gascun.
3. Health Protection Surveillance Centre, Seroepidemiology unit (HPSC SEU).
   Laura Whitton, Melissa Brady, Katie O'Brien, Jane Finucane, Claire Dillon, Fiona Culkin, Ellen Perry, Miriam Kelly, Michael Carton, Lois O'Connor.
4. The National Serosurveillance Programme Steering Committee.
   Further information on the Steering Committee members can be found here.

For further information on the National Serosurveillance Programme see here

Appendix

Representativeness

Table A1. Binomial exact test results for the comparison of proportions for sex and age-group between the SARS-CoV-2 sample in this study and the Irish population according to the National Census of Ireland 2022 (8).

Sample		Study N	Study %	Population N	Population %	P-value
Female	3-4 years	128	4.72	59302	5.67	0.034
	5-11 years	433	15.98	240129	23.0	<0.001
	12-17 years	901	33.26	210864	20.2	<0.001
Male	3-4 years	159	5.87	62687	6.0	0.808
	5-11 years	439	16.21	251801	24.1	<0.001
	12-17 years	649	23.96	220358	21.1	<0.001
Total N		**2709**		**1045141**		

Unadjusted seroprevalence estimates by sex and age-group

Table A2. Unadjusted SARS-CoV-2 seroprevalence estimates in children in Ireland, 01 February 2024 to 19 June 2024.

Sample	Age-group (years)	Count	S+/N+ count	S+/N+ (%)	S+/N+ 95% CI	S+ count	S+ (%)	S+ 95% CI	N+ count	N+ (%)	N+ 95% CI
All		2709	2645	97.6	97.0, 98.1	2563	94.6	93.7, 95.4	2520	93.0	92.0, 93.9
Female		1462	1431	97.9	97.0, 98.5	1399	95.7	94.5, 96.6	1364	93.3	91.9, 94.5
Male		1247	1214	97.3	96.3, 98.1	1164	93.3	91.8, 94.6	1156	92.7	91.1, 94.0
	3-4	287	267	93.0	89.5, 95.4	247	86.1	81.6, 89.6	248	86.4	82.0, 89.9
	5-11	872	843	96.7	95.3, 97.7	800	91.7	89.7, 93.4	795	91.2	89.1, 92.9
	12-17	1550	1535	99.0	98.4, 99.4	1516	97.8	97.0, 98.4	1477	95.3	94.1, 96.2
Female	3-4	128	118	92.2	86.2, 95.7	106	82.8	75.3, 88.4	109	85.2	78.0, 90.3
	5-11	433	421	97.2	95.2, 98.4	409	94.5	91.9, 96.2	394	91.0	87.9, 93.3
	12-17	901	892	99.0	98.1, 99.5	884	98.1	97.0, 98.8	861	95.6	94.0, 96.7
Male	3-4	159	149	93.7	88.8, 96.5	141	88.7	82.8, 92.7	139	87.4	81.4, 91.7
	5-11	439	422	96.1	93.9, 97.6	391	89.1	85.8, 91.7	401	91.3	88.3, 93.6
	12-17	649	643	99.1	98.0, 99.6	632	97.4	95.8, 98.4	616	94.9	92.9, 96.4

S+/N+ = any sample that tests positive for spike OR nucleocapsid protein-specific IgG antibodies

S+ = any sample that tests positive for spike protein-specific IgG antibodies

N+ = any sample that tests positive for nucleocapsid protein-specific IgG antibodies

Adjusted spike and nucleocapsid seroprevalence estimates by sex and age-group:

S+ seroprevalence was 87.1% (95% CI: 82.5-90.7) in the 3–4 year age group, 92.9% (95% CI: 90.8-94.5) in the 5–11-year age group, and 99.0% (95% CI: 98.2-99.7) in the 12-17 year age group, appendix Table A3 A similar pattern was observed across age-groups stratified by sex, with the highest estimates in the 12-17 year age-group and the lowest estimates in the 3-4 year age-group for both males and females. N+ seroprevalence was 86.8% (95% CI: 82.3-90.3) in the 3-4 year age group, 91.6% (95% CI: 89.5-93.3) in the 5-11 year age group, and 95.8% (95% CI: 94.6-96.7) in the 12-17 year age group. A similar pattern was observed across age-groups stratified by sex, with the highest estimates in the 12-17 year age-group and the lowest estimates in the 3-4 year age-group, appendix Table A3.

Table A3. Adjusted S+ and N+ seroprevalence estimates in children in Ireland, 01 February 2024 to 19 June 2024

Sample	Age-group (years)	Count	%	S+ count	S+ (%)	S+ 95% CI	N+ count	N+ (%)	N+ 95% CI
All		2709	100	2563	95.8	94.9, 96.6	2520	93.5	92.4, 94.4
Female		1462	54	1399	94.5	93.0, 95.8	1364	93.8	92.3, 94.9
Male		1247	46	1164	96.9	95.7, 97.8	1156	93.2	91.6, 94.5
3-4		287	10.6	247	87.1	82.5, 90.7	248	86.8	82.3, 90.3
5-11		872	32.2	800	92.9	90.8, 94.5	795	91.6	89.5, 93.3
12-17		1550	57.2	1516	99.0	98.2, 99.7	1477	95.8	94.6, 96.7
Female	3-4	128	4.7	106	83.8	76.2, 89.4	109	85.6	78.3, 90.7
	5-11	433	15.9	409	95.6	93.0, 97.5	394	91.4	88.3, 93.8
	12-17	901	33.3	884	99.4	98.2, 100	861	96.0	94.5, 97.2
Male	3-4	159	5.9	141	89.8	83.8, 93.9	139	87.8	81.7, 92.2
	5-11	439	16.2	391	90.1	86.8, 92.8	401	91.8	88.8, 94.1
	12-17	649	23.9	632	98.6	97.0, 99.6	616	95.4	93.4, 96.8

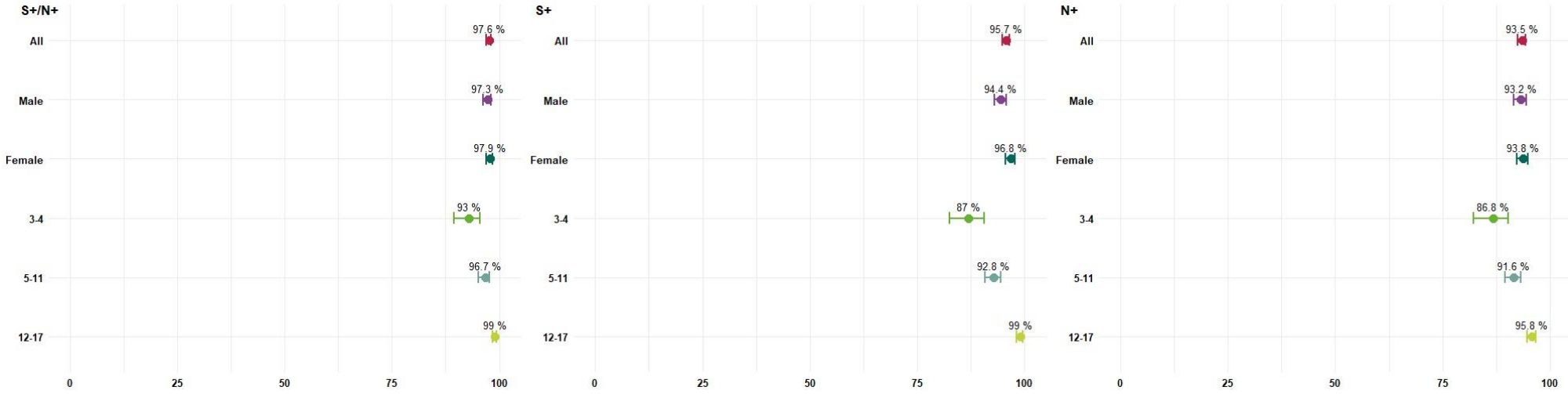

Figure A1. Adjusted SARS-CoV-2 seropositivity estimates by sex and by age-group: plot 1:S+/N+, plot 2: S+, plot 3: N+.

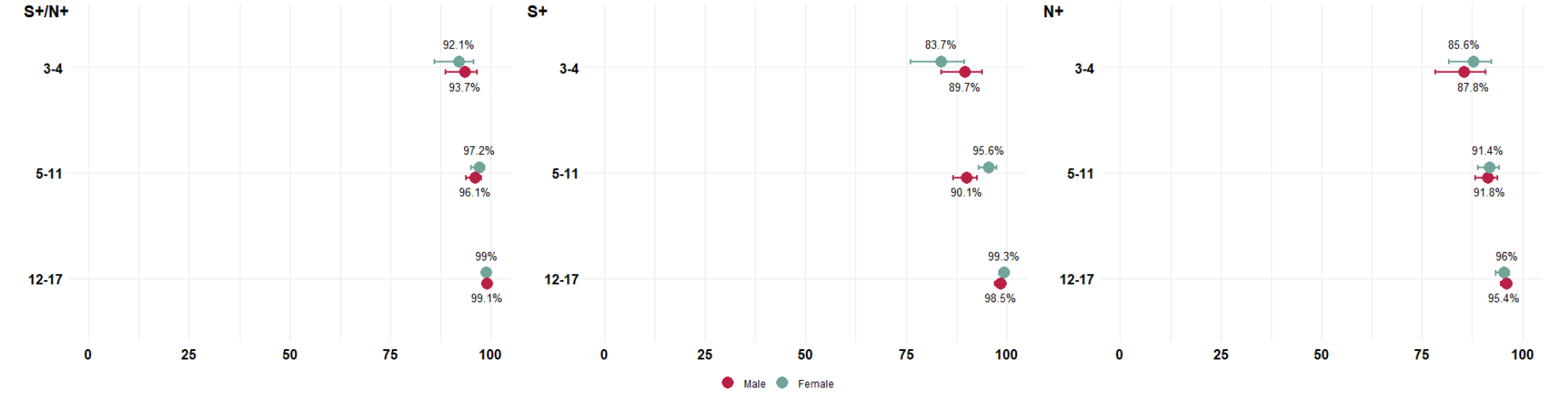

Figure A2. Adjusted SARS-CoV-2 seropositivity estimates by age-group, stratified by sex: plot 1:S+/N+, plot 2: S+, plot 3: N+

Quantitative SARS-CoV-2 antibody levels

Table A4. Summary of quantitative SARS-CoV-2 antibody levels in children aged 3-17 years, 01 February 2024 to 19 June 2024.

		Spike protein-specific IgG levels (BAU/ml)						Nucleocapsid protein-specific IgG levels (AU/ml)					
Sample	Count	min	max	median	mean	SD	IQR	min	max	median	mean	SD	IQR
All	2709	0	5680	209.8	805.7	1271.8	48.8-1022.6	0.069	340	66.7	97.9	92.4	12.7-176.0
Male	1247	0	5680	165.3	815.5	1335.9	37.5-1013.1	0.072	340	56.9	93.2	92.6	10.1-166.5
Female	1462	0.128	5680	252.0	797.2	1214.9	59.5-1023.8	0.069	337	76.0	101.8	92.0	15.3-181.8
3-4	287	0.114	5680	45.4	169.7	495.6	15.2-118.3	0.072	307	27.3	64.4	81.2	3.2-101.0
5-11	872	0.028	5680	87.9	339.7	746.4	24.1-289.4	0.069	337	44.8	86.8	91.4	8.5-158.0
12-17	1550	0	5680	550.5	1185.5	1458.7	132.2-1695.7	0.072	340	93.2	110.3	92.6	21.2-193.0

SD = standard deviation, **IQR** = interquartile range, Abbott Architect detectable upper limit = 40,000 AU/ml (5,680 BAU/ml)

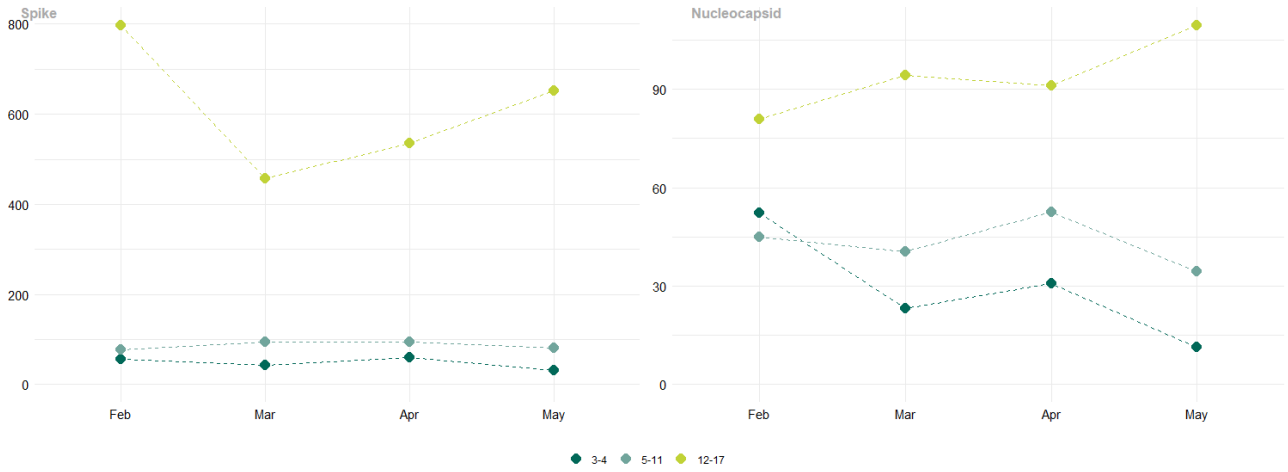

Figure A3. Median spike and nucleocapsid antibody (IgG) levels (BAU/mL) over time by age-group (years)

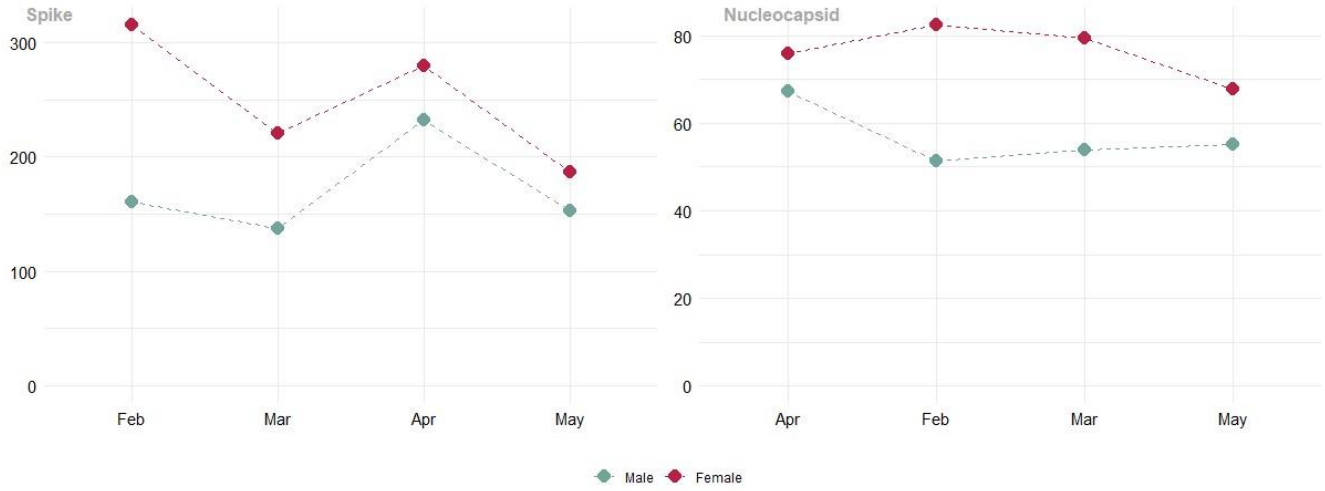

Figure A4. Median spike and nucleocapsid antibody (IgG) levels (AU/mL) over time by sex, February-May 2024

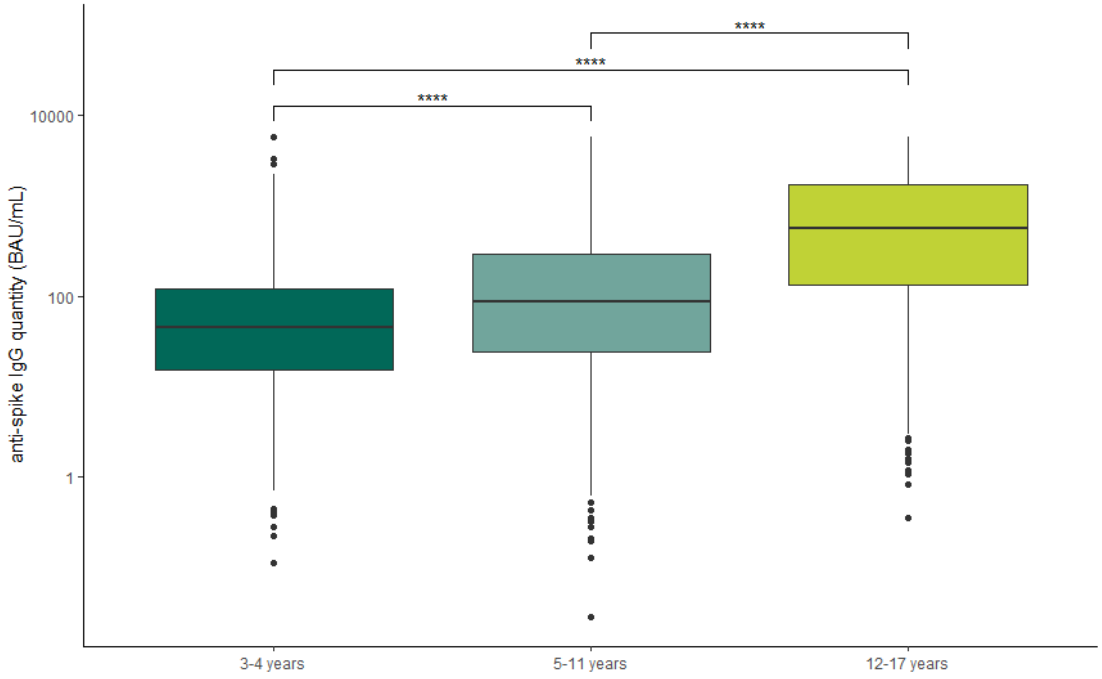

Figure A5. Spike IgG antibody levels (BAU/ml, log10 scale) by age-group. Mean spike IgG levels were significantly higher in 12-17 year olds compared to 3-4 year olds ($p \leq 0.0001$), significantly higher in 5-11 year olds compared to 3-4 year olds ($p \leq 0.0001$), and significantly higher in 12-17 year olds compared to 5-11 year olds ($p \leq 0.0001$).

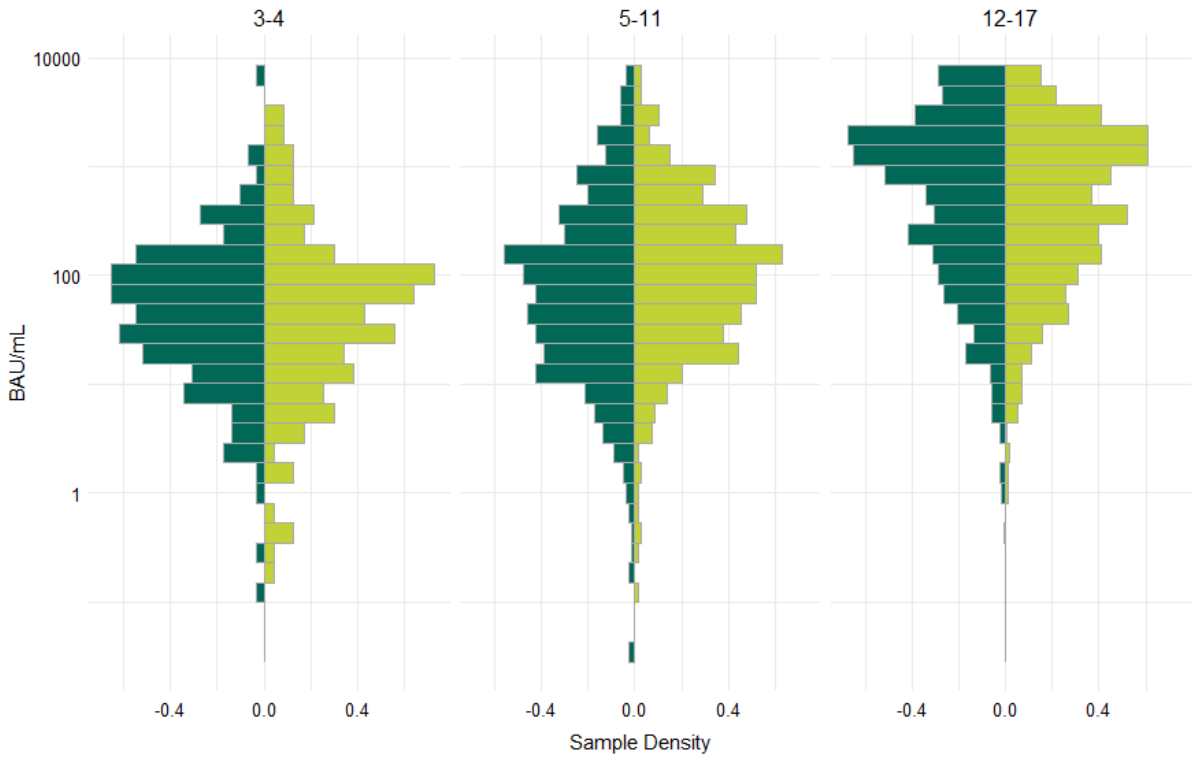

Figure A6. Distribution of spike IgG antibody levels (BAU/ml, log10 scale) by sex: female (light green), male (dark green) and age-group.

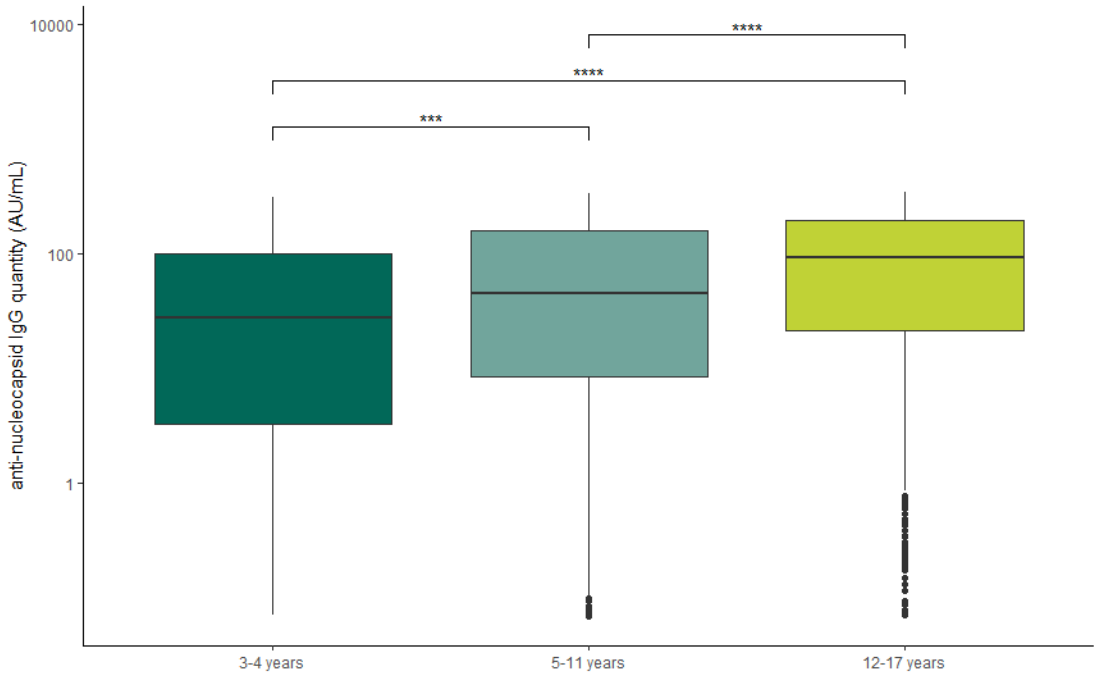

Figure A7. Nucleocapsid IgG antibody levels (AU/ml, log10 scale) by age-group. Mean nucleocapsid IgG levels were significantly higher in 12-17 year olds compared to 3-4 year olds ($p \leq 0.0001$), significantly higher in 5-11 year olds compared to 3-4 year olds ($p \leq 0.001$), and significantly higher in 12-17 year olds compared to 5-11 year olds ($p \leq 0.0001$).

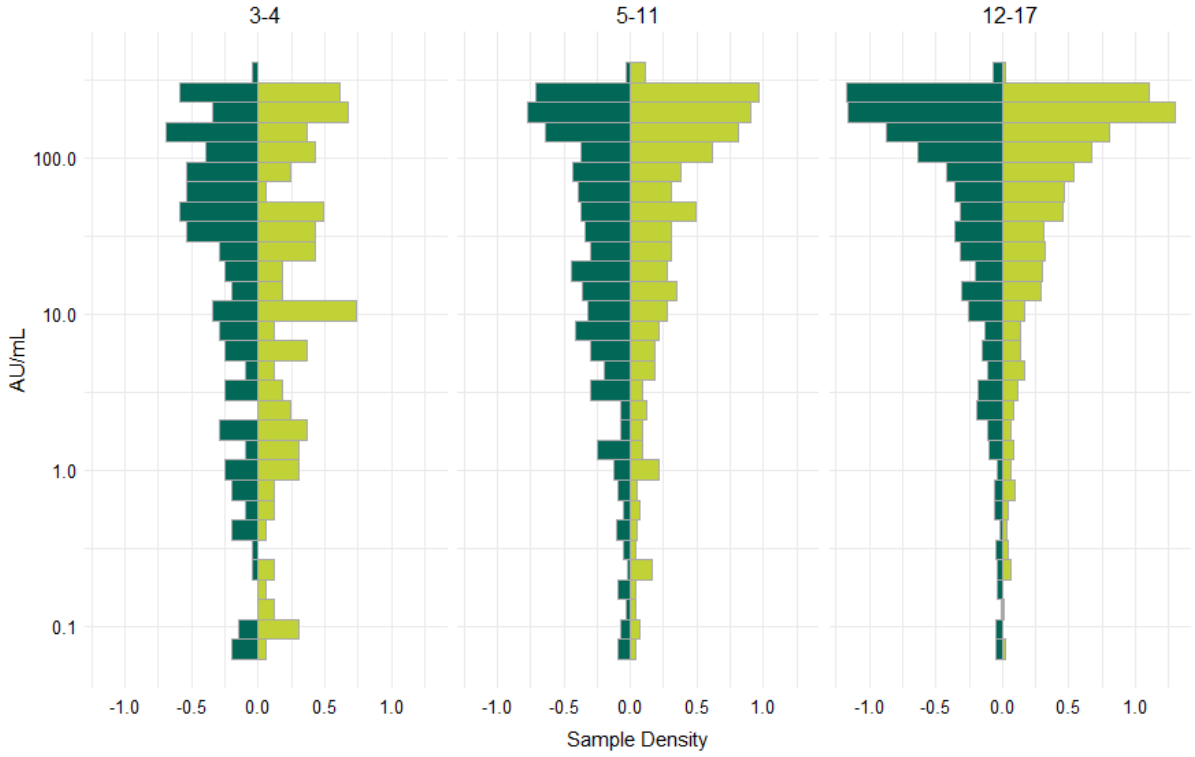

Figure A8. Distribution of nucleocapsid IgG antibody levels (AU/ml, log10 scale) by sex: female (light green), male (dark green) and age-group.

SARS-CoV-2 seroprevalence over time by sex and age-group

Table A5. Adjusted seroprevalence over time from February to May 2024 by sex and age-group

Sample	Month	Count	S+/N+ count	S+/N+ (%)	S+/N+ 95% CI
Male	Feb	240	239	99.6	97.7, 100
	Mar	271	260	95.9	92.8, 97.7
	Apr	504	491	97.4	95.6, 98.5
	May	230	222	96.5	93.2, 98.2
Female	Feb	229	225	98.2	95.6, 99.3
	Mar	338	332	98.2	96.2, 99.2
	Apr	612	605	98.9	97.6, 99.4
	May	278	264	94.9	91.7, 97.0
3-4	Feb	38	36	94.7	82.6, 98.5
	Mar	59	54	91.5	81.5, 96.3
	Apr	85	83	97.6	91.8, 99.4
	May	98	87	88.7	80.9, 93.6
5-11	Feb	156	154	98.7	95.4, 99.7
	Mar	220	210	95.4	91.8, 97.5
	Apr	356	345	96.9	94.5, 98.3
	May	140	134	95.7	90.9, 98.0
12-17	Feb	275	274	99.6	98.0, 100
	Mar	330	328	99.4	97.8, 99.8
	Apr	675	668	99.0	97.9, 99.5
	May	270	265	98.1	95.7, 99.2

Table A6. Total number of samples tested for SARS-CoV-2 IgG by age group and month, 2024

Age-group (years)	February	March	April	May	June
3-4	38	59	85	98	7
5-11	156	220	356	140	0
12-17	275	330	675	270	0
Total	469	609	1116	508	7