April 2022

Seroprevalence of antibodies to SARS-CoV-2, Ireland: findings from blood donor residual sera surveillance 18 October 2021 – 14 January 2022

Key Points

- Over a 12 week period between 18 October 2021 and 14 January 2022, trends in SARS-CoV-2 quantitative antibody levels were measured on a weekly basis in adult blood donors 20 years of age and older.
    - The overall seroprevalence of SARS-CoV-2 was 98.5% (95%CI 97.1, 99.8) when adjusted for the sensitivity and specificity of the antibody test used.
    - Overall seroprevalence rates were highest in those aged 20-29 years (99.7%, 95% CI 98.6, 100.0), and in those aged 70-79 years (100.0%, 95%CI 97.0, 100.0).
    - There was no difference observed in overall seropositivity rates by sex.
    - Seroprevalence rates in the sample were higher than national completed vaccination (uptake) rates (to 2 January 2022) for those aged 20-49. In the 20-29 year age group, for example, with a vaccination uptake rate of 88%, a seroprevalence of 99.0% (95%CI 98.2, 99.4) was observed.
    - Anti-N positive results (identifying those with previous SARS-CoV-2 infection) increased from 8% to 22% over the surveillance period. Those aged 20-29 years consistently showed the highest rates of previous infection, at 43.5% (95%CI 31.3, 56.6) by 9 January 2022.

HSE Health Protection Surveillance Centre. Seroprevalence of antibodies to SARS-CoV-2, Ireland: results from the Irish Blood Transfusion Service residual sera surveillance study. Dublin: HSE HPSC; 2022.

- Reported cases in CIDR showed a similar increase in infection rates over the surveillance period, with 8.3% of the 20-79 year olds in Ireland with a recorded COVID-19 diagnosis at the beginning of the period, rising to 14.6% by the end of the period. However, sample seroprevalence is generally higher than cumulative infection proportions each week, likely due to under-ascertainment of cases.

- Using the seroprevalence estimates by age-group as an approximation for the proportion in that age-group with a previous SARS-CoV-2 infection, we estimated that as of 26 December 2021, for 20-29 year olds, 1 in 2 cases of SARS-CoV-2 were recorded in CIDR, while for 30-49 year olds just over 4 in 5 cases were recorded. For those aged 50+ years it is estimated 3 in 5 SARS-CoV-2 cases were recorded.

- Median quantitative antibody levels trended upwards across the latter half of the 12-week surveillance period. Initial median quantitative antibody levels were 307 BAU/mL for the week beginning 17 October 2021, and by the week commencing 9 January 2022, median antibody levels had risen to 2,684 BAU/mL.

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Background

The National Serosurveillance Programme (NSP) is led by the Health Protection Surveillance Centre's (HPSC) Sero-Epidemiology Unit (SEU), working in partnership with the UCD National Virus Reference Laboratory (NVRL) Serosurveillance Unit (SSU), the acute-hospital Laboratory Surveillance Network (LSN) and the Irish Blood Transfusion Service (IBTS). It is overseen by a national multi-disciplinary and multi-sectoral Steering Committee.

At the request of the Department of Health, the SEU in HPSC and the IBTS carried out a study of SARS-CoV-2 prevalence using residual sera from blood donors in the adult population over a 12-week period from October 2021 to January 2022. The aim of this surveillance was to provide up to date estimates of SARS-CoV-2 seroprevalence in adults, including quantitative assessment of antibody levels by age and sex which may indicate if there is population waning of antibodies, and to determine any under ascertainment in case-based surveillance. This is the surveillance report providing results from the 12-week study.

Methods

Data

All three fixed site blood donation clinics in Ireland, two of which are in Dublin and one in Cork, participated in the cross-sectional weekly collection of residual sera over a 12-week period from the week beginning 17 October 2021 to 14 January, 2022. There was a one week break at Christmas, week beginning 26 December 2021.

Sequential sampling of blood donors aged 20 years and older took place until a target of 500 specimens was reached per week, or no other eligible specimens were available. Further eligibility criteria included specimens that were of sufficient volume, and specimens that were not apheresis donations, haemolysed, icteric, or lipaemic.

Specimens selected were anonymised after retrieving demographic details including date of birth, date of specimen collection, age, sex, and laboratory results. They were aliquoted the week of specimen collection. Specimens were identifiable only via a unique, unlinked SEU identification number assigned sequentially at the time of sample selection. These anonymised data were sent in weekly batches by secure electronic means to the HPSC SEU. All specimens were stored for the time period necessary to complete the testing and were discarded as per the IBTS protocol. Results data were held securely within HPSC using Excel. Access to the data was restricted to members of the HPSC SEU team only. As seroprevalence is a core surveillance activity for which the HPSC is legally mandated, no individual donor consent was required.

Population data were taken from the Central Statistics Office population estimates of 2021 provided by the HSE-National Health Intelligence Unit ('April 2021/H1'). Data were aggregated into the following age groups for analysis: 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and 70-79 years.

Data on laboratory confirmed cases of COVID-19 notified to HPSC were extracted from the Computerised Infectious Disease Reporting system (CIDR) on 7 February 2022 for the period of 1 March 2020 to midnight 26 December, 2021. These data are provisional and subject to ongoing review, validation, and update, and as a result the figures in this report may differ from previously published figures.

Vaccination uptake data by sex and age group were obtained from HPSC and extracted from Ireland's national COVID-19 immunisation system, COVAX. These data were aggregated into the following age groups for the analysis: 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and 70-79 years. Vaccinated persons were collated from COVAX data through to midnight 2 January 2022 to provide an approximate 14-day window for comparison with IBTS sample data, allowing for development of antibody response to vaccination.

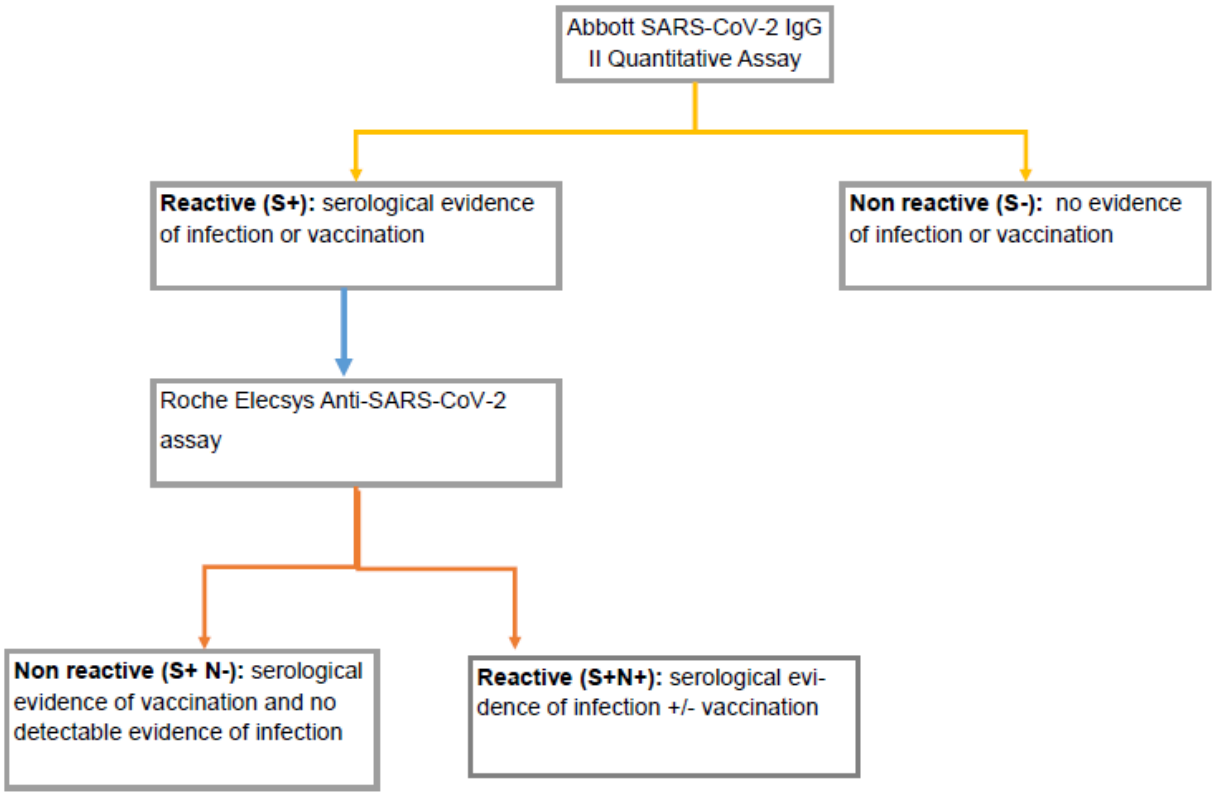
Tests

Laboratory testing and interpretation took place at the IBTS national Donor Screening Laboratory, Central Pathology Laboratory, and St James's Hospital (SJH).

Four structural proteins are encoded by the SARS-CoV-2 genome, including the spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins. Selected specimens were first screened using the Abbott SARS-CoV-2 IgG II Quantitative Assay, which detects antibodies to SARS-CoV-2 spike protein (anti-S). Specimens with a result of at least 50.0 arbitrary units per millilitre (AU/mL) are considered positive or reactive (S+). The Abbott SARS-CoV-2 IgG II Quantitative Assay has a manufacturer's stated Positive Percent Agreement (PPA) of 98.75% (93.25, 99.94) at ≥ 15 days post PCR diagnosis, and a Negative Percent Agreement (NPA) of 99.55% (99.15, 99.76).

Anti-S reactive specimens were subsequently tested in St James's Hospital (SJH) laboratory using the Roche Elecsys Anti-SARS-CoV-2 assay which qualitatively detects immunoglobulin G (IgG) antibodies to the SARS-CoV-2 nucleocapsid protein (anti-N). Vaccines currently approved for use in Ireland target the S protein, and it is not expected that individuals will produce an immunological response to E, M, or N proteins following vaccination. As such, anti-N reactivity was used to determine antibody responses due to infection, and specimens with a cut-off index of ≥ 1.0 are considered positive (S+N+). The Roche Elecsys Anti-SARS-CoV-2 assay has a manufacturer's stated sensitivity of 99.5% (97.0, 100) at ≥ 14 days post PCR diagnosis, and a clinical specificity of 99.80% (99.69, 99.88). Figure 1 illustrates this testing algorithm via the Abbott and Roche platforms.

Figure 1. IBTS 12-week surveillance testing algorithm



Quantitative measurements

Quantitative measurements of antibodies were obtained from the Abbott SARS-CoV-2 IgG II Quantitative Assay. In order to facilitate comparison with international literature, the raw data were converted into the WHO International Standard for anti-SARS-CoV-2 immunoglobulin, which is measured in binding antibody units per millilitre (BAU/mL). Thus the results from the Abbott SARS-CoV-2 IgG II Quantitative Assay were converted from AU/mL into BAU/mL using the manufacturer's suggested conversion of AU/mL*0.142. [1], [2]

Statistical methods

Descriptive statistics were used to explore the data with data management and analysis carried out using R version 4.1.2. The seroprevalence was adjusted for the misclassification or imperfect sensitivity and specificity in the application of the diagnostic testing using the Rogan Gladen-estimator (see Technical Notes for further details). Unless stated otherwise, adjusted results are presented.

Cumulative data from CIDR are 14 days in arrears from IBTS sample collection weeks to allow for comparison of reported COVID-19 infection notifications against seroprevalence data.

Results

Anti-S seroprevalence (S+)

In all, 5,226 valid specimens from the donation clinics were provided for analysis over the 12-week surveillance period, 3,416 (65.4%) males and 1,810 (34.6%) females (table 1).

Table 1. Demographic characteristics of total sample, week beginning 17 October 2021 – 14 January 2022

Characteristic		Number	Percent
Sex	Male	3416	65.4
	Female	1810	34.6
Age	Median age (years)	45	-
	Mean age (years)	45	-
	Age range (years)	20-78	-
	20-29	816	15.6
	30-39	1216	23.2
	40-49	1142	21.9
	50-59	1231	23.6
	60-69	731	14.0
	70-79	90	1.7
Collecting site	Dublin	4238	81.1
	Cork	988	18.9
Total		**5226***	

*5,350 specimens in total were returned to HPSC SEU, 68 were excluded from analysis as they fell outside the sampling frame (less than 20 years) and 56 apheresis specimens were excluded from analysis.

Adjustment had a small effect, increasing estimates of anti-S seropositivity by approximately 1% (table 2). The adjusted overall anti-S seropositivity rate was 98.4% (95%CI 98.0, 99.0). Anti-S seroprevalence rates were similar across age and sex categories.

Table 2. Unadjusted and adjusted overall anti-S seropositivity by age group and sex, week beginning 17 October 2021 – 14 January 2022

Characteristic		Number Seropositive	Unadjusted Prevalence	95% Confidence Interval	Adjusted Prevalence	95% Confidence Interval
Age group (years)	20-29	804	98.5	97.4, 99.2	99.7	98.6, 100.0
	30-39	1183	97.3	96.2, 98.1	98.5	97.4, 99.2
	40-49	1102	96.5	95.3, 97.4	97.6	96.4, 98.6
	50-59	1192	96.8	95.7, 97.7	98.0	96.8, 98.8
	60-69	713	97.5	96.1, 98.4	98.7	97.3, 99.6
	70-79	90	100.0	95.9, 100.0	100.0	97.0, 100.0
Sex	Female	1774	98.0	97.3, 98.6	99.2	98.4, 99.7
	Male	3310	96.9	97.3, 97.4	98.1	97.4, 98.6
Total		**5084**	**97.3**	**96.8, 97.7**	**98.4**	**98.0, 99.0**

The HSE's COVID-19 vaccination programme commenced in late December 2020, with eligibility according to risk group, employment status (healthcare workers) and descending

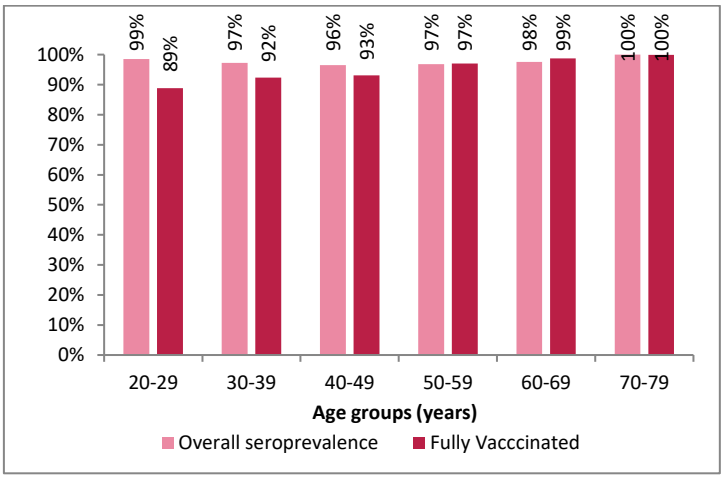
age.[3] An ecological comparison of overall anti-S seroprevalence in the IBTS sample and vaccination uptake stratified by age cohort is shown in figures 2a and 2b. According to COVAX [4], fully vaccinated refers to individuals on a two-dose vaccination plan who have received their first and second doses, and individuals on a single dose vaccine plan who have received a vaccination.

The HSE's COVID-19 booster vaccine programme commenced the week of 26 September, 2021 with rollout primarily by age and immunocompromised eligibility criteria. According to COVAX, secondary course vaccinated/booster dose refers to individuals who have completed a primary course (fully vaccinated) and have received a booster dose, while primary course vaccinated/third dose refers to immunocompromised individuals who have received two doses initially and require an additional third dose as part of their primary course treatment. Age stratified secondary course vaccinated/booster dose and primary course vaccinated/third dose uptake rates are shown in table 3 and figure 2b. By the end of the surveillance period, 86% of 70-79 year olds had received a booster dose, with a linear trend down the age groups closing at 28% booster uptake in the 20-29 year olds.

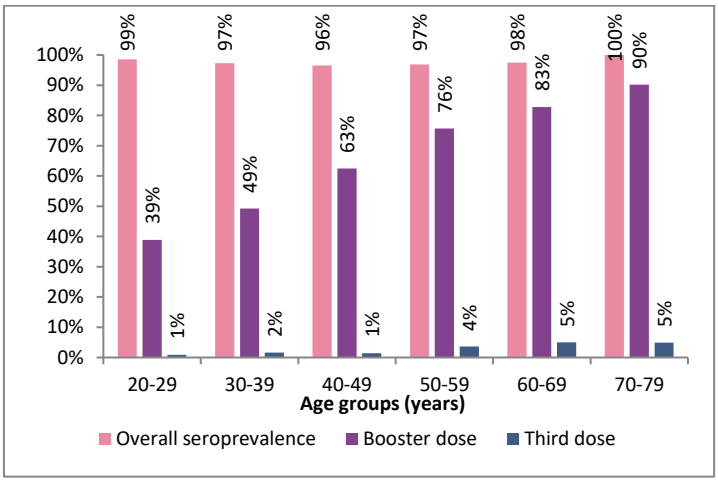
Anti-S seropositivity rates in the sample are higher than population vaccination uptake rates in the 20-49 age cohorts.

Figure 2 Age stratified anti-S seropositivity rates and vaccination uptake*, 17 October 2021 – 14 January 2022

(a)



(b)



*Data source: HPSC COVID-19 Vaccination Uptake in Ireland Weekly Report, 05/01/2022. Fully vaccinated refers to individuals on a two-dose vaccination plan who have received their first and second doses, and individuals on a single dose vaccine plan who have received a vaccination. Secondary course vaccinated/booster dose refers to individuals who have completed a primary course (fully vaccinated) and have received a booster dose, while primary course vaccinated/third dose refers to immunocompromised individuals who have received two doses initially and require an additional third dose as part of their primary course treatment.

Table 3. Uptake of booster and third dose vaccinations by IBTS age cohorts

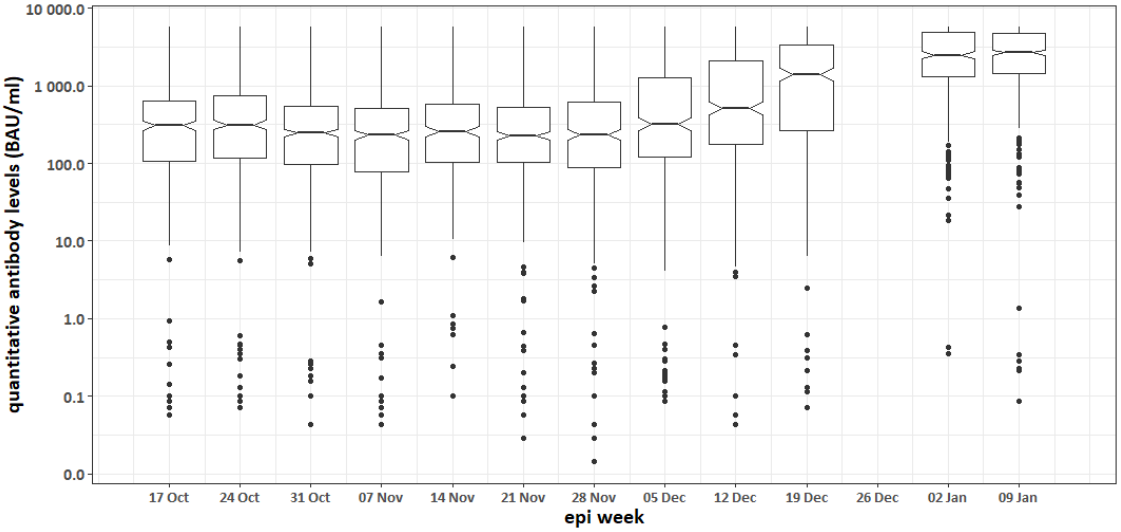
Age group (years)	Booster Doses Administered	% of Fully Vaccinated Population	Third Doses Administered	% of Fully Vaccinated Population
20-29	144,099	28%	5,134	1%
30-39	230,265	38%	10,176	2%
40-49	385,430	56%	18,639	3%
50-59	429,077	71%	22,266	4%
60-69	389,761	80%	24,563	5%
70-79	300,282	86%	16,593	5%

Data source: HPSC COVID-19 Vaccination Uptake in Ireland Weekly Report, 05/01/2022

Quantitative antibody measures

Median quantitative antibody levels as measured by the Abbott SARS-CoV-2 IgG II Quantitative Assay of the overall sample have trended upwards across the latter half of the 12-week surveillance period (figure 3). Initial median quantitative antibody levels were 307 BAU/mL for the week beginning 17 October 2021, and by the week commencing 9 January 2022 median antibody levels had risen to 2,684 BAU/mL.

Figure 3. Median quantitative anti-S antibody levels by week of sample collection, 17 October 2021 – 14 January 2022, all ages 20-79 years.

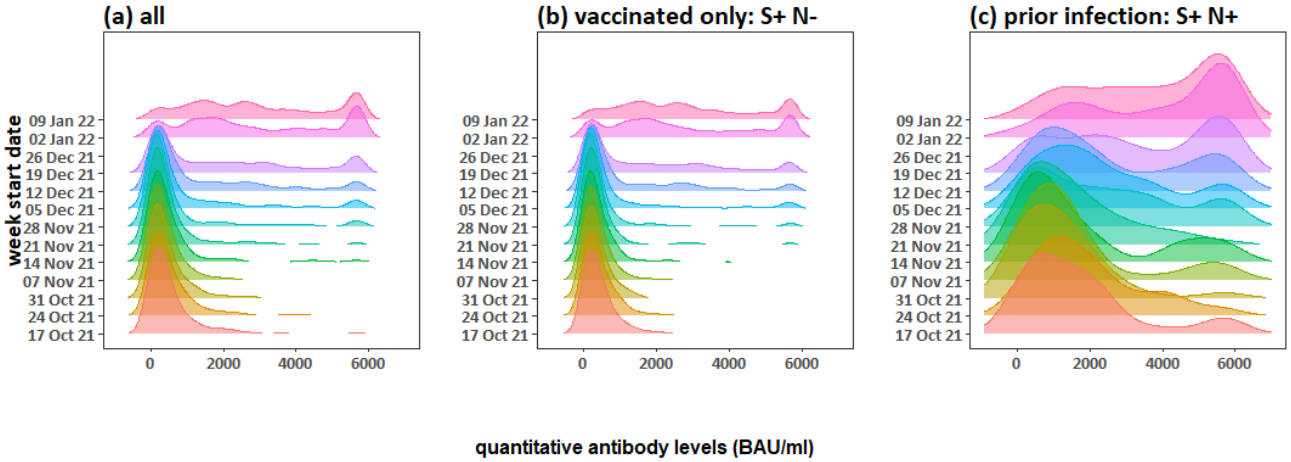


Note: the y-axis is log scale.

The distribution of quantitative anti-S antibody levels for the whole sample are displayed in figure 4a, those with serological evidence of vaccination only (S+N-) in figure 4b and those with a prior infection, who may or may not be vaccinated (S+N+), in figure 4c. As the data for figures 4a and 4b have a large overlap, the patterns are similar, where for approximately the first five weeks of surveillance, the distribution of quantitative anti-S levels is concentrated at the lower end of the scale. In tandem with the booster vaccination rollout, the antibody level distribution starts to move to the higher end of the scale, eventually leading to an approximate bimodal distribution of quantitative antibody levels by week 12 of the surveillance period.

In contrast, for the S+N+ subgroup, i.e. those with serological evidence of previous infection, the quantitative antibody level distribution appears to have wider variation throughout the surveillance period (figure 4c), though the effect of booster vaccinations may also be contributing to this effect as the S+N+ subgroup likely contains vaccinated individuals.

Figure 4. Distribution of quantitative anti-S antibody levels by week, 17 October 2021 – 14 January 2022

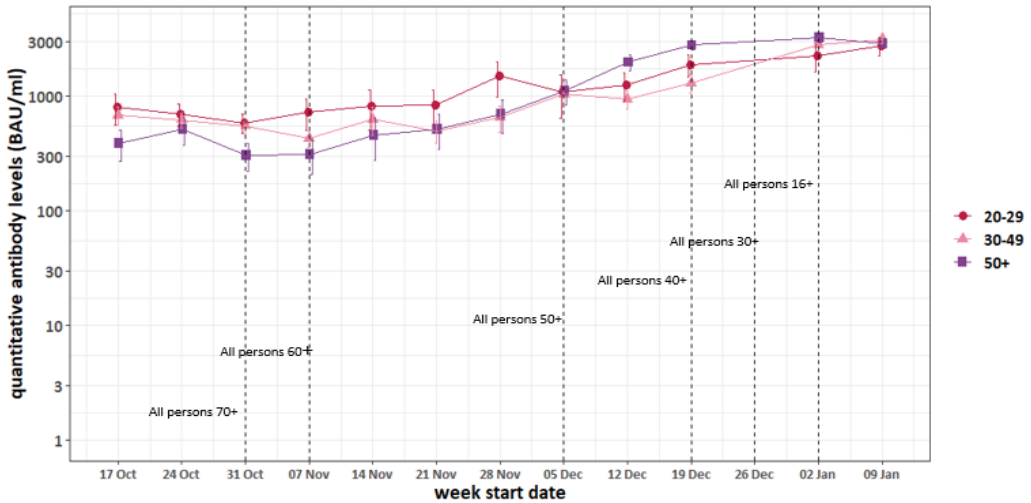


(a) Number of observations = 5,226, (b) number of observations = 4,355, (c) number of observations = 726

The administration of booster doses and third doses was available for all individuals aged 16 years and older by the close of the twelve-week surveillance period.[5]

Initially, mean quantitative antibody levels in the 50+ years cohort were lower than in the younger age groups, however the effect of the booster programme and subsequent rise in antibody levels for this cohort can be seen from 21 November onwards (figure 5). The other cohorts had later rising antibody levels, and by the end of the 12-week period, the three age groups were measuring similar levels.

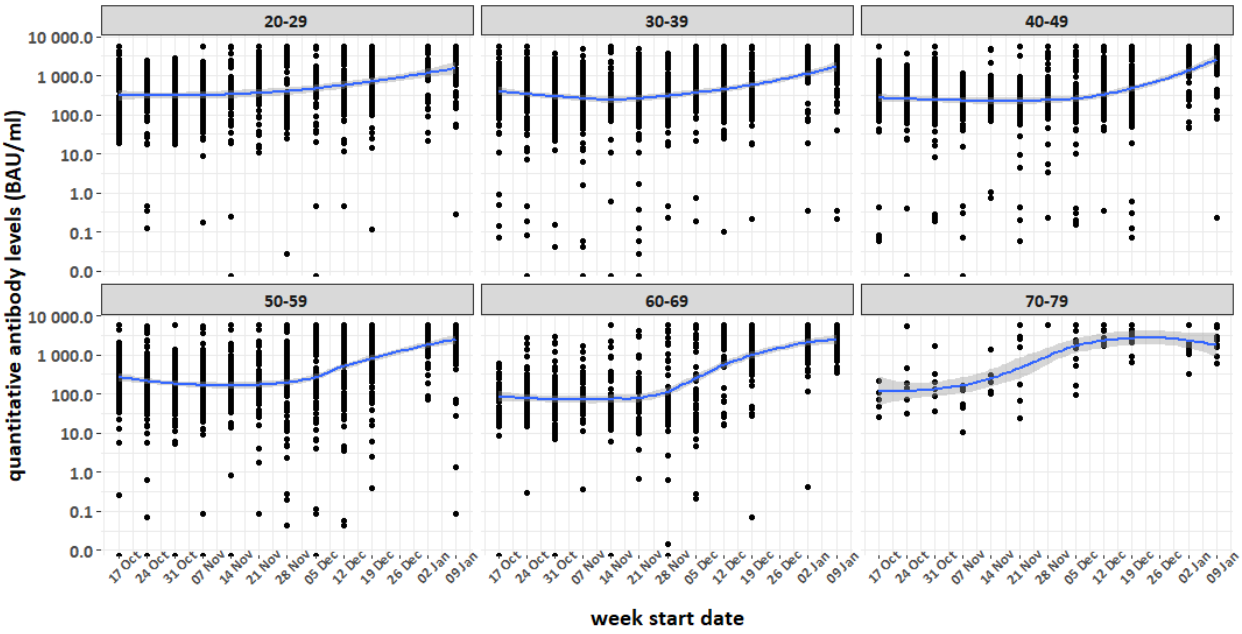
Figure 5. Mean quantitative anti-S antibody levels by age and by week of sample collection, 17 October 2021 – 14 January 2022



Note: Vertical dashed line indicates commencement week of booster for eligible age group

When the quantitative anti-S antibody levels are further disaggregated into 10 year age groups (figure 6), the antibody levels rose the earliest in the 70-79 year olds, and by the end of the surveillance period show signs of a plateau and perhaps the beginning of a decline. The younger age groups, which started from a higher base level showed a later and less steep rise.

Figure 6. Age stratified quantitative anti-S antibody levels with trend line, 17 October 2021 – 14 January 2022

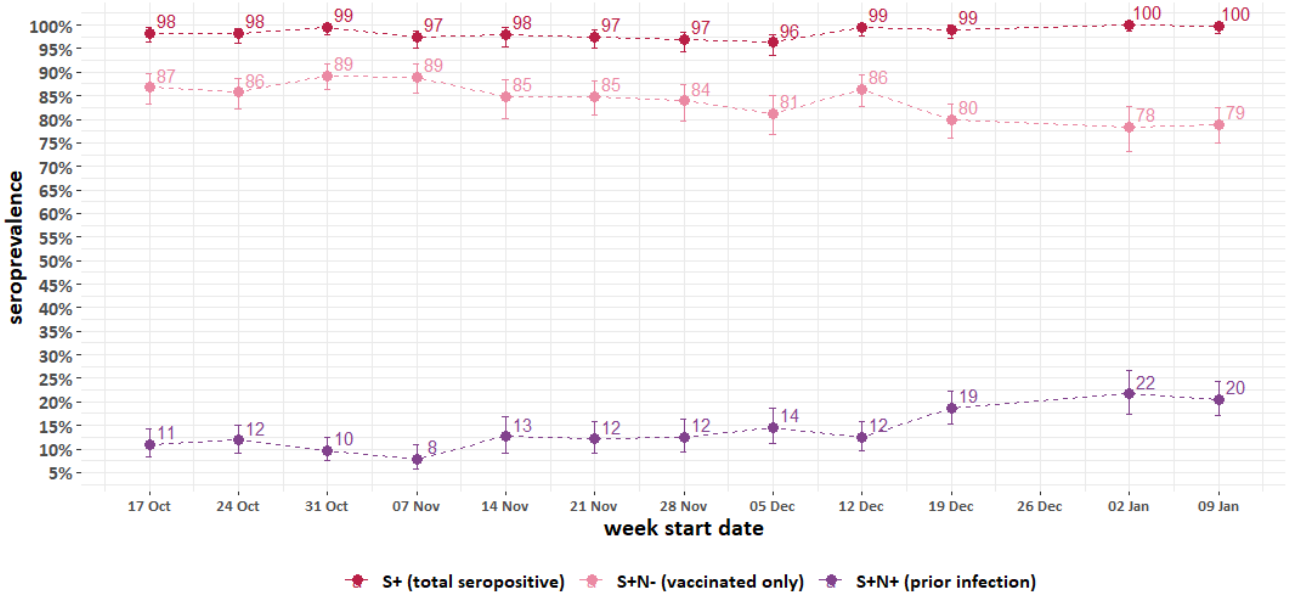


Note: the y-axis is log scale

Anti-N seroprevalence (S+N+)

Sample participants who were anti-S reactive (S+) were subsequently sent for anti-N testing in order to distinguish donors who had serological evidence of a previous SARS-CoV-2 infection. While overall S+ seropositivity remained relatively stable across the 12 weeks ranging from 96% to 100% (figure 7), the proportion of the sample who were S+N+, indicating previous infection, approximately doubled from 11% at the beginning of the period (17 October 2021) to 20% by the end of the 12 weeks (9 January 2022). The infection prevalence estimates represent exposure at least 14 days prior, so the final prevalence estimate relate to cases up to 26 December 2021.

Figure 7. Overall seropositivity (S+), previous vaccination (S+N-), and natural infection (S+N+)* proportions by week, 17 October 2021 – 14 January 2022



***** Individuals in this group may or may not be vaccinated

Table 4 shows a weekly comparison of the anti-N reactive subgroup (S+N+) against cumulative laboratory confirmed cases of COVID-19 reported to CIDR. The reported confirmed case counts were dated 14 days prior to the start of each IBTS sample week to allow for a detectable antibody response in the sample for comparison.[6], [7]

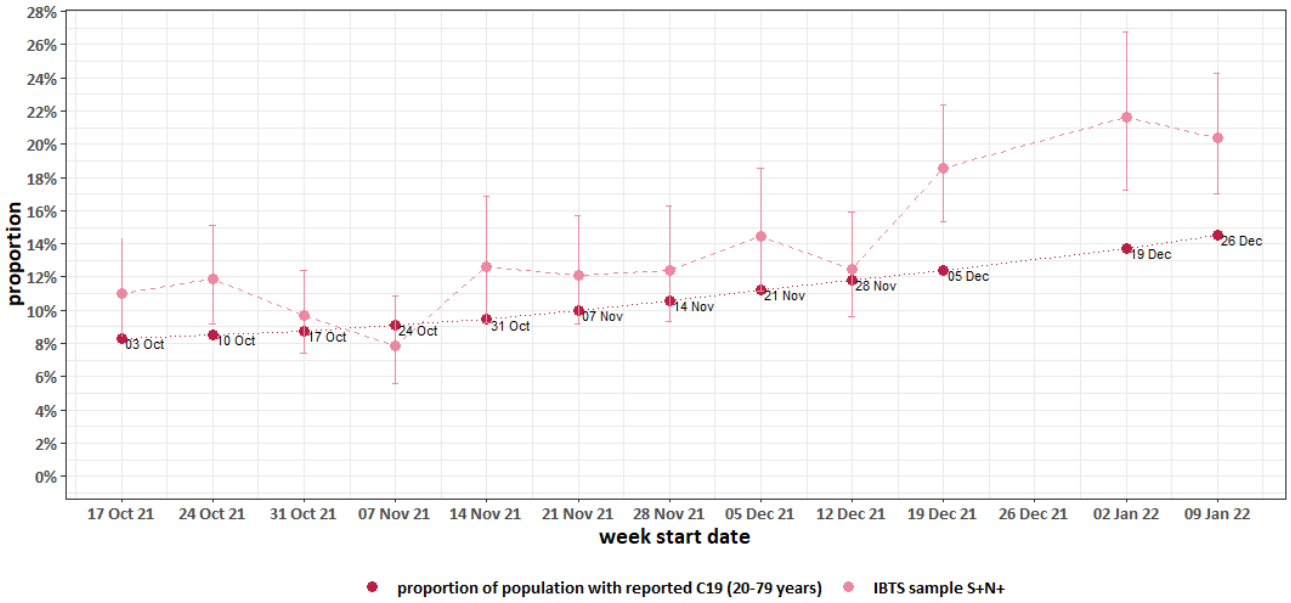
Table 4. Population proportion of COVID-19 cases reported to CIDR and IBTS S+N+ prevalence estimates by week*

CIDR week	Cumulative reported cases	Population %	IBTS sample week	Sample prevalence estimate	Lower CI	Upper CI
03/10/2021	286387	8.3%	17/10/2021	11.0%	8.4%	14.3%
10/10/2021	293375	8.5%	24/10/2021	11.9%	9.2%	15.1%
17/10/2021	301935	8.8%	31/10/2021	9.7%	7.4%	12.4%
24/10/2021	312496	9.1%	07/11/2021	7.9%	5.6%	10.9%
31/10/2021	324741	9.4%	14/11/2021	12.6%	9.2%	16.9%
07/11/2021	343568	10.0%	21/11/2021	12.1%	9.2%	15.7%
14/11/2021	363994	10.6%	28/11/2021	12.4%	9.3%	16.3%
21/11/2021	385874	11.2%	05/12/2021	14.5%	11.2%	18.5%
28/11/2021	405973	11.8%	12/12/2021	12.5%	9.7%	15.9%
05/12/2021	427297	12.4%	19/12/2021	18.6%	15.3%	22.3%
19/12/2021	472604	13.7%	02/01/2022	21.6%	17.3%	26.7%
26/12/2021	500859	14.6%	09/01/2022	20.4%	17.0%	24.2%

*Cumulative data from CIDR are 14 days in arrears from IBTS sample collection weeks to allow for comparison of reported COVID-19 infection notifications against seroprevalence data. There was no IBTS data collection the week beginning 26 December . All counts are for individuals aged 20-79 years only.

While both sources show an increase in infection rates over the surveillance period, the cumulative infection proportions reported in CIDR appear lower over the surveillance period than the sample seroprevalence rates (figure 8). Using the seroprevalence estimate as an approximation for the proportion for 20-79 year olds with a previous SARS-CoV-2 infection, we estimated that as of 26 December 2021, 7 in 10 cases of SARS-CoV-2 were recorded in CIDR.

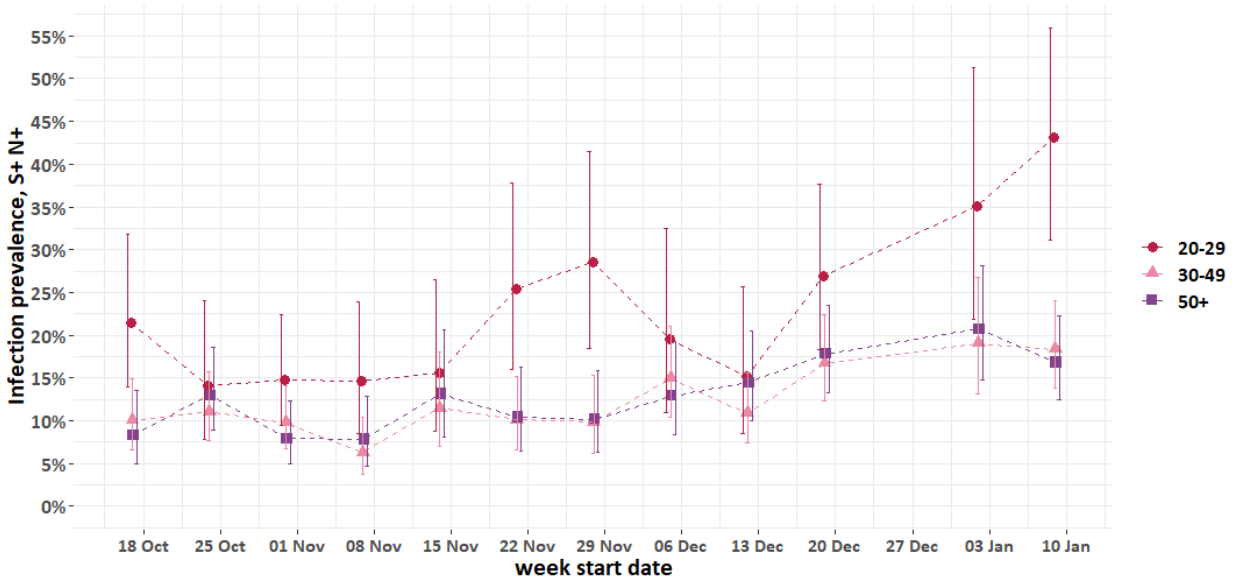
Figure 8. Cumulative confirmed COVID-19 cases reported to CIDR and IBTS S+N+ prevalence estimates by week*



*Cumulative data from CIDR are 14 days in arrears from IBTS sample collection weeks to allow for comparison of reported COVID-19 infection notifications against seroprevalence data. There was no IBTS data collection the week beginning 26 December. All counts are for individuals aged 20-79 years only.

Anti-N seropositivity in the sample showed variation when stratified by age (figure 9). The youngest age group consistently had the highest anti-N positivity rates across the surveillance period, indicating a higher proportion of individuals with serological evidence of infection with SARS-CoV-2 in the weeks prior to donation than the older age groups. The 30-49 years and 50+ years groups were similar in both the rate of anti-N reactivity each week and the pattern over time; initially flat and then trending upwards in the latter half of the surveillance period. By week beginning 9 January, those in the 20-29 age group had estimated anti-N seropositivity of 43.5% (95%CI 31.3, 56.6) while those in the 30-49 and 50+ age groups had anti-N prevalence estimates of 18.2% (95%CI 13.5, 23.9) and 16.6% (95%CI 12.1, 22.2) respectively (further details in Appendix A, table A2). The seroprevalence for this period corresponds to cumulative cases up to week beginning 26 December 2021.

Figure 9. Anti-N (S+N+) seropositivity rates by age and week, 17th October 2021 – 14th January, 2022



Using the seroprevalence estimates by age-group as an approximation for the proportion in that age-group with a previous SARS-CoV-2 infection, we estimated that as of 26 December 2021, for 20-29 year olds, 1 in 2 cases of SARS-C0V-2 were recorded in CIDR, while for 30-49 year olds just over 4 in 5 cases were recorded. For those aged 50+ years it is estimated 3 in 5 SARS-CoV-2 cases were recorded (Appendix A, table A2).

Discussion

Timely and accurate information on population seroprevalence is critical to inform proactive, targeted public health interventions, vaccination policy and treatment interventions. Seroprevalence data complement data from other surveillance systems, and can be used to estimate the true proportion of the population that has been infected. Surveillance of residual serum/plasma from blood donors can be used to monitor trends in seroprevalence in blood donors, approximate community prevalence, and is logistically more feasible to achieve and less costly than community surveys.[8]

This surveillance report shows that SARS-CoV-2 anti-S seropositivity is high in the blood donor population of 20-79 year olds, primarily reflecting the high vaccination rates of adults in Ireland. The overall anti-S seropositivity showed little variation by age and sex.

Anti-S seroprevalence rates were higher than national rates of fully vaccinated individuals for the younger age groups of 20-49 years. Those aged 20-29 showed the greatest disparity; vaccination uptake rates were 88% in the general population while seroprevalence was 99% amongst blood donors tested during this surveillance period. While the results indicated that 20-29 year olds consistently had the highest rates of antibodies indicating previous infection at a rate of 43% by the end of the surveillance period, the higher overall anti-S seropositivity compared to national vaccination rates may also be an artefact of the ‘heathy donor’ effect in

the population under surveillance, i.e. blood donors may be more likely to have received a vaccination when offered.

When the results indicating previous infection are compared to population proportions of confirmed cases of COVID-19 reported to CIDR, the sample seroprevalence was higher for most comparative weeks. This disparity increased in late December 2021, indicating a wider circulation of the virus in the community than that detected through case based surveillance, possibly due to the presence of the Omicron variant of SARS-CoV-2, and the associated surge in cases that led to an increased pressure on surveillance and testing capacity.[9] Although Ireland's contact tracing and COVID-19 testing infrastructure is robust, this data indicates an under ascertainment of confirmed cases using traditional methods of surveillance, especially during periods of infection surges where there is increased pressure on public health and testing capacity. Incorporating serosurveillance methods in conjunction with established surveillance practices may allow for the capture of asymptomatic cases, and are independent of changes in testing policy that affect the comprehensiveness of surveillance data being collected.

Initial antibody response, SARS-CoV-2 IgG antibodies to the spike protein (anti-S) and to the nucleocapsid protein (anti-N), can vary at the individual level, both due to disease severity and immunosuppression. In particular, some individuals may not mount any antibody response. Evidence surrounding waning antibody levels indicates that waning varies by individual, by target antigen, by antibody isotope, and by the assay used in measurement. The literature would suggest that waning is most likely to occur in older age groups, among men, and among individuals with immunosuppression.[10],[11] The duration of the surveillance may not have been sufficient to capture significant trends in anti-N waning, however the anti-S levels of the 70-79 group give an indication of a plateau over the final four weeks. Rapid antibody decline after vaccinations for other diseases is not uncommon, and evidence suggests that the protection offered by antibodies against serious consequences of infection persists. There remains a need to continue to monitor and investigate the impact of immunosenescence and other factors on antibody decline.

Research is ongoing to better understand what antibody levels mean in terms of protection against COVID-19. At a population level, higher antibody levels correlate with protection against infection; however, it is unclear whether this convention applies at the individual level. Antibody levels indicating protection may also be unequal across variants of the virus. Nevertheless, serosurveillance provides valuable information on the proportion of the population that has been exposed to SARS-CoV-2, as it includes asymptomatic and unreported infections that generally remain undetected using case-based surveillance systems.

Limitations

The information collected is a simple dataset, and only includes data readily available within the IBTS laboratory information management systems (LIMS). No information was available on vaccination status or underlying conditions of the individuals from whom the specimens

were sourced. Information on fully vaccinated and boosted individuals by age group in the whole population, available from COVAX, was used for comparison.

The residual serum/plasma specimens included were confined to those aged between 20 and 79 years of age, and were sourced from blood donors. There is uncertainty as to the representativeness of the blood donor sample compared to the general Irish population. Blood donor behaviour may differ systematically and result in a distinctly different risk of exposure to infection, thus not accurately representing community seroprevalence. However, the IBTS donor population used in this surveillance is homogenous and relatively stable due to samples only being sourced from fixed clinic sites, which normalises the differences in risk of exposure within the group, and provides a stable signal of their overall antibody trends from infection and vaccination over time.

Blood donors are subject to strict eligibility criteria, and as such these populations will not capture individuals with chronic inflammatory diseases, individuals with cancer or other immunodeficiencies, individuals on immunosuppressants, or other high-risk cohorts. However, studies have shown that Irish blood donors experience similar rates of infection to the general population, which may mitigate the impact of the so-called healthy donor effect. [12], [13] During the course of the surveillance period, the IBTS donor deferral policies shifted in response to the changing landscape of the pandemic. Donor deferral periods after full recovery from COVID-19 shortened from 28 days to 14 days in November 2021, and post vaccination deferral periods shortened from 7 days to 72 hours in December 2021.[14] These changes may have impacted quantitative antibody level measurements, and in turn impacted seropositivity rates overall. However, it should be noted that the sensitivity of the Roche assay (indicating prior infection) is 99.5% (97.0, 100) from at least 14 days post infection, which would include the majority of symptomatic blood donors in this surveillance report period, given the donor deferral period following infection.

Males are overrepresented in the sample due in part to early inclusion at one clinic of apheresis donations that are primarily sourced from men. Due to the anonymised nature of the results received by the HPSC SEU, these could not be excluded initially. From the fourth week of the surveillance period onward apheresis donations were excluded from specimen sampling at source, and ultimately the total sample approximated the age and sex profile of all blood donors in 2021 from the three sites.

The test sensitivity was measured as its ability to detect antibodies 14 days or longer following infection or vaccination; antibodies might not have been detected in specimens from persons tested earlier than this time period post infection or vaccination. However, IBTS policy excluded symptomatic donors from donating within 14 days of COVID-19 infection. While the majority of SARS-CoV-2-infected individuals seroconvert following SARS-CoV-2 infection, antibodies are not generated in a small minority of cases. Similarly, antibodies targeting the S1 domain of the SARS-CoV-2 spike protein are generated following vaccination, but might not be generated at measurable amounts in a small minority of cases. Independent evaluations of test performance were not carried out; manufacturer's reported sensitivity and specificity rates were used.

Serological tests target specific SARS-CoV-2-induced antibodies. However, results only provide a partial picture of the immune response against the virus. They may not reflect immune protection at the site of infection (i.e. respiratory tract), or T-cell mediated responses. The induction of SARS-CoV-2-specific memory T-cells is important for long-term protection and play a vital role in virus clearance. T-cells may be maintained even if there are not measurable levels of serum antibodies in the blood. This limits the reliance on antibody levels alone as a proxy for the existence and duration of immunity.

Technical notes

1. Epidemiological weeks are as outlined on the HPSC website.
2. Further information available on HPSC website: https://www.hpsc.ie/a-z/nationalserosurveillanceprogramme/
3. The seroprevalence was adjusted for the misclassification or imperfect sensitivity (the proportion of true positives that have been correctly identified) and specificity (the proportion of true negatives that have been correctly identified) in the application of the diagnostic testing. If the sensitivity and specificity of a test is known, we can get an approximately unbiased estimate of the true prevalence using the Rogan Gladen-estimator [15]
   Thus, the adjusted prevalence is estimated by:

$$prev_{adj} = \frac{prev + Sp - 1}{\mathrm{Se} + \mathrm{Sp} - 1}$$

   Where $prev$ is the unadjusted seroprevalence, Sp is the specificity of the test and Se is the sensitivity of the test.
   The associated confidence interval is similarly adjusted. The confidence interval is approximate because it assumes that the values of the sensitivity and specificity are known rather than estimated. If they are only estimates, then this can be taken into account using the estimates given in Greiner & Gardner.[16]

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Acknowledgements :

National Serosurveillance Programme (NSP) Steering Committee – Appendix B

Steering Committee - Health Protection Surveillance Centre (hpsc.ie)

Dr Suzanne Cotter and Piaras O'Lorcain, HPSC for providing vaccination uptake figures from COVAX.

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Appendix A – Supplementary material

Table A1. Unadjusted and adjusted anti-N seropositivity by week, 17 October 2021 – 14 January 2022

IBTS sample week	Number anti-n reactive	Total number sample	Unadjusted prevalence	CI Lower	CI Upper	Adjusted prevalence	CI Lower	CI Upper
17/10/2021	52	456	11.4%	8.8	14.6	**11.0%**	8.4	14.3
24/10/2021	61	499	12.2%	9.6	15.4	**11.9%**	9.2	15.1
31/10/2021	59	585	10.1%	7.9	12.8	**9.7%**	7.4	12.4
07/11/2021	38	455	8.4%	6.2	11.3	**7.9%**	5.6	10.9
14/11/2021	40	309	12.9%	9.7	17.1	**12.6%**	9.2	16.9
21/11/2021	51	410	12.4%	9.6	16.0	**12.1%**	9.2	15.7
28/11/2021	48	376	12.8%	9.8	16.5	**12.4%**	9.3	16.3
05/12/2021	55	372	14.8%	11.5	18.8	**14.5%**	11.2	18.5
12/12/2021	59	460	12.8%	10.1	16.2	**12.5%**	9.7	15.9
19/12/2021	94	500	18.8%	15.6	22.5	**18.6%**	15.3	22.3
02/01/2022	66	303	21.8%	17.5	26.8	**21.6%**	17.3	26.7
09/01/2022	103	501	20.6%	17.3	24.3	**20.4%**	17.0	24.2

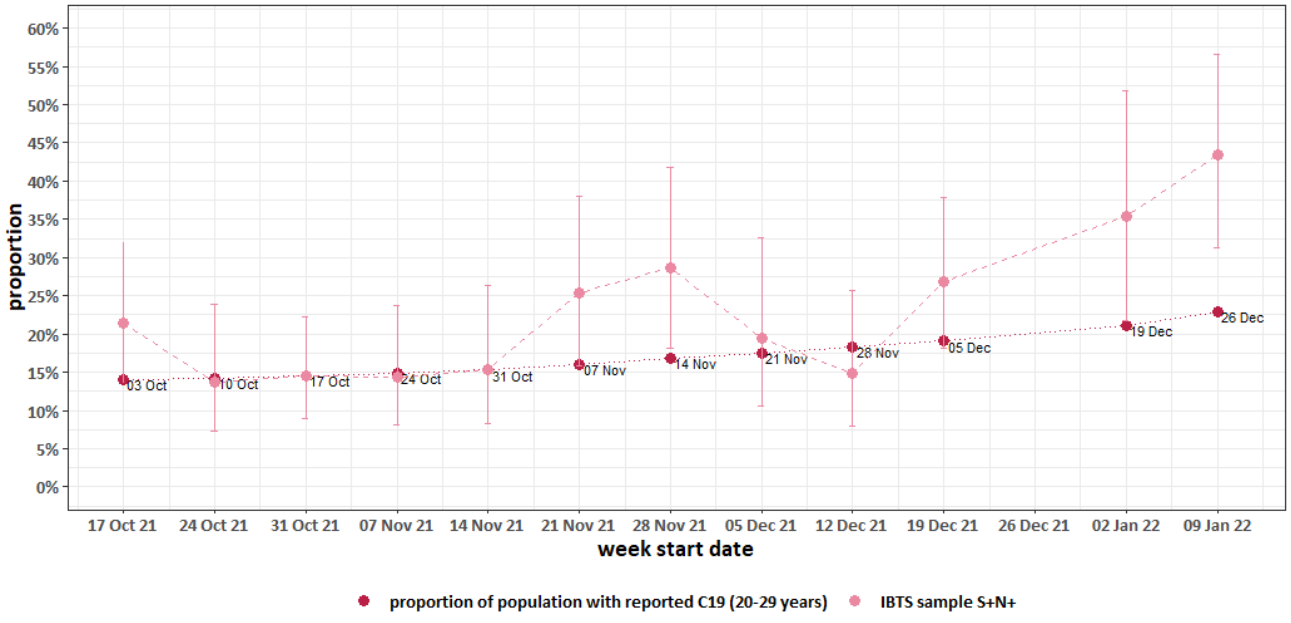
Table A2. Population proportion of COVID-19 cases reported to CIDR and IBTS S+N+ prevalence estimates by week, by age group 17 October 2021 – 14 January 2022

CIDR week	Cumulative reported cases	2021 population	Proportion of population with C19 record	IBTS sample week	Sample prevalence estimate	CI Lower	CI Upper
Age group: 20-29 years							
03/10/2021	82249	587898	**14.0%**	17/10/2021	**21.4%**	13.6%	31.9%
10/10/2021	83704	587898	**14.2%**	24/10/2021	**13.8%**	7.4%	23.9%
17/10/2021	85342	587898	**14.5%**	31/10/2021	**14.5%**	9.0%	22.3%
24/10/2021	87294	587898	**14.8%**	07/11/2021	**14.3%**	8.1%	23.8%
31/10/2021	89727	587898	**15.3%**	14/11/2021	**15.3%**	8.3%	26.4%
07/11/2021	94108	587898	**16.0%**	21/11/2021	**25.4%**	15.8%	38.0%
14/11/2021	98643	587898	**16.8%**	28/11/2021	**28.6%**	18.2%	41.8%
21/11/2021	103229	587898	**17.6%**	05/12/2021	**19.4%**	10.6%	32.6%
28/11/2021	107564	587898	**18.3%**	12/12/2021	**14.9%**	8.0%	25.6%
05/12/2021	111968	587898	**19.0%**	19/12/2021	**26.9%**	18.1%	37.9%
19/12/2021	123901	587898	**21.1%**	02/01/2022	**35.3%**	21.7%	51.8%
26/12/2021	134485	587898	**22.9%**	09/01/2022	**43.5%**	31.3%	56.6%
Age group: 30-49 years							
03/10/2021	119024	1399547	**8.5%**	17/10/2021	**9.6%**	6.2%	14.6%
10/10/2021	121949	1399547	**8.7%**	24/10/2021	**10.7%**	7.3%	15.4%
17/10/2021	125677	1399547	**9.0%**	31/10/2021	**9.4%**	6.2%	13.7%
24/10/2021	130267	1399547	**9.3%**	07/11/2021	**5.8%**	3.1%	10.0%
31/10/2021	135670	1399547	**9.7%**	14/11/2021	**11.1%**	6.6%	17.8%
07/11/2021	143940	1399547	**10.3%**	21/11/2021	**9.7%**	6.2%	14.9%

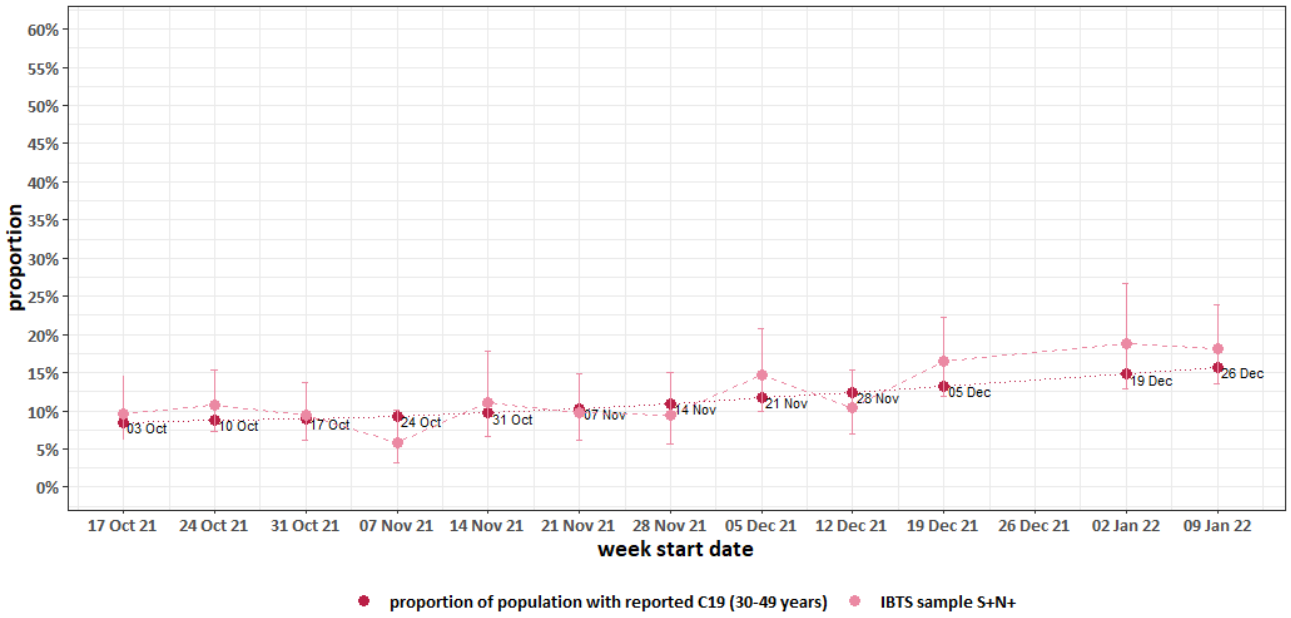
14/11/2021	153030	1399547	**10.9%**	28/11/2021	**9.4%**	5.6%	15.1%
21/11/2021	163318	1399547	**11.7%**	05/12/2021	**14.6%**	10.0%	20.8%
28/11/2021	172944	1399547	**12.4%**	12/12/2021	**10.5%**	6.9%	15.4%
05/12/2021	183952	1399547	**13.1%**	19/12/2021	**16.5%**	11.9%	22.3%
19/12/2021	206812	1399547	**14.8%**	02/01/2022	**18.8%**	12.8%	26.8%
26/12/2021	219766	1399547	**15.7%**	09/01/2022	**18.2%**	13.5%	23.9%
Age group: 50+ years							
03/10/2021	85114	1453077	**5.9%**	17/10/2021	**7.9%**	4.5%	13.2%
10/10/2021	87722	1453077	**6.0%**	24/10/2021	**12.6%**	8.4%	18.4%
17/10/2021	90916	1453077	**6.3%**	31/10/2021	**7.4%**	4.5%	11.9%
24/10/2021	94935	1453077	**6.5%**	07/11/2021	**7.4%**	4.1%	12.6%
31/10/2021	99344	1453077	**6.8%**	14/11/2021	**12.8%**	7.7%	20.4%
07/11/2021	105520	1453077	**7.3%**	21/11/2021	**10.0%**	6.0%	15.9%
14/11/2021	112321	1453077	**7.7%**	28/11/2021	**9.8%**	5.9%	15.6%
21/11/2021	119327	1453077	**8.2%**	05/12/2021	**12.6%**	8.0%	19.1%
28/11/2021	125465	1453077	**8.6%**	12/12/2021	**14.1%**	9.6%	20.3%
05/12/2021	131377	1453077	**9.0%**	19/12/2021	**17.6%**	12.9%	23.4%
19/12/2021	141891	1453077	**9.8%**	02/01/2022	**20.5%**	14.5%	28.2%
26/12/2021	146608	1453077	**10.1%**	09/01/2022	**16.6%**	12.1%	22.2%

Figure A1: Cumulative confirmed COVID-19 cases reported to CIDR and IBTS S+N+ prevalence estimates by week*

(a) 20-29 years



(b) 30-49 years


60%
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proportion
03 Oct
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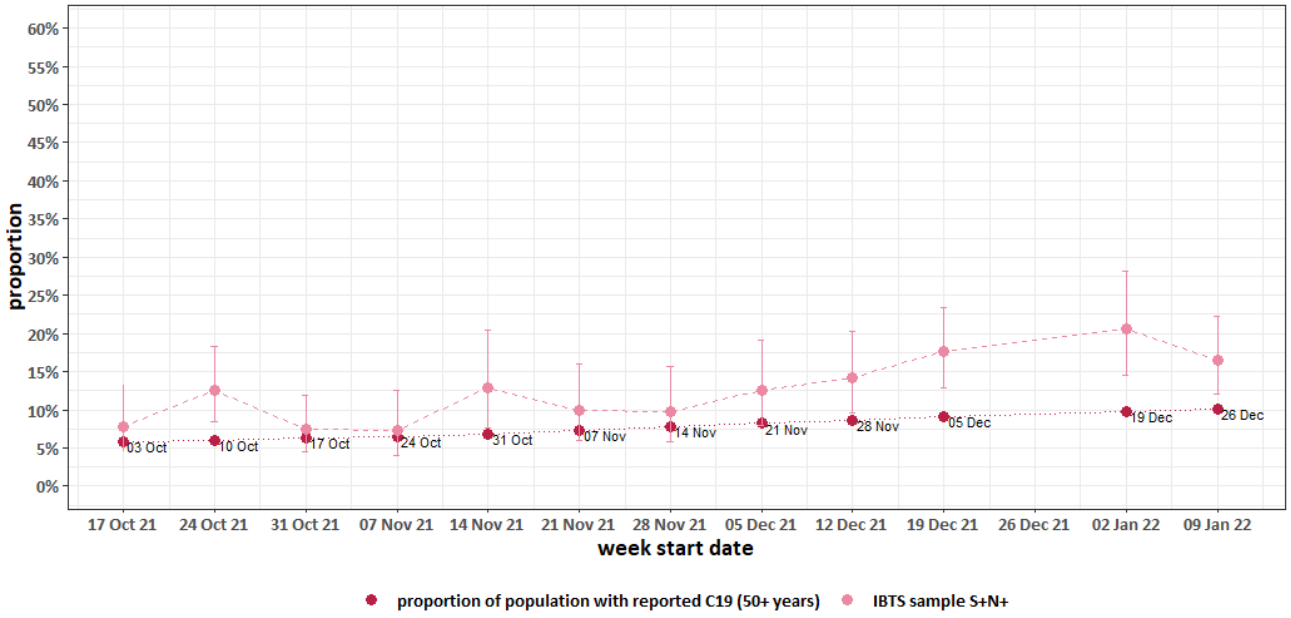
26 Dec
17 Oct 21
24 Oct 21
31 Oct 21
07 Nov 21
14 Nov 21
21 Nov 21
28 Nov 21
05 Dec 21
12 Dec 21
19 Dec 21
26 Dec 21
02 Jan 22
09 Jan 22
week start date
proportion of population with reported C19 (30-49 years)
IBTS sample S+N+

(c) 50+ years


60%
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24 Oct 21
31 Oct 21
07 Nov 21
14 Nov 21
21 Nov 21
28 Nov 21
05 Dec 21
12 Dec 21
19 Dec 21
26 Dec 21
02 Jan 22
09 Jan 22
week start date
proportion of population with reported C19 (50+ years)
IBTS sample S+N+

Appendix B – NSP Steering Committee Membership

NAME	TITLE/AFFILATION
Prof. Noel McCarthy (Chair)	Professor of Population Health Medicine, Trinity College Dublin
Ms Dee Burke	Laboratory Manager, National Virus Reference Laboratory
Dr Suzanne Cotter	Specialist in Public Health Medicine, Health Protection Surveillance Centre
Dr John Cuddihy	Director, Health Protection Surveillance Centre
Dr Cillian De Gascun	Consultant Virologist & Director, National Virus Reference Laboratory
Dr Lorraine Doherty	National Clinical Director, Health Protection
Dr Richard Drew	Consultant Clinical Microbiologist, Rotunda Hospital
Dr Damian Griffin	Consultant Chemical Pathologist, Galway University Hospital, representing Faculty of Pathology Chemical Pathologists
Dr Derval Igoe	Specialist in Public Health Medicine, Health Protection Surveillance Centre
Ms Bernadette Jackson	Point of Care Manager, Naas General Hospital, representing the Academy of Clinical Science and Laboratory Medicine
Dr Lucy Jessop	National Director, National Immunisation Office
Prof. Mary Keogan	Consultant Clinical Immunologist, Beaumont Hospital
Dr Ann Leonard	Quality Innovative Manager, Tallaght University Hospital, representing Peri Analytic and Laboratory Medicine Society
Dr Siobhan Ni Bhrian	National Lead, Integrated Care, HSE, nominated by the Office of the Chief Clinical Officer.

Dr Nuala O'Connor	GP Clinical lead COVID 19, representing Irish College of General Practitioners
Dr Niamh O'Flaherty	Consultant Clinical Microbiologist, Irish Blood Transfusion Service
Dr Siobhan O'Sullivan	Chief Bioethics Officer, Department of Health
Dr Margaret O'Sullivan	Specialist in Public Health Medicine, Department of Public Health , HSE South
Dr Shari Srinivasan	Consultant Chemical Pathologist, Beaumont Hospital