December 2021

Seroprevalence of antibodies to SARS-CoV-2, Ireland: results from National Serosurveillance Programme(NSP) Pilot, October 2021

Key Points

- Results from the pilot study undertaken in October 2021 to test the processes involved in the serosurveillance programme using residual serum/plasma from adults aged 20-69 years of age show:
    - The seroprevalence of SARS-CoV-2 in residual serum and plasma specimens sourced from general practice in October 2021 was 91.7% (95% CI 89.4-93.5), when adjusted for the sensitivity and specificity of the antibody test used.
    - Seropositivity varied by county of residence, with lower rates in Donegal at 81.7%, (95% CI 77.7-88.4) and higher rates in Dublin at 94.3% (95% CI 91.1-96.6).
    - Seropositivity in those aged 20-29 years was 86.1% (95% 79.4-91.0), lower than that in those aged 40-49 years which was 97.3% (95% CI 93.0-99.4).
    - There was no difference in seropositivity rates by sex.
    - Seroprevalence rates in the sample were higher than national completed vaccination uptake rates for all age groups except for those aged 50-59 years and 60-69 years. In the 60-69 year age group, despite a vaccination uptake rate of 99.7%, seroprevalence was lower at 91.7% (95% CI 86.1-95.3), a statistically significant difference.

HSE Health Protection Surveillance Centre. Seroprevalence of antibodies to SARS-CoV-2, Ireland, results from pilot. Dublin: HSE HPSC; 2021.

The National Serosurveillance Programme comprises the following partners:

1. The Laboratory Serosurveillance Network (LSN)

The following hospitals participated in the pilot

Beaumont Hospital	St. Vincent's University Hospital
Cork University Hospital	Tallaght University Hospital
Letterkenny University Hospital	University Hospital Galway
St James' Hospital	University Hospital Limerick

2. UCD National Virus Reference Laboratory Serosurveillance unit (NVRL SSU)

3. Health Protection Surveillance Centre, Seroepidemiology unit (HPSC SEU)

HSE Health Protection Surveillance Centre. Seroprevalence of antibodies to SARS-CoV-2, Ireland, results from pilot. Dublin: HSE HPSC; 2021.

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Background

The National Public Health Emergency Team (NPHET) endorsed a proposal from the National Clinical Director Health Protection, Health Service Executive on 27th August 2020 for the establishment of a national seroepidemiology surveillance system, including a seroepidemiology unit (SEU) in Health Protection at the HSE Health Protection Surveillance Centre (HPSC). Funding for the National Serosurveillance Programme (NSP) was formally agreed in June, 2021.

The NSP is led by the HPSC SEU, working in partnership with the UCD National Virus Reference Laboratory (NVRL) Serosurveillance Unit (SSU) and acute-hospital Laboratory Surveillance Network (LSN). It is overseen by a national multi-disciplinary and multi-sectoral Steering Committee. The surveillance system will conduct systematic sampling of residual general practice specimens from Clinical Chemistry laboratories within the LSN at regular intervals, with analysis for infectious disease antibodies at the UCD NVRL. The SEU will report on the cumulative seroprevalence of SARS-CoV-2 and in the future other infectious diseases of public health concern by age group, sex and region.

Prior to full implementation of the NSP, a pilot was undertaken with the purpose of testing logistical aspects of the surveillance system. This is the surveillance report providing results from the pilot.

Methods

Eight acute-hospital laboratories participated in the pilot to test surveillance processes for the new National Serosurveillance Programme.

HPSC SEU provided a sampling frame to participating acute-hospital Clinical Chemistry laboratories, indicating quotas of specimens to be provided. In all, 100 specimens were requested from each laboratory:10 males and 10 females across the age groups 20-29, 30-39, 40-49, 50-59, 60-69 years.

Laboratories selected residual serum or plasma specimens, sourced from general practice, that were collected in one of two weeks, 11th-15th October or 18th-22nd October. Processed samples were aliquoted and submitted in anonymised batch format to the UCD NVRL, the week following specimen collection. Each specimen was identifiable only through a unique, unlinked SEU ID number. In a separate process, demographic details including the SEU ID, date of specimen collection, sex, date of birth, and county of residence were sent by secure electronic means to HPSC SEU.

Antibodies to SARS-CoV-2 were detected using the Abbott SARS-CoV-2 IgG II Quantitative Assay, which detects antibodies to SARS-CoV-2 spike (S) protein (Anti-S) at the NVRL SSU. Qualitative results were provided to SEU.

Seroprevalence is presented by age group, sex and by county of residence. Adjusted results are also given to account for the sensitivity and specificity of the test used (details in Technical

Notes). Adjustment had a small effect, increasing estimates of seropositivity by approximately 1% (Table 2). Where not stated, adjusted results are given.

Vaccination uptake data by sex and age group were obtained from HPSC and extracted from COVAX. Denominator population profiles were taken from CSO 2020 population estimates**.** As seroprevalence is a core surveillance activity, for which the HPSC is legally mandated, no individual patient consent was required.

Results

In all, 787 valid specimens from the eight participating laboratories were provided for analysis, 388 males, 399 females. Demographic characteristics of specimens are outlined in Table 1.

Table 1. Demographic characteristics of specimens, October 10th – 23rd 2021

Characteristic		Number	Percent
Sex	Male	388	49.3
	Female	399	50.7
Age	Median age (years)	45	-
	Mean age (years)	45	-
	Age range (years)	20-69	-
	20-29	148	18.8
	30-39	162	20.6
	40-49	157	19.9
	50-59	160	20.3
	60-69	160	20.3
County of residence	Dublin	340	43.2
	Cork	100	12.7
	Donegal	99	12.6
	Galway	67	8.5
	Limerick	59	7.5
	Mayo	26	3.3
	Clare	24	3.0
	Wicklow	23	2.9
	Kildare	22	2.8
	Tipperary	17	2.2
	Roscommon	7	0.9
	Meath	2	0.3
	Kerry	1	0.1
Total		**787***	**100.0**

*791 specimens in total were returned to HPSC SEU, four were excluded from analysis as they fell outside the sampling frame (less than 20 years or greater than 69 years).

The adjusted seropositivity rate was 91.7% (95%CI 89.4-93.5). This varied by age group, as shown in Table 2 and Figure 1. Rates by sex were similar.

Seropositivity rates appeared to be lower in the younger age groups (20-39 years) compared with older age-groups (40-59 years) (table 2 and figure 1). In addition, the 91.7% seropositivity (95%CI 86.1 - 95.3) of the oldest age group (60-69 years) was also lower than that for the 40-59 year group. The HSE's COVID-19 booster vaccine campaign commenced

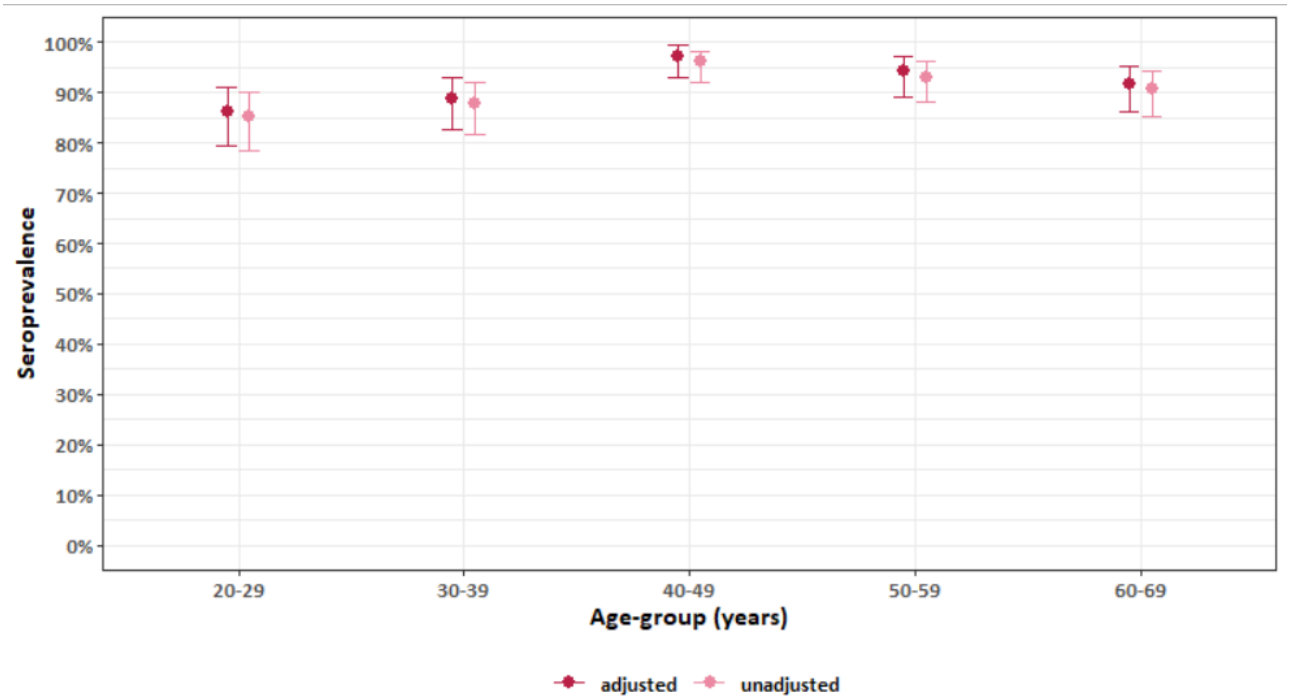
in the week of 26th September, 2021 according to age and immunocompromised eligibility criteria. During the two week period of the NSP Pilot, epidemiological weeks 41 and 42, the administration of additional (third) vaccine doses was underway for those aged 60 and older, and immunocompromised dose vaccines were underway for those aged 10 years and older (6).

Table 2. Unadjusted and adjusted seropositivity by age group, sex, and county of residence, October 10th – 23rd 2021

Characteristic		Number seropositive	Unadjusted Percent	95% Confidence interval		Adjusted Percent	95% Confidence interval	
Age group (years)	20-29	126	85.1	78.5	90.0	86.1	79.4	91.0
	30-39	142	87.7	81.7	91.9	88.7	82.6	92.9
	40-49	151	96.2	91.9	98.2	97.3	93.0	99.4
	50-59	149	93.1	88.1	96.1	94.2	89.1	97.3
	60-69	145	90.6	85.1	94.2	91.7	86.1	95.3
Sex	F	363	91.0	87.8	93.4	92.0	88.8	94.5
	M	350	90.2	86.8	92.8	91.3	87.8	93.9
County of residence	Dublin	317	93.2	90.1	95.5	94.3	91.1	96.6
	Cork	89	89.0	81.4	93.7	90.0	82.3	94.9
	Donegal	80	80.8	72.0	87.4	81.7	72.7	88.4
	Galway	63	94.0	85.6	97.7	95.1	86.6	98.8
	Limerick	54	91.5	81.6	96.3	92.6	82.6	97.5
	Mayo	24	92.3	75.9	97.9	93.4	76.7	99.0
	Clare	22	91.7	74.2	97.7	92.7	74.9	98.9
	Wicklow	21	91.3	73.2	97.6	92.4	74.0	98.8
	Kildare	20	90.9	72.2	97.5	92.0	72.9	98.6
	Tipperary	14	82.4	59.0	93.8	83.3	59.5	94.9
	Roscommon	7	100.0	64.6	100.0	100.0	65.2	100.0
	Kerry	1	100.0	5.1	100.0	*	*	*
	Meath	1	50.0	2.6	97.4	*	*	*
Total (pilot sites)		**713**	**90.6**	**88.4**	**92.4**	**91.7**	**89.4**	**93.5**

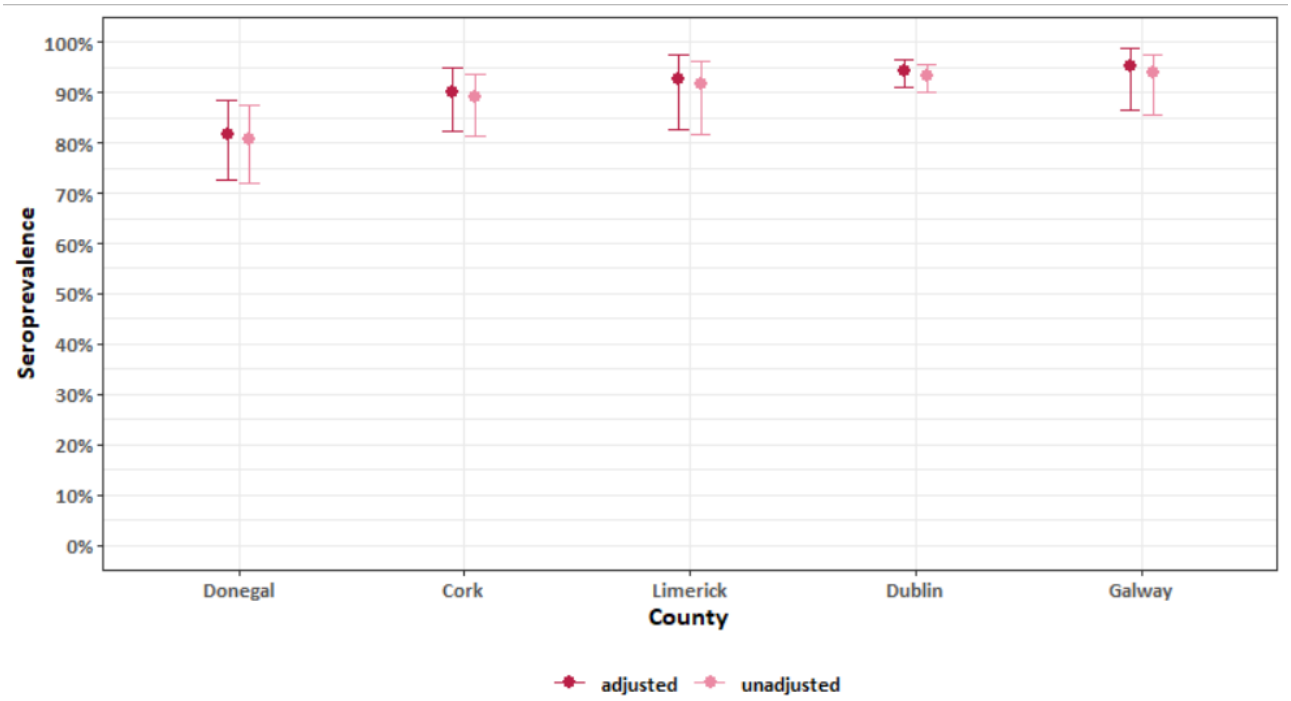
*Not estimated due to insufficient sample size

Figure 1. Unadjusted and adjusted seropositivity with 95% Confidence intervals by age group, October 10th – 23rd 2021



Focusing on counties Donegal, Cork, Limerick, Dublin and Galway with larger sample sizes, there may be an indication of a geographical effect (table 2 and figure 2), but further analysis is required.

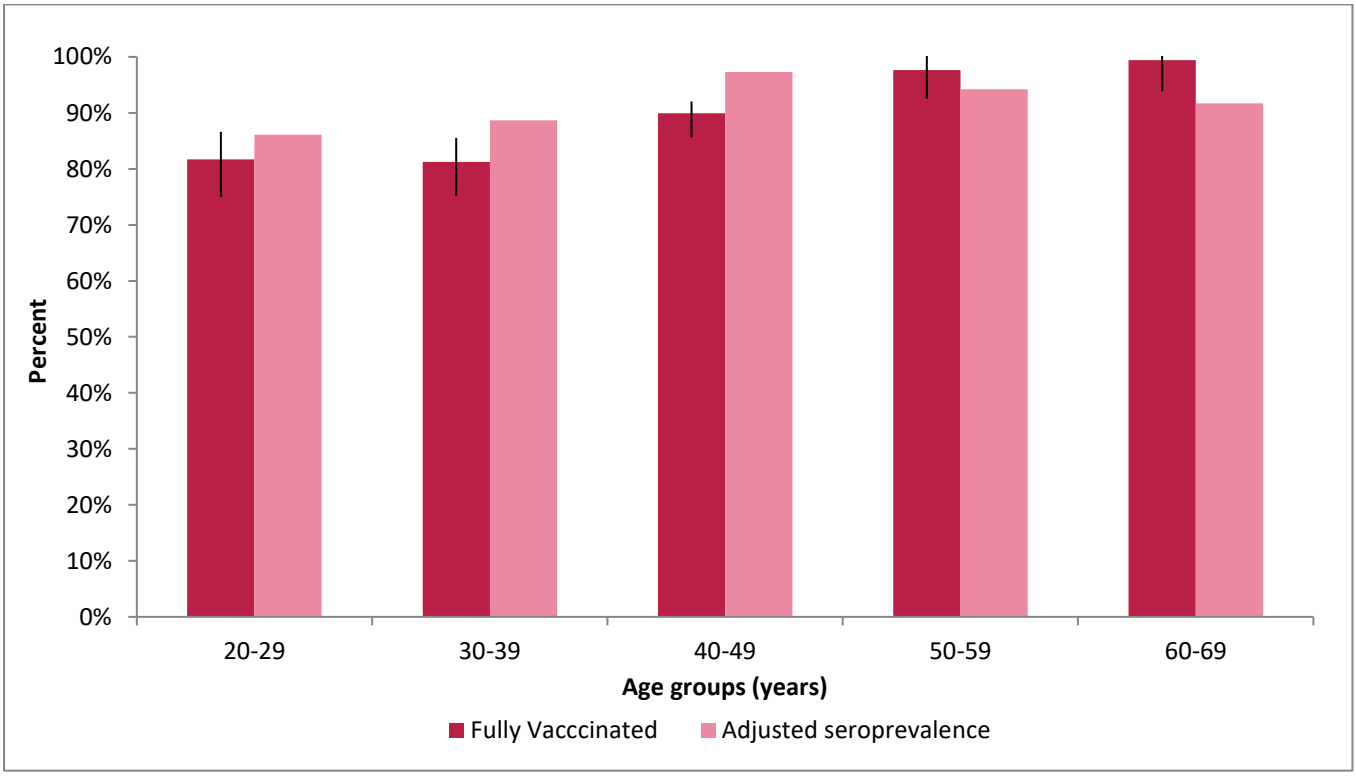
Figure 2. Unadjusted and adjusted seropositivity by county of residence*, October 10th – 23rd 2021



*Only counties with n>50 specimens were adjusted for test sensitivity and specificity and are shown in figure 2

Figure 3 shows adjusted seropositivity and vaccination uptake by age group. For the purposes of this report, HPSC has defined fully vaccinated as persons who were at least 14 days post completion of one dose of a 1-dose regimen, or both doses of a 2-dose regimen.

Figure 3. Adjusted seropositivity and vaccination uptake by age group, October 10th – 23rd 2021



Source: COVAX (Cumulative fully vaccinated data were collated from epidemiological week 39)

Limitations

As this was a pilot, the number of specimens included was smaller than that proposed for future collections, leading to less precision in the results.

The assay used for the measurement of antibody positivity for the pilot did not allow us to distinguish between antibodies generated or synthesised as a result of vaccination or following natural infection. Quantitative antibody results were not available for this analysis. Independent evaluations of test performance were not carried out; sensitivity and specificity rates were as reported by Abbott.

We believe that the sample selected primarily reflects the population who have had tests ordered by their GPs, but may also include routine repeat bloods requested by consultants, that have been ordered by GPs. While it is a proxy for community seroprevalence, it may not be representative of people in the community who do not have healthcare needs requiring blood testing or access to healthcare. A recent survey of Irish General Practices identified that Irish people consult with their GP or Practice Nurse 5.9 times per year giving context to use of residual specimens sourced from General Practice (1). However, information on the proportion of those attending who have blood tests taken within general practice is not

available. It is also likely that this consultation rate is affected by higher consultation rates in younger and older vulnerable populations.

The information collected in this surveillance system is a simple dataset, including only data that are readily available within the 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 individuals by agegroup in the whole population, available from COVAX, was used for comparison.

The residual serum/plasma specimens included in the pilot were confined to those aged between 20 and 69 years of age. The seroprevalence rates by age group and county in the pilot were not adjusted for the underlying demographic profiles of the counties.

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. SARS-CoV-2-infected individuals seroconvert following SARS-CoV-2 infection, and antibodies targeting the S1 domain of the SARS-CoV-2 spike protein are generated following vaccination. However antibodies are not generated in a small minority of cases.

Discussion

Timely and accurate information on population seroprevalence is critical to inform proactive, targeted public health interventions and vaccination policy. Seroprevalence data complements data from other surveillance systems, and can be used to estimate the true proportion of the population that remain susceptible to infection. Surveillance of residual serum/plasma from general practice can be used to approximate community prevalence, and is logistically more feasible to achieve and less costly than community surveys.(2)

From this pilot study it can be seen that SARS-CoV-2 anti-spike seropositivity is generally high in this population of 20-69 year olds, mainly reflecting the high vaccination rates of adults in Ireland. The seropositivity shows small variation by age, with the 40-49 year olds having the highest level of positivity. The lower seropositivity of the 20-29 year olds may be due to lower vaccination coverage or perhaps due to some very recent vaccination in this age group that is not yet detectable serologically. There are insufficient data to say whether the statistically significant lower seropositivity rates observed in the oldest age group in the pilot (60-69 years) are due to waning antibodies or other unmeasured variables, e.g. time since vaccination, presence of comorbidities and reason for visiting a GP.

The Abbott Architect SARS-CoV-2 IgG II anti-spike assay used in the pilot does not distinguish between vaccination-derived antibodies and those produced following natural infection, limiting interpretation of the findings. In future rounds, the preferred assay to be used by the NSP will facilitate this differentiation.

Adjusted seroprevalence rates were higher than national rates of fully vaccinated individuals for all age groups except those aged 50-59 years and 60-69 years. For those aged 60-69

years, this difference was statistically significant. This may be associated with vaccine effectiveness waning, but as comparisons between the groups are ecological, inferences cannot be made about the causes for the differences observed. For future rounds, older age groups will be included; if this effect is also seen in those aged 70-79 years of age, this will highlight the need for additional work to understand the impact of immunosenescence. In future rounds, the intention is also to measure quantitative antibody levels, which will provide more information on potential waning of immunity against infection by age group over time when examined in repeated cross sectional collection cycles.

For those aged 40-49 years of age, seroprevalence was significantly higher than reported vaccination rates. Vaccination rates were almost 90%, but seroprevalence was 97%, indicating that approximately 70% of those who were unvaccinated are apparently immune, which may be due to either natural infection, some bias in the sample attending GP for blood tests, and random error.

The lower seropositivity seen in Donegal compared with Dublin/Galway may be associated with the different age profiles, SARS-CoV-2 natural infection rates, vaccine uptake in these regions and possible vaccination of Donegal residents in Northern Ireland. In future, the results will be adjusted for demographic profile in the counties and vaccination rates in the counties will also be examined.

Public health implications

As part of the HPSC's ongoing remit to protect the health of the Irish people as the national centre for surveillance of communicable diseases, the establishment of the National Serosurveillance Programme will facilitate identification of changes in SARS CoV 2 seroprevelance at a community level.

Seroprevalence data generated by the NSP and participating partners will help to identify variance in population immunity in an attempt to guide public health measures e.g. the introduction or removal of non-pharmaceutical interventions at the popularion level. Seroprevalence data will also aid in ongoing epidemiological models being used to project scenarios for the trajectory of the disease and to monitor transmission trends.

Once established, the surveillance system will be in a position to provide information on the spread of other infectious diseases of public health importance in the population, and to inform planning of vaccination programmes and other preventative activities and interventions.

Technical notes

1. Population Data

Population data were taken from CSO 2020 estimates. Data were aggregated into the following age groups for the analysis: 20-29 years, 30-39 years, 40-49 years, 50-59 years and 60-69 years.

2. Adjustments for sensitivity and specificity of the test

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 (3)

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 (4). In this report we assume the sensitivity of the Abbott Architect SARS-CoV-2 IgG Assay is 98.81% (95%CI 93.56-99.94) and specificity is 99.55%100% (99.15, 99.76) as reported in (5).

3. Definition of Epidemiological week

Epidemiological weeks are as outlined on the HPSC website.

4. Vaccination Uptake Data

Vaccination uptake data were extracted from Covax on 25/11/2021. Data were aggregated into the following age groups for the analysis: 20-29 years, 30-39 years, 40-49 years, 50-59 years and 60-69 years. For the purposes of this report, individuals were considered fully vaccinated when they had completed 1 dose of a 1-dose vaccine regimen, or 2 doses of a 2-dose vaccine regimen. Fully vaccinated persons were collated from epidemiological week 39 to ensure a 14-day window had passed to compare against NSP pilot data.

Further information available on HPSC website

https://www.hpsc.ie/a-z/nationalserosurveillanceprogramme/

Acknowledgements

This pilot would not have been possible without the enthusiasm, dedication and commitment of all of the following individuals and organisations. The National Serosurveillance Programme would like to thank each and every one for their contribution to this important initiative.

Laboratory Surveillance Network (LSN) Pilot Participants

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National Serosurveillance Programme (NSP) Oversight Group

Membership in Appendix A

National Serosurveillance Programme (NSP) Steering Committee

Membership in Appendix B

Sincere thanks are also extended to Suzanne Cotter and Piaras O'Lorcain, HPSC for providing vaccination uptake figures from COVAX.

Report prepared by:

HPSC SEU Team, 02/12/2021

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Appendix A – NSP Oversight Group Membership

Dr Lorraine Doherty	National Clinical Director, Health Protection (Chair)
Dr John Cuddihy	Director, Health Protection Surveillance Centre
Dr Cillian De Gascun	Director, National Virus Reference Laboratory
Dr Jeff Connell (alternate)	Assistant Director, Principal Clinical Scientist, National Virus Reference Laboratory
Dr Suzanne Cotter	Specialist in Public Health Medicine, HPSC, HPSC Lead for immunisation and vaccine preventable diseases
Dr Shari Srinivasan	Consultant Chemical Pathologist, Beaumont Hospital, and Chair RCPI Faculty of Pathology Chemical Pathology group
Professor Mary Keogan	Clinical Lead National Clinical Programme for Pathology & Consultant Immunologist Beaumont Hospital
Dr Niamh O'Flaherty	Consultant Microbiologist, Irish Blood Transfusion Service
Dr Lelia Thornton	Specialist in Public Health Medicine, HPSC
Dr Derval Igoe	Specialist in Public Health Medicine, HPSC

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