PRECISE 5: COVID-19 in healthcare workers in Ireland: A prospective cohort study.

Louise Marron[1,2], Liam Townsend[3], Lisa Domegan[1], Katie O'Brien[1], Cathal Walsh[1,4], PRECISE Study Steering Group, Catherine Fleming[5], Colm Bergin[3,6]

On behalf of the PRECISE Steering Group

(Prevalence of COVID-19 Antibodies in Irish Healthcare Workers)

Authors affiliations

[1]Health Protection Surveillance Centre, 25-27 Middle Gardiner Street, Dublin 1, Ireland

[2]ECDC Fellowship Programme, Field Epidemiology path (EPIET), European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

[3]Department of Infectious Diseases, St James's Hospital, Dublin, Ireland

[4]Biostatistics Unit, Trinity College Dublin, Dublin, Ireland

[5]Department of Infectious Diseases, University Hospital Galway, Galway, Ireland

[6]Department of Clinical Medicine, Trinity College, Dublin, Ireland

PRECISE Study Steering Group Members and Affiliations

Dr Lorraine Doherty, National Clinical Director Strategic Public Health, HSE, and Chair of PRECISE Steering Group; Professor Colm Bergin, Consultant Physician in Infectious Diseases and Site Lead for PRECISE study, St. James's Hospital, Dublin, Ireland; Dr Niall Conlon, Consultant Immunologist, St. James's Hospital, Dublin, Ireland; Dr Lisa Domegan, Principal Epidemiologist, HSE-HPSC, Dublin, Ireland; Dr Catherine Fleming, Consultant in Infectious Diseases and Site Lead for PRECISE study, Galway University Hospital, Galway, Ireland; Dr Cillian de Gascun, Director, UCD National Virus Reference Laboratory, University College Dublin, Dublin, Ireland; Joan Gallagher, Programme Manager, Office of the Director for National Health Protection, National Health Protection Office, Dublin, Ireland; Professor Mary Keogan, Consultant Immunologist Beaumont Hospital and Clinical Lead, National Clinical Programme for Pathology, HSE, Ireland; Dr Noirin Noonan, Consultant in Occupational Medicine, St. James's Hospital, Dublin, Ireland; Professor Cliona O'Farrelly, Chair in Comparative Immunology, Trinity College Dublin, Ireland, Dr Deirdre Sugrue, Consultant in Occupational Medicine, Dr Gregory Martin, Director Health Protection Surveillance Centre, National Clinical Lead for Health Protection Surveillance, Dr Johnathan McGrath, Department of Infectious Diseases, St James's Hospital, Dublin, Ireland, Dr Claire Kenny, Department of Infectious Diseases, University Hospital Galway, Galway, Ireland

17th June 2024

Table of contents

List of abbreviations

Anti-N	Anti-Nucleocapsid
Anti-S	Anti-Spike
aOR	adjusted Odds Ratio
CI	Confidence Interval
BMI	Body Mass Index
COI	Cut Off Index
COVAX	National COVID-19 vaccination information system
COVID-19	Coronavirus Disease 2019
ED	Emergency Department
EU	European Union
GDPR	General Data Protection Regulations
GP	General Practitioner
UHG	University Hospital Galway
HCA	Healthcare Assistant
HCW	Healthcare Worker
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
IgG	Immunoglobulin G
IQR	Interquartile Range
ISO week	International Organization for Standardization week
OR	Odds Ratio
PCR	Polymerase Chain Reaction
IPC	Infection Prevention and Control
PPE	Personal Protective Equipment
PRECISE	Prevalence of COVID-19 in Irish Healthcare Workers
RR	Relative Risk
RSV	Respiratory Syncytial Virus
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SJH	St James's Hospital
TUH	Tallaght University Hospital
UK	United Kingdom
VIF	Variance Inflation Factor

List of tables

List of figures

Executive summary

Introduction

Hospital HCWs have an ongoing high exposure risk to SARS-CoV-2 and are a high-risk population for SARS-CoV-2 infection, despite high rates of COVID-19 vaccination and prior infection. We aimed to describe the evolving epidemiology of COVID-19, the serological response to SARS-CoV-2 infection and COVID-19 vaccination, and to identify the factors associated with seropositivity and with SARS-CoV-2 incident infection in hospital HCWs.

Methods

Prevalence of COVID-19 in Irish Healthcare Workers (PRECISE) is a series of multicentre seroprevalence studies among healthcare workers (HCWs) in two hospital sites in Ireland in Galway and Dublin. PRECISE 5 was a prospective multi-site, longitudinal cohort study. All HCWs aged 18 years and older (n = 9,100) in the two hospital sites were invited to participate. Enrolment began in November 2022 and was completed in December 2022. Participants were followed up over a nine-month time-period until September 2023. At entry to the study, serological status was assessed by measuring anti-nucleocapsid (anti-N) and anti-spike (anti-S) antibodies. An enrolment questionnaire recorded demographic data, clinical risk factors for severe SARS-CoV-2 infection, and history of previous SARS-CoV-2 infection and/or COVID-19 vaccination. Clinical risk factors for severe SARS-CoV-2 infection were self-reported at enrolment and included the presence of an underlying medical condition associated with sub-optimal response to vaccination or immunocompromise. For the duration of the study period, monthly questionnaires collected data on SARS-CoV-2 incident infections, including symptoms and absence from work, as well as COVID-19 vaccination history. For all participants, vaccination status was verified using the national COVID-19 vaccination database (COVAX). A descriptive analysis of all questionnaire responses was conducted to describe the baseline characteristics of participants and the characteristics of incident infections, including severity. Univariable and multivariable linear regression models identified the factors associated with anti-N antibody levels. Adjusted odds ratios (aOR) were calculated using logistic regression to identify factors associated with anti-N antibody status, incident infection and symptomatic incident infection.

Results

The participation rate in PRECISE 5 was 13.8% (n = 1,260). At entry to the study, 4.3% (n = 54) were unvaccinated, 91.2% (n = 1,149) had received at least one COVID-19 booster vaccination and 34.1% (n = 430) had received a second booster vaccination. Overall, 99.8% (n = 1,258) of the study population were anti-S antibody positive at enrolment and 79.8% (n = 1,006) had serological evidence of prior infection (anti-N antibody positive). Those with an underlying clinical risk factor for

severe infection were less likely to be anti-N antibody positive compared to those without a risk factor (aOR 0.40, 95% CI 0.23, 0.70, p-value = 0.001). Those aged 40-49 and those aged 50 years and older were also less likely to be anti-N antibody positive compared to those aged 18-29 years (aOR 0.50, 95% 0.27, 0.91, p-value = 0.025 and aOR 0.41 95% CI 0.22, 0.74, p-value = 0.004 respectively). In multiple linear regression, increasing time from last COVID-19 vaccination was associated with increasing anti-N antibody titres (p-value <0.001).

Those with an Asian ethnicity had 7-fold higher odds of being anti-N antibody positive compared to those with a White Irish ethnicity (aOR 7.81, 95% CI 2.27, 28.26, p-value = 0.001). HCAs were the only occupational group with a higher adjusted odds of anti-N positivity, with a 3.5-fold higher odds of anti-N antibody positivity compared to those in administrative roles (aOR 3.49, 95% CI 1.23, 11.14, p-value = 0.024), while those in allied healthcare professional roles and those categorised as being in an 'other' role had a lower odds of anti-N positivity.

At enrolment, 69.6% (n = 877) reported a previous SARS-CoV-2 infection, diagnosed using a laboratory Polymerase Chain Reaction (PCR) test in 46.4% (n = 585). During the study period, 21.7% (n = 274) reported an incident infection. The number of incident infections reported peaked in December 2023, reflecting the national epidemiology of SARS-CoV-2 infection during the study period. The diagnosis of incident infection was made by antigen test in 83.9% (230/274), PCR testing was used to diagnose incident infection in 14.6% (40/274). Of all incident infections, 60.6% were asymptomatic and for all infections, symptomatic and asymptomatic, the median number of days off work was 5 days (IQR 3-7 days). There were no hospital admissions among any participants during the study period and no participant required supplemental oxygen support.

Having at least one underlying clinical risk factor for acquiring severe SARS-CoV-2 infection was associated with an increased odds of incident infection (aOR 1.67, 95% CI 1.04, 2.65, p-value = 0.031). The odds of incident infection was 86% (aOR 1.86, 95% CI 1.24, 2.84, p-value = 0.003) higher among those who reported ≥ 180 days since last infection compared with those who reported infection within 180 days. Being anti-N antibody positive was protective (aOR 0.27, 95% CI 0.18, 0.40, p-value <0.001) against incident infection, however, 62% of participants who reported an incident infection were anti-N positive. There was no association between reporting an incident infection and time since last COVID-19 vaccination.

Discussion

This study indicated a high seroprevalence and an ongoing high risk of incident SARS-CoV-2 infection among hospital HCWs in Ireland, despite high rates of vaccination, prior infection and seropositivity.

The findings of this study indicated that the pattern of hospital HCW infection follows national trends and showed the absence of severe illness in a highly vaccinated hospital HCW cohort, emphasising the benefits of COVID-19 vaccination. However, ongoing incident infections among hospital HCWs continue to impact healthcare service provision and are an important consideration for healthcare service planning, particularly for winter planning, in anticipation of likely surges in respiratory infections.

There has been a shift in diagnostics used to diagnose infection among HCWs, from PCR to antigen testing, reflecting changes in national testing policies. PCR testing may be more sensitive in high-risk clinical settings. The high proportion of asymptomatic infections suggest a benefit to increased testing among HCWs particularly during surge periods of infection. Additionally, given high rates of SARS-CoV-2 infection despite vaccination, robust infection prevention and control (IPC) measures continue to be required to reduce exposure risk and prevent transmission in healthcare settings.

Increasing time since last SARS-CoV-2 infection (180 days or more) and having at least one clinical risk factor for severe infection such as immunocompromise due to immunosuppressive medication e.g., steroids or underlying comorbidities such as cancer, were associated with reporting an incident infection during this study period. Negative anti-N antibody status at enrolment was also associated with having a risk factor for severe SARS-CoV-2 infection and was associated with age over 40 years. Additionally, increasing anti-N antibody titres were associated with increasing time from last COVID-19 vaccination, this may suggest that SARS-CoV-2 infection risk and subsequent associated anti-N antibody positivity increases by time since vaccination.

Therefore, ongoing targeted vaccination campaigns for HCWs, particularly for those in older age groups (40 years and older) and with underlying risk factors and with increased time (180 days or more) since last SARS-CoV-2 infection are supported by the findings of this study. Nationally and internationally, as vaccine fatigue emerges as an important public health issue, supporting HCW vaccine decision making with vaccination information materials, explaining the rationale for targeted vaccination and ease of access to vaccinations will be important to improve and maintain COVID-19 vaccination uptake among HCWs to minimise the risk of infection, serious illness, and transmission in healthcare settings.

Recommendations

The following are recommendations arising from the findings of this study:

1. The findings of this study support continued targeted vaccination programmes for HCWs, particularly those in older age groups (40 years and older), those with underlying clinical risk factors for severe SARS-CoV-2 infection and those with increased time since last SARS-CoV-2 infection and/or vaccination (180 days or more). The findings should be shared with key stakeholders involved in the COVID-19 vaccination programme e.g., Chief Clinical Officer, Chief Medical Officer, the National Immunisation Advisory Committee, and the National Immunisation Office. The findings should also be communicated to occupational health departments in hospitals and others involved in the rollout of vaccination programmes among HCWs.

2. In the context of vaccine fatigue and lower than expected uptake of COVID-19 vaccines among HCW in the 2023/2024 season, the findings of this study should inform the development of targeted vaccination communication and education materials for all HCWs to emphasise the benefits of vaccination at preventing severe illness among hospital HCWs as well as the need to protect vulnerable patients and the healthcare service.

3. COVID-19 vaccination programmes should be particularly targeted among HCWs to those who are at higher risk of SARS-CoV-2 infection e.g., those in older age groups (40 years and older), those with risk factors for severe SARS-CoV-2 infection, those who have a longer time since last infection and/or vaccination (180 days or more), as well as those working as healthcare assistants and HCWs from ethnic minority groups. Strengthening surveillance of infection among HCWs would allow for identification of HCWs with increased time since last infection. Engaging vaccine champions and peer vaccinators in hospital sites from groups at higher risk of infection as well as improving vaccine accessibility, where possible, should be considered to communicate key messages about the benefits of vaccination to HCWs, patients and the healthcare system.

4. The risk of infection and transmission in healthcare settings despite vaccination emphasise the importance of adherence to infection prevention and control (IPC) guidance. IPC guidance should be regularly reviewed in clinical settings to ensure optimisation and adherence to guidance. Risk assessments in healthcare settings should be dynamic and reviewed regularly, particularly during surge periods of infection to guide the use of increased IPC measures, including consideration for increased testing among HCWs e.g., in outbreak settings.

5. Surge capacity plans that incorporate anticipated staff absences due to COVID-19 should be developed to allow for continued provision of scheduled and unscheduled care in the health service, including during surge periods of SARS-CoV-2 infection. This is of particular importance to those involved in winter planning.

6. Seropositivity among healthcare workers should not be used as a marker of immunity from infection. Planned detailed immunological studies to further understand the immunological factors associated with SARS-CoV-2 infection may be useful to further inform this discussion in the hospital HCW population in Ireland.

7. The impact of SARS-CoV-2 infection on the hospital HCW workforce should be further evaluated with an economic evaluation, this is planned as part of further PRECISE studies.

1 Introduction

Prevalence of COVID-19 in Irish Healthcare Workers studies (PRECISE) is a series of multicentre seroprevalence studies among hospital healthcare workers (HCWs) in two hospitals in Ireland. Previous PRECISE studies have indicated that HCWs in two hospital sites in Ireland are an engaged cohort, with a high COVID-19 vaccination coverage of 98% for the primary vaccination series,[1] and high rates of SARS-CoV-2 infection compared to the general population.[2] Previous PRECISE studies have also identified that seroprevalence risk in hospital HCWs is up to six times higher than community seroprevalence for SARS-CoV-2.[2]

Given changes to national testing policy and the limited use of Polymerase Chain Reaction (PCR) testing in the general population,[3] HCWs may undergo PCR or antigen testing more frequently than those in the community and hospital HCW infection may precede or follow each wave of COVID-19 infection in the community. Therefore, studies among hospital HCWs may provide timely information in relation to SARS-CoV-2 surges in the community.

COVID-19 immunity is an evolving area of research due to SARS-CoV-2 infections occurring despite robust anti-spike (anti-S) Immunoglobulin G (IgG) in vaccinated individuals and uncertainty about the duration of infection-acquired immunity.[4] As SARS-CoV-2 immunity following both infection and vaccination appears to wane over time requiring booster vaccination,[5] it is important to understand the impact of prior SARS-CoV-2 infection and COVID-19 vaccination on an individual's response to exposure to with the virus. There is also a need to identify predictors of incident infection, which may inform and guide targeted administration and timing of booster vaccination doses.

Understanding the epidemiology of COVID-19 in hospital HCWs and the factors associated with incident infection and seropositivity within this highly vaccinated cohort with high rates of prior infection is therefore important for several reasons including:

- To inform public health communication in relation to the benefits of vaccination at preventing severe illness.
- To provide information for health service planners to further estimate the impact of SARS-CoV-2 infection on the hospital HCW workforce including COVID-19 related absences.
- To inform communication to vaccination policy makers to guide decisions about the need for and optimal timing of additional booster doses for HCW and within the population.

The research question for this study was therefore, *what is the evolving epidemiology of COVID-19 among hospital HCWs in Ireland and what are the factors associated with serological status and incident infection, including the impact of COVID-19 vaccination and prior SARS-CoV-2 infection?*

2 Methods

2.1 Aim

To describe the evolving epidemiology of COVID-19, the serological response to SARS-CoV-2 infection and COVID-19 vaccination, and to identify the factors associated with seropositivity and with SARS-CoV-2 incident infection in hospital HCWs in two hospitals in Ireland.

2.2 Objectives

The specific objectives were as follows:

2.2.1 Objective 1

To describe the evolving epidemiology of incident SARS-CoV-2 infections and COVID-19 severity in hospital HCWs.

2.2.2 Objective 2

To describe the serological status of the hospital HCW population in two hospitals in Ireland and to identify the factors associated with anti-nucleocapsid (anti-N) antibody positivity and anti-N antibody levels in HCWs, including demographic factors, clinical factors (e.g., clinical risk factors for severe SARS-CoV-2 infection such as underlying immunocompromise) and history of SARS-CoV-2 infection and/or COVID-19 vaccination.

2.2.3 Objective 3

To estimate the number and proportion of incident SARS-CoV-2 infections and to identify the factors associated with incident SARS-CoV-2 infection in the HCW population in two hospitals in Ireland.

2.2.4 Objective 4

To estimate COVID-19 vaccination coverage among hospital HCWs.

2.3 Study design and population

PRECISE 5 was a prospective multi-site, longitudinal cohort study of hospital HCWs in two geographic areas of Ireland (Galway and Dublin). PRECISE 5 was an opt-in study and all HCWs aged 18 years and older in two hospitals (University Hospital Galway (UHG) and St James's Hospital (SJH), Dublin) were eligible to enrol. HCWs included catering, cleaning, and security staff in the participating hospitals. Any HCW aged under 18 years was excluded. Enrolment for PRECISE 5 began in November 2022 and was completed in December 2022. Participants were followed up over a nine-month time-period until September 2023.

2.4 Recruitment of participants

All HCWs in the participating hospitals (Total n = 9,100) were informed of PRECISE 5 through a communication campaign with circulation of information regarding the study. This campaign

involved a poster with a QR code and website address for the secure Castor online research portal. An electronic participant information leaflet was available on this portal. Those who wished to participate created a unique ID upon log in and were emailed a consent form which could be signed electronically. The participant was able to download their electronic consent form for their own records.

2.5 Data collection

2.5.1 Questionnaire

Once consented electronically, all participants in PRECISE 5 were asked via email to complete an online enrolment questionnaire (Appendix A), via the Castor secure online portal. This enrolment questionnaire included demographic details, role in the hospital and self-reported COVID-19 vaccination history, underlying clinical risk factors and medical history relating to prior COVID-19 infections.

To capture incident COVID-19 infections during the study period and associated disease severity and self-reported information on COVID-19 vaccination, participants completed monthly questionnaires over the nine-month study period. In the monthly questionnaire, participants were asked if they had an incident SARS-CoV-2 infection (yes/no) (defined as a self-reported positive SARS-CoV-2 PCR test and/or SARS-CoV-2 antigen test) in the previous month and related questions about:

- Date of infection (self-reported)
- How infection was confirmed (self-reported PCR or antigen positive)
- Presence of symptoms (yes/no)
- Symptom duration (in days)
- Symptom severity (days in bed due to illness, consultation with a General Practitioner (GP) (yes/no), Emergency Department (ED) attendance (yes/no), hospital admission (yes/no) and length of hospital stay (in days), supplemental oxygen (yes/no))
- Number of days of absence from work due to an incident SARS-CoV-2 infection

2.5.2 Verification of vaccination status

As part of the enrolment questionnaire and for each monthly questionnaire, participants were asked if they had been vaccinated in the previous month (yes/no) and the self-reported date and brand of vaccination. For all participants, where data were available, self-reported COVID-19 vaccination status was verified from the Health Service Executive (HSE) Centralised Vaccination Database (COVAX) in Ireland. This verified vaccination information was linked with serological and questionnaire data. Vaccination status, (e.g., vaccinated with primary course or vaccinated with primary course and booster 1), was defined based on national definitions of vaccination status

(Appendix B). Only COVAX verified vaccination history for participants were included in this study; for each vaccination, i.e. primary vaccination course and subsequent booster doses, participants who self-reported vaccination but who had no verified vaccination on COVAX were not considered vaccinated for a given dose/vaccination status.

2.5.3 Serological study

At enrolment in the study, all participants were given a link to Swiftqueue, a secure online facility through which participants could schedule a phlebotomy appointment. For the serological study, participants were asked to donate 3mls of whole blood. Blood samples were analysed by laboratories in each hospital site using the Roche Elecsys Anti-SARS-CoV-2 assay for detection of anti-N antibodies (as a measure of previous infection) and the Roche Elecsys-S Anti-SARS-CoV-2 assay for detection of anti-S antibodies (as a measure of vaccine response). As per the manufacturer guidelines on the titre level thresholds, a cut-off of ≥1.0 cut-off index (COI) in the Roche Elecsys Anti-SARS-CoV-2 assay and ≥0.8 U/mL in the Roche Elecsys-S Anti-SARS-CoV-2 assay was considered positive. The upper limit of quantification for the commercial Roche Elecsys-S Anti-SARS-CoV-2 assay is 250 U/mL.

In participants with a COVID-19 vaccination history, detectable anti-S antibodies were assumed anti-S positive in response to vaccination. Detectable anti-N antibodies were assumed anti-N positive in response to previous SARS-CoV-2 infection.

2.6 Operational definitions

2.6.1 Definition of key outcome variables

Self-reported infection

A history of previous self-reported infection at enrolment was defined as a response of "Yes" to the question that asked if the participant had ever had a COVID-19 infection. For calculation of time intervals in relation to self-reported infection (i.e. time from self-reported infection to enrolment and time from self-reported infection to incident infection), only infections where the participant self-reported a valid date of infection were included. A valid date of infection was defined as an infection reported after the first COVID-19 case was notified in Ireland (02/03/2020) and prior to the participants date of enrolment in the study (between 07/11/2022 and 02/12/2022). A person with no history of SARS-CoV-2 infection was defined as a person with no self-reported infection at enrolment (i.e. did not provide a "Yes" response to the question at enrolment that asked if the participant had ever had a COVID-19 infection).

Serological status

The classification of a participant as being anti-N antibody positive or anti-N antibody negative was based on the threshold of (≥0.8 U/mL). Based on the initial anti-N serological results, and self-reported previous SARS-CoV-2 infection status at enrolment, all participants were classified into four categories at enrolment as follows:

- Participants with detectable anti-N antibodies, above the threshold for positivity (≥0.8 U/mL), and a self-reported history of SARS-CoV-2 infection.
- Participants with an anti-N antibody level below the threshold for positivity, and with no self-reported SARS-CoV-2 infection.
- Participants with detectable anti-N antibodies, above the threshold for positivity (≥0.8 U/mL), and no self-reported history of SARS-CoV-2 infection, presumed to have had a previous unrecognised SARS-CoV-2 infection.
- Participants with anti-N antibodies below the threshold for positivity and a history of self-reported infection, who may have lost anti-N positivity over time.

Incident infection

An incident infection was defined as a self-reported SARS-CoV-2 infection after the date of a participant's enrolment to the study (between 07/11/2022 and 02/12/2022) and prior to the date of study completion (01/09/2023). Two additional variables to define an incident infection were created. The first (*incident infection*) included all self-reported incident infections during the nine-month study period. The second (*plausible date of incident infection*) included only those who had an incident infection with a plausible incident infection date. This was defined as an incident infection reported as occurring 30 days after the last self-reported incident infection. For calculation of the time interval from the date of last vaccination to the date of incident infection or date last self-reported infection at enrolment to incident infection, the date of the first self-reported incident infection was used. A severe incident infection was defined as requiring hospital admission and/or supplemental oxygen.

2.7 Data analysis

2.7.1 Descriptive analysis

Following data cleaning, descriptive statistical analysis was undertaken.

- The baseline characteristics for the study population overall and by participating hospital were calculated.
- Additional descriptive analysis of those who were anti-N antibody positive at enrolment compared to those who were anti-N antibody negative at enrolment was undertaken.

- Descriptive analysis comparing those who were anti-N antibody negative but with a history of self-reported SARS-CoV-2 infection to those who were anti-N antibody positive with a history of self-reported infection was also undertaken to identify participant characteristics associated with a potential waning/loss of anti-N positivity following SARS-CoV-2 infection.
- Additionally, a descriptive analysis of those who self-reported an incident infection during the study period compared to those who did not was undertaken, including descriptive analysis of those with symptomatic incident infection compared to those who reported incident infection but did not report symptoms.

The descriptive analyses included participant demographics, the presence of specific underlying clinical risk factors for severe SARS-CoV-2 infection, COVID-19 vaccination status, and self-reported prior SARS-CoV-2 infection(s) at enrolment to the study, baseline seropositivity at enrolment, classification by serological/vaccination history, time from last COVID-19 vaccination and time from last SARS-CoV-2 infection to enrolment.

Additionally, the epidemiology and clinical characteristics (including severity) of self-reported incident SARS-CoV-2 infection over the nine-month study time-period was analysed overall and by hospital site.

For categorical variables, frequencies and percentages were calculated and for continuous variables medians with interquartile ranges (IQRs) were calculated. Comparison between groups was made using the Chi-square test for proportions for categorical variables and the Mann-Whitney U test for comparison of medians for continuous variables.

2.7.2 Regression analysis

Univariable and multivariable logistic regression analysis calculated crude and adjusted odds ratios (ORs) with 95% confidence intervals (95% CI) to investigate the factors associated with incident SARS-CoV-2 infection (with a plausible infection date reported) and with anti-N antibody positivity at enrolment. Additionally, the factors associated with anti-N antibody level at enrolment were identified using simple and multiple linear regression models. Results were reported as β coefficients with 95% CIs. The distribution of the anti-N antibody level variable was assessed and underwent log transformation prior to inclusion in the linear models.

Variables known to be associated with the outcomes (age and sex) were chosen for inclusion *a priori* in the multivariable analysis. Along with age and sex, variables which, following univariable analysis, had a p-value of <0.05 were included in the multivariable models, as long as they did not correlate and result in multicollinearity (e.g., country of birth and ethnicity). This was assessed by calculating

the variance inflation factor (VIF). A VIF > 5 was considered to indicate multicollinearity. For all linear models, the assumptions of linear regression were verified. For the logistic regression models, the variability in the dependent variable explained by each model was assessed by calculation of the Nagelkerke R^2 test. The goodness of fit each model was assessed using a Hosmer-Lemeshow test (p-value > 0.05 indicated a good model fit).

Additionally, a sensitivity analysis used log binomial regression to calculate adjusted relative risks (aRRs) with 95% CI to identify the factors associated with incident SARS-CoV-2 infection. The results of the logistic regression analysis and the log binomial analysis were compared examining the direction, strength and significance of the associations.

All data analysis was conducted using R version 4.2.3. A data dictionary for all variables collected in the baseline and monthly questionnaire is included as Appendix C.

2.8 Ethical and data protection considerations

Ethical approval for PRECISE 5 was granted from the SJH/Tallaght University Hospital (TUH) joint Research Ethics Committee (GCREC 15/09/2022 C.A. 2860, TUH/SJH REC 2022-Nov-23002300). The online platform Castor EDC used for data collection complies with all the relevant regulatory compliance legislation, including EU Data Protection Directives, ICH E6 Good Clinical Practice, 21 CFR Part 11, and HIPAA and EU (Annex 11). They are also officially ISO 27001 and ISO 9001 certified. Castor EDC are compliant with the requirements under General Data Protection Regulations (GDPR).[6] Multiple published studies have utilised and referenced Castor EDC in their publication, including previous PRECISE studies.[2]

SJH and UHG were joint data controllers for PRECISE studies. Each hospital determined their own data processing activities and prospectively approved the governance arrangements, and a data sharing agreement was in place between the two sites. A data protection impact assessment was jointly undertaken by the two participating hospital sites in October 2020 at the commencement of the PRECISE studies, and this remains in place.

For PRECISE 5, the data collected were pseudonymised by the data controller before being processed by the data processor, to ensure pseudonymity for any participant in the study. The data controller had a password protected file with additional information on participants that was not shared with the data processor. Therefore, if a participant wished to withdraw their data at any time, the data controller could identify the participant and remove them from any future data processing.

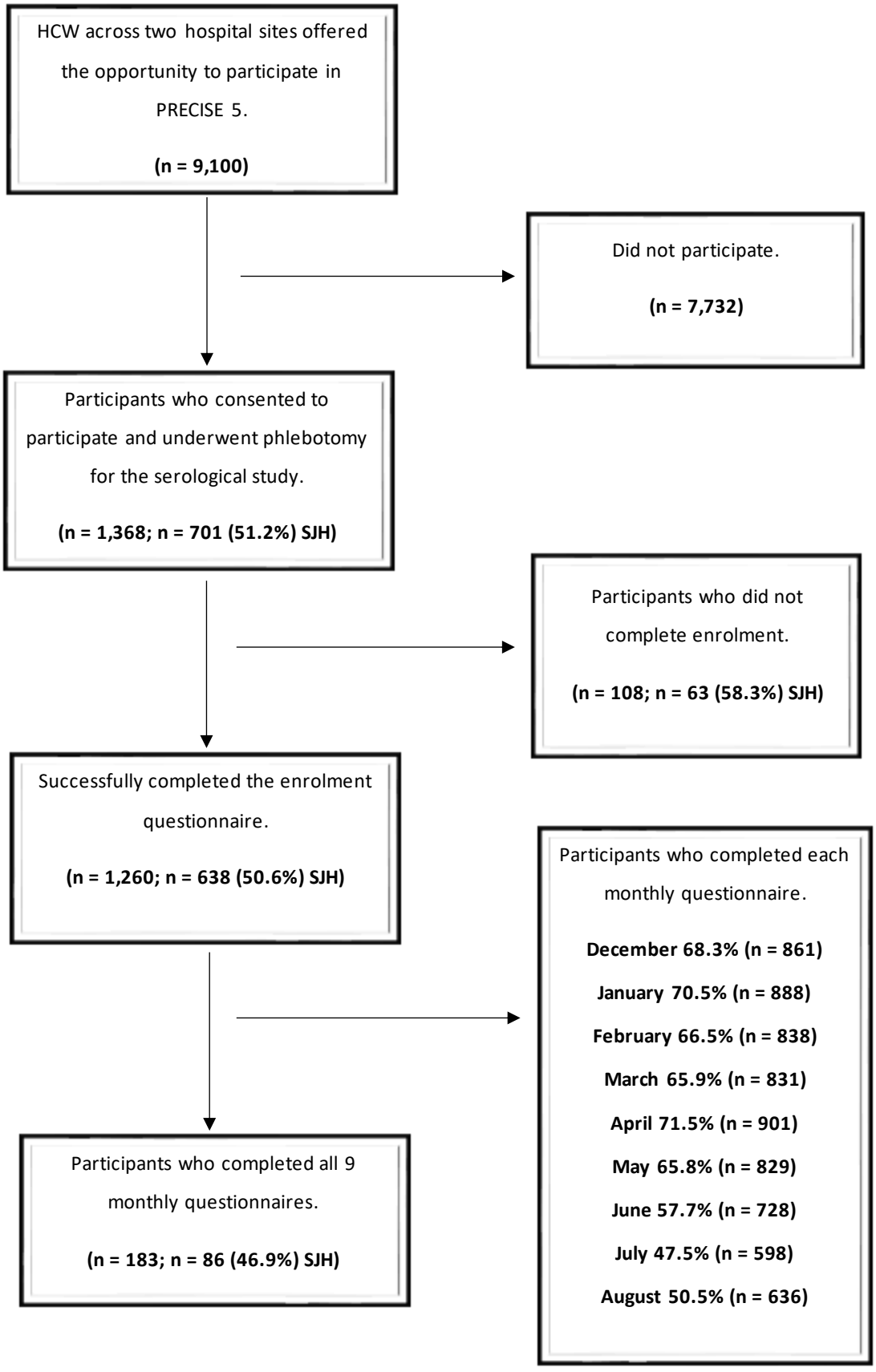
The PRECISE Steering Committee remained in place to provide oversight and reported back quarterly to the Health Protection Surveillance Centre (HPSC) on PRECISE studies.

3 Results

3.1.1 Study participation

The estimated total eligible population across the two hospital sites was 9,100. In total, 1,368 participants from the two hospital sites consented to participate and underwent phlebotomy for the serological study. A total of 1,260 hospital HCWs across the two sites completed the enrolment questionnaire, 50.6% (n = 638) from SJH and 49.4% (n = 622) from UHG. The participation rate for PRECISE 5 was therefore 13.8% (1,260/9,100). Monthly participation was over 65% for each month with the exception of the summer months; June (57.7%), July (47.5%) and August (50.5%) (Figure 1).

Figure 1 Flowchart of participation in PRECISE 5



3.1.2 Demographics

There were demographic differences between sites; participants in SJH were older, median age was 44 years (IQR 35-51) compared to 41.5 years (IQR 31-51) in UHG (p-value= 0.001) (Table 1). There were differences in occupation across sites with a higher proportion of participants in a clinical role from UHG (69% vs 61%, p-value = 0.004) (Table 2). Of the study population in both sites, 78% were born in Ireland and 78.9% identified as having white Irish ethnicity. However, there were differences by site for both ethnicity and country of birth; a higher proportion of participants in UHG reported their country of birth as being within the European Union (EU) or the United Kingdom (UK) (p-value= 0.031). There were no significant differences in underlying clinical risk factor status between the two participating sites with 9.0% (n=113) of the total study population reporting a clinical risk factor for severe SARS-CoV2 infection (Table 2) (Appendix D).

3.1.3 COVID-19 vaccination status at enrolment

Overall, 4.3% of the study population were unvaccinated (3.3% in SJH and 5.3% in UHG) while 4.5% had received their primary course only (5.0% in SJH and 4.0% in UHG) (p-value = 0.007). In total, 91.2% of participants had received at least one COVID-19 booster vaccination. A higher proportion of participants in SJH had completed their second booster vaccination at enrolment (38.2% vs 29.9%, p-value = 0.007) and were within 180 days of last vaccination (41.2 vs. 33.6%, p-value= 0.016), compared to participants in UHG (Table 2).

3.1.4 Anti-S antibody status at enrolment

Overall, 99.8% (1,258/1,260) of the study population were anti-S antibody positive at enrolment. All participants from SJH (n = 620) were anti-S antibody positive (Table 2).

3.1.5 Prior infection at enrolment

Previous SARS-CoV-2 infection was reported at enrolment by 69.6% (n = 877). There were similar rates of self-reported previous infection at enrolment reported across the two sites (68.8% vs 70.4%, p-value = 0.576) (Table 2Table 1). Among all study participants, laboratory PCR tests were the most commonly used test type among participants to confirm SARS-CoV-2 diagnosis at enrolment, 46.4% reported using PCR, compared to 22.4% who used antigen tests. There were differences in the sites in the test types used to diagnose self-reported infection. A higher proportion in SJH reported using laboratory confirmed PCR tests (48.6% vs. 44.2%), while a lower proportion reported using antigen tests (19.1% vs 25.7%) compared to UHG (p-value= 0.048) (Table 2). Among only those who self-reported a prior SARS-CoV-2 infection at enrolment and who provided information on test type (n = 867), 32.5% reported using antigen tests, while the remainder (67.5%) reported using a laboratory PCR test (Table 2).

Serological evidence of prior infection was present for 79.8% (n = 1,006) and there were no differences in the proportion of those who were anti-N positive across the two hospital sites (Table 2). However, there were differences in the median titres of anti-N antibodies with higher median titres measured from participants in UHG, 14.4u/dL (IQR 2.5-69.3) in UHG compared to 11.9u/dL (IQR 1.8-58.1) in SJH (p-value= 0.030) (Table 1).

Among those who self-reported prior SARS-CoV-2 infection, 93.7% (n = 822) were anti-N antibody positive while 6.2% (n = 54) were anti-N antibody negative despite reporting prior infection. Participants who were anti-N antibody negative despite reporting prior infection were older, median age 45 years (IQR 39-51) vs. 41 years (IQR 32-49), (p-value= 0.030), and had a longer time from last self-reported infection to serological testing at enrolment, 281 days (201-325) vs. 235 days (IQR 139-308), (p-value = 0.012). A higher proportion reported an acquisition risk factor for severe SARS-CoV-2 infection (22.2% vs. 7.5%, p-value <0.001) (Table 3).

Overall, 30.4% (n = 383) of the study population did not report a previous SARS-CoV-2 infection at enrolment (31.2% (SJH) and 29.6% (UHG), p-value= 0.576) (Table 2). In total, 15.8% (199/1,260) of the study population reported no history of SARS-CoV-2 infection and were anti-N antibody negative; this was 51.9% (199/383) of all those who did not self-report a previous SARS-CoV-2 infection. However, 14.6% (184/1,260) reported no infection but were anti-N antibody positive suggesting that 48.0% (184/383) of those who did not report previous SARS-CoV-2 infection may have had undiagnosed infection (Table 2). In 81% of hospital HCWs, their self-reported infection status aligned with their anti-N antibody status at enrolment (Table 2).

Table 1. Descriptive characteristics of the study population by hospital site and overall (n = 1,260): Continuous variables

	St James's Hospital (n = 638)		University Hospital Galway (n = 622)		Total (n) (n = 1,260)		p-value[a]
Exposure	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Age (years)	44	35-51	41.5	31-51	43	33-51	**0.001**
BMI	25.7	23.1-29.6	25.4	23-29.1	25.6	23.1-29.2	0.366
Anti nucleocapsid antibody level (U/ml)	11.9	1.8-58.1	14.4	2.5-69.3	12.9	2.2-65	**0.030**
Time from last COVID-19 vaccination to enrolment (days)	334	58-363	347	60-365	344	59-364	0.145
Time from last SARS-CoV-2 infection to enrolment (days)	232	138-312	239	144-308	237	140-311	0.762

[a]Mann-Whitney U test was used for comparison of medians for continuous variables.

Table 2. Descriptive characteristics of the study population by hospital site and overall (n = 1,260): Categorical variables

		St James's Hospital (n = 638)		University Hospital Galway (n = 622)		Total (n) (n = 1,260)		p-value[a]
		n	**%**	**n**	**%**	**n**	**%**	
Age category (years)	18-29	77	12.1	134	21.5	211	16.7	**<0.001**
	30-39	146	22.9	141	22.7	287	22.8	
	40-49	223	35.0	172	27.7	395	31.3	
	50+	192	30.1	175	28.1	367	29.1	
Sex	Female	512	80.3	488	78.5	1000	79.4	0.473
	Male	126	19.7	134	21.5	260	20.6	
Occupation	Administration	157	24.6	68	10.9	225	17.9	**<0.001**
	Allied Health Professional	102	16.0	60	9.6	162	12.9	
	General Support	35	5.5	26	4.2	61	4.8	
	Healthcare assistant	26	4.1	29	4.7	55	4.4	
	Laboratory	56	8.8	58	9.3	114	9.0	
	Medical/dental	71	11.1	117	18.8	188	14.9	
	Nursing/midwifery	183	28.7	220	35.4	403	32.0	
	Other role*	8	1.3	44	7.1	52	4.1	
Clinical role**	Clinical	391	61.3	430	69.1	821	65.2	**0.004**
	Non-clinical	247	38.7	192	30.9	439	34.8	

Contd.

Table 2. Descriptive characteristics of the study population by hospital site and overall (n = 1,260): Categorical variables (continued)

		St James's Hospital (n = 638)		University Hospital Galway (n = 622)		Total (n) (n = 1,260)		p-value[a]
Exposure		**n**	**%**	**n**	**%**	**n**	**%**	
Country of birth	Ireland	512	80.3	471	75.7	983	78.0	**0.031**
	European Union/United Kingdom	54	8.5	81	13.0	135	10.7	
	Other country	72	11.3	70	11.3	142	11.3	
Ethnicity	White Irish	520	81.5	471	75.7	991	78.7	**<0.001**
	Any other White Background	61	9.6	83	13.3	144	11.4	
	Asian background	49	7.7	41	6.6	90	7.1	
	Other***	8	1.3	27	4.3	35	2.8	
BMI category (< 30 or 30 and over)	BMI 30 and over	136	21.3	112	18.0	248	19.7	0.079
	BMI less than 30	439	68.8	470	75.6	909	72.1	
	Missing	63	9.9	40	6.4	103	8.2	
Risk factor for severe SARS-CoV-2 infection	No	571	89.5	576	92.6	1147	91.0	0.067
	Yes	67	10.5	46	7.4	113	9.0	
Anti-Nucleocapsid antibody	Negative (n)	139	21.8	114	18.3	253	20.1	0.148
	Positive (n)	499	78.2	507	81.5	1006	79.8	
	Missing	0	0.0	1	0.2	1	0.1	
Anti-Spike antibody	Negative (s)	0	0.0	1	0.2	1	0.1	0.493
	Positive (s)	638	100.0	620	99.7	1258	99.8	
	Missing	0	0.0	1	0.2	1	0.1	
Vaccination status at enrolment	Unvaccinated	21	3.3	33	5.3	54	4.3	**0.007**
	Primary course only	32	5.0	25	4.0	57	4.5	
	Primary course and booster 1 only	341	53.4	378	60.8	719	57.1	
	Primary course, booster 1 and booster 2	244	38.2	186	29.9	430	34.1	
Last COVID-19 vaccination to enrolment	180 days or more	354	55.5	380	61.1	734	58.3	**0.016**
	Less than 180 days	263	41.2	209	33.6	472	37.5	
	Unvaccinated	21	3.3	33	5.3	54	4.2	
Self-reported SARS-CoV-2 infection	No infection reported	199	31.2	184	29.6	383	30.4	0.576
	Infection reported	439	68.8	438	70.4	877	69.6	

Contd.

Table 2. Descriptive characteristics of the study population by hospital site and overall (n = 1,260) Categorical variables (continued)

		St James's Hospital (n = 638)		University Hospital Galway (n = 622)		Total (n) (n = 1,260)		p-value[a]
Exposure		**n**	**%**	**n**	**%**	**n**	**%**	
Number of SARS-CoV-2 infections	No infection reported	199	31.2	184	29.6	383	30.4	0.792
	One infection only reported	338	53.0	335	53.9	673	53.4	
	Two infections only reported	88	13.8	94	15.1	182	14.4	
	Three infections only reported	12	1.9	9	1.4	21	1.7	
	Incomplete data	1	0.2	0	0.0	1	0.1	
Test type (self-reported)	Antigen test	122	19.1	160	25.7	282	22.4	**0.048**
	Laboratory PCR test	310	48.6	275	44.2	585	46.4	
	No previous infection reported	199	31.2	184	29.6	383	30.4	
	No test information provided	1	0.2	0	0.0	1	0.1	
	Test type unknown	6	0.9	3	0.5	9	0.7	
Infection category	Infection reported and anti-N positive	411	64.4	411	66.1	822	65.2	0.410
	No infection reported and anti-N negative	111	17.4	88	14.1	199	15.8	
	Infection reported but anti-N negative	28	4.4	26	4.2	54	4.3	
	No infection reported but anti-N positive	88	13.8	96	15.4	184	14.6	
	Incomplete data	0	0.0	1	0.2	1	0.1	
Time from last SARS-CoV-2 infection	180 days or more	268	42	283	45.5	551	43.7	0.418
	Less than 180 days	151	23.7	143	23	294	23.3	
	No prior infection reported	199	31.2	184	29.6	383	30.4	
	No valid infection date reported	20	3.1	12	1.9	32	2.5	

[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5)

*Reported as other (not specified) and also includes those who reported occupation as perfusionist, neurophysiologist, phlebotomist, pharmacist, physicist

**Clinical role included those who reported their occupation as Allied Health Professional, Dentist, Doctor, Healthcare Assistant, Midwife, Nurse, Neurophysiologist, Perfusionist, Technician, Phlebotomist, Pharmacist. All other occupations were classified as non-clinical.

***Including mixed background and African and other black background

Table 3. Comparison of those who self-reported prior SARS-CoV-2 infection and were anti-N antibody positive (n = 822) and those who self-reported prior SARS-CoV-2 infection and were anti-N antibody negative (n=54): Continuous variables

	Anti-N positive (n = 822)		Anti-N negative (n = 54)		Total (n = 876)		p-value[a]
Exposure	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Age (years)	41	32-49	45	39-51	42	32-50	**0.030**
Time from last vaccination to enrolment (days)	352	63-365	256	54-367	352	62-365	0.407
Time from last infection to enrolment (days)	235	139-308	281	201-325	237	140-311	**0.012**

[a]Mann-Whitney U test was used for comparison of medians for continuous variables.

Table 4. Comparison of those who self-reported prior SARS-CoV-2 infection and were anti-N antibody positive (n = 822) and those who self-reported prior SARS-CoV-2 infection and were anti-N antibody negative (n=54): Categorical variables

		Anti-N positive (n = 822)		Anti-N negative (n = 54)		Total (n = 876)		p-value[a]
		n	**%**	**n**	**%**	**n**	**%**	
Age category	18-29	156	19	6	11.1	162	18.5	0.077
(years)	30-39	206	25.1	8	14.8	214	24.4	
	40-49	256	31.1	23	42.6	279	31.8	
	50+	204	24.8	17	31.5	221	25.2	
Sex	Female	646	78.6	46	85.2	692	79	0.327
	Male	176	21.4	8	14.8	184	21	
Risk factor for severe SARS CoV-2 infection	No	760	92.5	42	77.8	802	91.6	**<0.001**
	Yes	62	7.5	12	22.2	74	8.4	
Time from last COVID-19 vaccination	≥180 days	529	64.4	29	53.7	558	63.7	0.123
	< 180 days	259	31.5	24	44.4	283	32.3	
	Unvaccinated	34	4.1	1	1.9	35	4	
Time from last SARS-CoV-2 infection	≥180 days	511	62.2	39	72.2	550	62.8	0.307
	< 180 days	281	34.2	13	24.1	294	33.6	
	None*	30	3.6	2	3.7	32	3.7	

[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5) and the Mann-Whitney U test was used for comparison of medians for continuous variables. *No valid infection date reported

3.1.6 Associations with anti-N antibody positivity at enrolment

Participants who were anti-N antibody positive at enrolment (n = 1,006) were younger compared to those who were anti-N antibody negative (n =253); median age 42 years, (IQR 32-50) compared to median age 47 years (IQR 39-54), (p-value <0.001) (Table 5). Differences in the proportion of those who were anti-N antibody positive were most marked in those in older age groups; 26% of those who were anti-N antibody positive were aged 50 years and older (n = 262), compared to 41% of those who were anti-N antibody negative (n = 105), (p-value <0.001). Positive anti-N antibody status was also associated with a shorter time interval since last self-reported infection among those who were anti-N antibody positive (235 days (IQR 139-308)) compared to those who were anti-N antibody negative (281 days (IQR 201-325) (p-value = 0.012). A higher proportion of those who were anti-N negative reported no previous infection compared to those who were anti-N antibody positive (78.7% vs. 18.3%, p-value <0.001) (Table 5).

A lower proportion of those who were anti-N antibody positive had received a second COVID-19 booster vaccination, compared to those who were anti-N antibody negative (29.9% vs 51.0%, p-value <0.001). Positive anti-N antibody status was associated with an increased time since last vaccination; 351 days among those who were anti-N antibody positive compared to 84 days among those who were anti-N antibody negative (p-value = 0.001) (Table 5).

Negative anti-N antibody status was associated with having a known acquisition risk factor for severe SARS-CoV-2 infection, a higher proportion of those who were anti-N antibody negative had an acquisition risk factor compared to those who were anti-N antibody positive (14.6% vs. 7.6%, p-value <0.001).

There were also differences in anti-N antibody status by occupational group (p-value = 0.037), country of birth (p-value = 0.024) and ethnicity (p-value <0.001) (Table 5). Among those who were anti-N antibody positive, a higher proportion were medical/dental, nursing/midwifery and healthcare assistant (HCA) staff compared to those who were anti-N negative. The greatest differences by ethnicity were among those who were anti-N antibody positive, a higher proportion reported an Asian background ethnicity compared to those who were anti-N antibody negative (8.3% vs. 2.8%, p-value <0.001) (Table 5).

Table 5. Descriptive characteristics of participants who were anti-N antibody positive (n = 1,006) vs. those who were anti-N antibody negative (n = 253) at enrolment: Continuous variables

	Anti-N positive (n = 1,006)		Anti-N negative (n= 253)		Total (n=1,259)		p-value[a]
Exposure	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Age (years)	42	32-50	47	39-54	43	33-51	**<0.001**
BMI	25.6	23.1-29.1	25.5	23-29.9	25.6	23.1-29.2	0.713
Time from last vaccination to enrolment (days)	351	61-364	84	54.25-363	344	59-364	**0.001**
Time from last infection to enrolment (days)	235	139-308.25	281	201.25-324.75	237	140-311	**0.012**

[a]Mann-Whitney U test was used for comparison of medians for continuous variables.

Table 6. Descriptive characteristics of participants who were anti-N antibody positive (n = 1,006) vs. those who were anti-N antibody negative (n = 253) at enrolment: Categorical variables

		Anti-N positive (n = 1,006)		Anti-N negative (n= 253)		Total (n=1,259)		p-value[a]
		n	**%**	**n**	**%**	**n**	**%**	
Age category (years)	18-29	187	18.6	24	9.5	211	16.8	**<0.001**
	30-39	244	24.3	42	16.6	286	22.7	
	40-49	313	31.1	82	32.4	395	31.4	
	50+	262	26.0	105	41.5	367	29.2	
Sex	Female	789	78.4	210	83.0	999	79.3	0.129
	Male	217	21.6	43	17.0	260	20.7	
Hospital site	St James's Hospital	499	49.6	139	54.9	638	50.7	0.148
	University Hospital Galway	507	50.4	114	45.1	621	49.3	
Occupation	Administration	171	17.0	54	21.3	225	17.9	**0.037**
	Allied Health Professional	118	11.7	44	17.4	162	12.9	
	General Support	49	4.9	12	4.7	61	4.8	
	Healthcare assistant	49	4.9	6	2.4	55	4.4	
	Laboratory	92	9.1	22	8.7	114	9.1	
	Medical/dental	157	15.6	31	12.3	188	14.9	
	Nursing/midwifery	332	33.0	70	27.7	402	31.9	
	Other role	38	3.8	14	5.5	52	4.1	
Clinical role	Clinical	668	66.4	152	60.1	820	65.1	0.070
	Non-clinical	338	33.6	101	39.9	439	34.9	

Contd.

Table 6. Descriptive characteristics of participants who were anti-N antibody positive (n = 1,006) vs. those who were anti-N antibody negative (n = 253) at enrolment: Continuous variables (continued)

		Anti-N positive (n = 1,006)		Anti-N negative (n= 253)		Total (n=1,259)		p-value[a]
Exposure		**n**	**%**	**n**	**%**	**n**	**%**	
Country of birth	Ireland	789	78.4	193	76.3	982	78.0	**0.024**
	European Union/United Kingdom	97	9.6	38	15.0	135	10.7	
	Other country	120	11.9	22	8.7	142	11.3	
Ethnicity	White Irish	798	79.3	192	75.9	990	78.6	**<0.001**
	Any other White Background	99	9.8	45	17.8	144	11.4	
	Asian background	83	8.3	7	2.8	90	7.1	
	Other*	26	2.6	9	3.6	35	2.8	
Body Mass Index (BMI) category	BMI 30 and over	190	18.9	58	22.9	248	19.7	0.143
	BMI less than 30	736	73.2	172	68.0	908	72.1	
	Missing	80	8.0	23	9.1	103	8.2	
Risk factor for severe SARS-CoV-2 infection	No	930	92.4	216	85.4	1146	91.0	**0.001**
	Yes	76	7.6	37	14.6	113	9.0	
Vaccination status at enrolment	Unvaccinated	46	4.6	8	3.2	54	4.3	**<0.001**
	Primary course only	53	5.3	4	1.6	57	4.5	
	Primary course and booster 1 only	606	60.2	112	44.3	718	57.0	
	Primary course, booster 1 and booster 2	301	29.9	129	51.0	430	34.2	
Time from last COVID-19 vaccination	180 days or more	623	61.9	110	43.5	733	58.2	**<0.001**
	Less than 180 days	337	33.5	135	53.4	472	37.5	
	Unvaccinated	46	4.6	8	3.2	54	4.3	
Prior SARS-CoV-2 infection	No infection reported	184	18.3	199	78.7	383	30.4	**<0.001**
	Infection reported	822	81.7	54	21.3	876	69.6	
Time from last SARS-CoV-2 infection	180 days or more	511	50.8	39	15.4	550	43.7	**<0.001**
	Less than 180 days	281	27.9	13	5.1	294	23.4	
	No prior infection reported	184	18.3	199	78.7	383	30.4	
	No valid infection date reported	30	3.0	2	0.8	32	2.5	

*(Including mixed background and African and other black background)

[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5) and the Mann-Whitney U test was used for comparison of medians for continuous variables.

3.1.7 Factors associated with anti-N antibody status at enrolment

Those aged 40-49 and those aged 50 years and older were less likely to be anti-N antibody positive compared to those aged 18-29 years (aOR 0.50, 95% 0.27, 0.91, p-value = 0.025 and aOR 0.41 95% CI 0.22, 0.74, p-value = 0.004, respectively) (Table 7). Additionally, those with an acquisition risk factor for SARS-CoV-2 infection were 60% less likely to be anti-N antibody positive compared to those without a risk factor (aOR 0.40, 95% CI 0.23, 0.70, p-value < 0.001).

Those with a history of self-reported infection had 16-fold higher unadjusted odds of being anti-N antibody positive (OR 16.46, 95% CI 11.79, 23.33, p-value <0.001), compared to those without a previous self-reported infection (aORs were not calculated for this covariate due to multicollinearity with the time since last SARS-CoV-2 infection variable). Examining time since last infection, in the adjusted logistic regression model, those with no prior SARS-CoV-2 infection reported at enrolment were 96% less likely to be anti-N antibody positive compared to those who self-reported a recent infection (within 180 days of enrolment) (aOR 0.04, 95% CI 0.02, 0.07, p-value <0.001).

Those with an Asian ethnicity had 7-fold higher odds of being anti-N antibody positive compared to those with a White Irish ethnicity (aOR 7.81, 95% CI 2.27, 28.26, p-value = 0.001). HCAs were the only occupational group with a higher adjusted odds of anti-N positivity, with a 3.5 fold higher odds of anti-N antibody positivity compared to those in administrative roles (aOR 3.49, 95% CI 1.23, 11.14, p-value = 0.024), while those in allied healthcare professional roles and those categorised as being in an 'other' role had a lower odds of anti-N positivity (Table 7).

At enrolment, those who had received a booster 2 vaccination were less likely to be anti-N antibody positive compared to those who were unvaccinated (OR 0.41, 95% CI 0.17, 0.84, p-value = 0.023). Additionally, those who were vaccinated 180 days or more prior to enrolment and those who were unvaccinated had a higher odds of being anti-N antibody positive compared to those vaccinated within 180 days of enrolment, however these difference did not reach statistical significance (aOR 1.27, 95% CI 0.87, 1.84, p-value = 0.214 and aOR 2.09, 95% CI 0.82, 5.99, p-value = 0.139). (Table 7).

3.1.8 Factors associated with anti-N antibody levels at enrolment

In the adjusted model, anti-N antibody titres decreased with each year of increasing age (p-value <0.001) and with having an acquisition risk factor for SARS-CoV-2 infection (p-value = 0.011). Anti-N antibody titres increased with increasing time from last COVID-19 vaccination (p-value <0.001) and having a history of previous SARS-CoV-2 infection (p-value <0.001) as well as having an Asian background ethnicity (p-value = 0.033). In the simple linear model, anti-N antibody titres were lower among those having received a second booster vaccination at enrolment (Table 8).

Table 7. Factors associated with anti-N antibody positivity

	Crude				Adjusted[b]			
	Crude OR	**Lower CI**	**Upper CI**	**p-value**	**Adjusted OR[b]**	**Lower CI[b]**	**UpperCI[b]**	**p-value[b]**
Age category (years)								
18-29	-	-	-	-	-	-	-	-
30-39	0.75	0.43	1.27	0.284	0.64	0.33	1.21	0.173
40-49	**0.49**	**0.29**	**0.79**	**0.004**	**0.50**	**0.27**	**0.91**	**0.025**
50+	**0.32**	**0.19**	**0.51**	**<0.001**	**0.41**	**0.22**	**0.74**	**0.004**
Sex								
Female	-	-	-	-	-	-	-	-
Male	1.34	0.94	1.95	0.109	1.57	0.98	2.56	0.063
Ethnicity								
White Irish	-	-	-	-	-	-	-	-
Any other White Background	**0.53**	**0.36**	**0.78**	**0.001**	0.69	0.39	1.22	0.199
Asian background	**2.85**	**1.39**	**6.88**	**0.009**	**7.81**	**2.27**	**28.62**	**0.001**
Other*	0.70	0.33	1.59	0.357	1.59	0.50	5.20	0.432
Country of birth								
Ireland	-	-	-	-	-	-	-	-
EU/UK	**0.62**	**0.42**	**0.95**	**0.023**	0.68	0.37	1.24	0.202
Other country	1.33	0.84	2.21	0.240	0.53	0.21	1.37	0.182
Risk factor for severe SARS-CoV-2 infection								
No	-	-	-	-	-	-	-	-
Yes	**0.48**	**0.32**	**0.73**	**0.001**	**0.40**	**0.23**	**0.70**	**0.001**
Occupation								
Administration	-	-	-	-	-	-	-	-
Allied healthcare professional	0.85	0.53	1.35	0.481	**0.50**	**0.27**	**0.92**	**0.026**
General support	1.29	0.66	2.7	0.478	0.89	0.36	2.23	0.792
Healthcare assistant	**2.58**	**1.12**	**7.01**	**0.039**	**3.49**	**1.23**	**11.14**	**0.024**
Laboratory	1.32	0.77	2.34	0.328	0.85	0.42	1.76	0.666
Medical/Dental	1.60	0.98	2.64	0.061	0.74	0.38	1.44	0.372
Nursing/midwifery	**1.50**	**1.00**	**2.23**	**0.048**	1.02	0.61	1.70	0.936
Other role**	0.86	0.44	1.75	0.659	**0.36**	**0.15**	**0.87**	**0.020**

Contd.

Table 7. Factors associated with anti-N antibody positivity (continued)

	Crude OR	Lower CI	Upper CI	p-value	Adjusted OR[b]	Lower CI[b]	UpperCI[b]	p-value[b]
Time since COVID-19 vaccination at enrolment								
Less than 180 days	-	-	-	-	-	-	-	-
180 days or more	**2.27**	**1.71**	**3.02**	**<0.001**	1.27	0.87	1.84	0.214
Unvaccinated at enrolment	**2.30**	**1.12**	**5.39**	**0.035**	2.09	0.82	5.88	0.139
Time since last self-reported SARS-CoV-2 infection at enrolment (days)								
Less than 180 days	-	-	-	-	-	-	-	-
180 days or more	0.61	0.31	1.12	0.128	0.62	0.31	1.17	0.154
No prior infection reported	**0.04**	**0.02**	**0.07**	**<0.001**	**0.04**	**0.02**	**0.07**	**<0.001**
Previous SARS-CoV-2 infection* **								
No previous infection reported	-	-	-	-	-	-	-	-
Previous infection reported	**16.46**	**11.79**	**23.33**	**<0.001**	-	-	-	-
COVID-19 vaccination status at enrolment* **								
Unvaccinated	-	-	-	-	-	-	-	-
Primary course	2.30	0.68	9.10	0.195	-	-	-	-
Primary course and booster 1	0.94	0.40	1.94	0.878	-	-	-	-
Primary course, booster 1 and booster 2	**0.41**	**0.17**	**0.84**	**0.023**	-	-	-	-

[b]Multivariable logistic regression model adjusted for age category, sex, ethnicity, country of birth, acquisition risk, occupation, time since infection at enrolment, time since vaccination at enrolment

*Including mixed background and African and other black background

**Reported as other (not specified) and also includes those who reported occupation as perfusionist, neurophysiologist, phlebotomist, pharmacist, physicist

*** Excluded from multivariable analysis due to multicollinearity

For the logistic multivariable model, n = 1227, Nagelkerke R^2 = 43.7% , Hosmer Lemeshow test p-value = 0.6325

Table 8. Factors associated with anti-N antibody titre levels

	Crude				Adjusted[a]			
Exposure	**Estimate**	**Lower CI**	**Upper CI**	**p-value**	**Estimate[a]**	**Lower CI[a]**	**Upper CI[a]**	**p-value[a]**
Age (years)	**-0.0485**	-0.0605	-0.0366	**<0.001**	**-0.0263**	-0.0373	-0.0153	**<0.001**
Time from last COVID-19 vaccination to enrolment (days)	**0.0027**	0.0019	0.0035	**<0.001**	**0.0014**	0.0007	0.0021	**<0.001**
Time from last SARS-CoV-2 infection to enrolment (days)	-0.0004	-0.0010	0.0002	0.218	-	-	-	-
Sex (Ref: Female)								
Male	0.1856	-0.1575	0.5287	0.289	0.2465	-0.0522	0.5452	0.106
Risk status (Ref: No risk)								
Yes	**-0.8157**	-1.2997	-0.33167	**0.001**	**-0.5443**	-0.9654	-0.1231	**0.011**
Ethnicity (Ref: White Irish)								
Any other white background	-0.5577	-0.9946	-0.1209	**0.012**	-0.1629	-0.6015	0.2758	0.466
Asian background	**0.8792**	0.3399	1.4185	**0.001**	**0.8330**	0.0679	1.5982	**0.033**
Other*	0.0195	-0.8229	0.8619	0.964	0.3864	-0.5364	1.3093	0.412
Country of birth (Ref: Ireland)								
European Union/United Kingdom	-0.4534	-0.9040	-0.0028	**0.049**	-0.3728	-0.8243	0.0787	0.105
Other	0.5670	0.1263	1.0078	**0.012**	0.2118	-0.4489	0.8724	0.530
Previous SARS-CoV2 infection (Ref: No)								
Yes	**2.6614**	2.3977	2.9250	**<0.001**	**2.5539**	2.2867	2.8211	**<0.001**
COVID-19 vaccination status (Ref: Unvaccinated)**								
Primary course	0.1514	-0.7615	1.0643	0.745	-	-	-	-
Primary course and booster 1	-0.1399	-0.8183	0.5384	0.686	-	-	-	-
Primary course, booster 1 and booster 2	**-1.2946**	-1.9886	-0.6005	**<0.001**	-	-	-	-

[a]Multivariable linear regression model adjusted for age, sex, time from vaccination to enrolment, acquisition risk factor, ethnicity, country of birth, previous infection.

*Including mixed background and African and other black background

** Excluded from multivariable analysis due to multicollinearity

For the linear multivariable model total n = 1,207, adjusted R^2 = 29.2% p-value < 0.001

3.1.9 Incident infections

During the study period, 21.7% (n = 274) of participants reported at least one incident infection. Among those who reported an incident infection (n = 274), 86.5% (n = 237) had one incident infection, 12.8% (n = 35) reported two incident infections and 0.7% (n = 2) reported having three or more incident infections. The highest number of incident infections were reported in Week 51 2022 with smaller peaks of infection observed in week 11 2023 and week 32 2023 (Figure 2, Figure 3 and Figure 4).

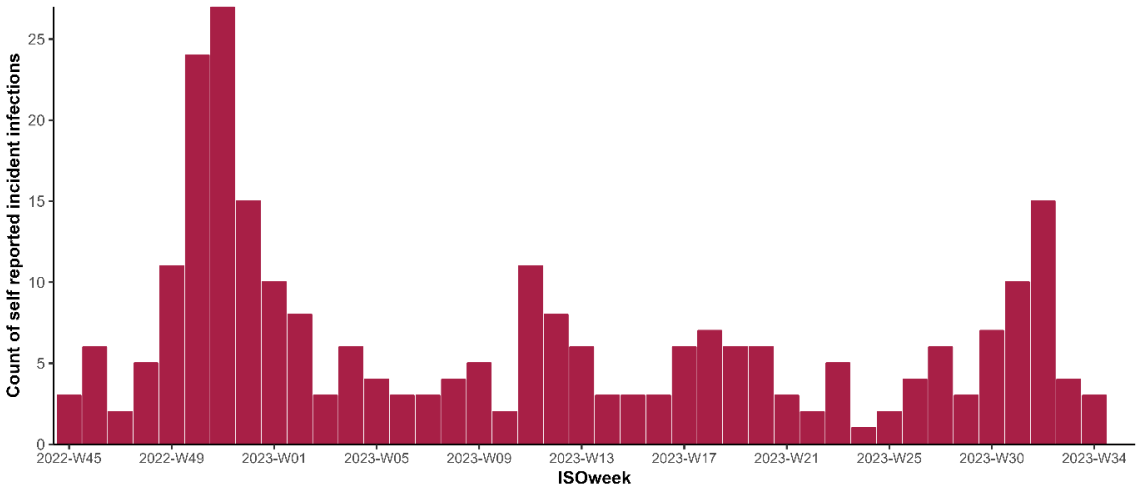


Figure 2. Number of self-reported incident infection by week of symptom onset during the study period (ISO week 45 2022 to ISO week 34 2023) (n = 274)

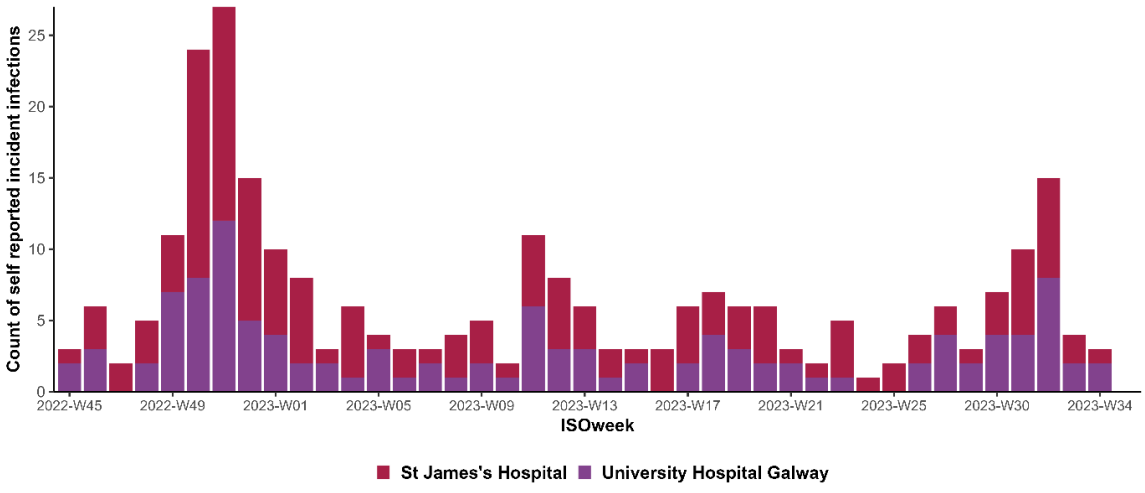


Figure 3. Number of self-reported incident infection by week of symptom onset and hospital site during the study period (ISO week 45 2022 to ISO week 34 2023) (n = 274)

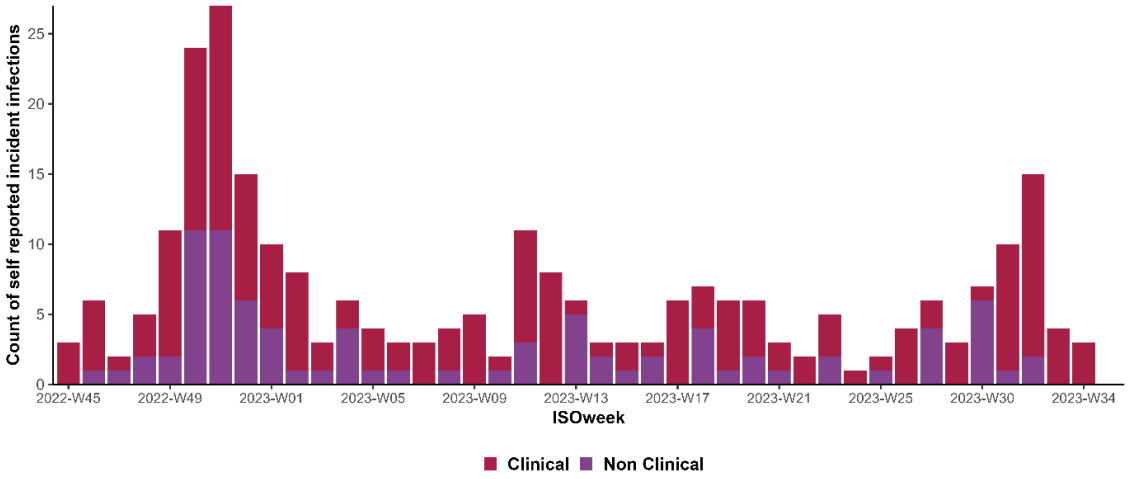


Figure 4. Number of self-reported incident infection by week of onset of symptoms and clinical and non-clinical role during the study period (ISO week 45 2022 to ISO week 34 2023) (n= 274)

Severity of incident infections

There were no differences in the severity of incident infections by hospital site (Table 9). Among all participants who self-reported a SARS-CoV-2 incident infection during the study period, 38.3% reported a symptomatic infection and the median duration of symptoms was 7 (IQR 4-10) days. For all infections, symptomatic and asymptomatic, the median duration of days in bed with an incident infection was 3 (IQR 0-5) days and the median number of days off work was 5 (IQR 3-7) days (Figure 5 and Figure 6). There were no hospital admissions among any participants during the study period and no participant required supplemental oxygen support; 12.4% (34/274) attended a GP on at least one occasion, while 0.4% (1/274) attended an ED. The diagnosis of incident infection was made by antigen test in 83.9% (230/274); laboratory PCR testing was used to diagnose incident infection in 14.6% (40/274). The median time from last vaccination to incident infection was 308 (IQR 126-428) days and the median time from last infection was 391 (IQR 274-506) days (Table 9).

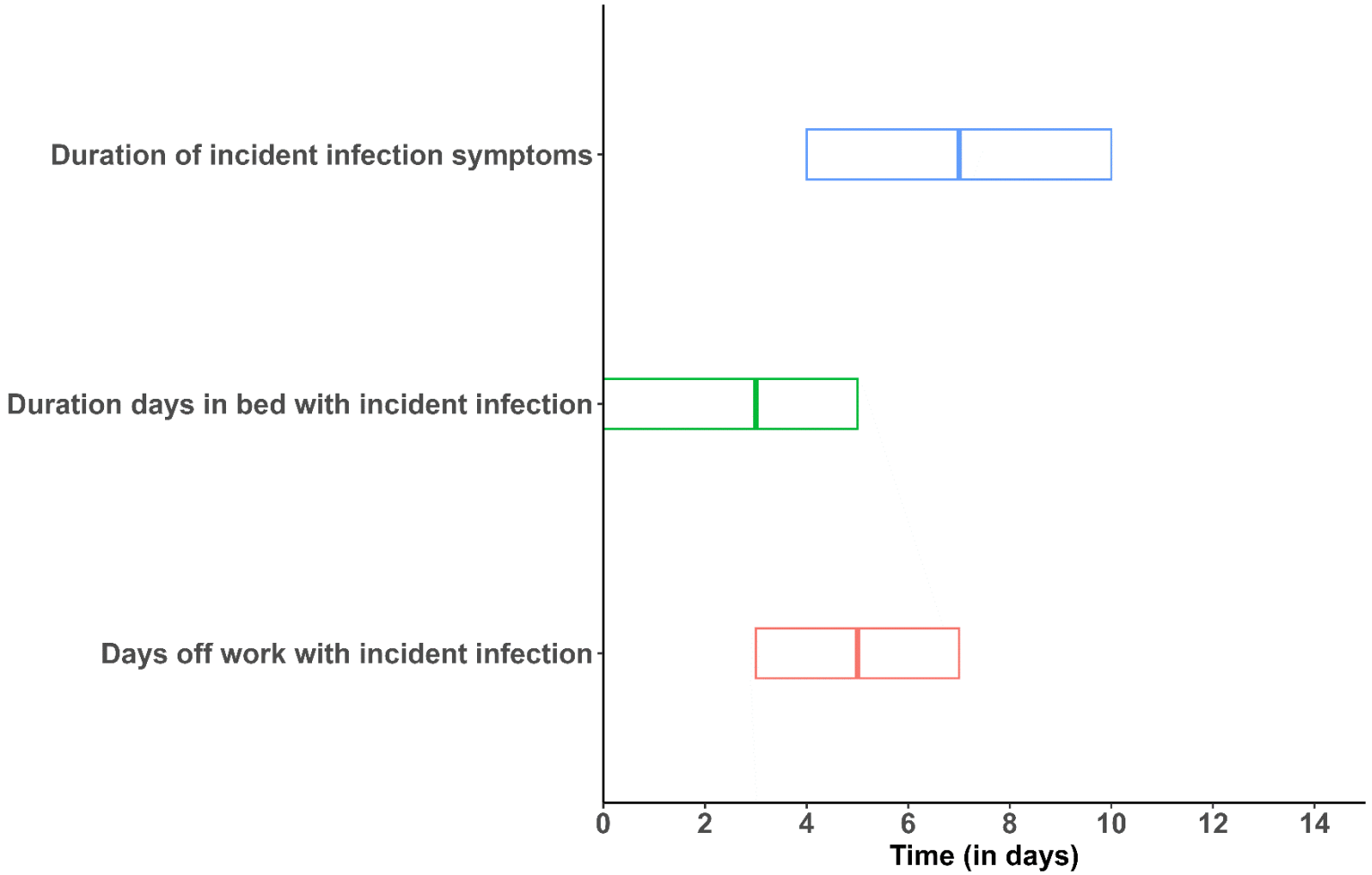


Figure 5. Median (IQR, range) for duration of symptoms with a SARS-CoV-2 incident infection (n = 274)

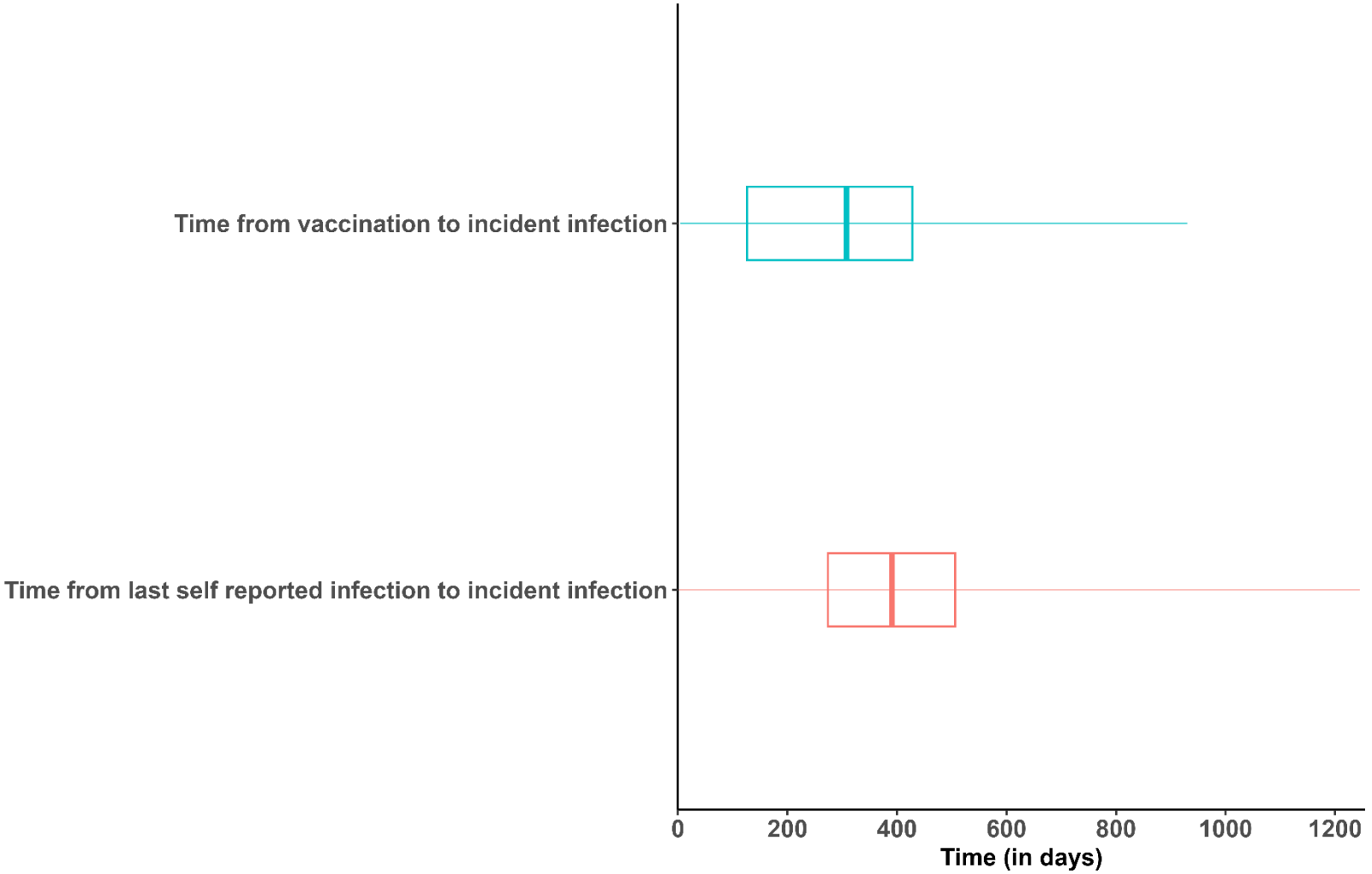


Figure 6. Median (IQR, range) for time since last COVID-19 vaccination and last SARS-CoV-2 infection for those with a SARS-CoV-2 incident infection (n = 258)*

***Only those who reported a valid date of incident infection include**

Table 9. Severity of self-reported incident SARS-CoV-2 infection by clinical site and overall (n = 274): Continuous variables

	St James's Hospital (n = 151)		University Hospital Galway (n = 123)		Total (n = 274)		p-value[a]
Exposure	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Duration of incident infection symptoms (days)	7	5-9	6	4-16	7	4-10	0.853
Duration in bed with incident infection (days)	3	1-5	2	0-4	3	0-5	0.117
Duration of hospitalisation with incident infection (days)	0	0	0	0	0	0	-
Duration off work with incident infection	5	3-7	5	3-6	5	3-7	0.568
Time from last COVID-19 vaccination (days)	279	119-408	355	151-461	308	126-428	0.101
Time from last self-reported SARS-CoV-2 infection (days)	404	275-537	359	273-490	391	274-506	0.138

Table 10. Severity of self-reported incident SARS-CoV-2 infection by clinical site and overall (n = 274): Categorical variables

		St James's Hospital (n = 151)		University Hospital Galway (n = 123)		Total (n = 274)		p-value[a]
Exposure		**n**	**%**	**n**	**%**	**n**	**%**	
Symptomatic incident infection	No symptoms reported	92	60.9	74	60.2	166	60.6	0.747
	No symptom data provided	1	0.7	2	1.6	3	1.1	-
	Symptomatic	58	38.4	47	38.2	105	38.3	-
Attended General Practitioner (GP)	Attended GP once	18	11.9	13	10.6	31	11.3	0.221
	Attended GP twice	0	0	3	2.4	3	1.1	-
	Did not state if attended GP	132	87.4	105	85.4	237	86.5	-
	No GP questionnaire data completed	1	0.7	2	1.6	3	1.1	-
Attended Emergency Department (ED)	Attended ED once	1	0.7	0	0	1	0.4	0.499
	Did not state if attended ED	149	98.7	121	98.4	270	98.5	-
	No ED questionnaire data completed	1	0.7	2	1.6	3	1.1	-
Test type	Antigen test	129	85.4	101	82.1	230	83.9	0.593
	Laboratory PCR test	20	13.2	20	16.3	40	14.6	-
	No test data provided	1	0.7	2	1.6	3	1.1	-
	Test type unknown	1	0.7	0	0	1	0.4	-

[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5) and the Mann-Whitney U test was used for comparison of medians for continuous variables.

Of all participants, 258 self-reported an incident infection with a plausible date of infection (as defined in Section 2.6.1) (Table 11). Among those who reported an incident SARS-CoV-2 infection, a higher proportion had an acquisition risk factor compared to those who did not report an incident infection (13.2% vs. 7.9%, p-value = 0.014).

A lower proportion of those who reported an incident infection during the study period, were anti-N antibody positive (62.0% vs. 84.3%, p-value <0.001) and the median anti-N antibody titre at enrolment was lower among those who reported an incident infection during the study period compared to those who did not (3.9 U/mL vs. 15.7 U/mL, p-value <0.001).

Additionally, a lower proportion of those who reported an incident SARS-CoV-2 infection had a prior infection reported at enrolment (62.0% vs. 71.3%, p-value = 0.006) and had reported a prior SARS-CoV-2 infection within 180 days of enrolment (14.3% vs. 25.9%, p-value <0.001) compared to those who did not report an incident infection. There were no differences by age, sex, hospital site, occupation, vaccination status at enrolment or time from last vaccination to enrolment (Table 11).

There were also no differences in the characteristics of those who reported a symptomatic incident infection compared to those who did not report symptoms or in the factors associated with reporting a symptomatic incident infection (Appendix E).

Those who had reported a prior SARS-CoV-2 infection at enrolment had 34% (OR 0.66, 95% CI 0.49, 0.88, p-value = 0.005) lower odds of having an incident infection compared to those with no prior infection. However, those who were 180 days or more after their self-reported infection at enrolment had an 86% (aOR 1.86, 95% CI 1.24, 2.84, p-value = 0.003) increased odds of incident infection compared to those who reported an incident infection within 180 days of enrolment. Those who had an underlying risk factor for severe SARS-CoV-2 infection had a 67% (OR 1.67, 95% CI 1.04, 2.65, p-value = 0.031) higher odds of reporting an incident infection. Those who were anti-N antibody positive had a 73% (aOR 0.27, 95% CI 0.18, 0.40, p-value <0.001) lower odds of an incident SARS-CoV-2 infection during the study period compared with those who were anti-N antibody negative (Table 13). Comparison between log binomial and logistic regression models showed that the direction of the association was the same for all measures of association (RRs and ORs) with similar magnitude and minimal differences in the logistic and log-binomial models (Appendix F and G).

Table 11. Characteristics of participants who reported an incident infection (n = 258) * compared to those who did not report an incident infection (n = 909): Continuous variables

	Incident infection (n = 258)		No incident infection (n = 909)		Total (n = 1,167)		p-value[a]
Exposure	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Age (years)	44	35-52	43	33-51	43	33-51	0.371
BMI	25.6	23.2-29.1	25.6	23.1-29.2	25.6	23.1-29.2	0.946
Anti-Nucleocapsid antibody titre at enrolment (U/mL)	3.9	0.1-22.5	15.7	3.2-72.0	12.9	2.2-65.0	**<0.001**

[a] Mann-Whitney U test was used for comparison of medians for continuous variables.

Table 12. Characteristics of participants who reported an incident infection (n = 258) * compared to those who did not report an incident infection (n = 909): Categorical variables

		Incident infection (n = 258)		No incident infection (n = 909)		Total (n = 1,167)		p-value
Exposure		**n**	**%**	**n**	**%**	**n**	**%**	
Age category	18-29	35	13.6	146	16.1	181	15.5	0.504
	30-39	64	24.8	198	21.8	262	22.5	
	40-49	77	29.8	295	32.5	372	31.9	
	50+	82	31.8	270	29.7	352	30.2	
Sex	Female	216	83.7	717	78.9	933	79.9	0.104
	Male	42	16.3	192	21.1	234	20.1	
Hospital site	St James's Hospital	145	56.2	451	49.6	596	51.1	0.072
	University Hospital Galway	113	43.8	458	50.4	571	48.9	
Occupation	Administration	48	18.6	162	17.8	210	18	0.227
	Allied Health Professional	42	16.3	104	11.4	146	12.5	
	General Support	11	4.3	44	4.8	55	4.7	
	Healthcare assistant	7	2.7	41	4.5	48	4.1	
	Laboratory	21	8.1	87	9.6	108	9.3	
	Medical/dental	30	11.6	141	15.5	171	14.7	
	Nursing/midwifery	91	35.3	289	31.8	380	32.6	
	Other role	8	3.1	41	4.5	49	4.2	
Clinical role	Clinical	173	67.1	584	64.2	757	64.9	0.447
	Non-clinical	85	32.9	325	35.8	410	35.1	

Contd.

Table 12. Characteristics of participants who reported an incident infection (n = 258) * compared to those who did not report an incident infection (n = 909): Categorical variables (continued)

		Incident infection (n = 258)		No incident infection (n = 909)		Total (n = 1,167)		p-value[a]
Exposure		**n**	**%**	**n**	**%**	**n**	**%**	
Country of birth	Ireland	214	82.9	697	76.7	911	78.1	0.097
	European Union/United Kingdom	23	8.9	106	11.7	129	11.1	
	Other	21	8.1	106	11.7	127	10.9	
Ethnicity	White Irish	217	84.1	709	78.0	926	79.3	**0.027**
	Any other White Background	24	9.3	108	11.9	132	11.3	
	Asian background	16	6.2	64	7.0	80	6.9	
	Other**	1	0.4	28	3.1	29	2.5	
BMI category	BMI 30 and over	49	19	181	19.9	230	19.7	0.858
	BMI less than 30	187	72.5	661	72.7	848	72.7	
	Missing	22	8.5	67	7.4	89	7.6	
Risk factor for severe SARS-CoV-2 infection	No	224	86.8	837	92.1	1061	90.9	**0.014**
	Yes	34	13.2	72	7.9	106	9.1	
COVID-19 vaccination status	Unvaccinated	6	2.3	43	4.7	49	4.2	0.364
	Primary course only	11	4.3	41	4.5	52	4.5	
	Primary course and booster 1	144	55.8	508	55.9	652	55.9	
	Primary course, booster 1 and booster 2	97	37.6	317	34.9	414	35.5	
Prior SARS-CoV-2 infection	No infection reported	98	38.0	261	28.7	359	30.8	**0.006**
	Infection reported	160	62.0	648	71.3	808	69.2	
Time from last COVID-19 vaccination	180 days or more	152	58.9	515	56.7	667	57.2	0.229
	Less than 180 days	100	38.8	351	38.6	451	38.6	
	Unvaccinated	6	2.3	43	4.7	49	4.2	
Time from last SARS-CoV-2 infection	180 days or more	114	44.2	394	43.3	508	43.5	**<0.001**
	Less than 180 days	37	14.3	235	25.9	272	23.3	
	No prior infection reported	98	38.0	261	28.7	359	30.8	
	No valid infection date reported	9	3.5	19	2.1	28	2.4	
Anti-Nucleocapsid antibody category	Negative (n)	97	37.6	143	15.7	240	20.6	**<0.001**
	Positive (n)	160	62.0	766	84.3	926	79.3	
	Missing	1	0.4	0	0	1	0.1	

* This includes only those with a plausible date of incident infection; defined as an incident infection reported as occurring 30 days after the last self-reported incident infection.**Including mixed background and African and other black background ethnicity[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5)

Table 13. Factors associated with an incident SARS-CoV-2 infection

	Crude				Adjusted*			
Exposure	**OR[a]**	**Lower CI**	**Upper CI**	**p-value**	**OR***	**Lower CI***	**Upper CI***	**p-value***
Age category								
18-29	-	-	-	-	-	-	-	-
30-39	1.35	0.85	2.16	0.207	1.34	0.83	2.20	0.240
40-49	1.09	0.70	1.72	0.709	0.95	0.60	1.53	0.827
50+	1.27	0.82	1.99	0.296	0.99	0.62	1.60	0.953
Sex								
Female	-	-	-	-	-	-	-	-
Male	0.73	0.50	1.04	0.087	0.73	0.49	1.07	0.110
Ethnicity								
White Irish	-	-	-	-	-	-	-	-
Any other White Background	0.73	0.45	1.14	0.180	**0.60**	**0.36**	**0.97**	**0.042**
Other**	**0.55**	**0.30**	**0.94**	**0.040**	0.59	0.32	1.04	0.082
Risk factor for severe SARS-CoV-2 infection								
No	-	-	-	-	-	-	-	-
Yes	**1.76**	**1.13**	**2.7**	**0.010**	**1.67**	**1.04**	**2.65**	**0.031**
Time since last self-reported SARS-CoV-2 infection at enrolment								
Less than 180 days	-	-	-	-	-	-	-	-
180 days or more	**1.84**	**1.24**	**2.78**	**0.003**	**1.86**	**1.24**	**2.84**	**0.003**
No self-reported infection	**2.38**	**1.58**	**3.66**	**<0.001**	1.28	0.78	2.10	0.327
Anti-Nucleocapsid antibody category								
Negative (n)	-	-	-	-	-	-	-	-
Positive (n)	**0.31**	**0.23**	**0.42**	**<0.001**	**0.27**	**0.18**	**0.40**	**<0.001**
Anti-Nucleocapsid antibody titre	**0.99**	**0.99**	**0.99**	**<0.001**	-	-	-	-
Prior SARS-CoV-2 infection								
No prior infection	-	-	-	-	-	-	-	-
Prior infection	**0.66**	**0.49**	**0.88**	**0.005**	-	-	-	-

[a]Odds Ratio

*Adjusted for age category, sex, ethnicity, risk factor for severe SARS-CoV-2 infection, time since last infection, anti-N antibody category

**Including mixed background and African and other black background ethnicity

For the multivariable model total n = 1138, Naglekerke R^2 = 10.6%, Hosmer Lemeshow test p-value = 0.5963

4 Discussion

4.1 Serological findings

Similar to other PRECISE studies, the hospital HCWs who participated in PRECISE 5 had a high rate of prior SARS-CoV-2 infection and COVID-19 vaccination.[1,2,7] Overall, 80% of HCWs who participated in this study had serological evidence of SARS-CoV-2 infection at enrolment. This aligns with national seroprevalence data which is estimated to be 78% from primary care sources and 86% among blood donors.[8] This suggests that seroprevalence among participants in this study is similar to seroprevalence in the general population. Previous PRECISE studies reported a higher risk of SARS-CoV-2 seropositivity among hospital HCWs.[2,7]

In 81% of hospital HCWs, their self-reported infection status aligned with their anti-N antibody status at enrolment, suggesting that self-reported infection status was accurate among the majority of study participants. Among those whose status did not align, 15% had no prior SARS-CoV-2 infection reported but were anti-N antibody positive, suggesting undiagnosed infection. However, the remaining 4.2% had reported prior infection but were anti-N antibody negative. This status was associated with increasing time from last infection, increasing age and having an acquisition risk factor for severe SARS-CoV-2 infection, suggesting that anti-N antibody positivity may have waned over time. Additionally, among all study participants, negative anti-N antibody status at enrolment was also associated with having a risk factor for severe SARS-CoV-2 infection and older age, suggesting that anti-N positivity may wane particularly in these subgroups. In this study, increasing anti-N titres were associated with increasing time from last COVID-19 vaccination, this may suggest that infection risk and subsequent associated anti-N antibody positivity increases by time since vaccination.

There were differences observed in seropositivity by ethnicity and occupation. Those with an Asian background ethnicity and those whose occupation was reported as a HCA were more likely to be anti-N antibody positive at enrolment, suggesting recent prior SARS-CoV-2 infection. These findings align with risk factors for SARS-CoV-2 seropositivity reported in previous PRECISE studies.[2,7]

At enrolment in PRECISE 5, participants in SJH were more likely to have received a second COVID-19 vaccine booster, likely reflecting the on-site rollout of the booster programme in SJH prior to the commencement of the study. A higher proportion of participants who were anti-N antibody negative at enrolment had received their second booster vaccine, suggesting that receiving the second booster vaccine may have increased immunity and provided protection from recent SARS-CoV-2 infection.

4.2 Incident infection

In this study, incident infections continued to occur in hospital HCWs despite high vaccination coverage; 96% had received at least a primary vaccination course at enrolment. Overall, 22% of HCWs reported an incident infection during the study time period, 98% of whom were vaccinated and 39% vaccinated within 180 days of enrolment. This finding is consistent with the fact that COVID-19 vaccines provide limited protection against acquisition of infection.[9-12] However, vaccination provides protection against serious illness,[9,12,13] and in this highly vaccinated hospital HCW cohort, this protection was evident by the fact that there were no hospitalisations associated with SARS-CoV-2 infection reported. This finding is important to inform public health communication in relation to the benefits of COVID-19 vaccination at preventing severe illness.

Having at least one underlying clinical risk factor for acquiring severe SARS-CoV-2 infection was associated with higher likelihood of incident infection, supporting the recommendations prioritising booster vaccination among those in risk groups to boost immunity and to provide sustained protection against serious illness.[14]

Additionally, a self-reported SARS-CoV-2 incident infection was associated with increased time since last infection. This finding aligns with previous studies that have reported that while a history of prior SARS-CoV-2 infection is associated with a lower risk of re-infection,[15] this protection decreases over time.[12,16,17] Incident infections were also associated with lower anti-N antibody titres and anti-N antibody negative status. However, 62% of incident infections in this study were reported among those who were anti-N antibody positive. This suggests that seropositivity among hospital HCWs should not be considered a marker of immunity from re-infection. Internationally, anti-S antibody levels have been shown to provide protection against re-infection.[4] However, an assessment of the association between anti-S levels and incident infections was not possible in this study, as the upper limit of quantification for the commercial Roche Elecsys-S Anti-SARS-CoV-2 assay prevented an assessment of titre levels of anti-S antibodies over time with the median equalling the upper limit of 250 U/mL.

The methods of SARS-CoV-2 diagnosis among hospital HCW were different at enrolment compared to the diagnosis of incident infections during the study period. The majority of incident infections were diagnosed with antigen tests compared to infections prior to enrolment where the majority were diagnosed using laboratory PCR testing. National COVID-19 testing policies were stable during winter 2022/2023 but changed to a clinically driven model with restriction of widespread PCR testing in April 2023.[18] This change in testing patterns among hospital HCWs likely reflects this change in

national testing policy and the associated wider use of antigen testing among hospital HCWs for SARS-CoV-2 diagnosis.

While there were no hospitalisations with SARS-CoV-2 reported during the study period, 38% of HCWs reported a symptomatic infection resulting in a median duration of seven days absent from work. All cases (those who reported symptoms and those who did not) reported a median of five days absence from work. The pattern of incident infections reported in this study among hospital HCWs reflected the national epidemiology of SARS-CoV-2 infection during the study period (Appendix H) with a peak of infection in December 2023.[19] This finding suggests that patterns of infection among hospital HCWs likely reflect the pattern of SARS-CoV-2 infection nationally, and that cases and associated absences among hospital HCWs may occur during the same time period that infection and hospitalisation rates are increased nationally,[19] likely impacting healthcare resilience.

4.3 Public health implications

SARS-CoV-2 infections continue to impact the hospital HCW workforce, and the findings of this study add to the understanding of the pattern and duration of this impact and are therefore important to inform healthcare service planning. It is likely that illness and associated absence among hospital HCWs will occur during surge periods of infection in the population and therefore there is a need for surge planning to ensure that there is capacity to maintain the provision of scheduled and unscheduled care. This is particularly important for winter planning when peaks of SARS-CoV-2 infection may coincide with other respiratory virus surges e.g., influenza and respiratory syncytial virus (RSV).

Additionally, the high proportion of asymptomatic incident infections (61%) reported in this study (and previous PRECISE studies), and the associated risk of asymptomatic transmission of SARS-CoV-2 in healthcare settings, highlight the importance of vaccination of both HCW and those in vulnerable groups to reduce the risk of infection and transmission in healthcare settings and to provide sustained protection against severe disease. This is particularly important among those who are vulnerable to severe SARS-CoV-2 infection, e.g., those in older age groups or with underlying clinical conditions associated with severe illness.[14]

The occurrence of incident infections despite high vaccination coverage among hospital HCWs suggest that vaccination alone will not prevent infection and associated transmission in healthcare settings. In particular, the high levels of asymptomatic SARS-CoV-2 infection reported in this study suggest that infection may be unrecognised which may increase the risk of transmission. Increased targeted SARS-CoV-2 testing among hospital HCWs e.g., during surge periods of infection, may be beneficial to detect asymptomatic SARS-CoV-2 infection to inform action to minimise risk of

transmission. Additionally, particularly for those with mild symptoms, PCR testing may be more sensitive than antigen tests which may be beneficial in high-risk clinical settings (or during outbreaks) to improve diagnostic yield.[20,21] Other recommended strategies to reduce transmission are also required, including, prompt detection of infection and implementation of infection prevention and control (IPC) precautions including appropriate use of personal protective equipment (PPE) and maximising ventilation where possible.[22] Additionally, HCWs should not attend work if they have symptoms of COVID-19 or any acute respiratory infection, even after vaccination.[22]

While in this study, there was no association between an incident SARS-CoV-2 infection and time since last COVID-19 vaccination, there was some evidence of protection afforded by vaccination. There was an absence of severe illness in this highly vaccinated cohort and additionally anti-N antibody titre levels increased by time since last COVID-19 vaccination which may suggest more recent infection in those with a longer time since last vaccination. Therefore, the findings of this study along with the known waning of the immunity afforded by vaccination over time,[23] and the limited protection from infection afforded by prior SARS-CoV-2 infection,[16,24] the high exposure risk to SARS-CoV-2 among HCWs and the impact of SARS-CoV-2 infections on the hospital HCW workforce, support the continued recommendation for regular targeted booster campaigns for HCWs.

The objectives of the national COVID-19 vaccination programme include protecting healthcare capacity.[14] While the optimal timing of booster vaccination doses for HCW and within the population remains the subject of ongoing discussion and research,[25,26] ensuring maximal protection during likely surge periods of respiratory infection should continue to be a priority for vaccination policy makers and for those involved in winter planning e.g., a continued autumn booster campaign for HCWs to provide optimal protection during the expected respiratory virus season.

Further work will be required to maintain high vaccination coverage among HCWs. Vaccination campaigns should be particularly targeted by age and the presence of underlying risk factors for severe infection among the hospital HCW population as well as the general population. Among HCWs, targeting and encouraging vaccination among those in older age groups, with higher risk of infection or associated complications and those with increased time since last infection and/or vaccination (180 days or more) may be beneficial. Strengthening surveillance of infection among HCWs would allow for identification of HCWs with increased time since last infection.

While overall vaccination uptake among HCWs was high in this study, only 34% had received a booster 2 vaccine at enrolment in November and December 2022. Rollout of booster 2 vaccinations for HCWs began on 7th September 2022 (Personal correspondence, National Immunisation Office).

In the 2023/2024 season as of 11/04/2024, COVID-19 booster vaccination uptake rate among HCWs was suboptimal (19%, provisional data from HPSC). Nationally and internationally, vaccine fatigue is emerging as an important public health issue impacting COVID-19 vaccination uptake.[27] While further understanding and investigation of the factors associated with vaccine fatigue is required, communication of the findings of this study in relation to the benefits of vaccination at preventing severe illness and the rationale for targeted vaccination programmes, may be useful to inform the development of vaccination information materials to counter vaccine fatigue among the hospital HCW population. This could be further supported by vaccination education programmes for HCWs, clear communication about the benefits of vaccination, supporting ongoing convenient access to vaccinations (e.g., on site administration) as well as engagement of peer vaccinators and vaccine champions to improve and maintain vaccination uptake among HCWs.[27-31]

4.4 Limitations

There was a low participation rate of 13% in PRECISE 5. This may have introduced bias and may limit the generalisability of the findings to the hospital HCW population. Participation in the monthly questionnaires was also low with only 15% (183/1260) participants completing all monthly questionnaires over the study period. Therefore, the number and proportion of incident infections may have been over or underestimated. Participation in the summer months (June, July and August) was lower compared to other months. This finding could inform the timing of data collection among HCWs for future PRECISE studies.

The self-reported survey data reported in this study might be unreliable. Specifically, data on self-reported incident infection including date of incident infection may not be accurate and additionally, asymptomatic infections may not have been recognised by participants. Self-reported risk factor status and self-reported prior infection at enrolment might also be unreliable. However, verification of self-reported infection with serology indicated that the majority of participants self-reported infection status aligned with their serological status.

While questions on underlying clinical risk factors for severe SARS-CoV-2 infection were included in the study questionnaire data on all risk factors for severe infection were not collected. Therefore, the proportion of participants with an underlying clinical risk factor may have been underestimated.

An assessment of titre levels of anti-S antibodies over time in this study was not possible due to the upper limit of quantification for the commercial Roche Elecsys-S Anti-SARS-CoV-2 assay.

5 Conclusion

This study has added to the understanding of the evolving epidemiology of COVID-19 infection in HCWs and shown a high seroprevalence and ongoing risk of incident SARS-CoV-2 infection among hospital HCWs in Ireland, despite high rates of both vaccination, prior infection and seropositivity. The findings have indicated that the pattern of hospital HCW infection follows national trends and have shown the absence of severe illness in a highly vaccinated hospital HCW cohort, emphasising the benefits of COVID-19 vaccination. However, ongoing incident infections among hospital HCWs continue to impact healthcare service provision and are an important consideration for healthcare service planning, particularly for winter planning, in anticipation of likely surges in respiratory infections. There has been a shift in diagnostics used to diagnose infection among HCWs, from PCR to antigen testing, reflecting changes in national testing policies. The high proportion of asymptomatic incident infections suggest that there may be a benefit to increased testing among HCWs, particularly during surge periods of infection. Additionally, given high rates of SARS-CoV-2 infection despite vaccination, robust infection prevention and control measures continue to be required to reduce exposure risk and prevent transmission in healthcare settings.

Ongoing targeted vaccination campaigns for HCWs, particularly for those in older age groups and with underlying risk factors and increased time since last SARS-CoV-2 infection and/vaccination (180 days or more) are supported by the findings of this study. Nationally and internationally, as vaccine fatigue emerges as an important public health issue, supporting HCW vaccine decision making with vaccination information materials and ease of access to vaccinations will be important to improve and maintain COVID-19 vaccination uptake among HCWs.

6 Recommendations

The following are recommendations arising from the findings of this study:

1. The findings of this study support continued targeted vaccination programmes for HCWs, particularly those in older age groups (40 years and older), those with underlying risk factors for severe SARS-CoV-2 infection and those with increased time since last SARS-CoV-2 infection and/or vaccination (180 days or more). The findings should be shared with key stakeholders involved in the COVID-19 vaccination programme e.g., Chief Clinical Officer, Chief Medical Officer, the National Immunisation Advisory Committee, and the National Immunisation Office. The findings should also be communicated to occupational health departments in hospitals and others involved in the rollout of vaccination programmes among HCWs.

2. In the context of vaccine fatigue and lower than expected uptake of COVID-19 vaccines among HCW in the 2023/2024 season, the findings of this study should inform the development of targeted vaccination communication and education materials for all HCWs to emphasise the benefits of vaccination at preventing severe illness among hospital HCWs as well as the need to protect vulnerable patients and the healthcare service.

3. COVID-19 vaccination programmes should be particularly targeted among HCWs to those who are at higher risk of SARS-CoV-2 infection e.g., those in older age groups (40 years and older), those with risk factors for severe SARS-CoV-2 infection, those who have a longer time since last infection and/or vaccination (180 days or more), as well as those working as healthcare assistants and HCWs from ethnic minority groups. Strengthening surveillance of infection among HCWs would allow for identification of HCWs with increased time since last infection. Engaging vaccine champions and peer vaccinators in hospital sites from groups at higher risk of infection as well as improving vaccine accessibility, where possible, should be considered to communicate key messages about the benefits of vaccination to HCWs, patients and the healthcare system.

4. The risk of infection and transmission in healthcare settings despite vaccination emphasise the importance of adherence to IPC guidance. IPC guidance should be regularly reviewed in clinical settings to ensure optimisation and adherence to guidance. Risk assessments in healthcare settings should be dynamic and reviewed regularly, particularly during surge periods of infection to guide the use of increased IPC measures, including consideration for increased testing among HCWs e.g., in outbreak settings.

5. Surge capacity plans that incorporate anticipated staff absences due to COVID-19 should be developed to allow for continued provision of scheduled and unscheduled care in the health service, including during surge periods of SARS-CoV-2 infection. This is of particular importance to those involved in winter planning.

6. Seropositivity among healthcare workers should not be used as a marker of immunity from infection. Planned detailed immunological studies to further understand the immunological factors associated with SARS-CoV-2 infection may be useful to further inform this discussion in the hospital HCW population in Ireland.

7. The impact of SARS-CoV-2 infection on the hospital HCW workforce should be further evaluated with an economic evaluation, this is planned as part of further PRECISE studies.

References

1. McGrath J, Kenny C, Nielsen CS, Domegan L, Walsh C, Rooney P, et al. SARS-CoV-2 epidemiology, antibody dynamics, and neutralisation capacity in Irish healthcare workers in the era of booster COVID-19 vaccinations. Frontiers in Medicine. 2023;10. 10.3389/fmed.2023.1078022
2. Allen N, Riain UN, Conlon N, Ferenczi A, Carrion Martin AI, Domegan L, et al. Prevalence of antibodies to SARS-CoV-2 in Irish hospital healthcare workers. Epidemiology and infection. 2021;149:e157. 10.1017/s0950268821000984
3. Health Protection Surveillance Centre. Public health advice for the management of COVID-19 cases and contacts. Ireland: HPSC; 2023.
4. Atti A, Insalata F, Carr EJ, Otter AD, Foulkes S, Wu MY, et al. Antibody correlates of protection against Delta infection after vaccination: A nested case-control within the UK-based SIREN study. The Journal of infection. 2023;87(5):420-7. 10.1016/j.jinf.2023.07.007
5. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman L, Haas EJ, et al. Waning Immunity after the BNT162b2 Vaccine in Israel. New England Journal of Medicine. 2021. 10.1056/NEJMoa2114228
6. Health Service Executive. Data Protection Policy. HSE; 2019 [Available from: https://www.hse.ie/eng/gdpr/hse-data-protection-policy/hse-data-protection-policy.pdf].
7. Allen N, Brady M, Ni Riain U, Conlon N, Domegan L, Carrion Martin AI, et al. Prevalence of Antibodies to SARS-CoV-2 Following Natural Infection and Vaccination in Irish Hospital Healthcare Workers: Changing Epidemiology as the Pandemic Progresses. Frontiers in Medicine. 2022;8. 10.3389/fmed.2021.758118
8. Health Protection Surveillance Centre. Seroepidemiology of COVID-19 in Ireland Data Hub - updated 18/12/2023. Ireland: HPSC; 2023.
9. Song S, Madewell ZJ, Liu M, Longini IM, Yang Y. Effectiveness of SARS-CoV-2 vaccines against Omicron infection and severe events: a systematic review and meta-analysis of test-negative design studies. Frontiers in public health. 2023;11. 10.3389/fpubh.2023.1195908
10. Higdon MM, Wahl B, Jones CB, Rosen JG, Truelove SA, Baidya A, et al. A Systematic Review of Coronavirus Disease 2019 Vaccine Efficacy and Effectiveness Against Severe Acute Respiratory Syndrome Coronavirus 2 Infection and Disease. Open forum infectious diseases. 2022;9(6):ofac138. 10.1093/ofid/ofac138
11. Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. Lancet (London, England). 2022;399(10328):924-44. 10.1016/S0140-6736(22)00152-0
12. Bobrovitz N, Ware H, Ma X, Li Z, Hosseini R, Cao C, et al. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. The Lancet Infectious diseases. 2023;23(5):556-67. 10.1016/s1473-3099(22)00801-5
13. Feikin DR, Abu-Raddad LJ, Andrews N, Davies MA, Higdon MM, Orenstein WA, et al. Assessing vaccine effectiveness against severe COVID-19 disease caused by omicron variant. Report from a meeting of the World Health Organization. Vaccine. 2022;40(26):3516-27. 10.1016/j.vaccine.2022.04.069
14. National Immunisation Advisory Committee. NIAC Immunisation Guidelines: Chapter 5a COVID-19. Ireland: RCPI; 2023.
15. Hall VJ, Foulkes S, Charlett A, Atti A, Monk EJM, Simmons R, et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). The Lancet. 2021;397(10283):1459-69. 10.1016/S0140-6736(21)00675-9
16. Stein C, Nassereldine H, Sorensen RJD, Amlag JO, Bisignano C, Byrne S, et al. Past SARS-CoV-2 infection protection against re-infection: a systematic review and meta-analysis. The Lancet. 2023;401(10379):833-42. 10.1016/S0140-6736(22)02465-5

17. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman LS, Ash N, et al. Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. New England Journal of Medicine. 2022;386(23):2201-12. 10.1056/NEJMoa2118946
18. Health Service Executive. Winter Plan October 2022-March 2023. Ireland: HSE; 2022.
19. Health Protection Surveillance Centre. Weekly report on the epidemiology of COVID-19 in Ireland, Week 34, 2023. Ireland: HPSC; 2023.
20. Chu VT, Schwartz NG, Donnelly MAP, Chuey MR, Soto R, Yousaf AR, et al. Comparison of Home Antigen Testing With RT-PCR and Viral Culture During the Course of SARS-CoV-2 Infection. JAMA internal medicine. 2022;182(7):701-9. 10.1001/jamainternmed.2022.1827
21. Wells CR, Pandey A, Moghadas SM, Singer BH, Krieger G, Heron RJL, et al. Comparative analyses of eighteen rapid antigen tests and RT-PCR for COVID-19 quarantine and surveillance-based isolation. Communications Medicine. 2022;2(1):84. 10.1038/s43856-022-00147-y
22. Health Protection Surveillance Centre. Acute Hospital Infection Prevention and Control Precautions for Possible or Confirmed COVID-19 in a Pandemic Setting. Ireland: HPSC; 2023.
23. Higdon MM, Baidya A, Walter KK, Patel MK, Issa H, Espié E, et al. Duration of effectiveness of vaccination against COVID-19 caused by the omicron variant. The Lancet Infectious diseases. 2022;22(8):1114-6. 10.1016/s1473-3099(22)00409-1
24. Chemaitelly H, Nagelkerke N, Ayoub HH, Coyle P, Tang P, Yassine HM, et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection. Journal of Travel Medicine. 2022;29(8). 10.1093/jtm/taac109
25. European Centre for Disease Prevention and Control. Interim public health considerations for COVID-19 vaccination roll-out during 2023. Stockholm: ECDC; 2023.
26. National Immunisation Advisory Committee. Recommendations for the 2023 COVID-19 vaccination strategy. Ireland: Rotal College of Physicians Ireland; 2023.
27. Stamm TA, Partheymüller J, Mosor E, Ritschl V, Kritzinger S, Alunno A, et al. Determinants of COVID-19 vaccine fatigue. Nature medicine. 2023;29(5):1164-71. 10.1038/s41591-023-02282-y
28. Tuckerman J, Kaufman J, Danchin M. Effective Approaches to Combat Vaccine Hesitancy. The Pediatric infectious disease journal. 2022;41(5):e243-e5. 10.1097/inf.0000000000003499
29. Madran B, Kayı İ, Beşer A, Ergönül Ö. Uptake of COVID-19 vaccines among healthcare workers and the effect of nudging interventions: A mixed methods study. Vaccine. 2023;41(31):4586-93. 10.1016/j.vaccine.2023.06.022
30. Dubé E, Leask J, Wolff B, Hickler B, Balaban V, Hosein E, et al. The WHO Tailoring Immunization Programmes (TIP) approach: Review of implementation to date. Vaccine. 2017;36. 10.1016/j.vaccine.2017.12.012
31. Casey SM, Burrowes SAB, Hall T, Dobbins S, Ma M, Bano R, et al. Healthcare workers' attitudes on mandates, incentives, and strategies to improve COVID-19 vaccine uptake: A mixed methods study. Human vaccines & immunotherapeutics. 2022;18(6):2144048. 10.1080/21645515.2022.2144048

Appendices

Appendix A. PRECISE 5 Questionnaire

PRECISE-5 Questionnaire A (At Study Registration):

1. Name:
2. Date of birth:
3. Job role: from dropdown menu
4. Site: from dropdown menu
5. Country of Birth: from dropdown menu
6. Ethnicity: from dropdown menu
7. Vaccinated for COVID-19: yes/no
8. If yes: Vaccination brand (s) and date(s) of vaccination
9. Height
10. Weight
11. Immunosuppressed: Dropdown menu:
    a. Steroids
    b. Biologics
    c. Rituximab/Methotrexate
    d. Transplant recipient
    e. Treated for cancer in the last one year
    f. Other
    g. Not applicable
12. Previous COVID-19 infection yes/no
13. If Yes:
    a. Date of first infection. Indicate if this was an Antigen test or PCR test
    b. Date of second infection (if applicable). Indicate if this was an Antigen test or PCR test
    c. Date of third infection (if applicable). Indicate if this was an Antigen test or PCR test
    d. Date of fourth infection (if applicable). Indicate if this was an Antigen test or PCR test
    e. Date of fifth infection (if applicable). Indicate if this was an Antigen test or PCR test

PRECISE-5 Questionnaire B (Post-reporting of an incident infection):

1. Confirm Name:
2. Confirm Date of Birth:
3. Confirm date of Positive SARS-CoV-2 PCR test or positive Antigen test
4. Number of days of symptoms experienced
5. Do you still have symptoms currently
6. Severity of infection (number of days in bed)
7. Were you admitted to hospital (yes/no)
8. If yes: for how many days
9. Number of days absent from work that was required (how many rostered days did you miss)

Appendix B. Definition of COVID-19 vaccination status

Primary series course completed

This is two doses of a two-dose vaccine course or one dose of a single Janssen (JCOVDEN) vaccine, including those who are immunocompromised (as per the NIAC guidelines) and have received an extra, third (primary) dose as an extended primary course. Those with one dose schedules are considered fully vaccinated 14 days or more after receipt of the second dose. Those with two dose schedules are considered fully vaccinated 14 days or more after receipt of the dose. Those with a two-dose schedule are considered fully vaccinated 7 days of more after receipt of the third dose.

First booster dose

Completed a primary series course and have received a first booster dose. Considered to be vaccinated with a first booster 7 days or more after receipt of the first booster dose.

Second booster dose

Completed a primary series course and have received a second booster dose. Considered to be vaccinated with a second booster 7 days or more after receipt of the second booster dose.

Third booster dose

Completed a primary series course and have received a third booster dose. Considered to be vaccinated with a third booster 7 days or more after receipt of the third booster dose.

Fourth booster dose

Completed a primary series course and have received a fourth booster dose. Considered to be vaccinated with a third booster 7 days or more after receipt of the fourth booster dose.

Not vaccinated

No record of COVID-19 vaccination.

Appendix C. Data dictionary

Original variables for baseline questionnaire and month 1 questionnaire (repeated each month) with the initial coding in the original datafile are shown below.

Variable name	Definition of variable	Variable type	Initial coding
Enrolment questionnaire variables			
Age	Age in years at the time of enrolment to the study	numeric	age in years as whole number
Sex	Sex of participant	categorical	0 = female 1 = male
Hospitalsite_1	Hospital the participant was working in at time of enrolment	categorical	0 = SJH 1 = UHG
JOB_1	Professional group of participant from drop down menu	categorical	Administration Allied health professional Building and maintenance Catering Dental Doctor Driver Healthcare attendant Laboratory Midwifery Other Porter Security Technician 0 = Missing

Contd.

Variable name	Definition of variable	Variable type	Initial coding
pat_country_1	Participants country of birth	categorical	Australia Bahrain Bosnia & Herzegovina Botswana Brazil Bulgaria Canada China Colombia Croatia Denmark France Germany Honduras Hungary India Ireland Italy Latvia Libya Lithuania Malaysia Mauritius Moldova Nepal New Zealand Nigeria Pakistan Philippines Poland Portugal Romania Saudia Arabia South Africa

Contd.

Variable name	Definition of variable	Variable type	Initial coding
			Sudan Switzerland Trinidad & Tobago Ukraine United Arab Emirates United Kingdom United States of America Venezuela Zambia Zimbabwe 0 = Missing
ETH_1	Participants ethnicity	categorical	Any other white background Asian or Asian Irish - Any other Asian background Asian or Asian Irish - Chinese Black or black Irish - African Black or black Irish - Any other black background Other (including mixed background) white Irish white Irish traveller 0 = Missing
Height	Participants self-reported height in cm	numeric	Numeric 0/blanks = Missing
Weight	Participants self-reported weight in kg	numeric	Numeric 0/00/blank = Missing
CoVaxYesNo_2	Has the participant's vaccination status been verified on COVAX	categorical	yes/no
VaccinationStatus_1	What is the participant's vaccination status - either verified on COVAX or by hospital occupational health department. ***Yes means that the participant has received at least one COVID-19 vaccine.***	categorical	yes/no 0 = missing

Variable name	Definition of variable	Variable type	Initial coding
Vaccinated Status RECODE	Participant vaccinated for COVID-19. ***Variable calculated based on answers to the two previous questions.***	categorical	Vaccinated/Not vaccinated
VacDate1_1	Participants date of first vaccination	date	dd-mm-yyyy 0/implausible dates
VacType1_1	Vaccination brand for participants first vaccination	categorical	Astra zeneca Janssen/Johnson and Johnson Moderna New moderna bivalent New pfizer bivalent other Pfizer Spikevax Unsure 0 = Missing
VacDate2_1	Participants date of second vaccination	date	dd-mm-yyyy 0/implausible dates = Missing
VacType2_1	Vaccination brand for participants second vaccination	categorical	Astra zeneca Janssen/Johnson and Johnson Moderna New moderna bivalent New pfizer bivalent other Pfizer Spikevax Unsure 0 = Missing
VacDate3_1	Participants date of third vaccination	date	dd-mm-yyyy 0/implausible dates = Missing

Contd.

Variable name	Definition of variable	Variable type	Initial coding
VacType3_1	Vaccination brand for participants third vaccination	categorical	Astra zeneca Janssen/Johnson and Johnson Moderna New moderna bivalent New pfizer bivalent other Pfizer Spikevax Unsure 0 = Missing
VacDate4_1	Participants date of fourth vaccination	date	dd-mm-yyyy 0/implausible dates = Missing
VacType4_1	Vaccination brand for participants fourth vaccination	categorical	Astra zeneca Janssen/Johnson and Johnson Moderna New moderna bivalent New pfizer bivalent other Pfizer Spikevax Unsure 0 = Missing
VacDate5_1	Participants date of fifth vaccination	date	dd-mm-yyyy 0/implausible dates = Missing

Contd.

Variable name	Definition of variable	Variable type	Initial coding
VacType5_1	Vaccination brand for participants fifth vaccination	categorical	Astra zeneca Janssen/Johnson and Johnson Moderna New moderna bivalent New pfizer bivalent other Pfizer Spikevax Unsure 0 = Missing
Number of Vaccines Received	Number of COVID-19 vaccines that the participant has received (self-reported or verified (COVAX))	numeric	0 1 2 3 4
Riskstatus	underlying medical condition reported by participant	categorical	yes/no/not known 0 = Missing
Medications_Conditions#Biologic_Agents	Is the participant taking a biologic agent	categorical	0/1 0= no 1= yes
Medications_Conditions#Rituximab	Is the participant taking Rituximab	categorical	0/1 0= no 1= yes
Medications_Conditions#Methotrexate	Is the participant taking methotrexate	categorical	0/1 0= no 1= yes
Medications_Conditions#Steroids	Is the participant taking steriods: 40mg daily for a week or 20mg daily for 14 days	categorical	0/1 0= no 1= yes

Contd.

Variable name	Definition of variable	Variable type	Initial coding
Medications_Conditions#Not_applicable	Medication not specified	categorical	0/1 0= yes 1= no
SeriousConditions#Transplant_Recipient	Is the participant a transplant recipient	categorical	0/1 0= no 1= yes
SeriousConditions#Treated_for_Cancer	Has the participant been treated for cancer in the past 12 months	categorical	0/1 0= no 1= yes
SeriousConditions#Not_Applicable	Serious condition (not in dropdown)	categorical	0/1 0= yes 1= no
InfectionYesNo_1	Has the participant had a previous COVID-19 infection ever (self-reported)	categorical	yes/no 0
Infection1test_1	For the participants first COVID-19 infection, was this confirmed with PCR or antigen test?	categorical	Antigen test Laboratory PCR test Not known 0 = Missing
infectiondate1_1	The date of the participants first infection	date	dd-mm-yyyy 0/implausible dates = Missing
Infection2test_1	For the participants second COVID-19 infection, was this confirmed with PCR or antigen test?	categorical	Antigen test Laboratory PCR test Not known 0 = Missing
infectiondate2_1	The date of the participants second infection	date	dd-mm-yyyy 0/implausible dates

Contd.

Variable name	Definition of variable	Variable type	Initial coding
Infection3test_1	For the participants third COVID-19 infection, was this confirmed with PCR or antigen test?	categorical	Antigen test Laboratory PCR test Not known 0 = Missing
infectiondate3_1	The date of the participants third infection	date	dd-mm-yyyy 0/implausible dates
Infection4test_1	For the participants fourth COVID-19 infection, was this confirmed with PCR or antigen test?	categorical	Antigen test Laboratory PCR test Not known 0 = Missing
ResultsYesNo_1	If patient consented to receive serology results	categorical	yes/no 0 = Missing
Monthly survey for participants: Month 1 variables shown below and repeated for months 1 to 9			
Infection Survey 1 Completion Rate	Proportion of questions completed by participant in survey 1	numeric	Numeric
Infection Survey 1	Did participant have a new self-reported COVID infection in month 1	categorical	yes/no blanks
COVID19datemonth1	If participant had a new self-reported COVID-19 infection in month 1, what was the self-reported date of COVID infection	date	dd-mm-yyyy blanks
COVID19testconfirmed 1month	If participant had a new self-reported COVID-19 infection in month 1,how was the COVID infection confirmed in month 1	categorical	Antigen test Laboratory PCR test Not known blanks
Symptomspresent Month 1	If participant had a new self-reported COVID-19 infection in month 1, were they symptomatic	categorical	yes/no blanks
Symptomslength Month 1	If participant had a new self-reported COVID-19 infection in month 1 and was symptomatic what was the duration of symptoms in days	numeric	Numeric Blanks/0 = Missing

Contd.

Variable name	Definition of variable	Variable type	Initial coding
daysinbed Month 1	If participant had a new self-reported COVID-19 infection in month 1and was symptomatic how many days were they in bed	numeric	Numeric Blanks/0 = Missing
Gpattendance Month 1	If participant had a new self-reported COVID-19 infection in month 1, did they attend GP	categorical	yes/no blanks
Edattendance Month 1	If participant had a new self-reported COVID-19 infection in month 1, did they attend ED	categorical	yes/no blanks
Hospitadmittance Month 1	If participant had a new self-reported COVID-19 infection in month 1, were they admitted to hospital	categorical	yes/no blanks
Hospitaldays Month 1	If participant had a new self-reported COVID-19 infection in month 1, and were admitted to hospital what was the length of stay in days	numeric	Numeric Blanks/0
Supplementaloxygen Month 1	If participant had a new self-reported COVID-19 infection in month 1and were admitted to hospital, did they require supplemental oxygen	categorical	yes/no
Daysoffwork Month 1	If participant had a new self-reported COVID-19 infection in month 1, how many days were they off work	numeric	Numeric Blanks/0 = Missing
Vaccination Month 1	Had participant been vaccinated within month 1	categorical	yes/no blanks
VaccinationDate Month 1	If the participant was vaccinated in month 1 what was the date of vaccination	data	dd-mm-yyyy blanks
Vaccinebrand Month 1	If the participant was vaccinated in month 1 what was the brand of vaccination	categorical	Astra zeneca Janssen/Johnson and Johnson Moderna New moderna bivalent New pfizer bivalent other Pfizer Spikevax Unsure

Contd.

Serology variables			
Anti-SARS-CoV-Nucleocapsid	antibody titre for anti-SARS-CoV-Nucleocapsid	numeric	numeric titre level insufficient
Anti-SARS-CoV-Nucleocapsid Interpretation	classification as Anti-SARS-CoV-Nucleocapsid Positive or Negative	categorical	Positive (N) Negative (N)
Anti-SARS-CoV-Spike	antibody titre for anti-SARS-CoV-Spike	numeric	numeric titre level up to max of 250 > 250 insufficient
Anti-SARS-CoV-Spike Interpretation	classification as Anti-SARS-CoV-Spike Positive or Negative	categorical	Positive (S)/Negative (S)
COVAX variables			
Primary Course Dose 1	Vaccination brand for the first dose of a primary COVID-19 vaccination course	categorical	0 = Missing AstraZeneca Declined COVAX access Janssen Moderna NA No No castor code found Not recorded on COVAX Not vaccinated at P5, no COVAX account Other Pfizer
Administration Date_pc1	Date of administration of the first dose of a primary COVID-19 vaccination course	date/categorical	dd/mm/yyyy Declined COVAX access NA No castor code found Not recorded on COVAX/ Not vaccinated at P5, no COVAX account Unknown

Contd.

Variable name	Definition of variable	Variable type	Initial coding
Primary Course Dose 2	Vaccination brand for the second dose of a primary COVID-19 vaccination course	categorical	0 = Missing AstraZeneca Declined COVAX access Janssen Moderna NA No No castor code found Not recorded on COVAX Not vaccinated at P5, no COVAX account Other Pfizer
Administration Date_pc2	Date of administration of the second dose of a primary COVID-19 vaccination course	date/categorical	dd/mm/yyyy Declined COVAX access NA No castor code found Not recorded on COVAX/ Not vaccinated at P5, no COVAX account Unknown
Additional Dose	Vaccination brand for an additional dose of a primary COVID-19 vaccination course	categorical	0 = Missing AstraZeneca Declined COVAX access Janssen Moderna NA No No castor code found Not recorded on COVAX Not vaccinated at P5, no COVAX account Other Pfizer

Contd.

Variable name	Definition of variable	Variable type	Initial coding
Administration Date_add_dose	Date of administration of an additional dose of a primary COVID-19 vaccination course	date/categorical	dd/mm/yyyy Declined COVAX access NA No castor code found Not recorded on COVAX/ Not vaccinated at P5, no COVAX account Unknown
Booster 1	Vaccination brand for a first COVID-19 booster	categorical	0 = Missing AstraZeneca Declined COVAX access Janssen Moderna NA No No castor code found Not recorded on COVAX Not vaccinated at P5, no COVAX account Other Pfizer
Administration Date_b1	Date of administration of first COVID-19 booster	date/categorical	dd/mm/yyyy Declined COVAX access NA No castor code found Not recorded on COVAX/ Not vaccinated at P5, no COVAX account Unknown

Contd.

Variable name	Definition of variable	Variable type	Initial coding
Booster 2	Vaccination brand for a second COVID-19 booster	categorical	0 = Missing AstraZeneca Declined COVAX access Janssen Moderna NA No No castor code found Not recorded on COVAX Not vaccinated at P5, no COVAX account Other Pfizer
Administration Date_b2	Date of administration of second COVID-19 booster	date/categorical	dd/mm/yyyy Declined COVAX access NA No castor code found Not recorded on COVAX/ Not vaccinated at P5, no COVAX account Unknown

Appendix D. Clinical risk factors for severe SARS-CoV-2 infection reported by participants

Table AD1. Specific risks reported by participants by hospital site*

		St James's Hospital		University Hospital Galway		Total		p-value[a]
		n	%	n	%	n	%	
Risk factor for severe SARS-CoV-2 infection	No	571	89.5	576	92.6	1147	91	0.067
	Yes	67	10.5	46	7.4	113	9	
Biologic agent	Not on biologic	631	98.9	618	99.4	1249	99.1	0.547
	Taking biologic	7	1.1	<5	0.6	11	0.9	
Rituximab	Not on rituximab	637	99.8	622	100	1259	99.9	1
	Rituximab	<5	0.2	0	0	<5	0.1	
Methotrexate	Not on Methotrexate	634	99.4	621	99.8	1255	99.6	0.374
	Methotrexate	4	0.6	<5	0.2	5	0.4	
Steroids	Not on steriods	622	97.5	612	98.4	1234	97.9	0.323
	Steriods	16	2.5	10	1.6	26	2.1	
Medication not specified	On medication (not specified)	25	3.9	19	3.1	44	3.5	0.445
	Not on medication	613	96.1	603	96.9	1216	96.5	
Transplant	Not a transplant recipient	638	100	621	99.8	1259	99.9	0.494
	Transplant recipient	0	0	<5	0.2	<5	0.1	
Cancer treatment	No cancer treatment	636	99.7	616	99	1252	99.4	0.173
	Cancer treatment	<5	0.3	6	1	8	0.6	
Condition unspecified	Has risk factor (not specified)	10	1.6	12	1.9	22	1.7	0.672
	No condition	628	98.4	610	98.1	1238	98.3	

*Counts between 1 and 4 changed to < 5 for each site and overall

[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5) and the Mann-Whitney U test was used for comparison of medians for continuous variables.

Appendix E. Symptomatic incident SARS-CoV-2 infection

Table AE1 Characteristics of those who reported a symptomatic incident SARS-CoV-2 infection (n = 101), compared to those who reported no symptoms (n = 157): Continuous variables

	Symptomatic (n= 101)		No symptoms reported (n = 157)		Total (n = 258)		p-value[a]
Exposure	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Age	43	33-51	44	35-53	44	35-52	0.811
BMI	25.1	23.1-29.1	25.8	23.4-29.1	25.6	23.2-29.1	0.718
Anti Nucleocapsid antibody titre at enrolment (U/ml)	6.3	0.1-26.4	3.1	0.1-19.7	3.9	0.1-22.5	0.116

Table AE1 Characteristics of those who reported a symptomatic incident SARS-CoV-2 infection (n = 101), compared to those who reported no symptoms (n = 157): Categorical variables

		n	%	n	%	n	%	p-value[a]
Age category	18-29	11	10.9	24	15.3	35	13.6	0.200
	30-39	32	31.7	32	20.4	64	24.8	
	40-49	27	26.7	50	31.8	77	29.8	
	50+	31	30.7	51	32.5	82	31.8	
Sex	Female	85	84.2	131	83.4	216	83.7	1.000
	Male	16	15.8	26	16.6	42	16.3	
Hospital site	St James's Hospital	56	55.4	89	56.7	145	56.2	0.946
	University Hospital Galway	45	44.6	68	43.3	113	43.8	
Occupation	Administration	16	15.8	32	20.4	48	18.6	0.825
	Allied Health Professional	18	17.8	24	15.3	42	16.3	
	General Support	4	4	7	4.5	11	4.3	
	Healthcare assistant	3	3	4	2.5	7	2.7	
	Laboratory	6	5.9	15	9.6	21	8.1	
	Medical/dental	10	9.9	20	12.7	30	11.6	
	Nursing/midwifery	41	40.6	50	31.8	91	35.3	
	Other	3	3	5	3.2	8	3.1	

Contd.

Table AE1. Characteristics of those who reported a symptomatic incident SARS-CoV-2 infection (n = 101) compared to those who reported no symptoms (n = 157) (continued)

		Symptomatic (n= 101)		No symptoms reported (n = 157)		Total (n = 258)		p-value[a]
		n	%	n	%	n	%	
Clinical role	Clinical	75	74.3	98	62.4	173	67.1	0.066
	Non-clinical	26	25.7	59	37.6	85	32.9	
Country of birth	Ireland	82	81.2	132	84.1	214	82.9	0.834
	European Union/United Kingdom	10	9.9	13	8.3	23	8.9	
	Other	9	8.9	12	7.6	21	8.1	
Ethnicity	White Irish	80	79.2	137	87.3	217	84.1	0.144
	Any other White Background	14	13.9	10	6.4	24	9.3	
	Asian background	7	6.9	9	5.7	16	6.2	
	Other* (Including mixed background and African and other black background)	0	0	1	0.6	1	0.4	
BMI category	BMI 30 and over	21	20.8	28	17.8	49	19	0.696
	BMI less than 30	72	71.3	115	73.2	187	72.5	
	Missing	8	7.9	14	8.9	22	8.5	
Risk factor for severe SARS-CoV-2 infection	No	88	87.1	136	86.6	224	86.8	1.000
	Yes	13	12.9	21	13.4	34	13.2	
COVID-19 vaccination status	Unvaccinated	3	3	3	1.9	6	2.3	0.668
	Primary course only	6	5.9	5	3.2	11	4.3	
	Primary course and booster 1 only	56	55.4	88	56.1	144	55.8	
	Primary course, booster 1 and booster 2 only	36	35.6	61	38.9	97	37.6	
Self-reported prior SARS-CoV-2 infection at enrolment	No infection reported	35	34.7	63	40.1	98	38	0.452
	Infection reported	66	65.3	94	59.9	160	62	

Contd.

Table AE1. Characteristics of those who reported a symptomatic incident SARS-CoV-2 infection (n = 101) compared to those who reported no symptoms (n = 157) (continued)

		Symptomatic (n= 101)		No symptoms reported (n = 157)		Total (n = 258)		p-value[a]
		n	%	n	%		n	%
Time from last COVID-19 vaccination	180 days or more	61	60.4	91	58	152	58.9	0.759
	Less than 180 days	37	36.6	63	40.1	100	38.8	
	Unvaccinated	3	3	3	1.9	6	2.3	
Infection/serology status	Infection reported and anti-N positive	61	60.4	83	52.9	144	55.8	0.384
	No infection reported and anti-N negative	28	27.7	54	34.4	82	31.8	
	Infection reported but anti-N negative	4	4	11	7	15	5.8	
	No infection reported but anti-N positive	7	6.9	9	5.7	16	6.2	
	Incomplete data	1	1	0	0	1	0.4	
Anti-Nucleocapsid antibody status	Negative (n)	32	31.7	65	41.4	97	37.6	0.166
	Positive (n)	68	67.3	92	58.6	160	62	
	Missing	1	1	0	0	1	0.4	

* Including mixed background and African and other black background

[a]Comparison between groups was made using the Chi-square test for proportions for categorical variables (Fisher's exact test was used when cell counts were < 5) and the Mann-Whitney U test was used for comparison of medians for continuous variables.

Table AE2. Factors associated with a symptomatic incident SARS-CoV-2 infection: Logistic regression

	Unadjusted				Adjusted*			
Exposure	**OR**	**Lower CI**	**Upper CI**	**p-value**	**OR***	**Lower CI***	**Upper CI***	**p-value***
Age category								
18-29								
30-39	2.18	0.93	5.33	0.077	2.11	0.9	5.19	0.093
40-49	1.18	0.51	2.84	0.706	1.2	0.51	2.93	0.673
50+	1.33	0.58	3.16	0.511	1.37	0.59	3.29	0.468
Sex								
Female								
Male	0.95	0.47	1.86	0.879	0.97	0.48	1.93	0.935
Clinical role								
Yes								
No	**0.58**	**0.33**	**0.99**	**0.049**	0.6	0.34	1.04	0.074

*Adjusted for age category, sex, and clinical role

For the multivariable model, n = 258, Nagelkerke R^2 = 4.1%, Hosmer Lemeshow test p-value= 0.571

Appendix F. Factors associated with an incident SARS-CoV-2 infection: Log binomial regression

Exposure	RR[a]	Lower CI	Upper CI	p-value	RR*	Lower CI*	Upper CI*	p-value*
Age category								
18-29	-	-	-	-	-	-	-	-
30-39	1.27	0.88	1.87	0.206	1.28	0.90	1.88	0.182
40-49	1.07	0.75	1.56	0.716	1.02	0.72	1.49	0.913
50+	1.18	0.84	1.72	0.358	1.05	0.74	1.54	0.776
Sex								
Female	-	-	-	-	-	-	-	-
Male	0.77	0.56	1.03	0.092	0.75	0.54	1.00	0.059
Ethnicity								
White Irish	-	-	-	-	-	-	-	-
Any other White Background	0.79	0.53	1.13	0.236	0.74	0.49	1.04	0.109
Other**	**0.61**	**0.36**	**0.96**	**0.049**	**0.56**	**0.33**	**0.87**	**0.018**
Risk factor for severe SARS-CoV-2 infection								
No	-	-	-	-	-	-	-	-
Yes	**1.57**	**1.13**	**2.09**	**0.004**	**1.57**	**1.14**	**2.07**	**0.003**
Time since last self-reported SARS-CoV-2 infection at enrolment								
Less than 180 days	-	-	-	-	-	-	-	-
180 days or more	**1.65**	**1.19**	**2.35**	**0.004**	**1.69**	**1.22**	**2.41**	**0.002**
No self-reported infection	**2.01**	**1.44**	**2.87**	**<0.001**	**2.12**	**1.52**	**3.03**	**<0.001**
Anti-N antibody category								
Negative (n)	-	-	-	-	-	-	-	-
Positive (n)	**0.42**	**0.34**	**0.52**	**<0.001**	-	-	-	-
Anti-Nucleocapsid antibody titre	**0.99**	**0.99**	**0.99**	**<0.001**	-	-	-	-
Prior infection								
No prior infection	-	-	-	-	-	-	-	-
Prior infection	**0.71**	**0.57**	**0.89**	**0.002**	-	-	-	-

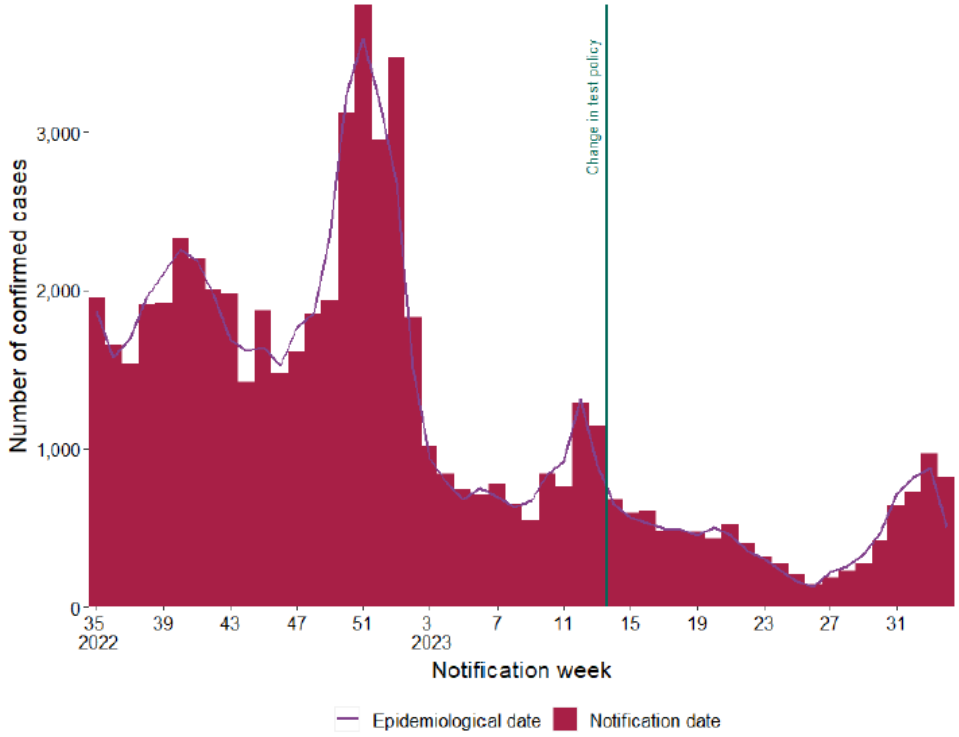
[a]Relative risk *Adjusted for age category, sex, ethnicity, risk factor for severe SARS-CoV-2 infection and time since last infection **Including mixed background and African and other black background.

Appendix G. Factors associated with a symptomatic incident SARS-CoV-2 infection: Log binomial regression

Exposure	RR	Lower CI	Upper CI	p-value	RR*	Lower CI*	Upper CI*	p-value*
Age category								
18-29	-	-	-	-	-	-	-	-
30-39	1.59	0.96	2.94	0.096	1.52	0.92	2.8	0.133
40-49	1.12	0.65	2.1	0.709	1.13	0.66	2.13	0.669
50+	1.2	0.71	2.25	0.520	1.21	0.72	2.26	0.500
Sex								
Female	-	-	-	-	-	-	-	-
Male	0.97	0.61	1.42	0.879	0.99	0.62	1.44	0.967
Clinical role								
Yes	-	-	-	-	-	-	-	-
No	0.71	0.48	0.99	0.059	0.74	0.5	1.05	0.106

*Adjusted for age category, sex, and clinical role

Appendix H. Epidemiology of COVID-19 in Ireland during the PRECISE 5 study period



**The line green vertical line represents a change in testing policy; since week 13 2023, community testing centres are closed and PCR testing is only performed based on clinical assessment*

Figure AH1. Number of confirmed cases by notification and epidemiological date in Ireland between week 35 2022 and week 34 2023*

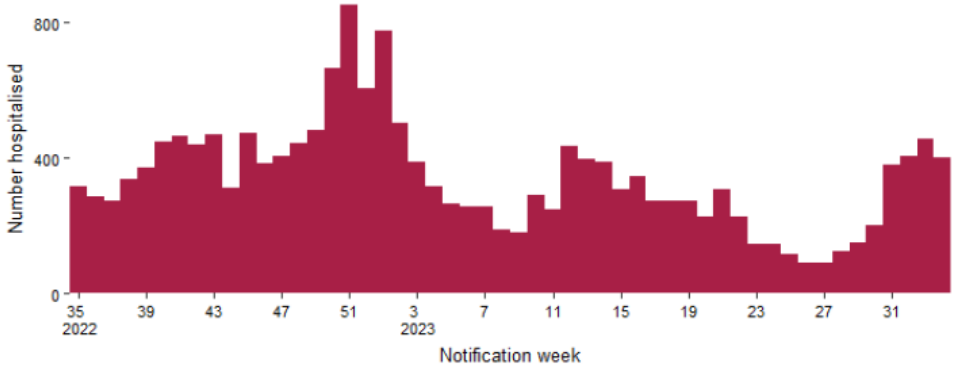


Figure AH2. Hospitalisations among confirmed CVID-19 cases in Ireland between week 35 2022 and week 34 2023