Prevalence of Antibodies to SARS-CoV-2 natural infection and post-vaccination in Irish Hospital Healthcare Workers (PRECISE 2)

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Summary (main body page 7)

Background

Hospital healthcare workers (HCW) are at increased risk of contracting SARS-CoV-2 infection. We aimed to determine the seroprevalence of SARS-CoV-2 antibodies in HCW in Ireland, and to compare the seroprevalence in the same HCW at two points in time. Two tertiary referral hospitals in Irish cities with diverging community incidence and seroprevalence were identified; COVID-19 had been diagnosed in 10.2% and 1.8% of staff respectively by the time of the first cross-sectional study (PRECISE 1, October 2020, during the second wave of the pandemic in Ireland). Community seroprevalence after the first wave of the pandemic was 3.1% and 0.6% respectively. Results of PRECISE 1 showed an overall SARS-CoV-2 seroprevalence of 15% in SJH and 4.1% in UHG, with higher adjusted relative risk (aRR) for male sex, age group 18-29, Asian ethnicity, direct patient contact, role of nurse or healthcare assistant, living with others and living with other HCW (1) (2).

This document pertains to the second cross-sectional study (PRECISE 2), which took place six months after PRECISE 1 (in April 2021, during the decline of the third wave of the pandemic in Ireland). By April 2021, occupational health data showed that COVID-19 infection had been diagnosed in 18.5% and 9.2% of staff in SJH and UHG respectively. PRECISE 2 took place four months after the start of vaccination at both sites. The aim of PRECISE 2 was to assess changes in overall seroprevalence with progression of the pandemic, and to further identify HCW risks for seropositivity (demographic, work-related and living arrangements). We also aimed to assess serological response to vaccination in the vaccinated cohort, and to examine changes in individual serostatus over the six-month period between PRECISE 1 and PRECISE 2 for those staff members who participated both times.

Methods

All staff of both hospitals (N=9038) were invited to participate in an online questionnaire and blood sampling for SARS-CoV-2 antibody testing in April 2021, in a similar manner to in October 2020 (1). We measured anti-nucleocapsid (N) antibodies and anti-spike (S) antibodies on all samples, using the Roche Elecsys anti-SARS-CoV-2 and Roche Elecsys anti-SARS-CoV-2 S immunoassays, respectively. A participant was presumed to have had COVID-19 infection at some stage if anti-N antibody was detected, or if anti-S antibody was detected without a history of vaccination. Detection of anti-S antibody in vaccinated participants was considered to be as a result of vaccination. All vaccines available to participants were as part of a two-dose regime. A participant was considered fully vaccinated at ≥14 days after the second dose vaccine. Frequencies and percentages for positive SARS-CoV-2 antibody were calculated and adjusted relative risks (aRR) for participant characteristics were calculated using multivariable regression analysis. Participants common to both serosurveys had their results linked to assess antibody loss or gain.

Results

Seroprevalence of past infection

5085 HCW participated in PRECISE 2 (56% response rate). Seroprevalence of antibodies to SARS-CoV-2 (indicative of past infection) was 21% and 13% in SJH and UHG respectively. The adjusted relative risk (aRR) for hospital data combined was higher for working in SJH, age 18-29, male sex, Black ethnicity, lower level of education, role of healthcare assistant (HCA), role of nurse, living with other HCW, and working directly with patients. Risk factors differed by hospital. Of those that were seropositive, 19% had never had symptoms consistent with COVID-19 infection, and 26% had never been diagnosed with COVID-19 infection.

PRECISE 1 versus PRECISE 2; summary of findings

Findings common to both

- Demographic risk factors: younger age group, males, and minority ethnic groups.
- Living arrangement risk factor: living with other HCWs.
- Work-related risks: close patient contact (especially with COVID-19 patients), especially HCAs, followed by nurses.
- The proportion of infections that had been previously undiagnosed remains high (although decreased from 39% to 26%).

Main differences in findings

- Expected rise in overall seroprevalence following the third wave of the COVID-19 pandemic nationally.
- Different ethnic group highlighted in each study (October 2020 Asian ethnicity, April 2021 Black ethnicity)
- Lower level of education associated with seropositivity in April 2021.
- Seroprevalence by role; large increase in seroprevalence amongst general support staff

Serological Response to Vaccination

Ninety-five percent of participants (4854/5085) had started or completed a COVID-19 vaccination course; 81% (4130/5085) of participants had received two doses of vaccine. All recipients of two vaccine doses had detectable anti-S antibodies in response to vaccination. There were 23 breakthrough infections in participants who had received their second dose of vaccine ≥14 days prior to PCR-confirmed infection, representing 0.6% (23/4111) of all fully vaccinated participants. There were 93 infections in participants who had received only 1 dose of the vaccine, or had received their 2nd dose <15 days before their infection, representing 13% (93/724) of partially vaccinated participants. Ninety-nine percent (713/716) of partially vaccinated participants had detectable anti-S antibodies.

Change in Antibody Response over time (six-months) from PRECISE 1 to PRECISE 2

In total, 3,313 participants were common to both PRECISE 1 (October 2020) and PRECISE 2 (April 2021). Of those participants who took part in both phases and were antibody positive in October 2020 (n=360), 90% (325/360) remained antibody positive. Among the 3,313, 9.7% (35/360) who were previously seropositive became seronegative, and 7.9% (235/2953) who were previously seronegative became seropositive.

Conclusion

The increase in seroprevalence from October 2020 to April 2021 reflects the magnitude of the third wave of the pandemic in both locations. Risk was higher in the hospital situated in a higher density area with higher community incidence throughout the COVID-19 pandemic. These findings highlight community incidence as one of the main risks to HCW. Workplace related factors also increased risk; risk was higher for HCW with close patient contact. Hospital outbreaks, hospital infrastructure, and social and demographic factors also may have

played a role in the differing seroprevalence at each site, and within each role group. However, in the absence of real time genomic sequencing, the attributable risk attributable of the workplace versus the household/community cannot be further defined.

We identified living with other HCW as an independent risk factor for seropositivity in both studies; to the best of our knowledge there is no other published literature commenting specifically on this risk factor. The other risk factors that we identified are consistent with the published literature, including age, male sex, having direct patient contact, being a HCA or a nurse, and being of Black, Asian ethnicity. Ninety percent of those who were seropositive in October 2020 and participated in April 2021, remained seropositive.

The antibody response to vaccination is reassuring, however we did show confirmed infection in a small minority of fully vaccinated participants; further studies are needed to correlate serological and T cell response with functional immunity. Specific vaccine effectiveness studies are needed to characterise breakthrough infections post vaccination and to estimate protection from infection, particularly with the ongoing emergence of variants of concern. With emerging evidence of reduction in transmission from vaccinated individuals, the authors strongly endorse immediate vaccination of all HCW. Messaging to HCW regarding the role and limits of vaccination need to be clear and should include the ongoing risk of infection and transmission. Ongoing adherence to all infection prevention and control standards in the healthcare setting and household are paramount in light of the proportion of undiagnosed infections, and the breakthrough infections in fully vaccinated participants. Easy access to testing of HCW with symptoms (including mild symptoms) and in the setting of close contact with a confirmed case of COVID-19 infection should continue, and vaccinated HCW with PCR-confirmed SARS-CoV-2 infection should be actively assessed to advance understanding of the reasons for breakthrough infection. This should include seeking further

information on patient biological factors, whole genome sequencing (WGS) of the virus from breakthrough infection HCW cases, and/or index cases identified by follow-up.

Main Body

Background

COVID-19 infection in hospital healthcare workers

Healthcare workers, and those they live with, are at increased risk of contracting SARS-CoV-2 viral infection (3) (4) (5). Detectable antibody to SARS-CoV-2 is an excellent indicator of COVID-19 infection (6). A high proportion of the COVID-19 infections notified in Ireland have been in hospital healthcare workers (HCW) and antibody seroprevalence has been shown to be up to six times as high as the background community seroprevalence (7) (8) (1). Understanding the transmission and potential immunity dynamics of SARS-CoV-2 in hospitals in Ireland is important in mitigating transmission at hospital level and adds valuable information to the growing evidence base on the transmission patterns of COVID-19 among HCW.

Antibody response following infection and vaccination

Natural infection has been shown to produce humoral and cellular immunity and whilst this may decline over time, durable memory responses are seen; infection-induced immunity has been shown to protect for up to nine months (9) (10). Although the duration of the detectable antibody response to SARS CoV2 can vary depending on the antigenic target and method of detection (11) (12), there is emerging evidence of a rich and sustained memory response in many individuals. Vaccines have been shown to be protective both against infection and

against symptomatic disease (13) (14) (15) (16). Vaccination is also associated with lower viral loads and decreased duration of oropharyngeal PCR positivity which are very likely to correlate with decreased transmissibility (17). Vaccine-induced immunity produces a more robust response the adaptive immune system therefore vaccination is likely to produce a sustained immune response with immunological memory and sustained protection, including against variants of concern (VoC) (18) (19). Immunity after natural infection may not protect against re-infection with variants of concern (20), while vaccine-induced immunity is reduced, but not lost, against variants of concern (21) (22) (23). Robust B and T cell responses to vaccination have been shown for both mRNA vaccines and viral vector vaccines (24). Antibody response has been shown to correlate with protective immunity against infection (25).

The spike (S) and nucleocapsid (N) proteins are two of the main immunogens of the coronavirus proteins (26). Commercial SARS-CoV-2 antibody assays can detect antibodies to these structural proteins. Natural infection can produce either anti-N antibodies, anti-S antibodies, both anti-N and anti-S antibodies, or neither antibody. Currently available vaccines against COVID-19 infection produce anti-S antibodies only.

Study sites – 2020 epidemiology

St. James's Hospital (SJH) is a tertiary referral hospital in the south inner city of Dublin, the capital city of Ireland (population 1.2 million) and has almost 4,700 employees and just over 1000 beds. From March-May 2020 (first wave of the pandemic in Ireland, (27)) 9.6% of the staff of SJH tested positive for SARS-CoV-2 infection via polymerase chain reaction (PCR), and by the start of October (the start of the second wave of the pandemic in Ireland, (27)) 10.2% of staff had tested positive by PCR. University Hospital Galway (UHG) is a

comparable tertiary referral hospital with almost 4400 employees and over 500 beds, located in Galway, in the West of Ireland (population 80,000); 1.8% of its HCW had a PCR-confirmed infection at some stage during the time-period from March-May 2020 and this remained at 1.8% until the start of October 2020.

SJH is one of the largest acute hospitals in Dublin city; UHG is the main acute hospital serving the city of Galway. Both hospitals received patients with COVID-19 infection throughout the first wave of the COVID-19 pandemic in Ireland, and breakdown by ward and specialty is similar.

The community incidence of COVID-19 infection in County Galway was significantly lower than in County Dublin during the first and second waves of the pandemic in Ireland (27). The community seroprevalence was assessed by the Study to Investigate COVID-19 Infection in People Living in Ireland (SCOPI) (28) in June/July 2020 (at the end of the first wave). Seroprevalence was found to be significantly lower in the West of Ireland (Sligo) at 0.6% compared with the greater Dublin area at 3.1% (28) (29).

The first part of the PRECISE Study (PRECISE 1) was conducted in October 2020, during the second wave of the pandemic in Ireland, and prior to national roll-out of COVID-19 vaccination. This was a cross-sectional seroprevalence study of antibodies to SARS-CoV-2 in all HCW at each of these hospital sites. Results of PRECISE 1 showed an overall SARS-CoV-2 seroprevalence of 15% in SJH and 4.1% in UHG. Almost 40% of infections had been previously undiagnosed, and at least 16% of infections were asymptomatic. Risk for seropositivity was higher for healthcare assistants, nurses, daily exposure to patients (especially patients with confirmed/suspected COVID-19 infection), age 18-29 years, living

with other HCW, Asian ethnicity and male sex (1) (2). The HCW seroprevalence was six times higher than community seroprevalence (28).

Study sites - 2021 epidemiology

The gap in COVID-19 incidence between Galway and Dublin during the third wave of the COVID-19 pandemic was narrower than during the first two waves; for a 2 week period in late January 2021 the 14-day incidence for Galway approached that of Dublin (30). At the start of this second seroprevalence study in April 2021, the incidence was 181/100,000 in Dublin and 83/100,000 in Galway (31). By the start of April 2021 (third wave of the pandemic in Ireland, (32)) the cumulative incidence of PCR-confirmed infections in HCW in SJH and UHG had risen to 18.5% and 9.2% respectively.

The purpose of this repeat cross-sectional study (PRECISE 2) was to re-assess the prevalence of anti-SARS-CoV-2 antibodies in HCW in these two hospitals following the third, and larger, wave of the pandemic in Ireland, and to relate risk of COVID-19 infection in HCW to demographic, living arrangements and work-related factors in order to inform ongoing risk reduction activities. We aimed to assess:

1. Changes in overall seroprevalence over a six-month period in these distinct geographical areas.
2. Serological response to COVID-19 vaccination in the vaccinated sub-group.
3. Changes in individual serostatus over time (six-months) for those who participated in PRECISE 1 and PRECISE 2 (note detailed analysis in the Addendum).

Methods

Study Design and participants

This was a cross-sectional study of the seroprevalence of circulating antibodies to SARS-CoV-2, carried out from the 19th-28th April 2021, with longitudinal linking of participants who also took part in the first serosurvey (PRECISE 1) carried out from the 14th-23rd October 2020. All staff members of both hospitals (N=9038) were invited to participate in an online self-administered consent process and online questionnaire, followed by blood sampling for SARS-CoV-2 antibody testing in April 2021, in the same manner as PRECISE 1 (1). Electronic consent and patient reported outcomes were captured using Castor; an eClinical platform that enables decentralised clinical trials (33). Following completion of the online consent and questionnaire, participants were automatically directed to an online platform to book a blood test on site at their place of work (34). Technical support and walk-in phlebotomy clinics were provided for participants who had difficulty with the online consent process. Information collected in the questionnaire included demographic information, contact details, place and type of work, level of contact with patients, previous COVID-19 symptoms and testing, history of close contact with a confirmed case of COVID-19, living arrangements and history of COVID-19 vaccination, including dates and type of vaccine. Blood samples were processed anonymously via a unique participant identifier (MRN), which was generated by the online blood booking system. This MRN was later used by the study team to link results to individual participants to deliver results. Results were sent by text message to all participants on an opt-out basis. Results were discussed in person with any participant who requested this.

All vaccinated study participants received their SARS-CoV-2 vaccine as part of a two-dose regimen, of either the Comirnaty (Pfizer/BioNTech) vaccine, the Vaxzevria (formerly AstraZeneca) vaccine or the Moderna vaccine. The National Immunisation Advisory Committee (NIAC) currently states that recipients of the Vaxzevria (AstraZeneca) may not have optimal protection until 15 days after the second dose of vaccine, recipients of the Moderna vaccine may not have optimal protection until 14 days after the second dose of vaccine, and recipients of the Comirnaty (Pfizer/BioNTech) vaccine may not have optional protection until 7 days after the second dose of vaccine (35). It's generally accepted that SARS-CoV-2 vaccine recipients may not have optimal protection until ≥15 days after the second vaccine dose (16). For the purposes of this study, a participant was considered fully vaccinated at ≥14 days after receipt of the second dose of vaccination, in line with Irish guidelines (35). A participant was considered partially vaccinated ≥14 days after receipt of the first dose of vaccination (35,36). A participant was considered to have started a vaccination course once one dose of vaccine had been received at any stage prior to the study.

Laboratory Methods

All samples were tested using the Roche Elecsys anti-SARS-CoV-2 and the Roche Elecsys anti-SARS-CoV-2 S immunoassays detecting total antibodies (including IgG) to the nucleocapsid and spike proteins of the SARS-CoV-2 virus, respectively (37). Thresholds for positive results were as per manufacturers' guidelines (37) (38). Participants with detectable anti-N antibodies were presumed to have had previous natural infection. Participants with detectable anti-S antibodies, and no reported history of COVID-19 vaccination were also presumed to have had natural infection. Participants with detectable anti-S antibodies and a history of COVID-19 vaccination were presumed to have these anti-S antibodies in response to vaccination.

Statistical analysis

Frequencies and percentages were calculated for sociodemographic, epidemiological, and clinical characteristics. Participants were deemed seropositive (i.e. assumed to have had past infection with SARS-CoV-2) if they had detectable anti- N antibodies, or if they had detectable anti-S antibodies but had not been previously vaccinated. Characteristics of those who were seropositive were compared to those who were not seropositive, using the chi-square test. Univariate logistic regression was used to calculate relative risks along with their 95% confidence intervals to assess the association between characteristics of the study participants and SARS-CoV-2 seropositivity. Multivariable regression analysis was conducted to control for negative and positive confounding and to calculate adjusted relative risks (aRR). No explicit finite population correction or reweighting was carried out. All analysis was conducted in Stata 15.1 (StataCorp LCC. 2019. College Station, TX 77845: USA).

Ethical approval and Funding

Ethical approval was obtained from the National Research Ethics Committee (NREC) for COVID-19, Study Number 20-NREC. COV-101 (33). Ethical approval was revised in February 2021 to allow the study to take into account the rollout of COVID-19 vaccination in Ireland – this involved changes to the study questionnaire, and the addition of anti-spike antibody testing on all samples. This work was supported financially by the Irish Health Service Executive COVID-19 budget.

Results

1. SARS-CoV-2 seroprevalence (past infection)

Participation rates and demographics

All staff working in SJH and UHG (9,038 people) were invited to participate in the study. In total 5,108 (57%) blood samples were collected and of those 99% (n=5,085) had a matching questionnaire (questionnaires were deemed to be completed if at least 80% of the questions were answered). In SJH, 63% (2945/4692) of staff participated in both questionnaire and blood sample. In UHG, 49% (2140/4346) of staff participated in both questionnaire and blood sample.

Age and sex of participants were similar in both hospitals (Table 1a). On combined hospital data, 78% of participants were female. Median age was 40 years (IQR 30-49); 5.5% of participants were aged 60 or older. By ethnicity; 75% of participants were white Irish (71% in SJH and 80% in UHG), 12% were Asian (16% in SJH and 6.0% in UHG), and 2.3% were of African or any other black background (2.3% in SJH and 2.2% in UHG). Ninety-one percent of participants lived with other people and 31% lived with other HCW. The highest proportion (37%) of participants were nursing staff, 21% were allied healthcare staff, 14% medical/dental staff (12% in SJH and 17% in UHG), 13% administration staff, 7.2% general support staff (8.3% SJH and 5.7% UHG), 5.7% health care assistants (HCA) and 2.1% other healthcare staff.

Participation by staff grouping was similar in both hospitals; allied health staff had the highest response rate in both hospitals (82% and 67% participation in SJH and UHG respectively) and HCAs had the lowest response rate in both hospitals (42% and 35% participation in SJH and UHG respectively). Participants broadly reflected the HCW

breakdown of the staff in both hospitals, with allied health staff slightly over-represented (+5.1%), and HCAs, administration staff, medical/dental staff and nursing/midwifery staff slightly under-represented (for details on participation by HCW role see Table A-D, Annex).

Table 1a Participant characteristics by hospital and total number of participants, PRECISE 2, April 2021

Participant characteristics		St James's Hospital (N=2,945)		University Hospital Galway (N=2,140)		P-value*	Total (N=5,085)	
		n	**%**	**n**	**%**		**N**	**%**
Age groups	18-29	653	22	455	21	0.431	1,108	22
	30-39	765	26	565	26		1,330	26
	40-49	811	28	603	28		1,414	28
	50-59	565	19	386	18		951	19
	≥60	151	5.1	131	6.1		282	5.5
Sex	Female	2,278	77	1,681	79	0.309	3,959	78
	Male	667	23	459	21		1,126	22
Ethnicity	Irish (white)	2,091	71	1,707	80	<0.001	3,798	75
	Any other white background	257	8.7	219	10		476	9.4
	Asian background	470	16	129	6.0		599	12
	African/other black background	69	2.3	48	2.2		117	2.3
	Other	58	2.0	37	1.7		95	1.9
Country of birth	Ireland	2,025	69	1605	75	<0.001	3,630	71
	United Kingdom	134	4.6	161	7.5		295	5.8
	India	225	7.6	68	3.2		293	5.8
	Philippines	198	6.7	16	0.7		214	4.2
	Poland	26	0.9	59	2.8		85	1.7
	USA	21	0.7	34	1.6		55	1.1
	Other	316	11	197	9.2		513	10
Education	Primary	20	0.7	2	0.1	<0.001	22	0.4
	Secondary	409	14	200	9.3		609	12
	Third level	1,280	43	964	45		2,244	44
	Post-graduate	1,236	42	974	46		2,210	43
Role	Admin	403	14	273	13	<0.001	676	13
	Medical/dental	357	12	356	17		713	14
	Nursing/ midwifery	1097	37	794	37		1,891	37
	Allied health	612	21	432	20		1,044	21
	General support	243	8.3	122	5.7		365	7.2
	Health care assistant	179	6.1	112	5.2		291	5.7
	Other	54	1.8	51	2.4		105	2.1
Lives with	Alone	270	9.2	194	9.1	0.603	464	9.1
	With others	2,667	90.	1,943	90.8		4,610	90.7
	Missing	8	0.3	3	0.1		11	0.2
Lives with HCW	Yes	928	32	643	30	0.284	1,571	31
	No	1,964	67	1,448	68		3412	67
	Missing	53	1.8	49	2.3		102	2.0

*Calculated using the chi-square test

Previous exposure, symptoms and testing

COVID-19 related characteristics of participants differed by hospital (Table 1b). Overall, 22% of participating HCWs reported that their main type of daily work involved contact with patients with suspected or confirmed COVID-19 (25% of participants in SJH and 19% of participants in UHG), a further 49% reported that their main type of daily work involved contact with patients without suspected COVID-19 infection (46% in SJH and 53% in UHG), and 28% had little or no patient contact (29% in SJH and 28% in UHG). Symptoms consistent with COVID-19 had occurred at some stage in 47% of SJH staff and 37% of UHG staff. Among the 43% of participants (in both hospitals) who had symptoms at some stage; 30% of these were mild symptoms (equal to a cold or less), 12% were significant symptoms (similar to influenza, bed-ridden), and 0.9% were severe symptoms (requiring hospitalisation). A higher proportion of participants in SJH experienced significant symptoms (14%) when compared to UHG (9.4%).

In terms of self-reported previous laboratory-confirmed COVID-19 infection, 18% of participants in SJH and 14% of participants in UHG reported that they had previously tested positive by PCR. Among those who were previously PCR positive, 21% did not have symptoms at the time of PCR testing (18% in SJH and 26% in UHG).

Table 1b COVID-19 related characteristics by hospital and total number of participants, PRECISE 2, April 2021

Participant characteristics		St James's Hospital		University Hospital Galway		P-value*	Total **(N=5,085)**	
		(N=2,945)		**(N=2,140)**				
				n %	**n %**	**N**	**%**	
Daily contact with COVID-19 patients	Contact with	726	25	410	19	<0.001	1136	22
	Contact with patients without COVID-19	1,362	46	1,138	53		2,500	49
	No patient contact	857	29	592	28		1,449	28
Previous COVID-19 symptoms	No symptoms	1571	53	1342	63	<0.001	2913	57
	Had symptoms	1374	47	797	37		2171	43
	Missing	0	0.0	1	0.0		1	0.0
Severity of symptoms	No symptoms	1571	53	1342	63	<0.001	2913	57
	Mild symptoms	932	32	570	27		1502	30
	Significant symptoms	420	14	201	9.4		621	12
	Severe (hospitalised)	21	0.7	26	1.2		47	0.9
	Type of symptoms	1	0.0	0	0.0		1	0.0
	Missing	0	0.0	1	0.0		1	0.0
Previous positive COVID-19 PCR test	No	2427	82	1846	86	<0.001	4273	84
	Yes	518	18	294	14		812	16
Symptoms at time of previous positive PCR test	No	95	18	77	26	<0.001	172	21
	Yes	423	82	217	74		640	79
Severity of symptoms at time of PCR test	No symptoms	95	18	77	26	<0.001	172	21
	Mild symptoms	162	31	94	32		256	32
	Significant symptoms	248	48	103	35		351	43
	Severe (hospitalised)	12	2.3	20	6.8		32	3.9
	Missing	1	0.2	0	0.0		1	0.1

*Calculated using the chi-square test

SARS-CoV-2 seroprevalence by site

In SJH, seroprevalence among participants was 21%. Seroprevalence was 27% in those who reported having daily contact with COVID-19 patients, 22% in those who reported having daily contact with patients without suspected COVID-19 infection, and 16% in those who had little or no patient contact. In UHG, seroprevalence among participants was 13%. Seroprevalence was 17% in those who reported having daily contact with COVID-19 patients, 15% in those who reported having daily contact with patients without suspected COVID-19 infection, and 6.1% in those who had little or no patient contact.

Seroprevalence by HCW role

By professional subgroup in SJH, seroprevalence was highest among HCAs (39%), followed by nursing/midwifery staff (26%), general support staff (25%), administrative staff (16%), medical/dental staff (15%), allied health professionals (15%), and other healthcare staff (7.4%) (other healthcare staff had small numbers and included those working in education and research, videographers, undefined technicians and others who did not further define their role). Details of seroprevalence (and 95% Confidence Intervals (CI)) by sociodemographic characteristics and by COVID-19 characteristics are shown in table 2a and 2b respectively.

By professional subgroup in UHG, seroprevalence was highest among HCAs (21%), followed by medical/dental staff (17%), general support staff (17%), nursing/midwifery staff (14%), other healthcare staff (12%), administrative staff (7.7%), and allied health professionals (6.7%). Details of seroprevalence and 95% CIs by sociodemographic characteristics and by COVID-19 characteristics are shown in table 2c and 2d respectively.

The combined data for both hospitals showed that HCAs were significantly more likely than other professional groups to be seropositive, with 32% of those participating in the study being seropositive. Seroprevalence in general support staff was second highest at 22%, followed by nursing/midwifery (21%). Prevalence of SARS-CoV-2 seropositivity for both hospitals combined, by participant characteristics and by COVID-19 characteristics are shown in Table 2e and 2f, Annex. The term ‘general support staff’ includes a range of hospital staff roles; by general support role, seroprevalence was highest among catering staff (28%) and domestic/cleaning staff (22%); a detailed breakdown by hospital is shown in Table 2g, Annex.

Table 2a Prevalence of SARS-CoV-2 seropositivity by participant characteristics, St James's Hospital, PRECISE 2, April 2021

Participant characteristics		Total	SARS-CoV-2 seropositive		
		N	**n**	**% (95% CI)**	**p-value***
Overall		2945	623	21 (20 - 23)	-
Age groups (years)	18-29	653	159	24 (21 - 28)	0.184
	30-39	765	154	20 (17 - 23)	
	40-49	811	157	19 (17 - 22)	
	50-59	565	119	21 (18 - 25)	
	Over 60	151	34	23 (16 - 30)	
Sex	Female	2,278	471	21 (19 - 22)	0.240
	Male	667	152	23 (20 - 26)	
Ethnicity	Irish (white)	2,091	401	19 (18 - 21)	<0.001
	Any other white background	257	56	22 (17 - 27)	
	Asian background	470	122	26 (22 - 30)	
	African or any other black background	69	29	42 (30 - 55)	
	Other	58	15	26 (15 - 39)	
Country of birth	Ireland	2,025	386	19 (17 - 21)	0.001
	United Kingdom	134	25	19 (12 - 26)	
	India	225	60	27 (21 - 33)	
	Philippines	198	53	27 (21 - 34)	
	Poland	26	8	31 (14 - 52)	
	USA	21	4	19 (5.4 - 42)	
	Romania	40	12	30 (17 - 47)	
	Nigeria	25	18	72 (51 – 88)	
	Other	251	57	23 (18 - 28)	
Education	Primary	20	7	35 (15 - 59)	<0.001
	Secondary	409	105	26 (22 - 30)	
	Third level	1,280	301	24 (21 - 26)	
	Post-graduate	1,236	210	17 (15 - 19)	
Role	Admin	403	64	16 (12 - 20)	<0.001
	Medical/dental	357	55	15 (12 - 20)	
	Nursing/ midwifery	1097	281	26 (23 - 28)	
	Allied health	612	89	15 (12 - 18)	
	General support	243	60	25 (19 - 31)	
	Health care assistant	179	70	39 (32 - 47)	
	Other	54	4	7.4 (2.1 - 18)	
Lives with	Alone	270	42	16 (11 - 20)	0.019
	With others	2,667	578	22 (20 - 23)	
	Missing	8	3	38 (8.5 - 76)	
Lives with HCW	Yes	928	234	25 (22 - 28)	<.001
	No	1,964	376	19 (17 - 21)	
	Missing	53	13	25 (14 - 38)	

*Calculated using the Chi-square test

Table 2b Prevalence of SARS-CoV-2 seropositivity by COVID-19 related characteristics, St James's Hospital, PRECISE 2, April 2021

COVID-19 related characteristics		Total	SARS-CoV-2 seropositive		
		N	**n**	**% (95% CI)**	**p-value***
Daily contact with COVID-19 patients	Contact with COVID-19 patients	726	196	27 (24 - 30)	<0.001
	Contact with patients without COVID-	1,362	293	22 (19 - 24)	
	No patient contact	857	134	16 (13 - 18)	
Previous COVID-19 symptoms	No symptoms	1571	121	7.7 (6.4 - 9.1)	<0.001
	Had symptoms	1374	502	37 (34 - 39)	
	Missing	0	0	-	
Severity of symptoms	No symptoms	1571	121	7.7 (6.4 - 9.1)	<0.001
	Mild symptoms	932	228	24 (22 - 27)	
	Significant symptoms	420	262	62 (58 - 67)	
	Severe (hospitalised)	21	12	57 (34 - 78)	
	Missing	1	0	-	
Previous positive COVID-19 PCR test	No	2427	190	7.8 (6.8 - 9.0)	<0.001
	Yes	518	433	84 (80 - 87)	
Symptoms at time of previous positive PCR	No	95	51	54 (43 - 64)	<0.001
	Yes	423	382	90.3 (87 - 93.0)	
Severity of symptoms at time of PCR test	No symptoms	95	51	54 (43 - 64)	<0.001
	Mild symptoms	162	143	88 (82 - 92.8)	
	Significant symptoms	248	227	91.5 (87 - 94.7)	
	Severe (hospitalised)	12	12	100 (74 - 100)	
	Missing	1	0	-	

*Calculated using the Chi-square test

Table 2c Prevalence of SARS-CoV-2 seropositivity by participant characteristics, University Hospital Galway, PRECISE 2, April 2021

Participant characteristics		Total	SARS-CoV-2 seropositive		
		N	**n**	**% (95% CI)**	**p-value***
Overall		2140	275	13 (11 - 14)	-
Age groups (years)	18-29	455	90	20 (16 - 24)	<0.001
	30-39	565	84	15 (12 - 18)	
	40-49	603	51	8.5 (6.4 - 11)	
	50-59	386	39	10 (7.3 - 14)	
	Over 60	131	11	8.4 (4.3 - 15)	
Sex	Female	1,681	198	12 (10 - 13)	0.005
	Male	459	77	17 (13 - 21)	
Ethnicity	Irish (white)	1,707	194	11 (10 - 13)	0.002
	Any other white background	219	38	17 (13 - 23)	
	Asian background	129	26	20 (14 - 28)	
	African or any other black background	48	10	21 (10 - 35)	
	Other	37	7	19 (8.0 - 35)	
Country of birth	Ireland	1605	181	11 (10 - 13)	<0.001
	United Kingdom	161	19	12 (7.3 - 18)	
	India	68	16	24 (14 - 35)	
	Poland	59	12	20 (11 - 33)	
	USA	34	7	21 (8.7 - 38)	
	Philippines	16	1	6.3 (0.2 - 30)	
	Nigeria	10	1	10 (0.3 - 45)	
	Romania	5	3	60 (14 - 95)	
	Other	182	39	19 (13 - 36)	
Education	Primary	2	0	-	0.485
	Secondary	200	28	14 (10 - 20)	
	Third level	964	133	14 (12 - 16)	
	Post-graduate	974	114	12 (10 - 14)	
Role	Admin	273	21	7.7 (4.8 - 12)	<0.001
	Medical/dental	356	61	17 (13 - 21)	
	Nursing/ midwifery	794	114	14 (12 - 17)	
	Allied health	432	29	6.7 (4.5 - 9.5)	
	General support	122	21	17 (11 - 25)	
	Health care assistant	112	23	21 (13 - 29)	
	Other	51	6	12 (4.4 - 24)	
Lives with	Alone	194	19	10 (6.0 - 15)	0.180
	With others	1,943	256	13 (12 - 15)	
	Missing	3	0	-	
Lives with HCW	Yes	643	106	16 (14 - 20)	0.001
	No	1448	164	11 (10 - 13)	
	Missing	49	5	10 (3.4 - 22)	

*Calculated using the Chi-square test

Table 2d Prevalence of SARS-CoV-2 seropositivity by COVID-19 characteristics, University Hospital Galway, PRECISE 2, April 2021

COVID-19 related characteristics		Total	SARS-CoV-2 seropositive		
		N	**n**	**% (95% CI)**	**p-value***
Daily contact with COVID-19 patients	Contact with COVID-19 patients	410	69	17 (13 - 21)	<0.001
	Contact with patients without COVID-19	1,138	170	15 (13 - 17)	
	No patient contact	592	36	6.1 (4.3 - 8.3)	
Previous COVID-19 symptoms	No symptoms	1342	48	3.6 (2.6 - 4.7)	<0.001
	Had symptoms	797	227	28 (25 - 32)	
	Missing	1	0	-	
Severity of symptoms	No symptoms	1342	48	3.6 (2.6 - 4.7)	<0.001
	Mild symptoms	570	107	19 (16 - 22)	
	Significant symptoms	201	102	51 (48 - 58)	
	Severe (hospitalised)	26	18	69 (44 - 86)	
	Missing	0	0	-	
Previous positive COVID-19 PCR	No	1846	45	2.4 (1.8 - 3.2)	<0.001
	Yes	294	230	78 (73 - 83)	
Symptoms at time of previous positive PCR	No	77	36	47 (35 - 58)	<0.001
	Yes	217	194	89 (85 - 93.2)	
Severity of symptoms at time of PCR test	No symptoms	77	36	47 (35 - 58)	<0.001
	Mild symptoms	94	83	88 (80 - 94.0)	
	Significant symptoms	103	93	90.3 (83 - 95.2)	
	Severe (hospitalised)	20	18	90.0 (68 - 99.0)	
	Missing	0	0	-	

*Calculated using the Chi-square test

Asymptomatic SARS-CoV-2 infection

The combined data for both hospitals shows that 19% (169/898) of seropositive participants had asymptomatic SARS-CoV-2 infection at some stage (i.e. they were seropositive in this study but reported never having symptoms of COVID-19). Asymptomatic infection by ethnic group was highest among those of African or other black background (36%), followed by white Irish background (20%), other white background (19%), Asian (12%), and other background (9.1%), but confidence intervals overlap. The breakdown was similar by hospital location; breakdown of asymptomatic infection by hospital and HCW role is shown in Table 2h, Annex.

Among those that had asymptomatic infection (antibody positive and never had symptoms), 33% (55/169) had been previously diagnosed positive by PCR, and 67% (114/169) had not. Among these 114 with previously undiagnosed asymptomatic infection, 73% (83/114) were white Irish, 12% (14/114) were of other white background, 8.8% (10/114) Asian, 4.4% (5/114) African or other black background, and 1.8% (2/114) other background.

Seropositivity by previous diagnosis and symptoms

Sixteen percent (812/5085) of participants reported having had a PCR-confirmed infection with COVID-19 at some stage. Of these, 82% (663/812) were seropositive and 18% (149/812) were seronegative, Table 2f. This meant that 3.6% (149/4187) of all participants who were seronegative had previously had a PCR-confirmed infection with COVID-19. Breakdown by hospital is shown in Tables 2b and 2d. The majority of those reporting a previous confirmed COVID-19 infection were symptomatic at the time of their positive PCR (640/812; 79%), Table 2f. Seroprevalence among those that were symptomatic (576/640; 90%) was significantly higher than seroprevalence among those who were asymptomatic at the time of their confirmed COVID-19 infection (87/172; 51%), ($p<.001$).

In total, 29% (1480/5085) of participants reported that they had experienced symptoms at some stage but had never had a positive PCR test. Of these, 121/1480 (8.2%) were seropositive. Thirty-two of these 121 participants who had never been tested by PCR reported significant COVID-19 like symptoms at some stage.

Undiagnosed SARS-CoV-2 infection

In total, 898 participants (623 in SJH and 275 in UHG) were seropositive. Of these, 235/898 (26%) had never been diagnosed with COVID-19 infection, representing 4.6% (235/5085) of the total study population. The majority of these undiagnosed infections were SJH employees

(190/235; 81%). In SJH, 30% (190/623) of those who were seropositive had never previously been diagnosed, and in UHG 16% (45/275) of those who were seropositive had never previously been diagnosed.

Just over half of those with undiagnosed infection (121/235; 51%) had experienced COVID-19 like symptoms at some stage; of those 74% (89/121) had experienced mild symptoms and 26% (32/121) had experienced significant symptoms. This proportion of undiagnosed participants who experienced only mild symptoms (89/121, 74%) was much higher than the proportion of diagnosed participants who experienced only mild symptoms (226/576; 34%) (Table E, Annex).

By ethnicity, the highest proportion (160/235; 68%) of HCWs with undiagnosed infection was white Irish, 14% (33/235) were Asian, 12% (28/235) were of other white background, 3% (6/235) were of African or other black background, and 3% (8/235) were of other ethnic background. Most participants with undiagnosed infection reported daily patient contact in their role (192/235; 82%); 36% (84/192) had daily contact with COVID-19 patients and 46% (108/192) had daily contact with patients without suspected COVID-19 infection. By professional role, 42% (98/235) of undiagnosed HCWs were nurses, 12% (28/235) were HCAs and 9% (20/235) were in medical/dental roles (of which 18 were doctors). The proportion of undiagnosed participants that were medical/dental professionals was higher in UHG (18%) than in SJH (6.3%). Detailed analysis of undiagnosed infection by HCW role and by hospital location is shown in Table 2i, Annex.

Risk factors for seropositivity

Characteristics of those participants who were seropositive compared with those who were seronegative for both hospitals combined are shown in Tables 2e and 2f (Annex). Those of male sex, and those in the 18-29-year age group had a higher seroprevalence; 20% of all participating males had detectable antibody versus 17% of females (p=.008), and 22% of all participants aged 18-29 were seropositive (p<.001). By ethnicity 33% of participants of African or other black background were seropositive, versus 16% of white Irish participants (p<.001). By country of birth, seroprevalence was highest in participants born in Nigeria (54%), Romania (33%), and India (26%), but it should be noted that there were a low number (<100) of participants born in either Nigeria or Romania. Seroprevalence decreased with increasing education level (from 32% for those with primary level education to 15% of those with post-graduate level education, p<.001). Seroprevalence was 32% for HCAs, 22% for general support staff, 21% for nurses, 16% for medical/dental staff, 13% for admin staff, 11% for allied health staff and 10% for other staff (p<.001). Eighteen percent of those living with others were seropositive, compared to 13% of those living alone (p=.008), and 22% of those living with other HCWs were seropositive compared with 16% of those not living with HCWs (p<.001). Twenty-three percent of those who had daily contact with COVID-19 patients were seropositive, compared to 19% of those who had daily contact with patients without COVID-19, and 12% of those who had little or no patient contact (p<.001).

By hospital, seroprevalence was higher in SJH (21%; 95% CI 20-23) when compared to UHG (13%; 95% CI 11-14) (p<.001). The characteristics of participants who were seropositive in each hospital are shown in Tables 2a-2d. The main differences in seropositivity between the two hospitals were for age, sex, education and living arrangements. For UHG, younger age groups had higher seropositivity (20% seropositivity among 18-29 year-olds versus 10% seropositivity among 50-59 year-olds, p<.001), but this

was not observed for SJH (Tables 2a and 2c). For UHG there was also higher seroprevalence amongst those of male sex (17% seropositivity among males versus 12% seropositivity among females, p=.005), but this difference was less pronounced for SJH. For SJH, seroprevalence decreased with increasing education level (p<.001), but this was not observed in UHG. The association between being seropositive and living arrangements was stronger in SJH compared to UHG; in SJH, 22% of participants that were living with other people were seropositive compared to 16% of participants that were living alone (p=.019). The association between seropositivity and living with other HCWs was strong in both hospitals. The differences in breakdown by professional subgroup are described above.

On multivariable analysis by hospital, in SJH the aRR of seropositivity was statistically significant for the following characteristics: being a healthcare assistant (aRR 1.9, 95% CI 1.4-2.6, p<.001), being a nurse (aRR 1.5, 95% CI 1.1-2.0, p=0.008), being of African or other black background (aRR 1.8, 95% CI 1.3-2.4, p<.001), secondary level education (aRR 1.5, 95% CI 1.2-1.9, p=0.002), and living with other HCW (aRR 1.2, 95% CI 1.0-1.4, p=0.011), see Table 3a.

In UHG, the aRR of seropositivity was statistically significant for the following characteristics: daily contact with COVID-19 patients (aRR 2.1, 95% CI 1.4-3.3, p=0.001), daily contact with patients without suspected or confirmed COVID-19 (aRR 1.9, 95% CI 1.3-2.9, p=0.001), being aged 18-29 years (aRR 1.7, 95% CI 1.2-2.4, p=0.004).

On multivariable analysis of the combined hospital data, the adjusted relative risk (aRR) of seropositivity was statistically significant for the following characteristics: working in SJH (aRR 1.5, 95% CI 1.3-1.8, p<.001), being a healthcare assistant (aRR 1.8, 95% CI 1.3-2.3,

p<.001), being of African or other black background (aRR 1.7, 95% CI 1.3-2.2, p<.001), secondary level education (aRR 1.4, 95% CI 1.1-1.8, p=0.002), being a nurse (aRR 1.4, 95% CI 1.0-1.8, p=0.022), daily contact with COVID-19 patients (aRR 1.4, 95% CI 1.1-1.7, p=0.002), daily contact with patients without suspected or confirmed COVID-19 (aRR 1.3, 95% CI 1.1-1.5, p=0.013), being 18-29 years of age (aRR 1.3, 95% CI 1.1-1.6, p=0.002), being male (aRR 1.2, 95% CI 1.0-1.4, p=0.016), and living with other HCW (aRR 1.2, 95% CI 1.0-1.4, p=0.007), Table 3c.

Table 3a Association between risk factors and SARS-CoV-2 seropositivity, St James's Hospital, PRECISE 2, April 2021

Participant characteristics		Unadjusted relative risk (95% CI)	P-value	Adjusted relative risk (95% CI)	P-value
Age groups (years)	18-29	1.2 (0.9 - 1.4)	0.174	1.2 (1.0 - 1.5)	0.107
	30-39	1.0 (0.8 - 1.2)	0.677	1.0 (0.8 - 1.3)	0.909
	40-49	0.9 (0.7 - 1.1)	0.437	1.0 (0.8 - 1.2)	0.887
	50-59	Ref.		Ref.	
	Over 60	1.1 (0.8 - 1.5)	0.697	1.0 (0.8 - 1.5)	0.655
Sex	Female	Ref.		Ref.	
	Male	1.1 (0.9 - 1.3)	0.237	1.2 (1.0 - 1.4)	0.104
Ethnicity	Irish (white)	Ref.		Ref.	
	Any other white background	1.1 (0.9 - 1.5)	0.312	1.1 (0.8 - 1.4)	0.516
	Asian background	1.4 (1.1 - 1.6)	0.001	1.1 (0.9 - 1.3)	0.571
	African or other black background	**2.2 (1.6 - 2.9)**	**<0.001**	**1.8 (1.3 - 2.4)**	**<0.001**
	Other	1.3 (0.9 - 2.1)	0.187	1.3 (0.8 - 2.0)	0.249
Country of birth	Ireland	Ref.			not entered
	India	1.4 (1.1 - 1.8)	0.005		
	Philippines	1.4 (1.1 - 1.8)	0.007		
	United Kingdom	1.0 (0.7 - 1.4)	0.908		
	Poland	1.6 (0.9 - 2.9)	0.108		
	USA	1.0 (0.4 - 2.4)	0.999		
	Romania	1.6 (1.0 - 2.5)	0.065		
	Nigeria	3.8 (2.9 - 4.9)	<0.001		
	Other	1.2 (0.9 - 1.5)	0.162		
Education	Primary	2.1 (1.1 - 3.8)	0.020	1.6 (0.9 - 2.9)	0.115
	Secondary	**1.5 (1.2 - 1.9)**	**<0.001**	**1.5 (1.2 - 1.9)**	**0.002**
	Third level	1.4 (1.2 - 1.6)	<0.001	1.2 (1.0 - 1.4)	0.103
	Post-graduate	Ref.		Ref.	
Role	Admin	Ref.		Ref.	
	Doctor\Dental	1.0 (0.7 - 1.4)	0.857	0.9 (0.6 - 1.3)	0.673
	Nursing	**1.6 (1.3 - 2.1)**	**<0.001**	**1.5 (1.1 - 2.0)**	**0.008**
	HCA	**2.5 (1.8 - 3.3)**	**<0.001**	**1.9 (1.4 - 2.6)**	**<0.001**

	General support	1.6 (1.1 - 2.1)	0.006	1.3 (0.9 - 1.8)	0.152
	Allied HCW	0.9 (0.7 - 1.2)	0.559	0.9 (0.7 - 1.3)	0.754
	Other	0.5 (0.2 - 1.2)	0.123	0.4 (0.2 - 1.1)	0.093
Lives with	Alone	Ref.			not entered
	With others	1.4 (1.0 - 1.9)	0.024		
Lives with HCW	No	Ref.		Ref.	
	Yes	**1.3 (1.1 - 1.5)**	**<0.001**	**1.2 (1.0 - 1.4)**	**0.011**
Workplace exposure to COVID-19 patients	No patient contact	Ref.		Ref.	
	Daily contact with patients without COVID-19	1.4 (1.1 - 1.7)	0.001	1.2 (0.9 - 1.4)	0.270
	Daily contact with COVID-19 patients	1.7 (1.4 - 2.1)	<0.001	1.2 (1.0 - 1.5)	0.090
Previous COVID-19 like symptoms	No	Ref.			not entered
	Yes	4.7 (3.9 - 5.7)	<0.001		
Severity of symptoms	No symptoms	Ref.			not entered
	Mild symptoms	3.2 (2.6 - 3.9)	<0.001		
	Significant symptoms	8.1 (6.7 - 9.8)	<0.001		
	Severe symptoms (hospitalisation)	7.4 (4.9 - 11.2)	<0.001		

Table 3b Association between risk factors and SARS-CoV-2 seropositivity, University Hospital Galway, PRECISE 2, April 2021

Participant characteristics		Unadjusted relative risk (95% CI)	P-value	Adjusted relative risk (95% CI)	P-value
Age groups (years)	18-29	**2.0 (1.4 - 2.8)**	**<0.001**	**1.7 (1.2 - 2. 4)**	**0.004**
	30-39	1.5 (1.0 - 2.1)	0.034	1.3 (0.9 - 1.9)	0.120
	40-49	0.8 (0.6 - 1.2)	0.380	0.8 (0.5 - 1.2)	0.304
	50-59	Ref.		Ref.	
	Over 60	0.8 (0.4 - 1.6)	0.570	0.8 (0.4 - 1.5)	0.501
Sex	Female	Ref.		Ref.	
	Male	1.4 (1.1 - 1.8)	0.004	1.3 (1.0 - 1.7)	0.097
Ethnicity	Irish (white)	Ref.		Ref.	
	Any other white background	1.5 (1.1 - 2.1)	0.009	1.3 (1.0 - 1.7)	0.078
	Asian background	1.8 (1.2 - 2.6)	0.002	1.2 (0.8 - 1.8)	0.333
	African or other black background	1.8 (1.0 - 3.2)	0.036	1.3 (0.7 - 2.4)	0.388
	Other	1.7 (0.8 - 3.3)	0.142	1.4 (0.7 - 2.8)	0.328
Country of birth	Ireland	Ref.			not entered
	India	2.1 (1.3 - 3.3)	0.001		
	Philippines	0.6 (0.1 - 3.7)	0.543		
	United Kingdom	1.0 (0.7 - 1.6)	0.841		
	Poland	1.8 (1.1 - 3.0)	0.027		
	USA	1.8 (0.9 - 3.6)	0.080		
	Romania	5.3 (2.6 - 11)	<0.001		
	Nigeria	0.9 (0.1 - 5.7)	0.899		
	Other	1.7 (1.2 - 2.4)	0.001		
Education	Primary	-			not entered
	Secondary	1.2 (0.8 - 1.8)	0.361		
	Third level	1.2 (0.9 - 1.5)	0.168		
	Post-graduate				
Role	Admin	Ref.		Ref.	
	Doctor\Dental	2.2 (1.4 - 3.6)	0.001	0.9 (0.5 - 1.5)	0.660
	Nursing	1.9 (1.2 - 2.9)	0.006	1.0 (0.6 - 1.6)	0. 901
	HCA	2.7 (1.5 - 4.6)	<0.001	1.5 (0.8 - 2.7)	0.180
	General support	2.2 (1.3 - 3.9)	0.005	1.1 (0.6 - 2.1)	0.704

	Allied HCW	**0.9 (0.5 - 1.5)**	**0.622**	**0.6 (0.3 - 1.0)**	**0.053**
	Other	1.5 (0.6 - 3.6)	0.331	0.8 (0.3 - 1.8)	0.533
Lives with	Alone	Ref.			not entered
	With others	1.3 (0.9 - 2.1)	0.188		
Lives with HCW	No	Ref.		Ref.	
	Yes	1.5 (1.2 - 1.8)	0.001	1.1 (0.9 - 1.4)	0.317
Workplace exposure to COVID-19 patients	No patient contact	Ref.		Ref.	
	Daily contact with patients without COVID-19	**2.5 (1.7 - 3.5)**	**<0.001**	**1.9 (1.3 - 2.9)**	**0.001**
	Daily contact with COVID-19 patients	**2.8 (1.9 - 4.1)**	**<0.001**	**2.1 (1.4 - 3.3)**	**0.001**
Previous COVID-19 like symptoms	No	Ref.			not entered
	Yes	8 (5.9 - 10.7)	<0.001		
Severity of symptoms	No symptoms	Ref.			not entered
	Mild symptoms	5.2 (3.8 - 7.3)	<0.001		
	Significant symptoms	14.2 (10.4 - 19.3)	<0.001		
	Severe symptoms (hospitalisation)	19.4 (13.3 - 28.2)	<0.001		

Table 3c Association between risk factors and SARS-CoV-2 seropositivity, both hospitals, PRECISE 2, April 2021

Participant characteristics		**Unadjusted relative risk (95% CI)**	**P-value**	**Adjusted relative risk (95% CI)**	**P-value**
Hospital	Galway University Hospital	Ref.			
	St James's Hospital	**1.6 (1.4 - 1.9)**	**<0.001**	**1.5 (1.3 - 1.8)**	**<0.001**
Age groups (years)	18-29	**1.4 (1.1 - 1.6)**	**0.001**	**1.3 (1.1 - 1.6)**	**0.002**
	30-39	1.1 (0.9 - 1.3)	0.427	1.1 (0.9 - 1.3)	0.299
	40-49	0.9 (0.7 - 1.1)	0.209	1.0 (0.7 - 1.1)	0.569
	50-59	Ref.		Ref.	
	Over 60	1.0 (0.7 - 1.3)	0.794	1.0 (0.7 - 1.3)	0.948
Sex	Female	Ref.		Ref.	
	Male	**1.2 (1.1 - 1.4)**	**0.007**	**1.2 (1.0 - 1.4)**	**0.016**
Ethnicity	Irish (white)	Ref.		Ref.	
	Any other white background	1.3 (1.0 - 1.5)	0.020	1.2 (1.0 - 1.4)	0.120
	Asian background	1.6 (1.3 - 1.8)	<0.001	1.1 (0.9 - 1.3)	0.206
	African or other black background	**2.1 (1.6 - 2.8)**	**<0.001**	**1.7 (1.3 - 2.2)**	**<0.001**

	Other	1.5 (1.0 - 2.1)	<0.001	1.3 (0.9 - 1.9)	0.145
Country of birth	Ireland	Ref.			not entered
	India	1.7 (1.3 – 2.0)	<0.001		
	Philippines	1.6 (1.3 - 2.1)	<0.001		
	United Kingdom	1.0 (0.7 - 1.3)	0.749		
	Poland	1.5 (1.0 - 2.2)	0.040		
	USA	1.3 (0.8 - 2.2)	0.364		
	Romania	2.1 (1.4 - 3.2)	<0.001		
	Nigeria	3.5 (2.5 - 4.8)	<0.001		
	Other	1.4 (1.1 - 1.7)	0.002		
Education	Primary	2.2 (1.2 – 4.0)	0.014	1.6 (0.9 - 2.9)	0.138
	Secondary	**1.5 (1.2 - 1.8)**	**<0.001**	**1.4 (1.1 - 1.8)**	**0.002**
	Third level	1.3 (1.2 - 1.5)	<0.001	1.1 (1.0 - 1.3)	0.133
	Post-graduate	Ref.		Ref.	
Role	Admin	Ref.		Ref.	
	Doctor\Dental	1.3 (1.0 - 1.7)	0.051	1.0 (0.7 - 1.4)	0.973
	Nursing	1.7 (1.3 - 2.1)	<0.001	1.4 (1.0 - 1.8)	0.022
	HCA	**2.5 (2.0 - 3.3)**	**<0.001**	**1.8 (1.3 - 2.3)**	**<0.001**
	General support	1.8 (1.3 - 2.3)	<0.001	1.2 (0.9 - 1.7)	0.144
	Allied HCW	0.9 (0.7 - 1.2)	0.424	0.8 (0.6 - 1.1)	0.119
	Other	0.8 (0.4 - 1.4)	0.381	0.7 (0.3 - 1.2)	0.134
Lives with	Alone	Ref.			not entered
	With others	1.4 (1.1 - 1.8)	0.010		
Lives with HCW	No	Ref.		Ref.	
	Yes	**1.3 (1.2 - 1.5)**	**<0.001**	**1.2 (1.0 - 1.4)**	**0.007**
Workplace exposure to COVID-19 patients	No patient contact	Ref.		Ref.	
	Daily contact with patients without COVID-19	**1.6 (1.3 - 1.9)**	**<0.001**	**1.3 (1.1 - 1.5)**	**0.013**
	Daily contact with COVID-19 patients	**2.0 (1.7 - 2.4)**	**<0.001**	**1.4 (1.1 - 1.7)**	**0.002**
Previous COVID-19 like symptoms	No	Ref.			not entered
	Yes	5.8 (4.9 - 6.8)	<0.001		
Severity of symptoms	No symptoms	Ref.			not entered
	Mild symptoms	3.8 (3.2 - 4.6)	<0.001		
	Significant symptoms	10.1 (8.6 - 11.9)	<0.001		
	Severe symptoms (hospitalisation)	11.0 (8.5 - 14.3)	<0.001		

2. Antibody response to vaccination

In total, 95% (4854/5085) of participants had received at least one vaccine dose at the time of this study; 14% (724/5085) had received one dose only, 81% (4130/5085) had received two doses, and 4.5% (231/5085) had not received any vaccine doses. In SJH 78% (2290/2945) were fully vaccinated and 19% (546/2945) had received 1st dose of vaccination only, for a total of 96% (2836/2945) participants in SJH having started or completed vaccination. In UHG 86% (1840/2140) were fully vaccinated and 8.3% (178/2140) had received 1st dose vaccination only, for a total of 94% (2018/2140) of participants in UHG having received at least one dose of vaccine. The majority of partially vaccinated HCW (680/724) had received Vaxzevria vaccine; roll out of this vaccine was in February 2021 and therefore these participants were not yet due the second dose due to the longer dosing interval of 12 weeks. Vaccination uptake by ethnicity was similar, with 142/3661 (3.9%, 95% CI 3.3-4.6)) of White Irish participants being unvaccinated, compared to 30/571 (5.2%, 95% CI 3.7-7.4) of Asian participants and 7/110 (6.4%, 95% CI 3.1-13) of Black participants. The vaccines received are shown in Table 4.

Table 4. COVID-19 vaccination status and vaccine brand received by participants, both hospitals, April 2021, PRECISE 2

	Started or completed vaccination^ **n/N (%)**	**Fully vaccinated*** **n/N (%)**
Hospital data combined	**4854/5085 (95.5%)**	**4130/ 5085 (81%)**
	Pfizer 4156/5085 (82%)	Pfizer 4116/5085 (81%)
	Vaxzevria 686/5085 (9.5%)	Vaxzevria 6/5085 (0.1%)
	Moderna 8/5085 (0.2)	Moderna 4/5085 (0.08%)
	I don't know 6/5085 (0.1)	I don't know 2/5085 (0.04%)
SJH	**2836/2945 (96.3%)**	**2290/ 2945 (78%)**
	Pfizer 2305/ 2945 (78%)	Pfizer 2286/ 2945 (78%)
	Vaxzevria 526/2945 (18%)	Vaxzevria 3/2945 (0.1%)
	Moderna 4/2945 (0.1%)	Moderna 1/2945 (0.03%)
UHG	**2018/2140 (94.3%)**	**1840/ 2140 (86%)**
	Pfizer 1849/2140 (86%)	Pfizer 1830/2140 (86%)
	Vaxzevria 161/2140 (7.5%)	Vaxzevria 3/2140 (0.1%)
	Moderna 4/2140 (0.2%)	Moderna 3/2140 (0.1%)
	I don't know 2/2140 (0.09%)	I don't know 2/2140 (0.09%)

^defined as anyone who had received a first dose of vaccine at any stage prior to the study

*defined as ≥14 days after receipt of second dose of vaccine

All fully vaccinated participants (4130/4130, 100%) had detectable anti-S antibodies. Of those that had received one dose of vaccine only, 713/724 (98%) had detectable anti-S antibodies. Of the 724 that had received only one dose of vaccine, 716 of them had received their vaccine >14 days prior to blood sampling for our study, and 713/716 (99.6%) had detectable anti-S antibodies.

SARS-CoV-2 infection post vaccination

In total, 116 participants reported that they had PCR-confirmed SARS-CoV-2 infection since vaccination; of those 82/116 (71%) had received one vaccine dose only and 34/116 (29%) had received their second dose; 23/116 (20%) of these were fully vaccinated i.e. had received their second dose ≥ 15 days before their positive PCR, representing 0.6% (23/4130) of all participants that received two doses and 0.6% (23/4111) of fully vaccinated participants. There were 93 infections in partially vaccinated participants (received only 1 dose of the vaccine or had received their 2nd dose <15 days before their infection) representing 93/724 (13%; 95% CI 11 - 16) of partially vaccinated participants having had a PCR-confirmed infection post vaccination compared to 23/4111 (0.6%; 95% CI 0.4 - 0.8) of fully vaccinated participants (p-value= <.001 (chi-square)). All fully and partially vaccinated participants with breakthrough infection had anti-spike antibodies detected; 21/23 of those fully vaccinated had anti-spike detected at >250u/ml (the other two had antibody levels 133u/ml and 242u/ml respectively) and 88/93 of those partially vaccinated had anti-spike detected at >250u/ml (range of 81-202u/ml for the other 5/93).

Of the 23 breakthrough infections in fully vaccinated participants, all had received the Pfizer vaccine. (It is noted that this was the most commonly received vaccine as it was the first vaccine to be rolled out, and also that the vaccine schedule for the Pfizer vaccine meant that

the other vaccines would have less time for breakthrough cases in fully vaccinated recipients to be observed ie. the majority of those that received Vaxzevria vaccine had not yet received their second dose by the time of the study). The median interval between first and second vaccine dose was 21 days (as recommended before 18th January 2021). For those 23 participants, the median number of days between second vaccine dose and PCR positive test was 30 days (IQR 25-50 days). Five (22%) had symptoms at the time of the positive PCR test and 18 (78%) did not have symptoms. While all 23 participants had detectable anti-S antibodies as expected post vaccination, notably, only 6/23 (26%, 95%CI: 11-49) had detectable anti-N antibodies in response to their infection, compared to 663/812 (82%, 95%CI: 79-84, p-value= <.001 (Chi-squared) of all participants in the study with previous PCR-confirmed infection having detectable anti-N antibodies. For the 17 that were anti-N negative after their confirmed infection, the median number of days between PCR positivity and blood sample was 52 days (range 9-67). Characteristics of participants with breakthrough infection are shown in Table F annex. The majority (78%) were working in SJH, 65% were female and by age group the highest proportion (35%) was aged 40-49 years. By ethnicity, just over half (52%) were white Irish and 35% were Asian. Thirty-nine percent had daily contact with COVID-19 patients, and 57% lived with other HCWs.

PRECISE 1 and PRECISE 2 comparison

Comparison of participation rates and participant demographics

All staff working in SJH and UHG (9,038 people) were invited to participate in both PRECISE 1 (October 2020) and PRECISE 2 (April 2021). Overall, participation was lower in PRECISE 2 (5,085 participants) than in PRECISE 1 (5,787 participants) (1). In SJH, 63% (2945/4692) of staff participated in PRECISE 2; a slight decrease on 65% participation in

PRECISE 1, and in UHG, 49% (2140/4346) of staff participated in PRECISE 2, a considerable decrease on 63% participation in PRECISE 1. The decrease in participation rate in UHG was similar across professional subgroups. The distribution of participants in PRECISE 1 and 2 was similar by age group, sex, and education level. By ethnicity, a slightly higher proportion of participants in PRECISE 2 were Asian (12%) when compared to PRECISE 1 (10%). By professional subgroup a slightly higher proportion of participants were allied healthcare workers (19% in PRECISE 1 versus 21% in PRECISE 2; p=0.035), a slightly higher proportion were HCAs (5.7% in PRECISE 2 versus 4.9% in PRECISE 1, p=0.790), and a lower proportion were medical/dental professionals (14% in PRECISE 2 versus 17% in PRECISE 1; p<0.001). A significantly lower proportion of participants in PRECISE 2 had ever experienced symptoms consistent with COVID-19 (47% of participants in SJH, and 37% in UHG) when compared to participants in PRECISE 1 (55% of participants in SJH, and 45% in UHG), (p<.001) (1). In terms of self-reported previous laboratory-confirmed COVID-19 infection, a significantly higher proportion of participants in PRECISE 2 reported having previously tested positive by PCR (18% of participants in SJH, and 14% in UHG), compared to PRECISE 1 (9.6% of participants in SJH, and 2.7% in UHG) (p<.001). (39).

Comparison of crude seroprevalence

A comparison of crude seroprevalence in PRECISE 1 (October 2020) and in PRECISE 2 (April 2021) by participant characteristics and by hospital is shown in Table 5. In SJH, the seroprevalence significantly increased from 15% in PRECISE 1 to 21% in PRECISE 2 (p<.001), and in UHG the seroprevalence significantly increased from 4.1% in PRECISE 1 to 13% in PRECISE 2 (p<.001). For both hospitals combined, seroprevalence increased from 10% in PRECISE 1 to 18% in PRECISE 2. For SJH by ethnic group, the increase in

seroprevalence was most pronounced for HCWs of African or other black background (from 23% in PRECISE 1 to 42% in PRECISE 2; p=0.020). Increase in seroprevalence in SJH was also significant for those of white Irish ethnicity (from 13% to 19%; p<.001) but the increase was not significant for HCWs of Asian ethnicity. By education level in SJH, increase in seroprevalence was highest for HCWs with primary education (from 15% in PRECISE 1 to 35% in PRECISE 2) but this increase was not significant due to low numbers of participants in this group. The increase was also high for those of secondary level education and it was significant (from 13% to 26%; p<.001). By professional subgroup in SJH, increase in seroprevalence was highest for general support staff (from 12% in PRECISE 1 to 25% in PRECISE 2; p<.001) and for HCAs (from 27% in PRECISE 1 to 39% in PRECISE 2; p=0.017). For UHG by ethnic group, the increase in seroprevalence was also most pronounced for HCWs of African or other black background (from 2.1% in PRECISE 1 to 21% in PRECISE 2; p=0.004). Increase in seroprevalence among HCWs of Asian ethnicity was significant (from 7.1% to 20%; p<.001) as was the increase among those of White Irish ethnicity (from 3.7% to 11%; p<.001). By professional subgroup in UHG, increase in seroprevalence was also highest for general support staff (from 1.7% in PRECISE 1 to 17% in PRECISE 2; p<.001) and for HCAs (from 6.2% in PRECISE 1 to 21% in PRECISE 2; p=0.001). By age group in UHG, the seroprevalence increased from 4.7% in PRECISE 1 to 20% in PRECISE 2 for younger HCWs aged 18-29 years (p<.001), (for SJH a small increase was observed for this age group but it was not significant).

For both hospitals combined by ethnic group, the increase in seroprevalence was most pronounced for HCWs of African or other black background (from 14% in PRECISE 1 to 33% in PRECISE 2; p=0.001). By education level, increase in seroprevalence was highest for HCWs with primary education (from 14% in PRECISE 1 to 32% in PRECISE 2) but was not

significant due to low numbers in this subgroup (p=0.121). For those of secondary education the increase was also high (from 8.9% to 22%) and it was significant (p<0.001). By professional subgroup, increase in seroprevalence was highest for general support staff (from 7.6% in PRECISE 1 to 22% in PRECISE 2; p<.001) and for HCAs (from 18% in PRECISE 1 to 32% in PRECISE 2; p<.001).

Change in Antibody Response over time (six-months) from PRECISE 1 to PRECISE 2

In total, 3,313 participants were common to both PRECISE 1 and 2. For the purposes of this part of the study, to facilitate direct comparison of individuals who participated in both studies, antibody positivity was defined as a detectable antibody on the Roche Elecsys anti-N total antibody assay, which was used in both studies. This excluded 16 participants who participated both times and had detectable anti-N antibodies on the Abbott Architect IgG assay which was also used in PRECISE 1 but not used in PRECISE 2. (These 16 participants did not have detectable anti-N antibodies on the Roche assay in PRECISE 1).

In total, 17.9% (595/3313) of matched qualifying participants were ever seropositive in PRECISE 1 or 2; 10.9% (360/3313) were positive in PRECISE 1, 16.9% (560/3313) were positive in PRECISE 2, and 9.8% (325/3313) were seropositive in both PRECISE 1 and 2. Of those participants who took part in both phases and were antibody positive in PRECISE 1 (n=360), 90% (325/360) remained antibody positive. Among the 3,313, 9.7% (35/360) who were previously seropositive became seronegative (i.e. they seroreverted), and 7.9% (235/2953) who were previously seronegative became seropositive. There were no participant characteristics that were significantly associated with seroreversion, further detail on the longitudinal change in antibody response is included in the addendum to this report (page 74 – 82).

Table 5 Comparison of SARS-CoV-2 seroprevalence October 2020 and April 2021, by hospital

Participant characteristics		St James's Hospital			University Hospital Galway			Both hospitals		
		% Oct -20	% Apr -21	% change	% Oct -20	% Apr -21	% change	% Oct -20	% Apr -21	% change
Overall seroprevalence		15	21	6.2	4.1	13	8.8	10	18	7.7
Age groups (years)	18-29	20	24	4.3	4.7	20	15.1	13	22	9.5
	30-39	15	20	5.1	6	15	8.9	10	18	7.9
	40-49	13	19	6.4	3.5	8.5	5.0	8.2	15	6.5
	50-59	13	21	8.1	1.5	10	8.6	7.7	17	8.9
	Over 60	17	23	5.5	2.7	8.4	5.7	9.9	16	6.1
Sex	Female	15	21	5.7	3.5	12	8.3	9.4	17	7.5
	Male	16	23	6.8	6.3	17	10.5	12	20	8.3
Ethnicity	Irish (white)	13	19	6.2	3.7	11	7.7	8.6	16	7.1
	Any other white background	17	22	4.8	6.3	17	11.1	11	20	8.7
	Asian background	24	26	2.0	7.1	20	13.1	19	25	5.7
	African or any other black background	23	42	19	2.1	21	18.7	14	33	19
	Other	13	26	13	-	19	-	6.9	23	16
Country of birth	Ireland	13	19	6.1	3.9	11	7.4	8.7	16	6.9
	United Kingdom	16	19	2.7	3.7	12	8.1	9.3	15	5.6
	India	23	27	3.7	8.2	24	15.3	18	26	7.9
	Philippines	27	27	-0.2	8.0	6.3	-1.8	25	25	0.2
	Poland	29	31	1.8	6.3	20	14	14	24	9.5
	USA	14	19	5.0	-	21	-	5.0	20	15
	Other	16	28	12	4	28	23.5	10	25	15
Education	Primary	15	35	20	0.0	0.0	0.0	14	32	18
	Secondary	13	26	13	3.0	14	11	8.9	22	13
	Third level	18	24	5.5	4.3	14	9.5	11	19	8.3
	Post-graduate	14	17	3.0	4.1	12	7.6	9.0	15	5.7
Role	Admin	10	16	5.9	1.2	7.7	6.5	6.0	13	6.6
	Medical/dental	14	15	1.4	6.9	17	10.2	10	16	6.3
	Nursing/ midwifery	21	26	4.6	4.7	14	9.7	13	21	7.9
	Allied health	10	15	4.5	2.5	6.7	4.2	6.7	11	4.6
	General support	12	25	13	1.7	17	15.5	7.6	22	15
	Health care assistant	27	39	12	6.2	21	14.3	18	32	14
	Other	11	7.4	-3.6	1.4	12	10.4	5.5	9.5	4.0
Lives with	Alone	8.2	16	7.4	3.1	10	6.7	5.9	13	7.2
	With others	16	22	5.7	4.2	13	9.0	10	18	8.1
	Missing	11	38	27	-	-	-	9.1	27	18
Lives with HCW	Yes	21	25	4.2	4.9	16	11.6	13	22	8.6
	No	13	19	6.0	3.8	11	7.5	8.5	16	7.3
	Missing	17	25	8.0	2.1	10	8.1	9.9	18	7.7
Daily contact with COVID-	Contact with COVID-19 patients	21	27	6.0	7.1	17	9.7	15	23	8.3
	Contact with patients without COVID-19	17	22	4.5	4.6	15	10.3	11	19	7.5

19 patients	No patient contact	9.5	16	6.1	1.3	6.1	4.8	5.9	12	5.8
Previous COVID-19 symptoms	No symptoms	5.8	7.7	1.9	1.3	3.6	2.3	3.2	5.8	2.6
	Had symptoms	23	37	14	7.5	28	21	17	34	17
Previous positive COVID-19 PCR test	No	6.8	7.8	1.0	1.5	2.4	0.9	4.2	5.5	1.3
	Yes	94.9	84	-11	97.3	78	-19.1	95.4	82	-14

Discussion

Participation and demographics

Our participants were similar in age and sex to those in other European studies (40) (41) (42). The participation rate was slightly lower for PRECISE 2 compared to PRECISE 1 (56% vs 64%). Overall, however, this is still a good uptake rate for an institutional opt-in study, comparable to other European studies (43) and included representation from all HCW groups, including the traditionally harder-to-reach groups such as general support staff and healthcare assistants, who may not engage as frequently with hospital communications platforms. Importantly, representation was similar across staff roles for PRECISE 1 and PRECISE 2, and overall participant demographics were similar in both studies, and therefore the data are likely to be comparable.

Overall seroprevalence

The overall seroprevalence of antibodies to SARS-CoV-2 in SJH rose from 15% in October 2020 to 21% in April 2021. The overall seroprevalence of antibodies to SARS-CoV-2 in UHG rose from 4.1% in October 2020 to 13% in April 2021. The combined overall seroprevalence for the two hospitals increased from 10% in October 2020 to 18% in April 2021. To the best of our knowledge there are no published studies evaluating SARS-CoV-2 seroprevalence in HCW in Europe in 2021.

In terms of the difference in seroprevalence between the two hospitals, we believe this to be related to local community incidence, to social and demographic factors, and to local work practices. The difference in seroprevalence between the two sites primarily reflects the difference in community incidence, with a corresponding higher seroprevalence seen in the

staff SJH, in the more densely populated capital city of Dublin, which has had higher community incidence throughout the pandemic thus far. Other studies have also shown community incidence to be one of the main factors impacting risk to HCW (44) (45). The rise in seroprevalence at both sites reflects the magnitude of the third wave of the pandemic at both sites. The relatively higher increase in seroprevalence in UHG compared to SJH likely reflects the fact that the community incidence in the Galway area approached that of the Dublin incidence during this third COVID-19 wave (30). A higher community incidence means that HCW are more likely to be exposed by the nature of their work which involves direct contact with other people, both patients and other HCW. While this risk disproportionately affected those with closer patient contact, the risk to HCW was higher than in the community, even for those who reported little or no patient contact.

The difference in overall seroprevalence was also likely to have been impacted by differences in hospital infrastructure, work-practices, bed-flow management, and the differing demographic and social factors by HCW role at each site. Broad work-place practices in both hospitals have been similar throughout the pandemic, including ward-based medical teams and universal use of face-masks. There were no issues with personal protective equipment (PPE) availability in either of the hospitals involved in our study at any stage thus far during the pandemic, and where staff were re-deployed to improve the hospital's capacity to deal with the outbreak, staff were not deployed to areas that would have been outside of their scope of practice, and all staff had training on the correct use of PPE. Both hospitals experienced multiple outbreaks during the 3rd wave of the pandemic, however the absence of real time genomic sequencing precludes identifying the role of hospital outbreaks in influencing the overall seroprevalence. It is also difficult to identify the contribution of the workplace versus the community/ household/ social factors to the attributable risk to HCW. It

is likely that many of these transmissions took place in the household, where higher attack rates are seen (46). It is also unclear as to the timing of arrival of different VOCs to each location, and the potential impact of this on changes in overall seroprevalence.

The overall seroprevalence was higher than the European average of 8.5% in a recently published meta-analysis (47), however this meta-analysis only took into account studies published up until August 2020. Individual studies across Europe in the first year of the pandemic showed a wide range of SARS-CoV-2 seroprevalence among HCW (1-45%) (40) (42) (48) (49) (50) (51). A recently published large study in Italian showed a seroprevalence of 12% in HCW, however the serological testing was conducted in April and May 2020 (43). Assumably the seroprevalence amongst HCW has risen across the rest of Europe since then, as our study shows it has in Ireland, however there are no published data for comparison.

Our study compared seroprevalence among the same HCW group at two points in time six months apart. A German study evaluated seroprevalence at 3 points in time, all in 2020, and found low seroprevalence among HCW at all three points in time (52). A Japanese study found much lower seroprevalence rates both before and after their second wave of the pandemic (<1% at both points in time, also both in 2020) (53).

Seroprevalence by role and type of patient contact

Daily contact with patients with known/suspected COVID-19 infection was associated with higher seroprevalence, followed by daily contact with patients without known or suspected COVID-19 infection. Having little or no patient contact carried the lowest seroprevalence. This reflected the findings of PRECISE 1 and has also been shown by other studies (54) (55) (56). In terms of working role, being a nurse or a HCA carried a higher aRR, likely also reflecting the close patient contact involved in performing these roles. The highest

seroprevalence was seen amongst HCAs; this was also a key finding of PRECISE 1, and this seroprevalence almost doubled over the six months between PRECISE 1 and 2. This finding has also been shown in other large European studies (43).

The seroprevalence among general support staff (which includes domestic and catering staff, maintenance, security and porters) trebled from PRECISE 1 to PRECISE 2, giving them the second highest seroprevalence of any working role in PRECISE 2. This increase was in both locations and was across all groups in this category (Table 2f, Annex). This was possibly related to outbreaks amongst these staff groups, though it was not clear whether these outbreaks were related to the workplace or not. There may be improper compliance with use of PPE, and fatigue with ICP as the pandemic has progressed. There are likely to also be other social factors involved that our study was not designed to assess.

The seroprevalence amongst medical staff showed one of the largest increases in UHG (from 6.9% to 17%) (Table 5). This may be related to social practices; many doctors working in UHG are not from Galway, and live and socialise together (in UHG 53% of doctors reported living with other HCW compared to 43% in SJH). In SJH, the smallest relative increase between PRECISE 1 and PRECISE 2 (from 14% to 15%) was amongst the medical staff. This resulted in medical staff having the joined-lowest seroprevalence of any role group in SJH by April 2021. Although the overall uptake among medical staff was similar to PRECISE 1, including of those who were seropositive in PRECISE 1, it is possible that medical staff who knew they had already had COVID-19 infection were less interested in participating in the study and availing of serology testing. Other studies have shown that medical staff are more likely to get vaccinated promptly against other infectious diseases (57), including influenza; occupational health data from SJH in 2019 showed that 60% of doctors received the influenza vaccine compared to 23% of nursing staff. In our study, 93%

of doctors had completed vaccination and 99% (684/692) had started vaccination, compared to only 81% of all staff having completed vaccination by the time of the study. This may indicate that doctors sought vaccination quicker than other role groups after its roll-out but does not explain the difference between the two hospitals. Overall this data shows that medical staff in SJH were less likely to be infected, and more likely to be diagnosed when they did get infected.

Previous symptoms and testing

Only 82% of participants with previous PCR-confirmed infection had detectable antibodies, compared to 95% of PRECISE 1 participants. This may be related to antibody waning over time for those in whom the reported infection occurred in the first wave of the pandemic. There may also be participants who were vaccinated, and therefore the anti-S antibody detected in PRECISE 2, assumed to be due to vaccination, may have been present before vaccination in response to previous infection. The longitudinal analysis of those participants common to PRECISE 1 and 2 below contains more detail on loss of antibody in those who were seropositive in PRECISE 1.

Nineteen percent of participants with detectable antibodies reported never having experienced symptoms that were consistent with infection with COVID-19, compared to 16% in PRECISE 1. This falls within the broad range reported by other studies (58). Those who had a symptomatic infection had a higher rate of antibody positivity than those who had an asymptomatic infection (90% versus 51%). This is also in keeping with other published data (59).

Over a quarter of participants reported having COVID-19 like symptoms at some stage but never having a positive PCR. This highlights the potential overlap in symptoms with other circulating viruses, including rhinoviruses which were circulating widely over the winter of 2020/21 in Ireland, and is a reminder of the impossibility of clinically excluding COVID-19 infection in HCW with symptoms, including in those with only mild symptoms, especially over the winter period. It also highlights the complexity involved in developing case definitions and testing guidelines.

Undiagnosed infections

In both hospitals, the seroprevalence was higher than the known PCR-confirmed diagnoses of COVID-19 infection of the same timeframe (21% vs 18% in SJH, and 13% vs 9.2% in UHG) though this gap was narrower than for PRECISE 1, assumably due to increased awareness and testing. Twenty-six percent of the infections in our study were undiagnosed, with 4.6% of all participants having had an undiagnosed infection. Almost half of these undiagnosed infections were asymptomatic (which was significantly higher than the rate of asymptomatic infections in those who had diagnosed COVID-19 infection). This proportion of undiagnosed infection has decreased from 39% in PRECISE 1, however still a quarter of infections had been undiagnosed despite both hospitals having onsite PCR testing available to HCW with symptoms or close contact with a confirmed case of COVID-19 from mid-March 2020. Although the majority of these infections were associated with only mild symptoms, it is still possible that these undiagnosed HCW were working during the infectious period, with potential for onwards transmission to patients and other staff members if proper use of PPE and other infection prevention and control (IPC) measures were not strictly adhered to. Easy access to testing, early detection of infection, and ongoing adherence to standard infection control precautions at all times, as well as the appropriate use of PPE including face masks in

the hospital setting, irrespective of symptoms remain important (60). This finding also supports the recommendation for screening of asymptomatic staff, including vaccinated staff in certain when a patient case of hospital-acquired infection, or hospital outbreak of infection with COVID-19 occurs. The exact role and methodology of routine asymptomatic screening, either widespread or in certain HCW, also remains to be defined.

Risk factors for antibody positivity

The main risk factors identified to be statistically significantly associated with antibody positivity (in decreasing order of aRR) were being a HCA, being of Black ethnicity, working in SJH, having secondary level education as opposed to post-graduate level education, being a nurse, having daily contact with patients (especially those known or suspected to have COVID-19 infection), being age 18-29, living with other HCW and being male. When broken down by hospital, the main risk factors identified to be significantly associated with SARS-CoV-2 antibody positivity differed. Seroprevalence by age and sex were similar to previously published literature, and similar to the findings of PRECISE 1 (1) (2) (47). Similar findings of increased risk direct patient contact, the role of HCA, and working with patients with COVID-19 infection have also been reported in the literature (42) (47) (61) (62).

Apart from the changes in seroprevalence by role discussed above, there were two main new findings on multivariate analysis from PRECISE 2 in comparison to PRECISE 1. Firstly, level of education emerged as an independent risk factor for seropositivity, with lower level of education being associated with higher seropositivity. Lower socio-economic status has been previously noted to correlate with increased risk of COVID-19 infection, and increased risk of poor clinical outcomes (63) (64). It is also associated with HCW role.

The second notable new finding was a change in the seropositivity by ethnic group; the seroprevalence amongst those of Black ethnicity trebled (from 14% (16/113) to 43% (39/117), for an aRR of 1.7 (95% CI 1.3-2.2, p<.001). They were also more likely to be asymptomatic, but not more likely to have an undiagnosed infection. The seroprevalence amongst those of Romanian nationality was also high for both hospitals combined, though numbers were small. Those of Asian ethnicity had a higher risk of seropositivity in PRECISE 1, but this finding was no longer significant in PRECISE 2. Both of these ethnic groups, as well as other minority ethnic groups which were likely under-represented in our study, have been shown to have increased risk in other studies (47) (65) (66) (67). There are likely to be social factors contributing to these ethnicity-related findings in both hospitals that our study did not measure.

Living with other HCW carried an increased risk for seropositivity, similar to our previous findings. This supports the theory that a proportion of the HCW contracting COVID-19 are doing so in their home environment. This finding was stronger in SJH than in UHG, where the community incidence was higher and the density of shared living space is also likely to be higher due to smaller spaces and more expensive accommodation in the capital city. Other studies have found correlation between size of household and antibody positivity (40) as well as higher risk of COVID-19 with a known household contact (68). To the best of our knowledge ours is the first study to comment on a significant risk of antibody positivity in HCW living with other HCW. This finding was common to both PRECISE 1 and 2.

Antibody response to vaccination

Most participants were either fully or partially vaccinated. All fully vaccinated participants, and the majority of partially vaccinated participants, had detectable anti-S antibodies. Other

studies have also shown high rates of seropositivity after both first and second dose vaccination (36) (69) (70) .

There were less breakthrough infections in those fully vaccinated than in those partially vaccinated (13% versus 0.6% of participants reported infection post first and second vaccine respectively), despite the fact that almost all of these participants had detectable antibodies. The 23 breakthrough infections, in 0.6% of the fully vaccinated study population, are in keeping with the rate of breakthrough infections experienced internationally (71). These breakthrough infections serve as a reminder that vaccination does not prevent infection acquisition, even in the setting of confirmed serological response to vaccination. Most of those with breakthrough infections had no symptoms, in keeping with the literature on vaccine effectiveness in reduction of severe symptoms and hospitalisation (19) (72) however the numbers are too small for any statistical comparison with symptoms in those who were unvaccinated. It would be prudent for all IPC measures to remain in place in the hospital setting, including for vaccinated HCW, while research is ongoing into the effects of vaccination on infection acquisition and onwards transmission, including with VOCs. Vaccinated HCW should not be exempt from measures discussed above in relation to minimising the rate of undiagnosed infections (access to testing, adherence to standard IPC precautions and inclusion in screening of asymptomatic staff in the case of a hospital outbreak).

It is also notable that of the 23 confirmed infections in fully vaccinated participants, only 6 of these participants had developed anti-N antibodies in response to their infection. Of the 17 that were anti-N negative, median number of days between PCR positivity and sampling mid-point was 52 (range 9-67) so it is surprising that the majority of these had not mounted an

anti-N antibody response (73). This low number of seroconversions might suggest that anti-N antibodies as a marker of natural infection post vaccination are unreliable. It raises the questions of whether the pre-existing spike antibodies alter the way the virus interacts with the immune system, with less production of anti-N antibodies. The numbers are very small but further research is warranted as this would be a very important point as we try to measure seroconversion and seroprevalence going forward in a post-vaccination era. To the best of our knowledge there are no published data to date commenting on this. Of the 17 that were anti-N negative, median number of days between PCR positivity and sampling mid-point was 52 (range 9-67) so it is surprising that the majority of these had not mounted an anti-N antibody response (73). This low number of seroconversions might suggest that anti-N antibodies may be insensitive as a marker of natural infection post vaccination. It is possible that early viral neutralisation, perhaps even at mucosal surfaces, might modify the natural humoral response and limit the development of anti-N antibodies. Studies are continuing to rely on anti-N as a marker of seropositivity related to natural infection, including in vaccinated individuals (74). To the best of our knowledge there are no published data to date that have identified a comparative reduction in anti-N seroconversion following natural infection in vaccinated individuals. Further research of individuals with well-defined vaccine breakthrough infections are required, as this information will be critical in determining how best to assess seroprevalence in vaccinated cohorts.

Sustained Antibody Response over six-months

Ninety percent of participants who were common to both studies, and were seropositive in PRECISE 1, still had antibodies at the time of PRECISE 2. The duration of antibody response in the literature is varied (11) (12), and further studies are still needed to directly correlate

sustained antibody positivity with protection from re-infection, especially as the pandemic progresses and further VOCs emerge.

Limitations

This study has several limitations. Firstly, information on COVID-19 symptoms and PCR test results were self-reported and thus could be biased. Secondly, although the uptake rate was good for an opt-in study, it was lower than the uptake for PRECISE 1; declining interest in research in the area of COVID-19 is a natural phenomenon as the pandemic progresses. Many staff at this point in time already knew they had been infected and therefore may have less interest in participating and availing of serology testing. Most staff had been vaccinated and therefore may also have a degree of comfort that produces less interest in knowing their antibody status. PRECISE 2 took place during the third wave of the pandemic in Ireland, which was the largest in magnitude and the longest. Other limitations include that WGS testing results were not available, particularly for those infected after full vaccination, and also that information on biological factors, e.g. co-morbidities, was not available. Although the communication strategy was an important part of the recruitment process, the study took part during our third wave of the pandemic, during Level 5 restrictions - the highest level of COVID-19 national restrictions - and therefore also relied heavily on engagement with information technology (IT) platforms (email, messenger groups, hospital intranet) and less on face-to-face announcements. Thirdly, as with all opt-in studies, there may be a selection bias. Those who had been vaccinated may have had less interest in participating due to less curiosity about their own serostatus, and therefore we may have underestimated the overall vaccination status of the workforce. Conversely, those who were unvaccinated may have had a fear of having to announce their vaccine-status to the study team, despite results not being linked to occupational health records, and those who had been vaccinated may have been

more likely to participate as they may be more likely to have health seeking behavior. The online consent process, questionnaire, and blood test booking system risks exclusion of those who are less literate in IT. This was identified as a potential limitation from the start, and attempts were made to mitigate this selection bias. Multilanguage information and plain English were used, and groups identified as potentially at risk of exclusion on this basis were targeted directly for inclusion in the study, with small-group sessions to aid consent and questionnaire completion and walk-in clinics for phlebotomy. We do not have individual level information on reasons for non-participation, or socio-demographic status of non-participants for comparison, but level of uptake by professional role was deemed to be representative of the hospital HCW population in both hospitals. The absence of real time genomic sequencing data precludes identifying the role of hospital outbreaks in influencing the overall seroprevalence, as well as drawing any definite conclusions regarding attributable risk to the workplace versus the community for HCW.

Detection of anti-spike antibody in conjunction with a self-reported history of vaccination was considered to be as a response to vaccination. It is possible that some of these participants may have detectable anti-spike antibody related to natural infection; these were not counted when assessing overall seroprevalence of presumed past infection, and therefore this overall seroprevalence may be an underestimate. Seroprevalence could also be underestimated because recent infection could be missed as several days are required for seroconversion of SARS-CoV-2 infection. Finally, some false negatives and false positives are expected with all laboratory tests. When the estimate of seroprevalence is adjusted using the manufacturer's stated specificity of 99.8% and sensitivity of 99.5%, (the seroprevalence does not change (18%; 95% CI 17% - 19%).

Conclusion and Recommendations

This study is a unique comparison between two hospitals in areas of differing community incidence over time, in which IPC measures were the same. The overall seroprevalence of antibodies to SARS-CoV-2 of 21% in SJH and 13% in UHG reflect the difference in community incidence in each area and the difference in rates of confirmed infections among the HCW of each hospital. Risk was higher in the hospital situated in a higher density area with higher community incidence throughout the COVID-19 pandemic. The rise in seroprevalence from 15% to 21% in SJH in and from 4.1% to 13% in UHG between October 2020 and April 2021 reflect the magnitude of the third wave of the pandemic in each location. This data compounded the findings of PRECISE 1, highlighting the local community incidence as one of the most significant risk factors for acquisition of COVID-19 infection in HCW. It is also likely that social and demographic factors, and local work practices influenced the overall seroprevalence. The lack of real time genomic sequencing precludes identifying the role of hospital outbreaks in influencing the overall seroprevalence, as well as drawing conclusions regarding attributable risk to the healthcare environment versus the community or household.

Other risk factors common to both PRECISE 1 and 2 included demographic risk factors (younger age group, male and Black or Asian ethnic group) and work-place related risk factors representing close patient contact, including the role of HCA. We identified living with other HCW as an independent risk factor for seropositivity in both studies; to the best of our knowledge there is no other published literature commenting specifically on this risk factor. The other risk factors that we identified are consistent with the published literature.

The comparison between PRECISE 1 and 2 highlights similar features throughout the pandemic, but also the changing epidemiology with different waves. The main differences in the findings of PRECISE 1 and PRECISE 2 were related to role, ethnicity and level of education, showing that certain risks may change with different waves of the pandemic. The large increase in the seropositivity among general support staff and higher seroprevalence among doctors in UHG compared to SJH are difficult to fully explain and may relate to social factors. While both studies highlighted minority ethnic groups as more at risk, the group highlighted in each study was different. Level of education, which has been shown internationally to play a role, emerged as a new significant finding in PRECISE 2. This, coupled with the findings of risk related to ethnicity, may suggest that, even a year and a half into the pandemic, some groups may not have been adequately reached by messaging and education, and ongoing efforts need to be made in this regard.

The degree of previously undiagnosed infections highlights the need for ongoing universal adherence to infection control guidance including the use of appropriate PPE in the hospital setting, as well as the importance of early case detection. It is essential that HCW have easy access to testing, even with mild or no symptoms, and even in the post vaccination setting. (75). We recommend ongoing risk assessment in the setting of a hospital outbreak, and where indicated, screening of HCW, including those without symptoms, and including those who are vaccinated.

Ninety percent of those who were anti-body positive (anti-N) in October 2020 and took part in April 2021 were remained positive (anti-N). Further research is needed to understand the anti-N seroconversion following natural infection in vaccinated individuals to inform optimal assessment of seroprevalence in vaccinated cohorts.

The antibody response to vaccination is reassuring, however we did show confirmed infection in a small minority of fully vaccinated participants; further studies are needed to correlate serological response with functional immunity. Formal vaccine effectiveness studies are needed to monitor how effective COVID-19 vaccines are in hospital HCW and to estimate duration of protection from infection, particularly with the ongoing emergence of variants of concern. With emerging evidence of reduction in transmission from vaccinated individuals, the authors strongly endorse immediate vaccination of all HCW. Messaging to HCW regarding the role and limits of vaccination need to be clear and should include the ongoing risk of infection and transmission. Ongoing adherence to all infection prevention and control standards in the healthcare setting and household are paramount. Easy access to testing of HCW with symptoms (including mild symptoms and including those who are vaccinated) and in the setting of close contact with a confirmed case of COVID-19 infection should continue, and vaccinated HCW with PCR-confirmed COVID-19 infection should be actively assessed to advance understanding of the reasons for breakthrough infection. This should include whole genome sequencing (WGS) of the virus from HCW with breakthrough infection and/or of virus from index cases identified by follow-up.

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Conflict of Interest

None of the authors have any conflicts of interest to declare.

Data Availability Statement

This dataset is not available to the public for ethical reasons of data protection as certain individuals may be identifiable from the data.

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Annex

Table A Response rate by HCW type, PRECISE 2, April 2021

HCW role	St James's Hospital response rate			University Hospital Galway response Rate			Combined response rate		
	N	n	%	N	n	%	N	n	%
Admin	693	403	58%	639	273	43%	1332	676	51%
Medical/dental	621	357	57%	814	356	44%	1435	713	50%
Nursing/ midwifery	1802	1097	61%	1689	794	47%	3491	1,891	54%
Allied health	742	612	82%	648	432	67%	1390	1,044	75%
General support	412	243	59%	240	122	51%	652	365	56%
Health care assistant	422	179	42%	316	112	35%	738	291	39%
Other	-	54		-	51		-	105	
Total	4692	2945	63%	4346	2140	49%	9038	5085	56%

Table B Comparison of all staff and study participants in St James's Hospital by healthcare worker role, PRECISE 2, April 2021

HCW role	St James's Hospital all staff		St James's Hospital response study participants		Difference	
	N	%	n	%	n	%
Admin	693	15%	403	14%	290	-1.1%
Medical/dental	621	13%	357	12%	264	-1.1%
Nursing/ midwifery	1802	38%	1097	37%	705	-1.2%
Allied health	742	16%	612	21%	130	5.0%
General support	412	8.8%	243	8.3%	169	-0.5%
Health care assistant	422	9.0%	179	6.1%	243	-2.9%
Other	-	-	54	1.8%	-	-
Total	4692	100%	2945	100%	1747	-

Table C Comparison of all staff and study participants in University Hospital Galway by healthcare worker role, PRECISE 2, April 2021

HCW role	University Hospital Galway all staff		University Hospital Galway response study participants		Difference	
	N	%	n	%	n	%
Admin	639	15%	273	13%	366	-1.9%
Medical/dental	814	19%	356	17%	458	-2.0%
Nursing/ midwifery	1689	39%	794	37%	895	-1.6%
Allied health	648	15%	432	20%	216	5.3%
General support	240	5.5%	122	5.7%	118	0.2%
Health care assistant	316	7.2%	112	5.2%	204	-2.0%
Other	-	-	51	2.4%	-	-
Total	4364	100%	2140	100%	2224	-

Table D Comparison of all staff and study participants by healthcare worker role, PRECISE 2, April 2021

HCW role	All invited staff		All study participants		Difference	
	N	%	n	%	n	%
Admin	1332	15%	676	13%	656	-1.5%
Medical/dental	1435	16%	713	14%	722	-1.9%
Nursing/ midwifery	3491	39%	1,891	37%	1600	-1.5%
Allied health	1390	15%	1,044	21%	346	5.1%
General support	652	7.2%	365	7.2%	287	0.0%
Health care assistant	738	8.2%	291	5.7%	447	-2.5%
Other		-	105	2.1%	-	-
Total	9028	100%	5085	100%	3943	-

Table E Characteristics of HCWs with SARS-CoV-2 seropositivity (n=898), by hospital, PRECISE 2, April 2021

Participant characteristics		St James's Hospital Dublin		University Hospital Galway		Both Hospitals	
		n	%	n	%	n	%
Overall		623	21%	275	13%	898	18%
Median age (IQR)		39 (29-49)		35 (27-44)		38 (29-48)	
Age groups (years)	18-29	159	26%	90	33%	249	28%
	30-39	154	25%	84	31%	238	27%
	40-49	157	25%	51	19%	208	23%
	50-59	119	19%	39	14%	158	18%
	Over 60	34	5.5%	11	4.0%	45	5.0%
Sex	Female	471	76%	198	72%	669	74%
	Male	152	24%	77	28%	229	26%
Ethnicity	Irish (white)	401	64%	194	71%	595	66%
	Any other white background	56	9.0%	38	14%	94	10%
	Asian background	122	20%	26	9.5%	148	16%
	African/other black background	29	4.7%	10	3.6%	39	4.3%
	Other	15	2.4%	7	2.5%	22	2.4%
Country of birth	Ireland	386	62%	181	66%	567	63%
	United Kingdom	25	4.0%	19	6.9%	44	4.9%
	India	60	10%	16	5.8%	76	8.5%
	Philippines	53	8.5%	1	0.4%	54	6.0%
	Poland	8	1.3%	12	4.4%	20	2.2%
	USA	4	0.6%	7	2.5%	11	1.2%
	Romania	12	1.9%	3	1.1%	15	1.7%
	Nigeria	18	2.9%	1	0.4%	19	2.1%
	Other	57	9.1%	35	13%	92	10%
Education	Primary	7	1.1%	0	0.0%	7	0.8%
	Secondary	105	17%	28	10%	133	15%
	Third level	301	48%	133	48%	434	48%
	Post-graduate	210	34%	114	41%	324	36%
Role	Admin	64	10%	21	7.6%	85	9.5%
	Medical/dental	55	8.8%	61	22%	116	13%
	Nursing/ midwifery	281	45%	114	41%	395	44%
	Allied health	89	14%	29	11%	118	13%
	General support	60	10%	21	7.6%	81	9.0%
	Health care assistant	70	11%	23	8.4%	93	10%
	Other	4	0.6%	6	2.2%	10	1.1%
Lives with	Alone	42	6.7%	19	6.9%	61	6.8%
	With others	578	92.8%	256	93%	834	92.9%
	Missing	3	0.5%	0	0.0%	3	0.3%
Lives with HCW	Yes	234	38%	106	39%	340	38%
	No	376	60%	164	60%	540	60%
	Missing	13	2.1%	5	1.8%	18	2.0%
Daily contact with COVID-19 patients	Contact with COVID-19 patients	196	31%	69	25%	265	30%
	Contact with patients without COVID-19	293	47%	170	62%	463	52%
	No patient contact	134	22%	36	13%	170	19%

Previous COVID-19 symptoms	No symptoms	121	19%	48	17%	169	19%
	Had symptoms	502	81%	227	83%	729	81%
	Missing	0	0.0%	0	0.0%	0	0.0%
Severity of symptoms	No symptoms	121	19%	48	17%	169	19%
	Mild symptoms	228	37%	107	39%	335	37%
	Significant symptoms	262	42%	102	37%	364	41%
	Severe (hospitalised)	12	1.9%	18	6.5%	30	3.3%
	Missing	0	0.0%	0	0.0%	0	0.0%
Previous positive COVID-19 PCR test	No	190	30%	45	16%	235	26%
	Yes	433	70%	230	84%	663	74%
Symptoms at time of previous positive PCR test	No	51	12%	36	16%	87	13%
	Yes	382	88%	194	84%	576	87%
Severity of symptoms at time of PCR test	No symptoms	51	12%	36	16%	87	13%
	Mild symptoms	143	33%	83	36%	226	34%
	Significant symptoms	227	52%	93	40%	320	48%
	Severe (hospitalised)	12	2.8%	18	7.8%	30	4.5%
	Missing	0	0.0%	0	0.0%	0	0.0%

Table 2e Prevalence of SARS-CoV-2 seropositivity by participant characteristics, both hospitals, PRECISE 2, April 2021

Participant characteristics		Total	SARS-CoV-2 seropositive		
		N	**n**	**% (95% CI)**	**p-value***
Overall		5085	898	18 (17 - 19)	
Hospital	St James's Hospital	2,945	623	21 (20 - 23)	<0.001
	University Hospital Galway	2,140	275	13 (11 - 14)	
Age groups (years)	18-29	1108	249	22 (20 - 25)	<0.001
	30-39	1330	238	18 (16 - 20)	
	40-49	1414	208	15 (13 - 17)	
	50-59	951	158	17 (14 - 19)	
	Over 60	282	45	16 (12 - 21)	
Sex	Female	3,959	669	17 (16 - 18)	0.008
	Male	1,126	229	20 (18 - 23)	
Ethnicity	Irish (white)	3,798	595	16 (15 - 17)	<0.001
	Any other white background	476	94	20 (16 - 24)	
	Asian background	599	148	25 (21 - 28)	
	African or any other black background	117	39	33 (25 - 43)	
	Other	95	22	23 (15 - 33)	
Country of birth	Ireland	3,630	567	16 (14 - 17)	<0.001
	United Kingdom	295	44	15 (11 - 20)	
	India	293	76	26 (21 - 31)	
	Philippines	214	54	25 (20 - 32)	
	Poland	85	20	24 (15 - 34)	
	USA	55	11	20 (10 - 33)	
	Romania	45	15	33 (20 - 49)	
	Nigeria	35	19	54 (31 - 71)	
	Other	433	92	21 (17 - 25)	
Education	Primary	22	7	32 (14 - 55)	<0.001
	Secondary	609	133	22 (19 - 25)	
	Third level	2,244	434	19 (18 - 21)	
	Post-graduate	2,210	324	15 (13 - 16)	
Role	Admin	676	85	13 (10 - 15)	<0.001
	Medical/dental	713	116	16 (14 - 19)	
	Nursing/ midwifery	1,891	395	21 (19 - 23)	
	Allied health	1,044	118	11 (9.4 - 13)	
	General support	365	81	22 (18 - 27)	
	Health care assistant	291	93	32 (27 - 38)	
	Other	105	10	10 (4.7 - 17)	
Lives with	Alone	464	61	13 (10 - 17)	0.008
	With others	4,610	834	18 (17 - 19)	
	Missing	11	3	27 (6.0 - 61)	
Lives with HCW	Yes	1,571	340	22 (20 - 24)	<0.001
	No	3412	540	16 (16 - 17)	
	Missing	102	18	18 (11 - 26)	

*Calculated using the chi-square test

Table 2f Prevalence of SARS-CoV-2 seropositivity by COVID-19 related characteristics, both hospitals, PRECISE 2, April 2021

COVID-19 related characteristics		Total	SARS-CoV-2 seropositive		
		N	**n**	**% (95% CI)**	**p-**
Daily contact with COVID-19 patients	Contact with COVID-19 patients	1136	265	23 (21 - 26)	<0.001
	Contact with patients without COVID-19	2,500	463	19 (17 - 20)	
	No patient contact	1,449	170	12 (10 - 14)	
Previous COVID-19 symptoms	No symptoms	2913	169	5.8 (5.0 - 6.7)	<0.001
	Had symptoms	2171	729	34 (32 - 36)	
	Missing	1	0	-	
Severity of symptoms	No symptoms	2913	169	5.8 (5.0 - 6.7)	<0.001
	Mild symptoms	1502	335	22 (20 - 24)	
	Significant symptoms	621	364	59 (55 - 63)	
	Severe (hospitalised)	47	30	64 (49 - 77)	
	Missing	1	0	-	
Previous positive COVID-19 PCR test	No	4273	235	5.5 (4.8 - 6.2)	<0.001
	Yes	812	663	82 (79 - 84)	
Symptoms at time of previous positive PCR test	No	172	87	51 (43 - 58)	<0.001
	Yes	640	576	90.0 (87 - 92.2)	
Severity of symptoms at time of PCR test	No symptoms	172	87	51 (43 - 58)	<0.001
	Mild symptoms	256	226	88 (84 - 92.0)	
	Significant symptoms	351	320	91.2 (88 -	
	Severe (hospitalised)	32	30	93.8 (79 -	
	Missing	1	0	-	

*Calculated using the chi-square test

Table 2g Prevalence of SARS-CoV-2 seropositivity for general support staff, by role and hospital, PRECISE 2, April 2021

Role	**St James's Hospital**			**University Hospital Galway**			**Both hospitals**		
	Total	**Seropositive**		**Total**	**Seropositive**		**Total**	**Seropositive**	
	N	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**
Domestic/ Cleaning	62	15	24%	45	9	20%	107	24	22%
Catering	83	23	28%	18	5	28%	101	28	28%
Maintenance	27	6	22%	24	1	4.2%	51	7	14%
Security	33	6	18%	14	3	21%	47	9	19%
Porter	20	6	30%	13	1	7.7%	33	7	21%
Chaplain	11	3	27%	2	0	0.0%	13	3	23%
Other	7	1	14%	0	0	-	7	1	14%
Driver	0	0	-	6	2	33%	6	2	33%
Total	**243**	**60**	**25%**	**122**	**21**	17%	**365**	**81**	**22%**

Table 2h Prevalence of asymptomatic SARS-CoV-2 infection, by hospital location and ethnicity, PRECISE 2, April 2021

		Total seropositive	Asymptomatic SARS-CoV-2 infection		
		N	**n**	**% (95% CI)**	**p-value***
St James's Hospital	Total	623	121	19 (16 - 23)	0.009
	Irish (white)	401	82	20 (17 - 25)	
	Other white background	56	13	23 (13 - 36)	
	Asian	122	13	11 (5.8 - 18)	
	African or other black	29	11	38 (21 - 58)	
	Other	15	2	13 (1.7 - 40)	
Galway University Hospital	Total	275	48	17 (13 - 22)	0.531
	Irish (white)	194	35	18 (13 - 24)	
	Other white background	38	5	13 (4.4 - 28)	
	Asian	26	5	19 (6.6 - 39)	
	African or other black	10	3	30 (6.7 - 65)	
	Other	7	0	-	
Both hospitals	Total	898	169	19 (16 - 22)	0.010
	Irish (white)	595	117	20 (17 - 23)	
	Other white background	94	18	19 (12 - 29)	
	Asian	148	18	12 (7.4 - 19)	
	African or other black	39	14	36 (21 - 53)	
	Other	22	2	9.1 (1.1 - 29)	

*Calculated using the Chi-square test

Table 2i Undiagnosed SARS-CoV-2 infection, by HCW role and hospital location, PRECISE 2, April 2021

	St James's Hospital		**University Hospital Galway**		**Both hospitals**	
	n	**%**	**n**	**%**	**n**	**%**
Admin	19	10%	5	11%	24	10%
Medical/dental	12	6.3%	8	18%	20	8.5%
Nursing/ midwifery	79	42%	19	42%	98	42%
Allied health	32	17%	6	13%	38	16%
General support	22	12%	4	8.8%	26	11%
Health care assistant	26	14%	2	4.4%	28	12%
Other	0	0.0%	1	2.2%	1	0.4%
Total	190	100%	45	100%	235	100%

Table F. Characteristics of fully vaccinated participants with PCR confirmed infection i.e. vaccine breakthrough cases, both hospitals (n=23), PRECISE 2, April 2021

Participant characteristics		**PCR positive ≥14 days after second vaccine dose (N=23)**	
		n	**%**
Hospital	St James's Hospital	18	78%
	University Hospital Galway	5	22%
Age groups	18-29	2	8.7%
	30-39	6	26%
	40-49	8	35%
	50-59	5	22%
	≥60	2	8.7%
Sex	Female	15	65%
	Male	8	35%
Ethnicity	Irish (white)	12	52%
	Any other white background	1	4.3%
	Asian background	8	35%
	African or other black background	2	8.7%
	Other	0	0.0%
Country of birth	Ireland	12	52%
	United Kingdom	0	0.0%
	India	4	17%
	Philippines	4	17%
	Poland	1	4.3%
	USA	0	0.0%
	Other	0	0.0%
Education	Primary	0	0.0%
	Secondary	2	8.7%
	Third level	11	48%
	Post-graduate	10	43%
Role	Admin	0	0.0%
	Medical/dental	0	0.0%
	Nursing/ midwifery	10	43%
	Allied health	5	22%
	General support	2	8.7%
	Health care assistant	4	17%
	Other	2	8.7%
Workplace exposure to COVID-19 patients	No patient contact	2	8.7%
	Daily contact with COVID-19 patients	9	39%
	Daily contact with patients without COVID-19	12	52%
Lives with	Alone	1	4.3%
	With others	22	96%
	Missing	0	0.0%
Lives with HCW	Yes	13	57%
	No	10	43%
Vaccine type	Pfizer	23	100%
	Other	0	0.0%
Symptoms at the time of positive PCR test	Yes	5	22%
	No	18	78%

Report Addendum

Prevalence of Antibodies to SARS-CoV-2 natural infection and post-vaccination in Irish Hospital Healthcare Workers (PRECISE 2)

Report version 2.0 19th October 2021

Introduction

This is an addendum to the PRECISE 2 study report and it details analysis of the longitudinal change in SARS-CoV-2 antibody status among participants during the six-month period between the PRECISE 1 study (October 2020) and the PRECISE 2 study (April 2021).

The aim of this longitudinal analysis was to examine changes in individual serostatus over the six-month period for those staff members who participated both times, and to assess the association between characteristics of the study participants and SARS-CoV-2 seroreversion.

There are three main parts to the analysis; seroreversion, antibody retention, and seroconversion:

- Seroreversion refers to the loss of previously detectable antibodies in the blood. For this study a person was considered to have 'seroreverted' if they had a positive SARS-CoV-2 serology test in October 2020 and a negative SARS-CoV-2 serology test in April 2021.
- Antibody retention refers to the persistence of detectable antibodies in the blood. In this study a person was considered to have maintained antibody positivity between both phases of the study if they had a positive SARS-CoV-2 serology test in October

2020 and a positive test again in April 2021, and they did not have a PCR-confirmed SARS-CoV-2 infection during that interval.

- Seroconversion refers to the development of detectable antibodies in the blood. For this study a person was considered to have 'seroconverted' if they had a negative SARS-CoV-2 serology test in October 2020 and a positive SARS-CoV-2 serology test in April 2021.

Methods

Data matching

Linkage of the PRECISE 1 and PRECISE 2 datasets was carried out based on probabilistic methods, matching on a minimum of two participant identifiers from the following; Name, Initials, Date of Birth, Phone number and Email address. Matching was carried out using Microsoft Excel software (Microsoft, Redmond, Washington, USA). All partial matches were reviewed manually and participants with partial matched data were contacted individually to confirm any errors in spelling of name or date of birth.

Laboratory methods

For the longitudinal analysis, participants were deemed seropositive if they were positive on the Roche Elecsys anti-SARS-CoV-2 immunoassay, as this assay was used in both phases of the PRECISE study. The assay detects total antibodies to the nucleocapsid protein of the SARS-CoV-2 virus; a positive test was deemed to be an indicator of natural infection, the rationale for this is described in the PRECISE 2 main report.

Statistical methods

The chi-square distribution was used to compute confidence intervals (CI) and p-values. Binary logistic regression was used to calculate relative risks along with their 95% CIs, to assess the association between symptom severity and SARS-CoV-2 seroreversion, adjusted for time since PCR positive test. PCR positivity refers to the date of most recent PCR positive test, the analysis was adjusted for participants who were positive in PRECISE 1 and had a subsequent PCR confirmed infection (indicating re-infection) (n=5 matched participants). All analysis was conducted in Stata 15.1 (StataCorp LCC. 2019. College Station, TX 77845: USA).

Results

In total, 3,313 qualifying study participants participated in both PRECISE 1 (October 2020) and PRECISE 2 (April 2021). Demographics of these 3,313 are shown in Table A, Annex 2. Eighteen percent (595/3313) were ever seropositive in PRECISE 1 or PRECISE 2; 11% (360/3313) were positive in PRECISE 1, 17% (560/3313) were positive in PRECISE 2, and 9.8% (325/3313) were seropositive in both PRECISE 1 and PRECISE 2 (Table 1).

Addendum **Table 1** Comparison of individual serological results in PRECISE 1 (October 2020) and PRECISE 2 (April 2021), Roche (anti-N) total antibody assay

Serological result **PRECISE 1**	Serological result **PRECISE 2**		
	Negative	**Positive**	**Total**
Negative	2718	235	2953
Positive	35	325	360
Total	2753	560	3313

Seroreversion

Of the 360 participants that were seropositive in PRECISE 1, 9.7% (n=35) experienced seroreversion (loss of previously detected antibody), i.e. they were seropositive in PRECISE 1 (October 2020) but seronegative in PRECISE 2 (April 2021). The proportion and 95% confidence intervals (CI) of participants that experienced seroreversion by demographic characteristics are shown in Table 2a. There were no participant characteristics that were significantly associated with seroreversion.

The proportion of participants that experienced seroreversion increased with decreasing symptom severity, but this was not statistically significant (Table 2b). The proportion was 15% among those who had never experienced symptoms of COVID-19, 9.9% among those who had experienced mild symptoms, 8.3% among those who had experienced significant[1] (i.e. moderate) symptoms, and 5.3% among those who had experienced severe symptoms.

Of the 360 participants who experienced seroreversion, 228 (63%) reported having had a previous PCR confirmed infection. The interval between date of previous PCR confirmed infection and the PRECISE 2 study ranged from 2 months to 13 months. There were no participants who experienced seroreversion and whose interval between PCR positive test and PRECISE 2 study was ≤10 months but this should be interpreted with caution due to low numbers in this group. Seroreversion was 15% for those whose interval was 13 months, 5.2% for those whose interval was 12 months, and 16% whose interval was 11 months (confidence intervals overlap) (Table 2b). Seroreversion (and 95% CIs) by symptom severity among those previously PCR positive is shown in Figure 1.

[1] Does not refer to statistical significance. Participants answered "I had significant symptoms (similar to a flu or worse, but I was not admitted to hospital)"

When symptom severity was adjusted for time since PCR confirmed infection, a similar trend was observed (the highest risk of seroreversion was observed for those that had not previously experienced COVID-19 symptoms; aRR 2.0 (95% CI 0.2-25)), but this was not significant (p=0.439) (Table 3a). Analysis of time since PCR positivity adjusted for symptom severity is shown in Table 3b, and was also not significant.

Addendum **Table 2a** Proportion and 95% CI of PRECISE 1 participants that experienced seroreversion (October 2020 to April 2021), by demographic characteristics

Participant characteristics		**Total**	**Experienced seroreversion**		
		N	**n**	**% (95% CI)**	**p-value***
All		360	35	9.7 (6.9-13)	
Age groups (years)	18-29	96	9	9.4 (4.4-17)	0.483
	30-39	110	14	13 (7.1-20)	
	40-49	79	8	10 (4.5-19)	
	50-59	59	4	6.8 (1.9-16)	
	≥60	16	0	-	
Sex	Female	271	31	11 (7.9-16)	0.055
	Male	89	4	4.5 (1.2-11)	
Ethnicity	Irish (white)	242	25	10 (6.8-15)	0.324
	Any other white background	45	7	16 (6.5-29)	
	Any Asian background	64	3	4.7 (1.0-13)	
	Any African or black background	8	0	-	
	Other	1	0	-	
Country of birth	Ireland	232	25	11 (7.1-15)	0.304
	United Kingdom	23	3	13 (2.8-34)	
	India	29	2	6.9 (0.8-23)	
	Philippines	31	1	3.2 (0.1-17)	
	Poland	6	2	33 (4.3-78)	
	USA	3	0	-	
	Other	36	2	5.6 (0.7-19)	
Education	Primary	2	0	-	0.193
	Secondary	32	2	6.3 (0.8-21)	
	Third level	181	13	7.2 (3.9-12)	
	Post-graduate	145	20	14 (8.6-20)	
Role	Admin	30	3	10 (2.1-27)	0.319
	Medical/dental	50	7	14 (5.8-27)	
	Nursing/ midwifery	184	15	8.2 (4.6-13)	
	Allied health	47	7	15 (6.2-28)	
	General support	19	3	16 (3.4-40)	
	Health care assistant	27	0	-	
	Other	3	0	-	
Lives with	Alone	18	2	11 (1.4-35)	0.929
	With others	341	33	9.7 (6.8-13)	
	Missing	1	0	-	
Lives with HCW	Yes	147	14	8.8 (4.8-15)	0.625
	No	206	21	10 (6.5-15)	
	Missing	7	0	11 (0.3-48)	
Daily contact with COVID-19 patients	Contact with COVID-19 patients	85	11	13 (6.6-22)	0.420
	Contact with patients without COVID-19	214	20	9.3 (5.8-14)	
	No patient contact	61	4	6.6 (1.8-16)	

*Calculated using the chi-square test

Addendum **Table 2b** Proportion and 95% CI of PRECISE 1 participants that experienced seroreversion (October 2020 to April 2021), by previous symptoms and by date of previous PCR confirmed infection

Participant characteristics		**Total**	**Experienced seroreversion**		
All		**N**	**n**	**% (95% CI)**	**p-value***
		360	35	9.7 (6.9-13)	
Previous COVID-19 symptoms	No symptoms	47	7	15 (6.2-28)	0.199
	Had symptoms	313	28	9 (6.0-13)	
Severity of symptoms	No symptoms	47	7	15 (6.2-28)	0.540
	Mild symptoms	162	16	9.9 (5.8-16)	
	Significant (moderate) symptoms	132	11	8.3 (4.2-14)	
	Severe (hospitalised)	19	1	5.3 (0.1-26)	
Previous positive COVID-19 PCR test	No	132	15	11 (6.5-18)	0.424
	Yes	228	20	8.8 (5.4-13)	
Number of months since most recent PCR positive test	1	0	0	-	0.349
	2	1	0	-	
	3	1	0	-	
	4	0	0	-	
	5	0	0	-	
	6	5	0	-	
	7	9	0	-	
	8	1	0	-	
	9	0	0	-	
	10	4	0	-	
	11	50	8	16 (7.2-29)	
	12	116	6	5.2 (1.9-11)	
	13	41	6	15 (5.6-29)	
Symptoms at time of most recent PCR test	No symptoms	17	2	12 (1.5-36)	0.917
	Mild symptoms	83	8	9.6 (4.3-18)	
	Significant (moderate) symptoms	111	9	8.1 (3.8-15)	
	Severe (hospitalised)	17	1	5.9 (0.1-29)	

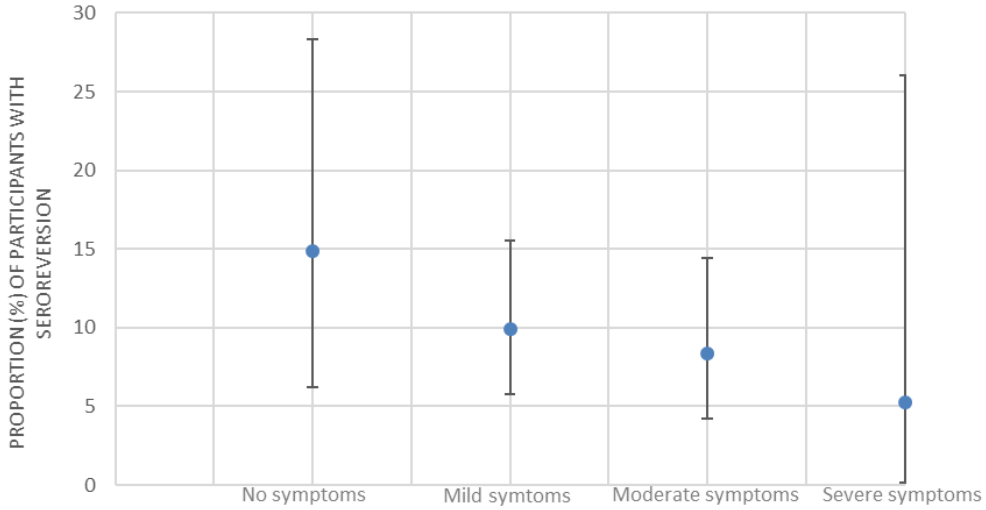
*Calculated using the chi-square test

Addendum **Table 3a** Association between symptom severity and seroreversion (October 2020 to April 2021) among PRECISE participants, controlled for time since PCR confirmed infection

Participant characteristics		**Adjusted relative risk**	
		% (95% CI)	**p-value**
Symptoms at time of previous positive PCR test	No symptoms	2.0 (0.2-25)	0.439
	Mild symptoms	1.7 (0.2-13)	0.590
	Significant (moderate)	1.4 (0.2-10)	0.733
	Severe (hospitalised)	Ref.	

Addendum **Table 3b** Association between time since PCR confirmed infection and seroreversion (October 2020 - April 2021) among PRECISE participants, controlled for symptom severity

Participant characteristics		Adjusted relative risk	
		% (95% CI)	**p-value**
Number of months since most recent PCR positive test	≤11	Ref.	
	12	0.4 (0.2-1.2)	0.101
	13	1.1 (0.4-2.9)	0.843



Addendum **Figure 1** Proportion (%) and 95% CIs of PRECISE participants that experienced seroreversion between PRECISE 1 (October 2020) and PRECISE 2 (April 2021), by COVID-19 symptom severity

Antibody retention

Ninety percent (325/360) of those who were seropositive in PRECISE 1 were also seropositive in PRECISE 2. Of those, five reported having had PCR confirmed infection on two separate occasions, three had their second episode of infection in October 2020 and two had their second episode in January 2021. The remaining 98% (320/325) did not report having had a PCR confirmed infection since October 2020 and are presumed to have maintained antibody positivity between both phases of the study.

Seroconversion

Of the 560 matched participants that were seropositive in PRECISE 2, 235 were seronegative in PRECISE 1, i.e. they seroconverted between October 2020 and April 2021.

Characteristics of those 235 participants are shown in Table B (Annex 2).

Limitations

Limitations of the longitudinal analysis included that part of the PRECISE study was questionnaire-based, therefore data on participant demographics, prior PCR-confirmed SARS-CoV-2 infection and prior COVID-19 symptoms were self-reported. Answers were inconsistent for some participants and these were clarified where possible.

Data linkage was based on probabilistic methods which is a common challenge in epidemiological studies where there is no unique participant identifying code that is common to all datasets included in the study. In total, 2% (n=87) of participants could not be matched and were excluded from longitudinal analysis. The match rate of 98% was deemed sufficient for this study.

Annex 2

Annex 2 **Table A** Characteristics of participants who took part in both PRECISE 1 (October 2020) and PRECISE 2 (April 2021)

Participant characteristics*		**Total (N=3,313)**	
		N	**%**
Age group	18-29	633	19
	30-39	856	26
	40-49	967	29
	50-59	664	20
	≥60	193	5.8
Sex	Female	2,625	79
	Male	688	21
Ethnicity	Irish (white)	2,615	79
	Any other white background	287	8.7
	Any Asian background	314	9.5
	Any African or black background	59	1.8
	Other	38	1.1
Country of birth	Ireland	2487	75
	United Kingdom	222	6.7
	India	154	4.6
	Philippines	112	3.4
	Poland	48	1.4
	USA	33	1.0
	Other	257	7.8
Education	Primary	11	0.3
	Secondary	373	11
	Third level	1407	42
	Post-graduate	1522	46
Role	Admin	450	14
	Medical/dental	422	13
	Nursing/ midwifery	1265	38
	Allied health	740	22
	General support	214	6.5
	Health care assistant	149	4.5
	Other	73	2.2
Lives with	Alone	296	8.9
	With others	3,013	90.9
	Missing	4	0.1
Lives with HCW	Yes	986	30
	No	2,259	68
	Missing	68	2.1
Daily contact with COVID-19 patients	Contact with COVID-19 patients	489	15
	Contact with patients without COVID-19	1,820	55
	No patient contact	1,004	30

*based on answers given in the PRECISE 1 study

Annex 2 **Table B** Characteristics of matched participants who seroconverted between PRECISE 1 (October 2020) and PRECISE 2 (April 2021)

Participant characteristics*		**Total (N=235)**	
		N	**%**
Age groups	18-29	63	27
	30-39	59	25
	40-49	59	25
	50-59	40	17
	≥60	14	6.0
Sex	Female	187	80
	Male	48	20
Ethnicity	Irish (white)	181	77
	Any other white background	18	7.7
	Any Asian background	20	8.5
	Any African or black background	6	2.6
	Other	10	4.3
Country of birth	Ireland	173	74
	United Kingdom	11	4.7
	India	12	5.1
	Philippines	5	2.1
	Poland	5	2.1
	USA	2	0.9
	Other	27	11
Education	Primary	2	0.9
	Secondary	40	17
	Third level	122	52
	Post-graduate	71	30
Role	Admin	27	11
	Medical/dental	22	9.4
	Nursing/ midwifery	107	46
	Allied health	29	12
	General support	22	9.4
	Health care assistant	24	10
	Other	4	1.7
Lives with	Alone	14	6.0
	With others	221	94
Lives with HCW	Yes	92	39
	No	141	60
	Missing	2	0.9
Daily contact with COVID-19 patients	Contact with COVID-19 patients	43	18
	Contact with patients without COVID-19	144	61
	No patient contact	48	20

*based on answers given in the PRECISE 1 study