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BMJ Open Seroprevalence of SARS-CoV-2 infection in healthcare workers in a large teaching hospital in the North West of England: a period prevalence survey

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ABSTRACT

Objectives Since its emergence in late 2019, SARS-CoV-2 has caused a global pandemic that has significantly challenged healthcare systems. Healthcare workers have previously been shown to have experienced higher rates of infection than the general population. We aimed to assess the extent of infection in staff working in our healthcare setting.

Design A retrospective analysis of antibody results, compared with staff demographic data, and exposure to patients with COVID-19 infection.

Setting A large teaching hospital in the North West of England.

Participants 4474 staff in diverse clinical and non-patient facing roles who volunteered for SARS-CoV-2 antibody testing by the Roche Elecsys assay between 29 May and 4 July 2020.

Results Seroprevalence was 17.4%. Higher rates were seen in Asian/Asian British (OR 1.61, 95% CI 1.27 to 2.04) and Black/Black British (OR 2.08, 95% CI 1.25 to 3.45) staff. Staff working in any clinical location were more likely to be seropositive (OR 2.68, 95% CI 2.27 to 3.15). Staff were at an increased risk of seropositivity as the 'per 100 COVID-19 bed-days change' increased in the clinical area in which they worked (OR 1.12, 95% CI 1.10 to 1.14). Staff working in critical care were no more likely to have detectable antibodies than staff working in non-clinical areas. Symptoms compatible with COVID-19 were reported in 41.8% and antibodies were detected in 30.7% of these individuals. In staff who reported no symptoms, antibodies were detected in 7.7%. In all staff who had detectable antibodies, 25.2% reported no symptoms.

Conclusions Staff working in clinical areas where patients with COVID-19 were nursed were more likely to have detectable antibodies. The relationship between seropositivity in healthcare workers and the increase in 'per 100 COVID-19 bed-days' of the area in which they worked, although statistically significant, was weak, suggesting other contributing factors to the risk profile. Of staff with detectable antibodies and therefore evidence of prior infection, a quarter self-reported that they had experienced no compatible symptoms. This has implications for potential unrecorded transmission in both staff and patients.

Strengths and limitations of this study

- This is a large dataset of antibody results in healthcare staff who perform a broad range of roles in a large English teaching hospital.
- We have been able to compare seropositivity in clinical staff with the level of exposure to patients with COVID-19 by looking at patient movements.
- Small numbers of respondents in some clinical areas has prevented the ability to elucidate further which areas are genuine outliers that could indicate specific good practice or inadequacies leading to lower or higher staff infection rates.
- This study used a single antibody assay (Roche Elecsys) so all results in this study are comparable; however, other centres have used different assays, which means that comparison between sites is not straightforward.
- The Roche antibody assay is most sensitive after at least 21 days following infection and there is growing evidence of declining titres with time; therefore, false negative results could have been generated.

INTRODUCTION

SARS-CoV-2 has spread globally following its first identification in Wuhan, China in December 2019.^{1–3} The WHO declared this to be a pandemic on 11 March 2020,⁴ and to date (8 September 2020) there have been almost 27 million recorded cases and 900 000 deaths globally.⁵ Cases were first identified in the UK on 31 January 2020 and to date (8 September 2020) there have been 350 000 confirmed cases and over 41 500 deaths.^{6,7}

Studies have shown varying rates of infection in healthcare workers. These infections were determined as current, by detection of viral RNA by PCR, or as prior infection, by the detection of specific antibodies. National data from May 2020 shows increased rates of infection in patient-facing and resident-facing

health/social care staff (1.87%) compared with working people in other, non-healthcare associated roles (0.32%).⁸ Analysis of registered deaths has shown that male healthcare workers had a higher death rate from COVID-19 compared with the general working population.⁹ Rates of infection detected in healthcare workers have varied geographically. Rates of 2%–3% asymptomatic infections have been described in some settings,^{10 11} while higher rates were seen in a London Hospital, with a peak of 7.1%, at the time that coincided with the peak in their local population.¹² Houlihan and colleagues demonstrated rates of SARS CoV-2 infection of 44% in one cohort of patient-facing healthcare workers in London during a similar time period.¹³ Rates of 14% and 18% were described in symptomatic healthcare workers in March 2020, in Newcastle and Sheffield, respectively.^{14 15} A study of 554 healthcare workers in Birmingham showed that seroconversion had occurred in 24.4%. Higher rates were seen in housekeeping (34.5%), acute medicine (33.3%), and general internal medicine (30.3%). Lower rates were seen in critical care (14.8%) and the emergency department (13.3%).¹⁶ Oxford University Hospitals showed evidence of SARS-CoV-2 infection in 11% of their surveyed staff, also with higher rates seen in patient facing areas, including acute medicine.¹⁷

The emergence of this novel virus means that we have much to learn about its biology, host immunological response, and variable rates of infection. Additionally, there is a need to investigate the impact on the infection rate of the healthcare work force and the effectiveness of processes used to mitigate this. Here, we aimed to conduct a period prevalence study to ascertain the proportion of staff who had been infected with SARS-CoV-2.

METHODS

Setting

Lancashire Teaching Hospitals NHS Foundation Trust (LTH) is one of the largest acute Trusts in the UK, providing district general hospital services to 370 000 people in Chorley, Preston and South Ribble and specialist care to 1.7 million people across Lancashire and South Cumbria. Approximately, 700 beds are split over two sites, Royal Preston Hospital and Chorley and South Ribble District Hospital. It employs circa 8500 staff, equating to circa 7600 full-time equivalents. In our Teaching Hospital setting the assessment, segregation and management of suspected COVID-19 patients were performed in alignment with Public Health England (PHE) guidance at the time. The trust was largely closed to elective admissions during this period and patients with COVID-19 were cared for throughout the trust. Patients were segregated on admission and placed in Green (COVID-19 not suspected), Amber (COVID-19 suspected but not confirmed) and Red (COVID-19 confirmed) areas. It was not possible to separate these areas into different wards; wards tended to have a mix of different types of patients, although separated into different bays, with bay doors

closed. Isolation of all suspected cases in side-rooms was also not possible due to large numbers of admissions. Most suspected cases were nursed in Amber bays, pending the results of COVID-19 swabs and medical review. Throughout the first peak of the epidemic (March–July 2020), the hospital followed PHE guidance on the use of personal protective equipment (PPE).

Participants

We undertook a retrospective, anonymised analysis of SARS-CoV-2 antibody results in staff members at LTH between 29 May and 4 July 2020. All staff, regardless of role, were offered a serum antibody test for SARS-CoV-2 using the Roche Elecsys total immunoassay method (Roche Diagnostics, Burgess Hill, UK). The sensitivity and specificity were determined for the Roche Elecsys assay by an in house verification using 160 known positive RT-PCR patient samples and 199 prepandemic negative samples. Specificity was 100% and a maximum sensitivity of 92% was found to be at day 21. Additionally, both within and between batch precision was calculated using positive and negative patient samples. For all samples, the %CVs were less than 5%. All staff were required to give written consent for the test, which included continued agreement to adhere to local infection prevention and control policies regardless of the outcome of the test.

Self-report survey

Staff were additionally asked to self-report via a questionnaire whether they had previously tested positive for SARS-CoV-2 (by PCR), and whether they had experienced any compatible symptoms (online supplemental material 1). All staff who experienced compatible symptoms were excluded from work and offered a SARS-CoV-2 PCR. Staff with a confirmed diagnosis could return to work 10 days after the positive test if they were well. Staff who tested negative were permitted to return to work if they were well enough to do so. Self-reported PCR was used as some individuals may have accessed pillar two testing outside of the trust and these results would not be accessible. Location of work, and individual demographic data collected from the consent forms were cross-referenced with electronic staff records.

Trust-wide COVID-19 data

Information was retrieved from the Trust's Patient Administration System (PAS, QuadraMed, Texas, USA). This system logs every patient bed move with a date and a time. In mid-March, LTH introduced dashboards (Qlikview, Pennsylvania, USA) which combined COVID-19 test data with patient location data from the PAS. Bed movements of COVID-19 positive patients were analysed, including ward, and bed-space check-in and check-out dates and times. The dashboard included data on the first positive COVID-19 test performed in that visit; the date of sample collection and the date of the report. All inpatient bed-days in the hospital visit after the first positive COVID-19 sample were included in the analysis and designated

'COVID-19 positive inpatient bed-days'. These data were analysed to 8 July 2020, which encompassed the first peak of incidence in our trust, and was used to assess varying exposure to patients with COVID-19 in different clinical areas.

There were 872 COVID-19 infected inpatients identified by PCR at LTH; 244 patients died; 610 patients were discharged home; 18 patients remained in hospital as of 8 July 2020. In total, these patients represented 9239 COVID-19 positive inpatient bed days. A total of 42 clinical locations were identified and the number of COVID-beds days were estimated for each location. These locations included clinical areas with no patients with COVID-19, such as the entire Women's and Children's Division. Other workplaces such as offices, pathology and pharmacy were designated as a single non-clinical location with no patients with COVID-19.

Statistical analysis

Summary statistics were used for descriptive analyses. Sensitivity and specificity were calculated with the standard formulae. The primary modelling framework was binary logistic regression for which the outcome was a positive or negative antibody test. The demographic predictors in the logistic regression were age (as a quantitative covariate), gender and ethnicity. Ethnicity was categorised into six ethnic groups and a seventh group which comprised all respondents for whom ethnicity was unknown. This approach allowed only those of known ethnicity to contribute to the estimates for their ethnic group but allowed all respondents to contribute to estimates for age, gender and environmental location. Location was initially categorised into two types; non-clinical and clinical locations. Location was also classified into 43 separate locations, the first being all non-clinical locations combined and the remainder being 42 different clinical locations. Each of the clinical locations was ascribed an estimated number of COVID-19 bed-days as described above. Finally, location was classified into four main types comprising all non-clinical locations, emergency department, critical care and all remaining clinical locations combined. Logistic regressions that included individual locations were restricted to those locations with at least 30 participants to avoid large confidence intervals and over-parameterisation.

Logistic regression models prevalence using a linear model for the logarithm of the odds where odds are defined as the ratio of the positive outcomes to the negative outcomes. Results are presented as ORs where the OR measures the extent to which one group has a different risk of the positive outcome relative to a reference group. Thus, an OR of 2.0 implies that this group has twice the odds of a positive outcome compared with the reference group. The reference group thus always has an OR of 1.0. Higher risk groups have an OR greater than 1.0 and lower risk groups have an OR of less than 1.0. The reference groups in this study were male gender, white UK or ROI ethnicity and zero COVID-19 bed days. The modelling

approach allows locations to be compared for prevalence after adjustment has been made for demographic differences between different locations. Statistical analyses were performed using IBM SPSS.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research. Results will be made available to all staff and patients via our usual communication channels.

RESULTS

Summary statistics

Staff with incomplete data (37/4511) were excluded in the data analysis stage. These staff were excluded because age and gender were not known, the antibody test result was invalid, or there was a major inconsistency in the demographic data. This resulted in 4474 individuals being included in all analyses except where individual location ORs were estimated. In this case, exclusion of locations with fewer than 30 participants resulted in 4189 individuals included. Staff who presented for antibody testing were representative of Trust staff in regard to age, sex, ethnicity and staff type when compared with workforce staff records (data not shown) and hence results presented are unlikely to contain any inherent bias. Antibodies were detected in 777 (17.4%) individuals (table 1).

Demographic characteristics

Older staff were less likely to be seropositive (OR 0.988, 95% CI 0.982 to 0.994, $p < 0.001$) per 1 year change (table 2). Staff who were Asian/Asian British (OR 1.61, 95% CI 1.27 to 2.04) and black/black British (OR 2.08, 95% CI 1.25 to 3.50) were more likely to have detectable antibodies than staff of white UK/ROI ethnicity when corrected for age, gender and clinical location (table 2).

Locations

Staff working in any clinical location where patients with COVID-19 were nursed were more likely to be seropositive (OR 2.68, 95% 2.27 to 3.15) when corrected for age, sex and ethnicity (table 2). There was a positive association of staff seropositivity per 100 COVID-19 bed-day increase in the clinical area in which they worked (OR 1.12, 95% 1.10 to 1.14, $p < 0.001$). The relationship between COVID-19 bed days and staff seropositivity was significant, but weak. The superimposed trend line through the logarithm of the odds ratios (treated as single points) illustrates the substantial non-conformity with a linear relationship with COVID-19 bed-days (figure 1). Staff working in either the emergency department or in critical care were no more likely to have detectable antibodies than staff working in non-clinical areas (table 3). Patients with COVID-19 were cared for throughout the trust and the 'COVID-19 bed days' demonstrates the range of potential staff exposure across medical and surgical wards. Of note however, the increased risk of seroconversion of staff working in the

Table 1 Summary statistics of respondents to invitation to undergo antibody testing (n=4474)

Demographic characteristics		
Gender: n (%)	Male	980 (21.9)
Age: mean (SD)	Years	42.5 (13.2)
Ethnicity: n (%)	Asian/Asian British	492 (11.0)
	Black/black British	79 (1.8)
	Chinese	21 (0.5)
	Mixed	66 (1.5)
	White UK and ROI	3143 (70.3)
	White other	123 (2.7)
	Unknown	550 (12.3)
Environmental characteristics		
Locations: n (%)	Non-clinical	2728 (61.0)
	Emergency department	305 (6.8)
	Critical care	209 (4.7)
	Other clinical locations	1232 (27.5)
Clinical characteristics		
PCR result: n (%)	Positive	209 (4.7)
	Negative	541 (12.1)
	Not performed	3698 (82.7)
	Inconclusive	16 (0.4)
	Unknown	10 (0.2)
Symptoms: n (%)	Yes	1871 (41.8)
	No	2547 (56.9)
	Unknown	56 (1.3)
Antibody result: n (%)	Positive	777 (17.4)
	Negative	3697 (82.6)

emergency department only just failed to reach significance (OR 1.38, 95% 0.98 to 1.93, $p=0.062$). One medical ward demonstrated the largest positive trend to staff seropositivity (OR 15.36, 95% CI 7.21 to 32.74); however, the relatively small number of responders generated a wide CI (table 3).

Prevalence and symptoms

Most staff responded to the question regarding whether they had experienced symptoms compatible with COVID-19 (4418/4474). Of these responders, 41.8% (1871/4474) reported symptoms. Antibodies were detected in 574/1871 (30.7%) individuals who reported symptoms, and 196/2547 (7.7%) individuals who reported no symptoms (table 4). Of those with antibodies detected, 25.2% (196/777) reported no symptoms. Sensitivity and specificity of self-reported symptoms as an indication of COVID-19 infection were 74.5% (95% CI 71.3% to 77.6%) and 64.5% (95% CI 62.9% to 66.0%), respectively.

Table 2 OR from the binary logistic regression for demographic characteristics and location type (n=4474)

	OR	95% CI	P value
Age per 1 year change	0.988	0.982 to 0.994	<0.001
Male (reference category)	1.000		
Female	1.060	0.868 to 1.293	0.568
White UK and ROI (reference category)	1.000		
Asian/Asian British	1.608	1.266 to 2.042	<0.001
White other	1.275	0.792 to 2.051	0.317
Black/black British	2.080	1.254 to 3.449	0.005
Mixed	0.722	0.351 to 1.487	0.377
Chinese	0.619	0.179 to 2.145	0.449
Unknown ethnicity	1.441	1.140 to 1.823	0.002
Non-clinical location (reference category)	1.000		
Clinical location	2.675	2.268 to 3.154	<0.001

Testing for SARS-CoV-2 by PCR was reported by 772 individuals. A valid result was recorded or available for 746 of these staff members (staff who recorded that they were not informed of their result, and invalid results were excluded). A small number of staff (n=5) self-reported a positive SARS-CoV-2 PCR but tested antibody negative. Antibodies were detected in 79 members of staff who self-reported a negative PCR.

DISCUSSION

We report a large dataset of SARS-CoV-2 antibody results for staff performing various roles in a large teaching hospital. We are not aware of any other published dataset of comparable size, nor of any that have used this Roche antibody assay in healthcare workers. Our finding of 17.4% seroprevalence in our staff compares to a range of 7%–44% in other studies.^{12–17} Differences in the number of staff infections have varied geographically. This is likely to be multifactorial and the number of infections in the local community is likely to contribute. By the end of this study period (early July 2020), it was estimated that seroprevalence in the North West of England as a whole was approximately 8%.¹⁸ It is also noteworthy that numerous antibody assays are being used nationally and their different performance characteristics may contribute to these differences. Our findings that staff working in most clinical areas are more likely to have been infected with SARS-CoV-2 than non-clinical staff are concordant with other studies. Likewise, the finding that lower rates of infection in staff working in the emergency or critical care departments demonstrated in this study has been noted previously.¹⁶ Higher rates of infection in black and ethnic minority individuals have also been reported nationally.¹⁹

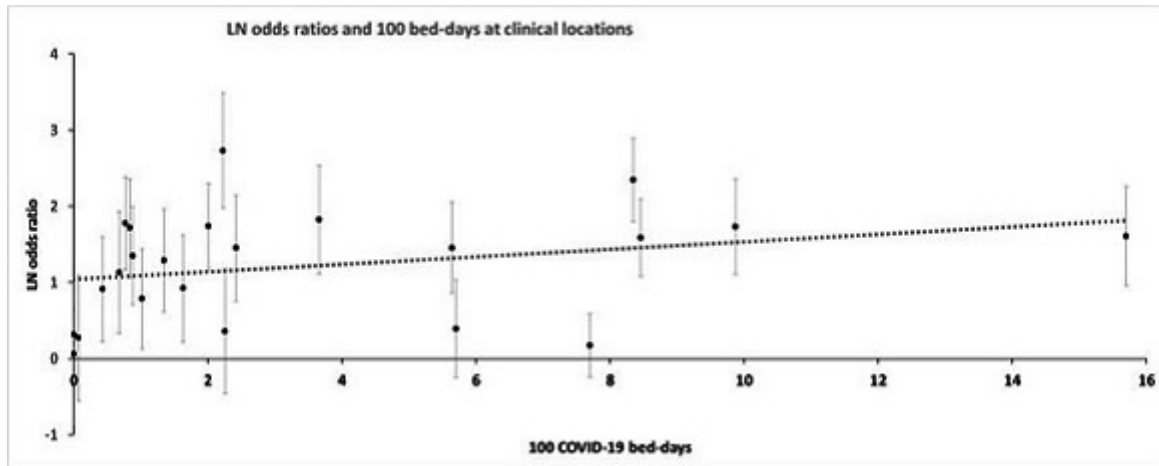


Figure 1 ORs for individual clinical locations relative to a non-clinical location against COVID-19 bed-days at each location; points are ORs, bars are 95% CIs and dashed line illustrates the trend through ORs treated as points.

Table 3 COVID-19 bed-days and OR for seropositivity from the binary logistic regression for demographic characteristics and the 24 different locations with 30 or more respondents (n=4189); only ORs for locations shown

Location	Staff N (%)	OR	95% CI	P value	COVID-19 bed-days
Non-clinical location (reference category)	3013 (67.3%)	1.000			0
Emergency department	305 (6.8%)	1.377	0.984 to 1.927	0.062	0
Critical care unit	209 (4.7%)	1.190	0.783 to 1.808	0.416	770
Medical	34 (0.8%)	15.364	7.209 to 32.741	<0.001	223
Medical	56 (1.3%)	10.455	6.045 to 18.084	<0.001	835
Medical	32 (0.7%)	6.203	3.041 to 12.656	<0.001	366
Surgical	45 (1.0%)	5.917	3.222 to 10.864	<0.001	77
Surgical	53 (1.2%)	5.691	3.242 to 9.989	<0.001	201
Medical	43 (1.0%)	5.646	3.016 to 10.567	<0.001	987
Surgical	40 (0.9%)	5.569	2.923 to 10.610	<0.001	84
Medical	40 (0.9%)	5.003	2.612 to 9.583	<0.001	1570
Medical	68 (1.5%)	4.892	2.944 to 8.129	<0.001	846
Surgical	49 (1.1%)	4.297	2.370 to 7.790	<0.001	564
Surgical	36 (0.8%)	4.270	2.126 to 8.575	<0.001	242
Medical	44 (1.0%)	3.863	2.032 to 7.342	<0.001	88
Medical	40 (0.9%)	3.629	1.837 to 7.171	<0.001	135
Medical	30 (0.7%)	3.096	1.392 to 6.888	0.006	68
Medical	43 (1.0%)	2.519	1.249 to 5.083	0.010	163
Surgical	44 (1.0%)	2.491	1.253 to 4.950	0.009	43
Surgical	53 (1.2%)	2.191	1.133 to 4.239	0.020	102
Medical	68 (1.5%)	1.479	0.778 to 2.815	0.233	570
Medical	44 (1.0%)	1.433	0.631 to 3.257	0.390	226
Surgical	45 (1.0%)	1.310	0.576 to 2.977	0.520	7
Medical	40 (0.9%)	1.063	0.410 to 2.753	0.901	0
Zero bed-days (reference category)		1.000			
Change per 100 bed-days		1.115	1.089 to 1.142	<0.001	

OR for 100 bed-days change also shown (n=4474).

Table 4 Symptoms and COVID-19 antibody prevalence

		Respondents' self-report:		
		Symptomatic (n=1871)	Asymptomatic (n=2547)	Non-response (n=56)
Antibody test negative:	PCR result:			
	Negative	375	85	2
	Positive	5	0	0
	Not performed	906	2261	47
	Inconclusive	7	3	0
	Unknown	4	2	0
	Total	(69.3%) 1297	(92.3%) 2351	49
Antibody test positive:	PCR result:			
	Negative	73	6	0
	Positive	199	3	2
	Not performed	293	186	5
	Inconclusive	6	0	0
	Unknown	3	1	0
	Total	(30.7%) 574	(7.7%) 196	7

The finding that the number of COVID-19 bed-days of a clinical area correlates with the prevalence of staff seropositivity is intuitive. However, this weak association suggests that factors other than the number of patients with COVID-19 in a clinical area contribute to the risk of staff infection. These could be numerous, and not limited to: adequacy and compliance with PPE, relative ventilation and air changes per hour, social distancing of staff groups within the clinical and recreational areas, and inappropriate de-escalation of patients with COVID-19 based on false-negative PCR results. This latter risk was somewhat mitigated by the introduction of fluid-resistant surgical masks in all patient-facing healthcare workers from early April. It was not possible to ascertain why some clinical areas have higher numbers of staff seroconversion than others. This is likely to be multifactorial and would require further investigation. The finding that a quarter of staff with antibodies reported no compatible symptoms indicates that asymptomatic infection occurred at significant levels and has implications for the control of this pandemic. It should be considered that onward transmission from such individuals may be possible if compliance with guidance regarding PPE and distancing is not followed.

Of the staff (2/5) whose positive PCR was performed at our trust, the PCR result preceded the antibody test by at least 21 days, allowing sufficient time to produce antibodies. These discrepancies could be a result of a false-positive PCR result, a false-negative antibody result, or a genuine case of no immune response being elicited. Likewise, it was not possible to definitively determine why some staff had demonstrable antibodies and a negative PCR result. This may be due to a myriad of reasons, including the timing or quality of the swab sampling, or

that the symptoms that prompted testing were due to another cause and individuals were previously, or subsequently, asymptotically infected with SARS-CoV-2.

This retrospective analysis has some limitations. First, although comparison with trust electronic staff records shows that our respondents are representative of the trust as a whole, there is a potential for ascertainment bias with staff who knew or believed that they were infected to be more likely to come forward for testing. The varying numbers of individuals in different clinical areas have generated wide confidence intervals. This reduces the ability to elucidate further which areas are genuine outliers that could indicate specific good practice or inadequacies leading to lower or higher staff infection rates. This study used a single antibody assay so all results in this study are comparable. However, other centres have used different assays, which means comparison of rates of staff infection between sites is not straightforward. Furthermore, the Roche antibody assay is most sensitive after at least 21 days following infection and there is growing evidence of declining titres with time. It is therefore possible that false negative results could be generated as a result of sampling staff prior to 21 days after infection, or due to waning antibody titres if infection occurred far earlier in the pandemic.

This COVID-19 pandemic has necessitated new ways of working and has led to innovation in healthcare systems. As the clinical presentation and progression have been more clearly characterised, along with a greater understanding of the diagnostic tools available, case finding (especially nosocomial infection) has improved. This should reduce the frequency in which infected patients are inappropriately de-escalated to non-COVID-19 areas, and therefore reduce further transmission, including to

staff. Our data clearly show that staff who work in clinical areas with large numbers of COVID-19 patients are more likely to have demonstrable SARS CoV-2 infection. However, this is not the only correlating factor. Using these data to further reduce the risk to healthcare workers in all settings must be a priority. Real-time data to show particular hotspots with high numbers of COVID-19 bed-days could prompt proactive staff surveillance, with enhanced audit of infection prevention and control practice in areas with suspected high rates of transmission.

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Contributors RJS and SH contributed equally to this research and should be acknowledged as such in the list of authors. All authors were involved in the conceptual design of this study. SH, MM and PW established the antibody test. PW established the PCR test. DO led the Trust's COVID-19 response and established the 'COVID bed days' dashboard. RJS and SH wrote the manuscript and analysed the initial data. MAH provided statistical analysis and advice. All authors were involved in manuscript review.

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