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Characterisation of the SARS-CoV-2 pandemic in healthcare workers within the United Kingdom: Risk factors for infection during four successive waves

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SUMMARY

Background: Healthcare workers were at a high risk of infection early in the SARS-CoV-2 pandemic. It is uncertain to what extent occupational, household and community factors contributed, and how this changed over time. We aimed to characterise the risk factors for infection over four successive waves of the pandemic in a large, UK healthcare worker cohort (SIREN).

Methods: Participants underwent fortnightly SARS-CoV-2 PCR testing and symptom/exposure questionnaire. Attack rates and adjusted OR of infection were calculated according to participant characteristics and exposures for each wave between 1st October 2020 and 30th August 2022.

Findings: 19,427 participants were included in the second wave, 20,260 in the third, 11,937 in the fourth, and 6503 in the fifth. The attack rates of infection were 9.1% (alpha), 6.6% (delta), 36.6% (omicron BA.1/2) and 15.9% (omicron BA.4/5), respectively.

Occupational risk factors were only apparent in the second wave, during which significant social distancing measures were in place. These were identified as working as a healthcare assistant, nurse or bedside therapist, and working on an inpatient ward. Occupational exposure requiring personal protective equipment was also a risk.

In subsequent waves, without social restrictions, occupational characteristics were not risk factors. Instead, living with others compared to living alone was a risk, particularly children. During the third wave (winter 2021–2022), having a colleague with COVID-19 was identified as a risk for the first time.

Interpretation: Our findings highlight clinical areas and occupational groups in which there may be scope to prevent healthcare-associated infections, particularly during winter pressures. Prospective studies targeting these are essential to establish which interventions are most effective. This study also underscores the importance of community circulation and exposures when considering healthcare workforce protection.

Introduction

The SARS-CoV-2 pandemic had global impact, with the majority of the world's population experiencing social distancing mandates, curfews and lockdowns for significant periods of 2020 and 2021 in order to control transmission, reduce deaths, and prevent the collapse of effective healthcare delivery.[1] Studies from multiple settings during the early waves of the pandemic suggest that healthcare workers, compared to the general population, were at a particularly high risk of infection.[2–5] In the United Kingdom (UK), during these periods of high incidence, illness within the workforce was also a considerable threat to staffing-levels and healthcare provision.[6,7] A deeper understanding of how occupational, household and community exposures contributed to these infection rates are essential for future preparedness.

The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study is a large multicentre cohort of over 44,000 healthcare workers recruited across 135 National Health Service (NHS) sites

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within the UK.[8] In previous work, we established certain occupational characteristics that put healthcare workers in England at risk of primary infection during the second wave of the pandemic, including working as a healthcare assistant and working in an emergency department or inpatient ward setting.[9] Since the second wave, which involved social distancing measures and the emergence of the alpha variant, the pandemic in the UK went through many developments and SIREN continued throughout.

To protect staff and healthcare delivery during future winter pressures and pandemics, we must understand the risk factors for infection within our workforce, and how these changed alongside evolving social distancing measures, with shifts in occupational, household and community exposure. During the pandemic in the UK, infection prevention and control (IPC) transmission-based precaution measures, including isolation/cohorting of patients and use of personal protective equipment (PPE) and respiratory protective equipment (RPE), were introduced in line with international guidance.[10,11] These measures were in addition to public health measures and national testing policies and implemented according to local risk assessments based on individual and organisational need, community-level incidence, and the social distancing measures and restrictions in place at the time.[12] Given this local variation and the lack of prospective controlled trials or high-quality observational studies on IPC measures in healthcare, it remains difficult to unpick the impact of each individual measure and establish how their effectiveness varied according to community and specific healthcare environment circumstance.

We aimed to determine infection rates and investigate the demographic, occupational, household and community factors associated with SARS-CoV-2 infection within UK healthcare workers during four distinct waves of the SARS-CoV-2 pandemic.

Methods

Study design

SIREN is a national multicentre prospective cohort study of healthcare workers (≥18 years) in the UK, participating in regular SARS-CoV-2 testing, with continuous follow-up since June 2020. Participants were initially consented for 12-months of active follow-up, with subsequent invitations to extend up to 33-months in total. The full study design and methods have been described previously.[8] Ethical approval was granted by the Berkshire Research Ethics Committee (IRAS ID 284460, REC reference 20/SC/0230).

Data collection and sources

At enrolment, participants completed a survey detailing demographic, household, and occupational characteristics. Throughout follow-up, they completed a fortnightly symptom and exposure (clinical, household and community) questionnaire and underwent fortnightly SARS-CoV-2 polymerase chain reaction (PCR) testing as per the SIREN protocol.[8] Vaccination data were obtained via the fortnightly questionnaires and through linkage to national vaccination registries. Index of multiple deprivation (IMD) was acquired according to postcode upon enrolment, where available.

Study period

SIREN has run continuously since June 2020, enrolling participants at pace early in the pandemic. For this analysis, we defined four periods of specific interest corresponding to periods of high infectivity (waves of infection) in both the SIREN cohort and nationally. These four periods were October 2020 to April 2021 (the second wave, predominantly the alpha variant), May to November 2021 (the third wave, predominantly the delta variant), December 2021 to April 2022 (the fourth wave, predominantly the omicron BA.1/2 variants), and May to August 2022 (the fifth wave, predominantly the omicron BA.4/5 variants).[13] The boundaries of the waves were chosen according to troughs in incidence, apart from the second wave where the observation period start date was chosen as a balance between incidence and cohort size, as recruitment was still active.

Outcome

The outcome in our analyses was a positive SARS-CoV-2 PCR test within the observation period, according to specimen date. An outcome could only occur once per participant within each wave.

Inclusion and exclusion criteria

Participants were included in each wave's cohort if they were under follow-up throughout the entirety of the wave and did not have a positive SARS-CoV-2 PCR test in the previous wave. We excluded participants who did not contribute to all demographic, occupational and household variables and, for the fourth and fifth waves, participants that had not received two doses of a COVID-19 vaccine upon entry to the wave.

Exposures

Static (captured on enrolment) and dynamic (fortnightly questionnaire) variables were included. Static variables consisted of gender, age, ethnicity, past medical history, whether the participant was patient-facing, occupational role, occupational setting, IMD quintile, type of household and region of residence.

Dynamic variables were self-reported clinical exposure and PPE use, known contact with a colleague with confirmed COVID-19, having a household member with confirmed COVID-19 and being contacted by a National Health Service (NHS) contact-tracing service (England, Northern Ireland and Wales: Test and Trace, Scotland: Test and Protect) or self-reporting a confirmed community contact.

Vaccination date was also captured, and a delay-to-vaccination linear variable created for each wave, defined as time to effective vaccine coverage within the wave (second wave: 21 days after first vaccine, third wave: 14 days after second vaccine, fourth and fifth waves: 14 days after booster vaccine).

Statistical analysis

The entire SIREN cohort was included to create an epidemic curve of the pandemic, with the calculation of fortnightly PCR positivity (number of positive PCR tests per 1000 participants tested) with 95% confidence intervals (CI). We then analysed each wave individually, including only those participants meeting the inclusion criteria described previously. For each wave's cohort, attack rates according to participant characteristics were calculated and adjusted odds ratios (aORs) of infection with 95% CIs were estimated through a mixed effects logistic regression model. Static characteristics were included as categorical variables (fixed effects) and vaccine delay included as a continuous variable (fixed effects), all nested within healthcare organisation-level clusters (random effects).

Further multi-variate analyses were performed to consider the dynamic clinical, household and community exposures reported by participants in each wave. For individuals that were infected within a wave, the questionnaire which included the date 14 days prior to their first positive PCR of an infection episode was included for analysis. This ensured that the questionnaire captured the most representative period of infection acquisition and that it was completed prior to the participant's knowledge of infection confirmation. This questionnaire was the only one that an infected participant

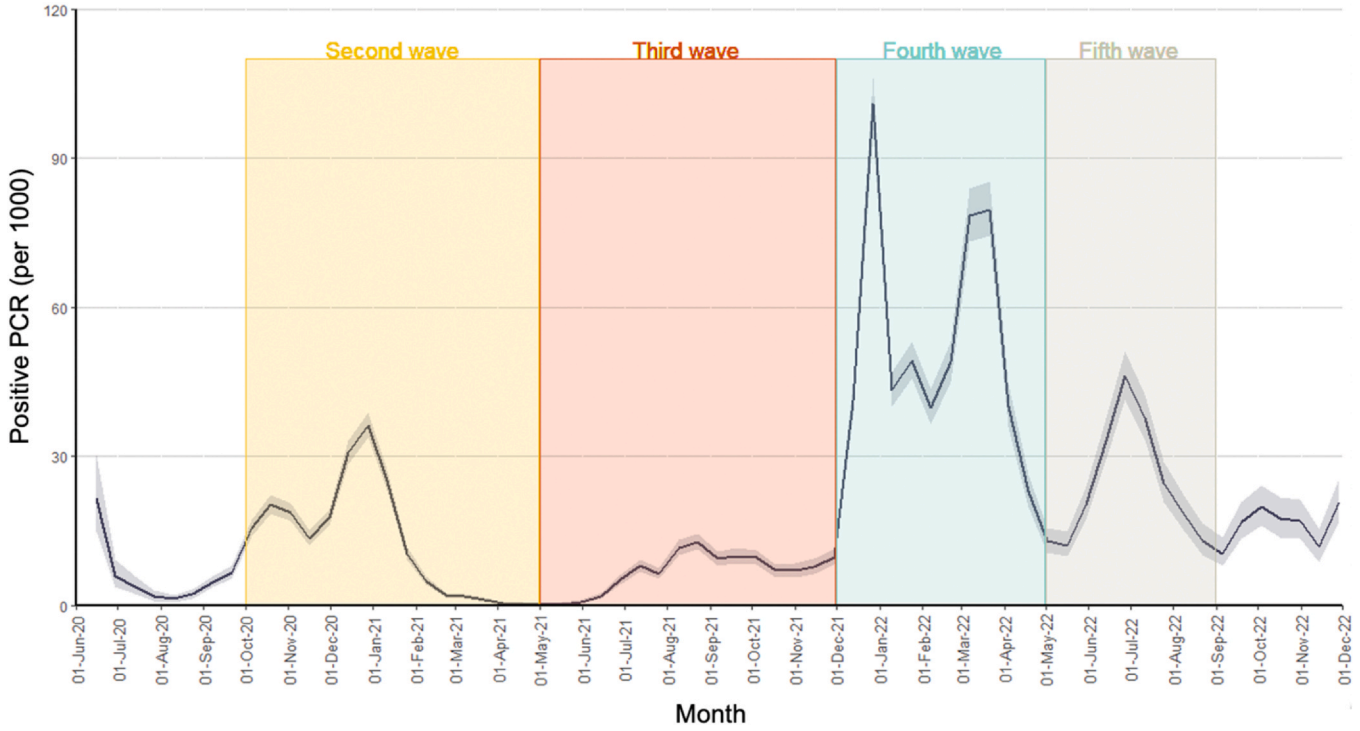

Fig. 1. Incidence of infection in SIREN participants during the SARS-CoV-2 pandemic in the United Kingdom.

contributed to the wave's analysis. For individuals who were not infected within a wave, data from all of their fortnightly questionnaires within the wave were included. Unadjusted odds ratios (ORs) and an adjusted odds ratio (aOR) of infection in participants reporting each exposure type in each wave were calculated with 95% CIs. Adjustment was by gender, age group and ethnicity as a priori variables in addition to exposure-specific participant characteristics that were considered potential confounders after a conceptual model exercise (occupational role and setting for clinical exposures, IMD quintile and household size for household exposures, and IMD quintile and region for community exposures).

All analyses were conducted using Stata Statistical Software: Release 17.0.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The views expressed are those of the authors.

Results

Between 18th June 2020 and 31st March 2021, 44,546 healthcare workers were recruited to the SIREN study. Fig. 1 shows the rate of infection in all SIREN participants between the first day of recruitment and 1st December 2022, and outlines the waves included in this study for further investigation. As recruitment in Northern Ireland, Scotland and Wales started later, only participants from England were under active follow-up for the duration of the second wave, and therefore included in the second wave analysis. For all other waves, participants were from across the UK.

The second wave peaked in the fortnight beginning 28th December 2020, with a PCR positivity rate of 36.3/1000 (95% CI 33.9 to 38.9/1000). The third wave peaked in the fortnight beginning 23rd August 2021, with a PCR positivity rate of 12.8/1000 (11.3 to 14.5/1000). The fourth wave peaked in the fortnight beginning 27th December 2021, with a PCR positivity rate of 100.9/1000 (95.8 to 106.2/1000). Finally, the fifth wave peaked in the fortnight beginning 27th June 2022, with a PCR positivity rate of 46.2/1000 (41.5 to 51.3/1000).

Fig. 2 shows the flowchart of participant inclusion and exclusion for further analysis. After the exclusion of participants that did not provide data for all demographic, occupational and household characteristics (1488 participants) and participants that had not received their first two vaccinations before the fourth (375 participants) and fifth (151 participants) waves, 19,427 participants contributed to the analyses for the second wave, 20,260 for the third wave, 11,937 for the fourth wave, and 6503 for the fifth wave. Fig. 3 shows the overall attack rate and the proportion of reinfections for each wave. Table 1 summarises the aOR of infection during each wave according to the demographic, occupational and household characteristics captured at enrolment. A more detailed table with numerator/denominators, attack rate and p values are available in the Supplementary Material.

The proportion of participants reporting each exposure and the aOR of infection are presented in Table 2. The questionnaire completion rate amongst participants with infection was 83.3% (1466/1760), 74.0% (990/1338), 84.0% (3659/4356) and 90.6% (938/1035) in the second, third, fourth and fifth waves respectively. Questionnaire completion in non-infected participants was 77.5% for the second wave (1.68 per participant per month), 71.0% for the third wave (1.54 per participant per month), 72.5% for the fourth wave (1.57 per participant per month) and 65.0% for the fifth wave (1.41 per participant per month).

Second wave

During the second wave, independent occupational risk factors for infection were working as a healthcare assistant (aOR 1.39, [1.09 to 1.77]), nurse (aOR 1.29 [1.05 to 1.57]), or bedside therapist (aOR 1.41 [1.01 to 1.98]), and working in any inpatient ward setting (aOR 1.67 [1.32 to 2.11]). Having clinical exposures requiring PPE use (aOR 2.08 [1.86 to 2.34] where PPE was used at every opportunity and 1.79 [1.08 to 2.97] with a self-reported suspected PPE breach) were also

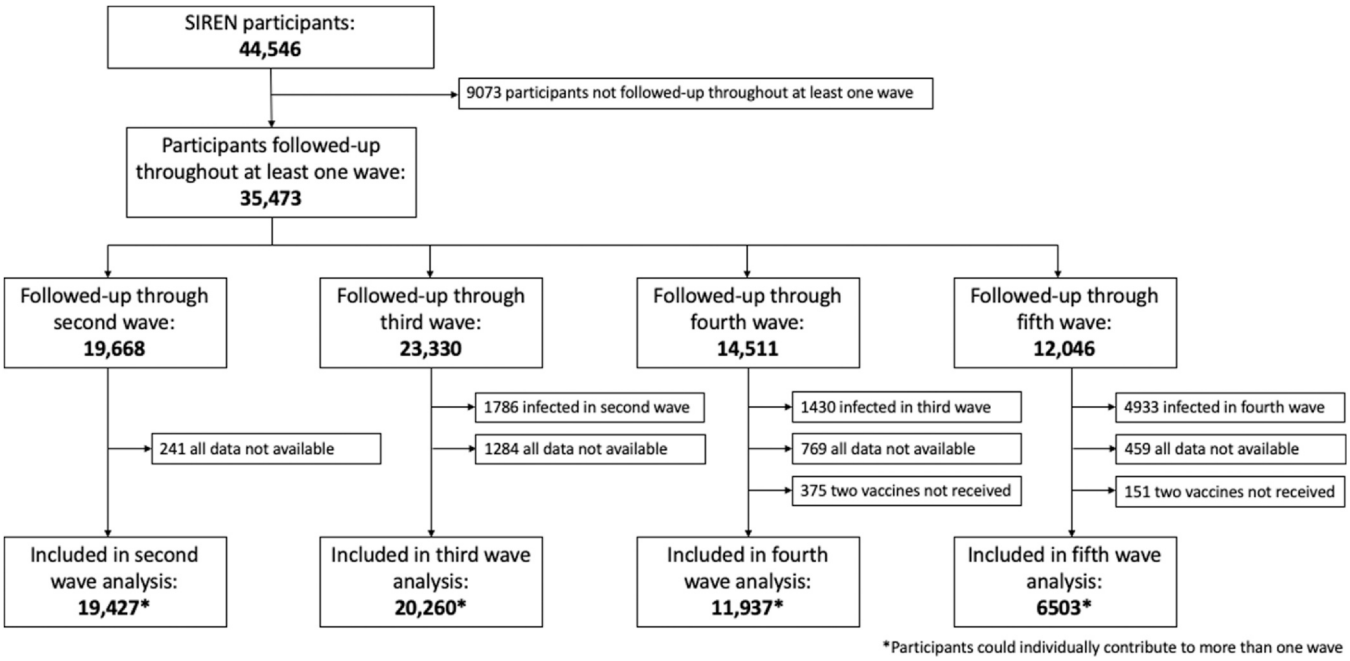

Fig. 2. Flowchart of SIREN participants included in this study.

associated with infection. Delay to first vaccine was a significant risk factor during the second wave, with each day of delay increasing a participant's risk of infection by 1.11% ($p < 0.001$). Despite these occupational risks, exposure risk factors with the highest relative risk were living with a household member with confirmed COVID-19 (aOR 10.73 [8.60 to 13.38]) and having a known community contact or national contract-tracing service alert (aOR 5.14 [4.19 to 6.30]).

Third wave

During the third wave, occupational risk factors were not found to be statistically significant. Deprivation according to IMD quintile was a new risk factor (IMD first quintile aOR 1.42 [1.17 to 1.74] and IMD second quintile aOR 1.35 [1.13 to 1.61] compared to IMD fifth quintile). Higher rates of infection were observed in participants

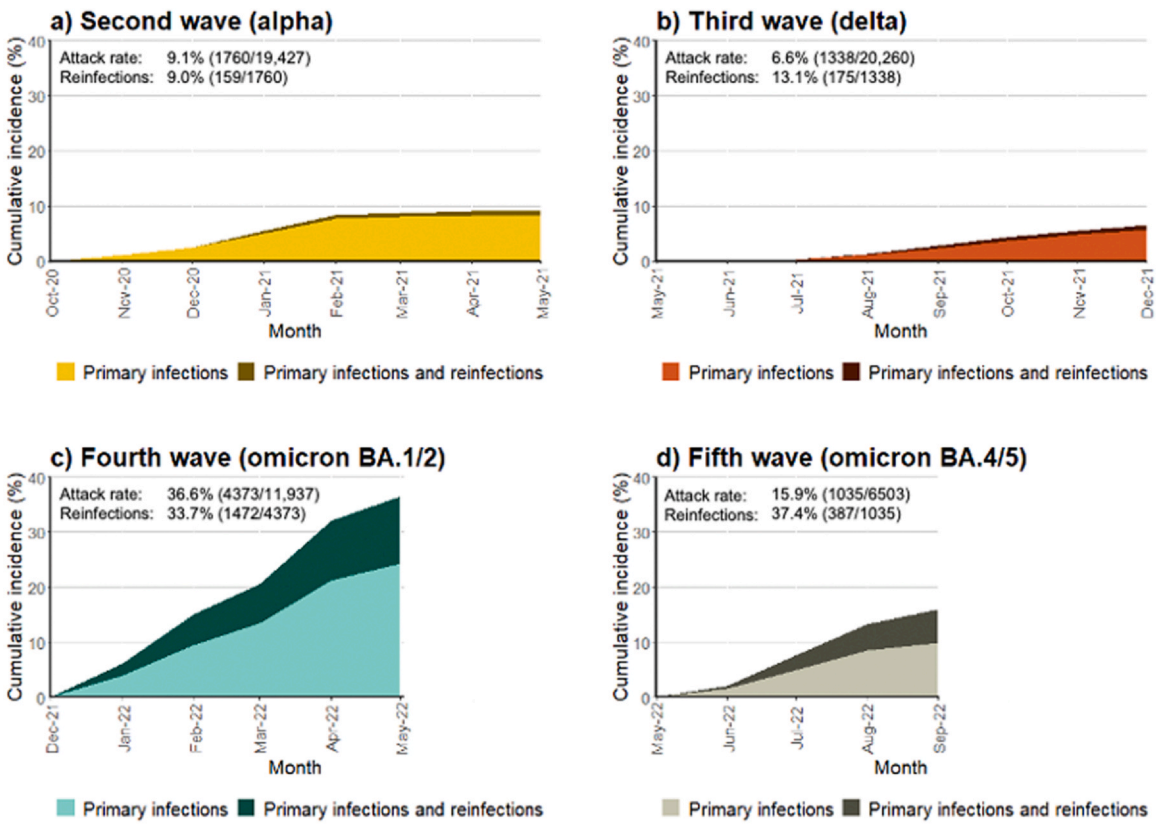

Fig. 3. Cumulative proportion of SIREN participants infected within each wave of the SARS-CoV-2 pandemic in the United Kingdom.

Table 1
SARS-CoV-2 infection during the United Kingdom's second, third, fourth and fifth wave of the pandemic according to SIREN participant demographic, occupational and household characteristics.

Participant characteristics	Second wave (n = 19,427)	Third wave (n = 20,260)	Fourth wave (n = 11,937)	Fifth wave (n = 6503)
	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Gender				
Female	*Ref*	*Ref*	*Ref*	*Ref*
Male	1.07 (0.92 to 1.23)	1.13 (0.96 to 1.32)	0.94 (0.84 to 1.05)	1.02 (0.83 to 1.25)
Age group				
18 to 25	1.73 (1.36 to 2.21)	1.37 (0.99 to 1.90)	1.63 (1.20 to 2.21)	0.45 (0.19 to 1.08)
25 to 34	1.04 (0.89 to 1.20)	0.99 (0.83 to 1.19)	1.56 (1.38 to 1.77)	0.96 (0.75 to 1.23)
35 to 44	0.98 (0.85 to 1.12)	1.17 (1.01 to 1.35)	1.29 (1.17 to 1.43)	0.83 (0.68 to 1.00)
45 to 54	*Ref*	*Ref*	*Ref*	*Ref*
55 to 64	0.89 (0.76 to 1.04)	0.94 (0.78 to 1.12)	0.90 (0.81 to 1.01)	0.91 (0.76 to 1.09)
Over 65	0.74 (0.45 to 1.20)	0.87 (0.50 to 1.51)	1.07 (0.80 to 1.44)	0.71 (0.42 to 1.21)
Ethnicity				
Asian	1.12 (0.93 to 1.35)	0.79 (0.62 to 1.01)	0.99 (0.85 to 1.16)	0.65 (0.45 to 0.92)
Black	0.80 (0.57 to 1.12)	0.98 (0.67 to 1.45)	0.60 (0.45 to 0.81)	0.73 (0.42 to 1.28)
White	*Ref*	*Ref*	*Ref*	*Ref*
Mixed ethnicity	0.49 (0.29 to 0.80)	1.22 (0.80 to 1.86)	1.01 (0.81 to 1.51)	1.16 (0.66 to 2.05)
Other ethnicity	0.69 (0.43 to 1.11)	0.65 (0.36 to 1.17)	0.88 (0.63 to 1.23)	0.82 (0.41 to 1.64)
Medical conditions				
No medical conditions	*Ref*	*Ref*	*Ref*	*Ref*
Immunocompromised	0.89 (0.60 to 1.30)	1.06 (0.73 to 1.55)	0.99 (0.77 to 1.27)	0.83 (0.52 to 1.33)
Chronic respiratory conditions	0.95 (0.82 to 1.12)	1.01 (0.85 to 1.20)	1.01 (0.90 to 1.14)	1.16 (0.94 to 1.43)
Chronic non-respiratory conditions	1.16 (0.98 to 1.36)	0.99 (0.82 to 1.19)	0.88 (0.77 to 1.00)	0.89 (0.71 to 1.12)
Patient-facing				
Yes	*Ref*	*Ref*	*Ref*	*Ref*
No	0.93 (0.76 to 1.14)	0.98 (0.80 to 1.21)	0.94 (0.82 to 1.08)	0.94 (0.73 to 1.20)
Occupational role				
Administrative/executive	*Ref*	*Ref*	*Ref*	*Ref*
Doctor	1.18 (0.92 to 1.52)	0.93 (0.71 to 1.22)	0.91 (0.76 to 1.09)	0.90 (0.66 to 1.24)
Nursing	1.29 (1.05 to 1.57)	0.92 (0.74 to 1.15)	1.03 (0.90 to 1.19)	0.81 (0.63 to 1.04)
Healthcare assistant	1.39 (1.09 to 1.77)	1.11 (0.85 to 1.46)	1.03 (0.85 to 1.25)	0.78 (0.55 to 1.11)
Midwife	0.98 (0.66 to 1.46)	1.07 (0.65 to 1.75)	0.77 (0.56 to 1.08)	1.01 (0.57 to 1.80)
Healthcare scientist	0.87 (0.61 to 1.23)	1.24 (0.90 to 1.69)	1.04 (0.83 to 1.30)	0.85 (0.56 to 1.28)
Pharmacist	0.84 (0.45 to 1.58)	0.96 (0.63 to 1.48)	0.79 (0.59 to 1.05)	0.87 (0.54 to 1.40)
Bedside therapist*	1.41 (1.01 to 1.98)	1.04 (0.75 to 1.44)	1.02 (0.82 to 1.28)	1.02 (0.69 to 1.52)
Student	1.23 (0.94 to 1.59)	1.01 (0.65 to 1.57)	1.09 (0.85 to 1.40)	0.70 (0.36 to 1.33)
Estates/porters/security	1.35 (0.73 to 2.47)	0.99 (0.65 to 1.52)	1.28 (0.94 to 1.75)	1.11 (0.67 to 1.84)
Other	1.19 (0.96 to 1.47)	0.89 (0.70 to 1.13)	1.02 (0.87 to 1.19)	0.87 (0.66 to 1.16)

Occupational setting				
Office	*Ref*	*Ref*	*Ref*	*Ref*
Patient-facing (non-clinical)	1.19 (0.87 to 1.64)	0.94 (0.66 to 1.33)	1.15 (0.92 to 1.44)	1.48 (1.01 to 2.19)
Outpatient	1.21 (1.00 to 1.48)	1.14 (0.93 to 1.41)	1.09 (0.95 to 1.24)	1.16 (0.91 to 1.49)
Maternity/labour ward	0.80 (0.37 to 1.71)	1.22 (0.71 to 2.07)	1.39 (0.93 to 2.07)	0.75 (0.36 to 1.54)
Ambulance/emergency department†	1.27 (0.80 to 2.01)	1.19 (0.85 to 1.66)	1.00 (0.76 to 1.33)	0.93 (0.57 to 1.50)
Inpatient wards	1.67 (1.32 to 2.11)	0.96 (0.77 to 1.20)	1.10 (0.94 to 1.27)	0.91 (0.69 to 1.19)
Intensive care	1.07 (0.83 to 1.38)	1.02 (0.73 to 1.42)	1.12 (0.91 to 1.38)	1.20 (0.80 to 1.81)
Theatres	0.97 (0.57 to 1.68)	1.33 (0.95 to 1.87)	1.06 (0.82 to 1.37)	1.08 (0.70 to 1.66)
Other	1.03 (0.87 to 1.22)	1.09 (0.89 to 1.34)	0.96 (0.85 to 1.09)	1.23 (0.96 to 1.56)
Index of Multiple Deprivation (IMD) quintile				
(Most deprived) 1	1.01 (0.84 to 1.22)	1.42 (1.17 to 1.74)	1.03 (0.89 to 1.19)	0.84 (0.63 to 1.11)
2	0.93 (0.79 to 1.10)	1.35 (1.13 to 1.61)	1.03 (0.91 to 1.16)	1.01 (0.81 to 1.27)
3	0.93 (0.80 to 1.08)	1.08 (0.91 to 1.28)	0.98 (0.87 to 1.09)	1.18 (0.97 to 1.45)
4	1.07 (0.93 to 1.24)	0.99 (0.83 to 1.17)	0.96 (0.86 to 1.07)	1.04 (0.86 to 1.26)
(Least deprived) 5	*Ref*	*Ref*	*Ref*	*Ref*
Household type				
Lives alone	*Ref*	*Ref*	*Ref*	*Ref*
Lives with others (no children)	1.06 (0.88 to 1.27)	1.34 (1.06 to 1.69)	1.23 (1.08 to 1.39)	1.12 (0.90 to 1.40)
Lives with others (including children)	1.09 (0.90 to 1.32)	2.45 (1.95 to 3.10)	1.57 (1.37 to 1.79)	1.01 (0.79 to 1.27)
Region				
East Midlands	0.83 (0.53 to 1.30)	1.14 (0.83 to 1.57)	0.81 (0.63 to 1.03)	0.62 (0.29 to 1.30)
East of England	0.59 (0.76 to 1.36)	0.83 (0.62 to 1.11)	0.85 (0.71 to 1.03)	1.15 (0.73 to 1.79)
London	*Ref*	*Ref*	*Ref*	*Ref*
North East	0.96 (0.37 to 2.49)	1.61 (1.09 to 2.38)	1.03 (0.76 to 1.39)	1.82 (0.89 to 3.70)
North West	1.04 (0.70 to 1.54)	1.12 (0.86 to 1.45)	1.04 (0.86 to 1.25)	1.22 (0.77 to 1.93)
Northern Ireland	N/A	0.26 (0.04 to 1.92)	1.34 (0.64 to 2.79)	4.16 (1.25 to 13.87)
Scotland	N/A	1.63 (1.29 to 2.06)	1.17 (0.97 to 1.40)	3.37 (2.17 to 5.23)
South East	0.92 (0.63 to 1.35)	1.03 (0.75 to 1.42)	0.92 (0.73 to 1.14)	1.27 (0.75 to 2.14)
South West	0.72 (0.50 to 1.03)	1.52 (1.15 to 2.00)	1.22 (0.97 to 1.55)	1.31 (0.66 to 2.59)
Wales	N/A	1.34 (0.96 to 1.86)	0.87 (0.64 to 1.19)	1.81 (0.96 to 3.41)
West Midlands	1.01 (0.66 to 1.55)	1.34 (0.99 to 1.80)	0.86 (0.67 to 1.07)	0.96 (0.58 to 1.59)
Yorkshire and the Humber	0.60 (0.38 to 0.95)	1.27 (0.95 to 1.71)	1.00 (0.80 to 1.25)	1.52 (0.89 to 2.60)

*Composed of occupational therapists, physiotherapists and speech and language therapists. †Includes paramedics. aOR = adjusted odds ratio, CI = confidence interval. Red = higher risk compared to reference, green = lower risk compared to reference, blue = comparable risk compared to reference, grey = reference.

who lived with others for the first time, particularly children (aOR 2.45 [1.95 to 3.10] in households with children and 1.34 [1.06 to 1.69] in households with other adults only, compared to living alone). Exposure questionnaires continued to find confirmed household and community COVID-19 contacts to be significantly associated with infection (aOR 9.00 [7.15 to 11.33] and 5.50 [4.48 to 6.77], respectively). The impact of appropriate vaccination (second vaccine) delay was less than that of the first vaccine in the second wave, increasing a participant's risk of infection by 0.13% (p = 0.023) per day.

Fourth wave

During the fourth wave, living with others remained a strong risk factor (aOR 1.57 [1.37 to 1.79] in households with children and 1.23 [1.08 to 1.39] in households with other adults only, compared to living alone). Whilst having a household or community contact with confirmed COVID-19 remained associated with infection (aOR 2.98 [2.73 to 3.26] and 2.23 [1.93 to 2.57 respectively), both aORs were significantly lower than for the preceding waves. Having a colleague with confirmed COVID-19 was associated with infection (aOR 1.15 [1.04 to 1.28]) for the first time. Delay to booster (third) vaccination increased a participant's risk of infection by 0.15% (p = 0.008) per day.

Fifth wave

During the fifth wave, there were no specific demographic, occupational or household characteristics associated with infection, but household exposure to COVID-19 remained associated (aOR 5.74 [4.84 to 6.81]). Delay to booster vaccination did not affect a participant's risk of infection (p = 0.855): though the majority of participants were vaccinated with a booster prior to the start of the wave.

Discussion

We monitored SARS-CoV-2 infection rates in our large healthcare worker cohort throughout four successive waves of the pandemic within the UK, with overall attack rates ranging from 6.6% in the

Table 2
Clinical, households and community exposures of SIREN participants associated with SARS-CoV-2 infection during the United Kingdom's second, third, fourth and fifth waves of the pandemic.

Reported participant exposures	Proportion reported in questionnaires associated with infection (n/N)	Proportion reported in questionnaires from participants not infected in wave (n/N)	Unadjusted OR (95% CI)	P value	Adjusted* OR (95% CI)	P value
Second wave						
PPE use in episodes of clinical contact						
With every contact and no breaches	58.5% (858/1466)	38.9% (80,786/207,893)	2.25 (2.03 to 2.50)	<0.001	2.08 (1.86 to 2.34)	<0.001
Less than every contact or breach reported	1.1% (16/1466)	0.8% (1639/207,893)	2.07 (1.26 to 3.41)	0.004	1.79 (1.08 to 2.97)	0.023
No episodes requiring PPE	40.4% (592/1466)	60.4% (125,468/207,893)	Ref	-	Ref	-
Contact with infected colleague						
Yes	1.9% (28/1466)	1.8% (3699/207,893)	1.07 (0.74 to 1.56)	0.706	1.06 (0.73 to 1.55)	0.753
Infected household member						
Yes	6.2% (91/1466)	0.6% (1192/207,893)	11.48 (9.21 to 14.30)	<0.001	10.73 (8.60 to 13.38)	<0.001
Known community contact / Test and Trace alert						
Yes	7.1% (104/1466)	1.4% (2855/207,893)	5.48 (4.48 to 6.72)	<0.001	5.14 (4.19 to 6.30)	<0.001
Third wave						
PPE use in episodes of clinical contact						
With every contact and no breaches	25.5% (252/990)	25.1% (51,213/204,124)	1.02 (0.88 to 1.17)	0.830	0.97 (0.83 to 1.13)	0.701
Less than every contact or breach reported	0.6% (6/990)	0.9% (1787/204,124)	0.69 (0.31 to 1.55)	0.370	0.63 (0.28 to 1.41)	0.261
No episodes requiring PPE	73.9% (732/990)	74.0% (15,1124/204,124)	Ref	-	Ref	-
Contact with infected colleague						
Yes	2.5% (25/990)	2.3% (4615/204,124)	1.12 (0.75 to 1.67)	0.577	1.11 (0.74 to 1.65)	0.619
Infected household member						
Yes	8.8% (87/990)	0.8% (1686/204,124)	11.57 (9.23 to 14.50)	<0.001	9.00 (7.15 to 11.33)	<0.001
Known community contact / Test and Trace alert						
Yes	10.5% (104/990)	2.0% (4142/204,124)	5.67 (4.61 to 6.96)	<0.001	5.50 (4.48 to 6.77)	<0.001
Fourth wave						
PPE use in episodes of clinical contact						
With every contact and no breaches	33.6% (1229/3659)	30.1% (17,940/59,605)	1.18 (1.10 to 1.26)	<0.001	1.08 (1.00 to 1.16)	0.058
Less than every contact or breach reported	1.9% (69/3659)	1.9% (1113/59,605)	1.06 (0.83 to 1.36)	0.618	0.93 (0.72 to 1.19)	0.560
No episodes requiring PPE	64.5% (2361/3659)	68.0% (40,552/59,605)	Ref	-	Ref	-
Contact with infected colleague						
Yes	11.6% (424/3659)	10.3% (6110/59,605)	1.15 (1.03 to 1.27)	0.010	1.15 (1.04 to 1.28)	0.008
Infected household member						
Yes	17.9% (656/3659)	6.4% (3803/59,605)	3.21 (2.93 to 3.51)	<0.001	2.98 (2.72 to 3.26)	<0.001
Known community contact / Test and Trace alert						
Yes	6.2% (226/3659)	2.7% (1615/59,605)	2.36 (2.05 to 2.73)	<0.001	2.23 (1.93 to 2.57)	<0.001
Fifth wave						
PPE use in episodes of clinical contact						
With every contact and no breaches	23.1% (217/938)	23.8% (7363/30,873)	0.96 (0.82 to 1.12)	0.605	0.91 (0.77 to 1.08)	0.276
Less than every contact or breach reported	1.6% (15/938)	1.6% (482/30,873)	1.01 (0.60 to 1.70)	0.959	0.93 (0.55 to 1.58)	0.800
No episodes requiring PPE	75.3% (706/938)	74.5% (22,998/30,873)	Ref	-	Ref	-
Contact with infected colleague						
Yes	8.3% (78/938)	7.1% (2192/30,873)	1.19 (0.94 to 1.50)	0.157	1.19 (0.94 to 1.51)	0.144
Infected household member						
Yes	20.1% (189/938)	4.2% (1291/30,873)	5.78 (4.87 to 6.85)	<0.001	5.74 (4.84 to 6.81)	<0.001
Known community contact						
Yes	0.4% (4/938)	0.4% (117/30,873)	1.12 (0.41 to 3.05)	0.818	1.14 (0.42 to 3.12)	0.794

n = numerator, N = denominator, OR = odds ratio, CI = confidence interval.

third wave (delta variant) to 36.6% in the fourth wave (the emergence of omicron BA.1/2 variants). The demographic, occupational, household and community risk factors for SARS-CoV-2 infection in healthcare workers shifted across the four waves, with occupational risks most apparent during the second wave.

The second wave differed considerably from latter waves in the UK, and was the only one during the time period of this cohort study during which there was enforced social distancing.[14] It was punctuated by the emergence of the first major variant of concern (alpha: first detected within SIREN on 9th November 2020), the introduction of the first COVID-19 vaccine (BNT162b2 [COMIRNATY]: 8th December 2020), and the second and third national lockdowns in England (5th November to 2nd December 2020 and 6th January 2021 onwards respectively). Whilst having a confirmed household or community contact with COVID-19 was a strong exposure risk factor for infection during this wave, living with others in general during this period of limited social mixing was not associated with infection in our healthcare worker cohort compared to living alone: the second wave had the lowest proportion (6.2%) of infected participants reporting a household contact. Together, these findings suggest a high relevance of occupational exposures with regards to relative risk during the second wave. Clinical exposure requiring PPE was associated with infection in the second wave only. Of note, participants self-reporting a PPE breach were at no higher risk of infection during these periods than those reporting PPE use without breach: there was complete overlap of CI for PPE use with or without breach in the second wave, with both having approximately a two-fold increase in SARS-CoV-2 positivity. There are several possible explanations for this: participants may not recall every clinical exposure or PPE breech, were unknowingly using PPE incorrectly, perhaps due to unfamiliarity, or overall the use of PPE during this wave did not afford complete protection.

After the lifting of social restrictions (the third wave), there was an occupational, household and community risk factor shift. Occupational characteristics within healthcare workers no longer appeared to contribute significant risk in the context of higher community SARS-CoV-2 circulation,[15] and living with others, particularly children, became a strong risk factor. Lower IMD quintiles being associated with infection as restrictions were lifted during the third wave suggest possible differences in household and community mixing patterns in these groups, compared to the highest IMD quintile, as restrictions lifted.

During the fourth wave, in winter 2021–2022, the only occupation-related exposure associated with infection (after the lifting of previous restrictions) was having a colleague with COVID-19, which strongly associated with infection. This could be due to differences in colleague-to-colleague mixing patterns compared to winter 2020–2021, outside the context of national social distancing measures. Whilst not statistically significant, there was also a signal of an association between occupational exposures requiring the use of PPE during the fifth wave and infection ($p = 0.058$).

Together, our findings reinforce the importance of considering the hierarchy of controls in pandemic contexts, whereby public health restrictions placed in the community and in healthcare settings, such as social distancing, can have a larger protective effect in hospitals than those measures lower down the hierarchy.[16]

It has been widely documented that healthcare workers in many settings were at increased risk of SARS-CoV-2 infection in the first wave, compared to the general population.[2–5] Compared to data from the UK's Office for National Statistics (ONS), we found the attack rates seen in healthcare workers during the second wave (9.1%, CI 8.7% to 9.5%) to be slightly higher than the UK's general population (8.1%, 'credible interval' 7.9% to 8.2%]), even in the context of patient-facing workforce vaccine prioritisation.[15] During the third wave, the healthcare worker attack rate was considerably less (6.6% versus 24.2%) than the general population, though children aged 12–16 years drove much of the community circulation during this period, reflected by the strong emergence of living with children as a risk factor for infection in our cohort. Our healthcare worker population had similar attack rates to the general population during the fourth wave (omicron BA.1/2) and lower attack rates during the fifth wave (omicron BA.4/5), perhaps due to the majority of our participants having received a booster (third) COVID-19 vaccination over winter 2021–2022.

During both winter periods included in our analysis, there were strong patient-facing workforce vaccination drives, and despite this, we found peak PCR positivity rate in our healthcare worker cohort to be higher than that found by ONS in the general population. In the second wave, we found a peak PCR positivity of 3.6% (CI 3.4% to 3.9%) compared to 1.5–3.0% in regional general populations in England, and in the fourth wave, we found a peak PCR positivity of 10.1% (CI 9.6% to 10.6%) compared to 5–10%.[17,18] These findings are reflected when comparing to other large prospective studies in the UK: REACT-1 found healthcare workers to have a higher risk of infection than the general population during the first and second wave of the pandemic,[19,20] with risk levelling out between July and September 2021 (the third wave).[21] Whilst we are unable to determine the reasons for these higher peaks of infection rate, there are multiple factors that may have contributed including how individuals travelled to and from work, how healthcare workers interacted with each other in the work environment, the ventilation in the hospital environment both in wards and staff areas, the numbers of infected individuals in the hospital, and the adherence to PPE and RPE worn by healthcare workers.

Our finding that younger participants, particularly under 25 years, were at a greater risk of infection are also reflected by REACT-1.[19,20,22–24] This might reflect general age-related differences in risk perception and social mixing behaviour,[25,26] or uncaptured confounders such as cohabiting with other essential workers.[27]

It should be noted that direct comparisons of cumulative incidence or peak incidence must be made with caution, given differences in wave definitions, the close contact and clustered nature of the hospitals, and testing availability between healthcare workers and the general population. Furthermore, ONS data analyses that considered their findings according to occupation types found mixed results with regards to healthcare workers, with broader definitions than those used in our inclusion and exclusion criteria.[28] We consider SIREN to be more appropriately positioned to measure the burden of the pandemic on the UK's secondary care healthcare workforce, and establish the occupational risk factors in these particular patient-facing populations and settings.

The main strengths of this study are that it is prospective, with the ability to survey participants with regards to their exposures prior to their infection status being known to them, and it is large with representation from across the four nations of the UK (England, Northern Ireland, Scotland and Wales), comprising data from over 30,000 participants throughout the workforce and over 500,000 exposure questionnaires. It is also comprehensive, capturing all PCR results available, even from samples taken outside of the SIREN study's protocol through linkage to national testing data.

One limitation to this study is that SIREN's primary aim was to study reinfection and vaccine effectiveness, rather than the intricacies of time-variable occupational risk factors for infection. Therefore, the data collection regarding these exposures, which relies on self-reporting and a brief follow-up questionnaire, are less detailed than from a purposefully designed prospective study. Data on specific PPE and RPE use has a high risk of reporting and recall bias, and our questionnaires focussed on perceived breaches that would have differed by definition according to dynamic local policies. In addition, fortnightly questionnaire did not detail specific PPE or RPE use for each encounter. We suspect that a large proportion of the organisation-level variation seen in each wave are due to

these uncaptured differences in policy. Capturing robust, individual PPE/RPE and occupational role/setting data requires purposefully designed controlled prospective studies, particularly during winter pressures, to provide higher quality evidence of the impact of occupational roles, staff behaviours and the built environment on infection risk.

Throughout the four waves included in this analysis there were incremental changes to IPC guidance over time.[10] As evidence emerged, there was an increased emphasis on some aspects, such as droplet/airborne routes, and less emphasis on the contact route and the need for measures such as additional cleaning. Risk pathway changes were made in August 2020 with further updates to risk assessment tools in July 2021, and there were isolation period changes September 2021. A further important change was moving from pandemic pathways back to transmission-based precautions in November 2021.[29] All of these are potentially important confounders when assessing workplace-related factors, and we currently lack evidence for their effectiveness. Our analysis shows novel insights into how these factors, along with changes in occupational, household and community exposures, contributed to a shifting healthcare worker population-at-risk.

In conclusion, we found that certain healthcare workers in specific settings were at a higher risk of SARS-CoV-2 infection during the second wave of the pandemic, with changes in the factors contributing to infection after the emergence of the omicron variants, highlighting the unpredictability of infection dynamics even within an established pandemic. The risk factors for infection shifted over the course of the pandemic, likely driven by differences in social mixing patterns between each wave. The finding that household and community factors were the main contributors to risk throughout successive waves, underscores the importance of considering exposures outside the hospital, in efforts to protect the healthcare workforce. Occupational factors were associated with infection risk during the second wave and highlight potential opportunities to interrupt transmission in healthcare settings. The evidence-base on effective interventions to protect healthcare staff remains underdeveloped and merits further research to inform policy and guidance to prepare for both future pandemics and seasonal pressures, particularly winter surges of respiratory viruses.[30] This study underscores the importance of purposefully designed prospective studies to measure IPC intervention effectiveness including PPE, RPE and ventilation, and to address possible contributory factors such as shared travel, shared healthcare worker households and other non-work based healthcare workers interactions.

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Author contributions

CSB, EJMM, JSR, SF and VJH: conceptualised the project. EJMM, KM and SF: curated and cleaned the data. EJMM: performed the formal analysis. EJMM and KM: designed the graphs and figures. CSB, EJMM, JSR, KM, SF, SH and VJH: interpreted the data. EJMM: drafted the manuscript. AA, CSB, JI, JSR, KM, SF, SH and VJH: critically revised the manuscript for intellectual content. All authors: read and approved the final manuscript.

EJMM and SF directly accessed and verified the underlying data.

Data availability

The metadata for this analysis will be available on reasonable request to researchers through the Health Data Research UK CO-CONNECT platform and available for secondary analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106393.

References

1. Mathieu E, Ritchie H, Rodés-Guirao L, Appel C, Gavrilov D, Giattino C, et al. Policy responses to the coronavirus pandemic. Published online at OurWorldInData.org; 2020. ⟨https://ourworldindata.org/coronavirus⟩.
2. Wei C-F, Lan F-Y, Hsu Y-T, Lowery N, Dibona L, Akkeh R, et al. *Risk of SARS-CoV-2 infection among essential workers in a community-based cohort in the United States. Front Public Health* 2022;**10**:878208. https://doi.org/10.3389/fpubh.2022.878208
3. Nguyen LH, Drew DA, Graham MS, Joshi AD, Guo C-G, Ma W, et al. *Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. Lancet Public Health* 2020;**5**(9):e475–83. https://doi.org/10.1016/S2468-2667(20)30164-X
4. Iversen K, Bundgaard H, Hasselbalch RB, Kristensen JH, Nielsen PB, Pries-Heje M, et al. *Risk of COVID-19 in health-care workers in Denmark: an observational cohort study. Lancet Infect Dis* 2020;**20**:1401–8. https://doi.org/10.1016/S1473-3099(20)30589-2
5. Mutambudzi M, Niedwiedz C, Macdonald EB, Leyland A, Mair F, Anderson J, et al. *Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants. Occup Environ Med* 2020(5):307–14. https://doi.org/10.1136/oemed-2020-106731
6. Health and Social Care Committee. Workforce burnout and resilience in the NHS and social care; 2021. ⟨https://committees.parliament.uk/work/494/workforce-burnout-and-resilience-in-the-nhs-and-social-care/publications/⟩.
7. NHS Digital. NHS sickness abscence rates; 2024. ⟨https://digital.nhs.uk/data-and-information/publications/statistical/nhs-sickness-absence-rates⟩.
8. Wallace S, Hall V, Charlett A, Kirwan PD, Cole M, Gillson N, et al. *Impact of prior SARS-CoV-2 infection and COVID-19 vaccination on the subsequent incidence of COVID-19: a multicentre prospective cohort study among UK healthcare workers – the SIREN (Sarscov2 Immunity & REinfection EvaluatioN) study protocol. BMJ Open* 2022(6):e054336. https://doi.org/10.1136/bmjopen-2021-054336
9. Pople D, Monk EJM, Evans S, Foulkes S, Islam J, Wellington E, et al. *Burden of SARS-CoV-2 infection in healthcare workers during second wave in England and impact of vaccines: prospective multicentre cohort study (SIREN) and mathematical model. BMJ* 2022;**378**:e070379. https://doi.org/10.1136/bmj-2022-070379
10. GOV.UK. COVID-19: infection prevention and control (IPC); 2022. ⟨https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control#full-publication-update-history⟩.
11. World Health Organization. Infection prevention and control in the context of coronavirus disease (COVID-19): a living guideline, 13 January 2023; 2023. ⟨https://www.who.int/publications/i/item/WHO-2019-nCoV-ipc-guideline-2023.1⟩.
12. GOV.UK. Coronavirus (COVID-19): guidance; 2024. ⟨https://www.gov.uk/government/collections/coronavirus-covid-19-list-of-guidance⟩.
13. Foulkes S, Monk EJM, Sparkes D, Hettiarachchi N, Milligan ID, Munro K, et al. *Early warning surveillance for SARS-CoV-2 omicron variants, United Kingdom, November 2021-September 2022. Emerg Infect Dis* 2023(1):184–8. https://doi.org/10.3201/eid2901.221293
14. Institute for Government. Timeline of UK government coronavirus lockdowns and restrictions; 2021. ⟨https://www.instituteforgovernment.org.uk/data-visualisation/timeline-coronavirus-lockdowns⟩.
15. Office for National Statistics. Coronavirus (COVID-19) infection survey technical article: cumulativeincidence of the percentage of people who have been infected with COVID-19 byvariant and age, England: 9 February 2023; 2023.
16. Health and Safety Executive. Managing risks and risk assessment at work; 2024. ⟨https://www.hse.gov.uk/simple-health-safety/risk/index.htm⟩.

17. Office for National Statistics. Regional and sub-regional estimates of coronavirus (COVID-19) positivity over time, UK: 12 January 2023. 2023. ⟨https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/regionalandsubregionalestimatesofcoronaviruscovid19positivityovertimeuk12january2023/2023-01-12⟩.
18. Office for National Statistics. Coronavirus (COVID-19) infection survey: characteristics of people testing positive for COVID-19 in countries of the UK, 20 May 2021; 2021. ⟨https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsinthecommunityinengland/characteristicsofpeopletestingpositiveforcovid19incountriesoftheuk20may2021⟩.
19. Riley S, Ainslie KEC, Eales O, Walters CE, Wang H, Atchison C, et al. *REACT-1 round 6 updated report: high prevalence of SARS-CoV-2 swab positivity with reduced rate of growth in England at the start of November 2020. medRxiv* 2020;**11**:18.20233932. https://doi.org/10.1101/2020.11.18.20233932
20. Riley S, Walters CE, Wang H, Eales O, Ainslie KEC, Atchison C, et al. *REACT-1 round 7 updated report: regional heterogeneity in changes in prevalence of SARS-CoV-2 infection during the second national COVID-19 lockdown in England. medRxiv* 2020:12.15.20248244. https://doi.org/10.1101/2020.12.15.20248244
21. Chadeau-Hyam M, Eales O, Bodinier B, Wang H, Haw D, Whitaker M, et al. *Breakthrough SARS-CoV-2 infections in double and triple vaccinated adults and single dose vaccine effectiveness among children in Autumn 2021 in England: REACT-1 study. EClinicalMedicine* 2022;**48**:101419. https://doi.org/10.1016/j.eclinm.2022.101419
22. Riley S, Eales O, Walters CE, Wang H, Ainslie KEC, Atchison C, et al. *REACT-1 round 8 final report: high average prevalence with regional heterogeneity of trends in SARS-CoV-2 infection in the community in England during January 2021. medRxiv* 2021:01.28.21250606. https://doi.org/10.1101/2021.01.28.21250606
23. Elliott P, Haw D, Wang H, Eales O, Walters CE, Ainslie KEC, et al. *Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant. Science* 2021;**374**(6574):eabl9551. https://doi.org/10.1126/science.abl9551
24. Elliott P, Bodinier B, Eales O, Wang H, Haw D, Elliott J, et al. *Rapid increase in omicron infections in England during December 2021: REACT-1 study. Science* 2022;**375**(6587):1406–11. https://doi.org/10.1126/science.abn8347
25. Herbec A, Brown J, Jackson SE, Kale D, Zatoński M, Garnett C, et al. *Perceived risk factors for severe Covid-19 symptoms and their association with health behaviours: findings from the HEBECO study. Acta Psychol* 2022 Feb;**222**:103458. https://doi.org/10.1016/j.actpsy.2021.103458
26. Gimma A, Munday JD, Wong KLM, Coletti P, van Zandvoort K, Prem K, et al. *Changes in social contacts in England during the COVID-19 pandemic between March 2020 and March 2021 as measured by the CoMix survey: a repeated cross-sectional study. PLoS Med* 2022;**19**(3):e1003907. https://doi.org/10.1371/journal.pmed.1003907
27. Song H, McKenna R, Chen AT, David G, Smith-McLallen. *The impact of non-essential business closure policy on Coivd-19 infection rates. Int J Health Econ Manag* 2021;**21**(4):387–426. https://doi.org/10.1007/s10754-021-09302-9
28. Rhodes S, Wilkinson J, Pearce N, Mueller W, Cherrie M, Stocking K, et al. *Occupational differences in SARS-CoV-2 infection: analysis of the UK ONS COVID-19 infection survey. J Epidemiol Community Health* 2022(10):841–6. https://doi.org/10.1136/jech-2022-219101
29. NHS England. National infection and prevention control manual (NIPCM) for England; 2022. ⟨https://www.england.nhs.uk/national-infection-prevention-and-control-manual-nipcm-for-england⟩.
30. Dunn K, Hamilton Hurwitz H, Paulo Toledo J, Schwaber MJ, Chu M, Chou R, et al. *Summary of WHO infection prevention and control guideline for covid-19: striving for evidence based practice in infection prevention and control. BMJ* 2024;**385**:q645. https://doi.org/10.1136/bmj.q645