ARHAI Scotland

Antimicrobial Resistance and Healthcare Associated Infection

NHS National Services Scotland

Rapid review of the literature – Risk of SARS-CoV-2 acquisition in healthcare workers

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Version history

Version	Date	Summary of changes
1.0	19/02/2021	Assessment of UK-based evidence
2.0	19/03/2021	Assessment of international (non-UK) evidence

Contents

1. Aim

To provide a rapid review of the scientific evidence base to determine the risk of healthcare worker (HCW) acquisition of SARS-CoV-2 in health and care settings.

2. Background

There has been growing concern surrounding the potentially increased risk of COVID-19 acquisition amongst healthcare workers (HCWs) in the UK compared to individuals in the general community.[1, 2] Of note, an open letter signed by almost 1500 HCWs, social care staff, teaching staff and other members of the public, stressed that current Infection Prevention and Control (IPC) measures are insufficient to protect against potential airborne transmission of SARS-CoV-2.[1] The British Medical Association (BMA) also published an open letter to Public Health England (PHE) detailing the need for wider use of respiratory protective equipment (RPE) when caring for all suspected or confirmed COVID-19 patients.[2]

Both letters state that use of RPE is associated with lower risk of SARS-CoV-2 acquisition to HCWs, however, the BMA letter does not provide citations to support this hypothesis, and the citations used to substantiate these claims in the NHS Fresh Air letter have several limitations. These include the use of serological testing to determine infection, observational study designs, lack of statistical power, and distinct differences in testing practices between HCWs and the general public.[1] A rapid review of the evidence surrounding the use of respirators in health and care settings for the prevention of nosocomial COVID-19 transmission has been conducted separately by ARHAI Scotland.[3]

Both open letters highlight that there is an urgent requirement to review the evidence regarding the risk of SARS-CoV-2 acquisition amongst HCWs.[1, 2]

3. Objectives

The following research question was considered:

> What is the risk of COVID-19 acquisition in healthcare workers providing care to suspected/confirmed COVID-19 patients in health and care settings?

4. Methodology

A rapid review of the literature was performed using two tailored search strategies (**Appendix 1**). The academic databases Medline and Embase were searched on 21 January 2021 to retrieve relevant literature. A further search was conducted on 11 February 2021 (**Appendix 1**). Additional hand searching was also conducted. Evidence was critiqued by four reviewers but not formally graded with the use of an appraisal tool owing to the rapid turnaround time. The studies appraised in this review assessed the risk of SARS-CoV-2 infection compared to risk in the general population, or according to occupation within the health and care setting, as it has been suggested that certain staff groups (e.g. front-line staff) may be of greater risk, particularly if working in departments with inadvertent contact with unconfirmed COVID-19 patients i.e. emergency departments. The laboratory methods adopted to assess risk were reverse-transcriptase polymerase chain reaction (RT-PCR) to detect SARS-CoV-2 RNA in nose and throat swab samples; or serological analysis, where blood serum samples were analysed for the presence of IgG or IgM SARS-CoV-2 antibodies. However, serological analysis is unreliable given the low sensitivity of the assays and the fact that not all individuals who have been infected with SARS-CoV-2 seroconvert. Consequently, the evidence from PCR studies and from serological studies is considered separately.

Studies were excluded if they did not provide a comparison of risk in HCWs according to HCW occupation or to that of the general population.

5. Results

A total of 329 and 228 studies were retrieved using search strategies A and B respectively, as detailed in **Appendix 1**. These studies consisted of both UK and international studies. A further 76 studies were found using citation searching and additional grey literature searching of online resources. A total of 232 and 226 studies were excluded following title and abstract screening of searches A and B, respectively; 57 were excluded in total during full-text screening or critical appraisal. Of the studies retrieved, several were excluded because they did not compare risk of HCW SARS-CoV-2 acquisition according to occupation or care setting, or to that of the general population.[4-29]

5.1 Risk of HCW COVID-19 infection in UK health and care settings

Following full-text screening, 30 studies were appraised that assessed the risk of HCW COVID-19 infection in UK health and care settings. Of these, 11 studies were excluded because they did not compare HCW risk by occupation or to the general population.6, 20, 26-35 Two studies were also excluded because they were narrative reviews and 5 additional studies were excluded based on methodological limitations.36-40 In summary, a total of 16 studies were appraised in greater detail; of these, 9 defined infection according to PCR positivity, 3 according to either PCR or serology, and 4 according to serology only.

5.1.1 UK HCW infection risk – PCR studies

Nine studies were assessed; two studies (both hospital-based) were eventually excluded due to their methodological limitations and an inability to determine the impact of potential confounders.[31, 41] This included a study by Zheng et al. (2020) that reported higher positivity rates in certain clinical specialties (e.g. medical & dental staff, nursing & midwifery) during March 2020, however statistical analysis was not performed to determine if differences were significant, there was no data provided regarding the population prevalence at the time in the area, the sample size was small and testing was not equally provided to all groups.[31] The second study (Hunter et al. 2010) reported no significant difference between staff groups (patient-facing, non patient-facing, low risk), but had a number of limitations which included; only those with symptoms being screened, not reporting staff roles for over a third of those tested, including only a small number of non-clinical staff, not providing a comparison with population prevalence and not testing for statistical significance.[41]

Of the seven included studies only two provided data regarding HCW occupational risk;[42, 43] the remaining studies assessed risk in HCWs compared to the general population or workers outside of health and care settings.[43-55] The majority of included studies (n = 5) assessed data from the early phase of the pandemic (March to June 2020);[42-44, 54, 55] one study collected data over 8 non-overlapping time-points between May 2020 to January 2021,[46-53] and one gathered data between March 2020 to January 2021.[45] Whilst there appeared to be a trend towards a higher risk of infection in HCWs in these studies (and in one study for HCWs in specific hospital wards), the heterogeneity in methodology and reporting periods between these studies prevented any meaningful comparison. Further, all studies had a number of limitations which impacted the validity of findings. Overall, the major limitation of the studies included in this section was that it was not possible to determine the exact source of infection or direction of transmission in the groups analysed. Therefore, there was no way of knowing if PCR positivity in HCWs was directly related to the workplace or indeed to patient care, or as a result of acquisition outside of the workplace in the community. The studies are discussed in detail below.

Rivett, et al. (2020) implemented a HCW screening programme at Cambridge University NHS Hospital Foundation Trust in April 2020.[56] Symptomatic HCWs and HCWs with symptomatic household contacts volunteered for screening. Additionally, asymptomatic screening was performed for staff working in wards considered to be at high risk of transmission (i.e. the ED and COVID-19 assessment unit) and for staff in contact with particularly vulnerable patients (i.e. haematology, oncology and transplant wards). A reactive approach to surveillance was also adopted, where asymptomatic screening was introduced in wards of concern (e.g. due to an increase in staff illness).[56] In total, 1,270 patient and non-patient facing HCWs underwent testing between 6 to 26 April, 2020, where 4.8% (n = 61) tested positive. Positivity was 3% (n = 31/1032) and 15.4% (n = 26/169) within the asymptomatic screening group and symptomatic screening group, respectively. As anticipated, symptomatic HCWs (and HCWs with symptomatic household contacts) were more likely to test positive than asymptomatic staff ($p<0.0001$). Wards were classified as 'red', if housing confirmed or probable COVID-19 inpatients; 'amber' for inpatients awaiting COVID-19 diagnosis or possible pre-symptomatic patients; or 'green', wards with no confirmed or suspected COVID-19 inpatients. A higher proportion of staff in red wards tested positive (5.1%, n = 19/372) compared to those in green wards (1.9%, n = 6/310; $p = 0.0389$).[56] This suggests that HCWs working in high-risk care settings are at greater risk of HCW infection however, a number of factors which may limit the validity of findings were not considered. Of note, there is a lack of information on staff movement between 'red', 'amber' and 'green' wards, as well as other factors that may have contributed to workplace transmission (e.g. compliance with IPC measures/PPE). Moreover, the number of staff who tested positive was small (n = 61), the programme was limited to one study site and the study duration was short. As supported by the authors, this study does not provide definitive evidence regarding HCW COVID-19 infection risk as the source of acquisition and direction of transmission cannot be determined.

Shah et al. (2020) performed a data linkage study to assess the risk of hospitalisation due to COVID-19 in Scottish HCWs and members of their households.[43] The findings relating to household members have been excluded from discussion as they are outside the scope of this review. HCWs employed by the NHS on 1 March 2020 were included in the analysis, where HCWs were defined as staff aged 16 to 65 years who provide direct or indirect patient care, i.e.

doctors and nurses; or IT and laboratory staff, respectively. Dental HCWs and staff working solely in paediatric roles were excluded. 158,445 HCWs were included, of whom 90,733 (57.3%) were patient-facing. The primary outcome of this study was hospital admission due to COVID-19, defined when the first positive PCR test occurred in hospital and/or the positive PCR test occurred 28 days prior to hospitalisation. 6,346 hospital admissions in Scotland met the criteria for the primary outcome during the study period (1 March to 6 June 2020). HCWs accounted for 11.6% (n = 243/6436) of admissions due to COVID-19; the risk of hospital admission due to COVID-19 was 0.20% (n = 181/90,733) for patient-facing HCWs and 0.07% (n = 23/32,615) for non-patient facing HCWs (p-values not provided). Patient-facing status was undetermined for 35,097 HCWs. Similar analysis, using the number of positive COVID-19 infections as the denominator, found that risk of hospital admission due to COVID-19 was 7.3% (n = 181/2485) for patient-facing staff and 11.5% (n = 23/200) for non-patient facing staff (p-values not provided). However, adjusting for age, sex, socioeconomic status and comorbidities, the hazard ratio of hospital admission for patient-facing HCWs was higher at 3.30 (95% confidence interval (CI) 2.13 – 5.13), compared to non-patient facing HCWs.

In the study by Shah et al. (2020), patient-facing HCWs were further sub-divided into the following groups: those who worked in ‘front door’ (e.g. paramedics), staff working in intensive care, HCWs in non-intensive care aerosol generating settings (i.e. respiratory medicine) and ‘other’. Staff who worked in ‘front door’ roles were of greatest risk of hospital admission (hazard ratio 2.09, 95% CI 1.49 – 2.94). The hazard ratio for hospital admission for staff working in non-intensive care involved in aerosol generating procedures was 1.[91] (95% CI 0.90 – 4.07). This finding was not statistically significant as the 95% CI crossed null. The hazard ratio of hospital admission for those working in the ICU was 1.22 (95% CI 0.29 – 5.09). Again, this finding was not significant as the 95% CI crossed the null, likely due to the small sample size (n = 1348), where less than 5 were admitted to hospital. Adjusting for age, sex, socioeconomic deprivation, occupation and part-time work status the hazard ratio of hospital admission was 3.07 (95% CI 1.73 – 5.43) for patient-facing HCWs compared to non-patient facing HCWs (p-values not provided). Lastly, adjusting for age and sex, Shah et al. (2020) estimated that risk of hospital admission was higher amongst individuals in patient-facing roles compared to the general population, the hazard ratios were 2.64 (95% CI 1.82 – 3.82), 4.18 (3.29 – 5.30) and 6.44 (95% CI 4.00 – 10.37) in March, April and May 2020, respectively (p = 0.01).[43] These findings should be interpreted with caution for the following reasons: As supported by the authors of this study, HCWs may have presented to healthcare settings earlier than the general population, or may have been more likely to be admitted to hospital. A lower threshold for presentation to healthcare settings or admission to hospitals amongst HCWs may have been apparent in the earlier phases of the pandemic. This is potentially due to the perceived exposure to COVID-19 due to contact with patients during direct patient care of COVID-19 cases, or inadvertent contact with cases who were asymptomatic or pre-symptomatic. Moreover, although differences in risk of hospital admission were observed between patient-facing and non-patient facing HCWs, patient-facing HCWs according to role, and patient-facing HCWs compared to the general population, there was a failure to take into account the duration of close contact with COVID-19 patients and movement between wards amongst HCWs.[43] Consequently, this study does not provide reliable evidence for increased risk of hospitalisation or infection in patient-facing HCWs.

The remaining studies in this section assessed risk of COVID-19 infection in HCWs compared to the general population with the use of various surveys and publicly available data.

The Office for National Statistics (ONS) performed a household survey pilot in England between 26 April to 30 May 2020 to assess risk of SARS-CoV-2 transmission, including all individuals living in private households, aged 2 years and older.[44] 19,723 self-administered nose and throat swab samples were collected; of these, swabs from 21 individuals living in 15 different households tested positive. Using this data, the authors estimated that an average of 0.10% of the community population in England were positive for COVID-19 at that time point (95% CI 0.05 – 0.18%). Further analysis limited to participants of working age found that positivity was 1.87% (95% CI 1.07 - 3.02%) in those working in patient-facing roles (i.e. doctors, nurses, social care workers in nursing homes and home care workers); versus 0.32% (95% CI 0.26 – 0.44%) amongst participants who did not report working in these types of roles.[44] Statistical testing was not performed to assess whether the higher prevalence in patient-facing roles was significant. Although the overall sample size in the ONS pilot survey was large (n = 19,723), the number of individuals who tested positive was very limited (n = 21). As a result, basing statistical analysis on these findings likely has limited validity. Limiting the validity of the findings further was the study's short duration period (2 weeks) and the use of a survey to assess risk factors, which may have introduced recall bias. Furthermore, comparing positivity amongst participants in patient-facing roles to those in all other roles encompasses participants who were working from home during lockdown. Such analysis therefore has limited value or generalisability. Instead, a comparison of infection between patient-facing HCWs and participants who still required to travel into work and interact with colleagues or customers, or non patient-facing HCWS, should have been performed to more accurately determine increased risk of COVID-19 amongst patient-facing HCWs. Overall, this study does therefore not provide reliable evidence for increased risk in patient-facing HCWs.

Nguyen et al. (2020) developed a smartphone application for use in both the USA and UK to assess the risk of COVID-19 infection amongst frontline HCWs compared to the general population, and if personal protective equipment (PPE) impacted risk of infection.[55] The application was available between 24 March 2020 to 23 April 2020. Use of the application was voluntary, where participants were able to enter demographic information, medical history, and any COVID-19 symptoms experienced and results of COVID-19 PCR tests. 2,810,103 participants used the application in the study period, of whom 2,627,695 were based in the UK. After excluding participants with <24 h of follow-up after initially using the app (n = 670,298) and those with a positive COVID-19 test at baseline (n = 4615), 99,795 front-line HCWs and 2,035,395 'general community' members were included in the study cohort (UK and USA). 3,450 incident reports of positive COVID-19 tests were recorded over 31,839,670 person-days in the UK general community, and 1,851 incident reports over 1,309,285 person days were reported amongst UK-based frontline HCWs.[55] Adjusting for the likelihood of receiving a COVID-19 test, the weighted hazard ratio of reporting a positive test in the UK and USA was 3.40 (95% CI 3.37 – 3.43) amongst front-line HCWs, compared to the general population, and 3.43 (95% CI 3.18 – 3.69) in the UK.[55] These findings should be interpreted with caution due to the introduction of volunteer bias and potential inaccuracy of data input into the application. Additionally, as supported by the authors, detailed information regarding HCW occupation and their nature of work (i.e. seniority level, PPE training, contact with COVID-19 patients, involvement with AGPs) and any non-work related activities that may have impacted risk of infection was not provided to take these confounders into consideration during analysis. Furthermore, use of a mobile application for data input may have excluded certain populations, limiting the generalisability of the findings. Lastly, participants were categorised as the 'general community' if they were not front-line HCWs. These participants may have worked in health and care settings, or worked in customer-facing roles. Therefore, categorising participants in this way may have biased the study findings towards the null.

A case-control study including data captured from the start of the pandemic in March 2020 to January 2021, was conducted in Scotland to investigate the risk of hospitalisation and severe COVID-19 amongst four groups: 1) teachers 2) household members of teachers, 3) healthcare workers and 4) household members of HCWs. In all of the analysis performed, only working aged individuals (21 to 65 years old) were included.[57] In this study, the 'general population' was defined as any working age adult, who were not teachers or HCWs, but were considered to be at increased risk of infection. However, there is lack of clarity surrounding why this population was of increased risk of infection. Datasets of teaching staff and HCWs were linked to an existing case-control dataset maintained by Public Health Scotland (PHS).

COVID-19 cases were defined as any individual with a positive PCR test; any inpatient discharged from hospital with a COVID-19 diagnosis (irrespective of any PCR testing) and any death where COVID-19 was named as a cause (underlying or primary), again, irrespective of any test results.[57] Cases were matched by age and sex to 10 randomly selected controls registered to the same general practice as the case, who did not meet the case definition. A total of 34,461 of 125,830 eligible HCWs (27.4%) were included in the analysis (both patient-facing and those whose patient contact status was unknown). Analysis of the case-control data was stratified according to the time period before and after schools re-opening: 1 March to 2 September 2020 and 3 September 2020 to 4 January 2021, respectively. In the period prior to schools reopening, HCWs had a higher adjusted rate ratio (aRR, 8.75, 95% CI 8.29-9.23) compared to the 'general population', whereas teachers had a lower aRR compared to the 'general population' (aRR 0.48; 95% CI 0.39-0.60). P-values were not provided to assess if the differences in aRR were statistically significant. In the period after schools re-opened (3 September 2020 to 4 January 2021) teachers and HCWs both had higher risk of infection than the general population, with the highest risk observed among healthcare workers (aRR 2.41; 95% CI 2.33-2.49 for HCWs and 1.42; 95% CI 1.35 – 1.49 for teachers). Overall, this study suggests that HCWs had greater risk of hospitalisation, severe COVID-19, and general COVID-19 infection compared to teachers and the general population. Testing practices for HCWs and the general population differed during the study period (March 2020 to January 2021). Due to limited capacity early in the pandemic, testing was prioritised for the management of clusters in residential and care settings and to minimise working days lost amongst key workers.[58] As a result, it is likely that in most cases, individuals within the general population would have only underwent testing after admission to healthcare settings with moderate or severe symptoms. Conversely, HCWs would have underwent testing even if symptoms were mild in order to minimise staff absences due to unnecessary self-isolation. The differences in testing dynamics between HCWs and the general population (including teachers) applies to more recent phases of the pandemic, as the general population is advised to self-isolate at home if experiencing COVID-19 symptoms, or following close contact with a positive case, without the need to confirm infection by PCR testing. The study also did not take into consideration the fact that teachers were working from home before schools reopened, whereas HCWs likely continued to use public transport, interact with colleagues sometimes without maintaining a physical distance, and interact with patients when mask-wearing in healthcare settings was not yet mandatory. There is also limited information provided on the roles of the HCWs, and the contact they had with patients, particularly those likely to have COVID-19 infection. Therefore, although this study suggests increased risk of infection, hospitalisation, and severe disease presentation amongst HCWs, the findings are arguably unreliable.

‘The Real-time Assessment of Community Transmission’ (REACT) Programme was commissioned by the Department of Health and Social Care to estimate community prevalence of SARS-CoV-2 in England. A series of cross-sectional ‘sub-studies’ were performed (REACT-1), where self-administered nose and throat swabs were collected from participants aged 5 years and over. Thus far, data from 8 rounds have been published for the following sampling periods; Round 1: 1 May to 1 June 2020; Round 2: 16 June to 7 July 2020; Round 3: 24 July to 11 August 2020; Round 4: 20 August to 8 September 2020; Round 5: 18 September to 5 October 2020; Round 6: 6 October to 2 November 2020; Round 7: 13 November to 3 December 2020 and finally, Round 8: 6 January to 22 January 2021.[46-53, 59] In all of the REACT-1 sub-studies, participants were randomly selected from the list of NHS patients in England, stratified at the level of lower-tier local authority (LTLA) to achieve similar levels of participants from each LTLA.59 Participants were invited to participate by letter. On average, the average response rate from the initial invitation letters was low (24.0%, range 22.0 – 30.5%) and the return rate of valid swab samples from those who volunteered to participate was 75.2% (range: 72.5 – 79.1%).[52, 60]

The REACT-1 series of sub-studies demonstrated that the overall estimated prevalence of SARS-CoV-2 varied in England during the time periods assessed. This is likely due to factors including the pandemic measures in place during different time periods to control community transmission (e.g. national lockdowns, tiered restrictions, mandatory mask-wearing and physical distancing). Consequently, it is not appropriate to compare prevalence estimates during different rounds of this study. The most recent round (6 to 22 January 2021) demonstrated that the overall weighted national prevalence was 1.57% (95% CI 1.49 – 1.66%, n = 2282/167,642).[52] Weighted national prevalence amongst health and care workers was 2.24% (95% CI 1.84 – 2.72%; n = 161/8259), compared to 1.79% (95%CI 1.61 – 2.0%, n = 531/30,239) amongst other essential or key worker). Adjusting for the aforementioned factors (gender, age, key worker status, ethnicity, household size and level of deprivation), adjusted odds ratio (aOR) for swab positivity was 1.48 (95% CI 1.25 – 1.77) for health and care workers versus 1.35 (95% CI 1.2 – 1.51) for other essential workers when compared to all other ‘regular’ workers in England.[52] P-values were not provided to investigate the statistical significance of these findings.

The estimates provided in Round 8 support those of previous rounds of the REACT-1 series of studies; namely, that swab-positivity was typically higher amongst health and care workers compared to the general population. Despite this reported increased prevalence amongst health and care workers, swab-positivity and aOR of prevalence amongst this group were relatively similar to those estimated for other essential workers. It is important to note that the findings from Round 1 (1 May to 1 June 2020) did not follow this trend. During this time period, the overall unadjusted prevalence in the total cohort was 0.13% (95% CI 0.11 – 0.15), but was higher for care home workers (CHWs) (0.71% (95% CI 0.24 – 2.06%) and HCWs 0.47% (0.30 – 0.75%) compared to other key workers, (0.17% (0.12 – 0.25%)). The aORs for swab-positivity were 8.3 (95% CI 2.9 – 9.5) and 5.2 (95% CI 2.9 – 9.5) for CHWs and HCWs, respectively, compared to all other workers.[48] These findings therefore suggest that odds of infection were markedly higher for CHWs and HCWs between 1 May to 1 June 2020. Risk of infection was likely higher in care home and acute healthcare settings during this time period, however, findings from the remainder of the REACT-1 studies support the fact that transmission dynamics have now changed, where odds of infection for staff in care settings have decreased and are mirroring that of community transmission.[51]

Overall, the series of REACT studies provides evidence that HCWs and CHWs may be at increased risk of SARS-CoV-2 infection compared to the general population and compared to other workers, however there are a number of study limitations that impact the validity of findings. Statistical testing was not performed to assess the statistical significance of the findings and the confidence intervals presented suggest that the differences in odds and prevalence presented are not significant as they are relatively wide and overlap. Additional limitations that should be considered when interpreting this evidence base include response bias, as demonstrated by the low average response rate following invitation to participate in the study (24.0%). Low participation may have over or under-represented certain groups, thus impacting the validity of the findings. Further bias was also introduced when using questionnaire data to gather epidemiological information. Importantly, only one round of findings stratified estimates on prevalence of infection according to direct or indirect patient contact and there was no information given on the contact time that HCWs and CHWs had with COVID-19 patients in any of the studies.

Public Health England (PHE) undertook a study to determine the proportion of domiciliary care workers in England who had COVID-19 infection, with or without symptoms, in June 2020.[54] Domiciliary care is provided to people living in their own homes who require additional support in order to maintain their independence and quality of life. Of 2,015 samples provided, 2 (0.1%, 95% CI 0.02%-0.40%) participants were found to be positive following PCR testing. This was in line with the estimated general population prevalence at that time (0.09%, 95% CI 0.04% - 0.19%). This study used a convenience sample. Selection of providers may have introduced bias due to the wide range of types of domiciliary care provider (in terms of type of care and client), their size, region in which they operate and impact of current infection rates on workload.[54] The estimate of prevalence therefore may not represent the true prevalence of COVID-19 in domiciliary care workers nationally. Those self-isolating due to symptoms or contact with a known case were likely underrepresented therefore prevalence may have been underestimated in the workforce as a whole. These limitations call into question the validity of the observed results.

Unpublished Scottish hospital outbreak reporting has shown a wide variation in the size of outbreaks and the numbers of HCWs affected in each. Some outbreaks have only involved HCWs, which is suggestive that acquisition amongst HCWs was not related to patient care. Lessons learned from outbreak reports have identified that activities out with the patient care area (i.e. break times, car sharing) may be a risk factor for HCW to HCW transmission that should be addressed to limit nosocomial transmission.

5.1.2 UK HCW Infection – Mixed methods (PCR or Serology)

Three studies critiqued for this reviewed adopted both serological and PCR analyses to estimate risk of SARS-CoV-2 infection in HCWs.[61-64] Two of these were later excluded due to the fact that analysis of risk factors for infection (i.e. staff role; speciality; contact with COVID-19 patients) was not stratified according to the test method used to confirm infection.61 Of note, although the supplementary file for the study by Eyre et al. (2020) demonstrated that additional multivariable analysis was performed for serology results only, these findings have also been excluded as sample sizes were not provided for the variables analysed (e.g. speciality and staff role).[61]

The remaining study by Shields et al. investigated both seroconversion and PCR-positivity in 554 asymptomatic HCWs working in University Hospitals Birmingham NHS Foundation Trust.[62, 63] Although PCR testing was performed, analysis of risk factors for PCR-positivity was not performed, likely due to the small sample size of staff who were PCR-positive (n = 13). Instead, analysis of risk factors was performed using results from serological analysis only. For this reason, this study will be discussed in the following section of this review.

5.1.3 UK HCW Infection – Serological analysis

Five studies were identified that used only serological analysis to assess HCW risk of SARS-CoV-2 infection.[62, 63, 65-68] The major limitation with these studies is that serology is not a reliable indicator of infection and cannot accurately pinpoint the timing of infection.

Four of the studies used serology to assess risk of infection according to HCW occupation or care-setting,[62, 63, 65-68] while the remaining study compared serology results in HCWs to those in non-HCWs. All of the studies included in this section were conducted between January and July 2020. Overall, these studies indicate that seroprevalence at that time was higher amongst HCWs compared to non-HCWs, and higher amongst staff providing direct patient care. Three studies highlighted that seroprevalence was lower amongst staff working in ICU wards compared to EDs, and higher amongst nurses compared to doctors.[62, 63, 66, 67] One study suggested that seropositivity decreased as seniority increased.[67] The studies are discussed in detail below.

Only one study compared seropositivity between HCWs and the general population. In the REACT-2 study,[65] 315,000 individuals aged 18 or over, living in England, from the NHS patient list were randomly selected between 20 June to 30 July 2020. 121,971 individuals agreed to participate, of whom 99,908 had valid test results alongside completed questionnaire data (31.76%, n = 99,908/315,000). IgG antibodies were detected in 5.6% (95% CI 5.4 – 5.7%; n = 5,544/94,364) of serum samples.[65] After adjusting for test performance and differences in response rate according to age, gender and level of deprivation, seroprevalence was estimated to be 6.0% (95% CI 5.8-6.1) in England during the study timeframe. Seroprevalence was estimated to be 11.7% (95% CI 10.5 -13.1) amongst HCWs with direct patient contact and 16.5% (95% CI 13.7 – 19.8) amongst CHWs with direct client contact.[65] Subsequently, odds of seroprevalence was estimated to be 2.09 (95% CI 1.86 – 2.35) and 3.09 (95% CI 2.51 – 3.80) for HCWs with direct patient contact and CHWs with direct client contact, respectively, compared to non-essential workers.[65] These findings suggest that HCWs and CHWs in contact with clients or patients have an increased risk of seroprevalence compared to non-essential workers. However, this study was performed in the early phases of the pandemic where community transmission dynamics differed due to lockdown. The authors also discussed the fact that there was a lower participation rate amongst ethnic minority groups and those living in deprived areas, therefore, the estimates produced may not be representative of the general English population.[65]

As previously mentioned, Shields et al. investigated both seroconversion and PCR-positivity in 554 asymptomatic HCWs working in University Hospitals Birmingham NHS Foundation Trust.[62, 63] Four hospitals participated in this study over a period of 24 hours, where percentage of positive infection by RT-PCR was 2.39% (n = 13 of 554). Samples from 513 of 554 HCWs were included in serological analysis, where seroconversion was highest amongst those working in housekeeping (34.5%; n = 10/29), acute medicine (33.3%, n = 10/30) and general internal medicine (30.3%, n = 30/99). Seroconversion was lowest for staff working in the ICU (14.8%; n = 9/61), emergency medicine (13.3%, n = 2/15) and general surgery (13.0%; n = 3/23).62, 63 Further analysis using the ICU department as a reference found that relative risk of seroconversion was 2.34 (95% CI 1.03 – 5.36, p = 0.04), 2.25 (95% CI 1.03 – 4.97) and 2.05 (95%CI 1.05 – 4.03, p = 0.04) for staff working in housekeeping, acute medicine, or general internal medicine, respectively.[62, 63] These findings should be interpreted with caution and due to the small sample size, particularly when stratified according to working area.

Jones et al. (2020) performed a prospective observational study in Bristol inviting all staff employed between January and June 2020 to participate, where 6,869 of 12,254 eligible HCWs underwent screening.[66] Overall seroprevalence was 9.38%, differing according to the ward in which staff worked. Seroprevalence was 2.5% and 16.2% for staff working in the ICU and acute medical unit, respectively. Moreover, seroprevalence for staff working in the respiratory and elderly care wards for COVID-19 inpatients was higher at 13.6% and 20.9%, respectively.[66] Statistical testing was not performed to determine the significance of the aforementioned findings. The odds of seroprevalence was estimated according to occupation. Of note, speciality registrars had statistically significant decreased odds of seroprevalence (aOR 0.62, 95% CI 0.41 – 0.91, p = 0.019), whereas healthcare assistants (aOR: 1.52, 95% CI 1.17 – 1.98); staff nurses (aOR 1.35, 95% CI 1.08 – 1.69, p = 0.0008), and doctors in foundation year 2 (aOR 2.11, 95% CI 1.40 – 3.13, p < 0.001) had increased odds of SARS-CoV-2 seroprevalence.[66] A number of limitations should be considered when drawing conclusions from this study. There is a risk of volunteer bias, as of the 12,254 HCWs and support staff eligible to participate during the study period, only 56% volunteered for serological testing.[66] This limitation is further supported by the fact that authors stated that particular sub-groups were found to be more likely to participate, namely older HCWs, females, white individuals, and permanent staff members (p <0.0001 for all).[66] Additionally, potential confounders, including compliance with PPE and other IPC measures, such as physical distancing in staff areas, were not taken into account in the analyses. It is unclear when the study itself was conducted as the findings were presented as a letter to the editor. Nevertheless, as HCWs employed in January to March 2020 were eligible to participate, the generalisability of these findings are limited as IPC measures and other wider pandemic responses differed during the early stages of the pandemic i.e. mask wearing was not yet mandatory in health and care settings.

Martin et al. (2020) performed a retrospective cohort study at the University Hospitals of Leicester (UHL) NHS Trust, where voluntary IgG testing for SARS-CoV-2 for all staff members commenced in May 2020.[67] Included in the analysis were 10,662 serology samples collected between 29 May 2020 and 13 July 2020, and seropositivity was found to be 10.8% (n = 1148/10,662). Similar to the findings presented by Jones et al. (2020), seropositivity was higher amongst nurses compared to doctors ($p = 0.002$). Additionally, seroprevalence decreased as medical practitioner or nursing seniority increased (Martin et al. 2020).[66, 67] Again, findings from this study have limited reliability as volunteer bias was present with participation limited to HCWs at one site, thus limiting generalisability. Moreover, the authors highlighted that issues regarding the sensitivity of the SARS-CoV-2 IgG assay used have been reported.[67]

Lastly, a seroprevalence study based in a tertiary-care hospital in London between 15 May 2020 and 5 June 2020 was performed to assess nosocomial transmission amongst HCWs. The study was conducted prior to the introduction of mandatory mask use in health and care settings. Participation was voluntary, where 2004 of 4000 HCWs employed participated.[68] Seropositivity was greatest for staff providing direct patient care in clinical environments (34.7%, $p < 0.005$) compared to all other exposure types (i.e. less/no patient contact in clinical environments; non-clinical environments with direct patient-contact; non-clinical environment with minimal to no direct patient contact; and shielding or working from home) when considered as one exposure group. Further analysis of seroprevalence according to ward-type found that seropositivity was highest amongst staff working in a COVID-19 dedicated ward with and without continuous positive airway pressure (42.0%, $p = 0.001$; 41.3%, $p < 0.005$, respectively), compared to the seroprevalence amongst staff working in all other ward types (operating theatres, non-COVID-19 wards, intensive care unit (ITU) and non-ward environments). Seropositivity was 26.0% (n = 206/792) amongst staff working in non-ward environments, compared to 35.3% (n = 428/1212), in staff working in all other ward types, $p < 0.005$. Overall, seroprevalence was lowest amongst staff working in the ITU (25.0%, n = 44/176). However, seroprevalence amongst ICU staff compared to staff working in all other ward types (32.3%, n = 590/1828) was not statistically significant ($p = 0.47$).[68] The evidence in this study regarding differential risk amongst HCWs is weak given its short duration, volunteer bias, lack of investigation of the confounding factors that may lead to seropositivity and how it correlates to any active infection (for example, PPE provision and compliance, ventilation provision), and lack of information regarding staff movement between ward types.

5.2 Risk of HCW COVID-19 infection in non-UK health and care settings

A total of 103 studies that assessed the risk of COVID-19 amongst HCWs in non-UK settings underwent full-text screening and/or appraisal. Of these, 19 were excluded as comparators were not assessed[4, 5, 7-9, 11-13, 15, 16, 18, 19, 21, 22, 24, 25, 69-71] and one was excluded as it was a narrative review.[72] A number of studies retrieved were excluded based on methodological limitations,[73-86] or due to failure to stratify data according to PCR or seropositivity.[78, 80-82] 42 international studies that used serological analysis were appraised,[39, 76, 77, 82, 86-128] and of these, one study using serology and PCR,[81] and 23 using serological analysis were considered suitable for full text assessment. Four studies compared risk of infection between HCWs and non-HCWs[101-104] whilst the remainder discussed HCW risk of infection according to occupation, care-setting, and/or degree of exposure to patients. Of these, 15 were performed in Europe;[82, 105-119] six in the USA (five of which were multi-site studies);[120-126] and two in Asia.[127, 128] Due to time constraints, the inherent limitations of serology as an indicator of infection and additional methodological limitations of the serological studies identified (i.e. small sample sizes, recall bias, volunteer bias, short study durations, and/or limited analysis to single-sites) it was decided to focus only on those international studies that used PCR positive to define infection.

5.2.1 Non-UK HCW infection risk – PCR studies

Ten studies used PCR data to define COVID-19 infection,[55, 129-136] where only one compared RT-PCR positivity between HCWs and the general population.[55] As previously discussed earlier in this review, Nguyen et al. (2020) developed a mobile phone application to gather RT-PCR data from HCWs and the general population. In the USA, the application was available between 29 March 2020 to 23 April 2020.[55] 182,408 participants based in the USA provided baseline information, of whom 4.8% (n = 134,885) reported being front-line HCWs. From the application data, incidence for infection was estimated at 3.96% for HCWs, and 0.33% amongst the general community. Taking into account both USA and UK data, the inverse probability-weighted hazard ratio (HR) for COVID-19 positivity for HCWs was 3.40 (95% CI 3.37 – 3.43) compared to the general population, after adjusting for age, sex, and the following co-morbidities: history of diabetes, lung disease, heart disease, kidney disease, smoking status and body-mass index. In the USA, the HR for COVID-19 positivity amongst HCWs compared to the general population was 1.97 (95% CI, 1.36, 2.85), $p < 0.0001$, thus was lower than the HR observed in the UK (3.43, 95% CI 3.18 – 3.69). As already discussed, the findings from this study should be interpreted with caution due to lack of information regarding HCW occupation, non-work related activities that may have impacted risk of infection, and lack of information about the nature of work amongst participants classed as the general community.

Studies performed in the USA,[129, 130] China[131] and Spain[132] assessed risk of COVID-19 infection according to degree of exposure to SARS-CoV-2 (e.g. due to contact with patients or working on wards treating COVID-19 patients). However, in these studies, there was a failure to take into account the movement of staff between high and low-risk care environments, or the degree of contact with COVID-19 patients, or patients in general. Risk factors for SARS-CoV-2 infection were also investigated using questionnaires or surveys, these are subject to recall bias, again limiting the validity of the study findings in this body of evidence.

Two studies performed cross-sectional analysis to assess risk factors for acquisition of COVID-19 infection amongst HCWs.[130, 133] These studies adopted a similar approach, whereby participants were recruited on a voluntary basis for PCR-testing and completion of a survey or questionnaire to gather data on risk factors for infection. Again, voluntary testing potentially introduced the risk of bias, where those working in high risk settings may have been more likely to present for testing, compared to those working in low-risk settings. Behaviours outside of the workplace (i.e. community method, working status of household members) may have also made certain HCWs more or less likely to present for testing.

Barrett et al. (2020) conducted a prospective cohort study in New Jersey, USA, from 24 March to 7 April 2020 to compare the incidence of COVID-19 infection in HCWs and non-HCWs. Non-HCWs were recruited from a university, and HCWs were recruited from two university-affiliated hospitals.130 0.4% (n = 1/283) of non-HCWs and 7.3% (n = 40/546) HCWs tested positive for SARS-CoV-2 by RT-PCR. Absolute risk of COVID-19 acquisition was therefore 7.0% greater for HCWs compared to non-HCWs (95% CI 4.7 – 9.3%; p-values not reported).[130] Further sub-group analysis of HCWs found that HCWs who reported caring for at least five patients with suspected or confirmed COVID-19 were more likely to be positive versus HCWs caring for fewer patients with confirmed or suspected COVID-19 (10.5% (n=24/226) versus 4.8% (n = 15/310), respectively; p-values not reported). The incidence of COVID-19 infection was higher amongst nurses (11.1%, n = 25/225) compared to attending physicians (1.8%, n = 2/112) and residents or fellow physicians (3.1%, n = 3/98) (p-values not reported).[130] This may be due to the fact that nurses reported spending a larger proportion of their time in patient rooms compared to attending physicians, residents and fellows; and because a higher proportion of nurses, compared to proportions of other staff roles, reported caring for five or more suspected COVID-19 patients. However, causation cannot be established due to the observational study design.

The authors state that PPE use was positively correlated with the number of patients treated with suspected or confirmed COVID-19 and that a higher incidence of SARS-CoV-2 infection was not observed for staff who had lower estimated percentage of patients for which PPE was used (i.e. use of gloves gowns and a surgical or N95 mask). However, statistical analysis was not performed to assess the significance of these findings. Further limitations of this study include a small sample size, volunteer bias due to the limited testing of staff and non-HCWs during the study period, and possible ascertainment bias as HCWs reported higher levels of contact with potential COVID-19 cases compared to non-HCWs. It is also important to note that lockdown restrictions were in place during the study period, thus non-HCWs likely had less interaction with people in general. This likely overestimated risk of infection amongst HCWs and limits the generalisability of this study.

Lombardi et al. (2020) performed a prospective study between 24 February and 31 March 2020, where HCW staff working in a hospital in Milan underwent testing if they were at risk of infection, defined as contact with a patient or colleague who tested positive for SARS-CoV-2. 1,573 HCWs were tested at least once in the study period and 139 (8.8%) tested positive (95% CI 7.5 – 10.3%).133 RT-PCR positivity varied according to occupation but was non-significant: 10.5% (n = 61/152) amongst physicians; 8.4% (n = 44/522) amongst nurses or midwives; 8.0% (n = 13/162) amongst healthcare assistants; and 3.6% (n= 5/137) amongst administrative staff (p = 0.15). Compared to clerical workers, the OR for HCW RT-PCR positivity was 4.16 (95% CI 1.55 – 11.1), 2.54 (95% CI 0.94 – 6.84), 2.27 (95% CI 0.78 – 6.86) and 2.61 (95% CI 8.88 – 7.69 - likely a typographical error in the CIs)), for physicians; nurses or midwives; healthcare assistants and healthcare technicians, respectively.[133] The wide and overlapping CIs for the ORs presented therefore mean that there is no reliable evidence on odds of infection according to occupation.

RT-PCR and/or whole genome sequencing (WGS) was adopted in three international studies to investigate the potential routes of COVID-19 transmission.[134-136] An investigation within a South African hospital involving 39 patients and 80 staff began on 4 April 2020, where it was subsequently hypothesised that nosocomial transmission likely occurred.[134] All cases underwent RT-PCR sequencing, where 23 samples (eight inpatient samples; nine HCW samples; one nursing home resident sample) underwent WGS for further investigation. Phylogenetic analysis of the A2a clade demonstrated that the sequences were over 99.9% identical, suggesting nosocomial transmission.[134] However, other routes of transmission cannot be ruled out given the limitations of this study, in particular, the small number of samples submitted for WGS, and reliance on circumstantial information.

Sikkema et al. (2020) also performed WGS to investigate HCW-to-HCW or HCW-to-patient transmission within 3 hospitals in the Netherlands between 2 March to 12 March 2020.[135] Symptomatic HCWs and hospitalised patients were screened by RT-PCR to confirm SARS-CoV-2 infection. Following WGS of 50 HCW and 18 patient samples, authors found no notable links in sequences between HCWs working on the same ward and between HCWs and inpatients.[135] The small sample size and limited testing performed limit the reliability and generalisability of these findings.

Lucey et al. (2020) performed WGS to investigate nosocomial transmission of SARS-CoV-2 in a tertiary hospital in Dublin, Ireland, between 7 March to 10 May 2020.[136] A number of outbreaks occurred in this hospital involving a number of different wards. One outbreak, where sequencing confirmed transmission, occurred in a single ward where many patients did not have direct contact with each other given lack of mobility. Given this fact the outbreak was attributed to HCW to patient transmission. Another cluster was associated with outbreaks on four different wards that were initially considered distinct due to the geographical location and the fact that the staff members do not interact. However, two HCWs were found to be 'floaters', i.e. they worked on different wards to care for patients who need a considerable amount of care. WGS also found one HCW within this cluster who did not have direct patient contact providing evidence to support transmission between HCWs in this outbreak.

6. Conclusions

Overall, the evidence base is inconclusive regarding the risk of SARS-CoV-2 acquisition in HCWs when caring for suspected or confirmed COVID-19 cases in UK settings, given the limitations of the studies described. Only seven UK studies and 10 international studies used PCR analysis to define infection. Collectively, these studies were unable to demonstrate a significantly greater risk of infection in HCWs compared to the general population. Whilst initial UK data may have suggested a greater risk in HCWs during the early phase of the pandemic, this is confounded by the differences in testing availability for HCWs and the public at that time. Only one study performed internationally compared infection between HCWs and non-HCWs. Although this study suggested increased risk of infection amongst HCWs compared to the general population, it had a number of limitations that impacted the rigour of its findings.

Of the five serological studies discussed that were performed in UK-settings, only one compared seroprevalence between HCWs and the general population. The remaining serological studies indicated that seroprevalence in the early phase of the pandemic (January to

July 2020) was higher amongst staff providing direct patient care, and lower amongst staff working in the ICU compared to other ward settings. However, in addition to discrepancies in testing during the early phases of the pandemic, it should be noted that serology is a less reliable proxy measure of infection compared to PCR analysis in that it cannot accurately pinpoint the time of active infection.

The overarching limitation of the evidence-base is the majority of studies were unable to demonstrate where HCWs were acquiring infection i.e. at work when caring for patients, at work when interacting with colleagues, or from the community and thus completely unrelated to their occupation. Only three studies attempted to assess transmission chains using WGS, and this suggested transmission from HCWs to HCWs and not acquisition related to patient care. From unreported Scottish hospital outbreak reporting, there is large variation in the involvement of HCWs in outbreaks with some settings reporting outbreaks involving only HCWs, suggestive of risk unrelated to patient care.

A further limitation of the evidence base is that studies were effectively point prevalence studies with varying methodology and background factors, making comparison challenging and limiting the generalisability of this evidence-base. Risk factors for infection were largely investigated using surveys, introducing recall bias. In the majority of studies, HCWs were recruited on a voluntary basis, another source of bias where confounding factors may have motivated some HCWs to undergo COVID-19 testing more than others. In all of the studies described, specific staff duties and contact time with COVID-19 patients was very unclear and there was minimal information provided regarding compliance with occupational-based control measures (e.g. PPE use, physical distancing, extended mask use, and compliance with community-based control measures (e.g. no household visiting)). In terms of risk according to health and care-setting occupation, a number of confounding factors were not considered in the studies discussed. Two important factors include differences in spatial structure and ventilation within the various settings. A further potential confounder is the experience of and training received by HCWs, as it has been suggested that certain groups (e.g. critical care staff) may have an increased awareness of IPC measures as a result of their training, in addition to greater experience in donning and doffing PPE appropriately.

The majority of studies were conducted during the period March to June 2020, in the early phase of the pandemic. This was prior to the roll out of expanded community and HCW testing, pre-mandatory mask use and physical distancing implementation. Lack of testing in the community at that time is likely to have underestimated the true prevalence of infection in the general population, leading to the overestimation of the proportion of infection experienced by

HCWs. Furthermore, testing of HCWs was largely limited to those who presented with more severe symptoms in healthcare settings, limiting the representation of those with mild symptoms, or asymptomatic carriage. Lastly, as the study duration periods were short, staff at home due to requirements to self-isolate or due to illness were likely unable to participate. Again, this may have over or under-estimated infection risk in certain staff groups. Only one study was conducted in the more recent phases of the pandemic, indicating that risk of infection is similar between HCWs and essential workers. This may suggest an influence of increased interaction with others which may be driving the infection rates and reflective of the transmission dynamics in the community. Further research is necessary to determine the drivers of transmission.

Overall, this rapid review highlights that there is a distinct paucity of rigorous research regarding the risk of SARS-CoV-2 infection amongst HCWs.

Appendix 1

The following search strategies were processed in OVID Embase and Medline on the 20 January 2021 (search A) and 11 February 2021 (search B). Studies were included if they compared HCW acquisition of SARS-CoV-2 according to profession, or compared HCW acquisition to the general community.

Search A

1. Healthcare worker*.mp.
2. Health care worker*.mp.
3. Healthcare personnel.mp.
4. Healthcare staff.mp.
5. Hospital staff.mp.
6. Clinician*.mp.
7. Physician*.mp.
8. Nurse*.mp.
9. HCW*.mp.
10. Acquisition.mp.
11. Hospital-acquired infection*.mp.
12. Nosocomial.mp.
13. Hospital transmission.mp.
14. In-hospital transmission.mp.
15. Seroprevalence.mp.
16. Seropositivity.mp.
17. Occupational risk.mp.

18. SARS-CoV-2.mp.
19. COVID-19.mp.
20. 2019-nCoV.mp.
21. novel coronavirus.mp
22. Anti-SARS-Cov-2.mp.
23. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
24. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
25. 18 or 19 or 20 or 21 or 22
26. 23 and 24 and 25
27. Remove duplicates from 26
28. Limit 27 to English language
29. Limit 28 to humans

Search B

1. Healthcare worker*.mp.
2. Health care worker*.mp.
3. Healthcare personnel.mp.
4. Healthcare staff.mp.
5. Care home staff.mp.
6. Social care staff.mp.
7. Domiciliary care.mp.
8. Nursing home.mp.
9. Acquisition.mp.

10. Nosocomial.mp.

11. Healthcare-acquired.mp.

12. Healthcare associated.mp.

13. Occupational risk.mp.

14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8

15. 9 or 10 or 11 or 12 or 13

16. 14 and 15

17. Limit 16 to COVID-19

18. Remove duplicates from 17

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