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Cumulative incidence of SARS-CoV-2 and associated risk factors among healthcare workers in the Eastern Cape, South Africa

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Abstract

Objectives: This study assesses the cumulative incidence of SARS-CoV-2 infection among healthcare workers (HCWs) during South Africa's first wave and examines the associated demographic, health-related, and occupational risk factors for infection.

Methods: Multi-stage cluster sampling was used in a cross-sectional study to recruit 1,309 HCWs from two academic hospitals in the Eastern Cape, South Africa over six weeks in November and December 2020. Prior test results for SARS-CoV-2 polymerase chain reaction (PCR) and participants' characteristics were recorded while a blood sample was drawn for detection of IgG antibodies against SARS-CoV-2 nucleocapsid protein. The primary outcome measure was the SARS-CoV-2 cumulative incidence rate, defined as the combined total of positive results for either PCR or IgG antibodies, divided by the total sample. The secondary outcome was significant risk factors associated with infection.

Results: Of the total participants included in the analysis (N=1295), the majority were female (81.5%), of black race (78.7%) and nurses (44.8%). A total of 390 (30.1%) HCWs had a positive SARS-CoV-2 PCR result and SARS-CoV-2 antibodies were detected in 488 (37.7%), yielding a cumulative incidence of 47.2% (n = 611). In the adjusted logistic regression model, being overweight (Adjusted odds ratio (AOR) = 2.15, 95% CI 1.44-3.20), obese (AOR = 1.37, 95% CI 1.02-1.85) and living with HIV (AOR = 1.78, 95% CI 1.38-2.08) were independently associated with SARS-CoV-2 infection. There was no significant difference in infection rates between high, medium and low COVID-19 exposure working environments.

Conclusions: The high SARS-CoV-2 cumulative incidence in the cohort was surprising this early in the epidemic and probably related to exposure both in and outside the hospitals. To mitigate the impact of SARS-CoV-2 among HCWs, infection prevention and control (IPC) strategies should target community transmission in addition to screening for HIV and metabolic conditions.

Strengths and limitations of this study:

- This is a large representative sample of the total workforce of the two hospitals, with a good spectrum of staff category.
- Combining the historical SARS-CoV-2 PCR results with the Nucleocapsid IgG enabled capturing of some of the asymptomatic and missed SARS-CoV-2 infections.
- This is one of the first studies to look at SARS-CoV-2 infection risk factors in a high exposure environment in Africa.

- A limitation is that HIV ELISA and CD4 counts were not tested, but relied on self-report, which may likely underestimate the burden of HIV in the cohort.

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Competing interests statement:
The authors declare no conflict of interest.

Keywords: COVID-19, cumulative infection rate, Eastern Cape, healthcare workers, SARS-CoV-2

Background

South Africa reported its first imported case of SARS-CoV-2 on 5 March 2020 and subsequently experienced high rates of transmission throughout the country. The first wave peaked in July 2020, the second wave in late December 2020 and a third wave occurred in June 2021, with total cases approaching 3 million.[1] The Eastern Cape ranked 4th out of South Africa's nine provinces for cumulative SARS-CoV-2 cases, with 290 898 cases recorded on 2 October 2021.[1]

Healthcare workers (HCWs) are responsible for providing acute in-hospital care for patients with moderate and severe COVID-19 who require oxygen support and other therapies.[2] The HCWs are exposed to infectious droplets and aerosols, putting them at increased risk for infection.[2] Despite infection prevention and control measures at the health facility level, HCWs still acquire SARS-CoV-2 at a higher rate than the general population.[2–4] A prospective study of 200 frontline HCWs in the United Kingdom (UK), during the first peak of viral transmission involving the collection of twice weekly nasopharyngeal swabs for reverse transcription polymerase chain reaction (RT-PCR) and monthly blood samples for serology, showed that 44% became infected. This was more than double the rate of the local population.[3] A smartphone application allowing self-reporting of positive SARS-CoV-2 PCR results was used in a survey of almost 100,000 UK and United States (US) HCWs. Incident cases in these HCWs

were almost 12-fold greater than in a two million comparator sample of the general population.[2] Another UK study found a SARS-CoV-2 seroprevalence of 16.3% among HCWs compared to a 5.9% national community rate.[4]

Reported information on SARS-CoV-2 infections among HCWs in Africa is scanty. Two hundred and twenty-two HCWs from single South African paediatric unit were included in a global comparative seroprevalence study (recruited June to August 2020), with a seropositivity of 10.36% (95% CI: 7-15.07).[5] A pre-print of a serosurvey of 500 HCWs in Blantyre, Malawi, reported a 12.3% positivity rate.[6] The Eastern Cape Department of Health reported a total of 11,262 HCWs infected with SARS-CoV-2 by 18 February 2021, with 262 deaths (2.3% fatality rate). The highest infection rates were among state-employed doctors and nurses (18.2% and 22.3%, respectively) compared to a 2.8% for the province as a whole.[7]

The potentially high SARS-CoV-2 exposure environment in hospitals enables acquisition of data on infection rates and associated risk factors amongst HCWs, that can assist in understanding the dynamics of SARS-CoV-2 transmission and the efficacy of infection prevention and control measures. In some studies, high-exposure clinical areas such as Accident & Emergency Units, acute medical wards and intensive care units have been associated with increased HCW infections when compared to administrative or support service areas.[8–10] Others have shown no difference between staff roles, suggesting that most infections were acquired outside of areas of patient contact, or outside of the hospital.[11,12] Inadequate availability or faulty use of personal protective equipment (PPE) are both factors shown to increase the risk of infection.[2,13] Male HCWs and those with at least one comorbidity also appear to have an increased risk of acquiring SARS-CoV-2 infection.[8,14] Outside the healthcare environment, a study of 3,802 SARS-CoV-2 tests performed in the UK found that infection risk was increased by male gender, age 40-64 years, black ethnicity, lower socio-economic status, chronic kidney disease, and obesity. In this study, smokers had a lower risk of infection.[15]

SARS-CoV-2 is a global pandemic, but has affected individual countries and their health systems to varying degrees. Explanations for this include a complex interaction of population and genetic vulnerabilities, social mitigation behaviour, and health system interventions. Due to the paucity of evidence around the impact of SARS-CoV-2 on HCWs in Africa, this study was undertaken to gain insights in this setting. Frere and Cecilia Makiwane hospitals are both

in the Eastern Cape Province in South Africa. This is an under-resourced province with a less robust healthcare system than that in some other provinces. Both facilities experienced high numbers of staff infections and absenteeism during the first wave of SARS-CoV-2, with considerable disruption to health service delivery. This study was conducted to assess the cumulative incidence of staff SARS-CoV-2 infections (symptomatic and asymptomatic), and their associated demographic, health-related, and occupational risk factors. Findings from the study may inform planning and improve IPC measures related to infections with SARS-CoV-2 and other respiratory viruses in the province.

Methods

Study design and settings

This observational cross-sectional study was conducted in two academic hospitals: Frere and Cecilia Makiwane, in the central region of the Eastern Cape, South Africa. Cecilia Makiwane is a regional hospital that provides levels one and two healthcare services to the residents of Buffalo City and the Amathole district. Frere hospital is a tertiary institution which serves as a referral hospital for four district municipalities: Buffalo City, Amathole, Chris Hani and Joe Gqabi. Together they serve a population of almost three million residents and have over 4,000 HCWs: doctors, nurses, pharmacists, allied workers and support staff (administration, laundry, kitchen and mortuary).[16]

Re-organisation of hospitals during the 'first wave'

At the onset of the first wave, local protocols were developed in accordance with the National Institute of Communicable Diseases Guidelines for the management of confirmed or suspected cases of COVID-19.[17] Designated COVID-19 units were created from the existing emergency units of the two hospitals. All individuals meeting the criteria for 'patient under investigation' and/or confirmed cases of COVID-19 were directed to the designated area within the emergency unit, where triaging and clinical evaluations were performed by the attending clinicians. In both hospitals, patients meeting the criteria for admission based on the severity of their condition and/or co-morbidities were admitted into designated COVID-19 wards. Patients who presented in critical condition were admitted into the hospitals' intensive care units. The head of the internal medicine department supervised in-patient admissions in both hospitals, thereby ensuring that the COVID-19 protocol was the same at both facilities. All clinicians working in the designated COVID-19 wards and emergency units received training on the effective use of PPE. In addition, the hospitals formed logistics committees comprising

senior managers of the hospital to ensure a constant supply of PPE for use by all personnel caring for patients with COVID-19. The Occupational Health and Safety (OHS) unit of each hospital created a database of COVID-19 infection among its HCWs. HCWs were required to submit confirmation of a SARS-CoV-2 PCR positive result as evidence of diagnosis and permission to proceed with the mandatory isolation of 10–14 days, in accordance with the guidelines.[17]

Participants

All categories of HCWs in the two hospitals were eligible to participate in the study. To ensure inclusivity of all HCWs, the study adopted a multi-stage cluster sampling technique. Risk profiles were categorised according to the exposure areas identified by Iversen et al.: 'high risk' if the HCWs worked in Accident & Emergency units, designated COVID-19 wards, and intensive care units (ICUs); 'intermediate risk' if HCWs worked in non-respiratory admission wards, outpatient departments (OPDs), and other clinical areas; and 'low risk' if the HCWs performed administrative tasks and other non-clinical duties.[8] Prior to recruitment, mass sensitisation about the study was conducted through union leaders, departmental heads and clinical managers. In addition, a communique was circulated across the two hospitals to create awareness of the study. Each working area was allocated specific days to allow those on night shifts as well as those who were off-duty to participate with minimal interruption to service delivery. In addition, a central recruitment area was created in each of the two hospitals to cater for HCWs who might have missed the dates allocated by their departments. There was no sample size calculation performed, but rather as many staff recruited as possible within the budgeted time frame for the study. The study was implemented between 4 November and 18 December 2020. SARS-CoV-2 vaccination for HCWs in South Africa only became available in March 2021.

Procedure

Each department/work area provided a dedicated station where HCWs completed a manual questionnaire and blood samples were drawn. Two research nurses and four assistants underwent training on the research process and study instrument over a three-day period prior to commencement of the study. The research nurses measured HCWs' height and weight according to standard protocols. Venous blood samples (about 5 mL) were drawn by the trained research nurses using an aseptic technique. All blood samples were tested for the IgG

antibodies against SARS-CoV-2 nucleocapsid protein by the National Health Laboratory Services in accordance with standard protocols.

To link the results of SARS-CoV-2 PCR tests recorded on the OHS databases with the SARS-CoV-2 IgG antibody tests, while maintaining confidentiality, a unique identifying number was used to encode the participants' details (names, date of birth and area of work) in the research register, which was accessible only to the investigators. The questionnaire data for the study were captured on the REDCap® online database of the South African Medical Research Council server.

Main outcome measures

Serum samples were analysed on an Abbott ARCHITECT *i*1000SR instrument using the Abbott SARS-CoV-2 IgG assay in accordance with the manufacturer's instructions. This is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG against the SARS-CoV-2 nucleoprotein. Strength of response in relative light units reflects quantity of IgG present, and is compared to a calibrator to determine the calculated index (specimen/calibrator [S/C]) for a sample (with positive at 1.4 or greater).This assay has a specificity of 99.9% from 1020 pre-COVID-19 serum specimens and a sensitivity of 100% at 17 days after symptom onset and 13 days after PCR positivity.[18]

Seropositivity was categorised as a binary outcome: a positive result of SARS-CoV-2 IgG was considered as evidence of prior infection (humoral immune response), while a negative result was considered as either non-exposure or as a decayed (lost) immune response.

Cumulative incidence: This was a combination of a SARS-CoV-2 diagnosis (positive SARS-CoV-2 PCR and/or positive SARS-CoV-2 IgG).

Missed SARS-CoV-2 infection: This was defined as seropositive SARS-CoV-2 IgG without any documented diagnosis of SARS-CoV-2. The latter included symptomatic individuals with negative SARS-CoV-2 PCR or who never tested and asymptomatic individuals who had not undergone PCR testing.

Covariates

Sociodemographic and clinical covariates were included in this study. Age, sex, race, highest level of education, profession and smoking status, among others, were self-reported in the questionnaire. Age was categorised by decades for the multivariate analysis. Exposure risks

(such as direct contact with patients with COVID-19) and training on the use of PPE were also obtained. Certain comorbidities (diabetes, hypertension, HIV, Tuberculosis, Chronic kidney disease, heart disease, Asthma/Chronic obstructive pulmonary disease, liver disease, cancer, pregnancy) or immunosuppressive therapy, that have been shown to increase the risk of acquiring SARS-CoV-2 were explored in the questionnaire.[2,8,13,15,19] A prior SARS-CoV-2 diagnosis was self-reported by the participants and validated through the OHS personnel database in each hospital. The questionnaire was completed by each participant, with assistance offered to those participants requiring it.

Data analysis

Data were exported from the REDCap® online database for analysis using the IBM SPSS version 25.0 software (IBM SPSS, Chicago, Illinois) after cross-checking for completeness and accuracy. The means ± standard deviations were estimated for continuous data and counts and proportions were estimated for categorical data for the sociodemographic characteristics of the participants. The proportion of HCWs with either a SARS-CoV-2 PCR diagnosis or positive IgG antibodies, or both, were reckoned as cumulative incidence in the study. The cumulative incidence was disaggregated by sociodemographic and clinical factors.

The associations between the cumulative incidence and risk factors (sociodemographic and clinical) were explored using the Pearson $\chi 2$ test. We fitted both unadjusted and adjusted multivariate logistic regression models to examine the independent risk factors for cumulative infection with SARS-CoV-2 among the HCWs in the study. Variable selection in the model analysis was guided by known risk factors reported previously in other studies.[8,13,15] A p-value less than 0.05 was considered statistically significant.

Ethical Considerations

The Walter Sisulu University Ethics Committee granted approval for the implementation of the study (Reference: 087/2020), as well as the Eastern Cape Provincial Department of Health and local hospitals ethics committee. Each participant provided written informed consent for the study. Participants' rights to privacy and the confidentiality of clinical data were respected during and after the study. The research process followed the Helsinki Declaration and local institutional policy. All hard copies of materials used in the study were locked securely and soft copies were password-protected in the computer in the research office.

Patient and public involvement

There was no public or patient involvement in the design, conduct or reporting of this research, as patients were not included. The healthcare worker participants were given their individual SARS-CoV-2 IgG results via cellular messaging. The main findings of the study will be shared with the respective hospital management teams.

Results

A total of 1,309 HCWs participated in the study from both hospitals, 656 from Frere Hospital and 653 from Cecilia Makiwane Hospital. Eleven blood samples for SARS-CoV-2 IgG serology were missing or rejected by the laboratory and were excluded from the final analysis. Data for another three participants were excluded due to missing data on the main outcome measures. Data for 1,295 HCWs were included in the final analysis.

Baseline characteristics of the participants (N = 1,295)

The participants were predominantly women (81.5%), black (78.7%), had undergone tertiary education (71.5%), and most had never smoked (91.0%). In terms of professional category, nurses predominated (44.8%), followed by support staff (28.8%) and medical doctors (13.6%). Most (77.1%) participants reported direct contact with patients with COVID-19 and had attended training on PPE use (79.4%) (Table 1).

SARS-CoV-2 cumulative incidence

SARS-CoV-2 infection was confirmed (PCR positive) in 390 participants (30.1%), and a SARS-CoV-2 IgG positive result occurred in 488 (37.7%), participants giving a cumulative incidence of 47.2% (611 HCWs). Of the 390 PCR positive cases, 123 (31.5%) were SARS-CoV-2 IgG negative at the time of study. One hundred and forty-six of 640 (22.8%) PCR negative cases were IgG positive indicating potentially false negative PCR tests or being tested at the incorrect time. The SARS-CoV-2 IgG picked up an additional 17.1% (n = 221) missed infections in this cohort (146 HCWs with negative PCR results and 75 who never tested) (Table 2).

Risk factors for SARS-CoV-2 infection among the HCWs

When examining sociodemographic and exposure risk factors for infection (Table 3), age, race, level of educational, smoking status, professional category, and work area were all significantly associated with SARS-CoV-2 infection ($p < 0.05$). Among the co-morbid conditions (Table 4), only Body Mass Index (BMI) was significantly associated with SARS-CoV-2 infection.

In an unadjusted logistic regression analysis (Table 5), female sex, coloured ethnicity, a primary education, active smokers, medical doctors and allied staff, use of public transport, and being overweight and obese were significantly associated with SARS-CoV-2 infection. However, in the adjusted logistic regression (Table 5), comorbidity with HIV, and being overweight and obesity were independently associated with SARS-CoV-2 infection. Individuals who were living with HIV were almost twice as likely to be infected with SARS-CoV-2 (Adjusted Odd Ratio [AOR] = 1.78; 95% Confidence Interval [CI]: 1.38-2.08). Individuals who were overweight were twice as likely to be infected with SARS-CoV-2 (AOR = 2.15; 95% CI 1.44-3.20). Similarly, those who were obese were slightly more likely to be infected with SARS-CoV-2 (AOR = 1.37; 95% CI 1.02-1.85).

Discussion

This cross-sectional survey of 1 295 HCWs from two large referral hospitals in the Eastern Cape Province combined two diagnostic modalities (SARS-CoV-2 PCR and SARS-CoV-2 IgG antibodies) to estimate the cumulative incidence of SARS-CoV-2 infection. The study showed a high rate of SARS-CoV-2 infection (47.2%) after the first wave of COVID-19 among the HCWs in the region. This rate is double the official figures reported for doctors and nurses subsequent to the second wave in the Eastern Cape province (18.2-22.3%).[7] The 30.1% SARS-CoV-2 PCR positivity is significantly higher than the pooled prevalence of 11% (95% CI; 7-15%) from a systematic review of 46 studies among HCWs worldwide.[20] Similarly the 37.7% SARS-CoV-2 IgG seropositivity is higher than the pooled prevalence of 7% (95% CI; 4-11%) of 27,445 HCWs in the same review.[20]

In order to obtain reliable epidemiologic data on the infection rate with SARS-CoV-2 for strategic planning, a minimum of two or more data sources should be combined. Findings from this study demonstrate the importance of combining PCR results with antibody testing within a population to assess more accurately the cumulative incidence of SARS-CoV-2 infection. Neither of the modalities alone was accurate in estimating the infection rate in the study as reflected by the 31.5% of IgG negative results in HCWs who had been documented as SARS-

CoV-2 PCR positive. These most likely represent cases of decay in the humoral immune response with IgG levels falling below the assay detection threshold over time. A study of the duration of SARS-CoV-2 IgG anti-nucleocapsid antibodies among 452 HCWs reported decline starting within 1 month after first positive PCR, with an estimated half-life of 85 days and 50% seronegative after 7 months.[21] On the other hand, SARS-CoV-2 IgG testing identified 17.1% of participants with infections that had been missed by PCR. Two thirds (146/221) of these missed infections reported negative PCR tests. These likely represent false negative PCR results; suboptimal sample collections, or swabs that were taken before or after the peak of viral shedding.[22–24] The other third (75/221) of the missed infections had never had a PCR test performed. These were likely asymptomatic infections or patients with mild symptoms that did not lead to PCR testing.

In terms of risk factors for SARS-CoV-2 infection among HCWs, the only significant risk factors in the adjusted multivariate logistic regression analysis were having an increased BMI (overweight or obese) and being HIV positive. While these factors have been reported as risks for infection among the general population in some reports[2,5,12,14,18], this is the first time they have been linked in a specifically HCW population. Stratifying areas of work into low, medium and high risk for SARS-CoV-2 exposure did not identify significant differences in infection risk, contrary to findings by Iversen et al.[8] There was also no difference in infection prevalence across different professions. These are important negative findings of this study, and contribute some insights into SARS-CoV-2 exposure and transmission in the hospital environment. Of interest for epidemiologic purposes are two pertinent questions. 'Why did doctors and nurses working in designated COVID-19 clinical areas not experience higher infection rates than non-clinical staff?' and 'Did improved use of PPE in these designated clinical areas effectively level this risk?'

Despite a large proportion (80%) of HCWs having been trained on the use of PPE, and they confirmed that PPEs were available for use, there was no correlation with SARS-CoV-2 infection in the cohort. A prospective study of SARS-CoV-2 infections among 10,034 UK HCWs, showed a lower risk of infection among ICU clinical staff, suggesting that training on PPE and strict adherence to infection control protocols protected staff in high risk areas.[9] While there were concerns about inadequate quantities and quality of PPE during the period prior to the study, there was never a total shortage of PPE for use in COVID-19 clinical areas in either of the two facilities. Another plausible explanation for the results could be the strict adherence

to symptom screening of all staff in the COVID-19 clinical areas throughout the period. Prompt diagnosis and isolation of infected individuals will prevent further spread among HCWs in the same work areas[2,3]. Furthermore, it was not infrequent for COVID-19 cases to be diagnosed in the non-COVID-19 clinical areas, which could account for similarly high proportions of staff infection in low, medium and high-risk clinical areas.

Transmission of SARS-CoV-2 between HCWs in the common areas during tea and lunch breaks, when staff interact socially with or without masks was not measured in the study, but is quite probable to have occurred to some degree. It was hypothesised that taking shared or public transport to work would increase the risk of infection compared to solo vehicle transport, but this was not found to be significant. At the time of this study, there were no community seroprevalence data with which to compare our findings. During the second epidemiologic wave, Sykes et al. reported a seropositivity rate of 63% among blood donors from the Eastern Cape, the highest among four provinces sampled in the country in January 2021.[25] This study only sampled 1,457 donors, a highly selected group of healthy volunteers from four provinces. It is therefore difficult to estimate the community prevalence at the time of our study. Notwithstanding, there is a strong possibility of a high- exposure environment outside of the hospitals in the region. A previous UK study found that having a household COVID-19 contact was the strongest risk factor for HCW infection [AOR 4.82; 95% CI 3.45–6.72].[9]

Being overweight or obese has been linked to increased susceptibility to SARS-CoV-2 infection, as well as to disease severity and increased mortality. A meta-analysis of 20 studies assessing obesity and risk of SARS-CoV-2 infection found an odds ratio of 1.46 (95% CI 1.30-1.65).[26] Poorer outcomes for respiratory viruses in the obese had been described prior to SARS-CoV-2 with the H1N1 influenza pandemic.[27] The mechanisms for the increased vulnerability to SARS-CoV-2 among the overweight and obese are complex. Obesity is associated with a pro-inflammatory phenotype and systemic low-grade inflammation.[27] Obesity dampens and delays both the innate and the adaptive immune response to infection with reduced efficacy of B- and T- cell responses. Obesity is also associated with poorer response to vaccination, likely through the same immune dampening effects.[27] This sample of HCWs revealed alarmingly high rates of being either overweight (22.7%) or obese (63.1%), which is a concern due to increased vulnerability to respiratory viral infections as well as the non-communicable disease risks linked such as type 2 diabetes mellitus, hypertension, cardiovascular diseases and certain cancers.[28]

There is epidemiological evidence for an increased susceptibility to SARS-CoV-2 with HIV infection. A systematic review and meta-analysis of almost 21 million people across multiple continents reported a risk ratio of 1.24 (95% CI 1.05-1.46) for SARS-CoV-2 infection among people living with HIV compared to those uninfected by HIV.[29] The HIV prevalence of 7.3% in this cohort may be an underestimate, given the self-reported nature of the data and some infected individuals may not have been diagnosed. The estimated adult HIV prevalence in the local district is 13.6%, as a comparison.[30] Data on CD4 cell counts and whether HIV infected HCWs were on antiretroviral therapy were not obtained in this study, but could have added more insights into the HIV-related risk. Like obesity, HIV is an important vulnerability to be managed among HCWs in relation to SARS-CoV-2 and other infections such as *Mycobacterium tuberculosis*.

Strengths and limitations

This is the first reported study to have combined two diagnostic modalities to estimate the cumulative incidence of SARS-CoV-2 infection among HCWs in South Africa. Findings will inform IPC policies in the region. However, this study does have some limitations. Due to the pragmatic nature of the local policy relating to PCR testing for SARS-CoV-2, testing was largely limited to symptomatic staff, which would have missed some asymptomatic infections. HIV serology and CD4 counts were not tested, but relied on self-reporting of individual HIV status, which may likely underestimate the burden of HIV in the cohort.

Conclusion

We report a high SARS-CoV-2 cumulative incidence of 47.2% after the first epidemiologic wave among HCWs from two referral hospitals in the Eastern Cape, South Africa. This is one of the highest reported in the literature and more than double that of the official figures for HCWs in the region. Being overweight or obese were significant risks for infection, and over 85% of HCWs fell into these categories. HIV infection was also associated with increased infection in the cohort. There were similar rates of infection across low, medium and high SARS-CoV-2 transmission risk areas, suggesting that significant transmission of infection occurred between colleagues or outside the workplace. Staff wellness programmes should address weight reduction and regular HIV testing and treatment, to mitigate vulnerabilities in this essential workforce.

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Table 1: Baseline characteristics of the participants (n = 1,295)

Variable	Frequency	Percentage
Sex		
Males	240	18.5
Females	1055	81.5
Age (years)		
18-25	71	5.49
26-35	325	25.12
36-45	349	26.97
46-55	346	26.74
>55	203	15.69
***Race**		
Black	1019	78.7
White	114	8.8
Coloured	98	7.6
Others	53	4.1
Level of Education		
Tertiary	925	71.5
Secondary	357	27.6
Primary	12	0.9
Smoking Status		
Never smoked	1178	91.0
Active smoker	72	5.6
Former smoker	44	3.4
Profession		
Medical doctors	176	13.6
Pharmacy staff	61	4.7
Nurses	580	44.8
Allied staff	105	8.1
Support staff	372	28.8
Direct contact with a confirmed COVID-19 case		
Yes	998	77.1
No	296	22.9
Attended PPE training		
Yes	1027	79.4
No	267	20.6

***n = 10 participants did not indicate their race group**
PPE = Personal protective equipment

Table 2. Confirmation of SARS-CoV-2 infection among the participants

Variables	IgG Positive (n; %)	IgG Negative (n; %)	Total (n; %)
PCR Positive	267 (68.5)	123 (31.5)	390 (30.1)
PCR Negative	146 (22.8)	494 (77.2)	640 (49.5)
Never tested	75 (28.4)	189 (71.6)	264 (20.4)
Total	488 (37.7)	806 (62.3)	1294 (100)

IgG = Immunoglobulin G; PCR = Polymerase chain reaction; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2

Table 3. Relationship between socio-demographic characteristics and SARS-CoV-2 by Pearson χ2 test

Variable	SARS-CoV-2 by PCR and/or IgG		p-values
	Yes (%)	**No** (%)	
All	n = 611 (47.2)	n = 683 (52.8)	
Sex			**0.007**
Males	95 (39.6)	145 (60.4)	
Females	517 (49.0)	538 (51.0)	
Age			0.628
<45 years	347 (46.6)	397 (53.4)	
>45 years	346 (54.7)	286 (45.3)	
Race			**<0.001**
Black	524 (51.4)	495 (48.6)	
White	30 (26.3)	84 (73.7)	
Coloured	29 (29.6)	69 (70.4)	
Others	18 (34.0)	35 (66.0)	
Level of Education			**0.003**
Tertiary	418 (45.2)	507 (54.8)	
Secondary	191 (53.5)	166 (46.5)	
Primary	02 (16.7)	10 (83.3)	
Smoking Status			**<0.001**
Never smoked	580 (49.2)	598 (50.8)	
Active smoker	17 (23.6)	55 (76.4)	
Former smoker	14 (31.8)	30 (68.2)	
Covid-19 exposure by Ward			**0.008**
High risk	151 (51.2)	144 (48.8)	
Medium risk	265 (42.7)	355 (57.3)	
Low risk	195 (51.5)	184 (48.6)	
Profession			**<0.001**
Medical doctors	55 (31.2)	121 (68.8)	
Pharmacy staff	28 (45.9)	33 (54.1)	
Nurses	311 (53.6)	269 (46.4)	
Allied staff	25 (23.8)	80 (76.2)	
Support staff	192 (51.6)	180 (48.4)	
Direct contact with a confirmed COVID-19 case			0.337
Yes	464 (46.5)	534 (53.5)	
No	147 (49.7)	149 (50.3)	
Attended PPE training			0.498
Yes	480 (46.7)	547 (53.3)	
No	131 (49.1)	136 (50.9)	

IgG = Immunoglobulin G; PCR = Polymerase chain reaction; PPE = Personal protective equipment; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2.
Support staff = Administration/Management staff (51/98; 52.0%), General workers (31/61; 50.8%), Kitchen staff (23/33; 69.7%), Porters (06/15; 40.0%), Stores/Sales staff (0/5), Mortuary staff (4/5; 80.0%), Laundry staff (23/39; 59.0%). *117 of the support staff did not indicate their duties.
Allied Workers = Radiology staff (9/37; 24.3%), Social workers (1), Physiotherapists (1), Dieticians (1), *68 of allied workers did not indicate their duties.

Table 4: Relationship between co-morbidities and SARS-CoV-2 by Pearson χ2 test

Variables	Positive SARS-CoV-2 PCR and/ or IgG		p-values
	Yes (%)	**No** (%)	
All	n = 611 (47.2)	n = 683 (52.8)	
***BMI**			**<0.001**
Underweight	4 (57.1)	3 (42.9)	
Normal weight	47 (26.7)	129 (73.3)	
Overweight	121 (41.4)	171 (58.6)	
Obese	434 (53.5)	378 (46.6)	
Diabetes			0.076
Yes	56 (54.4)	47 (45.6)	
No	555 (46.6)	636 (53.4)	
Hypertension			0.246
Yes	119 (50.6)	116 (49.4)	
No	492 (46.5)	567 (53.5)	
HIV			0.300
Yes	40 (42.1)	55 (57.9)	
No	571 (47.6)	628 (52.4)	
TB			0.141
Yes	11 (34.4)	21 (65.6)	
No	600 (47.5)	662 (52.5)	
Chronic Kidney Disease			0.074
Yes	07 (29.2)	17 (70.8)	
No	604 (47.6)	666 (52.4)	
Heart Disease			0.496
Yes	15 (53.6)	13 (46.4)	
No	596 (47.1)	670 (52.9)	
Asthma/COPD			0.143
Yes	31 (39.2)	48 (60.8)	
No	580 (47.7)	635 (52.3)	
Liver Disease			0.169
Yes	06 (31.6)	13 (68.4)	
No	605 (47.5)	670 (52.6)	
Cancer			0.515
Yes	8 (40.0)	12 (60.0)	
No	603 (47.3)	671 (52.7)	

BMI = Body mass index; IgG = Immunoglobulin G; TB = Tuberculosis; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2; COPD = Chronic obstructive pulmonary disease.

Table 5. Adjusted and unadjusted logistic regression model showing risk factors for SARS-CoV-2 infection among HCWs

Variables	UOR (95%CI)	p-value	AOR (95%CI)	p-value
Sex				
Males	Ref		Ref	
Females	1.48 (1.11-1.79)	**0.007**	1.09 (0.78-1.51)	0.595
Race				
Others	Ref		Ref	
Coloured	0.48 (0.27-0.86)	**0.015**	1.06 (0.55-2.06)	0.848
White	1.44 (0.71-2.91)	0.311	1.46 (0.69-3.07)	0.313
Black	0.91 (0.91-1.81)	0.789	1.28 (0.61-2.71)	0.504
Level of Education				
Tertiary	Ref		Ref	
Secondary	4.12 (0.89-18.91)	0.068	3.05 (0.62-14.85)	0.166
Primary	0.71 (0.56-0.91)	**0.008**	0.90 (0.67-1.22)	0.509
Smoking Status				
Never smoked	Ref		Ref	
Active smoker	0.48 (0.25-0.91)	**0.026**	0.65 (0.32-1.29)	0.222
Former smoker	1.51 (0.65-3.48)	0.334	1.77 (0.73-4.25)	0.199
Profession				
Support staff	Ref		Ref	
Allied staff	2.34 (1.60-3.42)	**<0.001**	1.92 (0.83-4.43)	0.124
Nurses	1.25 (0.73-2.16)	0.409	0.84 (0.35-1.99)	0.693
Pharmacy staff	0.93 (0.71-1.19)	0.545	0.88 (0.42-1.84)	0.747
Medical doctors	3.41 (2.08-5.58)	**<0.001**	1.52 (0.67-3.45)	0.316
COVID-19 Exposure by Ward				
Low risk	Ref		Ref	
Medium risk	0.69 (0.53-0.90)	0.006	1.19 (0.59-2.41)	0.749
High risk	0.97 (0.71-1.32)	0.883	0.88 (0.42-1.86)	0.611
Direct contact with a confirmed COVID-19 case				
No	Ref		Ref	
Yes	0.88 (0.67-1.14)	0.338	1.01 (0.75-1.36)	0.928
Attended PPE training				
Yes	Ref		Ref	
No	1.09 (0.83-1.42)	0.498	0.99 (0.74-1.33)	0.996
Use of public transport				
No	Ref		Ref	
Yes	0.63 (0.51-0.79)	**<0.001**	0.94 (0.69-1.17)	0.444
BMI				
Underweight	-		-	
Normal	Ref		Ref	
Overweight	3.15 (2.19-4.53)	**<0.001**	2.15 (1.44-3.20)	**<0.001**
Obese	1.62 (1.23-2.12)	**<0.001**	1.37 (1.02-1.85)	**0.033**
Diabetes				
No	Ref		Ref	
Yes	0.73 (0.48-1.09)	0.131	0.85 (0.55-1.32)	0.480
Hypertension				
No	Ref		Ref	
Yes	0.84 (0.63-1.12)	0.246	1.08 (0.78-1.48)	0.628
HIV				
No	Ref		Ref	
Yes	1.25 (0.81-1.19)	0.301	1.78 (1.38-2.08)	**0.012**

BMI = Body mass index; HCWs = Healthcare workers; PPE = Personal protective equipment; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2; UOR = Unadjusted odds ratio; AOR = Adjusted odds ratio

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	*6*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cumulative incidence of SARS-CoV-2 and associated risk factors among healthcare workers – a cross-sectional study in the Eastern Cape, South Africa

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Abstract

Objectives: This study assesses the cumulative incidence of SARS-CoV-2 infection among healthcare workers (HCWs) during South Africa's first wave and examines the associated demographic, health-related, and occupational risk factors for infection.

Methods: Multi-stage cluster sampling was used in a cross-sectional study to recruit 1,309 HCWs from two academic hospitals in the Eastern Cape, South Africa over six weeks in November and December 2020. Prior test results for SARS-CoV-2 polymerase chain reaction (PCR) and participants' characteristics were recorded while a blood sample was drawn for detection of IgG antibodies against SARS-CoV-2 nucleocapsid protein. The primary outcome measure was the SARS-CoV-2 cumulative incidence rate, defined as the combined total of positive results for either PCR or IgG antibodies, divided by the total sample. The secondary outcome was significant risk factors associated with infection.

Results: Of the total participants included in the analysis (n=1295), the majority were female (81.5%), of black race (78.7%) and nurses (44.8%). A total of 390 (30.1%) HCWs had a positive SARS-CoV-2 PCR result and SARS-CoV-2 antibodies were detected in 488 (37.7%), yielding a cumulative incidence of 47.2% (n = 611). In the adjusted logistic regression model, being overweight (Adjusted odds ratio (AOR) = 2.15, 95% CI 1.44-3.20), obese (AOR = 1.37, 95% CI 1.02-1.85) and living with HIV (AOR = 1.78, 95% CI 1.38-2.08) were independently associated with SARS-CoV-2 infection. There was no significant difference in infection rates between high, medium and low COVID-19 exposure working environments.

Conclusions: The high SARS-CoV-2 cumulative incidence in the cohort was surprising this early in the epidemic and probably related to exposure both in and outside the hospitals. To mitigate the impact of SARS-CoV-2 among HCWs, infection prevention and control (IPC) strategies should target community transmission in addition to screening for HIV and metabolic conditions.

Strengths and limitations of this study:

- This is a large representative sample of the total workforce of the two hospitals, with a good spectrum of staff category.
- Combining the historical SARS-CoV-2 PCR results with the Nucleocapsid IgG enabled capturing of some of the asymptomatic and missed SARS-CoV-2 infections.
- This is one of the first studies to look at SARS-CoV-2 infection risk factors in a high exposure environment in Africa.

- A limitation is that HIV ELISA and CD4 counts were not tested, but relied on self-report, which may likely underestimate the burden of HIV in the cohort.

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Competing interests statement:
The authors declare no conflict of interest.

Keywords: COVID-19, cumulative infection rate, Eastern Cape, healthcare workers, SARS-CoV-2

Background

South Africa reported its first imported case of SARS-CoV-2 on 5 March 2020 and subsequently experienced high rates of transmission throughout the country. The first wave peaked in July 2020, the second wave in late December 2020 and a third in June 2021, with total cases approaching 3 million.[1] The Eastern Cape ranked 4th out of South Africa's nine provinces for cumulative SARS-CoV-2 cases, with 290 898 cases recorded on 2 October 2021.[1]

Healthcare workers (HCWs) are responsible for providing acute in-hospital care for patients with moderate and severe COVID-19 who require oxygen support and other therapies.[2] The HCWs are exposed to infectious droplets and aerosols, putting them at increased risk for infection.[2] Despite infection prevention and control measures at the health facility level, HCWs still acquire SARS-CoV-2 at a higher rate than the general population.[2–4] A prospective study of 200 frontline HCWs in the United Kingdom (UK), during the first peak of viral transmission involving the collection of twice weekly nasopharyngeal swabs for reverse transcription polymerase chain reaction (RT-PCR) and monthly blood samples for serology, showed that 44% became infected. This was more than double the rate of the local population.[3] A smartphone application allowing self-reporting of positive SARS-CoV-2 PCR results was used in a survey of almost 100,000 UK and United States (US) HCWs. Incident cases in these HCWs were almost 12-fold greater than in a two million comparator sample of the general population.[2]

Another UK study found a SARS-CoV-2 seroprevalence of 16.3% among HCWs compared to a 5.9% national community rate.[4]

Reported information on SARS-CoV-2 infections among HCWs in Africa is scanty. Two hundred and twenty-two HCWs from single South African paediatric unit were included in a global comparative seroprevalence study (recruited June to August 2020), with a seropositivity of 10.36% (95% CI: 7-15.07).[5] A pre-print of a serosurvey of 500 HCWs in Blantyre, Malawi, reported a 12.3% positivity rate.[6] The Eastern Cape Department of Health reported a total of 11,262 HCWs infected with SARS-CoV-2 by 18 February 2021, with 262 deaths (2.3% fatality rate). The highest infection rates were among state-employed doctors and nurses (18.2% and 22.3%, respectively) compared to a 2.8% for the province as a whole.[7]

The high SARS-CoV-2 exposure environment in hospitals enables the study of SARS-CoV-2 transmission dynamics, and the efficacy of infection prevention and control measures. In some studies, high-exposure clinical areas such as Accident & Emergency Units, acute medical wards and intensive care units have been associated with increased HCW infections when compared to administrative or support service areas.[8–10] Others have shown no difference between staff roles, suggesting that most infections were acquired outside of areas of patient contact, or outside of the hospital.[11,12] Inadequate availability or faulty use of personal protective equipment (PPE) are both factors shown to increase the risk of infection.[2,13] Male HCWs and those with at least one comorbidity also appear to have an increased risk of acquiring SARS-CoV-2 infection.[8,14] Outside the healthcare environment, a study of 3,802 SARS-CoV-2 tests performed in the UK found that infection risk was increased by male gender, age 40-64 years, black ethnicity, lower socio-economic status, chronic kidney disease, and obesity. In this study, smokers had a lower risk of infection.[15]

SARS-CoV-2 is a global pandemic, but has affected individual countries and their health systems to varying degrees. Explanations for this include a complex interaction of population and genetic vulnerabilities, social mitigation behaviour, and health system interventions. Due to the paucity of evidence around the impact of SARS-CoV-2 on HCWs in Africa, this study was undertaken to gain insights in this setting. Frere and Cecilia Makiwane hospitals are situated in the Eastern Cape Province in South Africa. This is an under-resourced province with a relatively less robust healthcare system. Both facilities experienced high numbers of staff infections and absenteeism during the first wave of SARS-CoV-2, with considerable

disruption to health service delivery. This study was conducted to assess the cumulative incidence of staff SARS-CoV-2 infections (symptomatic and asymptomatic), and their associated demographic, health-related, and occupational risk factors. Findings from the study may inform planning and improve IPC measures related to infections with SARS-CoV-2 and other respiratory viruses in the province.

Methods

Study design and settings

This observational cross-sectional study was conducted in two academic hospitals: Frere and Cecilia Makiwane, in the central region of the Eastern Cape, South Africa. Cecilia Makiwane is a regional hospital that provides levels one and two healthcare services to the residents of Buffalo City and the Amathole district. Frere hospital is a tertiary institution which serves as a referral hospital for four district municipalities: Buffalo City, Amathole, Chris Hani and Joe Gqabi. Together they serve a population of almost three million residents and have over 4,000 HCWs: doctors, nurses, pharmacists, allied workers and support staff (administration, laundry, kitchen and mortuary).[16]

Re-organisation of hospitals during the 'first wave'

At the onset of the first wave, local protocols were developed in accordance with the National Institute of Communicable Diseases Guidelines for the management of confirmed or suspected cases of COVID-19.[17] Designated COVID-19 units were created from the existing emergency units of the two hospitals. All individuals meeting the criteria for 'patient under investigation' and/or confirmed cases of COVID-19 were directed to the designated area within the emergency unit, where triaging and clinical evaluations were performed by the attending clinicians. Patients meeting the criteria for admission based on the severity of their condition and/or co-morbidities were admitted into designated COVID-19 wards. Patients who presented in critical condition were admitted into the hospitals' intensive care units. All staff working in the designated COVID-19 wards and emergency units received training on the effective use of PPE. In addition, the hospitals formed logistics committees comprising senior managers of the hospital to ensure a constant supply of PPE for use by all personnel caring for patients with COVID-19. Health care workers were tested by SARS-CoV-2 PCR if they developed any attributable symptoms, or if they were judged to be close contacts of a known positive case. This was in accordance with the national guidelines.[17] The Occupational Health and Safety (OHS) unit of each hospital created a database of COVID-19 infection among its HCWs.

HCWs were required to submit confirmation of a SARS-CoV-2 PCR positive result to proceed with the mandatory isolation of 10–14 days.

Participants

All categories of HCWs in the two hospitals were eligible to participate in the study. To ensure inclusivity of all HCWs, the study adopted a multi-stage cluster sampling technique. Risk profiles were categorised according to the exposure areas identified by Iversen et al.: 'high risk' if the HCWs worked in Accident & Emergency units, designated COVID-19 wards, and intensive care units (ICUs); 'intermediate risk' if HCWs worked in non-respiratory admission wards, outpatient departments (OPDs), and other clinical areas; and 'low risk' if the HCWs performed administrative tasks and other non-clinical duties.[8] Prior to recruitment, mass sensitisation about the study was conducted through union leaders, departmental heads and clinical managers, and a circulated communique. Each working area was allocated specific days to allow those on night shifts as well as those who were off-duty to participate. In addition, a central recruitment area was created in each of the two hospitals to cater for HCWs who might have missed the dates allocated by their departments. There was no sample size calculation performed, but rather as many staff recruited as possible within the time frame for the study. The study was implemented between 4 November and 18 December 2020. SARS-CoV-2 vaccination for HCWs in South Africa only became available in March 2021.

Procedure

Each department/work area provided a dedicated station where HCWs completed a written questionnaire (included in supplementary material) and blood samples were drawn. Two research nurses and four assistants underwent training on the research process and study instrument over a three-day period prior to commencement. The research nurses measured HCWs' height and weight according to standard protocols. Venous blood samples (about 5 mL) were drawn by the trained research nurses using an aseptic technique. All blood samples were tested for the IgG antibodies against SARS-CoV-2 nucleocapsid protein by the National Health Laboratory Services in accordance with standard protocols.

To link the results of SARS-CoV-2 PCR tests recorded on the OHS databases with the SARS-CoV-2 IgG antibody tests, while maintaining confidentiality, a unique identifying number was used to encode the participants' details (names, date of birth and area of work) in the research register, which was accessible only to the investigators. The questionnaire data for the study

were captured on the REDCap® online database of the South African Medical Research Council server.

Main outcome measures

Serum samples were analysed on an Abbott ARCHITECT *i*1000SR instrument using the Abbott SARS-CoV-2 IgG assay in accordance with the manufacturer's instructions. This is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG against the SARS-CoV-2 nucleoprotein. Strength of response in relative light units reflects quantity of IgG present, and is compared to a calibrator to determine the calculated index (specimen/calibrator [S/C]) for a sample (with positive at 1.4 or greater).This assay has a specificity of 99.9% from 1020 pre-COVID-19 serum specimens and a sensitivity of 100% at 17 days after symptom onset and 13 days after PCR positivity.[18]

Seropositivity was categorised as a binary outcome: a positive result of SARS-CoV-2 IgG was considered as evidence of prior infection (humoral immune response), while a negative result was considered as either non-exposure or as a decayed (lost) immune response.

Cumulative incidence: This was a combination of a SARS-CoV-2 diagnosis (positive SARS-CoV-2 PCR and/or positive SARS-CoV-2 IgG).

Missed SARS-CoV-2 infection: This was defined as seropositive SARS-CoV-2 IgG without any documented diagnosis of SARS-CoV-2. The latter included symptomatic individuals with negative SARS-CoV-2 PCR or who never tested and asymptomatic individuals who had not undergone PCR testing.

Covariates

Sociodemographic and clinical covariates were included in this study. Age, sex, race, highest level of education, profession and smoking status, among others, were self-reported in the questionnaire. Age was categorised by decades for the multivariate analysis. Exposure risks (such as direct contact with patients with COVID-19) and training on the use of PPE were also obtained. Certain comorbidities (diabetes, hypertension, HIV, Tuberculosis, Chronic kidney disease, heart disease, Asthma/Chronic obstructive pulmonary disease, liver disease, cancer, pregnancy) or immunosuppressive therapy, that have been shown to increase the risk of acquiring SARS-CoV-2 were explored in the questionnaire.[2,8,13,15,19] A prior SARS-CoV-2 diagnosis was self-reported by the participants and validated through the OHS personnel

database in each hospital. The questionnaire was completed by each participant, with assistance offered to those participants requiring it.

Data analysis

Data were exported from the REDCap® online database for analysis using the IBM SPSS version 25.0 software (IBM SPSS, Chicago, Illinois) after cross-checking for completeness and accuracy. The means ± standard deviations were estimated for continuous data and counts and proportions were estimated for categorical data for the sociodemographic characteristics of the participants. The proportion of HCWs with either a SARS-CoV-2 PCR diagnosis or positive IgG antibodies, or both, were reckoned as cumulative incidence in the study. The cumulative incidence was disaggregated by sociodemographic and clinical factors.

The associations between the cumulative incidence and risk factors (sociodemographic and clinical) were explored using the Pearson $\chi 2$ test. We fitted both unadjusted and adjusted multivariate logistic regression models to examine the independent risk factors for cumulative infection with SARS-CoV-2 among the HCWs in the study. Variable selection in the model analysis was guided by known risk factors reported previously in other studies.[8,13,15] A p-value less than 0.05 was considered statistically significant.

Ethical Considerations

The Walter Sisulu University Ethics Committee granted approval for the implementation of the study (Reference: 087/2020), as well as the Eastern Cape Provincial Department of Health and local hospitals ethics committee. Each participant provided written informed consent for the study. Participants' rights to privacy and the confidentiality of clinical data were respected during and after the study. The research process followed the Helsinki Declaration and local institutional policy. All hard copies of materials used in the study were locked securely and soft copies were password-protected in the computer in the research office.

Patient and public involvement

There was no public or patient involvement in the design, conduct or reporting of this research, as patients were not included. The healthcare worker participants were given their individual SARS-CoV-2 IgG results via cellular messaging. The main findings of the study will be shared with the respective hospital management teams.

Results

A total of 1,309 HCWs participated in the study from both hospitals, 656 from Frere Hospital and 653 from Cecilia Makiwane Hospital. Eleven blood samples for SARS-CoV-2 IgG serology were missing or rejected by the laboratory and were excluded from the final analysis. Data for another three participants were excluded due to missing data on the main outcome measures. Data for 1,295 HCWs were included in the final analysis.

Baseline characteristics of the participants (n = 1,295)

The participants were predominantly women (81.5%), black (78.7%), had undergone tertiary education (71.5%), and most had never smoked (91.0%). In terms of professional category, nurses predominated (44.8%), followed by support staff (28.8%) and medical doctors (13.6%). Most (77.1%) participants reported direct contact with patients with COVID-19 and had attended training on PPE use (79.4%) (Table 1).

SARS-CoV-2 cumulative incidence

SARS-CoV-2 infection was confirmed (PCR positive) in 390 participants (30.1%). Three hundred and forty-two (87.7%) of these reported at least 1 COVID-19 symptom at the time of testing, 38 (9.7%) were asymptomatic, and 10 (2.6%) had incomplete data. A positive SARS-CoV-2 IgG result occurred in 488 (37.7%) participants, giving a cumulative SARS-CoV-2 incidence of 47.2% (611 HCWs). Of the 390 PCR positive cases, 123 (31.5%) were SARS-CoV-2 IgG negative at the time of study, representing decay of IgG levels to below the testing threshold. This rate of humoral decay over time for this cohort was used to extrapolate the estimated true IgG positivity from the recorded 488 IgG positive, calculated at 712.8 (55,0%) estimated SARS-CoV-2 IgG positive at any time point. One hundred and forty-six of 640 (22.8%) PCR negative cases were IgG positive indicating potentially false negative PCR tests or being tested at the incorrect time. The SARS-CoV-2 IgG picked up an additional 17.1% (n = 221) missed infections in this cohort (146 HCWs with negative PCR results and 75 who never tested) (Table 2).

Risk factors for SARS-CoV-2 infection among the HCWs

When examining sociodemographic and exposure risk factors for infection (Table 3), age, race, level of educational, smoking status, professional category, and work area were all significantly associated with SARS-CoV-2 infection ($p < 0.05$). Among the co-morbid conditions (Table 4), only Body Mass Index (BMI) was significantly associated with SARS-CoV-2 infection.

In an unadjusted logistic regression analysis (Table 5), female sex, coloured ethnicity, a primary education, active smokers, medical doctors and allied staff, use of public transport, and being overweight and obese were significantly associated with SARS-CoV-2 infection. However, in the adjusted logistic regression (Table 5), comorbidity with HIV, and being overweight and obesity were independently associated with SARS-CoV-2 infection. Individuals who were living with HIV were almost twice as likely to be infected with SARS-CoV-2 (Adjusted Odd Ratio [AOR] = 1.78; 95% Confidence Interval [CI]: 1.38-2.08). Individuals who were overweight were twice as likely to be infected with SARS-CoV-2 (AOR = 2.15; 95% CI 1.44-3.20). Similarly, those who were obese were slightly more likely to be infected with SARS-CoV-2 (AOR = 1.37; 95% CI 1.02-1.85).

Discussion

This cross-sectional survey of 1 295 HCWs from two large referral hospitals in the Eastern Cape Province combined two diagnostic modalities (SARS-CoV-2 PCR and SARS-CoV-2 IgG antibodies) to estimate the cumulative incidence of SARS-CoV-2 infection. The study showed a high rate of SARS-CoV-2 infection (47.2%) after the first wave of COVID-19 among the HCWs in the region. The estimated true SARS-CoV-2 IgG seroprevalence, using the calculated IgG degradation rate, was even higher at 55.0%. These rates are more than double the official figures reported for doctors and nurses subsequent to the second wave in the Eastern Cape province (18.2-22.3% PCR positive).[7] The 30.1% SARS-CoV-2 PCR positivity is significantly higher than the pooled prevalence of 11% (95% CI; 7-15%) from a systematic review of 46 studies among HCWs worldwide.[20] Similarly the 37.7% SARS-CoV-2 IgG seropositivity is higher than the pooled prevalence of 7% (95% CI; 4-11%) of 27,445 HCWs in the same review.[20]

In order to obtain reliable epidemiologic data on the infection rate with SARS-CoV-2 for strategic planning, a minimum of two or more data sources should be combined. Findings from this study demonstrate the importance of combining PCR results with antibody testing within a population to assess more accurately the cumulative incidence of SARS-CoV-2 infection. Neither of the modalities alone was accurate in estimating the infection rate in the study as

reflected by the 31.5% of IgG negative results in HCWs who had been documented as SARS-CoV-2 PCR positive. These likely represent cases of decay in the humoral immune response with IgG levels falling below the assay detection threshold over time. A study of the duration of SARS-CoV-2 IgG anti-nucleocapsid antibodies among 452 HCWs reported decline starting within 1 month after first positive PCR, with an estimated half-life of 85 days and 50% seronegative after 7 months.[21] On the other hand, SARS-CoV-2 IgG testing identified 17.1% of participants with infections that had been missed by PCR. Two thirds (146/221) of these missed infections reported negative PCR tests. These likely represent false negative PCR results; suboptimal sample collections, or swabs that were taken before or after the peak of viral shedding.[22–24] The other third (75/221) of the missed infections had never had a PCR test performed. These were likely asymptomatic infections or patients with mild symptoms that did not lead to PCR testing.

In terms of risk factors for SARS-CoV-2 infection among HCWs, the only significant risk factors in the adjusted multivariate logistic regression analysis were having an increased BMI (overweight or obese) and being HIV positive. While these factors have been reported as risks for infection among the general population in some reports[2,5,12,14,18], this is the first time they have been linked in a specifically HCW population. Stratifying areas of work into low, medium and high risk for SARS-CoV-2 exposure did not identify significant differences in infection risk, contrary to findings by Iversen et al.[8] There was also no difference in infection prevalence across different professions. These are important negative findings of this study, and contribute some insights into SARS-CoV-2 exposure and transmission in these hospital environments. Of interest for epidemiologic purposes are two pertinent questions. 'Why did doctors and nurses working in designated COVID-19 clinical areas not experience higher infection rates than non-clinical staff?' and 'Did improved use of PPE in these designated clinical areas effectively level this risk?'

Despite a large proportion (80%) of HCWs having been trained on the use of PPE, and they confirmed that PPEs were available for use, there was no correlation with SARS-CoV-2 infection in the cohort. A prospective study of SARS-CoV-2 infections among 10,034 UK HCWs, showed a lower risk of infection among ICU clinical staff, suggesting that training on PPE and strict adherence to infection control protocols protected staff in high risk areas.[9] While there were concerns about inadequate quantities and quality of PPE during the period prior to the study, there was never a total shortage of PPE for use in COVID-19 clinical areas in either

of the two facilities. Another plausible explanation for the results could be the strict adherence to symptom screening of all staff in the COVID-19 clinical areas throughout the period. Prompt diagnosis and isolation of infected individuals will prevent further spread among HCWs in the same work areas[2,3]. Furthermore, it was not infrequent for COVID-19 cases to be diagnosed in the non-COVID-19 clinical areas, which could account for similarly high proportions of staff infection in low, medium and high-risk clinical areas. Certain support staff categories were classified as 'low risk' but may have had transient exposure to COVID-19 patients, wards or potentially contaminated linen etc. e.g. porters, laundry and kitchen staff.

Transmission of SARS-CoV-2 between HCWs in the common areas during tea and lunch breaks, when staff interact socially with or without masks was not measured in the study, but is quite probable to have occurred to some degree. Almost 10% of the PCR positive staff were asymptomatic at the time of testing, and may have been responsible for some onward transmission of infection to colleagues. It was hypothesised that taking shared or public transport to work would increase the risk of infection compared to solo vehicle transport, but this was not found to be significant. At the time of this study, there were no community seroprevalence data with which to compare our findings. During the second epidemiologic wave, Sykes et al. reported a seropositivity rate of 63% among blood donors from the Eastern Cape, the highest among four provinces sampled in the country in January 2021.[25] This study only sampled 1,457 donors, a select group of healthy volunteers from four provinces. It is therefore difficult to estimate the community prevalence at the time of our study. Notwithstanding, there is a strong possibility of a high- exposure environment outside of the hospitals in the region. A previous UK study found that having a household COVID-19 contact was the strongest risk factor for HCW infection [AOR 4.82; 95% CI 3.45–6.72].[9]

Being overweight or obese has been linked to increased susceptibility to SARS-CoV-2 infection, as well as to disease severity and increased mortality. A meta-analysis of 20 studies assessing obesity and risk of SARS-CoV-2 infection found an odds ratio of 1.46 (95% CI 1.30-1.65).[26] Poorer outcomes for respiratory viruses in the obese had been described prior to SARS-CoV-2 with the H1N1 influenza pandemic.[27] The mechanisms for the increased vulnerability to SARS-CoV-2 among the overweight and obese are complex. Obesity is associated with a pro-inflammatory phenotype and systemic low-grade inflammation.[27] Obesity dampens and delays both the innate and the adaptive immune response to infection with reduced efficacy of B- and T- cell responses. Obesity is also associated with poorer response to vaccination, likely

through the same immune dampening effects.[27] This sample of HCWs revealed alarmingly high rates of being either overweight (22.7%) or obese (63.1%), which is a concern due to increased vulnerability to respiratory viral infections as well as the non-communicable disease risks linked such as type 2 diabetes mellitus, hypertension, cardiovascular diseases and certain cancers.[28]

There is epidemiological evidence for an increased susceptibility to SARS-CoV-2 with HIV infection. A systematic review and meta-analysis of almost 21 million people across multiple continents reported a risk ratio of 1.24 (95% CI 1.05-1.46) for SARS-CoV-2 infection among people living with HIV compared to those uninfected by HIV.[29] The HIV prevalence of 7.3% in this cohort may be an underestimate, given the self-reported nature of the data and some infected individuals may not have been diagnosed. The estimated adult HIV prevalence in the local district is 13.6%, as a comparison.[30] Data on CD4 cell counts and antiretroviral therapy use were not obtained in this study, but would have added more insight into the HIV-related risk. Like obesity, HIV is an important vulnerability to be managed among HCWs in relation to SARS-CoV-2 and other infections such as *Mycobacterium tuberculosis*.

Strengths and limitations

This is the first reported study to have combined two diagnostic modalities to estimate the cumulative incidence of SARS-CoV-2 infection among HCWs in South Africa. Findings will inform IPC policies in the region. However, this study does have some limitations. Due to the pragmatic nature of the local policy relating to PCR testing for SARS-CoV-2, testing was largely limited to symptomatic staff (87,7% of PCR positive staff were symptomatic), which would have missed some asymptomatic infections. HIV serology and CD4 counts were not tested, but relied on self-reporting of individual HIV status, which may likely underestimate the burden of HIV in the cohort.

Conclusion

We report a high SARS-CoV-2 cumulative incidence of 47.2% after the first epidemiologic wave among HCWs from two referral hospitals in the Eastern Cape, South Africa. This is one of the highest reported in the literature and more than double that of the official figures for HCWs in the region. Being overweight or obese were significant risks for infection, and over 85% of HCWs fell into these categories. HIV infection was also associated with increased

infection in the cohort. There were similar rates of infection across low, medium and high SARS-CoV-2 transmission risk areas, suggesting that significant transmission of infection occurred between colleagues or outside the workplace. Staff wellness programmes should address weight reduction and regular HIV testing and treatment, to mitigate vulnerabilities in this essential workforce.

Author contributorship

DS, VA, MS, JB, EJ, AP contributed to the conception and design of the study.
DS, VA, MS, JB, EJ, SA contributed to data collection. DS, VA, SA, AP contributed to data analysis. DS and VA drafted the article. DS, VA, MS, JB, EJ, AP, SA provided critical revision of the article and final approval for submission for publication.

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Data sharing

The study data isn't available in a repository, but sharing will be considered by request.

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Table 1: Baseline characteristics of the participants (n = 1,295)

Variable	Frequency	Percentage
Sex		
Males	240	18.5
Females	1055	81.5
Age (years)		
18-25	71	5.49
26-35	325	25.12
36-45	349	26.97
46-55	346	26.74
>55	203	15.69
***Race**		
Black	1019	78.7
White	114	8.8
Coloured	98	7.6
Others	53	4.1
Level of Education		
Tertiary	925	71.5
Secondary	357	27.6
Primary	12	0.9
Smoking Status		
Never smoked	1178	91.0
Active smoker	72	5.6
Former smoker	44	3.4
Profession		
Medical doctors	176	13.6
Pharmacy staff	61	4.7
Nurses	580	44.8
Allied staff	105	8.1
Support staff	372	28.8
Direct contact with a confirmed COVID-19 case		
Yes	998	77.1
No	296	22.9
Attended PPE training		
Yes	1027	79.4
No	267	20.6

***n = 10 participants did not indicate their race group**
PPE = Personal protective equipment

Table 2. Confirmation of SARS-CoV-2 infection among the participants

Variables	IgG Positive (n; %)	IgG Negative (n; %)	Total (n; %)
PCR Positive	267 (68.5)	123 (31.5)	390 (30.1)
PCR Negative	146 (22.8)	494 (77.2)	640 (49.5)
Never tested	75 (28.4)	189 (71.6)	264 (20.4)
Total	488 (37.7)	806 (62.3)	1294 (100)

IgG = Immunoglobulin G; PCR = Polymerase chain reaction; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2

Table 3. Relationship between socio-demographic characteristics and SARS-CoV-2 by Pearson χ2 test

Variable	SARS-CoV-2 by PCR and/or IgG		p-values
	Yes (%)	**No** (%)	
All	n = 611 (47.2)	n = 683 (52.8)	
Sex			**0.007**
Males	95 (39.6)	145 (60.4)	
Females	517 (49.0)	538 (51.0)	
Age			0.628
<45 years	347 (46.6)	397 (53.4)	
>45 years	346 (54.7)	286 (45.3)	
Race			**<0.001**
Black	524 (51.4)	495 (48.6)	
White	30 (26.3)	84 (73.7)	
Coloured	29 (29.6)	69 (70.4)	
Others	18 (34.0)	35 (66.0)	
Level of Education			**0.003**
Tertiary	418 (45.2)	507 (54.8)	
Secondary	191 (53.5)	166 (46.5)	
Primary	02 (16.7)	10 (83.3)	
Smoking Status			**<0.001**
Never smoked	580 (49.2)	598 (50.8)	
Active smoker	17 (23.6)	55 (76.4)	
Former smoker	14 (31.8)	30 (68.2)	
Covid-19 exposure by Ward			**0.008**
High risk	151 (51.2)	144 (48.8)	
Medium risk	265 (42.7)	355 (57.3)	
Low risk	195 (51.5)	184 (48.6)	
Profession			**<0.001**
Medical doctors	55 (31.2)	121 (68.8)	
Pharmacy staff	28 (45.9)	33 (54.1)	
Nurses	311 (53.6)	269 (46.4)	
Allied staff	25 (23.8)	80 (76.2)	
Support staff	192 (51.6)	180 (48.4)	
Direct contact with a confirmed COVID-19 case			0.337
Yes	464 (46.5)	534 (53.5)	
No	147 (49.7)	149 (50.3)	
Attended PPE training			0.498
Yes	480 (46.7)	547 (53.3)	
No	131 (49.1)	136 (50.9)	

IgG = Immunoglobulin G; PCR = Polymerase chain reaction; PPE = Personal protective equipment; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2.
Support staff = Administration/Management staff (51/98; 52.0%), General workers (31/61; 50.8%), Kitchen staff (23/33; 69.7%), Porters (06/15; 40.0%), Stores/Sales staff (0/5), Mortuary staff (4/5; 80.0%), Laundry staff (23/39; 59.0%). *117 of the support staff did not indicate their duties.
Allied Workers = Radiology staff (9/37; 24.3%), Social workers (1), Physiotherapists (1), Dieticians (1), *68 of allied workers did not indicate their duties.

Table 4: Relationship between co-morbidities and SARS-CoV-2 by Pearson χ2 test

Variables	Positive SARS-CoV-2 PCR and/ or IgG		p-values
	Yes (%)	**No** (%)	
All	n = 611 (47.2)	n = 683 (52.8)	
***BMI**			**<0.001**
Underweight	4 (57.1)	3 (42.9)	
Normal weight	47 (26.7)	129 (73.3)	
Overweight	121 (41.4)	171 (58.6)	
Obese	434 (53.5)	378 (46.6)	
Diabetes			0.076
Yes	56 (54.4)	47 (45.6)	
No	555 (46.6)	636 (53.4)	
Hypertension			0.246
Yes	119 (50.6)	116 (49.4)	
No	492 (46.5)	567 (53.5)	
HIV			0.300
Yes	40 (42.1)	55 (57.9)	
No	571 (47.6)	628 (52.4)	
TB			0.141
Yes	11 (34.4)	21 (65.6)	
No	600 (47.5)	662 (52.5)	
Chronic Kidney Disease			0.074
Yes	07 (29.2)	17 (70.8)	
No	604 (47.6)	666 (52.4)	
Heart Disease			0.496
Yes	15 (53.6)	13 (46.4)	
No	596 (47.1)	670 (52.9)	
Asthma/COPD			0.143
Yes	31 (39.2)	48 (60.8)	
No	580 (47.7)	635 (52.3)	
Liver Disease			0.169
Yes	06 (31.6)	13 (68.4)	
No	605 (47.5)	670 (52.6)	
Cancer			0.515
Yes	8 (40.0)	12 (60.0)	
No	603 (47.3)	671 (52.7)	

BMI = Body mass index; IgG = Immunoglobulin G; TB = Tuberculosis; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2; COPD = Chronic obstructive pulmonary disease.

Table 5. Adjusted and unadjusted logistic regression model showing risk factors for SARS-CoV-2 infection among HCWs

Variables	UOR (95%CI)	p-value	AOR (95%CI)	p-value
Sex				
Males	Ref		Ref	
Females	1.48 (1.11-1.79)	**0.007**	1.09 (0.78-1.51)	0.595
Race				
Others	Ref		Ref	
Coloured	0.48 (0.27-0.86)	**0.015**	1.06 (0.55-2.06)	0.848
White	1.44 (0.71-2.91)	0.311	1.46 (0.69-3.07)	0.313
Black	0.91 (0.91-1.81)	0.789	1.28 (0.61-2.71)	0.504
Level of Education				
Tertiary	Ref		Ref	
Secondary	4.12 (0.89-18.91)	0.068	3.05 (0.62-14.85)	0.166
Primary	0.71 (0.56-0.91)	**0.008**	0.90 (0.67-1.22)	0.509
Smoking Status				
Never smoked	Ref		Ref	
Active smoker	0.48 (0.25-0.91)	**0.026**	0.65 (0.32-1.29)	0.222
Former smoker	1.51 (0.65-3.48)	0.334	1.77 (0.73-4.25)	0.199
Profession				
Support staff	Ref		Ref	
Allied staff	2.34 (1.60-3.42)	**<0.001**	1.92 (0.83-4.43)	0.124
Nurses	1.25 (0.73-2.16)	0.409	0.84 (0.35-1.99)	0.693
Pharmacy staff	0.93 (0.71-1.19)	0.545	0.88 (0.42-1.84)	0.747
Medical doctors	3.41 (2.08-5.58)	**<0.001**	1.52 (0.67-3.45)	0.316
COVID-19 Exposure by Ward				
Low risk	Ref		Ref	
Medium risk	0.69 (0.53-0.90)	0.006	1.19 (0.59-2.41)	0.749
High risk	0.97 (0.71-1.32)	0.883	0.88 (0.42-1.86)	0.611
Direct contact with a confirmed COVID-19 case				
No	Ref		Ref	
Yes	0.88 (0.67-1.14)	0.338	1.01 (0.75-1.36)	0.928
Attended PPE training				
Yes	Ref		Ref	
No	1.09 (0.83-1.42)	0.498	0.99 (0.74-1.33)	0.996
Use of public transport				
No	Ref		Ref	
Yes	0.63 (0.51-0.79)	**<0.001**	0.94 (0.69-1.17)	0.444
BMI				
Underweight	-		-	
Normal	Ref		Ref	
Overweight	3.15 (2.19-4.53)	**<0.001**	2.15 (1.44-3.20)	**<0.001**
Obese	1.62 (1.23-2.12)	**<0.001**	1.37 (1.02-1.85)	**0.033**
Diabetes				
No	Ref		Ref	
Yes	0.73 (0.48-1.09)	0.131	0.85 (0.55-1.32)	0.480
Hypertension				
No	Ref		Ref	
Yes	0.84 (0.63-1.12)	0.246	1.08 (0.78-1.48)	0.628
HIV				
No	Ref		Ref	
Yes	1.25 (0.81-1.19)	0.301	1.78 (1.38-2.08)	**0.012**

BMI = Body mass index; HCWs = Healthcare workers; PPE = Personal protective equipment; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2; UOR = Unadjusted odds ratio; AOR = Adjusted odds ratio

ECHAS STUDY QUESTIONNAIRE – 2020v2.0

EASTERN CAPE HEALTHCARE WORKERS ACQUISITION OF SARS-COV-2

SECTION ONE – FOR ALL PARTICIPANTS (Mark chosen answers with a X, please answer truthfully)

1. Participant Identifier (PTID)						
2. Date of completion of questionnaire	d d	m m m	y y y y			
3. Consent has been read and understood	Yes	No				
4. Facility completed at	Frere	CMH				
5. Initials of field worker assisting form completion						
A. DEMOGRAPHIC INFORMATION						
1. Date of Birth	d d	m m m	y y y y			
2. Sex	Male	Female				
3. Ethnicity	Black	White	Coloured	Indian	Asian	Other
4. Suburb of primary residence						
5. Highest level of education	Primary	Secondary	Matric	Tertiary		
6. How many people including yourself live in your house/flat?						
B. RISK ASSESSMENT FOR SARS-COV-2						
7. Smoking status	Never smoked	Active smoker	Quit (>3 months)			
8. *If active smoker*: Average number of cigarettes per day						
9. *If active/former smoker*: Number of years smoking:	< 5	5-10	11-20	>20		
10. Diabetes	Yes	No				
11. Hypertension	Yes	No				
12. HIV	Yes	No	Prefer not to say			
13. On treatment for TB in 2020	Yes	No				
14. Previous TB treatment	Yes	No				
15. Chronic Kidney Disease	Yes	No				
16. Heart disease	Yes	No				
17. Chronic steroid use or any immunosuppressant drugs	Yes	No				
18. Asthma/COPD	Yes	No				
19. Liver disease	Yes	No				

ECHAS STUDY QUESTIONNAIRE – 2020v2.0

20. Cancer	Yes			No	
21. Currently pregnant?	Yes			No	
22. *If pregnant*, what is the gestational age (weeks):					
C. PERSONAL PROTECTIVE EQUIPMENT AT WORK (may be 'not applicable' [N/A] for non-clinical areas)					
23. Did you receive training in the correct use of PPE?	Yes	No	N/A		
24. Were FFP2/N95 masks available for you when needed?	Always	Most of the time	Some of the time	Never	N/A
25. Were surgical masks available for you when needed?	Always	Most of the time	Some of the time	Never	N/A
26. Were gloves available for you when needed?	Always	Most of the time	Some of the time	Never	N/A
27. Were protective gowns available for you when needed?	Always	Most of the time	Some of the time	Never	N/A
28. Was eye protection (goggles or face shield) available for you when needed?	Always	Most of the time	Some of the time	Never	N/A
29. Were you confident about your use of PPEs when dealing with patients with COVID-19?	Yes	No	Unsure	N/A	
D. COVID-19 VACCINE					
30. Do you believe that a vaccine is needed to end COVID-19 pandemic?	Yes			No	
31. Do you think every health worker should get COVID-19 vaccine when it becomes available?	Yes			No	
32. When COVID-19 vaccine becomes available; will you be willing to receive the vaccine?	Yes			No	
33. Do you think vaccines are generally safe?	Yes			No	
34. Have you ever refused vaccines in the past?	Yes			No	
35. Have you experienced adverse effects from vaccines before?	Yes			No	
E. EXPOSURE RISK ASSESSMENT					
36. Duty at work	Doctor	Nurse	Allied health	Management /admin	Porter
	Pharmacy	Kitchen	Radiology	Mortuary	Other: .....
37. <u>For doctors & nurses only</u>: where were you working during June to August?	Medical	Surgery	Casualty	ICU	O&G
	Paediatrics	Orthopaedics	Theatre	Other:	
38. Have you had direct contact with COVID-19 patients at work?	Yes			No	

ECHAS STUDY QUESTIONNAIRE – 2020v2.0

39. Have you had direct contact with COVID-19 cases outside of work?	Yes			No	
40. Do you take public transport to work?	Yes			No	
41. Have you ever had a SARS-CoV-2 swab PCR test(s) done?	Yes			No	
42. Have you ever had a **positive** SARS-CoV-2 PCR Result?	Yes			No	
43. Date of any **positive** SARS-CoV-2 PCR? (approximate if unsure of exact date)	d d		m m m		y y y y
44. Where was the test done?	NHLS	Pathcare	Ampath	Dischem	Other:
45. Were any of your household members diagnosed with COVID-19 around the same period as you?	Yes		No		Not applicable
46. *If yes to 45*, how many members tested positive?					
F. SYMPTOMS AT THE TIME OF TAKING THE SARS-CoV-2 SWAB (*Answer only if 'yes' selected in no.41)*					
47. Fever	Yes			No	
48. Cough	Yes			No	
49. Sore throat	Yes			No	
50. Shortness of breath	Yes			No	
51. Loss of smell	Yes			No	
52. Loss of taste	Yes			No	
53. Headache or body aches	Yes			No	
54. Diarrhoea and vomiting	Yes			No	
55. Fatigue/weakness/tiredness	Yes			No	
56. Red eyes (conjunctivitis)	Yes			No	
G. MANAGEMENT RECEIVED AFTER DIAGNOSIS OF COVID-19 (*Answer only if 'yes' selected in no.42)*					
57. Did you require hospitalization?	Yes			No	
58. Number of days hospitalised	<3	4-7	8-14	15-21	>21
59. Did you require Oxygen at any time?	Yes			No	
60. Were you admitted to ICU?	Yes			No	
61. Do you feel that you have fully recovered physically from COVID-19?	Yes			No	
62. How many 'sick days' have you taken due to COVID-19?	<7	7-14	15-21	22-28	>28

ECHAS STUDY QUESTIONNAIRE – 2020v2.0

H. PERSISTENCE OF COVID-19 SYMPTOMS (*Answer only if 'yes' selected in no.42)* (i.e. which, if any, of these symptoms are you still experiencing now?)		
63. Headaches	Yes	No
64. Weakness	Yes	No
65. Tiredness	Yes	No
66. Shortness of breath	Yes	No
67. Cough	Yes	No
68. Loss of taste/smell	Yes	No
69. Joint pain	Yes	No
70. Dizziness	Yes	No
71. Lack of appetite	Yes	No
72. Muscle pain (myalgia)	Yes	No
73. Chest pain	Yes	No
74. List other symptom(s)		
I. EMPLOYEE WELLNESS Are you currently experiencing any of the following?		
75. Anxiety about coming to work:	Yes	No
76. Low mood about coming to work:	Yes	No
77. Loss of interest in patient care:	Yes	No
78. Have you considered resigning/retiring from clinical work?	Yes	No
79. Do you need staff health referral?	Yes	No

SECTION 2: NURSE MEASUREMENTS & BLOOD SAMPLE FOR SARS-CoV-2 SEROLOGY (All participants)

80. Weight (Kg)		
81. Height (cm)		
82. Mid-upper arm circumference (cm)		
83. Bar Code (Specimen Identifier)		
84. Would you like to be notified of the blood results?	Yes	No

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	*6*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.