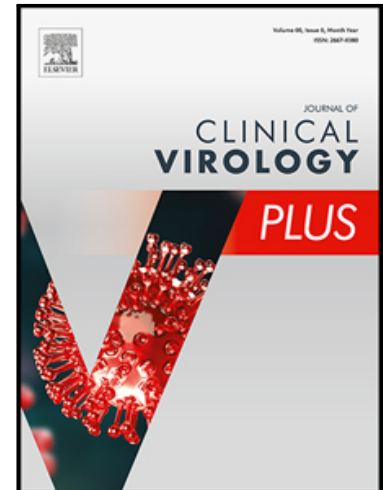


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Audit of vaccination status of health-care workers who tested positive for SARS-CoV-2.

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Summary

Multiple SARS-CoV-2 vaccinations have shown excellent efficacy during clinical trials. However, post vaccine surveillance is important to confirm 'real-world' findings of vaccine efficacy and safety. It is therefore imperative to identify individuals that become infected with SARS-CoV-2 post vaccination. We investigated the vaccination status of staff that had tested positive in a cohort of healthcare workers in one large tertiary hospital in the UK. At the time of the investigation, 8th December 2020 to 13th March 2021, 11,871 staff had been vaccinated and 225 staff tested positive for SARS-CoV-2. This period coincided with the second wave of SARS-CoV-2 infections in the UK which was driven by the Alpha variant. No healthcare workers who were double vaccinated had a positive PCR test for SARS-CoV-2 during this study period confirming vaccination with Pfizer BioNTec BNT162b2 gives excellent protection against infection of this variant.

Introduction

On the 8th December 2020 the world's first dose of COVID-19 vaccine, was given to a recipient outside of clinical trials. This dose of Pfizer BioNTec BNT162b2 was administered at University Hospital Coventry and Warwickshire NHS Trust (UHCW), a large tertiary hospital located in the West Midlands, England. Healthcare workers who receive their vaccine on the hospital site are only offered the Pfizer BioNTec BNT162b2. In rare circumstances where the Pfizer vaccination was contraindicated due to history of severe allergy, staff may have been vaccinated elsewhere with the AstraZeneca (ChAdOx1). At the time of this study these were the only two vaccines available in the

UK. Clinical trial data for the Pfizer vaccination recommended an interval of 21 days between first and second doses of vaccine and vaccine induced protection is considered to be achieved 14 days after the first vaccine dose. On the 30th December 2020 the Joint Committee on Vaccination and Immunisation (JCVI) decided to amend the vaccine schedule extent the interval between doses to 12 weeks, allowing more people to receive at least one dose of vaccine to maximise the short term impact at a time when cases of SARS-CoV-2 in the UK were high [1]. The subsequent speed at which the vaccination programme in the UK has been rolled has been phenomenal. As of May 2021 36,704,672 first doses and 20,287,403 second doses have been administered nationally [2]. Throughout the pandemic it has been clear that front-line healthcare workers are at high risk of acquiring SARS-CoV-2 infection and transmitting infection onto vulnerable groups of patients [3]. Due to this increased risk, healthcare workers were placed second on the JCVI prioritisation list [4]. Some healthcare workers who presented early for vaccine in the UK received 2 doses of BNT162b2 prior to the change in schedule. Post vaccine surveillance is important to confirm ‘real-world’ findings of vaccine efficacy and safety demonstrated within clinical trial settings, especially when the recommended regimen has been adapted. It is therefore imperative to identify individuals that become infected with SARS-CoV-2 post vaccination to better understand protection offered by vaccination and the signs and symptoms of disease in this cohort.

The SIREN study looked to understand impact of vaccination in healthcare workers in a group of staff who were undergoing regular asymptomatic screening for SARS-CoV-2 [5]. The roll-out of the vaccination programme requires further investigation as to the impact on the incidence of COVID-19 in healthcare workers to extend on the work that has been done by the SIREN study. Here we present the data from an audit of vaccination status of staff members at UHCW, who tested positive for SARS-CoV-2 by PCR between 8th December 2020 and 13th March 2021. This audit was carried out in the midst of the second wave in the UK which peaked in the last week of January 2021, the predominant variant in the UK at this time was Alpha (B.1.1.7).

Materials and Methods

UHCW is a tertiary university hospital of 1250 beds covering a wide range of specialities. There are approximately 13,000 staff who work across the organisation. Positive SARS-CoV-2 PCR test results from staff tested at UHCW were extracted from the laboratory information system covering the period of the 8th December 2020 to the 13th March 2021. Staff that had positive SARS-CoV-2 PCR results from a nasopharyngeal and throat swab were cross-referenced with vaccination data to identify which of those staff who had tested positive during this period had received at least one dose of vaccine.

Staff who tested positive >14 days after their first dose of vaccination were contacted to participate in a survey relating to their positive SARS-CoV-2 PCR result. The survey was conducted in April 2021 one month after the data collection period ended. Time from infection to answering the survey ranged from 1 -4 months, dependent on when they tested positive for SARS-CoV-2. The survey was delivered via telephone or email and captured information on job role, ethnicity, reason for seeking a SARS-CoV2 test, symptom timelines and any known contacts with a positive case of SARS-CoV-2.

Under the Governance Arrangements for Research Ethics Committees (GAfREC), studies where staff are being approached due to the nature of their role are exempt from requiring Research Ethics Committee (REC) approval. Therefore, local R&D approval was obtained via the COVID-19 Research Committee to carry out this project within UHCW NHS Trust.

Results and Discussion

Two hundred and twenty five staff that had tested positive for SARS-CoV-2 between the 8th December 2020 and 14th March 2021 were identified. Twelve staff were excluded due to inability to ascertain their vaccination status, reducing the cohort to 213 individuals (figure 1).

Of the 213 staff with a positive SARS-CoV-2 PCR test, 70 (33%) individuals had not received a single COVID-19 vaccination dose. Eighty four (39%) individuals had received a single dose of vaccine after their positive SARS-CoV-2 result. Therefore, no protection from vaccination would have been expected at the time they tested positive.

Fifty-nine staff (28%) had received their first dose of vaccine between 2 to 69 days before they tested positive for SARS-CoV-2. Of the 59 staff who received their vaccine prior to testing positive for SARS-CoV-2; Thirty three of these individuals tested positive for SARS-CoV-2 within 10 days of vaccination and were therefore most likely incubating the virus at the time of vaccination. Three staff tested positive at 10-14 days after vaccine administration so possibly incubating at the time of vaccination or shortly after having received the vaccine but would not have had sufficient time to mount a protective immune response.

Twenty three staff members were vaccinated >14 days before they tested positive for SARS-CoV-2 (range 15-69 days), and therefore failed to be protected from infection following a single vaccine dose (figure 1 and 2). All 23 health care workers had received Pfizer-BioNTech BNT162b2 vaccination. These 23 staff members were contacted and asked to partake in a survey regarding their infection. Seventeen responses were received (table I).

The majority of staff members were white British (76%). The most common reason for having a PCR test was due to ward outbreak surveillance screening (8) , followed by symptomatic screens (5), confirmation of positive asymptomatic lateral flow testing (3) and finally social contact with a positive case (1). The time from vaccination to become positive ranged from 15-69 days, with a median of 22.5 days. Three (17.6%) of the 17 staff members surveyed stated that they were asymptomatic at the time of testing and did not go onto develop any symptoms attributable to SARS-CoV 2 at all after their positive SARS-CoV-2 test. The remaining 14 staff members either had symptoms at the time of the testing, or developed symptoms in the 3 days after their test. None of these staff required medical intervention or hospitalisation. Ten staff members stated that they thought the transmission had occurred due to positive patient contact. Five staff members had contact with a positive household case. Two staff members had no known contact with individuals known to be infected with SARS-CoV-2. Surveys were conducted at the end of the study period, and therefore depending upon when the infection took place, there may be an element of recall bias when gathering information from study participants.

Cycle threshold (CT) values in SARS-CoV-2 infected individuals can range from low to high and is dependent on multiple factors; including the time the swab was taken in relation to the infectious period and the swabbing technique. It can be used as a crude indication of the amount of virus present in the oro/nasopharynx at the time of swabbing with a low CT value indicating a high level of viral RNA. CT values were reviewed from all positive SARS-CoV-2 PCR tests in this cohort and ranged from 16-35. Two individuals had swabs with CT values of <20 and could be considered to have a relatively high amount of viral RNA. Fifteen individuals had swabs with CT values ranging from 20-35 and could be considered to have a relatively low amount of viral RNA. Inferring a viral burden from CT values must be done with caution as a standard curve was not used. However, the fact that the majority of these staff members had swabs with relatively low amounts of viral RNA is an observation that requires further investigation to ascertain whether this is a vaccine affect or not.

This observation has been noted in other studies whereby vaccinated individuals have a reduction in the amount of virus detected by PCR [6].

It is of note that there was a significant number of staff (70; 32.9%) who had not at the time of the audit received a single dose of vaccine, when it had been available to them for approximately 3 months. While it is recommended to wait a minimum of 4 weeks after a positive test before receiving the COVID-19 vaccine [7], these staff tested positive >4 weeks before their vaccination status was ascertained. Interestingly the SIREN study also noted that vaccine coverage was significantly reduced in HCW's who had had prior infection with SARS-CoV-2 [5]. It would be interesting to explore the reasoning of HCW's reluctance to present for vaccination post-infection. Perhaps this is because of a fear of side effects; It has been observed that people who are vaccinated after natural infection have more severe but still self-limiting flu-like symptoms post vaccination compared to SARS-CoV-2 naive counterparts [8]. It may also be that staff who have been infected with SARS-CoV-2 are not presenting for vaccination due to altruistic reasons; they have antibodies to SAR-CoV-2 and are therefore choosing to delay their vaccination so someone else can go first. Data from SIREN interim analysis suggests that immunity from natural infection lasts at least 7 months in HCW's [9], therefore these individuals not being vaccinated at this stage of the pandemic is unlikely to have an impact on the national goal of reaching a level of population immunity that will reduce the number of hospitalisations associated with COVID-19. It must be noted that this is a cohort who are <65 years of age and whether this duration of protection can be extrapolated to those >65 or to those with underlying health conditions is unclear. This hesitancy in health care workers who have had a previous infection with SARS-CoV-2 to present for vaccination may need to be considered when designing communication strategies around vaccination and vaccine hesitancy in healthcare settings.

161 As of the 13th March 2021, 11,871 staff at UHCW had been vaccinated. Of those, 9488 had only one
162 dose and 2383 staff had received both doses. Four hundred and fifty six staff received their first
163 dose between the 28th February and the 13th March and would not have been considered protected
164 during this audit period. Therefore this gives us an infection rate of 0.2% in our vaccinated cohort
165 (23/11,415), and all staff that became infected had only received one dose of vaccine (Pfizer BioNTec
166 BNT162b2). It should be noted we may be slightly under reporting the number of the infections in
167 our staff cohort as some people may have chosen to be tested at an alternative testing centre which
168 would be outside of the scope of this audit. The infection rate observed in our cohort of staff is
169 comparable to the findings of Keehner *et al.* who found an infection rate of 0.4% from 14 days after
170 the first dose of vaccine [10]. None of the staff members who completed the survey at UHCW had
171 severe infection requiring hospital treatment. This is reassuring and confirms data from studies that
172 while not completely protective against infection, there is significant protection from hospitalisation
173 and death [11]. Reassuringly, none of the staff who tested positive during the study period had two
174 doses of vaccine.

175 This is an evaluation looking at the vaccination status of our staff that tested positive for SARS-CoV-2
176 in the period from the 8th December 2020 to the 13th March 2021. This study showed that a low
177 number of these infections (23 individuals) were from staff members who had been vaccinated in a
178 time frame that would have been considered protective. This gives confidence that the vaccination
179 programme is a success. However, we cannot comment on the longevity of protection offered from
180 vaccination and the coverage that will be offered against new variants that arise. Reassuringly, the
181 staff members in this audit were vaccinated while there were still very high rates of transmission
182 occurring in the community, and we were in the midst of a second wave with Alpha (B.1.1.7) being
183 the predominant strain. This wave peaked in the last week of January 2021. So while this data
184 offers real-world evidence that the vaccine is effective in preventing infections in health care
185 workers, there is clearly need for further research into the impact of vaccination on the amount of

virus present in the oro/nasopharynx and its role in transmission and whether this changes between different SARS-CoV-2 Variants.

Declaration of interests

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

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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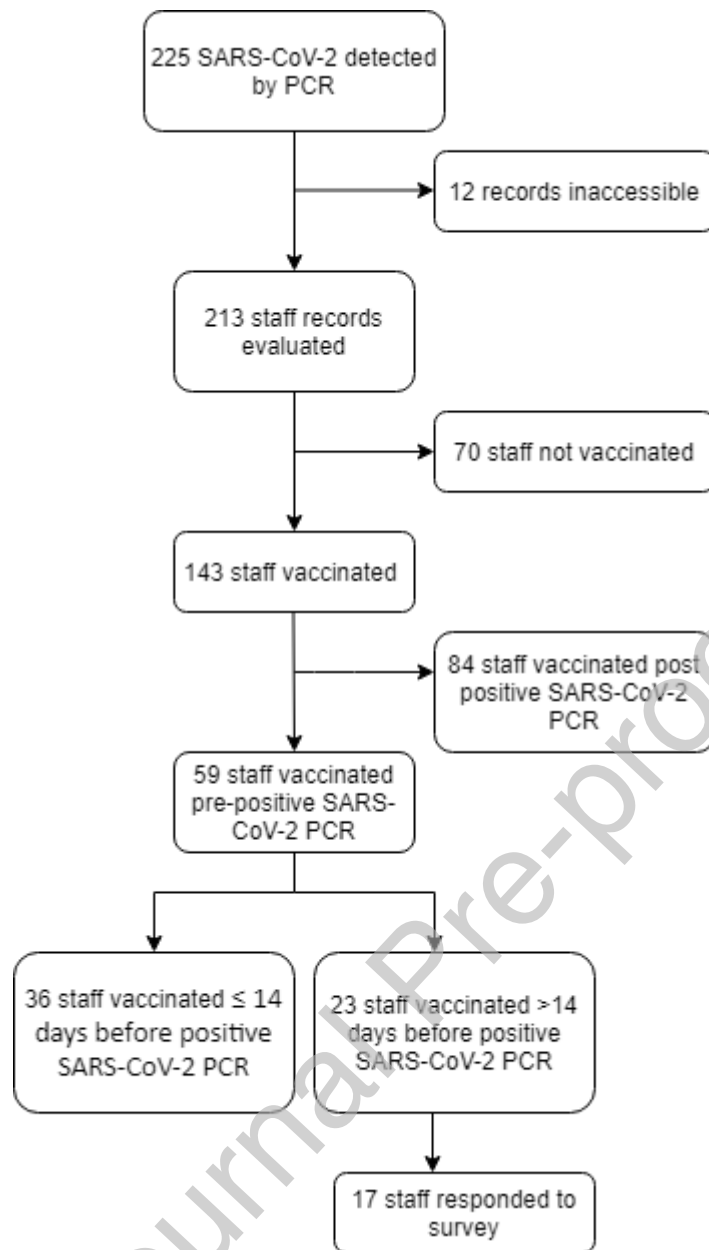


Figure 1: Breakdown of dataset

Table 1: Survey responses from staff members who tested positive for SARS-CoV-2 >14 days after vaccination.

Job role	Age (yrs)	Positive patient contact?	Ethnicity	Reason for SARS-CoV-2 testing	Number of days post vaccination until positive SARS-CoV-2 PCR	PCR CT value	PCR platform used	Symptoms present on day of test	New or additional symptoms within 3 days following the test	Any known SARS-CoV-2/ COVID contacts
Medical	31	Yes	White British	Positive lateral flow	30	21	Siemens kPCR	Coryza	Migraine Anosmia	Positive household contact
Nursing	57	Yes	White British	COVID outbreak: surveillance screen	20	20	Siemens kPCR	Fatigue	None	Confirmed case on ward.
Physiotherapist	27	Yes	White British	COVID outbreak: surveillance screen	16	32	Siemens kPCR	None	None	Confirmed case on ward.
Portering	50	No	White Irish	Symptomatic	15	33*	Abbott M2000	Cough Pyrexia	None	Positive household contact.
Administration	19	No	White British	In contact with a person who was feeling unwell.	17	17*	Abbott M2000	None	SOB Anosmia Ageusia	Positive household and social contact
Nursing	53	No	White British	Positive lateral flow	23	21	STARlet Seegene	Fatigue SOB Headache Sweating	None	None
Nursing	45	Yes	White British	Positive lateral flow	20	26	SRATlet Seegene	Coryza Flu-like illness Myalgia	SOB Anosmia Ageusia	None
Phlebotomist and health care assistant	40	Yes	Black African	Symptomatic	24	33	STARlet Seegene	'Itchy throat'	None	Positive household contact.
Mental health nursing	21	Yes	White British	COVID outbreak: surveillance	22	34	Siemens kPCR	None	Chest pain SOB	Confirmed case on ward.

				screen						
Specialist occupational therapist	26	Yes	White British	COVID outbreak: surveillance screen	18	34	Siemens kPCR	None	None	Confirmed case on ward.
Ward manager	33	Yes	White British	Symptomatic	53	30	STARlet Seegene	Cough Fatigue 'Severe' headache	None	Confirmed case on ward.
Health Care Assistant	57	Yes	White British	COVID outbreak: surveillance screen	27	35	Siemens kPCR	None	Severe leg pains	Confirmed case on ward.
Physiotherapist	32	Yes	White British	COVID outbreak: surveillance screen	31	24	STARlet Seegene	Sore throat	Cough Coryza Headache	Confirmed case on ward.
Trainee Advanced Nurse Practitioner	37	Yes	White British	COVID outbreak: surveillance screen	39	30	STARlet Seegene	Coryza Headache	Cough	Confirmed case on ward.
Health Care Assistant	49	Yes	British Indian	Symptomatic	64	28	Siemens kPCR	Coryza Fever Cough Myalgia	None	Positive household contact.
Nursing	52	Yes	Indian	Symptomatic	21	16	Siemens kPCR	Fever Shivering Headache Productive cough	None	Confirmed case on ward.
Activities Co-Ordinator	40	Yes	White British	COVID outbreak: surveillance screen	69	29	STARlet Seegene	None	None	Confirmed case on ward.

SOB: shortness of breath

*Cycle threshold (CT) values do not register the first 10 rounds of amplification. Results obtained from the Abbott M2000 have been adjusted to reflect this (10 CT's added). Standard curves were not used to generate CT values.

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