Single-dose BNT162b2 vaccine protects against asymptomatic SARS-CoV-2 infection

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Abstract

The BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) is being utilised internationally for mass COVID-19 vaccination. Evidence of single-dose protection against symptomatic disease has encouraged some countries to opt for delayed booster doses of BNT162b2, but the effect of this strategy on rates of asymptomatic SARS-CoV-2 infection remains unknown. We previously demonstrated frequent pauci- and asymptomatic SARS-CoV-2 infection amongst healthcare workers (HCWs) during the UK's first wave of the COVID-19 pandemic, using a comprehensive PCR-based HCW screening programme (Rivett et al., 2020; Jones et al., 2020). Here, we evaluate the effect of first-dose BNT162b2 vaccination on test positivity rates, and find a four-fold reduction in asymptomatic infection amongst HCWs ≥12 days post-vaccination. These data provide real-world evidence of short-term protection against asymptomatic SARS-CoV-2 infection following a single dose of BNT162b2 vaccine, suggesting that mass first-dose vaccination will reduce SARS-CoV-2 *transmission*, as well as the burden of COVID-19 *disease*.

Introduction

The UK has initiated mass COVID-19 immunisation, with healthcare workers (HCWs) given early priority because of the potential for workplace exposure and risk of onward transmission to patients. The UK's Joint Committee on Vaccination and Immunisation has recommended maximising the number of people vaccinated with first doses at the expense of early booster vaccinations, based on single-dose efficacy against symptomatic COVID-19 disease.[1-3]

At the time of writing, three COVID-19 vaccines have been granted emergency use authorisation in the UK, including the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech). A vital outstanding question is whether this vaccine prevents asymptomatic as well as symptomatic SARS-CoV-2 infection, or merely converts infections from symptomatic to asymptomatic. Sub-clinical infection following vaccination could continue to drive transmission. This is especially important because many UK HCWs have received this vaccine, and nosocomial COVID-19 infection has been a persistent problem.

Through the implementation of a 24 h-turnaround PCR-based comprehensive HCW screening programme at Cambridge University Hospitals NHS Foundation Trust (CUHNFT), we previously demonstrated the frequent presence of pauci- and asymptomatic infection amongst HCWs during the UK's first wave of the COVID-19 pandemic.[4] Here, we evaluate the effect of first-dose BNT162b2 vaccination on test positivity rates and cycle threshold (Ct) values in the asymptomatic arm of our programme, which now offers weekly screening to all staff.

Main text

Vaccination of HCWs at CUHNFT began on 8th December 2020, with mass vaccination from 8th January 2021. Here, we analyse data from two weeks spanning 18th to 31st January 2021, during which: (a) the prevalence of COVID-19 amongst HCWs remained approximately constant; and (b) we screened comparable numbers of vaccinated and unvaccinated HCWs. During this period, 4,408 (week 1) and 4,411 (week 2) PCR tests were performed on individuals reporting well to work, from a weekly on-site HCW population of ~9,000. We stratified HCWs <12 days or ≥12 days post-vaccination because this was the point at which protection against symptomatic infection began to appear in the phase III clinical trial.[2] In the post-vaccination groups, the median number of days between vaccination and testing were 7 (IQR 4-9; <12 day group) and 16 (14-18; ≥12 day group).

26/3,252 (0.8%, Wilson's interval 0.6-1.2%) tests from unvaccinated HCWs were positive (Ct<36), compared to 13/3,535 (0.4%, Wilson's interval 0.2-0.6%) from HCWs <12 days post-vaccination and 4/1,989 (0.2%, Wilson's interval 0.1-0.5%) tests from HCWs ≥12 days post-vaccination (p=0.023 and p=0.004, respectively; Fisher's exact test, Figure 1 and Table 1). This suggests a four-fold decrease in the risk of asymptomatic SARS-CoV-2 infection amongst HCWs ≥12 days post-vaccination, compared to unvaccinated HCWs, with an intermediate effect amongst HCWs <12 days post-vaccination.

A marked reduction in infections was also seen when analyses were repeated with: (a) inclusion of HCWs testing positive through both the symptomatic and asymptomatic arms of the programme (56/3,370 (1.7%, Wilson's interval 1.3-2.2%) unvaccinated vs 8/2,018 (0.4%, Wilson's interval 0.2-0.8%) ≥12 days post-vaccination, 4.2-fold reduction, p<0.0001); (b) inclusion of PCR tests which were positive at the limit of detection (Ct>36, 42/3,268 (1.3%, Wilson's interval 1.0-1.7%) vs 15/2,000 (0.7%, Wilson's interval 0.5-1.2%), 1.7-fold

reduction, p=0.07). In addition, the median Ct value of positive tests showed a non-significant trend towards increase between unvaccinated HCWs and HCWs ≥12 days post-vaccination (23.3 (IQR 13.5-33.0) to 30.3 (IQR 25.5-35.1), Figure), raising the possibility that vaccinated individuals who do go on to develop infection may have *lower* viral loads.

HCWs working in COVID-19 clinical areas were prioritised for vaccination, and a small number of clinically vulnerable HCWs were also given priority. Otherwise, vaccine allocation was arbitrary. Since asymptomatic infection was examined, the date of infection could have been earlier than the test date. These factors would all tend to lead to an underestimate of the vaccine's effect (bias towards the null). Because of the rapid decline in incidence of SARS-CoV-2 infection in the Cambridge community, this study could only examine the short-term impact of single-dose BNT162b2 vaccination. The frequency of prior SARS-CoV-2 infection[5] was similar in all groups (seroprevalence 7.1%, unvaccinated; 5.6%, <12 days post-vaccination; 5.7%, ≥12 days post-vaccination), suggesting that this did not confound our observations.

Taken together, our findings provide real-world evidence of short-term protection against asymptomatic SARS-CoV-2 infection after a single dose of BNT162b2 vaccine, at a time when the UK COVID-19 variant of concern 202012/01 (lineage B.1.1.7) accounted for the great majority of infections (24/29 sequenced isolates from asymptomatic HCWs). A four-fold reduction from 0.8% to 0.2% in asymptomatic infection is likely to be crucial in controlling nosocomial SARS-CoV-2 transmission. Nonetheless, protection is incomplete, suggesting that continuing asymptomatic HCW screening, social distancing, mask-wearing and strict hand hygiene remain vital.

Methods

HCW screening programme

We previously described protocols for staff screening, sample collection, and results reporting in detail.[4,6] In general, these methods remained unchanged throughout this study period. Two parallel streams of entry into the testing programme included (i) *HCW symptomatic*, and *HCW symptomatic household contact* screening arms and (ii) an *HCW asymptomatic* screening arm. Since our prior description of the screening programme, weekly asymptomatic testing is now offered to all CUHNFT staff. Testing was performed (i) at temporary on-site 'Pods'; and (ii) via self-swabbing kits collected by HCWs. Individuals

performed a self-swab of the oropharynx and anterior nasal cavity. Samples were subjected to RNA extraction and amplification using real-time RT-PCR, with all sample processing and analysis undertaken at the Cambridge COVID-19 Testing Centre (Lighthouse laboratory).

Vaccination

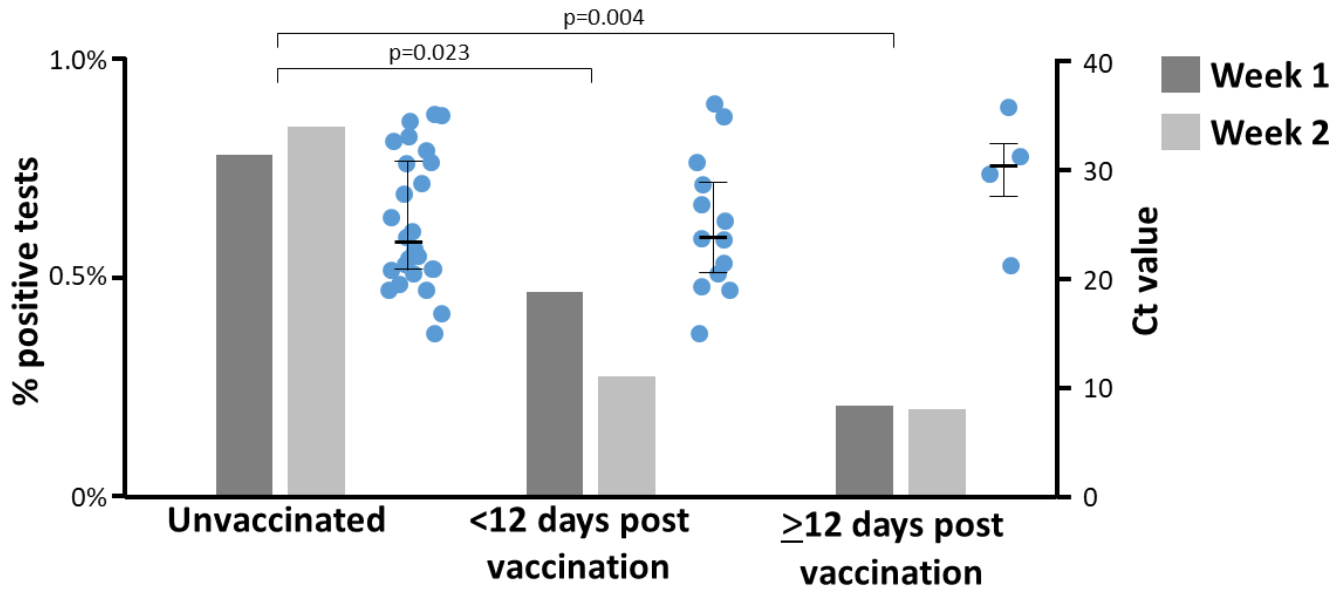
HCW vaccination began at CUHNFT on 8th December 2020, with appointments made by invitation only for all high risk HCWs working on-site. This was followed by self-booked appointments for HCWs working in designated COVID-19 clinical areas, from 8th January 2021 onwards. From 18th January 2021, vaccination was offered to all HCWs, with appointments made using the hospital's electronic patient record system 'MyChart'. All vials of Pfizer-BioNTech COVID-19 Vaccine (BNT162b2) were stored at -74˚C, before being transferred to storage at 2-8˚C. From the moment the vials were removed from the freezer they were given a 120 hour expiration date, of which 3 hours were dedicated to thawing the vaccines. All vaccine doses were administered intramuscularly by trained vaccinators, in accordance with the manufacturer's instructions. Vaccination was undertaken exclusively at an on-site vaccination centre, with mandatory mask-wearing and social distancing in place. HCWs remained at the on-site vaccination centre for a minimum observation period of 15 minutes after vaccination.

Data extraction and analysis

Swab result, vaccination details and serology data for HCWs were extracted directly from the hospital-laboratory interface software, Epic (Verona, Wisconsin, USA). Data were collated using Microsoft Excel, and the figure produced with GraphPad Prism (GraphPad Software, La Jolla, California, USA). Fisher's exact test was used for comparison of positive rates between groups, defined in the main text. Additionally, 95% confidence intervals were calculated using Wilson's method.

Ethics

This study was conducted as a service evaluation of the CUHNFT staff testing and vaccination services (CUHNFT clinical project ID ID3682). As a study of healthcare-associated infections, this investigation is exempt from requiring ethical approval under Section 251 of the NHS Act 2006 (see also the NHS Health Research Authority algorithm, available at http://www.hra-decisiontools.org.uk/research/, which concludes that no formal ethical approval is required).



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148 **Figure 1**: Proportion of positive screening tests for SARS-CoV-2 amongst HCWs from the
149 CUHNHFT asymptomatic screening programme (grey bars; week 1, 18/01/2021-24/01/2021;
150 week 2, 25/01/2021-31/01/2021) and Ct values of positive tests (CT<36; blue dots; both
151 weeks). RT-PCR targeting the SARS-CoV-2 ORF1ab genes was conducted at the Cambridge
152 COVID-19 Testing Centre (part of the UK Lighthouse Labs Network). For proportions of
153 positive screening tests, p values for pair-wise comparisons of unvaccinated HCWs with
154 HCWs <12 days or ≥12 days post-vaccination are shown (Fisher's exact test; both weeks).
155 For Ct values, medians ± interquartile ranges are shown.

	Unvaccinated			**<12 days since vaccination**			**≥12 days since vaccination**		
Week start	Total tests	Positive tests	%	Total tests	Positive tests	%	Total tests	Positive tests	%
28/12/2020	2097	16	0.8%	8	0	0.0%	6	0	0.0%
04/01/2021	4762	43	0.9%	93	0	0.0%	22	0	0.0%
11/01/2021	3273	27	0.8%	978	6	0.6%	30	0	0.0%
18/01/2021	2183	17	0.8%	1716	8	0.5%	483	1	0.2%
25/01/2021	1069	9	0.8%	1819	5	0.3%	1506	3	0.2%
01/02/2021	699	1	0.1%	758	1	0.1%	2825	1	0.0%

156 **Table 1:** Weekly numbers and proportions of positive SARS-CoV-2 test results spanning six
157 weeks around the main study period (indicated in grey).

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