

1 **Effectiveness of BNT162b2 mRNA vaccine against infection and COVID-19 vaccine**
2 **coverage in healthcare workers in England, multicentre prospective cohort study (the**
3 **SIREN study)**

4
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27

28 **ABSTRACT**

29 **Background**

30 BNT162b2 mRNA and ChAdOx1 nCoV-19 adenoviral vector vaccines have been rapidly
31 rolled out in the UK. We determined the factors associated with vaccine coverage for both
32 vaccines and documented the vaccine effectiveness of the BNT162b2 mRNA vaccine in our
33 healthcare worker (HCW) cohort study of staff undergoing regular asymptomatic testing.

34 **Methods**

35 The SIREN study is a prospective cohort study among staff working in publicly funded
36 hospitals. Baseline risk factors, vaccination status (from 8/12/2020-5/2/2021), and symptoms
37 are recorded at 2 weekly intervals and all SARS-CoV-2 polymerase chain reaction (PCR)
38 and antibody test results documented. A mixed effect proportional hazards frailty model
39 using a Poisson distribution was used to calculate hazard ratios to compare time to infection
40 in unvaccinated and vaccinated participants to estimate the impact of the BNT162b2 vaccine
41 on all (asymptomatic and symptomatic) infection.

42 **Findings**

43 Vaccine coverage was 89% on 5/2/2021. Significantly lower coverage was associated with
44 prior infection (aOR 0.59 95% confidence interval [CI] 0.54-0.64), female (aOR 0.72, 95% CI
45 0.63-0.82), aged under 35 years, being from minority ethnic groups (especially Black, aOR
46 0.26, 95% CI 0.21-0.32), porters/security guards (aOR 0.61, 95% CI 0.42-0.90), or midwife
47 (aOR 0.74, 95% CI 0.57-0.97), and living in more deprived neighbourhoods (IMD 1 (most) vs.
48 5 (least) (aOR 0.75, 95% CI 0.65-0.87). A single dose of BNT162b2 vaccine demonstrated
49 vaccine effectiveness of 72% (95% CI 58-86) 21 days after first dose and 86% (95% CI 76-
50 97) seven days after two doses in the antibody negative cohort.

51 **Conclusion**

52 Our study demonstrates that the BNT162b2 vaccine effectively prevents both symptomatic
53 and asymptomatic infection in working age adults; this cohort was vaccinated when the

54 dominant variant in circulation was B1.1.7 and demonstrates effectiveness against this
55 variant.

56 **Funding:** Public Health England and the Department of Health and Social Care; NIHR

57

58

60 **RESEARCH IN CONTEXT**

61 **Evidence before this study**

62 We searched PubMed and medRxiv for studies including “asymptomatic” and “symptomatic”
63 SARS-CoV-2 results after vaccination. Only a single paper existed for ChAdOx1 which
64 stated that it reduced all (symptomatic or asymptomatic) infection by 51.9% (95% CI 42.0-
65 60.1%). Three studies from Israel demonstrated that those who attended symptomatic
66 testing had reduced infections two weeks post vaccination; a single healthcare worker
67 cohort study in Israel, demonstrated vaccine effectiveness of 75% (95% CI 72 – 84%) from
68 15 to 28 days following the first dose of the BNT162b2 vaccine to reduce symptomatic
69 infection. No data on asymptomatic infection through routinely collected swabs
70 asymptomatic testing was available for the BNT162b2 vaccine.

71 **Added value of this study**

72 This is a large established cohort study in HCWs that enables accurate measurement of
73 asymptomatic and symptomatic infection rates in the vaccinated and unvaccinated
74 population.

75 It measures the impact of a single dose of vaccine over the first 8-week period. We have
76 estimated the vaccine effectiveness against all (symptomatic and asymptomatic) infection for
77 the BNT162b2 vaccine to be at least 70% 21 days after the first dose, which increased to at
78 least 85% seven days after the second dose.

79 It also highlights the vaccine coverage and uptake among hospital staff. Further
80 engagement is required in groups that have not yet accepted the vaccine offer.

81 **Implications of all the available evidence**

82 We provide strong evidence that vaccinating working age adults will substantially reduce
83 asymptomatic and symptomatic SARS-CoV-2 infection and therefore reduce transmission of
84 infection in the population. However, it does not eliminate infection risk completely and

85 therefore personal protective equipment, non-pharmaceutical interventions and regular
86 asymptomatic testing will need to be continued until prevalence of SARS-CoV-2 is extremely
87 low to reduce the risk of transmission in healthcare settings.

88 **INTRODUCTION**

89 Since the World Health Organization (WHO) declared the emergence of Coronavirus Disease
90 2019 (COVID-19) a pandemic on 11 March 2020, over 2.4 million people have died around
91 the world ¹, including over 120,000 people in the United Kingdom (UK) ². There has been an
92 unprecedented international effort by private and public institutions to develop a vaccine
93 against its causative agent, the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-
94 CoV-2).³ In less than a year, three COVID-19 vaccine candidates have been granted
95 Emergency Use Authorization by the UK Medicines and Healthcare products Regulatory
96 Agency (MHRA),⁴ with several more in the development pipeline. The BNT162b2 mRNA
97 (Pfizer-BioNTech) and ChAdOx1 nCoV-19 adenoviral (Oxford AstraZeneca COVID-19)
98 vaccines, were approved on 2 December and 30 December 2020 respectively, based on
99 interim analyses from phase 3 Randomized Controlled Trials (RCT)[6, 7],^{5,6} and were deployed
100 for use within seven days of authorisation.

101
102 Following advice from the Joint Committee on Vaccination and Immunisation (JCVI), the UK
103 Government selected a vaccination strategy with the aim of rapidly reducing hospitalisations,
104 severe outcomes and preventable deaths from COVID-19.⁷ The initial phase targeted
105 individuals at high-risk of severe COVID-19, such as care home residents and their carers,
106 people aged 80 years and over, and frontline HCWs, recognising this group's particular high
107 exposure and potential role in transmission. On 30 December, the JCVI published their
108 recommendation to delay the 2nd dose of the deployed coronavirus vaccines by up to 12 weeks
109 with the aim of optimising the public health impact of the vaccination campaign in the
110 population by doubling the number of people who would receive the first dose.⁸ By 19
111 February 2021, the UK had vaccinated more than 17.2 million people (25% of the population).⁹
112 However, population-level vaccine effectiveness studies are needed to assess the impact of
113 coronavirus vaccination in the real world and inform developments of the public health policy.

114

115 The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) Study is a large, multi-centre
116 prospective cohort study of HCWs and support staff in publicly funded (National Health Service
117 (NHS) hospitals in the United Kingdom.¹⁰ SIREN initially investigated the effect of prior
118 infection on protection against re-infection and was amended to investigate COVID-19 vaccine
119 effectiveness in January 2021.

120

121 In this study, we aimed to describe the factors associated with both BNT162b2 and ChAdOx1
122 nCoV-19 vaccine coverage and early vaccine effectiveness of BNT162b2 vaccine against all
123 (asymptomatic and symptomatic) infection in this large-scale cohort of HCWs in England.

124

125 **METHODS**

126 **Study design and setting**

127 The SIREN study is a prospective cohort study among staff working in the publicly funded
128 hospitals (NHS) across the UK. The SIREN protocol is described elsewhere.¹¹

129

130 **Participants**

131 HCWs, support staff and administrative staff working at hospital sites participating in SIREN,
132 who could provide informed consent and anticipated remaining engaged in follow-up for 12
133 months were eligible to join SIREN. Participants were excluded from this analysis if they
134 enrolled after 7 December 2020, had no PCR tests after 7 December 2020, or had insufficient
135 PCR and antibody data to complete cohort assignment.

136

137 **Variables**

138 The primary outcome variable for the vaccine coverage analysis was the binary 'ever
139 vaccinated' variable. Participants were categorised as 'ever vaccinated' if they had at least
140 one vaccine dose recorded from 8 December 2020 to 5 February 2021 from at least one of
141 the two vaccination data sources available. Data on vaccination date, manufacturer and batch

142 number was available for each dose. Second doses were excluded if they preceded the first
143 dose and marked as 'short interval' if they were less than 19 days after the first dose.

144

145 The primary outcome variable for the vaccine effectiveness analysis was a PCR confirmed
146 SARS-CoV-2 infection. This was defined as a new PCR positive result during follow-up for
147 the negative cohort and a reinfection during the follow-up in the positive cohort, irrespective of
148 symptom status.¹⁰ Participants were assigned into either the positive cohort (antibody positive
149 or history of infection (prior antibody or PCR positive)) or the negative cohort (antibody
150 negative with no prior positive test) at the beginning of the follow up period (7 December 2020).

151

152 **Data sources and measurement**

153 Vaccination data was obtained directly from participants completing the enrolment and follow-
154 up questionnaires and from linkage on personal identifiable information (NHS number,
155 surname, date of birth and postcode) to the National Immunisation Management System
156 (NIMS), the registry of COVID-19 vaccination in England.

157

158 SIREN participants undergo fortnightly asymptomatic PCR testing (anterior nasal swabs or
159 combined nose and oropharyngeal swabs) and monthly antibody testing at their site of
160 enrolment. In addition, hospitals introduced twice weekly asymptomatic testing using a lateral
161 flow device (LFD), Innova SARS-CoV-2 Antigen Rapid Qualitative Test (Innova), to all frontline
162 HCWs for twice weekly asymptomatic testing in November 2020. All positive LFD tests were
163 confirmed by PCR. Participants consent for the release of all SARS-CoV-2 PCR and antibody
164 test results before or after enrolment to the study team through the Public Health England
165 (PHE) national laboratory testing surveillance system. The SIREN SQL database runs
166 automated data linkage with the laboratory surveillance system daily to extract new positive
167 and negative test results.

168

169 Participants are requested to complete online questionnaires at enrolment and fortnightly
170 intervals, capturing data on demographics, symptoms, testing and exposures (household,
171 community and occupational). Index of Multiple Deprivation a measure of neighbourhood
172 relative deprivation, calculated by the Office of National Statistics, was obtained through
173 linkage on participant postcode.

174

175 Data was extracted from all sources on 08 February 2021.

176

177 **Bias reduction**

178 Data were collected on potential confounders, including site and participant demographics to
179 enable adjusted analysis. Analysis was restricted to one manufacturer only, where sufficient
180 follow-up time had accrued; data was truncated on participants with an unreliable date of
181 second dose (<19 days). Sample date of a PCR positive result was used as the event date
182 which may have introduced some misclassification of vaccination status relative to infection
183 or onset in the period shortly after vaccination and informed our decision to calculate
184 cumulative vaccine effectiveness after suitable intervals (21 days post first dose and 7 days
185 post second dose), in order to focus on infections acquired since vaccination after a sufficient
186 interval for biological protection.

187

188 **Study size**

189 Prior to vaccine introduction calculations of the precision of effectiveness estimates were
190 performed on an estimated cohort size of 40,000, 65% seronegative at baseline, coverage
191 averaging at 75% in the follow-up period, and incidence in the follow-up period ranging from
192 0.5% to 5%. Precision estimates around effectiveness of 60% and 90% gave 95% confidence
193 intervals ranging from the widest for a VE of 60% (95%CI: 39-74) to the narrowest for a VE of
194 90% (95%CI: 88-92).

195

196 **Person time at risk**

197 Follow-up time for all participants started on 7 December 2020, the day before vaccine roll-
198 out began, with all participants contributing at least one day of follow-up unvaccinated.
199 Participants moved from unvaccinated to vaccinated within their assigned cohort on the date
200 of the first vaccination dose. Participants contributed person-time to follow-up until either an
201 event of interest (i.e. a new PCR positive in the negative cohort or a reinfection in the positive
202 cohort); the date of the suspect second dose for those with an unreliable date of second dose;
203 the date of their first dose for those vaccinated with the ChAdOx1 vaccine; or the censored
204 date. We defined the end of follow-up in those who were not positive cases as the date of a
205 negative test or 05 February 2021 if the test was after this date, in order to avoid immortal time
206 bias. As symptomatic testing was done at any time of symptoms the most recent days could
207 be biased towards symptomatic testing, therefore, the end of follow-up was defined at a date
208 two days prior to the last date samples were available.

209

210 **Statistical methods**

211 Investigation of factors associated with vaccination was conducted using mixed effect
212 multivariable logistic regression model (with hospital site as a random effect) to investigate
213 confounding between demographic and occupational risk factors on the outcome variable
214 'ever vaccinated'. A backwards stepwise approach was used, removing variables from the
215 model sequentially with those with the least effect at univariable analysis removed first, and
216 goodness of fit was tested (likelihood ratio tests) after each change. Only the variables which
217 demonstrated strong evidence of association on vaccine coverage were retained in the final
218 model.

219

220 A mixed effect proportional hazards frailty model using a Poisson distribution was used to
221 calculate Hazard Ratios to compare time to infection in unvaccinated and vaccinated
222 participants to estimate the impact of the BNT162b2 vaccine on infection (including
223 asymptomatic and symptomatic as the primary outcome). As the main covariate of interest
224 (vaccination) changes as time elapses and the effect of vaccine changes over follow-up time,

225 we grouped time to infection into 12 vaccine intervals to analyse the short-term dynamics of
226 post vaccination protection in detail. The models were fitted by Poisson regression with a log
227 link, using COVID-19 infection as response, log of exposure times as an offset and dummies
228 for the time intervals as explanatory variables to allow for different piecewise constant
229 hazards.¹² The model fitting approach also provided estimates of the baseline hazard rates.
230 The hospital site was added into models as a random effect to account for the extra variation
231 and associated correlation that was not explained by risk/covariates variables. The frailty
232 model was also extended by including individual within the site as an addition random effect.
233 The results (not reported here) did not support heterogeneity among individuals after
234 controlling for site effect and therefore our final model does not include individual. The fixed
235 covariates included in the model were age, ethnicity, comorbidities, region, job role, frequency
236 of COVID-19 patient contact, patient-facing role, workplace setting. Hazard ratios from 21 days
237 after first dose and seven days after second dose were calculated using a weighted average
238 method, the point at which an immunological response to the vaccine dose should have been
239 provoked. Vaccine effectiveness was calculated as $1 - \text{adjusted Hazard Ratio (vaccinated}$
240 $\text{versus unvaccinated)}$.

241

242 Three models were run on different cohorts within the study population. The main model
243 included the full study population and adjusted for cohort assignment. Models were then run
244 on the two cohorts separately, to provide estimates of vaccine effectiveness in the susceptible
245 population (negative cohort) and the positive cohort with natural immunity following prior
246 SARS-CoV-2 infection.

247

248 **Ethics**

249 The study was approved by the Berkshire Research Ethics Committee, Health Research
250 Authority (IRAS ID 284460, REC reference 20/SC/0230) on 22 May 2020; the vaccine
251 amendment was approved on 12/1/2021. The study is registered with ISRCTN (Trial ID:
252 ISRCTN11041050).

253 **Reporting**

254 The study follows the Strengthening the Reporting of Observational studies in Epidemiology
255 (STROBE) guidelines and the checklists are included in the Supplementary Appendix.¹³

256

257 **RESULTS**

258 **Characteristics of participants included in the analysis**

259 By 7 December 2020, 29,378 participants were enrolled and maintained in SIREN for the
260 England cohort; 23,324 met the inclusion criteria and were included in this analysis from 104
261 hospitals¹. At the start date of follow-up (7 December 2020), 8,203 (35%) participants were
262 assigned to the positive cohort (antibody positive or had a previous antibody or PCR positive
263 test) and 15,121 (65%) were assigned to the negative cohort.

264

265 Most participants were female (84%; 19,692), of white ethnicity (89%; 20,424), in a patient-
266 facing role (86%; 20,054) and in a clinical discipline (66%; 15,502). A quarter (26%; n=5,874)
267 of participants had a reported medical condition; with asthma (n=2,893), obesity (n=1,988)
268 and diabetes (n=677) the most frequent.

269

270 The total follow-up time in this analysis was two calendar months and 1,106,905 participant
271 person-days, 710,587 person-days unvaccinated and 396,318 person-days vaccinated.
272 Participants were followed-up for a maximum of 59 days post first dose (median 21,
273 interquartile range: 13-31) and 39 days post second dose (median 23, interquartile range: 17-
274 28). Total person-days of follow-up in the negative cohort was 711,135 and 395,770 in the
275 positive cohort.

276

¹ Whilst recruitment of participants from Scotland and Northern Ireland began before 31/12/2020 their testing and vaccination data was not available for linkage by the study team at the time of this analysis, and therefore they were excluded. Recruitment of Welsh participants began in 2021.

277 **Vaccine coverage with the SIREN cohort up to 5 February 2021**

278 At least one dose of vaccine was administered to 20,641 (89%) participants by 5 February
279 2021; 94% (19,384) received the BNT162b2 vaccine and 6% (1,252) received the ChAdOx1
280 vaccine. Roll-out of the first dose of vaccine in this cohort peaked on 12 January 2021 (Figure
281 1). Two doses of vaccine were administered to a minority of participants (n=1,607, 8%) by 5
282 February 2021; 99.9% (n=1,605) received the BNT162b2 vaccine and 0.1% (n=2) received
283 the ChAdOx1 vaccine. The median length of time between first dose and second dose was
284 23 days; IQR: 21-26 days; range 19-28.

285

286 **Demographic, household and occupational factors associated with being vaccinated**

287 A description of the demographic, household and occupational factors associated with being
288 vaccinated, including the proportions vaccinated and odds ratios are presented in table 1. In
289 multivariable analysis, after controlling for all other risk factors and given site, having a prior
290 infection, gender, age, ethnicity, IMD score and staff group remained significantly associated
291 with vaccine coverage. Participants were less likely to have been vaccinated if they had a
292 prior infection (aOR 0.59, 95% CI 0.54-0.64), were female (aOR 0.72, 95% CI 0.63-0.82), were
293 aged under 35 (aOR 0.78, 95% CI 0.64-0.96), were from Black, Asian or minority ethnic
294 groups, especially if they were Black (aOR 0.26, 95% CI 0.21-0.32), lived in areas of higher
295 deprivation (IMD 1 (most) vs. 5 (least) aOR 0.75, 95% CI 0.65-0.87) or worked as a
296 porter/security/estates (aOR 0.61, 95% CI 0.42-0.90) or midwife (aOR 0.74, 95% CI 0.57-
297 0.97).

298

299 **Vaccine effectiveness against infection**

300 There were 977 new infections during 710,587 person days of follow-up in the unvaccinated
301 group, an incidence density of 14 infections per 10,000 person days of follow-up (table 2). In
302 the vaccinated group, 21 days after the first dose, there were 71 new infections (incidence
303 density 8 per 10,000 person-days of follow-up) and nine new infections seven days after the
304 second dose (incidence density of 4 per 10,000 person days of follow-up).

305

306 Classic COVID-19 symptoms (fever, cough, change/loss of taste or smell) were reported by
307 620 (63%) cases in the unvaccinated group 14-days before or after their positive test date;
308 139 (14%) had other symptoms²; 51 (5%) were asymptomatic; and 167 (17%) did not complete
309 the symptom status questionnaire within 2 weeks of their PCR test date. In comparison, of
310 the infections 21 days after first dose and seven days after second dose in the vaccinated
311 group, 32 (40%) had classic COVID-19 symptoms, 13 (16%) had other symptoms, 10 (13%)
312 were asymptomatic and 25 (31%) did not complete the symptom status questionnaire for the
313 time period.

314

315 After controlling for the other risk factors, cohort and at a given site, vaccine effectiveness
316 against infection 21 days after the first dose of BNT162b2 vaccine in the overall study
317 population was 70% (95% CI 53-87%) and increased to 85% (95% 74-96%) seven days
318 after the second dose (table 2). Protection was higher when the negative cohort was
319 modelled separately, and after adjustment for the other risk factors and at a given site;
320 vaccine effectiveness was 72% (95% CI 58-86%) 21 days after first dose and 86% (95% 76-
321 97%) 7 days after the second dose. There was insufficient information to separately
322 model the positive cohort at this analysis timepoint. The overall model showed that the
323 positive cohort already had 90% protection (95% CI 88-92%) compared to the negative
324 cohort following their natural infection (supplementary material).

325

326 Figures 2a and 2b show the trends in vaccine effectiveness measured over short post-
327 vaccination intervals in the full cohort and negative cohort; this demonstrated a reduced risk
328 of infection in vaccinated individuals immediately (0-3 days) following the first dose; there

² Participants were recorded as having 'other symptoms' if they reported ANY of the following symptoms: shortness of breath, sore throat, runny nose, headache, muscle aches, extreme fatigue, diarrhoea, nausea or vomiting or small itchy red patches on fingers or toes, on the follow-up questionnaire with a symptom onset date within 14-days before or after the PCR positive sample date.

329 was no significant effect between days 4-9, with a significant protection from infection
330 increasing from day 10 onwards, and plateauing after 21 days. Following the second dose
331 a similar pattern is observed. The hazard ratios, adjusted and unadjusted for each time
332 period post vaccination in the full cohort and the negative cohort are provided in Appendix A
333 Tables 3a & 3b.

334

335 **DISCUSSION**

336 Our follow-up of this large cohort of over 23,000 HCWs, whose prior SARS-CoV-2 infection
337 history is known for two months after vaccine roll-out provides unique real-world data on the
338 short-term vaccine effectiveness of the BNT162b2 vaccine against both symptomatic and
339 asymptomatic infection. The regular PCR-testing of participants, regardless of symptom
340 status, allowed for the detection of asymptomatic infection, an important proxy for reduction in
341 transmission. Two months after roll-out commenced, 89% of our cohort had received at least
342 one dose of COVID-19 vaccine; 8% had received two doses. We detected modest variability
343 in coverage, with lower coverage observed in participants with prior infection, from Black,
344 Asian and minority ethnic backgrounds, and living in areas of higher deprivation. We
345 estimated the vaccine effectiveness against infection for the BNT162b2 vaccine to be at least
346 70% 21 days after the first dose, increasing to at least 85% 7 days after the second dose in
347 our study population. This demonstrates that the BNT162b2 is effective against the B.1.1.7
348 variant given its predominance throughout the study period.¹⁴

349

350 The high vaccine coverage in SIREN may not be generalisable to UK HCWs or the general
351 population, as those who have self-selected to participate in a research study may not be
352 representative of UK HCWs or the population more generally.

353

354 With fewer of the cohort vaccinated with the ChAdOx1 vaccine, and the later roll-out resulting
355 in less follow-up time accrued, we are currently unable to investigate the effectiveness of the
356 ChAdOx1 vaccine within this study.

357

358 The analysis is based on PCR positivity, which may miss infections depending on the timing
359 of the infection relative to PCR testing or PCR sensitivity, which if differential by vaccination
360 status may lead to overestimation of the vaccine effect against all infections. However, given
361 our cohort, irrespective of vaccine status, attended fortnightly asymptomatic PCR testing
362 within SIREN, and additionally many also underwent twice weekly LFD testing with PCR
363 confirmation, we believe most infections during this period will have been detected. The cohort
364 will also have regular serological testing and the effect of seroconversion to both the S assay
365 (for vaccine) and N assay (for infection) will be estimated in the future.

366

367 Given the high vaccine coverage and small proportion of participants remaining unvaccinated,
368 the characteristics and exposures of this group may become sufficiently different from the
369 vaccinated cohort to undermine the validity of future analyses. However, given the short
370 follow-up period for this analysis, with all participants contributing follow-up time to the
371 unvaccinated group, we do not consider this would have introduced significant bias at this
372 stage.

373

374 Speculation of high levels of HCW vaccine hesitancy are not supported in our cohort study,
375 with almost 90% receiving at least one dose of vaccination within two months of roll-out.¹⁵
376 High and rapid vaccine HCW coverage was also reported in two single-centre cohort studies
377 in Israel, reporting 79% and 90% coverage six weeks after roll-out.^{16,17} Slightly lower uptake
378 of 65% was reported in a single UK trust which also reported similar disparities in vaccination
379 coverage by ethnicity.¹⁸ Our findings also indicated that age, gender and occupation were
380 associated with coverage, confirming a systematic review of 11 studies including 9,000
381 participants, on the intention of healthcare workers HCW to accept the COVID-19 vaccine,
382 which concluded that older age, male gender and being a doctor were factors associated with
383 increased willingness to get vaccinated.¹⁵ Conversely, the authors also found that people with
384 prior SARS-CoV-2 infection or co-morbidities expressed more willingness to take the vaccine,

385 not seen in our data. We also observed a significant trend of lower COVID-19 vaccination
386 coverage in those living in more deprived areas, corresponding to a population study of 23.4
387 million patients in the UK.¹⁹

388

389 Our analysis identified a reduced risk of infection in vaccinated individuals immediately (0-3
390 days) following the first dose, which cannot be plausibly explained by the immune response
391 to the vaccine; this is likely a deferral effect bias where those that are symptomatic, currently
392 PCR positive or have been recently exposed to a COVID-19 case may defer their
393 vaccination and be under-represented in accordance with national guidance.²⁰

394

395 We found a vaccine effectiveness, at a given site, of at least 70% overall (72% in the negative
396 cohort) against both asymptomatic and symptomatic infection, from 21 days post-first dose of
397 the BNT162b2 vaccine. This is comparable to a single-centre Israeli HCW cohort study
398 vaccine effectiveness of 75% (95% CI 72 – 84), 15-28 days following first dose of BNT162b2
399 vaccine ¹⁶. However, this study had no routine laboratory surveillance to pick up asymptomatic
400 cases and only detected cases if symptomatic, whereas SIREN had regular asymptomatic
401 testing; in addition, their adjustment for other potential risk factors was more limited.

402

403 Another population-level study in Israel reported a 51% reduction in PCR-confirmed SARS-
404 CoV-2 infections 13-24 days after individuals received the first dose of BNT162b2 vaccine,
405 compared to historical controls' 1-12 days ²¹. This mirrors the 52.4% (95% CI: 29.5 - 68.4)
406 vaccine efficacy estimated by Pfizer-BioNTech researchers, between the first and second
407 dose.⁶ Whilst follow up periods differed, the RCT included true controls and the Israeli study
408 included PCR-positivity regardless of symptom status compared to symptomatic confirmed
409 cases in the phase III BNT162b2 RCT. A preprint from researchers re-analysing the data from
410 the Israeli study using daily incidence of infection, calculated a vaccine effectiveness of 91%
411 at day 21 post-vaccination.²² This estimate is closer to the 92.6% vaccine efficacy 14–21 days

412 after the first dose, calculated by researchers using data submitted by the manufacturers to
413 the Food and Drug Administration from vaccine trials.²³

414

415 The differences in the vaccine effectiveness estimates may be due to the differences in
416 study design and populations included. Nonetheless, BNT162b2 is making a substantial
417 impact in reducing SARS-CoV-2 infection rates in vaccinated populations. A study with a
418 comparable methodology to SIREN, focussing on “Covid-19 Vaccine Effectiveness in
419 Healthcare Personnel in Clalit Health Services in Israel”, is currently underway
420 [ClinicalTrials.gov number NCT04709003], but results are awaited. A notable difference is
421 that people in Israel that have recovered from SARS-CoV-2 infection are not eligible for
422 vaccination at present;²⁴ therefore, their population studies do not include the seropositive
423 people that would be present in a general population. Weekly swabbing of a sub-set of
424 asymptomatic and symptomatic participants was carried out in the Oxford-AstraZeneca RCT
425 and investigators reported reduced viral load and PCR positivity in the COVID-19 vaccinated
426 participants; a signal that transmission may be reduced by their vaccine.²⁵ This is the first
427 study that describes the reduction in all cases of infection with BNT162b2.

428

429 Most data on vaccinated UK individuals are from people aged >75years old, where vaccine
430 effectiveness may be lower due to immunosenescence.²⁷ The SIREN cohort is taken from
431 working age people, making the conclusions more relevant for the overall adult population.
432 However, the healthy worker effect bias may underestimate the disease impact compared to
433 the general population.²⁸

434

435 Further work on this cohort is underway including measuring the impact of vaccination on
436 symptoms, serological responses, potential hospitalisations, and development of post-acute-
437 COVID. We will attempt to sequence infections occurring at least 21 days post vaccination to
438 determine proportion of novel variants.

439

440 This study clearly demonstrates that the vaccine does not prevent all cases of infection and
441 therefore HCWs will need to continue to wear personal protective equipment while caring for
442 all patients, observe physical distancing and other non-pharmaceutical measures in and
443 outside work and continue to perform regular asymptomatic testing (especially as typical
444 symptoms were reduced post vaccination) until COVID prevalence is considerably lower.

445

446 **Funding**

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461 **Trial Registration**

462 IRAS ID 284460, REC reference 20/SC/0230 Berkshire Research Ethics Committee, Health
463 Research Authority and Health and Care Research Wales approval granted 22 May 2020.

464 Trial registered with ISRCTN, Trial ID: ISRCTN11041050.

465 <https://www.isrctn.com/ISRCTN11041050>

466

467 **Author Contributions**

468 SH conceived this study, commented on the draft protocol, supervised the study, drafted and
469 edited the final manuscript. JLB, NA and VH wrote the first draft of the protocol and analysis
470 plan for the vaccine effectiveness sub-study. SF and VH cleaned and analysed data. VH and
471 BO performed the literature search and drafted the manuscript. AS performed the statistical
472 modelling of VE supervised by NA and AC. All authors contributed to the study design. All
473 authors contributed to drafting the protocol and revised the manuscript for important
474 intellectual content. All authors gave final approval of the version to be published.

475 **Conflict of interest statement**

476 The Immunisation and Countermeasures Division has provided vaccine manufacturers
477 (including Pfizer) with post-marketing surveillance reports on pneumococcal and
478 meningococcal infection which the companies are required to submit to the UK Licensing
479 authority in compliance with their Risk Management Strategy. A cost recovery charge is
480 made for these reports.

481 **Data sharing statement**

482 The metadata will be available through the HDR-UK Co-Connect platform and available for
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493 **References**

- 494 1. World Health Organization. WHO Coronavirus Diseases (COVID-19) Dashboard
495 2021. <https://covid19.who.int/> (accessed 16 February 2021).
- 496 2. Office for National Statistics. Coronavirus (COVID-19) latest insights. 2021.
497 <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19/latestinsights#deaths> (accessed 14 February 2021).
- 498 3. Sharma O, Sultan AA, Ding H, Trigg CR. A Review of the Progress and Challenges
499 of Developing a Vaccine for COVID-19. *Front Immunol* 2020; **11**: 585354-.
- 500 4. Medicines and Healthcare Regulatory Authority. MHRA guidance on coronavirus
501 (COVID-19). 2021. [https://www.gov.uk/government/collections/mhra-guidance-on-](https://www.gov.uk/government/collections/mhra-guidance-on-coronavirus-covid-19)
502 [coronavirus-covid-19](https://www.gov.uk/government/collections/mhra-guidance-on-coronavirus-covid-19) (accessed 14 February 2021).
- 503 5. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1
504 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised
505 controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021; **397**(10269): 99-111.
- 506 6. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA
507 Covid-19 Vaccine. *N Engl J Med* 2020; **383**(27): 2603-15.
- 508 7. Department of Health and Social Care. UK COVID-19 vaccine uptake plan. 2021.
509 [https://www.gov.uk/government/publications/covid-19-vaccination-uptake-plan/uk-covid-19-](https://www.gov.uk/government/publications/covid-19-vaccination-uptake-plan/uk-covid-19-vaccine-uptake-plan)
510 [vaccine-uptake-plan](https://www.gov.uk/government/publications/covid-19-vaccination-uptake-plan/uk-covid-19-vaccine-uptake-plan) (accessed 15 February 2021).
- 511 8. Department of Health and Social Care. Optimising the COVID-19 vaccination
512 programme for maximum short-term impact. 2021.
513 [https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-](https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-term-impact)
514 [statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-term-impact](https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-term-impact)
515 (accessed 14 February 2021).
- 516 9. Our World in Data. Coronavirus (COVID-19) Vaccinations. 2021.
517 <https://ourworldindata.org/covid-vaccinations> (accessed 18 February 2021).
- 518 10. Hall V, Foulkes S, Charlett A, et al. Do antibody positive healthcare workers have
519 lower SARS-CoV-2 infection rates than antibody negative healthcare workers? Large multi-
520

- 521 centre prospective cohort study (the SIREN study), England: June to November 2020.
522 *medRxiv* 2021: 2021.01.13.21249642.
- 523 11. Wallace S, Hall V, Charlett A, et al. SIREN protocol: Impact of detectable anti-SARS-
524 CoV-2 on the subsequent incidence of COVID-19 in 100,000 healthcare workers: do
525 antibody positive healthcare workers have less reinfection than antibody negative healthcare
526 workers? *medRxiv* 2020: 2020.12.15.20247981.
- 527 12. Holford TR. The Analysis of Rates and of Survivorship Using Log-Linear Models.
528 *Biometrics* 1980; **36**(2): 299-305.
- 529 13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The
530 Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement:
531 guidelines for reporting observational studies. *Lancet* 2007; **370**(9596): 1453-7.
- 532 14. Public Health England. Investigation of SARS-CoV-2 variants of concern in England.
533 Technical briefing 6. In: Care DoHaS, editor. 6 ed; 2021.
- 534 15. Galanis PA, Vraka I, Fragkou D, Bilali A, Kaitelidou D. Intention of health care
535 workers to accept COVID-19 vaccination and related factors: a systematic review and meta-
536 analysis. *medRxiv* 2020: 2020.12.08.20246041.
- 537 16. Amit S, Regev-Yochay G, Afek A, Kreiss Y, Leshem E. Early rate reductions of
538 SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients. *The Lancet*.
- 539 17. Abu Jabal K, Ben-Amram H, Beiruti K, et al. Impact of age, ethnicity, sex and prior
540 infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-
541 19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January
542 2021. *Eurosurveillance* 2021; **26**(6): 2100096.
- 543 18. Martin CA, Marshall C, Patel P, et al. Association of demographic and occupational
544 factors with SARS-CoV-2 vaccine uptake in a multi-ethnic UK healthcare workforce: a rapid
545 real-world analysis. *medRxiv* 2021: 2021.02.11.21251548.
- 546 19. MacKenna B, Curtis HJ, Morton CE, et al. Trends, regional variation, and clinical
547 characteristics of COVID-19 vaccine recipients: a retrospective cohort study in 23.4 million
548 patients using OpenSAFELY. *medRxiv* 2021: 2021.01.25.21250356.

- 549 20. Public Health England. Chapter 14a COVID-10, *the Green Book*.
550 [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_da](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961287/Greenbook_chapter_14a_v7_12Feb2021.pdf)
551 [ta/file/961287/Greenbook_chapter_14a_v7_12Feb2021.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961287/Greenbook_chapter_14a_v7_12Feb2021.pdf) (accessed 21 February 2021)
- 552 21 Chodick G, Tene L, Patalon T, et al. The effectiveness of the first dose of BNT162b2
553 vaccine in reducing SARS-CoV-2 infection 13-24 days after immunization: real-world
554 evidence. *medRxiv* 2021: 2021.01.27.21250612.
- 555 22. Hunter PR, Brainard J. Estimating the effectiveness of the Pfizer COVID-19
556 BNT162b2 vaccine after a single dose. A reanalysis of a study of 'real-world' vaccination
557 outcomes from Israel. *medRxiv* 2021: 2021.02.01.21250957.
- 558 23. Skowronski DDS, G. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.
559 *New England Journal of Medicine* 2021.
- 560 24. Israeli Ministry of Health. Vaccine Safety and Effectiveness. 2021.
561 <https://govextra.gov.il/ministry-of-health/covid19-vaccine/en-covid19-vaccine-faqs/>
562 (accessed 18 February 2021).
- 563 25. Emary RW, Golubchik T, Aley PK, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222)
564 Vaccine Against SARS-CoV-2 VOC 202012/01 (B.1.1.7). *The Lancet* 2021.
- 565 26. Office of National Statistics (ONS). Coronavirus (COVID-19) Infection Survey,
566 antibody data for the UK: 16 February 2021. 2021.
567 [https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsandd](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsurveyantibodydatafortheuk/16february2021)
568 [iseases/articles/coronaviruscovid19infectionsurveyantibodydatafortheuk/16february2021](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsurveyantibodydatafortheuk/16february2021)
569 (accessed 16 February 2021).
- 570 27. Aiello A, Farzaneh F, Candore G, et al. Immunosenescence and Its Hallmarks: How
571 to Oppose Aging Strategically? A Review of Potential Options for Therapeutic Intervention.
572 *Front Immunol* 2019; **10**(2247).
- 573 28. Shah D. Healthy worker effect phenomenon. *Indian J Occup Environ Med*. 2009.
- 574

Table 1: Characteristics of vaccinated and non-vaccinated SIREN participants and factors associated with vaccine coverage in multivariable logistic regression analysis, (n=23,324)

Characteristics	Not Vaccinated	Vaccinated	OR (95% CI)	p-value	aOR** (95% CI)	p-value
	n (%)	n (%)				
Prior COVID-19 infection*						
Negative	1405 (9.3)	13716 (90.7)	Reference			
Positive	1278 (15.6)	6925 (84.4)	0.56 (0.51-0.60)	<0.001	0.59 (0.54-0.64)	<0.001
Gender						
Male	333 (9.2)	3270 (90.8)	Reference			
Female	2346 (11.9)	17346 (88.1)	0.75 (0.67-0.85)	<0.001	0.72 (0.63-0.82)	<0.001
Other	4 (13.8)	25 (86.2)	0.64 (0.22-1.84)	0.404	0.94 (0.30-2.93)	0.913
Age group						
Under 25	136 (16.1)	711 (83.9)	Reference			
25-34	886 (19.7)	3614 (80.3)	0.78 (0.64-0.95)	0.014	0.78 (0.64-0.96)	0.018
35-44	650 (11.5)	4998 (88.5)	1.47 (1.20-1.80)	<0.001	1.45 (1.18-1.79)	<0.001
45-54	600 (8.4)	6566 (91.6)	2.09 (1.71-2.56)	<0.001	2.22 (1.80-2.73)	<0.001
55-64	382 (8.0)	4412 (92.0)	2.21 (1.79-2.73)	<0.001	2.31 (1.85-2.87)	<0.001
Over 65	29 (7.9)	340 (92.1)	2.24 (1.47-3.42)	<0.001	2.19 (1.42-3.37)	<0.001
Ethnicity						
White	2119 (10.4)	18305 (89.6)	Reference			
Mixed Race	69 (19.4)	287 (80.6)	0.48 (0.37-0.63)	<0.001	0.56 (0.43-0.75)	<0.001
Asian	250 (15.8)	1337 (84.2)	0.62 (0.54-0.71)	<0.001	0.65 (0.56-0.76)	<0.001
Black	162 (34.9)	302 (65.1)	0.22 (0.18-0.26)	<0.001	0.26 (0.21-0.32)	<0.001
Chinese	17 (12.7)	117 (87.3)	0.80 (0.48-1.33)	0.383	0.73 (0.43-1.25)	0.252
Other ethnic group	56 (17.8)	258 (82.2)	0.53 (0.40-0.71)	<0.001	0.54 (0.39-0.73)	<0.001
Prefer not to say	10 (22.2)	35 (77.8)	0.41 (0.20-0.82)	0.012	0.30 (0.14-0.65)	0.002
Pre-existing medical condition^						
No medical condition	2060 (11.8)	15390 (88.2)	Reference			
Immunosuppression	56 (11.7)	421 (88.3)	1.01 (0.76-1.33)	0.965	-	-

Chronic Respiratory conditions	305 (10.4)	2619 (89.6)	1.15 (1.01-1.31)	0.032	-	-
Chronic Non-Respiratory conditions	262 (10.6)	2211 (89.4)	1.13 (0.99-1.29)	0.079	-	-
Household size						
Just you	283 (12.1)	2063 (87.9)	Reference			
Two to four	2080 (11.2)	16494 (88.8)	1.09 (0.95-1.24)	0.213	-	-
Over four	297 (12.7)	2037 (87.3)	0.94 (0.79-1.12)	0.492	-	-
Prefer not to say	23 (32.9)	47 (67.1)	0.28 (0.17-0.47)	<0.001	-	-
Index of Multiple Deprivation						
5 (least deprived)	507 (9.0)	5107 (91.0)	Reference			
4	534 (9.7)	4947 (90.3)	0.92 (0.81-1.04)	0.199	1.02 (0.89-1.16)	0.795
3	591 (11.1)	4731 (88.9)	0.79 (0.70-0.90)	<0.001	0.92 (0.81-1.05)	0.216
2	577 (14.1)	3512 (85.9)	0.60 (0.53-0.69)	<0.001	0.78 (0.69-0.90)	<0.001
1 (most deprived)	436 (16.6)	2198 (83.4)	0.50 (0.44-0.57)	<0.001	0.75 (0.65-0.87)	<0.001
Not known	38 (20.7)	146 (79.3)	0.38 (0.26-0.55)	<0.001	0.53 (0.36-0.78)	0.001
Region						
Yorkshire and the Humber	239 (11.5)	1832 (88.5)	Reference			
East Midlands	248 (10.1)	2200 (89.9)	1.16 (0.96-1.40)	0.128	1.14 (0.80-1.62)	0.461
East of England	299 (10.8)	2462 (89.2)	1.07 (0.90-1.29)	0.437	1.12 (0.80-1.56)	0.505
London	444 (15.5)	2416 (84.5)	0.71 (0.60-0.84)	<0.001	1.00 (0.73-1.37)	1.000
North East	53 (9.7)	496 (90.3)	1.22 (0.89-1.67)	0.212	1.31 (0.76-2.26)	0.340
North West	350 (12.7)	2403 (87.3)	0.90 (0.75-1.07)	0.218	0.96 (0.70-1.32)	0.803
South East	247 (9.1)	2462 (90.9)	1.30 (1.08-1.57)	0.006	1.24 (0.91-1.71)	0.176
South West	464 (9.7)	4335 (90.3)	1.22 (1.03-1.44)	0.019	1.11 (0.82-1.49)	0.506
West Midlands	339 (14.3)	2035 (85.7)	0.78 (0.66-0.93)	0.007	0.87 (0.63-1.19)	0.380
Staff group						
Admin	377 (10.5)	3223 (89.5)	Reference			
Nursing/Healthcare Assistant	1275 (13.0)	8551 (87.0)	0.78 (0.69-0.89)	<0.001	0.96 (0.84-1.09)	0.515
Doctor	189 (7.5)	2332 (92.5)	1.44 (1.20-1.73)	<0.001	1.82 (1.49-2.22)	0.000
Midwife	88 (15.5)	478 (84.5)	0.64 (0.49-0.82)	<0.001	0.74 (0.57-0.97)	0.027
Specialist staff	156 (11)	1262 (89.0)	0.95 (0.78-1.15)	0.584	1.28 (1.04-1.57)	0.020
Estates/Porters/Security	38 (17.1)	184 (82.9)	0.57 (0.39-0.82)	0.002	0.61 (0.42-0.90)	0.012
Pharmacist	35 (10.0)	316 (90.0)	1.06 (0.73-1.52)	0.770	1.59 (1.09-2.33)	0.016

Healthcare Scientist	91 (11.1)	729 (88.9)	0.94 (0.74-1.19)	0.599	1.16 (0.90-1.49)	0.261
Other	434 (10.8)	3566 (89.1)	0.96 (0.83-1.11)	0.594	1.13 (0.97-1.31)	0.126
Occupation setting*						
Offices and laboratory (lower risk)	932 (11.2)	7384 (88.8)	Reference			
Patient facing non-clinical	112 (12.9)	757 (87.1)	0.85 (0.69-1.05)	0.138	-	-
Outpatient	469 (11.6)	3590 (88.4)	0.97 (0.86-1.09)	0.567	-	-
Inpatient wards and ambulance	498 (14)	3069 (86.0)	0.78 (0.69-0.87)	<0.001	-	-
Intensive Care (higher risk)	157 (13.0)	1053 (87.0)	0.85 (0.71-1.01)	0.071	-	-
Other	515 (9.7)	4788 (90.3)	1.17 (1.05-1.31)	0.006	-	-
Contact with patients or working in patient-facing areas						
No	330 (10.1)	2940 (89.9)	Reference			
Yes	2353 (11.7)	17701 (88.3)	0.84 (0.75-0.95)	0.006	-	-
Frequency of contact with COVID-19 patients in the workplace						
Never	793 (9.6)	7484 (90.4)	Reference			
Daily	871 (15.4)	4777 (84.6)	0.58 (0.52-0.64)	<0.001	-	-
Weekly	448 (10.8)	3688 (89.2)	0.87 (0.77-0.99)	0.029	-	-
Monthly	239 (11.3)	1883 (88.7)	0.83 (0.72-0.97)	0.021	-	-
Less than monthly	332 (10.6)	2809 (89.4)	0.90 (0.78-1.03)	0.113	-	-
All Participants	2683 (11.5)	20641 (88.5)				

*Ever antibody or PCR positive as of 07 December 2020; ^pre-existing medical condition categories: immunosuppression (cancers affecting the immune system in the last 5 years, rheumatological/autoimmune conditions and on immunosuppressive therapy, organ or bone marrow transplantation, asplenia), Chronic respiratory conditions (asthma, chronic respiratory disease), chronic non-respiratory conditions (diabetes, obesity, chronic heart disease, chronic kidney disease, chronic liver disease, other cancers, dementia, other neurological disorder and HIV) and no reported medical conditions. Where participants reported multiple conditions, they were assigned to a category dependent on which condition was considered by the study team to be the most severe.

*Occupation setting: 1 = office, laboratory, estates; 2: community pharmacy, hospital pharmacy, communal areas open to the public, mobile across areas (porters); 3: outpatient, radiology, day ward, general practice, renal dialysis unit; 4: inpatient ward, theatres, emergency department, maternity unit/labour ward, ambulance; 5: intensive care; Other

**multivariable model included and adjusted for: site (as a random effect), and fixed effects: prior infection status, age, gender, ethnicity, IMD, region and staff group

576 **Table 2: Effectiveness of the BNT162b2 COVID-19 vaccine against infection in SIREN**
 577 **participants, stratified by cohort, between 7 December 2020 and 5 February 2021,**
 578 **(n=23,324)**

Vaccine group	Total person time (days)	Number of PCR positives	Incidence Density per 10,000 person days	Unadjusted Hazard Ratio (95% CI)^	Adjusted Hazard Ratio (95% CI)*
Full cohort					
Unvaccinated	710587	977	14	Reference	Reference
d1 ≥21	87278	71	8	0.43 (0.23-0.64)	0.30 (0.15-0.45)
d2 ≥7	20978	9	4	0.23 (0.06-0.40)	0.15 (0.04-0.26)
Negative cohort					
Unvaccinated	442605	902	20	Reference	Reference
d1 ≥21	59748	66	11	0.33 (0.17-0.49)	0.28 (0.14-0.42)
d2 ≥7	14746	8	5	0.18 (0.04-0.31)	0.14 (0.03-0.24)
Positive cohort**					
Unvaccinated	267982	75	3	-	-
d1 ≥21	27530	5	2	-	-
d2 ≥7	6232	1	2	-	-

579 ^Unadjusted includes vaccine effect (period) only; *the full model was adjusted for site as a random effect,
 580 period, and fixed effects: age, gender, ethnicity, comorbidities, job role, frequency of contact with COVID-19
 581 patients, employed in a patient facing role, occupational exposure. **there was insufficient information to model
 582 the positive cohort separately so stratified hazard ratios are not available for the positive cohort.

583

584

FIGURES

Figure 1: Number of vaccinated SIREN participants by dose, manufacturer and day, 8 December 2020 to 5 February 2021 (n=20,641)

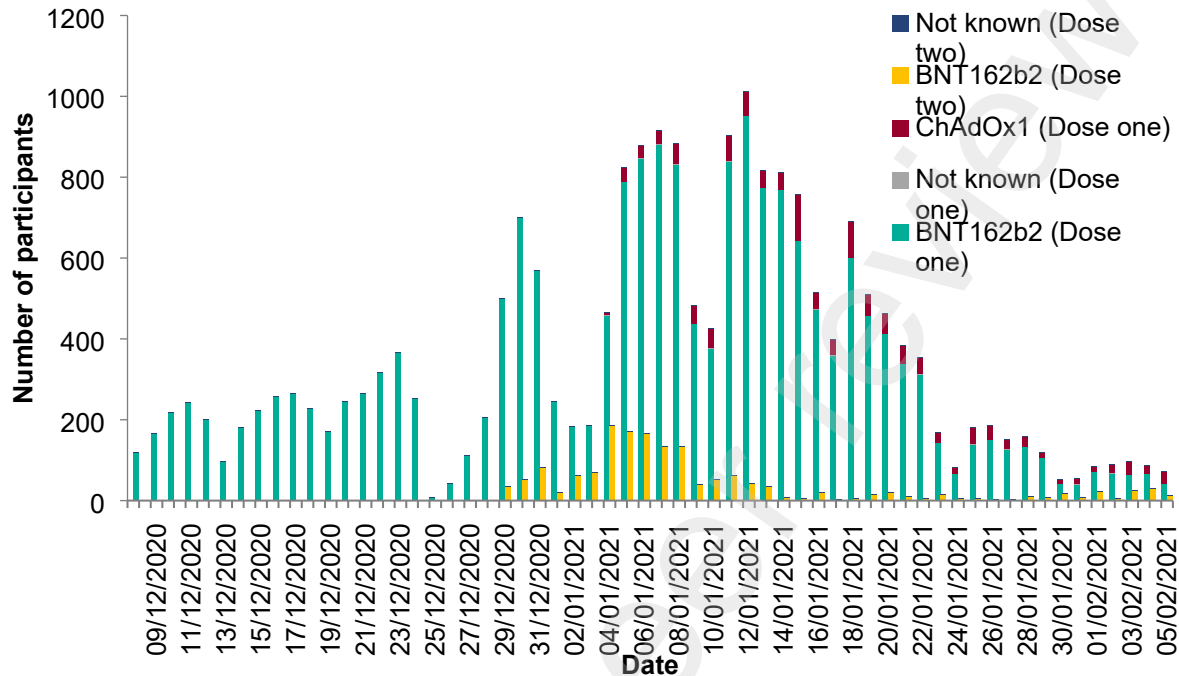


Figure 2a: Graph of adjusted Hazard Ratios at post-vaccination intervals, 7 December 2020 – 5 February 2021, full cohort (n=23,324)

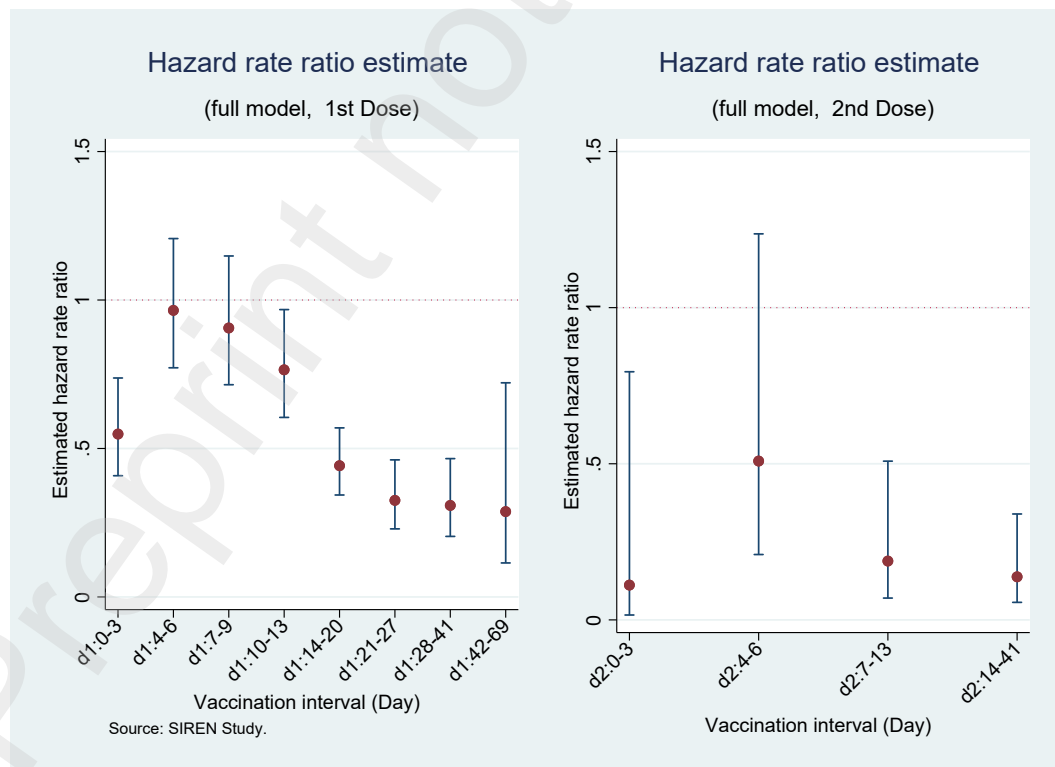


Figure 2b: Graph of adjusted Hazard Ratios at post-vaccination intervals, 7 December 2020 – 5 February 2021, negative cohort (n=15,121)

