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1 **Research Note**2 **Effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1**
3 **nCoV-19 vaccines against COVID-19 in health care workers: an**
4 **observational study using surveillance data**

5

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20

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23

24 **Abstract**

25 *Objectives:* Health care workers (HCWs), at increased risk of COVID-19, were among the
26 primary targets for vaccine campaigns. We aimed to estimate the effectiveness of the 3 first
27 COVID-19 vaccines available in Western Europe for their protection.

28 *Methods:* We merged two prospective databases that systematically recorded, in our
29 institution: i) HCWs positive for SARS-CoV-2 by RT-PCR on nasopharyngeal sample; ii)
30 HCWs who received at least one dose of COVID-19 vaccine. We excluded HCWs with
31 SARS-CoV-2 infection during the 6 months prior to the study. HCWs were categorized as
32 non-vaccinated if they received no vaccine and until first injection +13 days, partially
33 vaccinated from first injection +14 days to second injection +13 days, and fully vaccinated
34 thereafter.

35 *Results:* Of the 8,165 HCWs employed in our institution, 360 (4.4%) tested positive for
36 SARS-CoV-2 by RT-PCR during the study period (January 4th to May 17th 2021): Incidence
37 was 9.1% (8.2-10.0) in non-vaccinated HCWs; 1.2% (0.7-1.9) after one dose of ChAdOx1
38 nCoV-19; 1.4% (0.6-2.3), and 0.5% (0.1-1.0), after one, and two doses, of mRNA BNT162b2;
39 0.7% (0.1-1.9), and 0%, after one, and two doses, of mRNA-1273 ($P<0.0001$). Vaccine
40 effectiveness (Cox Model), was estimated at, respectively, 86.2% (76.5-91.0), 38.2% (6.3-
41 59.2), and 49.2% (19.1-68.1) 14 days after the first dose for ChAdOx1 nCoV-19, mRNA-
42 1273, and mRNA-BNT162b2; 100% (ND), and 94.6% (61.0-99.2) 14 days after the second
43 dose for mRNA-1273, and mRNA-BNT162b2.

44 *Conclusions:* In this real-world study, the observed effectiveness of COVID-19 vaccines in
45 HCWs was in line with the efficacy reported in pivotal randomized trials.

46

47 **Introduction**

48 Phase 3 clinical trials of COVID-19 vaccines evaluated the efficacy of two doses of
49 mRNA BNT162b2 (Pfizer), and mRNA-1273 vaccines (Moderna) at, respectively, 95%
50 (90.3%-97.6%), and 94.1% (89.3%-96.8%), for the prevention of COVID-19 [1, 2] . The
51 pivotal study of ChAdOx1 nCoV-19 vaccine (Astra-Zeneca) reported an efficacy of 62.1%
52 (41.0%-75.7%) [3]. This should not be interpreted as a superiority of the mRNA vaccines to
53 the latter, as these were not comparative studies: Indeed, study design, characteristics of the
54 population included, and profile of SARS-CoV-2 strains circulating during the study period
55 may impact the evaluation of vaccine efficacy. Hence, post-marketing observational studies
56 are complementary to randomized trials, as they document the effectiveness of vaccines in the
57 real life, and allow head-to-head comparisons. We aimed to estimate the vaccine effectiveness
58 of the three COVID-19 vaccines available for health care workers (HCWs) in France from
59 January to May 2021.

60

61 **Methods**

62 Rennes University Hospital is a 1500-bed hospital which serves as a referral centre for
63 Western France (population catchment area, 1.5 million inhabitants). All HCWs are registered
64 and followed-up by the department of occupational medicine, with two main objectives: i) to
65 protect them from occupational hazards; ii) to protect their patients. Since March 2020, a
66 database has been implemented to collect data on HCWs who test positive for SARS-CoV-2
67 by RT-PCR on nasopharyngeal samples, from any laboratory which performs these tests,
68 through the national system of health insurance. HCWs were tested in case of any symptom
69 suggestive of COVID-19, or for the purpose of contact tracing, when they were identified as
70 close contact of someone with SARS-CoV-2 infection. All HCWs with positive RT-PCR

71 were interviewed by phone within 48 hours of diagnosis, and data were collected on a
72 standardized questionnaire.

73 In January 4th 2021, we opened a COVID-19 vaccine centre in our hospital, to provide
74 free vaccine to HCWs, initially restricted to those aged 50 years and older (January-February),
75 then open to any HCWs willing to be vaccinated, following the national strategy. All vaccines
76 administered to HCWs were recorded in a database. Three COVID-19 vaccines have been
77 used in our hospital during the study period, according to authorizations of French drug
78 agency, and to their availability: mRNA BNT162b2 was available starting from January 4th,
79 ChAdOx1 nCoV-19 from February 8th, and mRNA-1273 from February, 23rd. The second
80 injection was scheduled 3-4 weeks after the first dose for the mRNA vaccines, and 12 weeks
81 after the first dose for ChAdOx1 nCoV-19. Following reports of severe thrombotic events
82 related to the ChAdOx1 nCoV-19 vaccine, its administration was interrupted on March 15th in
83 France, and restarted on March 20th, thereafter restricted to people aged 55 years and older.

84 The two databases (i.e., SARS-CoV-2 infected HCWs, and those who received COVID-
85 19 vaccines), were merged with the human resources database that includes all HCWs who
86 worked in the institution during the study period, from January 4th to May 17th 2021. HCWs
87 who tested positive for SARS-CoV-2 by RT-PCR within the 6 months before the COVID-19
88 vaccine campaign were excluded, as they were not immediately eligible to vaccination, and
89 were at low risk of COVID-19 during the survey. Data collected were anonymized before
90 analysis, and HCWs were informed of the study and its results through our institution website.
91 In accordance with French law, they did not have to provide written consent.

92 HCWs were categorized as non-vaccinated if they received no vaccine, or until the first
93 injection +13 days, partially vaccinated from the first injection +14 days to the second
94 injection +13 days, and fully vaccinated thereafter [4]. As only 10 HCWs had received their

95 second injection of ChAdOx1 nCoV-19 during the study period due to the 12-week interval,
96 we could not analyse the effectiveness of complete immunization with ChAdOx1 nCoV-19.

97 Statistical analyses included descriptive variables of HCWs who tested positive for SARS-
98 CoV-2, and those who did not. The 95% confidence intervals (CI) for proportions were based
99 on a binomial distribution. Multiple analyses were based on Cox models, with time-varying
100 vaccine status as the explanatory main variable, adjusted for age and occupation. Results are
101 presented as hazard risks (HR) with their 95%CI. Vaccine efficacy estimates were based on
102 the $100 \times (1 - \text{HR})$ formula, and CI extrapolated from HR 95%CI. Statistical analyses were
103 performed using the SAS® package, v9.4. A P value < 0.05 was considered as significant.

104

105 **Results**

106 We enrolled 8,165 HCWs, of whom 3,540 (43.4%) underwent at least one test for
107 SARS-CoV-2 by RT-PCR on nasopharyngeal samples (supplementary figure). Of the 8,165
108 HCWs, 360 (4.4%) tested positive during the study period, including 124 (34.4%) SARS-
109 CoV-2 variant alpha (B.1.1.7), and 1 (0.3%) variant beta (B.1.351) or gamma (P.1). HCWs
110 with positive RT-PCR were younger ($P < 0.001$), and more likely to be nurses, auxiliary
111 nurses, and household staff ($P < 0.0001$, Table 1). The incidence of positive RT-PCR was 9.1%
112 (8.2-10.0) in non-vaccinated HCWs, 1.2% (0.7-1.9) in those who received one dose of
113 ChAdOx1 nCoV-19, 1.4% (0.6-2.3), and 0.5% (0.1-1.0), respectively, for those who received
114 one dose, and two doses, of mRNA BNT162b2, and respectively 0.7% (0.1-1.9), and 0%, for
115 those who received one dose, and two doses, of mRNA-1273 ($P < 0.0001$). The vaccine
116 effectiveness, based on Cox Model (Table 2) was estimated at, respectively, 86.2% (76.5-
117 91.0), 38.2% (6.3-59.2), and 49.2% (19.1-68.1) 14 days after the first dose for ChAdOx1
118 nCoV-19, mRNA-1273, and mRNA-BNT162b2. It increased to 100% (ND), and 94.6%
119 (61.0-99.2) 14 days after the second dose for mRNA-1273, and mRNA-BNT162b2. We

120 performed sensitivity analyses based on Cox models restricted to HCWs who were tested at
121 least once by RT-PCR: the findings were very similar to the primary analyses. We performed
122 a subgroup analyses of vaccine efficacy restricted to the main variant during the study period
123 (alpha, B.1.1.7): HR were 0.44 [0.17-1.15] after one dose of ChAdOx1 nCoV-19, 0.96 [0.52-
124 1.78] after one dose of mRNA-1273, 0.45 [0.18-1.14] after one dose of mRNA-BNT162b2,
125 and 0.0 after two doses of mRNA-BNT162b2 (supplementary table).

126 **Discussion**

127 We found that the effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1
128 nCoV-19 vaccines against COVID-19 in HCWs was at least as good as reported by pivotal
129 randomized trials that led to their approval. Although these findings are merely confirmatory,
130 they are of value for the following reasons: First, inclusion criteria for randomized trials tend
131 to select the population most likely to respond, and this may especially apply for trials funded
132 by pharmaceutical companies. Hence, post-marketing studies performed in one of the main
133 target population (i.e. HCWs), with no restriction except previous severe allergy, are
134 welcome. Second, our study was performed while the variant B.1.1.7, referred to as 'UK
135 variant', was rapidly emerging (35.4% of SARS-CoV-2 infections during the study period).
136 Our findings that effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19
137 vaccines was maintained in this context partly address the concerns that vaccine efficacy may
138 be lower against this variant, as compared to SARS-CoV-2 strains circulating by the time
139 randomized trials were conducted.

140 Previous studies on vaccine effectiveness found similar findings for mRNA
141 BNT162b2: In Israel, the vaccine effectiveness was 29% (17%-39%) 14 days after one dose
142 of mRNA BNT162b2 vaccine in the general population, increasing to 90% (83%-94%) 7 days
143 after the second dose [5]. Jones et al. reported an incidence of 0.8% among non-vaccinated
144 HCWs as compared to 0.2% ($P=0.004$) in HCWs who had received mRNA BNT162b2

145 vaccine at least 12 days before enrolment [6]. Surprisingly, efficacy of ChAdOx1 nCoV-19 in
146 our study appears higher than previously [3]. Among HCWs, Shah et al estimated ChAdOx1
147 nCoV-19 effectiveness at 30% (22-37) 14 days after first dose, and 54% (30-70) 14 days after
148 the second dose [7].

149 Our study has limitations. First, as it was monocentric, its findings may not be
150 generalizable to other settings, given the variability of SARS-CoV-2 variants epidemiology.
151 Second, we could only evaluate vaccine effectiveness during the first months, as the study
152 ends 5 months after the COVID-19 vaccine campaign was started. With 35,217
153 persons.months, our study was not powered to evaluate vaccine effectiveness more than 3
154 months after the first dose. Thirdly, our study was based on passive surveillance, so that we
155 probably underestimated asymptomatic SARS-CoV-2 infection.

156 In conclusion, we found that the effectiveness of the 3 first COVID vaccines available
157 in western Europe, i.e. mRNA-BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19, was in
158 line with the efficacy reported in the pivotal randomized trials, in a large cohort of HCWs.

159

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162

163 **Conflict of interest**

164 None

165

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167 None

168 **Authors contribution**

189 Writing – Original draft: C.P.; Writing – Review & Editing: C.P., R.G., and P.T.

190 Conceptualization: C.P., R.G., E.T., F.B., S.P., S.H., and P.T. - Investigation: C.P., E.T., F.B.,

191 S.P., S.H., V.T., O.B., B.B., V.G., and C.R. Methodology: C.P., R.G., F.B., S.P., and S.H. –
192 Formal analysis: C.P., R.G., and P.T.

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218

1 **Table 1.** Comparison of health care workers (HCWs), according to tests for SARS-CoV-2 by
 2 RT-PCR on nasopharyngeal samples during the study period¹ (n=8165)

Characteristics	No test n=4625 (56.6%)	RT-PCR negative, n=3180 (39.0%)	RT-PCR Positive, n=360 (4.4%)	P Value
Age, years				
< 30	846 (45.0)	891 (47.4)	143 (7.6)	
30-39	1279 (56.7)	879 (39.0)	97 (4.3)	
40-49	1203 (59.7)	737 (36.6)	74 (3.7)	
50-59	1093 (63.4)	590 (34.2)	42 (2.4)	
≥ 60	204 (70.1)	83 (28.5)	4 (1.4)	<0.0001
median (range)	41.4 (19.5-72.1)	37.9 (18.5-70.9)	32.7 (19.5-61.6)	<0.0001
Occupation				
Administrative staff	591 (71.0)	229 (27.5)	12 (1.4)	
Household Staff	174 (52.7)	132 (40.0)	24 (7.3)	
Auxiliary nurses	767 (54.1)	566 (39.9)	84 (5.9)	
Health managers	95 (60.5)	58 (36.9)	4 (2.5)	
Nurses	1111 (52.9)	867 (41.3)	122 (5.8)	
Physicians	728 (55.7)	540 (41.4)	38 (2.9)	
Midwives	57 (80.3)	13 (18.3)	1 (1.4)	
Technical staff	417 (59.4)	270 (38.5)	15 (2.1)	
Laboratory staff	458 (56.6)	540 (41.4)	16 (2.0)	
Other care staff	227 (54.1)	169 (40.2)	24 (5.7)	<0.0001
Not available	14	15	20	
Vaccine status²				<0.0001
Non vaccinated	2193 (61.4)	1054 (29.5)	326 (9.1)	
mRNA BNT162b2				
Partially vaccinated	246 (50.7)	232 (47.8)	7 (1.4)	
Fully vaccinated	685 (59.2)	467 (40.4)	5 (0.4)	-
mRNA-1273				
Partially vaccinated	262 (56.6)	198 (42.8)	3 (0.7)	
Fully vaccinated	462 (52.2)	423 (47.8)	0 (0.0)	-
ChAdOx1 nCoV-19				
Partially vaccinated	776 (48.5)	806 (50.3)	19 (1.2)	
Fully vaccinated	1 (-)	0	0	-
Vaccine status (overall)				
Partially vaccinated	1284 (50.4)	1236 (48.5)	29 (1.1)	
Fully vaccinated	1148 (56.2)	890 (43.6)	5 (0.2)	<0.0001

3 ¹ Study period, January, 4th - May, 17th 2021

4 ² To express the delay between vaccine and positive RT-PCR test, HCWs were categorized as
 5 'partially vaccinated' between 14 days after the first dose, and 14 days after the second dose,
 6 and 'fully vaccinated' thereafter

7 Qualitative data are presented as number (%), quantitative data as median (range)

1 **Table 2.** Hazard Ratios and vaccine efficacy according to vaccine status (Cox Models¹,
 2 n=8165)

3

Variables ²	Number of events	Persons.months	HR [95%CI]	Vaccine Efficacy
Non-Vaccinated	326	25365	1 [ref]	
mRNA BNT162b2				
Partially vaccinated	7	1615	0.51 [0.32-0.81]	49.2 (19.1-68.1)
Fully vaccinated	5	3223	0.054 [0.008-0.39]	94.6 (61.0-99.2)
mRNA-1273				
Partially vaccinated	3	1073	0.62 [0.41-0.94]	38.2 (6.3-59.2)
Fully vaccinated	0	455	0.0 [ND]	
ChAdOx1 nCoV-19				
Partially vaccinated	19	3486	0.14 [0.08-0.24]	86.2 (76.5-91.0)
Fully vaccinated	-	2	-	

4

5 ¹ Study period, January 4th - May 17th 2021: 35,217 persons.months

6 ² To express the delay between vaccine and positive RT-PCR test, HCWs were categorized as
 7 'partially vaccinated' between 14 days after the first dose, and 14 days after the second dose,
 8 and 'fully vaccinated' thereafter

9 HR, hazard ratio; CI, Confidence interval; ND, not determined

10 All models were adjusted for age, and occupation, missing data = 15

11

12