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Research note

Effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19 vaccines against COVID-19 in healthcare workers: an observational study using surveillance data

Christophe Paris [1,*], Sophie Perrin [1], Stephanie Hamonic [2], Baptiste Bourget [1], Clémence Roué [1], Olivier Brassard [1], Emilie Tadié [1], Vincent Gicquel [3], François Bénézit [4], Vincent Thibault [5], Ronan Garlantézec [2], Pierre Tattevin [4]

[1] Service de Santé au Travail, Hôpital Pontchaillou, Centre Hospitalo-Universitaire, INSERM U1085 IRSET, 35033 Rennes, France
[2] Service d'Epidémiologie et de Santé Publique, Hôpital Pontchaillou, Centre Hospitalo-Universitaire, 35033 Rennes, France
[3] Pharmacie Centrale, Hôpital Pontchaillou, Centre Hospitalo-Universitaire, 35033 Rennes, France
[4] Maladies Infectieuses et Réanimation Médicale, Hôpital Pontchaillou, Centre Hospitalo-Universitaire, 35033 Rennes, France
[5] Laboratoire de Virologie, Hôpital Pontchaillou, Centre Hospitalo-Universitaire, 35033 Rennes, France

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ABSTRACT

Objectives: Healthcare workers (HCWs) at increased risk of coronavirus disease 2019 (COVID-19) were among the primary targets for vaccine campaigns. We aimed to estimate the protective efficacy of the first three COVID-19 vaccines available in Western Europe.
Methods: We merged two prospective databases that systematically recorded, in our institution: (a) HCWs positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by RT-PCR on nasopharyngeal samples, and (b) HCWs who received at least one dose of COVID-19 vaccine. We excluded HCWs with SARS-CoV-2 infection during the 6 months prior to the study. HCWs were categorized as non-vaccinated if they received no vaccine and until the first injection +13 days, partially vaccinated from the first injection +14 days to the second injection +13 days, and fully vaccinated thereafter.
Results: Of the 8165 HCWs employed in our institution, 360 (4.4%) tested positive for SARS-CoV-2 by RT-PCR during the study period (4th January to 17th May 2021). Incidence was 9.1% (8.2–10.0) in non-vaccinated HCWs, 1.2% (0.7–1.9) after one dose of ChAdOx1 nCoV-19, 1.4% (0.6–2.3) and 0.5% (0.1–1.0) after one and two doses of mRNA BNT162b2, 0.7% (0.1–1.9) and 0% after one and two doses of mRNA-1273 ($p < 0.0001$). Vaccine effectiveness (Cox model) was estimated at, respectively, 86.2% (76.5–91.0), 38.2% (6.3–59.2), and 49.2% (19.1–68.1) 14 days after the first dose for ChAdOx1 nCoV-19, mRNA-1273, and mRNA-BNT162b2, and 100% (ND) and 94.6% (61.0–99.2) 14 days after the second dose for mRNA-1273 and mRNA-BNT162b2.
Conclusions: In this real-world study, the observed effectiveness of COVID-19 vaccines in HCWs was in line with the efficacy reported in pivotal randomized trials. **Christophe Paris, Clin Microbiol Infect 2021;27:1699.e5–1699.e8**

Introduction

Phase III clinical trials of vaccines against coronavirus disease 2019 (COVID-19) evaluated the efficacy of two doses of mRNA BNT162b2 (Pfizer) and mRNA-1273 vaccines (Moderna) at, respectively, 95% (90.3–97.6%) and 94.1% (89.3–96.8%) for the prevention of COVID-19 [1,2]. The pivotal study of ChAdOx1 nCoV-19 vaccine (Astra-Zeneca) reported an efficacy of 62.1% (41.0–75.7%) [3]. This should not be interpreted as a superiority of the mRNA vaccines over the latter, as these were not comparative studies: indeed, study design, characteristics of the population included, and profile of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strains circulating during the study period may impact the evaluation of vaccine efficacy. Hence, post-marketing observational studies are complementary

* Corresponding author. Christophe Paris, Occupational Diseases Department, CHU Pontchaillou, F-33033 Rennes, France.
E-mail address: Christophe.paris@inserm.fr (C. Paris).

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to randomized trials, as they document the effectiveness of vaccines in real-life situations and allow head-to-head comparisons. We aimed to estimate the effectiveness of the three COVID-19 vaccines available for healthcare workers (HCWs) in France from January to May 2021.

Methods

Rennes University Hospital is a 1500-bed hospital which serves as a referral centre for Western France (population catchment area 1.5 million inhabitants). All HCWs are registered and followed up by the department of occupational medicine with two main objectives: (a) to protect them from occupational hazards, and (b) to protect their patients. Since March 2020, a database has been implemented to collect data on HCWs who test positive for SARS-CoV-2 by RT-PCR on nasopharyngeal samples, from any laboratory which performs these tests, through the national system of health insurance. HCWs were tested in case of any symptom suggestive of COVID-19, or for the purpose of contact tracing when they were identified as close a contact of someone with SARS-CoV-2 infection. All HCWs with positive RT-PCR were interviewed by phone within 48 hours of diagnosis, and data were collected on a standardized questionnaire.

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

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

HCWs were categorized as non-vaccinated if they received no vaccine or until the first injection +13 days, partially vaccinated from the first injection +14 days to the second injection +13 days, and fully vaccinated thereafter [4]. As only ten HCWs had received their second injection of ChAdOx1 nCoV-19 during the study period due to the 12-week interval, we could not analyse the effectiveness of complete immunization with ChAdOx1 nCoV-19.

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

Results

We enrolled 8165 HCWs, of whom 3540 (43.4%) underwent at least one test for SARS-CoV-2 by RT-PCR on nasopharyngeal samples (Supplementary Material Fig. S1). Of the 8165 HCWs, 360 (4.4%) tested positive during the study period, including 124 (34.4%) SARS-CoV-2 variant α (B.1.1.7), and one (0.3%) variant β (B.1.351) or γ (P.1). HCWs with positive RT-PCR were younger ($p < 0.001$) and more likely to be nurses, auxiliary nurses, and household staff ($p < 0.0001$, Table 1). The incidence of positive RT-PCR was 9.1% (8.2–10.0) in non-vaccinated HCWs, 1.2% (0.7–1.9) in those who received one dose of ChAdOx1 nCoV-19, 1.4% (0.6–2.3), and 0.5% (0.1–1.0), respectively, for those who received one dose and two doses of mRNA BNT162b2, and respectively 0.7% (0.1–1.9) and 0% for those who received one dose and two doses of mRNA-1273 ($p < 0.0001$). The vaccine effectiveness, based on the Cox model (Table 2), was estimated at, respectively, 86.2% (76.5–91.0), 38.2% (6.3–59.2), and 49.2% (19.1–68.1) 14 days after the first dose for ChAdOx1 nCoV-19, mRNA-1273, and mRNA-BNT162b2. It increased to 100% (ND) and 94.6% (61.0–99.2) 14 days after the second dose for mRNA-1273 and mRNA-BNT162b2. We performed sensitivity analyses based on Cox models restricted to HCWs who were tested at least once by RT-PCR; the findings were very similar to the primary analyses. We performed a subgroup analysis of vaccine efficacy restricted to the main variant during the study period (α, B.1.1.7): HR was 0.44 (0.17–1.15) after one dose of ChAdOx1 nCoV-19, 0.96 (0.52–1.78) after one dose of mRNA-1273, 0.45 (0.18–1.14) after one dose of mRNA-BNT162b2, and 0.0 after two doses of mRNA-BNT162b2 (Supplementary Material Table S1).

Discussion

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

Previous studies on vaccine effectiveness have found similar findings for mRNA BNT162b2. In Israel, the vaccine effectiveness was 29% (17–39%) 14 days after one dose of mRNA BNT162b2 vaccine in the general population, increasing to 90% (83–94%) 7 days after the second dose [5]. Jones et al. reported an incidence of 0.8% among non-vaccinated HCWs as compared to 0.2% (p 0.004) in HCWs who had received mRNA BNT162b2 vaccine at least 12 days before enrolment [6]. Surprisingly, the efficacy of ChAdOx1 nCoV-19 in our study appears higher than that previously found [3]. Among HCWs, Shah et al. estimated ChAdOx1 nCoV-19 effectiveness at 30% (22–37%) 14 days after the first dose, and 54% (30–70%) 14 days after the second dose [7].

Table 1
Comparison of healthcare workers (HCWs) according to tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by RT-PCR on nasopharyngeal samples during the study period[a] ($n = 8165$)

Characteristics	No test $n = 4625$ (56.6%)	RT-PCR-negative, $n = 3180$ (39.0%)	RT-PCR-positive, $n = 360$ (4.4%)	p
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 status[b]				<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

Qualitative data are presented as number (%), quantitative data as median (range).
[a] Study period, 4th January–17th May 2021.
[b] To express the delay between vaccine and positive RT-PCR test, HCWs were categorized as 'partially vaccinated' between 14 days after the first dose, and 14 days after the second dose, and 'fully vaccinated' thereafter.

Table 2
Hazard ratios (HR) and vaccine efficacy according to vaccine status (Cox Models[a], $n = 8165$)

Variables[b]	Number of events	Person-months	HR (95%CI)	Vaccine efficacy (95%CI)
Non-vaccinated	326	25,365	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	—	

CI, confidence interval; ND, not determined.
All models were adjusted for age and occupation; missing data = 15.
[a] Study period: 4th January–17th May 2021, 35 217 person-months.
[b] To express the delay between vaccine and positive RT-PCR test, healthcare workers were categorized as 'partially vaccinated' between 14 days after the first dose and 14 days after the second dose, and 'fully vaccinated' thereafter.

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

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

Author contributions

Writing—original draft: CP. Writing—review and editing: CP, RG and PT. Conceptualization: CP, RG, ET, FB, SP, SH and PT.

Investigation: CP, ET, FB, SP, SH, VT, OB, BB, VG and CR. Methodology: CP, RG, FB, SP and SH. Formal analysis: CP, RG and PT.

Transparency declaration

The authors declare no conflicts of interest. No funding was received for this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2021.06.043.

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