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Interim Estimates of Vaccine Effectiveness of Pfizer-BioNTech and Moderna COVID-19 Vaccines Among Health Care Personnel — 33 U.S. Sites, January–March 2021

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Throughout the COVID-19 pandemic, health care personnel (HCP) have been at high risk for exposure to SARS-CoV-2, the virus that causes COVID-19, through patient interactions and community exposure (1). The Advisory Committee on Immunization Practices recommended prioritization of HCP for COVID-19 vaccination to maintain provision of critical services and reduce spread of infection in health care settings (2). Early distribution of two mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) to HCP allowed assessment of the effectiveness of these vaccines in a real-world setting. A test-negative case-control study is underway to evaluate mRNA COVID-19 vaccine effectiveness (VE) against symptomatic illness among HCP at 33 U.S. sites across 25 U.S. states. Interim analyses indicated that the VE of a single dose (measured 14 days after the first dose through 6 days after the second dose) was 82% (95% confidence interval [CI] = 74%–87%), adjusted for age, race/ethnicity, and underlying medical conditions. The adjusted VE of 2 doses (measured ≥7 days after the second dose) was 94% (95% CI = 87%–97%). VE of partial (1-dose) and complete (2-dose) vaccination in this population is comparable to that reported from clinical trials and recent observational studies, supporting the effectiveness of mRNA COVID-19 vaccines against symptomatic disease in adults, with strong 2-dose protection.

A test-negative design case-control study of mRNA COVID-19 VE is underway, with HCP being enrolled at 33 sites across 25 U.S. states; the planned interim analysis presented in this report includes data collected during January–March 2021. A majority (75%) of enrolled HCP worked at acute care hospitals (including emergency departments), 25% worked in outpatient or specialty clinics, and <1% worked in long-term care facilities and urgent care clinics. HCP with the potential for exposure to SARS-CoV-2 through direct patient contact or for indirect exposure (e.g., through infectious materials) were eligible for enrollment. Case-patients and control participants (controls) were identified through routine employee testing performed based on site-specific occupational health practices. HCP with a positive SARS-CoV-2 polymerase chain reaction (PCR) or antigen-based test result and at least one COVID-19–like illness symptom were enrolled as case-patients, and HCP with a negative SARS-CoV-2 PCR test result, regardless of symptoms, were eligible for enrollment as controls. Controls were frequency matched to case-patients (aiming for a ratio of three controls per case-patient) by site and week of test. HCP who reported having received a positive SARS-CoV-2 PCR or antigen-based test result >60 days earlier (i.e., with a previous SARS-CoV-2 infection) were excluded. Information on demographics, COVID-19–like illness symptoms within 14 days before or after the testing date, and presence of underlying conditions and risk factors for severe COVID-19 were collected through HCP interviews or self-completed surveys. Medical records were reviewed to collect data on SARS-CoV-2 test dates, type, and results and on medical care sought for COVID-19–like illness. Vaccination records, including dates and type of COVID-19 vaccine received, were obtained from occupational health or other verified sources (e.g., vaccine card, state registry, or medical record).

1 https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html
2 Health care personnel are considered symptomatic if one or more of the following signs and symptoms are present 14 days before or after the test date: fever (documented ≥100.4°F [38.0°C] or subjective), chills, cough (dry or productive), shortness of breath, chest pain or tightness, fatigue or malaise, sore throat, headache, runny nose, congestion, muscle aches, nausea or vomiting, diarrhea, abdominal pain, altered sense of smell or taste, loss of appetite, or red or bruised toes or feet.
3 Underlying conditions grouped based on CDC guidelines identifying conditions associated or potentially associated with risk for severe COVID-19 illness. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

*https://www.cdc.gov/vaccines/covid-19/downloads/hcp-early-phase-protocol-508.pdf

https://www.cdc.gov/mmwr/summary/MMWRR20210618.htm

https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html
HCP were defined as unvaccinated if they had not received any COVID-19 vaccine doses or had received their first dose after the test date. The interval of 0–13 days from receipt of the first dose was defined as the time before first dose vaccine effect. The effectiveness of a single dose was measured during the interval from 14 days after the first dose through 6 days after the second dose. Because of the potential for vaccine-related reactions to influence HCP testing behaviors, sensitivity analyses of single-dose VE were conducted 1) excluding participants tested within 0–2 days of receiving the second dose and 2) measuring VE before receiving the second dose. Effectiveness of 2 doses was measured ≥7 days after the receipt of the second dose, consistent with the Pfizer-BioNTech clinical trial procedure (3). Sensitivity analyses measuring 2-dose effectiveness ≥14 days after the second dose were conducted, consistent with the Moderna clinical trial procedure (4). Conditional logistic regression was used to estimate matched odds ratios (mORs) adjusted for age, race/ethnicity, and presence of underlying conditions. VE was estimated as 100% × (1–mOR) for 1 or 2 doses, compared with no doses. Because of the small sample size, analyses could not be stratified by COVID-19 vaccine type. All statistical analyses were conducted using SAS (version 9.4; SAS Institute). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.**

As of March 18, 2021, 623 case-patients and 1,220 controls had been enrolled. The median ages of case-patients and controls were 38 years (range = 19–69 years) and 37 years (range = 19–76 years), respectively (Table 1). The majority of HCP (60% of case-patients and 64% of controls) worked in occupational categories with substantial anticipated direct patient contact and were aged 19–49 years (75% and 76%, respectively), female (84% and 82%, respectively), and non-Hispanic White (64% and 70%, respectively). Underlying conditions associated with increased risk for severe COVID-19 were reported by 77% of case-patients and 75% of controls. Case-patients were significantly more likely than controls to have fever (40% versus 23%, p<0.001), cough (56% versus 22%, p<0.001), or shortness of breath (26% versus 7%, p<0.001); 5% of case-patients and 14% of controls reported only mild symptoms (sore throat, headache, runny nose, or congestion; p<0.001); 17% of controls reported no symptoms. Only 12 (2%) case-patients and 10 (1%) controls had severe illness requiring hospitalization, and no deaths occurred in either group.

Ten percent of case-patients and 20% of controls had received 1 dose of COVID-19 vaccine ≥14 days before the test date, and 3% of case-patients and 15% of controls had received 2 doses ≥7 days before the test date (Table 2). Among vaccinated persons, 76% of case-patients and 78% of controls received the Pfizer-BioNTech vaccine; the remainder received the Moderna vaccine. The adjusted single-dose VE was 82% (95% CI = 74%–87%) and was similar for both 1-dose sensitivity analyses (before dose 2: VE = 74%, 95% CI = 62%–82%; excluding days 0–2 after dose 2: VE = 78%, 95% CI = 68%–84%). The adjusted 2-dose VE was 94% (95% CI = 87%–97%); effectiveness ≥14 days after the second dose was similar (VE = 90%, 95% CI = 77%–96%).

**This investigation was defined as having met the requirements for public health surveillance as defined in 45 C.F.R. part 46.102(d)(2) 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Discussion

This multisite test-negative design case-control study found that authorized mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) are highly effective against symptomatic COVID-19 among HCP. Effectiveness of a complete 2-dose regimen of these vaccines was estimated to be 94%, consistent with findings from two clinical trials (3,4). Although the case definition applied in this study was broader than that used in both clinical trials (3,4), 93% and 88% of cases included in this study met the respective Pfizer-BioNTech and Moderna trial case definitions. The results are also consistent with findings from an observational study among the general adult population from Israel (5), two cohort studies among HCP from the United Kingdom,†† and recently reported interim results from a U.S. cohort evaluation among HCP and frontline workers (6).

Effectiveness of a single dose, estimated to be 82% in this report, has also been demonstrated in phase III trials and recent observational studies. The estimated effectiveness found in this report is higher than estimates of single-dose effectiveness found in the Pfizer-BioNTech clinical trial (efficacy 52%; 95% CI = 30%–68%) (3) and an observational study from Israel (5). In the Israeli study, the Pfizer-BioNTech VE against symptomatic illness among the general adult population was 57% (95% CI = 50%–63%) and 66% (95% CI = 57%–73%) measured during 14–20 and 21–27 days, respectively, after the first dose (5). These differences might be related to the younger age of the HCP population in this study (<2% of participants aged ≥65 years) compared with the age of the Israeli study population (13% aged ≥70 years). In two cohort studies among HCP, the single-dose effectiveness of the Pfizer-BioNTech vaccine was consistent with the estimates in this report, with 72% effectiveness (95% CI = 58%–86%) 21 days after the first dose in a U.K. study (7) and 80% effectiveness (95% CI = 59%–90%) ≥14 days after the first dose in a U.S. cohort study (6). Because the single-dose

†† https://doi.org/10.1101/2021.03.09.21253218; https://doi.org/10.1101/2021.03.11.21253275
### TABLE 1. Characteristics of health care personnel case-patients and controls — 33 U.S. sites, January–March 2021

| Characteristic                                                                 | Case-patients* (N = 623) | Controls* (N = 1,220) |
|--------------------------------------------------------------------------------|--------------------------|-----------------------|
| **Age group, yrs**                                                             |                          |                       |
| Median (range)                                                                 | 38 (19–69)               | 37 (19–76)            |
| 19–49                                                                         | 470 (75)                 | 931 (76)              |
| 50–64                                                                         | 144 (23)                 | 257 (21)              |
| ≥65                                                                           | 7 (1)                    | 24 (2)                |
| Missing                                                                       | 2 (<1)                   | 8 (<1)                |
| **Sex**                                                                       |                          |                       |
| Male                                                                          | 99 (16)                  | 223 (18)              |
| Female                                                                        | 521 (84)                 | 996 (82)              |
| Other                                                                         | 3 (<1)                   | 1 (<1)                |
| **Race/Ethnicity**                                                            |                          |                       |
| White, non-Hispanic                                                           | 401 (64)                 | 853 (70)              |
| Black, non-Hispanic                                                           | 64 (10)                  | 64 (5)                |
| Hispanic/Latino                                                               | 81 (13)                  | 124 (10)              |
| Other†                                                                        | 77 (13)                  | 179 (15)              |
| **Anticipated level of HCP patient contact based on occupational category**    |                          |                       |
| Substantial§                                                                  | 375 (60)                 | 785 (64)              |
| Moderate§                                                                    | 60 (10)                  | 120 (10)              |
| Minimal**                                                                    | 147 (24)                 | 221 (18)              |
| Undefined††                                                                  | 41 (7)                   | 94 (8)                |
| **Presence of one or more underlying conditions or risk factors associated with increased risk for severe COVID-19** |                          |                       |
| Obesity (BMI >30 kg/m² or listed in medical record)                          | 217 (35)                 | 395 (32)              |
| Overweight (BMI 25–29 kg/m² or listed in medical record)                      | 186 (30)                 | 355 (29)              |
| Asthma                                                                       | 98 (16)                  | 211 (17)              |
| Hypertension                                                                  | 92 (15)                  | 159 (13)              |
| Diabetes mellitus§                                                            | 28 (4)                   | 57 (5)                |
| Immunocompromising condition***                                               | 25 (4)                   | 46 (4)                |
| Heart disease                                                                 | 15 (2)                   | 61 (5)                |
| Cerebrovascular disease                                                       | 2 (<1)                   | 4 (<1)                |
| Neurologic condition                                                         | 2 (<1)                   | 7 (<1)                |
| Chronic kidney disease                                                       | 1 (<1)                   | 5 (<1)                |
| Chronic obstructive pulmonary disease                                         | 1 (<1)                   | 6 (<1)                |
| Other chronic lung disease                                                   | 6 (<1)                   | 16 (1)                |
| Chronic liver disease                                                        | 2 (<1)                   | 6 (<1)                |
| Current or former smoking‡‡                                                  | 130 (21)                 | 255 (21)              |
| Pregnancy (proportion among female HCP)                                       | 13 (3)                   | 40 (4)                |
| **Reported symptoms of illness**                                              |                          |                       |
| Fever (measured temperature ≥100.4°F [38.0°C] or subjective)§§§              | 249 (40)                 | 281 (23)              |
| Cough (dry or productive)§§§                                                  | 348 (56)                 | 267 (22)              |
| Shortness of breath§§§                                                       | 161 (26)                 | 80 (7)                |
| Chills§§                                                                     | 275 (44)                 | 324 (27)              |
| Muscle pain§§                                                                 | 289 (46)                 | 342 (28)              |
| Altered sense of smell or taste§§§                                            | 351 (56)                 | 45 (4)                |
| Sore throat§§                                                                 | 215 (35)                 | 344 (28)              |
| Diarrhea§§                                                                    | 154 (25)                 | 173 (14)              |
| Nausea or vomiting§§                                                          | 132 (21)                 | 186 (15)              |
| Other symptoms§§                                                              | 560 (90)                 | 796 (65)              |
| **Hospitalized**                                                              | 12 (2)                   | 10 (1)                |
| **COVID-19 vaccine status**                                                   |                          |                       |
| Unvaccinated                                                                  | 340 (55)                 | 302 (25)              |
| Received ≥1 dose before test date, by vaccine type                           | 283 (45)                 | 918 (75)              |
| Pfizer-BioNTech                                                              | 214 (76)                 | 712 (78)              |
| Moderna                                                                       | 68 (24)                  | 200 (22)              |
| Mixed product††                                                               | 0                        | 1 (0.4)               |
| Missing product information                                                  | 1 (0.4)                  | 5 (0.5)               |

See table footnotes on the next page.
The findings in this report are subject to at least four limitations. First, testing for SARS-CoV-2 infection among HCP was based on occupational health practices at each facility, and no changes in routine testing practices were reported after vaccine introduction. If vaccinated HCP were less likely to obtain testing than unvaccinated HCP, the VE might have been underestimated. Alternatively, if postvaccination reactions increased the likelihood that vaccinated HCP would seek testing, the VE might have been overestimated. However, the sensitivity analysis excluding the interval of 0–2 days after receipt of dose 2, the interval during which most postvaccination reactions would be expected to occur, did not significantly change effectiveness estimates. Second, because of the limited sample size, effectiveness by vaccine product, presence of underlying medical conditions, and disease severity could not be estimated. In addition, because of limited statistical power, effectiveness estimates could not be adjusted for other potential confounders, such as use of personal protective equipment, occupational categories, or workplace or community exposures. Third, the VE estimates might not be generalizable to the U.S. adult population because racial/ethnic minority groups disproportionately affected by COVID-19 and who may have had higher exposure risks in the community were underrepresented in this population, and the overall HCP population was younger than the general U.S. adult population. However, the study’s geographic coverage was broad, representing the population of U.S. HCP, and vaccination data were obtained from multiple sources. Finally, although HCP with a known past infection was unknown could not be excluded. Data collection for this study is ongoing and will allow effectiveness to be evaluated by vaccine type and among HCP subgroups.

These interim results demonstrate that complete vaccination with authorized mRNA COVID-19 vaccines is highly effective in preventing symptomatic COVID-19 among HCP,
supporting the results of phase III trials and additional accruing evidence in recent observational studies. Real-world VE data are critical to guiding evolving COVID-19 vaccine policy. In addition to adherence to recommended infection control and prevention practices, a critical component of controlling the U.S. COVID-19 pandemic and protecting HCP is ensuring high coverage with safe and effective COVID-19 vaccines.

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