COVID-19 cases, hospitalizations and deaths after vaccination: a cohort event monitoring study, Islamic Republic of Iran

Ali Hosseinzadeh,† Sajad Sahab-Negah,‡ Sairan Nili,§ Roqayeh Aliyari,¶ Shahrbanoor Goli,* Mohammad Fereidouni,* Ali Alami,* Mohsen Shati,* Elham Ahmadnejad,* Shiva Mehravaran,† Mansoorfeh Fateh,* Hamidreza Khajeha,* Zahra Emamian,* Elahe Behmanesh,* Sepideh Mahdavi,* Mostafa Enayatrad,* Parvin Mangolian shahrbabaki,* Alireza Ansari-Moghadam,* Abtin Heidarzadeh,© Fariba Shahraiki-Sanavi,* Farshad Shokri-Ahadi,* Seyed Mohammad Hashemi Shahri,* Mahlagha Dehghan,* Mohammadreza Amini Moridani,© Hossein Sheibani,§ Maryam Abbasszadeh,* Reza Jafari,¶ Maryam Valikhani,¶ Ehsan Binesh,* Hamid Vahedi,* Reza Chaman,* Rozita Khodashahi,* Mahnaz Amini,* Farahzad Jabbari Azad,* Fariborz Rezaieitalab,¶ Saeid Amel Jamehdar,¶ Ali Eshraghi,* Hamid Sharifi,* Seyed Mehdi Hashemi Baygani,* Amin Mahdavi,* Abdollah Jafarzadeh,¶† Mehrdad Farokhnia,*† Saeedeh Ebrahimi,*† Abbas Pardakhty,*† Ebrahim Ghaderi,*† Hasan Soltani,¶† Sedigh Jadidoleslami,¶ Anoush Arianejad,¶ Hamed Gavili,¶ Borhan Moradveisi,*† Dina Motamedni,*† Hamed Zare,* Toba Kazemi*¶† & Mohammad Hassan Emamian*§

Abstracts in العربية, 简体中文, Français, Русский и Español at the end of each article.

Introduction

To end the ongoing global pandemic of coronavirus disease 2019 (COVID-19), it is imperative to have safe and effective vaccines that can provide immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. As of 10 June 2022, 364 vaccines against SARS-CoV-2 have been investigated, but only 37 of them have been used in Phase III clinical trials.¹

New vaccines are developed by companies and research centres using a broad range of techniques including viral vectors, inactivated vaccines, live weakened vaccines, deoxyribonucleic acid- (DNA) or ribonucleic acid- (RNA) based vaccines and protein-based vaccines.²,³ Each technique has advantages and disadvantages. For example, viral vector vaccines trigger robust immune responses that can result in long-term protection; however, they may also cause serious complications, such as immunity against the vector and coagulopathy.⁴ Inactivated vaccines, on the other hand, while safe for immunocompromised individuals,⁵ usually induce a much weaker immune response than viral vector-based vaccines.⁶

As of 12 January 2022, the World Health Organization (WHO) lists only nine COVID-19 vaccines that have been deemed safe and efficacious for emergency use in national immunization programmes.⁷ The approvals, however, are based on evidence from randomized controlled clinical trials whose samples may not necessarily be representative of the general population. Furthermore, only interim analyses were done for licensing purposes, the data did not allow the duration of protection to be determined and certain populations, such as pregnant women, were excluded. Therefore, active surveillance of the vaccines is needed through observational studies on the incidence of adverse events and COVID-19 cases and hospitalizations among vaccinated individuals over a defined period of time. To conduct...
an active safety surveillance study, a protocol for cohort event monitoring studies has been released by WHO.

To meet the need for such data in the Islamic Republic of Iran for four COVID-19 vaccines (i.e. AZD1222 Vaxzevria, CovIran\textsuperscript{a} vaccine, SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) or Sputnik V), we used the WHO protocol template for cohort event monitoring to design an observational study on the incidence of serious adverse events, adverse events of special interest and COVID-19 after each vaccine dose. We also sought to estimate the reactogenicity within 7 days of receiving each vaccine dose.\textsuperscript{10} In this paper, we report the incidence of COVID-19 cases, hospitalizations and deaths among a vaccinated sample of the population. It should be noted that the objective of this study was to determine the safety and efficiency of each vaccine in terms of adverse events and COVID-19 and is in no way related to WHO emergency approval, nor does it reflect the opinions of WHO.

**Methods**

In accordance with the cohort event monitoring template developed by WHO, we conducted a four-arm cohort study in seven cities in the Islamic Republic of Iran (Birjand, Kerman, Mashhad, Rasht, Sanandaj, Shahrud and Zahedan). The selection of the study sites was based on availability of tertiary care hospitals and an experienced investigator and also on the commitment of local authorities to support the study. We invited individuals 18 years or older who were receiving their first dose of SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV), Sputnik V, AZD1222 Vaxzevria or CovIran\textsuperscript{a} vaccine at a participating public vaccination site to participate. This study is part of a larger study,\textsuperscript{16} and here we report the incidence of COVID-19 cases, hospitalizations for COVID-19 and deaths due to COVID-19 by vaccine brand. The study methods have been fully described previously\textsuperscript{16} and we provide a summary as follows.

After enrolment, study staff interviewed the participants and collected their contact information and other data on vaccine brand, vaccination date, vaccine batch number, demographic characteristics (age, sex, years of education), previous COVID-19 and comorbidities (cancer, chronic cardiac, hepatic, mental, neurological, respiratory and renal diseases, diabetes, hypertension and immunodeficiency). To assess obesity, we also recorded self-reported weight and height and defined obesity as a body mass index $\geq 30$ kg/m\textsuperscript{2}. We actively followed participants until 3 months after their last dose of COVID-19 vaccine, if administered within 3 months of the first dose. For those receiving SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV), Sputnik V or CovIran\textsuperscript{a} vaccine, the expected follow-up time was 17 weeks, assuming an interval of up to 1 month between the first and second doses. For those receiving AZD1222 Vaxzevria, given that the interval between doses is 3 months, the expected follow-up time was 25 weeks.

During the follow-up period, participants completed questionnaires through telephone or web-based surveys at weekly intervals. We also retrieved vaccination dates and vaccine batch numbers of the second doses from national COVID-19 vaccination registries. The diagnosis of COVID-19 infection was based on self-reported reverse-transcription polymerase chain reaction (PCR) test or antibodies against SARS-CoV-2. We also checked medical
hospital records for unreliable responses (i.e. if the participant did not know the PCR results) and for patients admitted to intensive care units.

We considered participants lost to follow-up after two unsuccessful attempts to contact them by telephone, followed by one unsuccessful attempt to contact their next of kin. In case of loss to follow-up, we used data collected up to the last follow-up time in the analyses. We calculated the follow-up index (ratio) as: actual investigated follow-up period/potential follow-up duration.11

To factor in immunity status (time elapsed since vaccine dose administration), we considered the following immunity periods: non-immune period = first 14 days after the administration of the first dose; partial immunity period = period between 14 days after the first dose and 14 days after the second dose; full immunity period = period between 14 days after the second dose and the end of follow-up. We calculated incidence rates by dividing the total number of events by total person-days followed up, with their 95% confidence intervals (CI), for the total sample and by age, sex and immunity status. For the total follow-up period, we calculated incidence rates for events occurring 14 days after the first dose of the vaccine.

We used Cox proportional hazard regression models for survival analysis, with calendar time as the timescale and stratified by study sites to estimate the adjusted hazard ratios (HRs) for COVID-19 infection. We first used a univariate model with age, sex, education, vaccine brand, prior COVID-19 and comorbidities as covariates, and we only entered variables significant at $P < 0.1$ into the final stepwise Cox regression models.

**Ethical considerations**

The Institutional Review Board of Shahroud University of Medical Sciences, Islamic Republic of Iran (IR.SHMU. REC.1400.012) approved the study protocol, and we conducted all procedures in accordance with the Helsinki Declaration. Study participation was voluntary and all participants gave their written informed consent after trained staff had explained the study objectives and procedures and had answered participants’ questions.

**Results**

Between 7 April 2021 and 22 January 2022, we enrolled 89 783 participants in the study (Fig. 1). Table 1 presents the distribution of participants by vaccine brand and vaccination status, demographic characteristics, underlying diseases and follow-up status. The follow-up index was more than 98% for all vaccines.

The incidence rate of COVID-19 cases was 528.2 (95% CI: 514.0–542.7) per 1 000 000 person-days. For hospitalizations and deaths incidence rates were 55.8 (95% CI: 51.4–60.5) and 4.1 (95% CI: 3.0–5.5) cases per 1 000 000 person-days, respectively. Table 2 shows these rates for the different vaccine brands by sex, age and immunity status. Among the vaccine brands, the SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) had the highest rates of COVID-19 cases, hospitaliza-
tions and deaths. Participants 50 years and older had significantly higher rates of hospitalization and death compared with those younger than 50 years regardless of vaccine brand. In addition, with all vaccine brands, both hospitalization and death rates were significantly higher during the partial immunity period than the full immunity period.

The results of Cox proportional hazard regression for COVID-19 infection are shown in Table 3. Sputnik V and AZD1222 Vaxzevria provided significantly greater protection than the SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) during the partial immunity period. In the full immunity period, the SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) provided lower protection than the other three vaccines. History of COVID-19 significantly reduced the risk of reinfection, and most underlying diseases significantly increased the risk of COVID-19, including chronic neurological disorders and mental health disorders.

Table 4 shows the Cox proportional hazard regression for COVID-19 hospitalization. In the partial immunity period, AZD1222 Vaxzevria had significantly better effectiveness than the SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV), while in the full immunity period, no significant differences were found between vaccine brands. History of COVID-19 reduced the risk of hospitalization only in the partial immunity period. Most underlying diseases significantly increased the risk of COVID-19 hospitalization in the partial immunity period.

A total of 42 COVID-19–related deaths were registered; 17 (40.5%) occurred during the full immunity period (more than 14 days after administering the second dose). As such, the incidence of COVID-19 deaths per 1 000 000 person-days was 4.1 (95% CI: 3.0–5.5) overall (14 days after the first dose of vaccine till the end of follow-up) and 3.0 (95% CI: 1.9–4.8) during the full immunity period. The HR in the Cox regression model for COVID-19 death was not significantly different by vaccine brand in the full immunity period, but AZD1222 Vaxzevria provided better protection from death in the partial immunity period. Age (HR: 1.11; 95% CI: 1.04–1.17) and chronic renal diseases (HR: 5.13; 95% CI: 1.15–22.93) were associated with significantly higher risk of death (Table 5).

**Discussion**

Although vaccines provide adequate protection against SARS-CoV-2, their effectiveness never reaches 100%, and this protection is expected to further de-

| Variable                                      | SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) | Sputnik V | AZD1222 Vaxzevria | Coviran® vaccine |
|-----------------------------------------------|-----------------------------------------------------|-----------|------------------|------------------|
| Total, no. (%)                                | 31 690 (35.3)                                       | 20 195 (22.5) | 23 780 (26.5) | 14 118 (15.7)    |
| Date of completion of vaccination*            |                                                     |           |                  |                  |
| First quartile                                | 15 Aug 2021                                         | 1 Nov 2021 | 5 Sep 2021      | 12 Sep 2021      |
| Second quartile                               | 4 Sep 2021                                          | 8 Nov 2021 | 4 Nov 2021      | 13 Oct 2021      |
| Third quartile                                | 25 Sep 2021                                         | 22 Nov 2021 | 16 Dec 2021     | 16 Nov 2021      |
| Received second dose, no. (%)                 | 30 228 (95.4)                                       | 17 701 (87.7) | 21 379 (89.9) | 12 499 (88.5)    |
| Received third dose, no. (%)                  | 490 (1.5)                                           | 105 (0.52)   | 22 (0.1)      | 64 (0.5)        |
| Age in years, mean (SD)                       | 53.3 (16.0)                                         | 34.4 (11.1)  | 45.6 (18.3)   | 42.8 (13.2)      |
| Males, no. (%)                                | 15 535 (49.0)                                       | 11 129 (55.1) | 12 923 (54.3) | 7411 (52.5)      |
| Education in years, mean (SD)                 | 10.9 (5.4)                                          | 13.3 (3.5)   | 12.3 (5.2)     | 12.1 (4.3)      |
| Medical history, no. (%)                      |                                                     |           |                  |                  |
| Prior COVID-19 infection (self-reported)       | 7062 (22.3)                                         | 8549 (42.3)  | 6100 (25.7)    | 4205 (29.8)     |
| Obesity                                       | 3738 (11.8)                                         | 2158 (10.7)  | 2576 (10.8)     | 1384 (9.8)      |
| Diabetes                                      | 4275 (13.5)                                         | 339 (1.7)    | 1981 (8.3)     | 981 (7.0)       |
| Hypertension                                  | 5993 (18.9)                                         | 526 (2.6)    | 2988 (12.6)    | 1136 (8.1)      |
| Chronic cardiac diseases                      | 2962 (9.4)                                          | 242 (1.2)    | 1499 (6.3)     | 515 (3.7)       |
| Cancer                                        | 1007 (3.2)                                          | 19 (0.1)     | 75 (0.3)       | 30 (0.2)        |
| Chronic respiratory diseases                  | 861 (2.7)                                           | 188 (0.9)    | 446 (1.9)      | 230 (1.6)       |
| Chronic renal diseases                        | 601 (1.9)                                           | 64 (0.3)     | 255 (1.1)      | 128 (0.9)       |
| Chronic hepatic diseases                      | 260 (0.8)                                           | 52 (0.3)     | 139 (0.6)      | 82 (0.6)        |
| Chronic neurological diseases                 | 402 (1.3)                                           | 79 (0.4)     | 193 (0.8)      | 156 (1.1)       |
| Mental health disorders                       | 146 (0.5)                                           | 30 (0.2)     | 107 (0.5)      | 55 (0.4)        |
| Immunodeficiency                              | 64 (0.2)                                            | 19 (0.1)     | 30 (0.1)       | 12 (0.1)        |
| Follow-up index, %b                           | 98.4                                                | 98.6        | 99.4            | 98.6            |

© 2021 Ali Hosseinzadeh et al.

*The first quartile date is when a quarter of the participants received their second dose of vaccine; the second quartile date is when half of the participants received their second dose of vaccine; the third quartile date is when three quarters of the participants received their second dose of vaccine.

We calculated the follow-up index (ratio) as the: actual investigated follow-up period/potential follow-up duration.

COVID-19: coronavirus disease 2019; SD: standard deviation.
ccline as immunity wanes over time and new virus strains emerge. In fact, all COVID-19 vaccines have waning protection. However, vaccinated individuals who do become infected experience less severe symptoms and have much lower risk of hospitalization and death compared with unvaccinated people with similar risk factors. The results of our study showed overall breakthrough rates of 528.2, 55.8 and 4.1 per 1 000 000 person-days for COVID-19 cases, hospitalizations and deaths, respectively.

The main determinants of breakthrough rates were: time since vaccination; the genetic variant of SARS-CoV-2; comorbidities; age; waning immunity; level of community adherence to mitigation strategies; and epidemic severity. Therefore, it would be difficult to draw valid comparisons of breakthrough rates with other studies. For example, in Washington state in the United States of America, the rate of breakthrough infection among over 5 million fully vaccinated people increased from 1 per 5000 between 17 January and 21 August 2021, to 589 per 5000 between 17 January and 14 May 2022. In addition, the comparison of different vaccine brands in our study is misleading because the participants entered the study at different calendar times when the severity stage of the epidemic and the dominant variant were different. A higher rate of breakthrough infection has been reported for delta variants of SARS-CoV-2. The incidence of COVID-19 cases in fully vaccinated people was about 100 cases per 100 000 population in the United States during August to late November 2021 when the delta variant was the main variant. The incidence of deaths related to COVID-19 was 0.38 per 100 000 among the same group and over the same time. In addition, during the week of 1 May 2021, the median number of incident cases of COVID-19 in New York State among the vaccinated population was 2.4 cases per 100 000 person-days (range 0.7 to 6.8). Rates increased after the delta variant became the most prevalent circulating variant and reached 16.4 cases per 100 000 person-days (range 8.3 to 27.9) among vaccinated people.

In our study, with 17 registered deaths (0.028% of admitted patients), the mortality rate in fully vaccinated people was 3.0 per 1 000 000 person-days; this rate is much higher than the rate reported in Massachusetts in the United States (0.01%) but lower than Minnesota (0.032%). Differences in age and COVID-19 epidemic patterns, virus variants, vaccine effectiveness and health-care utilization are the main reasons for differences between results and these factors should be noted when comparing study results.

The lower incidence rates of COVID-19 hospitalization and death in the full immunity period compared with the partial immunity period in our study are consistent with previous reports.
on the effectiveness of COVID-19 vaccines. For example, analysis of National Immunization Management Service and the Coronavirus Clinical Information Network in the United Kingdom of Great Britain and Northern Ireland showed that out of 40,000 patients with COVID-19 who were admitted to hospital, 84% had not been vaccinated, 13% had only received their first vaccine dose and 3% had received both doses.\textsuperscript{26,27} It should be noted that participants in our study were enrolled at different times on the epidemic curve. For example, the SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) became available just before the onset of the fifth COVID-19 wave, while CovIran\textsuperscript{®} vaccine and SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) were the main brands used in the vaccination programme when COVID-19 incidence was at its peak in July 2021. Therefore, the occurrence of COVID-19 cases was affected by the time of entry of participants into the study. In addition, vaccines may lose their effectiveness over time as newer strains of the virus emerge. Even the age groups and comorbidities of participants varied by vaccine brands, and since the risk of infection differs by age and comorbidity, we cannot simply compare the incidence rates by vaccine brand. Thus, we used Cox regression analysis to adjust for important covariates and used calendar time as the time span.

Based on the results of the Cox regression analysis, AZD1222 Vaxzevria was most effective at preventing COVID-19 cases, hospitalizations and deaths, while the SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) had the lowest effectiveness, especially in the partial immunity period. A similar finding was recently reported in a large study conducted in the Islamic Republic of Iran.\textsuperscript{28} The results suggest that vector-based vaccines (Sputnik V and AZD1222 Vaxzevria) had better effectiveness than inactivated vaccines (SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) and CovIran\textsuperscript{®} vaccine).

The Cox regression models showed that individuals with chronic respiratory, renal and cardiac diseases, diabetes and obesity were at a higher risk of COVID-19 hospitalization, and a previous history of COVID-19 reduced this risk to less than half. Similar associations have been reported in other studies.\textsuperscript{26,27} A study has shown that prior SARS-CoV-2 infection significantly reduces the risk of breakthrough infection.\textsuperscript{29} Another factor associated with COVID-19 hospitalization was obesity. This outcome is most likely because obesity impairs immunity by altering the response of cytokines which increases susceptibility to infection, especially infections that require a rapid cellular immune response.\textsuperscript{26,27} In addition, obesity is linked to metabolic disorders and

### Table 3. Variables associated with COVID-19 cases: Cox regression analysis, Islamic Republic of Iran, 2021

| Independent variable | Partial immunity period\(a\) | Full immunity period\(a\) |
|----------------------|-----------------------------|--------------------------|
| Age, years           | 1.00 (0.99–1.00)            | 1.00 (0.99–1.01)          |
| Female sex           | 1.17 (1.08–1.27)            | 1.22 (1.13–1.32)          |
| Education, years     | 1.02 (1.01–1.03)            | 1.05 (1.04–1.06)          |
| Vaccine brand        |                             |                          |
| SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) | Reference | Reference |
| Sputnik V            | 0.66 (0.55–0.80)            | 0.73 (0.62–0.86)          |
| AZD1222 Vaxzevria    | 0.74 (0.67–0.82)            | 0.70 (0.61–0.80)          |
| CovIran\textsuperscript{®} vaccine | 0.93 (0.81–1.07) | 0.73 (0.63–0.86) |
| Prior COVID-19 infection | 0.56 (0.50–0.64) | 0.76 (0.69–0.84) |
| Chronic respiratory diseases | 1.28 (1.01–1.63) | 1.34 (1.03–1.75) |
| Chronic renal diseases | 1.33 (0.98–1.81) | 1.49 (1.07–2.07) |
| Chronic neurological diseases | 1.44 (1.05–1.98) | NA\textsuperscript{c} |
| Diabetes             | 1.12 (0.99–1.27)            | 1.17 (1.01–1.37)          |
| Chronic cardiac diseases | NA\textsuperscript{c} | 1.25 (1.05–1.48) |
| Mental health disorders | 1.82 (1.13–2.95) | NA\textsuperscript{c} |

CI: confidence interval; COVID-19: coronavirus disease 2019; HR: hazard ratio; NA: not applicable.  
\(a\) Defined as the period between the 14th day after the first dose and 14 days after the second dose.  
\(b\) Defined as the period between the 14th day after the second dose and the end of follow-up.  
\(c\) Not entered in the final stepwise Cox regression models as P > 0.1 in the univariate analysis.

### Table 4. Variables associated with COVID-19 hospitalization: Cox regression analysis, Islamic Republic of Iran, 2021

| Independent variable | Partial immunity period\(a\) | Full immunity period\(a\) |
|----------------------|-----------------------------|--------------------------|
| Age, years           | 1.03 (1.02–1.04)            | 1.03 (1.02–1.04)          |
| Female sex           | 1.02 (0.82–1.26)            | 0.98 (0.74–1.28)          |
| Education, years     | 1.02 (0.997–1.047)          | 1.02 (0.99–1.05)          |
| Vaccine brand        |                             |                          |
| SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV) | Reference | Reference |
| Sputnik V            | 0.62 (0.38–1.00)            | 0.86 (0.46–1.59)          |
| AZD1222 Vaxzevria    | 0.47 (0.36–0.61)            | 0.71 (0.48–1.08)          |
| CovIran\textsuperscript{®} vaccine | 0.91 (0.62–1.32) | 1.16 (0.73–1.84) |
| Prior COVID-19 infection | 0.42 (0.29–0.62) | 0.66 (0.44–1.00) |
| Chronic respiratory diseases | 1.96 (1.21–3.19) | NA\textsuperscript{c} |
| Chronic renal diseases | 2.05 (1.14–3.68) | 2.52 (1.33–4.80) |
| Chronic cardiac diseases | 1.38 (1.00–1.92) | NA\textsuperscript{c} |
| Diabetes             | 1.63 (1.23–2.16)            | 1.75 (1.25–2.44)          |
| Obesity              | 1.60 (1.22–2.11)            | NA\textsuperscript{c}    |

CI: confidence interval; COVID-19: coronavirus disease 2019; HR: hazard ratio; NA: not applicable.  
\(a\) Defined as the period between the 14th day after the first dose and 14 days after the second dose.  
\(b\) Defined as the period between the 14th day after the second dose and the end of follow-up.  
\(c\) Not entered in the final stepwise Cox regression models as P > 0.1 in the univariate analysis.
other critical diseases such as diabetes, hypertension, and cardiac and cerebrovascular diseases. Obesity and its related comorbidities have been shown to increase the cumulative risk of death in COVID-19 patients. Similar to our findings, other studies confirmed the association of chronic neurological and mental diseases with contracting COVID-19. Higher vulnerability to SARS-CoV-2 infection of participants with mental diseases may be attributed to their lower cooperation with preventive measures, which may also be true for people with dementia and Parkinson disease. However, more studies are needed to determine the exact reasons for the association between mental and neurological diseases and SARS-CoV-2 infection.

The main strengths of our study include its large sample size, the investigation and comparison of four vaccines, the active surveillance that was conducted, weekly follow-up of participants, and investigation and classification of all hospitalized participants. However, we could not determine virus variants and included no control group for investigating vaccine effectiveness, which can be considered limitations of our study.

In conclusion, COVID-19 breakthrough rates were relatively high in our study. AZD1222 Vaxzevria vaccine provided better protection from COVID-19 infection, hospitalization and death than the other three vaccines. All the vaccines had similar protection against COVID-19 hospitalization 14 days after the second dose. People with comorbidities had higher risk of contracting COVID-19 and hospitalization and should be prioritized for preventive interventions.

Acknowledgements
The first four authors contributed equally as first author to the article. The steering committee for COVID-19 vaccine studies at the Iranian Ministry of Health and Medical Education provided technical notes on data analysis and had full supervision of this study. We thank Professor Akbar Fotouhi, Dr Bita Mesgarpoor, Professor Gholam Moradi, Professor Farid Naji, Professor Masud Yusnesian and Professor Seyed Mohsen Zahraei.

Funding: This study was supported by Shahroud University of Medical Sciences (Grant Number: 99135), Vice-Chancellor for research and technology at the Iranian Ministry of Health and Medical Education (Grant Number: 2302) and World Health Organization (WHO Reference: 2021/1169483-0).

Competing interests: None declared.
COVID-19 cases after vaccination, Islamic Republic of Iran

Ali Hosseinzadeh et al.

Abstract

We conducted a cohort study on the surveillance of COVID-19 cases after vaccination, Islamic Republic of Iran. We recruited individuals aged 18 years or older who received their first COVID-19 dose between April 2021 and January 2022 in seven Iranian cities. Participants completed daily follow-up surveys for 17 weeks (25 weeks for AZD1222). The incidence rate was 528.2 per 100,000 people (95% CI: 514.0–542.7) for COVID-19 cases; the hospitalization rate was 4.1 per 100,000 people (95% CI: 3.0–5.5) for COVID-19 cases, and the death rate was 0.7% (95% CI: 0.6–0.8) for COVID-19 cases.

Results

Among the 89,783 participants, the incidence rate was 528.2 per 100,000 people (95% CI: 514.0–542.7) for COVID-19 cases; the hospitalization rate was 4.1 per 100,000 people (95% CI: 3.0–5.5) for COVID-19 cases, and the death rate was 0.7% (95% CI: 0.6–0.8) for COVID-19 cases.

Conclusion

The incidence of COVID-19 after vaccination was relatively low. In other words, the vaccine against COVID-19 reduced the risk of COVID-19, hospitalization, and death.

Résumé

Cas, hospitalisations et décès liés à la COVID-19 après la vaccination: étude de cohorte portant sur la surveillance des événements en République islamique d'Iran

Objectif Analyser l'incidence des cas, hospitalisations et décès liés à la maladie à coronavirus 2019 (COVID-19) chez les Iraniens vaccinés avec la Vaxzevria, Covifran®, le vaccin contre le SARS-CoV-2 (cellule Vero), le vaccin inactivé (InCoV) ou Sputnik V.

Méthodes Nous avons recruté des individus de minimum 18 ans ayant reçu leur première dose de vaccin contre la COVID-19 entre avril 2021 et janvier 2022 dans sept villes iraniennes. Les participants ont rempli des enquêtes de suivi hebdomadaires pendant 17 semaines (25 semaines pour AZD1222) afin de communiquer sur leur statut COVID-19 et rénaux et rénaux entraînaient un risque accru de contracter la COVID-19 après la vaccination.

Résultats Sur 89 783 participants recrutés, le taux d'infection à la COVID-19 après la vaccination était relativement élevé. D'autre part, le vaccin contre le SARS-CoV-2 (cellule Vero) s'est révélé moins efficace que les autres vaccins. Enfin, les personnes souffrant de comorbidités avaient plus de risques de contracter la COVID-19 et d'être hospitalisées; elles devraient donc être priorisées lors des interventions préventives.

Conclusion Le taux d'infection à la COVID-19 après la vaccination était relativement élevé. D'autre part, le vaccin contre le SARS-CoV-2 (cellule Vero) s'est révélé moins efficace que les autres vaccins. Enfin, les personnes souffrant de comorbidités avaient plus de risques de contracter la COVID-19 et d'être hospitalisées; elles devraient donc être priorisées lors des interventions préventives.

Резюме

Случаи заражения COVID-19, госпитализации и смерти после вакцинации: когортное исследование мониторинга событий, Исламская Республика Иран

Цель Изучить уровень заболеваемости коронавирусной инфекцией 2019 года (COVID-19) у участников исследования среди иранцев, вакцинированных вакциной AZD1222 Vaxzevria, Covifran®, SARS-CoV-2 (Vero Cell), инактивированной вакциной (InCoV) или вакциной Sputnik V.

Методы Авторы включили в исследование участников в возрасте от 18 лет, получивших первую дозу вакцины против COVID-19 в период с апреля 2021 г. по январь 2022 г. в семи иранских городах. Участники проходили еженедельные следующие обследования в течение 17 недель (25 недель для AZD1222) и сообщали о своем состоянии COVID-19 и госпитализации. Авторы использовали модели регрессии Кокса для оценки факторов риска заражения COVID-19, госпитализации и смерти.

Результаты Из 89 783 включенных участников показатели заболеваемости на 1 000 000 человеко-дней составили: 528.2 (95%-й ДИ: 514.0–542.7) для случаев заражения COVID-19;
Casos, hospitalizaciones y muertes por la COVID-19 tras la vacunación: un estudio de cohortes sobre el seguimiento de eventos en la República Islámica de Irán

Objetivo Analizar la incidencia de los casos, hospitalizaciones y muertes a causa de la enfermedad por coronavirus de 2019 (COVID-19) en los iraníes vacunados con Sputnik ADZ1222, la vacuna Coviran®, la vacuna contra el SARS-CoV-2 (célula Vero), la vacuna inactivada (InCoV) o la Sputnik V.

Métodos Se inscribieron personas de 18 años o más que recibieron su primera dosis de la vacuna contra la COVID-19 entre abril de 2021 y enero de 2022 en siete ciudades iraníes. Los participantes completaron encuestas de seguimiento semanales durante 17 semanas (25 semanas para ADZ1222) para informar sobre su estado de la COVID-19 y la hospitalización. Se utilizaron modelos de regresión de Cox para valorar los factores de riesgo de contraer la COVID-19, de ser hospitalizadas, por lo que deberían ser prioritarias para las intervenciones preventivas.

Resultados De los 89 783 participantes inscritos, las tasas de incidencia de los casos, hospitalizaciones y muertes fueron relativamente altas. La vacuna contra el SARS-CoV-2 (célula Vero), el vacímetro, la vacuna inactivada (InCoV) o la Sputnik V.

Referencias

1. COVID-19 vaccine tracker and landscape. Geneva: World Health Organization; 2022. Available from: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines [cited 2022 June 13].

2. Tregoning JS, Brown ES, Cheeseman HM, Flight KE, Higham SL, Lemm NM, et al. Vaccines for COVID-19. Clin Exp Immunol. 2020 Nov;202(2):162–92. doi: http://dx.doi.org/10.1111/cei.13517 PMID: 32953351

3. Thanh Le T, Andreadakis Z, Kumar A, Gómez Román R, Tollerien S, Saville M, et al. The COVID-19 vaccine development landscape. Nat Rev Drug Discov. 2020 May;19(5):305–6. doi: http://dx.doi.org/10.1038/s41573-020-00073-5 PMID: 32273591

4. Barros-Martins J, Hammerschmidt SL, Cossmann A, Odak I, Stankov MV, Morillas Ramos G, et al. Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination. Nat Med. 2021 Sep;27(9):1525–9. doi: http://dx.doi.org/10.1038/s41591-021-01449-9 PMID: 34261258

5. Monagle P, Ng AP, Linden M, Ignjatovic V, Farley A, Taoudi S, et al. Vaccine-induced immune thrombosis and thrombocytopenia syndrome following adenovirus vectored severe acute respiratory syndrome coronavirus 2 vaccination: a novel hypothesis regarding mechanisms and implications for future vaccine development. Immuno Cell Biol. 2021 Nov;99(10):1006–10. doi: http://dx.doi.org/10.10111/Imcb.12505 PMID: 34664030

6. Lim WW, Mak L, Leung GM, Cowling BJ, Peiris M. Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19. Lancet Microbe. 2021 Sep;2(9):e423. doi: http://dx.doi.org/10.1016/S2666 -5247(21)00107-4 PMID: 34308395

7. Iversen PL, Bava S. Inactivated COVID-19 vaccines to make a global impact. Lancet Infect Dis. 2021 Jun;21(6):746–8. doi: http://dx.doi.org/10.1016/S1473-3099(21)00020-7 PMID: 33548196

8. Coronavirus disease (COVID-19); vaccines [internet]. Geneva: World Health Organization; 2022. Available from: https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(COVID-19)-vaccines [cited 2022 May 18].

9. Protocol template to be used as template for observational study protocols: cohort event monitoring (CEM) for safety signal detection after vaccination with COVID-19 vaccines. Geneva: World Health Organization; 2021. Available from: https://apps.who.int/iris/handle/10665/342193 [cited 2022 May 18].

10. Alizari R, Mahdavi S, Enayatrad M, Sahab-Negah S, Nili S, Fereidooni M, et al. Study protocol: cohort event monitoring for safety signal detection after vaccination. Geneva: World Health Organization; 2021. Available from: https://apps.who.int/iris/handle/10665/342193 [cited 2022 May 18].

11. von Allmen RS, Weiss S, Tevaearai HT, Kuemmerli C, Tinner C, Carrel TP, et al. Completeness of follow-up determines validity of study findings: results of a prospective repeated measures cohort study. PLoS One. 2015 Oct 15;10(10):e0140817. doi: http://dx.doi.org/10.1371/journal.pone.0140817 PMID: 26469346

12. Yewdell JW. Individuals cannot rely on COVID-19 herd immunity: durable immunity to viral disease is limited to viruses with obligate viremic spread. PLoS Pathog. 2021 Apr 26;17(4):e1009509. doi: http://dx.doi.org/10.1371/ journal.ppat.1009509 PMID: 33901246

13. COVID-19 vaccine breakthrough weekly update [internet]. St Paul: Minnesota Department of Health; 2022. Available from: https://www.health.state.mn.us/diseases/coronavirus/stats/vbt.html [cited 2022 May 10].

14. Lipshitz M, Kramer F, Regov-Yochay G, Lustig Y, Balicer RD. SARS-CoV-2 breakthrough infections in vaccinated individuals: measurement, causes and impact. Nat Rev Immunol. 2022 Jan;22(1):57–65. doi: http://dx.doi.org/10.1038/s41577-021-00662-4 PMID: 34876702
15. SARS-CoV-2 vaccine breakthrough surveillance and case information resource. Shoreline, WA: Washington State Department of Health; 2022. Available from: https://doh.wa.gov/sites/default/files/2022-02/420-339-VaccineBreakthroughReport.pdf [cited 2022 May 28].
16. Christensen PA, Olsen RJ, Long SW, Subedi S, Davis JJ, Hodjat P, et al. Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas. Am J Pathol. 2022 Feb;192(2):320–31. doi: http://dx.doi.org/10.1016/j.ajpath.2021.10.019 PMID: 3474517
17. COVID data tracker. Rates of COVID-19 cases and deaths by vaccination status [internet]. Atlanta: Centers for Disease Control and Prevention, 2022. Available from: https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status [cited 2022 May 12].
18. Rosenberg ES, Dorabawila V, Easton D, Bauer UE, Kumar J, Hoen R, et al. COVID-19 vaccine effectiveness in New York State. N Engl J Med. 2022 Jan 13;386(2):116–27. doi: http://dx.doi.org/10.1056/NEJMoa2116063 PMID: 34942067
19. Breakthrough cases in Mass. Top 100,000; over 5 million fully vaccinated. NBC10 Boston. 2021 Dec 14. Available from: https://www.nbc10.com/news/coronavirus/breakthrough-cases-in-mass-top-100000-over-5-million-fully-vaccinated/2590370/ [cited 2022 May 15].
20. Egan C, Turtle L, Thorpe M, Harrison EM, Semple MG, Docherty AB; ISARIC4C Investigators. Hospital admission for symptomatic COVID-19 and impact of vaccination: analysis of linked data from the Coronavirus Clinical Information Network and the National Immunisation Management Service. Anaesthesia. 2022 Feb 18;77(5):605–8. doi: http://dx.doi.org/10.1111/anae.15677 PMID: 35178709
21. Iacobucci G. Covid-19: how is vaccination affecting hospital admissions and deaths? BMJ. 2021 Sep 7;374(2036):n2306. doi: http://dx.doi.org/10.1136/bmj.n2306 PMID: 34544731
22. Taherian Z, Rezaei M, Haddadpour A, Amini Z. The effect of COVID-19 vaccination on reducing the risk of infection, hospitalization, and death in Isfahan Province, Iran. Iran J Public Health. 2022 Jan;51(1):186–95. doi: http://dx.doi.org/10.18502/jiph.v51i1.8311 PMID:35223640
23. Jamali-Atergeleh H, Emamian MH, Goli S, Rohani-Rasaf M, Hashemi H, Fotouhi A. The risk factors of COVID-19 in 50–74 years old people: a longitudinal population-based study. Epidemiol Methods. 2021;10(1):20210024. doi: http://dx.doi.org/10.1515/embr-2021-0024
24. Poly TN, Islam MM, Yang HC, Lin MC, Jian WS, Hsu MH, et al. Obesity and mortality among patients diagnosed with COVID-19: a systematic review and meta-analysis. Front Med (Lausanne). 2021 Feb 5;8:620044. doi: http://dx.doi.org/10.3389/fmed.2021.620044 PMID: 33634150
25. Abu-Raddad LJ, Chemateilly H, Ayoub HH, Yousse FM, Benslimane FM, Al Khatib HA, et al. Association of prior SARS-CoV-2 infection with risk of breakthrough infection following mRNA vaccination in Qatar. JAMA. 2021 Nov 16;326(19):1930–9. doi: http://dx.doi.org/10.1001/jama.2021.19623 PMID: 34724027
26. Rojas-Oxornio SA, Cruz-Hernández TR, Drago-Serrano ME, Campos-Rodríguez R. Immunity to influenza: impact of obesity. Obes Res Clin Pract. 2019 Sep–Oct;13(5):419–29. doi: http://dx.doi.org/10.1016/j.orcp.2019.05.003 PMID: 31542241
27. Fortis A, García-Macedo R, Maldonado-Bernal C, Alarcon-Aguilar F, Cruz M. El papel de la inmunidad innata en la obesidad. Salud Publica Mex. 2012 Mar-Apr;54(2):171–7. Spanish. doi: http://dx.doi.org/10.1590/S0036-36342012000200014 PMID: 22535177
28. Mahamat-Saleh Y, Fiolet T, Rebeaud ME, Mulet M, Guihur A, El Fatouhi D, et al. Diabetes, hypertension, body mass index, smoking and COVID-19-related mortality: a systematic review and meta-analysis of observational studies. BMJ Open. 2021 Oct 25;11(10):e052777. doi: http://dx.doi.org/10.1136/bmjopen-2021-052777 PMID: 34697120
29. Liu L, Ni SY, Yan W, Lu QD, Zhao YM, Xu YK, et al. Mental and neurological disorders and risk of COVID-19 susceptibility, illness severity and mortality: a systematic review, meta-analysis and call for action. EJClinicalMedicine. 2021;40:101111. doi: http://dx.doi.org/10.1016/j.eclinm.2021.101111 PMID: 34514362