COVID-19 Vaccine Effectiveness using Test-Negative Case-Control Study in Severe Acute Respiratory Infections: Results from Eight Provinces in Iran

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COVID-19 situation in Iran and vaccine policies

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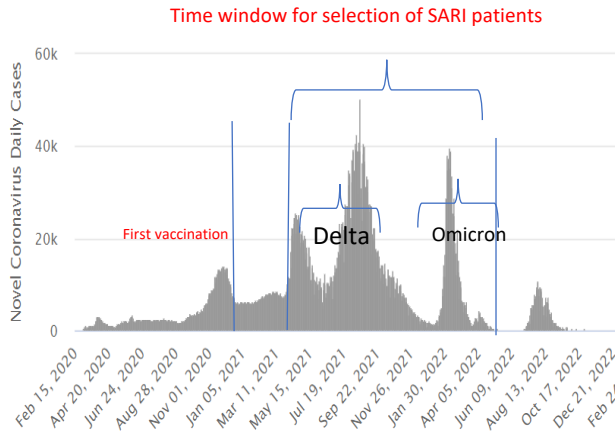
- Total number of confirmed cases till Oct 25, 2023=7,619,981
- First vaccine in 9th Feb, 2021 (11 moths after first COVID-19)
- Proportion of people with complete primary vaccination: 66.2%
- Proportion of people with booster vaccination: 34.02
- People aged ≥ 12 years old were eligible for vaccination



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Available vaccine in Iran

Name	Type	Country
Noora vaccine	Protein subunit	Iran
Soberna 02	Protein subunit	Cuba
Raz Cov Pars	Protein subunit	Iran
Spikogen	Protein subunit	Iran
Sputnik light	Non replicating viral vector	Russia
Sputnik V	Non replicating viral vector	Russia
Vaxzevria	Non replicating viral vector	UK
Covaxin	Inactivated	India
Fakhravac	Inactivated	Iran
COVIran Barekat	Inactivated	Iran
Covilo	Inactivated	China

Study objectives

- Objective 1: To estimate the CVE to reduce the chance of hospitalization, by type of vaccine, demographic variables, and by period of variants circulation
- Objective 2: To estimate the CVE to reduce the chance of sever outcome (ICU admission and/ or death) , by type of vaccine and demographic variables, period of variants circulation

Vaccination status and outcomes

- Exposure of interest:
  - Unvaccinated: A SARI patient is considered unvaccinated if they did not receive the COVID-19 vaccine, received it within 14 days before current hospitalization.
  - Vaccinated with one dose (partially vaccinated): An individual is considered partially vaccinated if they have received one dose of COVID-19 vaccine more than 14 days before the current hospitalization.
  - Fully vaccinated: Patients are considered fully vaccinated if they have received the second dose of the vaccine at least 14 days before current hospitalization.
  - Booster vaccination: Patients with a booster dose if they have received the primary vaccination along with an additional booster dose at least 7 days before current hospitalization.
- Outcome of interest:
  - Hospital admission: at least 24-hour hospital admission with SARI symptoms
  - Sever outcome: any hospital admission to ICU and/or died within hospital

Overview of study

- A test-negative case-control study using registered data
- 8 universities/provinces
- Time window for selecting cases and controls: April 30th, 2021-June 20th, 2022
- The primary sample size was intended to be 30450 SARI cases, but it decreased to 19360 SARI cases
- Data from Medical Care Monitoring Center (MCMC) and Electronic Health Record Portal (SIB) were linked
- Diagnosis of COVID-19 was based on RT-PCRs which have been done within few approved central laboratories within each university/province.

Laboratory methods and selection of cases and controls

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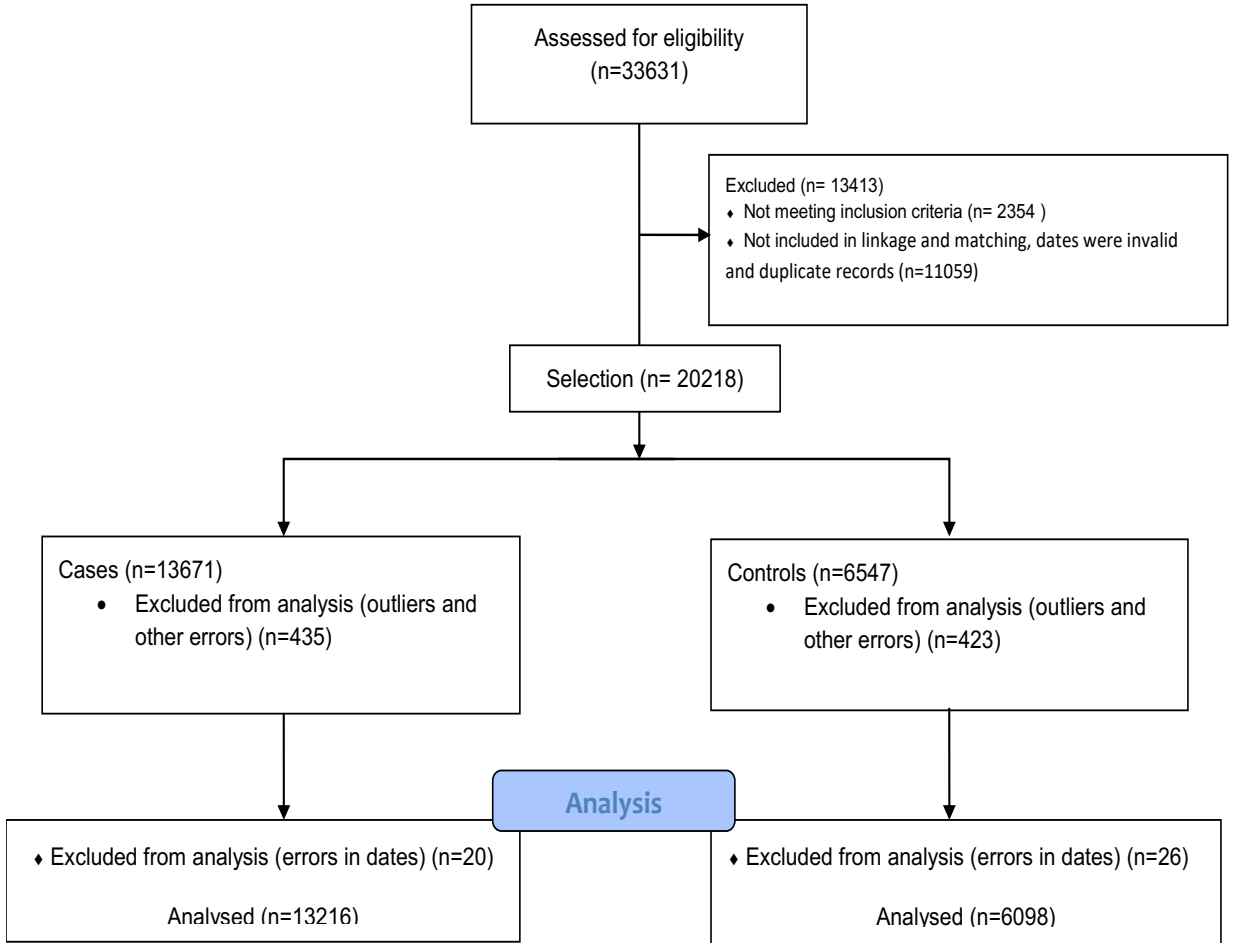
- Laboratory methods: specimen collection within hospital and primary care center
  - RT-PCR within selected and confirmed labs
- Cases defined as a patient hospitalized with SARI symptoms, with a positive RT-PCR, either within 48 hours of hospital admission or documented within 14 days before hospital admission
- Controls defined as patients hospitalized with SARI symptoms, with a negative RT-PCR on hospital admission, up to 48 hours after hospital admission

Selection of cases and controls



Data management and methods

- All participating universities were asked to link these two datasets using national ID.
- To recover missing information in MCMC, the data management team in each university used HIS of each hospital
- In each university, eligible hospitalized patients were classified as cases and controls and matched by hospital and time of hospitalization (no more than two weeks apart)
- Central team checked the quality of data by checking for outliers, impossible ranges, and missing data
- Cases and controls were described and compared using the frequency tables of all important variables, including both numbers and proportion. For continuous variables, median and interquartile range were reported.
- The VE computed as VE = (1 – OR)*100. A 95 % confidence interval computed around the point estimate calculated with univariable and multivariable logistic regression models for both outcomes.
- In order to adjust for confounding variables in multivariable logistic regression, we entered the variables with a p-value less than 0.2 in univariate analysis into the model. Age and number of comorbidities were highly correlated; therefore, we decided not to include comorbidity in the multivariable models

Results

Table 1: Characteristics of cases (n=13216) and controls (n=6098), April 30, 2021 to June 20, 2022, for Iran is among SARI patients

Variables		Number of cases/total 13216 (68.4%)	Number of controls/total 6098 (31.6%)	P value	Total 19314 (100%)
Age groups	12-44	4720(35.7)	2081 (34.1)	<0.001	6801 (35.2)
	45-64	4950 (37.5)	2081 (34.1)		7031 (36.4)
	>=65	3546 (26.8)	1936 (31.8)		5482 (28.4)
Sex	Female	7072 (53.5)	3120 (51.2)	0.002	10192 (52.8)
	Male	6144 (46.5)	2978 (48.8)		9122 (47.2)
Admitted to ICU		2650 (20.1)	1236 (20.3)	0.726	3886 (20.1)
Death		984 (7.4)	329 (5.4)		1313 (6.8)
Comorbidity*	0	9202 (69.6)	4088 (67.0)	<0.001	13290
	1	2501 (18.9)	1172 (19.2)		3673 (19.0)
	>=2	1513 (11.5)	838 (13.7)		2351 (12.2)
the patient has previous admission for COVID19		85 (0.6)	53 (0.9)	0.083	138 (0.7)
Hospital stays, median (IQR)		5 (4-6)	4 (3-6)	<0.001	5 (3-6)
O2 saturation on admission	<90	4520 (34.2)	1933 (31.7)	0.001	6453 (33.4)
	>=90	7305 (55.3)	3140 (51.5)		10445 (54.1)
	Missing	1391(10.5)	1025 (16.8)		2416 (12.5)

Vaccine status

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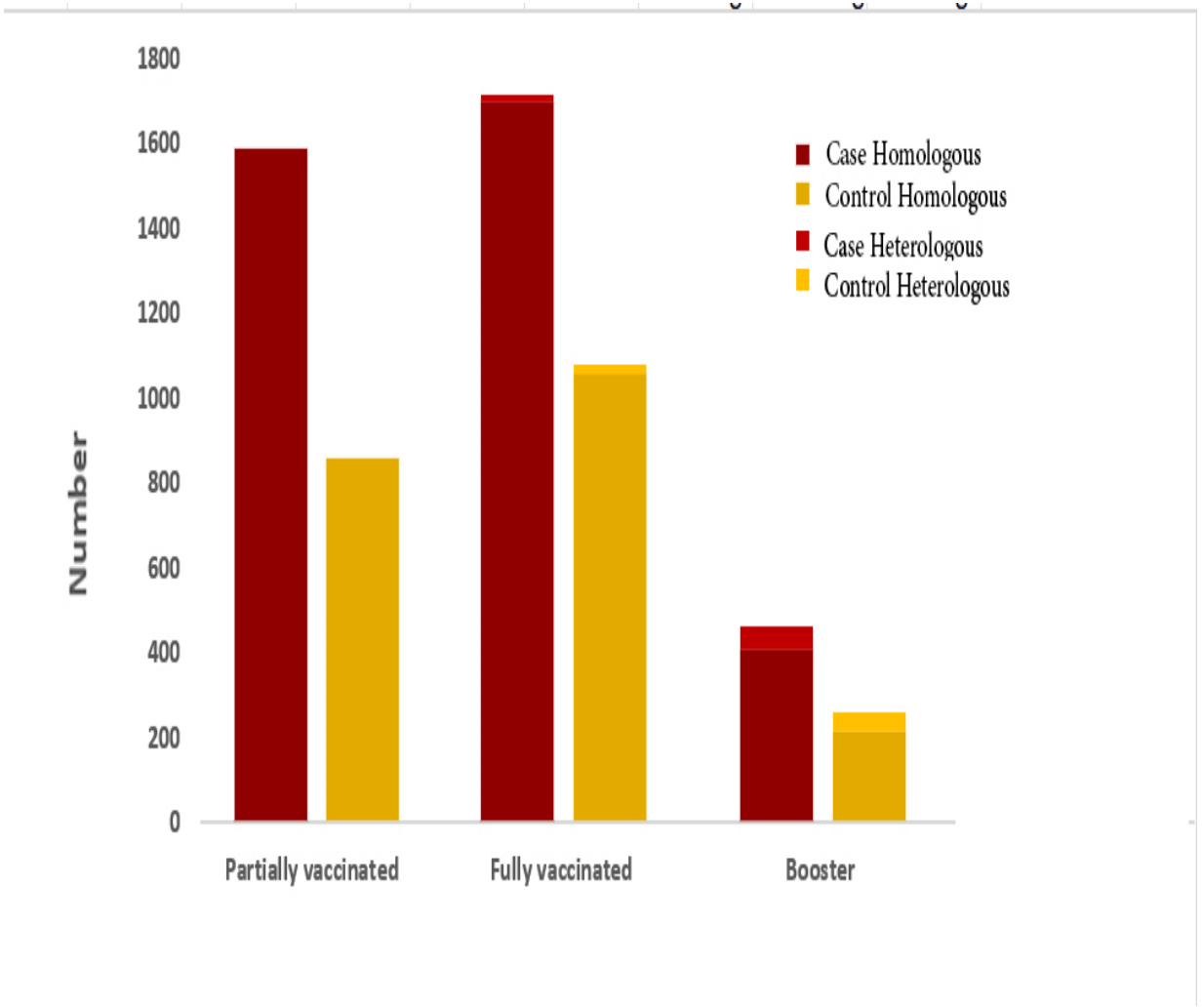
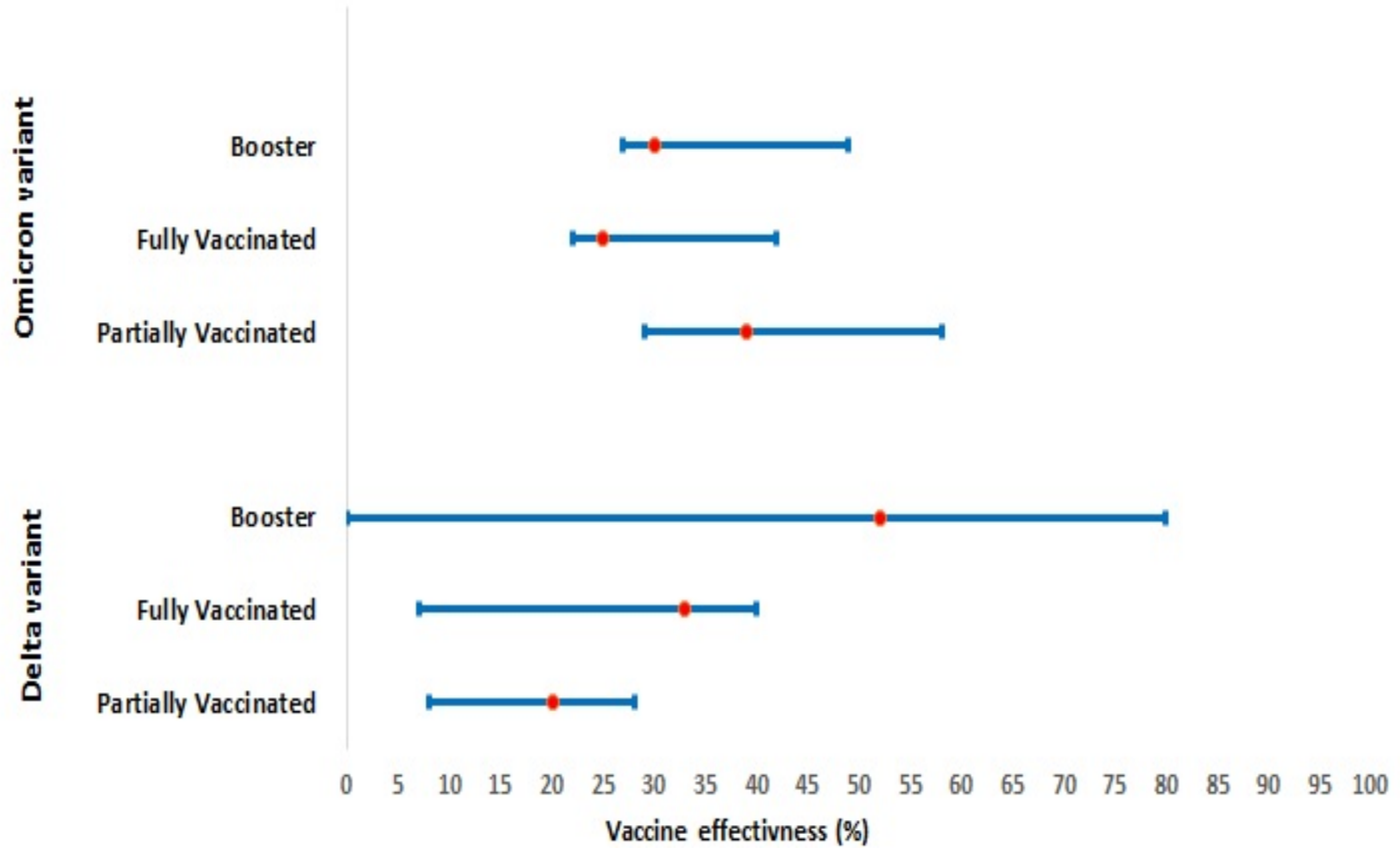
Table 2. Comparison of Vaccination Status between Cases and Controls by Vaccine Brand and Time Interval between Doses

Variables	Category	cases/total 13216 (68.4%)	controls/total 6098 (31.6%)	Total 19314 (100%)
Vaccine status	Un vaccinated	9451 (71.5)	3904 (64.0)	13355 (69.2)
	Partially vaccinated	1587 (12.0)	856 (14.0)	2443 (12.6)
	Fully vaccinated	1717 (13.0)	1079 (17.7)	2796 (14.5)
	Booster	461 (3.5)	259 (4.3)	720 (3.7)
Vaccine combination in fully vaccinated	Homologous	1710 (61.4)	1073 (38.6)	2783 (14.4)
	Heterologous	4 (44.4)	5 (56.6)	9 (0.0005)
Vaccine combination (booster dose)	homologous	419 (90.9)	230 (88.7)	649 (90.2)
	Mix-and-match	42 (9.1)	29 (11.3)	71 (9.8)



Vaccine effectiveness against hospital admission



Vaccine effectiveness against hospital admission

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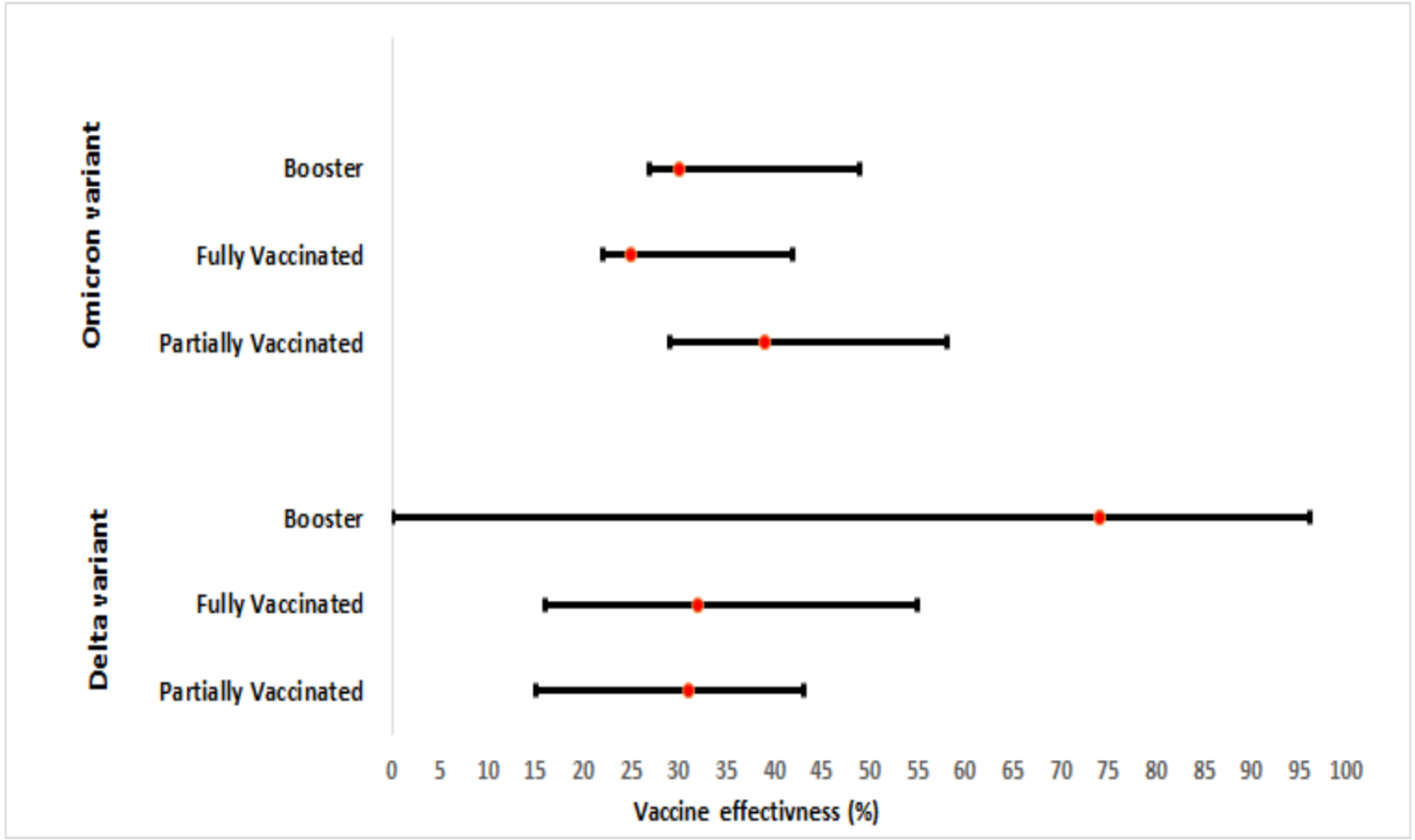
Crude and adjusted vaccine effectiveness against hospital admission, regardless of dominant variant of circulation							
		Total					
Variables	Population or exposure or study period	N (19314)	Cases;vacc / Controls; vacc	Crude VE	CI	Adjusted VE*	CI
All ages	Partially vaccinated	2443	1587/856	24	17-31	22	14-29
	Fully vaccinated	2796	1717/1079	35	29-40	35	29-41
	Booster vaccinated	720	461/259	27	14-38	33	16-47

Vaccine effectiveness against sever outcome



Vaccine effectiveness sever outcome

Crude and adjusted vaccine effectiveness against sever outcome regardless of dominant variant of circulation							
		Total					
Variables	**Population or exposure or study period**	**N (4483)**	**Cases;vacc / Controls; vacc**	**Crude VE**	**CI**	**Adjusted VE***	**CI**
All ages	Partially vaccinated	610	383/227	31	18-43	33	19-44
	Fully vaccinated	717	452/265	31	18-42	34	20-45
	Booster vaccinated	174	120/54	10	-26- 35	20	-29-50

Interpretation and limitations of VE estimates

1. The lower vaccine effectiveness against hospital admission and sever outcomes during the period of Omicron circulation is consistent with findings from other studies.
2. The effectiveness of the vaccine against hospital admission and sever outcomes are decreasing with age, which is consistent with other findings
3. The administration of booster doses is associated with increased effectiveness of the vaccine against hospital admission
4. The effectiveness of all vaccines against severe outcomes has decreased when compared to their effectiveness against hospital admission

limitations

- We used registered data with limited access to the full profiles of patients
  - No trends on oxygen saturation and trajectory of other risk factors
  - The presence of measurement errors is crucial for both the exposure (vaccine) and the classification of cases and controls. This non-differential error leads to an underestimation of the true vaccine effectiveness (VE) in our estimates.
  - In our case-control study, the number of cases is two times of controls. The best scenario for a case-control study is having the equal number of cases and controls.
  - Low coverage of vaccination in our sample did not allow us to calculate the vaccine effectiveness by province.

Conclusion

- The overall effectiveness of vaccines used in Iran was estimated to be less than optimal, partly due to the types of vaccines used and the classification errors inherent in the test-negative case-control study conducted using registered data.
- The progressive evolution of the virus necessitates the generation of new vaccines to be used for future waves.

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Thank you

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