VACCINE EFFECTIVENESS IN HCW AT TERTIARY CARE HOSPITALS OF KP, PAKISTAN: A COHORT STUDY

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COVID-19 situation in country and vaccine policies

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- In Pakistan, as of 25th October 2023, 1,580,631 confirmed cases with 30,656 deaths.

- Seven type of vaccines are approved and available in Pakistan:
  Sinopharm, Sinovac, Astrazeneca, Sputnik V, Pfizer, & Moderna

- Eligibility for vaccination:
  Vaccination in February 2021 in Pakistan. Healthcare workers were prioritized followed by elderly population.

- Variants of concerns in Pakistan:
  S & G clade strains of Wuhan Strain (1st wave)
  B.1 & B.6 variant of south Africa (2nd wave)
  B1.1.7 variant (3rd wave)
  Delta variant (4th wave)
  Omicron variant (5th wave)
  Omicron sub variant (6th wave)

Study objectives

- Primary Objective:
  - To measure VE against symptomatic PCR-confirmed SARS-CoV-2 infection amongst all hospital health workers eligible for vaccination.

- Secondary Objectives:
  - To measure VE against symptomatic PCR-confirmed SARS-CoV-2 infection amongst hospital health care workers eligible for vaccination and without evidence of previous infection (participants without previous infection)

  - To measure VE against symptomatic PCR-confirmed SARS-CoV-2 reinfection amongst hospital health workers eligible for vaccination and with evidence of previous infection (participants with previous infection)

Overview of study

- **Study design:** Retrospective Cohort Study

- **Study sites:** Affiliated teaching hospital of KMU;

(1) Mardan Medical Complex-Mardan; (2) Saidu Teaching Hospital-Swat; (3) DHQ Hospital-Kohat

- **Start, end date:** 20th November 2021-30th December 2022

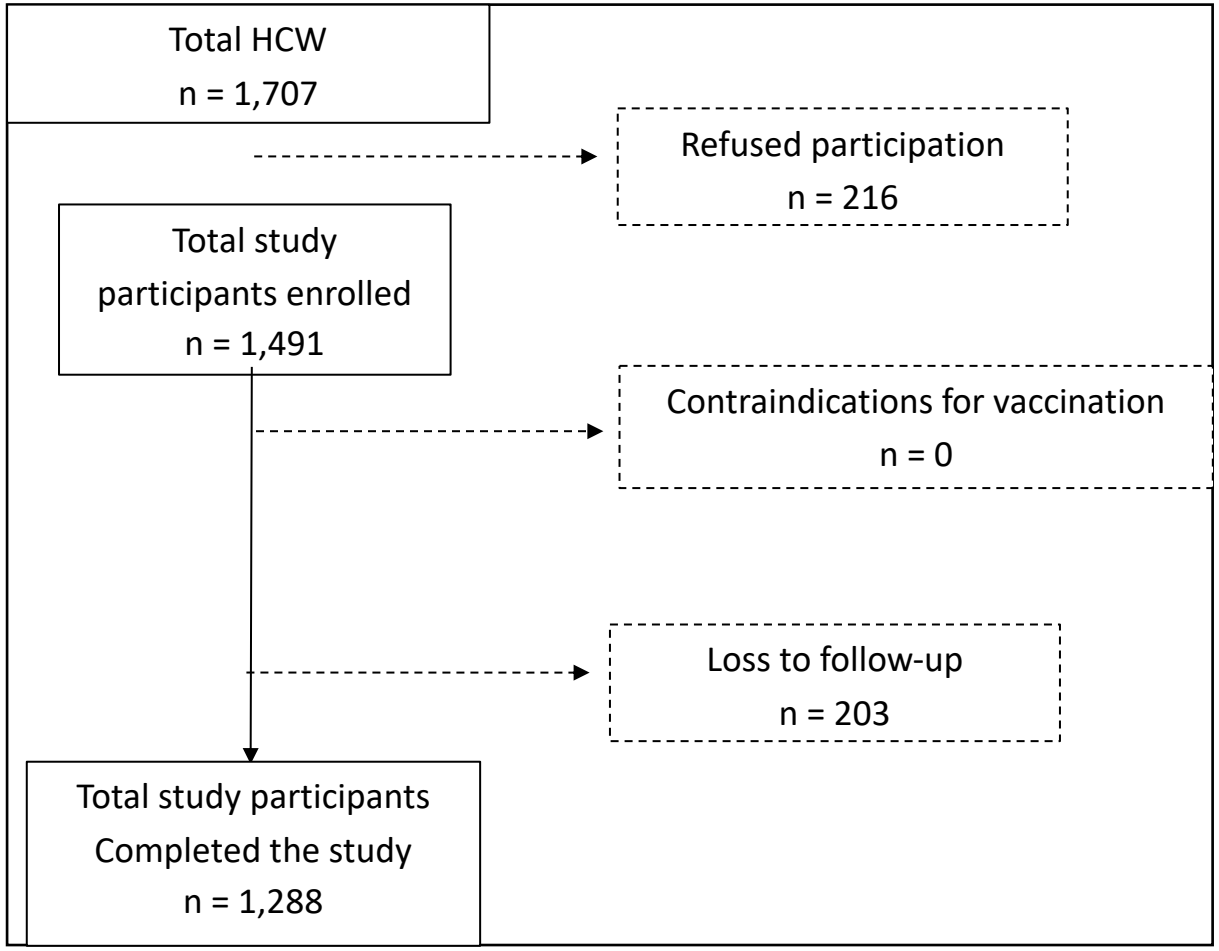
- **Eligibility criteria:** HCW who are working in tertiary care hospitals of the KP Province
- **Active follow-up:** Follow-up period (15 days) and testing timeline (symptoms-based)
  - Definition of "symptomatic infection" SARS-CoV-2 laboratory confirmation by RT-PCR in symptomatic participant, who had any of the following symptoms: acute onset Fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dysponea/SOB, anorexia/nausea/vomiting, diarrhea, altered mental status, anosmia, ageusia, or altered taste.

- **Data collection tools:** In hospital follow-up and on development of symptoms follow-up

- **Laboratory methods:** Rt-PCR test array

Study enrollment and sample size

- **Enrollment procedure** (flowchart, showing sample size, inclusion and exclusion criteria, laboratory methods)
- **Sample size** =1,491



Laboratory methods

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- **Specimen collection:** Nasopharyngeal Swab, Blood Sample (at baseline & Endline only)

- **Specimen storage, shipment and transport:** Storage at the hospital and then transported with WHO-CO to the National Institute of Health Lab Islamabad for testing

- **Specific serology tests used:** Anti-S antibodies for detection of vaccine related antibodies

Data management and methods

- **Data processing after REDCap download**, i.e., secondary variables Age, Gender, Vaccination status, Vaccine type were cleaned and coded according to the original data.

- **Queries raised by the technical team** has been resolved and the final data has been uploaded to the REDCap for pool analysis.

- **Descriptive analysis approach**, Chi-Square test was used to compare the participant characteristics by occurrence of symptomatic COVID-19 infection.

Statistical analysis

- **Measurement of End point for a participant** was defined as either **occurrence of the event**, **refuse to participate** in the study or **completion of the 24th follow-up** of the study.

- **Statistical analyses performed** (i.e. Cox proportional hazards with both adjusted and unadjusted models)
  - Two-dose vaccine effectiveness against symptomatic PCR confirmed COVID-19 infection for full cohort, and stratified by previous infection status.
  - Vaccine effectiveness = 1-HR

- Sensitivity analyses: E-value sensitivity analysis for the HR

Background characteristics Summary

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- We recruited a total of 1,491 participants in this study.
- The overall duration of follow-up for each of the study participant was twelve months (i.e. 24 follow-ups).
- A total of 1,288 study participants completed the study and the loss to follow-up rate was 13.8% (n=203).
- Mean age of the participants was 34.1 (8.6 SD) years and 25.2% (n=373) were female.
- Among the study participants, the prevalence of existing comorbid condition was 6.9% (n=103) and 17.5% (n=262) reported to have COVID-19 infection prior to COVID-19 vaccine administration.

Results: Participant characteristics

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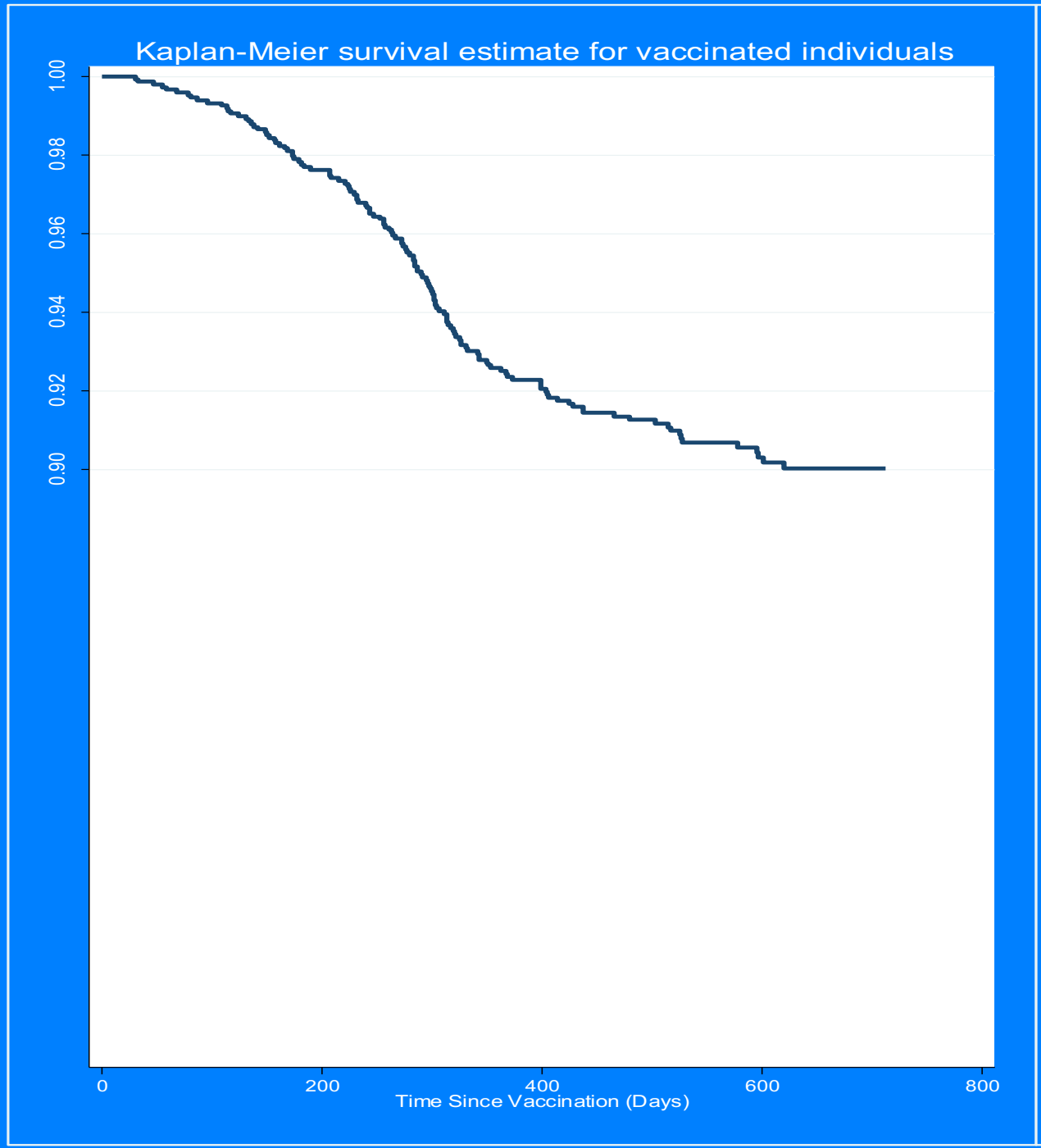
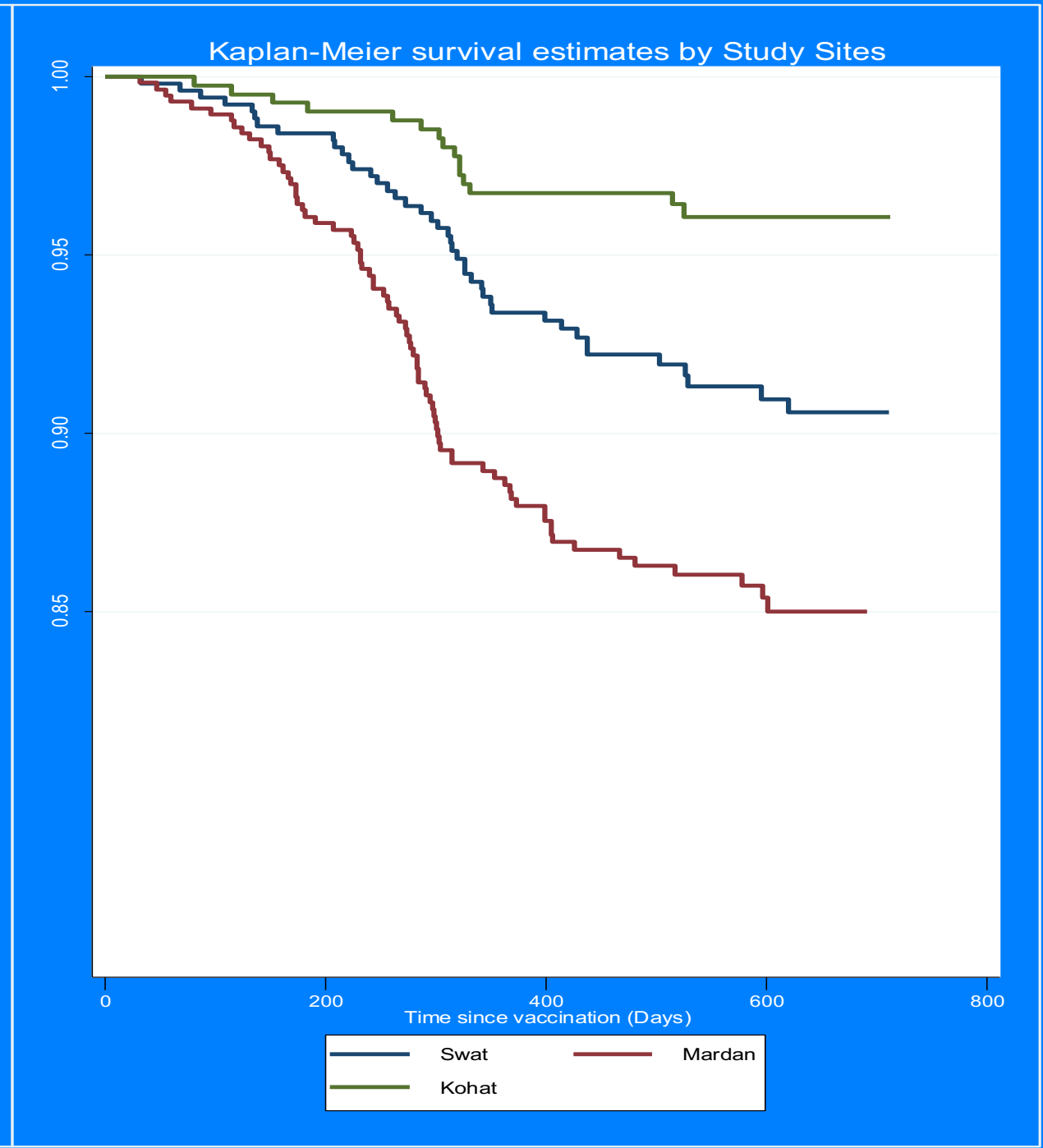
Characteristics of Participants	No Infection N (%) 1,357 (92.15)	Symptomatic COVID-19 Infection N (%) 134 (7.85)	Total N (%) 1,491
Sex			
Female	342 (25.2)	31 (23.13)	373 (25.02)
Male	1,015 (74.8)	103 (76.87)	1,118 (74.98)
Age in years			
19/29	498 (36.7)	48 (35.82)	546 (36.62)
30/39	522 (38.47)	61 (45.52)	583 (39.1)
40/49	242 (17.83)	17 (12.69)	259 (17.37)
50/60	95 (7)	8 (5.97)	103 (6.91)
Study Site			
Swat	467 (34.41)	42 (31.34)	509 (34.14)
Mardan	493 (36.33)	77 (57.46)	570 (38.23)
Kohat	397 (29.26)	15 (11.19)	412 (27.63)
Comorbid condition			
No	1,265 (93.22)	123 (91.79)	1,388 (93.09)
Yes	92 (6.78)	11 (8.21)	103 (6.91)
BMI Asian Cut-off			
Underweight	42 (3.1)	9 (6.72)	51 (3.42)
Normal weight	393 (28.96)	34 (25.37)	427 (28.64)
Overweight	297 (21.89)	25 (18.66)	322 (21.6)
Obese	625 (46.06)	66 (49.25)	691 (46.34)

Results: Participant characteristics (n=1,491)

World Health Organization

Characteristics of Participants	No Infection N (%) 1,357 (92.15)	Symptomatic COVID-19 Infection N (%) 134 (7.85)	Total N (%) 1,491
Smoking Status			
Non-Smoker	1,225 (90.27)	127 (94.78)	1,352 (90.68)
Ex-smoker	19 (1.4)	1 (0.75)	20 (1.34)
Current Smoker	113 (8.33)	6 (4.48)	119 (7.98)
Cadre			
Doctor	395 (29.11)	37 (27.61)	432 (28.97)
Nurses	420 (30.95)	35 (26.12)	455 (30.52)
Paramedical	114 (8.4)	12 (8.96)	126 (8.45)
Other	428 (31.54)	50 (37.31)	478 (32.06)
Previous infection			
No	1,103 (81.28)	106 (79.1)	1,209 (81.09)
Yes	254 (18.72)	28 (20.9)	282 (18.91)
Immunization status			
Partial	75 (5.53)	8 (5.97)	83 (5.57)
Complete	1,282 (94.47)	126 (94.03)	1,408 (94.43)
Type of Vaccine			
Other	66 (4.88)	6 (4.48)	72 (4.84)
Cansino	61 (4.51)	2 (1.49)	63 (4.24)
Sinovac	275 (20.33)	23 (17.16)	298 (20.04)
Sinopharm	951 (70.29)	103 (76.87)	1,054 (70.88)


Kaplan-Meier survival estimate for vaccinated individuals
1.00
0.98
0.96
0.94
0.92
0.90
0
200
400
600
800
Time Since Vaccination (Days)


Kaplan-Meier survival estimates by Study Sites
1.00
0.95
0.90
0.85
0
200
400
600
800
Time since vaccination (Days)
Swat
Mardan
Kohat

Results Obj1: Crude and adjusted VE estimates of the study participants (n=1,491)

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Two doses (all vaccines)	N	Total person-time (days)	Symptomatic COVID-19 PCR-confirmed infections	Incidence per 10,000 person-days	Unadjusted HR	(95% CI)	Adjusted HR	(95% CI)	Adjusted VE %
Total cohort									
Fully vaccinated (≥14d from 2nd dose)	1410	758227	126	1.7	0.74	0.4, 1.5	0.7	0.4, 1.6	30%
Participants without prior infection									
Fully vaccinated (≥14d from 2nd dose)	1162	624230	101	1.6	0.8	0.4, 1.8	0.8	0.3, 1.8	20%
Participants with prior infection									
Fully vaccinated (≥14d from 2nd dose)	248	133997	25	1.9	0.6	0.1, 2.4	0.6	0.1, 2.8	40%
Partially vaccinated (≥14d from 1st dose)	**Reference**								

Results Obj1: Crude and adjusted VE estimates of the study participants (n=1,491)

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	Unadjusted Results			Adjusted Results		
	HR	95% CI	p-value	HR	95% CI	p-value
Male	1.07	0.72, 1.60	0.74	0.98	0.60, 1.60	0.93
Age in Years						
19/29		Reference			Reference	
30/39	1.10	0.75, 1.60	0.63	1.35	0.90, 2.04	0.15
40/49	0.66	0.38, 1.15	0.14	0.82	0.44, 1.50	0.51
50/60	0.75	0.36, 1.60	0.46	1.14	0.50, 2.59	0.76
Study Site						
Swat	**2.39**	**1.32, 4.31**	**<0.001**	**2.42**	**1.29, 4.53**	**0.01**
Mardan	**4.11**	**2.36, 7.15**	**<0.001**	**4.12**	**2.32, 7.31**	**<0.001**
Kohat		Reference			Reference	
Have Comorbidity	1.19	0.64, 2.21	0.57	1.26	0.65, 2.43	0.50
Have no comorbidity		Reference			Reference	
BMI Asian Cut-offs						
Underweight	**2.44**	**1.17, 5.08**	**0.02**	**2.26**	**1.07, 4.79**	**0.03**
Normal Weight		Reference			Reference	
Overweight	0.97	0.58, 1.63	0.92	0.88	0.52, 1.49	0.64
Obese	1.16	0.77, 1.76	0.48	1.08	0.70, 1.65	0.74
Working Department						
Emergency	**0.20**	**0.06, 0.62**	**0.01**	**0.19**	**0.06, 0.61**	**0.01**
Surgical	1.14	0.64, 2.02	0.65	0.99	0.54, 1.83	0.99
Critical Unit	1.13	0.50, 2.57	0.76	1.13	0.49, 2.64	0.77
Medicine	1.21	0.70, 2.10	0.50	1.12	0.62, 2.03	0.71
Have previous infection	1.12	0.74, 1.70	0.59	1.03	0.67, 1.57	0.90
Fully immunized	0.74	0.36, 1.52	0.42	0.96	0.44, 2.09	0.92

Results: Crude and adjusted VE estimates: Participants having no prior infection (n= 1,209)

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	Unadjusted Results			Adjusted Results		
	HR	95% CI	p-value	HR	95% CI	p-value
Male	1.07	0.67, 1.70	0.78	0.98	0.55, 1.72	0.93
Age in years						
19/29		Reference			Reference	
30/39	1.22	0.79, 1.89	0.37	1.51	0.95, 2.39	0.08
40/49	0.83	0.46, 1.53	0.56	1.06	0.55, 2.05	0.85
50/60	0.99	0.46, 2.13	0.97	1.48	0.61, 3.59	0.39
Study Site						
Swat	**2.34**	**1.24, 4.42**	**0.01**	**2.50**	**1.26, 4.96**	**0.01**
Mardan	**3.76**	**2.06, 6.87**	**<0.001**	**4.06**	**2.17, 7.57**	**<0.001**
Kohat						
Having Co-morbidity	1.26	0.64, 2.49	0.51	1.16	0.55, 2.43	0.70
BMI Asian Cut-offs						
Underweight	2.23	0.92, 5.42	0.08	1.99	0.80, 4.95	0.14
Normal Weight						
Overweight	1.00	0.55, 1.80	0.99	0.88	0.48, 1.60	0.68
Obese	1.31	0.82, 2.09	0.26	1.18	0.73, 1.92	0.50
Working Department						
Emergency	**0.16**	**0.04, 0.65**	**0.01**	**0.16**	**0.04, 0.64**	**0.01**
Surgical	1.22	0.65, 2.27	0.54	1.08	0.55, 2.11	0.83
Critical Unit	1.39	0.57, 3.41	0.47	1.50	0.60, 3.76	0.39
Medicine	1.42	0.78, 2.58	0.26	1.39	0.73, 2.64	0.32
Cadre	0.86	0.51, 1.44	0.56	0.71	0.39, 1.31	0.28
Fully Immunized	0.80	0.35, 1.82	0.59	0.99	0.41, 2.39	0.98

Interpretation VE estimates

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- Over the course of the study, a total of **1,962 times symptoms** were developed by the study participants and all of these were tested with RT-PCR Assay test for diagnosis of COVID-19.

- Among the study participants, the **incidence of symptomatic COVID-19 infection was 10% (n=134)** over the 12-month follow-up.
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- The **overall vaccine effectiveness** over a period of two years was **30%** (95%CI 0-60). Among the participants having **no history of COVID-19 infection,** the overall vaccine effectiveness was **20%** (95% CI 0-70) while it was **40%** (95% CI 0-90)among those **who has COVID-19 infection prior to vaccination**.

- Among the incident cases of COVID-19, all of the **cases developed mild infection of SARS-CoV-2** and **none of these were admitted to the hospital.**

- On the multivariate cox proportional hazard model for the overall study participants, there was increased risk for the symptomatic COVID-19 infection in participants from **Mardan study site (HR: 4.12, 95% CI 2.32, 7.31)** and **Swat study site (HR: 2.42, 95% CI 1.29, 4.53)** and participants who were **underweight** on BMI Asian Cut-offs **(HR: 2.26, 95% CI 1.07, 4.79).**
- This association remained the same for participants who had no previous infection of COVID-19.

Limitations of VE estimates

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- History of COVID-19 prior to vaccination for COVID-19, majority diagnosed with agRDT and not further confirmed with the RT-PCR Assay test for COVID-19.

- Vaccine administration prior to the study could have resulted in under reporting of the vaccine effectiveness as the mean duration since vaccination is 585 days and first quarter of the duration is 458 days for 25% of the participants.

- Among the vaccine administered, majority were sinopharm and sinovac. The under reporting of other vaccines may result in low effectiveness of the vaccination.

- The increased number of cases in the first four months of 2022 may have been attributed to Omicron variant of SARS-COV-2 but we couldn’t perform the sequencing to further confirm its existing during that period.

Conclusion and recommendations

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- Conclusion:
  - Vaccination of COVID-19 proved to be effective against symptomatic COVID-19 infections in workers working in tertiary care hospitals of Pakistan. Booster dose of a COVID-19 vaccine provided additional benefit in reducing the symptomatic COVID-19 infection *(although p-value>0.05)*

- Recommendation:
  - All eligible adults should receive booster doses of an mRNA vaccine to boost their immunity against SARS-CoV-2.
  - The registration for the COVID-19 vaccination must be completed to ensure that all the participants have received the required vaccination.
  - All the health care workers (despite the cadre) working in health facilities must adopt the required SOPs for infection prevention and control measure while working in the hospitals for their own and patients' safety.

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Thank you

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