Effectiveness of BBIBP-CorV vaccine against severe outcomes of COVID-19 in Abu Dhabi, United Arab Emirates

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Background

- UAE collaborated with China's National Biotec Group for a phase III trial of the Sinopharm (BBIBP-CorV) vaccine.
- The vaccine was developed from the HB02 strain of SARS-CoV-2, inactivated with beta-propiolactone, and mixed with an aluminum-based adjuvant.
- The phase III trial found that two doses of the BBIBP-CorV vaccine, given three weeks apart, were 78% effective in preventing symptomatic COVID-19.
- The UAE government granted emergency approval for frontline workers in September 2020 and for public use in December 2020.
- The World Health Organization also approved the vaccine for global emergency use.
- UAE has one of the highest COVID-19 vaccination rates worldwide

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Methods (study design)

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Study population and design:	**Outcomes and covariates:**
• Retrospective cohort study in Abu Dhabi, UAE. • Included individuals aged 18 and older. • Data extracted from SEHA and Malaffi databases. • SEHA operates public healthcare facilities, provides COVID-19 vaccination, manages vaccine-related issues, and runs COVID-19 hospitals in Abu Dhabi.	• Investigated vaccine effectiveness for three COVID-19 outcomes: **hospitalization, critical care unit admission, and COVID-19–related death.** • Participants followed for three months from the baseline date (defined as 14 days after the second vaccine dose). • Adjusted vaccine effectiveness for covariates: age, sex, comorbidity, ethnicity, and entry month into the study. • Study period divided into three calendar month groups: Oct-Dec 2020, Jan-Apr 2021, and May-Jul 2021.

Methods (study design)

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Statistical analysis:

- Descriptive statistics summarized baseline characteristics (mean and SD for continuous, frequency tables for categorical).
- Compared categorical variables with Chi-squared or Fisher's exact tests.
- Compared continuous variables using unpaired t tests or, when necessary, Wilcoxon rank sum tests if normality assumption violated.

Matching procedure:

- Used Rolling Entry Matching (REM) in a 1:1 ratio.
- Vaccinated individuals completed their second dose before July 1, 2021.
- Unvaccinated individuals had not received any COVID-19 vaccine by the same date.
- Matched based on age, sex, ethnicity, and comorbidities.
- REM matched based on the entry date into the study (14 days after the second dose) to ensure the same exposure duration.
- Followed all individuals until September 30, 2021.

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Methods (study design)

Estimation of vaccine effectiveness:

- Used a Cox-proportional hazard model with time-varying coefficients to account for the proportional hazard assumption and the decline in vaccine effectiveness over time.
- For each of the three COVID-19 outcomes (hospital admission, critical care admission, death), measured the time from the baseline date to the event occurrence (in days).
- Excluded vaccinated individuals with less than two weeks between their 1st and 2nd vaccine dose, and those with a prior history of COVID-19 hospitalization.
- Removed individuals matched to these exclusions to maintain matching balance.
- Focused on participants with no prior history of COVID-19 outcomes for survival analysis.

Study objective:

- Evaluate real-world effectiveness of two doses of the inactivated BBIBP-CorV vaccine in preventing severe COVID-19 outcomes, such as hospital admissions, critical care admissions, and COVID-19 related deaths over a three-month period in Abu Dhabi, UAE.
- Assess vaccine effectiveness decline over time for each studied COVID-19 outcome.

Results
Study population and matching

- 1,832,583 individuals received two doses of inactivated BBIBP-CorV vaccine and completed their second dose before July 1st, 2021.
- 1,315,286 unvaccinated controls had not received any vaccine before July 1st, 2021.
- A Rolling Entry Matching (REM) procedure was used to match 1,153,515 vaccinated individuals with an equal number of unvaccinated controls.
- The matching was based on age and sex, resulting in a 1:1 ratio between the two groups.

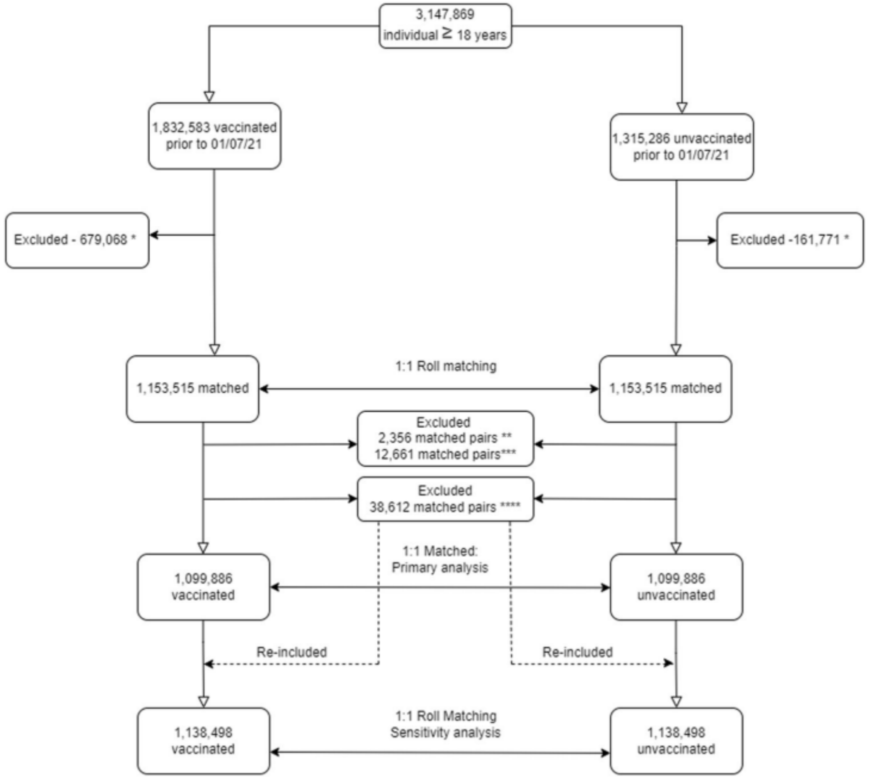

Fig. 1 Flowchart of study population and matching process. *Were not matched. **Vaccinated individuals with the interval between 1st and 2nd dose less than 2 weeks. Their corresponding matched unvaccinated individuals were also excluded. ***Individuals (Vaccinated & Unvaccinated) who had hospital admission prior to their baseline dates. Their corresponding matched individuals (Vaccinated & Unvaccinated) were also excluded. ****Unvaccinated individuals who received their first dose of the vaccine during their follow-up period (i.e. after their baseline date). Their corresponding matched vaccinated individuals were also excluded.

Results

Table 1 Demographic and Clinical Characteristics of the study participants at baseline.

Characteristics	Overall (*n*=2,199,772)	Non-vaccinated (*n* = 1,099,886)	Vaccinated (*n* = 1,099,886)
Median age (IQR)	35 (28-43)	34 (28-43)	35 (29-43)
Age group *n* (%)			
Less than 40 years	1,447,391 (66)	728,893 (66)	718,498 (65)
40-60 years	648,813 (29)	309,459 (28)	339,354 (31)
More than 60 years	103,568 (4.7)	61,534 (5.6)	42,034 (3.8)
Sex *n* (%)			
Female	798,999 (36)	397,981 (36)	401,018 (36)
Male	1,400,773 (64)	701,905 (64)	698,868 (64)
Ethnicity *n* (%)			
Arab	760,211 (35)	375,887 (34)	384,324 (35)
Asian	1,209,118 (55)	605,694 (55)	603,424 (55)
Other	230,443 (10)	118,305 (11)	112,138 (10)
Comorbidities *n* (%)			
Asthma	25,581 (1.2)	11,412 (1.0)	14,169 (1.3)
Chronic kidney disease	17,321 (0.8)	8055 (0.7)	9266 (0.8)
Diabetes	83,583 (3.8)	40,112 (3.6)	43,471 (4.0)
Heart disease	13,934 (0.6)	6433 (0.6)	7501 (0.7)
Hypertension	47,841 (2.2)	22,812 (2.1)	25,029 (2.3)
Immunodeficiencies	2641 (0.1)	1271 (0.1)	1370 (0.1)
Neoplasms	19,356 (0.9)	9525 (0.9)	9831 (0.9)
Respiratory diseases	3542 (0.2)	1680 (0.2)	1862 (0.2)
History of transplantation	1308 (<0.1)	656 (<0.1)	652 (<0.1)
Comorbidities *n* (%)			
No comorbidity	2,076,268 (94)	1,044,356 (95)	1,031,912 (94)
One comorbidity	70,096 (3.2)	29,750 (2.7)	40,346 (3.7)
2 or more comorbidities	53,408 (2.4)	25,780 (2.3)	27,628 (2.5)
Months of observation *n* (%)			
Oct-Dec 2020	131,850 (6.0)	65,925 (6.0)	65,925 (6.0)
Jan-April 2021	1,774,370 (81)	887,185 (81)	887,185 (81)
May-July 2021	293,552 (13)	146,776 (13)	146,776 (13)
Month of observation *n* (%)			
October 2020	1238 (<0.1)	619 (<0.1)	619 (<0.1)
November 2020	64,340 (2.9)	32,170 (2.9)	32,170 (2.9)
December 2020	66,272 (3.0)	33,136 (3.0)	33,136 (3.0)
January 2021	247,616 (11)	123,808 (11)	123,808 (11)
February 2021	801,792 (36)	400,896 (36)	400,896 (36)
March 2021	392,396 (18)	196,198 (18)	196,198 (18)
April 2021	115,710 (5.3)	57,855 (5.3)	57,855 (5.3)
May 2021	216,856 (9.9)	108,428 (9.9)	108,428 (9.9)
June 2021	192,334 (8.7)	96,167 (8.7)	96,167 (8.7)
July 2021	101,218 (4.6)	50,609 (4.6)	50,609 (4.6)

Details of ethnicities included in the other group are listed in Supplementary Table 11.

Results:
Overall effectiveness

- During the follow-up period of three months, there were
  - 3505 COVID-19 related hospitalizations (2889 in unvaccinated compared to 616 in vaccinated),
  - 653 critical care admissions (574 in unvaccinated compared to 79 in vaccinated), and
  - 99 deaths (87 in unvaccinated versus 12 in vaccinated) documented.

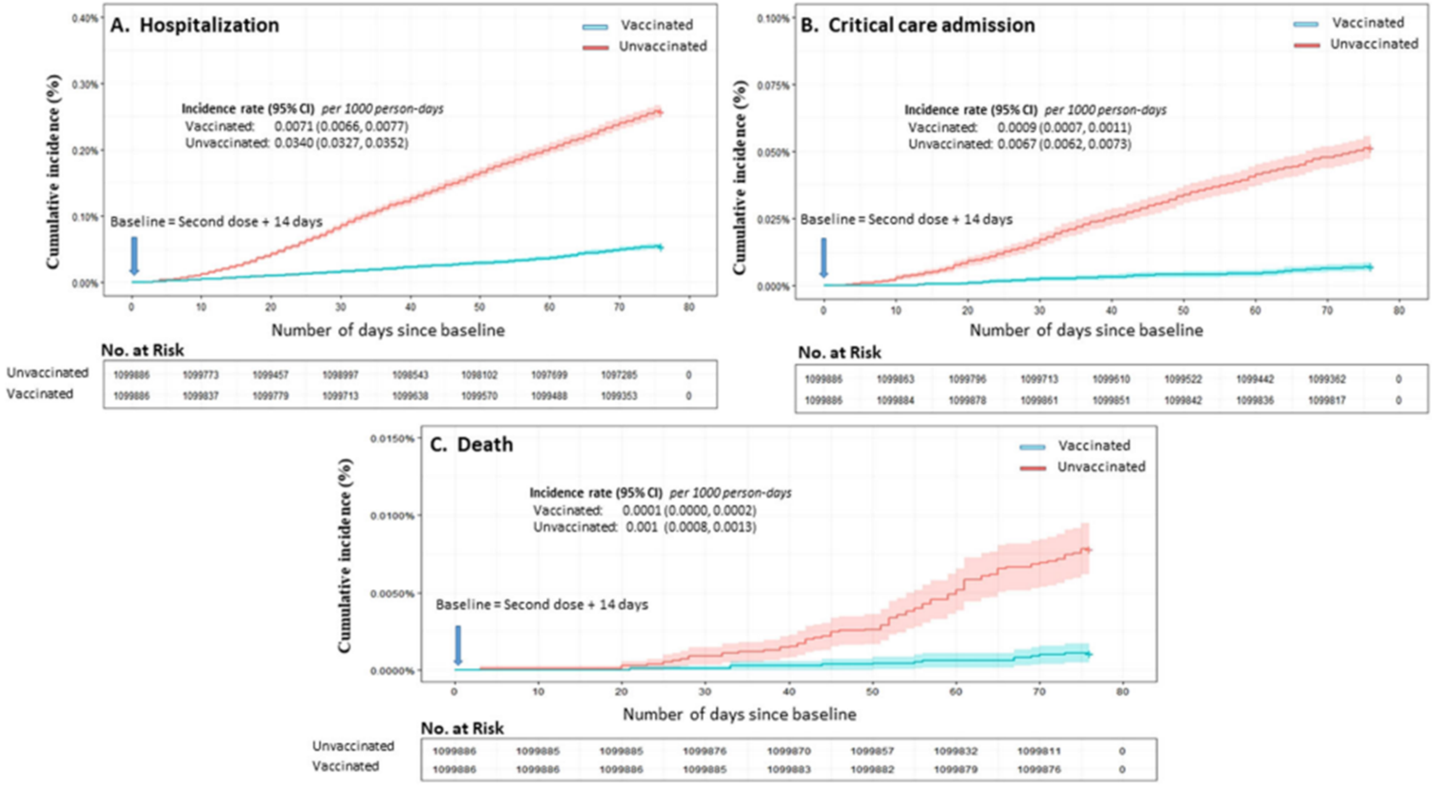

Fig. 2 Cumulative incidence of severe outcomes of COVID-19. The blue curve represents vaccinated subjects and the red curve represents unvaccinated individuals. The error bands represent the 95% confidence intervals. The No. at Risk table in each plot represents the number of participants at risk for the outcome at given follow-up times. **A** The cumulative incidence curve of hospitalization. **B** The cumulative incidence curve of critical care admission. **C** The cumulative incidence curve of death.

Results:
Vaccine effectiveness

Vaccine effectiveness at three months post complete vaccination:

- **79.6%** against COVID-19 related hospitalization (95% CI, 77.7–81.3, P < 0.001)
- **86%** against critical care admission (95% CI, 82.2–89.0, P < 0.001)
- **84.1%** against death (95% CI, 70.8–91.3, P < 0.001)

Results:
Effectiveness according to different risk factors

- **For hospital admission**: Age, sex, comorbidity, and the month of study entry had significant interactions.
- **For critical care admission**: Significant interactions were observed with sex, comorbidity, and the month of study entry.
- **For COVID-19 mortality**: Significant interactions were noted with comorbidity and the month of study entry.
- COVID-19 hospitalization effectiveness was higher in females (82.3%) compared to males ($p < 0.001$) and in individuals below 60 years old (84.7%) compared to those above 60 years of age ($p < 0.001$).

Results:
Effectiveness according to different risk factors

COVID-19 hospitalization:

- Higher effectiveness in females (82.3%) compared to males ($p < 0.001$).
- Higher effectiveness in individuals below 60 years old (84.7%) compared to those above 60 years of age ($p < 0.001$).
- Higher effectiveness among individuals with comorbidities (83.5%) compared to those without comorbid conditions ($p < 0.001$).
- Higher effectiveness during the months of October through December 2020 (97.5%) compared to the months between January 2021 and July 2021 ($p < 0.001$).

Critical care admission:

- Higher effectiveness among males (89.3%) compared to females ($p < 0.001$).
- Higher effectiveness in individuals with comorbidities (88.7%) compared to those without comorbidities ($p < 0.001$).
- Higher effectiveness during the months of October through December 2020 (98.8%) compared to the period between January 2021 and July 2021 ($p < 0.001$).

Death due to COVID-19:

- Highest effectiveness observed for patients with comorbidities (97.1%, $p < 0.001$)
- Higher effectiveness during the months of October through December 2020 (99.9%, $p < 0.001$).

The waning of effectiveness

- COVID-19 hospitalization effectiveness declined from **82.8%** at two months post complete vaccination to **62.1%** at six months post vaccination.
- While there was a gradual decline in vaccine effectiveness against COVID-19 hospitalization from two to six months, **no further decline occurred beyond six months.**
- Waning of protection was also observed in critical care admission. The effectiveness declined from **85.7%** at two months after complete vaccination to **72.8%** at six months post vaccination, without further decline from seven to twelve months post-vaccination.
- The decline in effectiveness against critical care admission was smaller compared to the decline in hospitalization effectiveness.

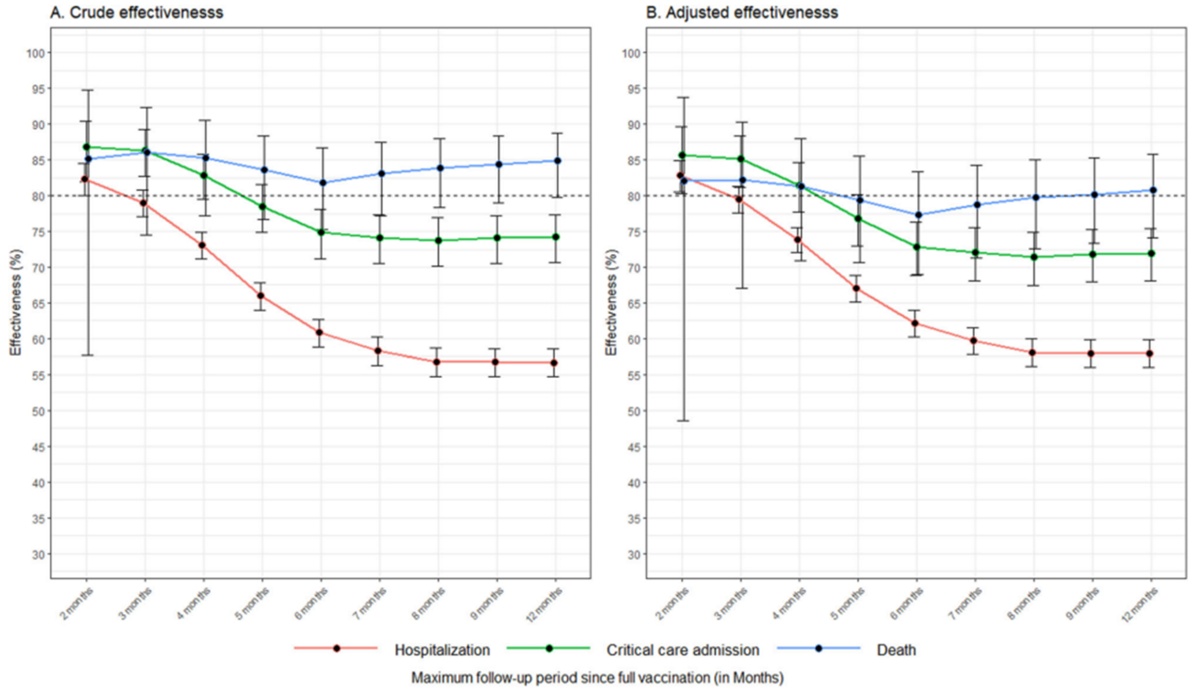

Fig. 3 Decline in vaccine effectiveness over 12 months of follow up. Vaccine effectiveness estimated at increasing follow-up periods using the Cox proportional hazard regression model. The red, green and blue curves indicate hospitalization, critical care admission and death respectively. Error bars represent the 95% confidence intervals of the true effectiveness, $n = 2{,}199{,}772$ individuals (1,099,886 vaccinated and 1,099,866 unvaccinated matched controls). **A** Effectiveness estimated without adjustment. **B** Effectiveness estimated adjusting for age, sex, presence of comorbidity, ethnicity, and the calendar month of entry into the study.

Discussion-1

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- The study's findings indicated lower effectiveness compared to a secondary analysis of the phase III trial, which reported 100% efficacy against severe COVID-19 cases, including both severe cases and deaths.
- The disparity in effectiveness may be attributed to the fact that the study used **real-world data**, **including high-risk populations**, and had **a longer follow-up period**, whereas the phase III trial had a median follow-up of only 77 days
- The **emergence of newer variants of concern of SARS-CoV-2** virus during this study period, which have been shown to escape vaccine-induced antibodies, may have also contributed to the lower effectiveness

Discussion-2

- We found that Vaccine effectiveness against hospitalization decreases with age, especially in the older (≥60 years) group.
- This aligns with other studies showing a link between COVID-19 vaccine effectiveness and age.
- The vaccine effectiveness in the older age group might be underestimated because AD- UAE regulations required hospitalization of all individuals above 65 with positive SARS-CoV-2 PCR tests, regardless of vaccination status, to protect this vulnerable population.
- Fewer deaths compared to other studies.
  - Could be due to proactive measures in Abu Dhabi, including hospitalizing high-risk patients regardless of symptoms or insurance.
  - All COVID-19 patients received standardized treatment in dedicated hospitals.

Discussion -3

- Vaccine effectiveness was notably high from October to December 2020, as this period coincided with the emergency use authorization vaccination rollout for frontline workers in the UAE and predated the emergence of concerning virus variants.
- The decline in vaccine effectiveness measured in three-month intervals during January to June 2021 is likely linked to the appearance of new SARS-CoV-2 variants, some of which were more transmissible and posed higher health risks

Discussion -4

- The twelve months follow-up revealed that the effectiveness of the vaccine started to decline after three months
- The decline in effectiveness is likely due:
  - to antigenic changes in newer SARS-CoV-2 variants that evade the vaccine-induced immune response.
  - This decline is also associated with a reduction in antibody levels, as observed in previous studies
- These findings provide a good rationale for the administration of booster doses in preventing severe outcomes of COVID-19

Study strengths:

- Utilized a large, comprehensive data set covering the entire population of Abu Dhabi.
- Matched data for age, sex, comorbidities, ethnicity, and observation month for standardized comparisons and reduced confounding factors.
- Provided a nearly 12-month follow-up period for precise estimation of overall effectiveness, effectiveness across risk factors, and waning of effectiveness over time.
- Measured vaccine effectiveness in three-month intervals (October–December 2020, January–April 2021, and May–July 2021), enabling control for waning effectiveness and the impact of variants of concern (wild-type virus, alpha variant, delta variant).

Study limitations:

- Focused solely on hospitalization, critical care admission, and death as outcomes, not assessing vaccine effectiveness against other outcomes like symptomatic infections or organ injury.
- Adjusted for factors like age, sex, ethnicity, and comorbidities but did not consider potential influencers like obesity, smoking, and occupation.
- Although we analyzed the decline in vaccine effectiveness over time, we couldn't entirely rule out the impact of changing circulating variants on waning effectiveness.
- Did not include infections as an outcome because of extensive COVID-19 screening in the UAE; the study primarily focused on severe and hospitalized COVID-19 cases for public health relevance.

Thank you

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