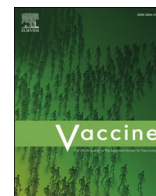


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Effectiveness of COVID-19 vaccine against SARS-CoV-2 infection among symptomatic COVID-19 patients in Uganda

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ABSTRACT

Background: COVID-19 vaccines significantly reduce severe disease outcomes, but uncertainty remains about long-term protection. We investigated vaccine effectiveness (VE) against SARS-CoV-2 infection over extended periods in the World Health Organisation AFRO-MoVE network studies in Africa.

Methods: Participants with COVID-19-like symptoms were recruited between 2023 and 2024 for a test-negative case-control study conducted across 19-healthcare centres in Uganda. Cases were symptomatic patients with any three of cough, sore-throat, coryza, among others, and PCR-confirmed SARS-CoV-2, while controls were SARS-CoV-2 PCR-negative. Vaccination was verified from vaccination cards, hospital-records, vaccination registry and self-reporting. VE was assessed through three measures: (a) Annual - patients vaccinated in the past 12-months regardless of dose vs those vaccinated >12-months before symptom onset plus unvaccinated; (b) Absolute - patients vaccinated in the past 12-months vs unvaccinated; and (c) Relative - patients vaccinated in the past 12-months vs those vaccinated >12-months before symptom onset. VE was calculated as 1- adjusted odds ratio for three patient groups based on days since the last dose; (1) <365, (2) 7–269 and (3) 270–364 while adjusting for age, sex, calendar-time and chronic conditions. The sensitivity analysis excluded patients that were previously infected with SARS-CoV-2.

Findings: In total, 1371 patients, 56 % female were recruited. Of these, 173 were classified as cases, with 97 (56 %) fully vaccinated compared to 701 (59 %) controls, $p = 0.830$. The overall adjusted VE was moderate, 45 % to 59 %, and remained consistent across the annual, absolute and relative measures. Sensitivity analysis showed consistently lower VE (32 % to 38 %) across all measures.

Interpretation: The results suggest that COVID-19 vaccination provides moderate protection against symptomatic SARS-CoV-2 infection up to 12-months after the last dose and highlight the importance of up-to-date vaccinations for high-risk individuals. The lack of clear COVID-19 seasonality in this and other African settings creates a challenge to selecting the optimal timing for annual vaccination.

Abbreviations: AFRO-MoVE, African Region Monitoring Vaccine Effectiveness; CA, California; COVID-19, Coronavirus Disease; KM, Kilometer; LSHTM, London School of Hygiene and Tropical Medicine; MRC, Medical Research Council; PCR, Polymerase Chain Reaction; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; USA, United States of America; UVRI, Uganda Virus Research Institute; VE, Vaccine Effectiveness; WHO, World Health Organisation.

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1. Introduction

The first coronavirus disease (COVID-19) case in Africa was reported in February 2020, with Uganda reporting her first case a month later [1]. Access to COVID-19 vaccines for African countries including Uganda was delayed until March 2021 [2], in contrast to regions like Europe, where countries like the United Kingdom began vaccinations as early as December 2020 [3]. Due to this delay, Uganda relied heavily on lockdowns and movement restrictions both within the country and across borders to curb severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission, measures that severely impacted economic livelihoods. Uganda's vaccination campaign began in March 2021, primarily using AstraZeneca ChAdOx1 vaccine and targeting groups at higher risk of infection such as frontline healthcare workers, security personnel, older adults, and individuals with chronic illnesses [2]. Later, other vaccines, including Pfizer (BNT162b2), Johnson & Johnson (Ad26.COV2.S), Moderna (mRNA-1273) and Sinopharm (BBIBP-CorV) were made available targeting the general population.

In March 2023, the Ministry of Health in Uganda established a multisectoral, multidisciplinary national COVID-19 task force to strengthen leadership and coordination of preparedness and response efforts including guiding the vaccination programme [4]. Although the vaccine uptake was lower than expected, the programme facilitated the easing of lockdowns. Towards the end of 2021, the Government of Uganda recommended COVID-19 vaccination for all eligible individuals aged at least 12 years. However, by June 2022, uptake remained low at 64 % with significant regional disparities [2]. Currently, uptake of these vaccines has slowed down substantially.

The introduction of COVID-19 vaccines significantly reduced severe disease outcomes such as hospitalisations and death [2,5,6]. Studies have reported strong vaccine effectiveness (VE), more than 80 % against COVID-19 (symptomatic disease) mainly in the developed world in the short, 6 months [7,8] and long term, 12 months [8] following

vaccination. These have not been studied in Uganda and many other African countries more so in the extended period. There is evidence that the effectiveness of some vaccines varies, being 20–50 % lower in Low- and Middle-Income countries [5]. There is limited literature on assessment of COVID-19 VE against SARS-CoV-2 infection in the medium to long term in Africa.

In early 2023, the World Health Organisation (WHO) through the African Region Monitoring Vaccine Effectiveness (AFRO-MoVE) network initiated a study in Africa to measure COVID-19 VE. We utilized data from the network's sites in Uganda to evaluate annual, absolute and relative measures of COVID-19 VE.

2. Methods

Study design: A test-negative case-control vaccine effectiveness (VE) study conducted to assess SARS-CoV-2 VE.

Study sites: Nineteen healthcare centres in six districts in Uganda; Lyantonde (1), Kyotera (1), Kalungu (2), and Masaka (3), primarily rural farming communities, located between 120 and 200 km to the southwest of Kampala, the capital; and Wakiso (5), partly encircling the capital, and Kampala (7), both predominantly urban populations in central Uganda (Fig. 1).

The healthcare centres were selected based on their willingness to participate, links to ongoing research projects, and prior designation as COVID-19 treatment centres or influenza sentinel surveillance sites.

Study population: Patients with SARS-CoV-2-like symptoms (defined below) who presented at designated study sites between 22 March 2023 and 26 March 2024.

Case-control definition: Cases were defined as patients aged 12 years and older who presented with COVID-19-like symptoms within the past 10 days and had a polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection in the laboratory at the Medical Research Council / Uganda Virus Research Institute and, London School of Hygiene and

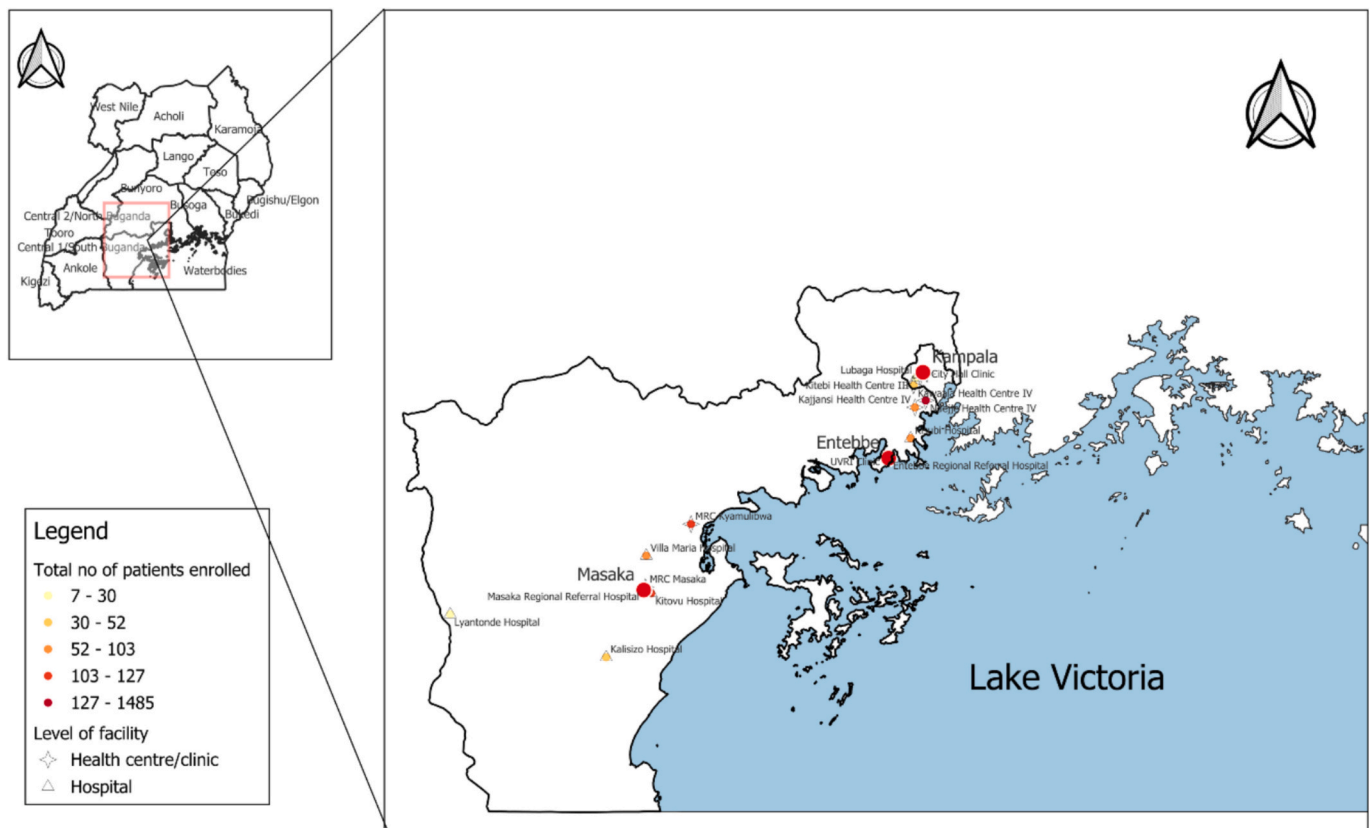


Fig. 1. Map of Uganda showing the distribution of healthcare centres included in the study.

Tropical Medicine (MRC/UVRI & LSHTM) Uganda Research Unit in Entebbe. Controls were similar to cases, but tested SARS-CoV-2 negative. Symptoms included at least three of the following: cough, fever, headache, sore throat, coryza, nasal congestion, general body weakness or fatigue, myalgia, dyspnoea, anorexia/nausea/vomiting, diarrhoea, altered mental status, loss of appetite, ageusia and anosmia.

Recruitment and SARS-CoV-2 vaccination: Study nurses at participating healthcare centres identified patients with COVID-19-like symptoms and provided them with study information. They addressed any queries, obtained written informed consent, and enrolled those willing to participate (Fig. 2).

They administered a questionnaire to collect data on social demographics and medical history, including pre-existing chronic health conditions. The questionnaire also included questions about any previous diagnosis of SARS-CoV-2 infection and the severity of current disease. Key vital signs, including heart rate, temperature, oxygen saturation and respiratory rate were recorded. Nasal and oropharyngeal swabs were collected for testing for SARS-CoV-2 infection. Additionally, the study team collected information on COVID-19 vaccination status through self-reports. This was further confirmed by reviewing vaccination documents such as vaccination cards, if available, and the Uganda national COVID-19 vaccination certification portal [9] to document the type, dose, and dates of vaccination on the questionnaire.

Testing for SARS-CoV-2: Nasal and oropharyngeal swabs collected were placed in viral transport media and transported to the MRC/UVRI & LSHTM Uganda Research Unit laboratory in Entebbe for testing. Real-time quantitative polymerase chain reaction (qPCR) using QuantStudio™ system Berlin protocol was used for testing.

Description of the study variables: Data were collected on age (recorded in completed years) and sex (categorized as male or female). Employment status was categorized into frontline healthcare workers, including those providing direct patient care such as doctors, nurses, laboratory technologists, and other clinical staff, and non-clinical staff, such as administrators, drivers, and other support staff. Smoking status

was categorized as current smoker, defined as individuals who smoke cigarettes or other tobacco products daily or occasionally, and former smokers, referring to those who previously smoked but no longer do. Disease severity was categorized into three levels: mild (no limitations to daily activities), moderate (limitations to daily activities) and severe (hospitalised, with or without oxygen therapy administered via a mask, nasal cannula or mechanical ventilation). Other collected variables included calendar time and presence of at least one chronic disease condition recognised as a risk factor for severe COVID-19. Data were collected on diabetes, heart disease, lung disease, asthma, cancer, hypertension, rheumatic disorders, liver disease, renal disease, and tuberculosis, all determined a priori.

2.1. Statistical methods

Sample size: We initially set out to recruit 3045 individuals (609 cases and 2436 controls). This estimate was based on the following assumptions: proportion of positive cases of 20 %, population vaccine coverage in negative controls of 20 %, vaccine effectiveness of 70 %, precision around VE estimate (lower 95 % CI boundary) of 10 %, and a 1:4 case-control matching ratio. In the end we enrolled 1371 participants (173 cases, 1198 controls). However, given the observed proportion of positive cases (12.6 %) and vaccine coverage in negative controls (67.8 %), it appears we would have needed to enrol 1796 (226 cases, 1570 controls). **Data management:** Study data were collected and managed using REDCap, a secure electronic data capture system [10] hosted at MRC/UVRI and LSHTM Uganda Research Unit. The data were then transferred to R statistical software (version 4.0; R Foundation for Statistical Computing, San Francisco CA, USA) for analysis. **Analysis:** To describe participants' vaccination status at enrolment, we defined full vaccination as receiving the complete recommended regimen for a given vaccine, either a single dose for a one-dose vaccine or both doses for a two-dose vaccine, at least 2 weeks prior to enrolment. Partial vaccination was defined similarly but applied to individuals who had received

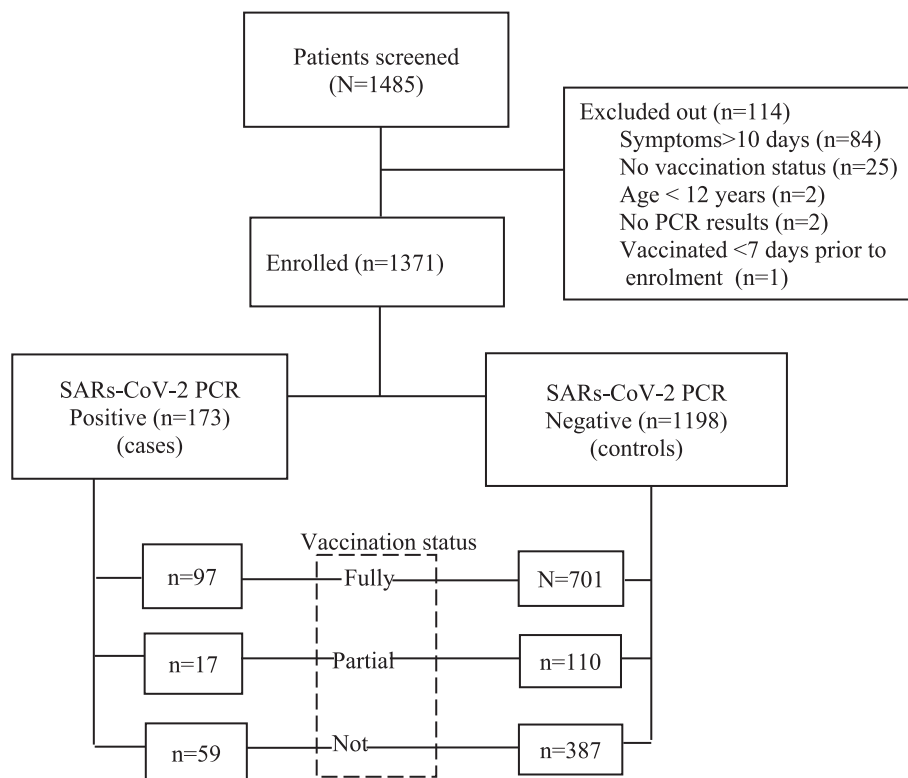


Fig. 2. Recruitment flowchart for SARS-CoV-2 vaccine effectiveness study in 19 healthcare centres in six districts of central and southwestern Uganda (March 2023 – March 2024).

only the first dose of a two-dose vaccine. Booster vaccination was defined as receiving one or more additional doses at least 6 months after full vaccination. Unvaccinated individuals were defined as those who had never received any SARS-CoV-2 vaccine. For the VE analysis, and in contrast to previous VE studies [7,11], we defined the vaccinated group (numerator) as individuals who received their last vaccine dose within the 12 months preceding symptom onset. The unvaccinated group (denominator) differed for each of the three VE analyses conducted: (a) Annual VE: included individuals who were never-vaccinated, as well as those whose last vaccine dose was administered more than 12 months before symptom onset. This is consistent with latest 2023 strategic advisory group of experts on immunization (SAGE) recommendations [12], which advise high-risk groups to receive a COVID-19 vaccine every 6–12 months; (b) Absolute VE: included only individuals who were never vaccinated; (c) Relative VE: included those whose last vaccine dose was more than 12 months before symptom onset. We summarised continuous variables using the mean and standard deviation or the median and interquartile range (IQR), while categorical variables were presented as counts and percentages. Patients' demographics, vaccination status and clinical characteristics were compared by case-control status using the Chi-squared test. We estimated VE as 1 minus the adjusted odds ratio, expressed as a percentage. VE was calculated for Annual, Absolute and Relative measures across three time strata based on number of days since last vaccine dose: (1) <365 days, (2) 7–269 days and (3) 270–364 days. The analysis was adjusted for age, sex, calendar time (with the date of swab modelled as either a categorical month variable or as restricted cubic spline), and the presence of at least one chronic condition as defined above. We further conducted a sensitivity analysis applying the same definitions as the primary analysis but excluding patients who self-reported a previous COVID-19 infection before vaccination.

3. Results

3.1. Participant characteristics

Between 22 March 2023 and 26 March 2024, 1371 patients (92 % of those screened) with COVID-19 like symptoms were recruited. Reasons for exclusion included having symptoms for more than 10 days and uncertainty about COVID-19 vaccination status, Fig. 2. The median age of those recruited was 31 years (IQR: 24–41), and the majority, 762 (56 %) were female. Nearly half (48 %) were from Wakiso district, the most highly populated district in Uganda, while 27 % were from Kampala, the capital city of Uganda. Most participants (95 %) had never smoked, 86 % reported no chronic disease and 81 % reported no previous diagnosis of COVID-19 as shown in Table 1. Among 1371 recruited patients, 173 (13 %) tested positive for SARS-CoV-2 and were classified as cases, while 1198 (87 %) were controls. Among cases, 97 (56 %) were fully vaccinated versus 701 (59 %) of controls ($p = 0.830$). A slightly higher proportion of cases than controls (23 % versus 15 %) had moderate-severe symptoms, a statistically significant difference ($p = 0.024$). Similarly, a higher proportion of cases than controls (19 % versus 12 %) had previously been diagnosed with COVID-19 ($p = 0.025$). Furthermore, a higher proportion of cases than controls (21 % versus 14 %) were aged ≥ 50 years ($p = 0.022$). Most vaccinated cases and controls had received AstraZeneca (ChAdOx1) COVID-19 vaccine (53 %) of all those vaccinated.

3.2. Vaccine effectiveness

Stratified by the number of days since the last COVID-19 vaccine dose, the adjusted VE ranged from 45 % to 59 % and was similar across the annual, absolute and relative measures, Table 2 and Fig. 3. In the sensitivity analysis, which excluded those who self-reported a previous COVID-19 infection, VE remained moderate at 32–38 % for all measures, but slightly lower than in the primary analysis.

Table 1

Participant characteristics overall and by case status in a SARS-CoV-2 vaccine effectiveness study across 19 healthcare centres in six districts of central and southwestern Uganda (March 2023 – March 2024, $N = 1371$).

Characteristic	All patients N = 1371 n (%)	Case SARS- CoV-2- positive = 173 n (%)	Control Test- negative = 1198, n (%)	χ^2 statistic	p- value
COVID-19 Vaccination status				0.374	0.830
Full vaccination [#]	798 (58.2)	97 (56.1)	701 (58.5)		
Partial vaccination*	127 (9.3)	17 (9.8)	110 (9.2)		
Unvaccinated	446 (32.5)	59 (34.1)	387 (32.3)		
Age (complete years)				5.251	0.022
< 50	1162 (84.8)	136 (78.6)	1026 (85.6)		
≥ 50	209 (15.2)	37 (21.4)	172 (14.4)		
Sex				0.766	0.382
Female	762 (55.6)	102 (59.0)	660 (55.1)		
Male	609 (44.4)	71 (41.0)	538 (44.9)		
Employment				3.121	0.077
Frontline/ health worker	349 (25.5)	54 (31.2)	295 (24.6)		
Others	1022 (74.5)	119 (68.8)	903 (75.4)		
Area of residence				0.669	0.716
Kampala	370 (27.0)	49 (28.3)	321 (26.8)		
Masaka	343 (25.0)	39 (22.5)	304 (25.4)		
Wakiso	658 (48.0)	85 (49.1)	573 (47.8)		
Smoking status				0.247	0.619
Current/ former	65 (4.7)	10 (5.8)	55 (4.6)		
Never	1306 (95.3)	163 (94.2)	1143 (95.4)		
Presence of chronic disease				1.448	0.229
No	1178 (85.9)	143 (82.7)	1035 (86.4)		
Yes	193 (14.1)	30 (17.3)	163 (13.6)		
HIV Status				1.030	0.598
Negative	1213 (88.5)	150 (86.7)	1063 (88.7)		
Positive	78 (5.7)	10 (5.8)	68 (5.8)		
Unknown	80 (5.8)	13 (7.5)	67 (5.6)		
Previous COVID-19 infection				7.379	0.025
No	1106 (80.7)	127 (73.4)	979 (81.7)		
Yes	178 (13.0)	33 (19.1)	145 (12.1)		
Unknown	87 (6.3)	13 (7.5)	74 (6.2)		
Current disease severity				5.069	0.024
Mild	1147 (83.7)	134 (77.5)	1013 (84.6)		
Moderate- severe	224 (16.3)	39 (22.5)	185 (15.4)		
Vaccine received				3.119	0.077
Not vaccinated	446 (32.5)	59 (34.1)	387 (32.3)		
AstraZeneca (ChAdOx1)	488 (35.6)	68 (39.3)	420 (35.1)		

(continued on next page)

Table 1 (continued)

Characteristic	All patients N = 1371 n (%)	Case SARS-CoV-2- positive = 173 n (%)	Control Test-negative = 1198, n (%)	χ^2 statistic	p-value
Pfizer (BNT162b2)	287 (20.9)	29 (16.8)	258 (21.5)		
JnJ (Ad26.COV2-S)	102 (7.4)	12 (6.9)	90 (7.5)		
Moderna (mRNA-1273)	33 (2.4)	4 (2.3)	29 (2.4)		
Sinopharm (BBIBP-CorV)	15 (1.1)	1 (0.6)	14 (1.2)		

Full vaccination: Defined as the administration of the recommended single dose for a one-dose vaccine, or both doses for a two-dose vaccine, completed at least 2 weeks prior to enrolment in the study; *Partial vaccination was defined as receiving only one dose for a two-dose vaccine, completed at least 2 weeks prior to enrolment in the study.

4. Discussion

We investigated the Annual, Absolute and Relative VE against symptomatic SARS-CoV-2 infection. Across the three measures, COVID-19 vaccination, on average, prevented nearly half of symptomatic infections within 12 months of receiving the last vaccine dose. Estimates were similar for all three measures of VE (Annual, Absolute and Relative) and for the different times since the last dose. The VE in our study was lower than that observed in other studies for a shorter period post-last dose of vaccination e.g. at 2–3 months [13,14]. However, our findings are consistent with and complement those from other studies

both in similar [15,16] and different settings [6,13,17]. In these latter studies, VE was 43 % at 112 days [6] and 34 % at >180 days [17] during the Omicron wave, suggesting a waning VE with time since last dose. The waning in vaccine protection has been previously observed in other studies [18]. The protection observed in our study for a similar time since last dose was slightly higher than that in the other studies [13,17] and in a systematic review by Nana Wu et al., which reported a significant decline in VE by 112 days post-vaccination, with further decrease to below 50 % by 280 days [6]. Most of the studies included in the systematic review were also done during the Omicron wave, but in high-income countries that have older populations than ours. In Africa, the general population median age is 19.4 years compared to 40 years in Europe, and 38 years in the United States [14]. Studies have shown higher COVID-19 vaccines real-world VE in younger populations [15]. The authors of the aforementioned systematic review further suggest a degradation in immunogenicity and this could highlight the need for up-to-date COVID-19 vaccination, regardless of previous number of doses. Though we recruited symptomatic patients, under one in four patients had moderate to severe disease among the positives, and no deaths were observed. Though the reasons for low death in Uganda are not yet clear, age demographics (youthful population), favorable weather and previous exposure to circulating coronaviruses, could have contributed [19].

We found that VE was lower in the sensitivity analysis, with protection falling to one in every three, when we excluded individuals who self-reported a previous COVID-19 infection. This suggests that previous infection, combined with vaccination may offer greater immune protection against subsequent infections. Indeed, studies have reported that VE against SARS-CoV-2 infection is strongest for individuals with hybrid immunity from previous infection and vaccination [20,21].

The strengths of this study included reasonable sample size to investigate VE beyond 6 months, although 95 % confidence intervals

Table 2

Annual, Absolute and relative COVID-19 vaccine effectiveness against symptomatic infection, stratified by time since vaccination, among 1371 patients at 19 health centres in six districts of central and southwestern Uganda (March 2023 – March 2024).

Days from last vaccination to symptom onset	Vaccinated cases /unvaccinated cases; Vaccinated controls /unvaccinated controls			VE ^a (95 % CI)		
	Annual	Absolute	Relative	Annual (%)	Absolute (%)	Relative (%)
<365	13/162; 163/1041	13/62; 163/405	13/100; 163/636	55 (17,76)	59 (19,79)	56 (17,77)
7–269	6/162; 84/1041	6/62; 84/405	6/100; 84/636	56 (–3,81)	57 (–5,82)	58 (1,83)
270–364	7/162; 79/1041	7/62; 79/405	7/100; 79/636	46 (–20,76)	53 (–10,80)	45 (–25,76)

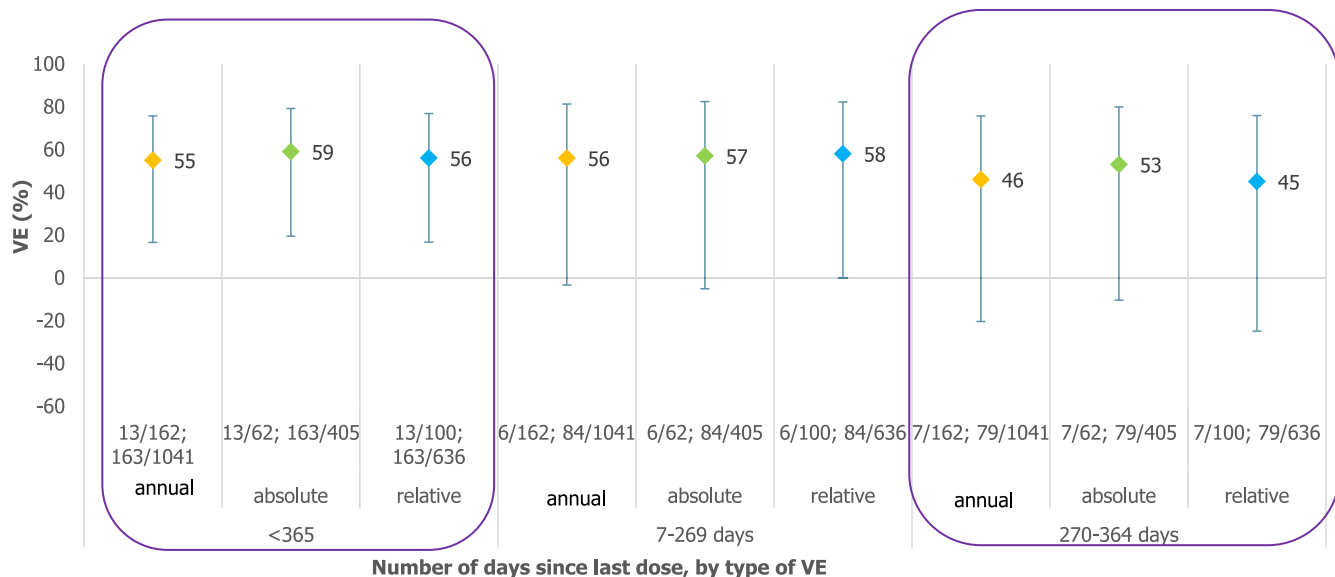


Fig. 3. Line graph showing, annual, absolute and relative COVID-19 % vaccine effectiveness against symptomatic infection, stratified by time since vaccination among 1371 patients at 19 health centres in six districts of central and southwestern Uganda (March 2023 – March 2024).

were wide. We were able to verify vaccination status from vaccination cards, hospital records and the Uganda Ministry of Health records. This helped to avoid misclassification of vaccination status. However, our study is not without limitations; potential unmeasured confounding could be present. Evidence in Uganda [22] and elsewhere [23,24] shows that vaccinated participants are usually different from those not vaccinated on many other prevention measures, therefore the list of confounders used for adjustment may not have been exhaustive. We were unable to accumulate the estimated sample size because of the low number of COVID-19 cases. Furthermore, fewer than 15 % of the patients self-reported previous COVID-19 diagnosis: the true proportion could be higher but affected by social desirability bias as SARS-CoV-2 infection in Uganda was stigmatized [25,26]; also, there are limited SARS-CoV-2 testing opportunities and interest in or need for testing for SARS-CoV-2 infection during minor symptoms.

5. Conclusion

In conclusion, similar results for Annual, Absolute and Relative VE measures could imply that most people in the study areas had already acquired some level of immunity from natural infection. We may not have been able to determine this because of limited SARS-CoV-2 testing opportunities in Uganda. Therefore, evaluating “annual” or “up-to-date” vaccination could be used in the future to align with recent WHO COVID-19 vaccine recommendation [12]. Results suggest moderate VE against symptomatic infection, therefore high-risk individuals should receive another COVID-19 vaccine every 12 months regardless of their previous vaccination history. Lack of clear COVID-19 seasonality in this and other African settings creates a challenge to selecting the optimal timing for annual vaccination.

Author contribution

Conceptualization, AA, AK, VA, TAO, GK, DS, AE, PK and ER; Methodology, AA, SK, VA, TAO, CS, JMWER; Software, VA, TAO, AK and AA; Validation, AA, VA, TAO, AK; Formal Analysis, AA, SC and VA; Investigation, SK, BNK, ER; Resources, SK, BNK, ER; Data Curation, VA, TAO, AK, AA; Writing – Original Draft Preparation, AA, SK, VA; Writing – Review & Editing, AA, SK, VA, TAO, AK, GK, DS, BNK, HKB, YTW, AK, JH, AKW, SC, JMM, AE, PK; Visualizations, AA, SK, VA, TAO, ER; Supervision, PK, ER; Project Administration, SK, TAO, BNK; Funding Acquisition, GK, AA, DS, AE, PK and ER.

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Institutional review board statement

The study received ethical approval from the Uganda Virus Research Institute Research Ethics Committee, reference; GC/127/952 on 22nd Feb 2023, the Uganda National Council for Science and Technology, reference HS2672ES on 7th Mar 2023, and the London School of Hygiene and Tropical Medicine Research Ethics Committee, reference 28,824 on 16th Mar 2023. The Uganda Ministry of Health, provided administrative clearance and support to use all participating hospitals and healthcare facilities. All participants provided written informed consent/assent for participation in the study. All methods were performed in accordance with the relevant guidelines and regulations.

Informed consent statement

Written informed consent and assent were obtained from all study participants before any study procedures were performed.

CRedit authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The data sharing policy and procedures to access data from which this manuscript was generated are accessible through <https://apps.mrcuganda.org/mrcdatavisibility>. Should any of the other researchers need to have access to the data from which this manuscript was generated, the processes to access the data are well laid out in the policy. The corresponding author can be contacted for any clarifications and/or support to access the data.

References

- [1] Olum R, Bongomin F. Uganda's first 100 COVID-19 cases: Trends and lessons. 2020.
- [2] King P, Wanyana MW, Migisha R, Kadobera D, Kwesiga B, Claire B, et al. COVID-19 vaccine uptake and coverage, Uganda, 2021–2022. *UNIPH. Bulletin* 2023;8.
- [3] Islam N, Shkolnikov VM, Acosta RJ, Klimkin I, Kawachi I, Irizarry RA, et al. Excess deaths associated with covid-19 pandemic in 2020: age and sex disaggregated time series analysis in 29 high income countries. *bmj* 2021;373.
- [4] Health UMo. COVID-19 Response Hub: Coordination structure. Accessed June 6, 2024, <https://covid19.gou.go.ug/coordination.html>.
- [5] van Dorst MM, Pyuza JJ, Nkurunungi G, Kullaya VI, Smits HH, Hogendoorn PC, et al. Immunological factors linked to geographical variation in vaccine responses. *Nat Rev Immunol* 2024;24(4):250–63.
- [6] Wu N, Joyal-Desmarais K, Ribeiro PA, Vieira AM, Stojanovic J, Sanuade C, et al. Long-term effectiveness of COVID-19 vaccines against infections, hospitalisations, and mortality in adults: findings from a rapid living systematic evidence synthesis and meta-analysis up to December, 2022. *Lancet Respir Med* 2023;11(5):439–52.
- [7] Lewis NM, Murray N, Adams K, Surie D, Gaglani M, Ginde AA, et al. Editors. Absolute and relative vaccine effectiveness of primary and booster series of COVID-19 vaccines (mRNA and adenovirus vector) against COVID-19 hospitalizations in the United States, December 2021–April 2022. *Open forum infectious diseases*. 2023. Oxford University Press US.
- [8] Lin D-Y, Zeng D, Gilbert PB. Evaluating the long-term efficacy of coronavirus disease 2019 (COVID-19) vaccines. *Clin Infect Dis* 2021;73(10):1927–39.
- [9] Health Umo. Uganda National COVID-19 Vaccination Certification Portal [Internet]. HISP Uganda. Assessed 28 October 2024. Available from, <https://epivac.health.go.ug/certificates/#/>.
- [10] RedCap, <https://projectredcap.org/resources/citations/>. Accessed on 25.10.2024.
- [11] Ku JH, Sy LS, Qian L, Ackerson BK, Luo Y, Tubert JE, et al. Effectiveness of a fourth dose of mRNA-1273 against COVID-19 among older adults in the United States: interim results from an observational cohort study. *Vaccine* 2023;41(29):4212–9.
- [12] WHO. SAGE updates COVID-19 vaccination guidance 2023. <https://www.who.int/news/item/28-03-2023-sage-updates-covid-19-vaccination-guidance>. Accessed on 05.06.2024.
- [13] Lin D-Y, Gu Y, Wheeler B, Young H, Holloway S, Sunny S-K, et al. Effectiveness of Covid-19 vaccines over a 9-month period in North Carolina. *New England Journal of Medicine* 2022;386(10):933–41.
- [14] Liu B, Stepien S, Dobbins T, Gidding H, Henry D, Korda R, et al. Effectiveness of COVID-19 vaccination against COVID-19 specific and all-cause mortality in older Australians: a population based study. *The Lancet Regional Health–Western Pacific* 2023;40.
- [15] Mweso O, Simwanza J, Malambo W, Banda D, Fwoloshi S, Sinyange N, et al. Test negative case–control study of COVID-19 vaccine effectiveness for symptomatic SARS-CoV-2 infection among healthcare workers: Zambia, 2021–2022. *BMJ Open* 2023;13(12):e072144.
- [16] Kassanjee R, Davies M-A, Heekes A, Mahomed H, Hawkridge AJ, Wolmarans M, et al. COVID-19 vaccine uptake and effectiveness by time since vaccination in the Western cape province, South Africa: an observational cohort study during 2020–2022. *medRxiv* 2024;2024(01). 24.24301721.
- [17] Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. *The Lancet* 2022;399(10328):924–44.
- [18] Nordström P, Ballin M, Nordström A. Risk of infection, hospitalisation, and death up to 9 months after a second dose of COVID-19 vaccine: a retrospective, total population cohort study in Sweden. *The Lancet* 2022;399(10327):814–23.
- [19] Njenga MK, Dawa J, Nanyingi M, Gachohi J, Ngere I, Letko M, et al. Why is there low morbidity and mortality of COVID-19 in Africa? *Am J Trop Med Hyg* 2020 Aug;103(2):564.
- [20] Almendares OM, Ruffin JD, Collingwood AH, Nolen LD, Lanier WA, Dash SR, et al. Previous infection and effectiveness of COVID-19 vaccination in middle-and high-school students. *Pediatrics* 2023;152(6):e2023062422.
- [21] Bobrovitz N, Ware H, Ma X, Li Z, Hosseini R, Cao C, et al. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. *Lancet Infect Dis* 2023;23(5):556–67.
- [22] Echoru I, Ajambo PD, Keirania E, Bukenya EE. Sociodemographic factors associated with acceptance of COVID-19 vaccine and clinical trials in Uganda: a cross-sectional study in western Uganda. *BMC Public Health* 2021;21(1):1106.
- [23] Domostawska-Żylińska K, Krysińska-Pisarek M, Czabanowska K, Sesa G. Vaccinated and unvaccinated risk perceptions and motivations for COVID-19 preventive measures based on EPPM—A polish qualitative pilot study. *Int J Environ Res Public Health* 2022;19(20):13473.
- [24] Lipovčan LK, Prizmić-Larsen Z, Franc R. Differences between COVID-19-vaccinated and unvaccinated participants from Croatia. *Croat Med J* 2022;63(6):508.
- [25] Amir K. COVID-19 and its related stigma: a qualitative study among survivors in Kampala, Uganda. *Stigma and Health* 2021;6(3):272.
- [26] Asio A, Massanja V, Kadobera D, Kwesiga B, Bulage L, Ario AR. Covid-19 related stigma among survivors in Soroti District, Uganda, march 2020 to December 2021. *UNIPH Quarterly Epidemiological Bulletin* 2023;8:1–17.