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MAJOR ARTICLE

COVID-19 Vaccine Effectiveness Against Progression to In-Hospital Mortality in Zambia, 2021–2022

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Background. Coronavirus disease 2019 (COVID-19) vaccines are highly effective for reducing severe disease and mortality. However, vaccine effectiveness data are limited from Sub-Saharan Africa. We report COVID-19 vaccine effectiveness against progression to in-hospital mortality in Zambia.

Methods. We conducted a retrospective cohort study among admitted patients at 8 COVID-19 treatment centers across Zambia during April 2021 through March 2022, when the Delta and Omicron variants were circulating. Patient demographic and clinical information including vaccination status and hospitalization outcome (discharged or died) were collected. Multivariable logistic regression was used to assess the odds of in-hospital mortality by vaccination status, adjusted for age, sex, number of comorbid conditions, disease severity, hospitalization month, and COVID-19 treatment center. Vaccine effectiveness of ≥1 vaccine dose was calculated from the adjusted odds ratio.

Results. Among 1653 patients with data on their vaccination status and hospitalization outcome, 365 (22.1%) died. Overall, 236 (14.3%) patients had received ≥1 vaccine dose before hospital admission. Of the patients who had received ≥1 vaccine dose, 22 (9.3%) died compared with 343 (24.2%) among unvaccinated patients ($P < .01$). The median time since receipt of a first vaccine dose (interquartile range) was 52.5 (28–107) days. Vaccine effectiveness for progression to in-hospital mortality among hospitalized patients was 64.8% (95% CI, 42.3%–79.4%).

Conclusions. Among patients admitted to COVID-19 treatment centers in Zambia, COVID-19 vaccination was associated with lower progression to in-hospital mortality. These data are consistent with evidence from other countries demonstrating the benefit of COVID-19 vaccination against severe complications. Vaccination is a critical tool for reducing the consequences of COVID-19 in Zambia.

Keywords. SARS-CoV-2; Africa; COVID-19 vaccines; COVID-19/mortality; SARS-CoV-2; Zambia; vaccine efficacy.

Since the onset of the novel coronavirus disease 2019 (COVID-19) pandemic, >170 000 persons have died of COVID-19 in Sub-Saharan Africa [1]. In Zambia, from March 20, 2020, to August 26, 2022, a total of 332 763 confirmed cases and 4016 confirmed deaths were recorded [2], although the true number of infections and deaths was likely greater [3, 4].

As of February 2022, African countries had received >587 million vaccine doses, enough to vaccinate ∼360 million people (which is ∼37% of the number of doses needed to reach vaccination targets) [1]. However, through April 2022, only 14.3% of the eligible population in Sub-Saharan Africa had been fully vaccinated [1]. The ChAdOx1-S COVID-19 vaccine became available in Zambia in April 2021, and ∼1 year later, ∼2.3 million persons had been fully vaccinated in Zambia (21.5% of persons aged ≥12 years, the eligible population) [2]. In addition to poor access to COVID-19 vaccines for much of 2021, several other challenges hindered vaccination programs in Zambia, including suboptimal access to preventive health care/routine immunization, under-resourced health care systems, inadequate cold chain systems, lack of awareness of benefits of vaccination, and vaccine misconceptions and misinformation [5–8].

COVID-19 vaccines have demonstrated excellent efficacy in clinical trials and good effectiveness in real-world observational studies, including against variants of concern and in people who have had prior COVID-19 infections [9–11]. In particular, COVID-19 vaccines substantially reduce the risk of severe disease and mortality [10, 12]. Yet, there is a paucity of vaccine efficacy and effectiveness data from countries in Sub-Saharan Africa. Most of the vaccine evidence from Africa has originated from South Africa, where several vaccine clinical trials have

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been conducted and observational vaccine effectiveness (VE) studies have been published [13–17]. A single dose of the Ad26.COV2.S vaccine was associated with lower hospitalizations and mortality during the Beta and Delta waves in South Africa [13], and additional evidence demonstrated effectiveness against COVID-19 hospitalizations during the Omicron wave [14]. In Zambia, full receipt of a primary COVID-19 vaccine was associated with lower rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and symptomatic illness during an outbreak in a prison when Omicron was the dominant variant [15]. However, data from other countries in Sub-Saharan Africa are limited to date.

Filling the COVID-19 vaccine evidence gap in Africa is important to counter misinformation and skepticism toward research from other parts of the world [18, 19]. Furthermore, SARS-CoV-2 epidemiology in Africa has differed from elsewhere, with fewer confirmed cases and deaths and lower symptomatic rates, yet high evidence of infection-induced immunity [20–22]. Furthermore, many countries in Sub-Saharan Africa have a high burden of people with HIV (PWH) and tuberculosis, which are conditions associated with increased risk of poor outcomes from COVID-19 [23, 24]. Lastly, differences in social and health system structures might impact vaccine delivery. Therefore, more real-world data on COVID-19 vaccines from countries in Africa are needed. We assessed COVID-19 VE against progression to in-hospital mortality in patients hospitalized with COVID-19 in Zambia.

Methodology

We conducted a retrospective cohort study of patients admitted to COVID-19 treatment centers in Zambia to assess COVID-19 VE against progression to in-hospital mortality between April 15, 2021 (when Zambia first began offering COVID-19 vaccines), and March 31, 2022. Since the pandemic onset, patients diagnosed with COVID-19 requiring in-patient admission in Zambia were admitted to COVID-19 treatment centers that had specifically designated isolation and treatment units staffed by clinicians and nurses trained in COVID-19 clinical management [25]. The COVID-19 clinical outcomes study was conceived during the early weeks of the COVID-19 epidemic in Zambia and eventually included 8 COVID-19 treatment centers in 5 cities: Lusaka (4 treatment centers), Ndola, Kitwe, Kabwe, and Livingstone [26]. Data on relative variant genome frequency by region from the Global Initiative on Sharing Avian Influenza Data (GISAID) were utilized to define the SARS-CoV-2 variant that was circulating during each wave [27]. ChAdOx1-S COVID-19 vaccine was the first vaccine type available in Zambia, and by late 2021, Ad26.COV2.S, mRNA-127, BNT162b2, and Sinopharm BBIBP-CorV were available in the country. An additional vaccine dose after completing a primary vaccine series (ie, "booster") became available in Zambia in January 2022.

Patients at participating COVID-19 treatment centers had demographic and clinical information collected at admission and during hospitalization until they were discharged or died. These data were retrospectively abstracted from clinical records using a standardized case record form adapted from the World Health Organization (WHO) [28] and entered into Research Electronic Data Capture (REDCap) electronic data capture tools by trained staff at a later date [29]. Data collection occurred throughout the study period but was primarily done following waves given the larger volume of patient records to abstract. Vaccination information was collected from patients during clinical care and recorded in their charts. Proof of vaccination included self-report and/or review of vaccine cards. For those with missing vaccine information, attempts were made to cross-reference the electronic national vaccine registry to improve data completeness. Severe COVID-19 was defined as having an oxygen saturation (SpO2) <90%, respiratory rate >30 breaths/minute, or need for oxygen therapy [30]. The number of self-reported comorbidities was summed for each patient, including cardiac disease, hypertension, diabetes, other pulmonary disease, HIV, tuberculosis (active or previous), asthma, kidney disease, liver disease, neurological disorders, asplenia, malignant neoplasms, and current smoking (each condition was given equal weight). History of prior COVID-19 was not available for patients, although the reliability of this history is not clear given a low case detection proportion in Zambia [3].

Full vaccination was defined as receiving the first dose of a 1-dose vaccine or second dose of a 2-dose vaccine ≥14 days before COVID-19 treatment center admission. Partial vaccination was defined as receiving the first dose of a 2-dose vaccine ≥14 days before admission but either not yet receiving the second dose or receiving the second dose ≤13 days before admission. Those vaccinated with their first COVID-19 vaccine dose ≤13 days before admission were considered indeterminate, and those with missing vaccine dates were classified as such. Because vaccination dates were missing for many patients with known vaccination status, we also created a separate category of patients who received ≥1 COVID-19 vaccine dose and used this as our primary predictor variable (with full/partial vaccination status being secondary analyses). The main outcome variable was categorized as discharged from hospital or died in the hospital. Length of stay was calculated as the days between admission and discharge or death. Patients whose vaccination status or hospitalization outcomes could not be determined were excluded from the analyses.

The analysis was restricted to patients admitted during the period that COVID-19 vaccines were available in Zambia (April 15, 2021, through March 31, 2022). We used the chi-square test and Student *t* test to compare categorical and continuous variables, respectively. We used multivariable logistic regression to calculate the odds of in-hospital mortality by

vaccination status, adjusting for age, sex, number of comorbid conditions, disease severity at admission, hospitalization month, and COVID-19 treatment center. VE was calculated as 1 minus the adjusted odds ratio times 100. We did secondary analyses to calculate VE by full/partial vaccination status, vaccine type, the predominant circulating variant (ie, Delta from April to November 2021 and Omicron [subvariants B1 and B2] [27] from December 2021 through March 2022 [31]), and HIV status. Additionally, we analyzed if there was an association between progression to in-hospital mortality and predominant variant periods (Delta vs Omicron waves), adjusting for patients' vaccination status.

RESULTS

Overall, 2385 persons had data on their hospitalization course abstracted at a COVID-19 treatment center in Zambia during April 2021 through March 2022. Of patients with data abstracted, 1821 (76.4%) had their COVID-19 vaccination status documented (815 [61.5%] persons had it documented during the Delta variant–predominant period and 1006 [94.9%] persons had it documented during the Omicron variant–predominant period). Among patients with known vaccination status, 1653 (69.3% of total) had a known hospitalization outcome (Figure 1).

The median age of participants (interquartile range [IQR]) was 47 (30–65) years, and females accounted for 852 (51.5%) patients (Table 1). Overall, 1065 (64.4%) patients reported having at least 1 comorbidity, with 266 (17.9%) patients reporting having HIV infection (compared with national prevalence of 11.1% in persons aged 15–49 years [32]). The average length of stay was 2.5 days, and 365 (22.1%) patients died during hospitalization.

Two hundred thirty-six (14.3%) patients had received ≥1 vaccine dose before hospital admission, of whom 55 (23.3%)

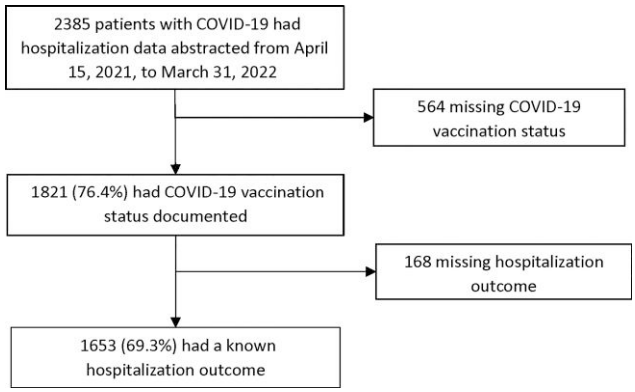

Figure 1. Sample size flow diagram for analysis of COVID-19 vaccine effectiveness against in-hospital mortality in Zambia, 2021–2022. Abbreviation: COVID-19, coronavirus disease 2019.

Table 1. Characteristics and Outcomes of Patients Admitted to COVID-19 Treatment Centers With Known Hospitalization Outcome in Zambia, 2021–2022

Characteristic	Overall (n = 1653)	Vaccinated (n = 236)	Unvaccinated (n = 1417)	*P* Value[a]
Age, median (IQR), y (No. miss = 3)	47 (30–65)	42 (29–61)	48 (30–66)	.10
Age group, No. (%) (No. miss = 3)	…	…	…	…
0–17 y	78 (4.7)	4 (1.7)	74 (5.2)	.02
18–29 y	322 (19.5)	57 (24.3)	265 (18.7)	…
30–44 y	370 (22.4)	60 (25.5)	310 (21.9)	…
45–59 y	331 (20.1)	48 (20.4)	283 (20.0)	…
≥60 y	549 (33.3)	66 (28.1)	483 (34.1)	…
Sex, No. (%)	…	…	…	…
Female	852 (51.5)	133 (56.4)	719 (50.7)	.13
Male	801 (48.5)	103 (43.6)	698 (49.3)	…
District, No. (%) (No. miss = 48)	…	…	…	…
Lusaka	715 (44.5)	99 (42.3)	616 (44.9)	<.01
Ndola	426 (26.5)	36 (15.4)	390 (28.4)	…
Kitwe	209 (13.0)	75 (32.1)	134 (9.8)	…
Livingstone	139 (8.7)	15 (6.4)	124 (9.0)	…
Kabwe	116 (7.2)	9 (3.8)	107 (7.8)	…
Comorbidity number, No. (%)[a]	…	…	…	…
0	588 (35.6)	81 (34.3)	507 (35.8)	.93
1	535 (32.3)	77 (32.6)	458 (32.3)	…
2	326 (19.7)	46 (19.5)	280 (19.8)	…
≥3	204 (12.3)	32 (13.6)	172 (12.1)	…
Comorbidities, No. (%)[b]	…	…	…	…
Hypertension (No. miss = 78)	564 (35.8)	79 (35.4)	485 (35.9)	.96
HIV (No. miss = 159)	266 (17.9)	35 (15.5)	231 (18.4)	.35
Diabetes (No. miss = 114)	222 (14.4)	41 (19.0)	181 (13.7)	.05
Severe COVID-19 at admission, No. (%)[c] (No. miss = 12)	872 (53.1)	83 (35.3)	789 (56.1)	<.01
Mean length of stay (range), d	2.5 (0–27)	1.9 (0–27)	2.6 (0–27)	<.01
Hospitalized ≥5 d, No. (%)	287 (17.4)	29 (12.3)	258 (18.2)	.03
Died during hospitalization, No. (%)	365 (22.1)	22 (9.3)	343 (24.2)	<.01
Timing of 1st vaccine dose, No. (%)	…	…	…	…
≥14 d before admission	…	85 (36.0)	…	…
0–13 d before admission	…	8 (3.4)	…	…
After admission	…	0 (0.0)	…	…
Unknown date	…	143 (60.6)	…	…
Vaccination status, No. (%)[d]	…	…	…	…
Fully	…	55 (23.3)	…	…

Table 1. Continued

Characteristic	Overall (n = 1653)	Vaccinated (n = 236)	Unvaccinated (n = 1417)	*P* Value[a]
Partially	…	30 (12.7)	…	…
Indeterminate	…	8 (3.4)	…	…
Unknown date	…	143 (60.6)	…	…
Median time since vaccination, d (IQR) (No. miss: 146)[e]	…	52.5 (28–107)	…	…
Vaccine type, No. (%) (No. miss = 27)	…	…	…	…
Ad26.COV2.S	…	121 (57.9)	…	…
ChAdOx1-S	…	84 (40.2)	…	…
BNT162b2	…	3 (1.4)	…	…
mRNA-127	…	1 (0.5)	…	…
Sinopharm BBIBP-CorV	…	0 (0.0)	…	…

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range.

[a]Chi-square test used for categorical variables and Student *t* test used for continuous variables.

[b]Comorbidities included cardiac disease, hypertension, diabetes, other pulmonary disease, HIV, tuberculosis (active or previous), asthma, kidney disease, liver disease, neurological disorder, asplenia, malignant neoplasm, and current smoking. Only the most common comorbidity options are shown in the table.

[c]Severe COVID-19 was defined as an oxygen saturation <90% on room air, respiratory rate >30 breaths per minute, or receiving oxygen therapy.

[d]Full vaccination defined as receiving the first dose of a 1-dose vaccine or second dose of a 2-dose vaccine ≥14 days before COVID-19 treatment center admission, partial vaccination defined as receiving the first dose of a 2-dose vaccine ≥14 days before admission but either not yet receiving the second dose or receiving the second dose ≤13 days before admission, and indeterminate vaccination status defined as receiving the first COVID-19 vaccine dose ≤13 days before admission.

[e]One hundred forty-six missing date since first dose received. Three of these persons had date of second dose, meaning they could be classified as fully vaccinated in prior analyses.

were fully vaccinated, 30 (12.7%) were partially vaccinated, 8 (3.4%) had an indeterminate vaccination status, and 143 (60.6%) were missing information on vaccination date(s) (Table 1). No patient had a record of receiving a third vaccine dose. The median time since receipt of a first vaccine dose (IQR) was 52.5 (28–107) days.

The average length of stay for patients with ≥1 vaccine dose was 1.9 days vs 2.6 days for unvaccinated patients ($P < .01$) (Table 1). Twenty-two (9.3%) patients reporting ≥1 vaccine dose died compared with 343 (24.2%) unvaccinated patients ($P < .01$). VE of ≥1 COVID-19 vaccine dose against progression to in-hospital mortality was 64.8% (95% CI, 42.3%–79.4%) (Table 2). VE of ≥1 vaccine dose during the period when Delta was dominant was 65.0% (95% CI, 22.5%–85.8%), and VE during the period when Omicron was dominant was 64.8% (95% CI, 31.4%–82.9%).

Among the 266 patients with HIV, 5 (14.3%) who had received ≥1 COVID-19 vaccine dose died compared with 61 (26.4%) who were unvaccinated ($P = .18$). VE of ≥1 COVID-19 vaccine dose against progression to in-hospital mortality among PWH was 53.6% (95% CI, −15.6% to 84.7%).

In-hospital mortality among patients in the study was higher during the Delta variant–predominant period than the Omicron variant–predominant period (31.1% vs 14.5%; $P < .01$; odds ratio, 2.7; 95% CI, 2.1–3.4) (Table 3). Adjusting for the different vaccination coverage of patients between waves

Table 2. COVID-19 Vaccine Effectiveness Against Progression to In-Hospital Mortality—Zambia, April 2021–March 2022

Vaccination Status	Deaths in Vaccinated Group,[a] No. (%)	Vaccine Effectiveness, % (95% CI)	
…	…	Crude VE	Adjusted VE[b]
≥1 vaccine dose (n = 236)	22 (9.3)	67.8 (50.4–80.1)	64.8 (42.3–79.4)
Vaccination status[c]	…	…	…
Full (n = 55)	6 (10.9)	61.7 (16.5–85.4)	60.9 (2.3–86.5)
Partial (n = 30)	4 (13.3)	51.8 (–24.7 to 85.9)	61.3 (–15.8 to 89.7)
Indeterminate (n = 8)	0 (0.0)	…	…
Unknown (n = 143)	12 (8.4)	71.3 (49.7–85.1)	63.4 (29.7–82.3)
Time period (predominant variant)[d,e]	…	…	…
April to November 2021 (Delta; n = 46)	8 (17.4)	55.3 (7.5–80.9)	65.0 (22.5–85.8)
December 2021 to March 2022 (Omicron; n = 190)	14 (7.4)	59.6 (30.2–78.3)	64.8 (31.4–82.9)
Vaccine type[d]	…	…	…
ChAdOx1-S (n = 84)	9 (10.7)	62.1 (32.9–80.5)	65.2 (33.5–83.1)
Ad26.COV2.S (n = 121)	10 (8.3)	69.9 (48.2–84.0)	61.1 (26.6–80.8)

Abbreviations: COVID-19, coronavirus disease 2019; VE, vaccine effectiveness.

[a]Three hundred forty-three (24.2%) patients died in the unvaccinated group (n = 1417).

[b]Adjusted for age, sex, number of comorbid conditions, disease severity at admission (defined as oxygen saturation <90% on room air, respiratory rate >30 breaths per minute, or receiving oxygen therapy), hospitalization month, and COVID-19 treatment center.

[c]Full vaccination defined as receiving the first dose of a 1-dose vaccine or second dose of a 2-dose vaccine ≥14 days before COVID-19 treatment center admission, partial vaccination defined as receiving the first dose of a 2-dose vaccine ≥14 days before admission but either not yet receiving the second dose or receiving the second dose ≤13 days before admission, and indeterminate vaccination status defined as receiving the first COVID-19 vaccine dose ≤13 days before admission.

[d]Estimate for receipt of ≥1 COVID-19 vaccine dose.

[e]In the Delta variant–predominant period, there were 706 unvaccinated patients, of whom 226 (32.0%) died during hospitalization. In the Omicron variant–predominant period, there were 711 unvaccinated patients, of whom 117 (16.5%) died during hospitalization.

Table 3. In-Hospital Mortality by COVID-19 Pandemic Period (Proxy for Predominant Variant) and Vaccination Status—Zambia, 2021–2022

Outcome	All Patients, No. (%)			Unvaccinated, No. (%)			≥1 Vaccine Dose, No. (%)		
	Delta Period (n = 752)	Omicron Period (n = 901)	*P* Value[a]	Delta Period (n = 706)	Omicron Period (n = 711)	*P* Value[a]	Delta Period (n = 46)	Omicron Period (n = 190)	*P* Value[a]
Severe illness at admission	552 (73.4)	320 (35.5)	<.01	517 (73.2)	272 (38.3)	<.01	35 (76.1)	48 (25.3)	<.01
Hospitalized ≥5 d	176 (23.4)	111 (12.3)	<.01	163 (23.1)	95 (13.4)	<.01	13 (28.3)	16 (8.4)	<.01
In-hospital mortality	234 (31.1)	131 (14.5)	<.01	226 (32.0)	117 (16.5)	<.01	8 (17.4)	14 (7.4)	.05

Delta period defined as April to November 2021 and Omicron period defined as December 2021 through March 2022.

Abbreviation: COVID-19, coronavirus disease 2019.

[a]Chi-square test or Fisher exact test where appropriate.

(6.1% during Delta vs 21.1% during Omicron) did not appreciably change the odds of in-hospital mortality (adjusted odds ratio, 2.4; 95% CI, 1.9–3.1).

DISCUSSION

Patients vaccinated against COVID-19 had lower progression to in-hospital mortality in Zambia, a finding that was consistent during periods when Delta and Omicron were the dominant variants circulating in the country. These data from Zambia expand on limited evidence of COVID-19 VE in Africa [5, 9–12]. COVID-19 vaccination uptake in Africa has lagged behind other regions, but these findings suggest that these vaccines are a critical tool for reducing morbidity and mortality from COVID-19. Sharing local evidence of the benefit of COVID-19 vaccine in Zambia might increase vaccine uptake.

The Omicron variant of SARS-CoV-2 has mutations that enable it to evade prior immunity, resulting in decreased VE [11]. However, protection from severe COVID-19 outcomes is the most conserved vaccine effect across different variants, especially following a booster dose [10, 33, 34]. In our study, there was no decrement in VE against progression to in-hospital mortality when Omicron was the predominant variant in Zambia (compared with when Delta was predominant). Patients in this analysis had been vaccinated relatively recently (ie, <2 months), which could explain the preserved VE [11]; additionally, data from before the Omicron surge in the United States indicate preserved VE against hospitalization for at least 6 months after receipt of a single-dose adenovirus vaccine [35, 36].

Even though VE remained similar between the Delta and Omicron waves in this study, the in-hospital mortality risk was lower during the Omicron wave. However, this mortality difference was not driven by higher vaccination coverage among patients during the Omicron wave. This finding is similar to those in a study by Modes et al. demonstrating that in 1 US hospital, fewer fully vaccinated patients died in-hospital during the Omicron wave compared with the Delta wave [37]. This suggests that other factors like patient characteristics (eg, greater proportion of patients with infection-induced immunity during the Omicron wave, higher-risk patients admitted during the Delta wave), system/environmental factors (eg, relative availability of hospital beds or oxygen supply in Zambia, which were much more constrained during the Delta wave than during the Omicron wave), and/or virus characteristics (eg, Omicron having lower replication competence in lung parenchyma [38]) could be responsible for the mortality difference by wave in Zambia [24].

Some clinical trials for COVID-19 vaccines included PWH, although the numbers were too small to derive definitive evidence of efficacy in PWH [16, 39]. Based on immunological studies, vaccines are expected to work well in this high-risk population [40]. The Ad26.COV2.S vaccine has been demonstrated to reduce hospitalizations and deaths among PWH in South Africa [13], and in Russia, the Gam-COVID-VAC vaccine was shown to be effective in PWH, especially for severe disease [41]. Although COVID-19 vaccination among PWH appeared to be effective against progression to in-hospital mortality in this study, the effect was not statistically significant. The inclusion of additional PWH in this study could provide clearer evidence on this important topic in Zambia, where there is a high burden of HIV [32].

Vaccinated patients in this study were also less likely than unvaccinated patients to be admitted to treatment centers with severe COVID-19, suggesting that vaccination also helped prevent this outcome. Although vaccine coverage in this study was low, it varied by geographic location, suggesting opportunities to learn from best practices in some areas to help other areas increase vaccine coverage. Zambia remains below targets adopted from the African Union [42], although in recent months it has made substantial strides at increasing coverage of the primary series (ie, 52.8% of the eligible population has received the primary series as of August 28, 2022, [2]). This has been accomplished through coordinated leadership by the government, leveraging existing health investments of programs like PEPFAR, and using a community-based approach to COVID-19 vaccine delivery.

Our study had several limitations. Data were not available describing either national COVID-19-related hospitalization numbers or COVID-19 hospitalization rates by facility, limiting our understanding of the study's generalizability. As with many studies conducted during emergency responses, data completeness for some key variables was a challenge that impacted our sample size and resulted in wide confidence intervals. Additionally, the lack of vaccination dose numbers and dates for many participants necessitate use of a nonstandard category (ie, ≥1 vaccine dose) for the primary analysis to avoid excessive loss of participants; the similarity of VE estimates for full and missing vaccination statuses could indicate that many patients with missing vaccination status were in fact fully vaccinated. Additionally, given high levels of infection-induced immunity in Africa [20], hybrid immunity likely confers substantial protection against severe consequences of COVID-19 in Zambia [43]. Variant periods were defined based on predominant variants in GISAID data in Zambia and not on sequencing results from patients in the study. HIV status was self-reported, which could have led to biased VE findings in PWH. Lastly, there are potentially other unaccounted-for confounders that could not be factored into the VE analysis.

Vaccination is a critical tool to reduce the consequences of the SARS-CoV-2 pandemic. COVID-19 vaccines have likely saved millions of lives globally [44]. These findings are among the first demonstrating the life-saving potential of COVID-19 vaccines in countries in Africa, and such real-world evidence could help increase vaccination in a region that lags behind the rest of the world by providing local evidence of vaccine benefits in preventing COVID-19 mortality. Substantially increasing COVID-19 vaccinations will help Zambia reach targets and reduce COVID-19 mortality in the country.

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Patient consent. Patients who provided verbal consent for clinical care at participating COVID-19 treatment centers were eligible for inclusion in the study. The study protocol was approved by the University of Zambia Biomedical Research Ethics Committee; it was also reviewed in accordance with the US Centers for Disease Control and Prevention (CDC) human research protection procedures and was determined to be research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes.

References

1. World Health Organization Regional Office for Africa (WHO AFRO). COVID-19 vaccination in the WHO African region; monthly bulletin. Available at: https://apps.who.int/iris/bitstream/handle/10665/354270/CV-20220513-eng.pdf.
2. Zambia National Public Health Institute. Zambia COVID-19 statistics; daily status update. Available at: https://www.facebook.com/ZMPublicHealth/.
3. Mulenga LB, Hines JZ, Fwoloshi S, et al. Prevalence of SARS-CoV-2 in six districts in Zambia in July, 2020: a cross-sectional cluster sample survey. Lancet Glob Health **2021;** 9:E773–E781.
4. Wang H, Paulson KR, Pease SA, et al. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21. Lancet **2022;** 399:1513–36.
5. Bobo P, Hines JZ, Chilengi R, et al. Leveraging Zambia's HIV program and civil society to accelerate COVID-19 vaccine uptake. Emerg Infect Dis. **In press**.
6. Carcelen AC, Prosperi C, Mutembo S, et al. COVID-19 vaccine hesitancy in Zambia: a glimpse at the possible challenges ahead for COVID-19 vaccination rollout in Sub-Saharan Africa. Hum Vaccin Immunother **2022;** 18:1–6.
7. Matenga TFL, Zulu JM, Davis LM, Chavula MP. Motivating factors for and barriers to the COVID-19 vaccine uptake: a review of social media data in Zambia. Cogent Public Heal. **In press**.
8. Nolen S. As vaccines trickle into Africa, Zambia's challenges highlight other obstacles. *New York Times*. December 11, **2021**. Available at: https://www.nytimes.com/2021/12/11/health/covid-vaccine-africa.html.
9. Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. Int J Infect Dis **2022;** 114:252–60.
10. Tenforde MW, Self WH, Gaglani M, et al. Effectiveness of mRNA vaccination in preventing COVID-19-associated invasive mechanical ventilation and death—United States, March 2021-January 2022. MMWR Morb Mortal Wkly Rep **2022;** 71:459–65.
11. Andrews N, Stowe J, Kirsebom F, et al. COVID-19 vaccine effectiveness against the Omicron (B.1.1.529) variant. N Engl J Med **2022;** 386:1532–46.
12. Plumb ID, Feldstein LR, Barkley E, et al. Effectiveness of COVID-19 mRNA vaccination in preventing COVID-19-associated hospitalization among adults with previous SARS-CoV-2 infection—United States, June 2021-February 2022. MMWR Morb Mortal Wkly Rep **2022;** 71:549–55.
13. Bekker L-G, Garrett N, Goga A, et al. Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke Study): results from a single-arm, open-label, phase 3B, implementation study. Lancet **2022;** 399:1141–53.
14. Collie S, Champion J, Moultrie H, Bekker L-G, Gray G. Effectiveness of BNT162b2 vaccine against Omicron variant in South Africa. N Engl J Med **2022;** 386:494–6.
15. Simwanza J, Hines JZ, Sinyange D, et al. COVID-19 vaccine effectiveness during a prison outbreak when Omicron was the dominant circulating variant—Zambia. Am J Trop Med Hyg **2022**. tpmd220368. Available at: https://www.medrxiv.org/content/10.1101/2022.05.06.22274701v1.
16. Food and Drug Administration. Vaccines and related biological products advisory committee meeting, February 26, 2021. FDA briefing document; Janssen Ad26COV2S vaccine for the prevention of COVID-19. **2021**. Available at: https://www.fda.gov/media/146217/download.
17. Madhi SA, Baillie V, Cutland CL, et al. Efficacy of the ChAdOx1 nCoV-19 COVID-19 vaccine against the B.1.351 variant. N Engl J Med **2021;** 384:1885–98.
18. Menezes NP, Simuzingili M, Debebe ZY, Pivodic F, Massiah E. What is driving COVID-19 vaccine hesitancy in Sub-Saharan Africa? *World Bank Blogs*. August 11, **2021**. Available at: https://blogs.worldbank.org/africacan/what-driving-covid-19-vaccine-hesitancy-sub-saharan-africa. Accessed June 27, 2022.
19. Africa Centres for Disease Control. COVID 19 vaccine perceptions: a 15 country study. **2021**. Available at: https://africacdc.org/download/covid-19-vaccine-perceptions-a-15-country-study/.

20. Lewis HC, Ware H, Whelan M, et al. SARS-CoV-2 infection in Africa: a systematic review and meta-analysis of standardised seroprevalence studies, from January 2020 to December 2021. BMJ Global Health. **In press**.
21. Salyer SJ, Maeda J, Sembuche S, et al. The first and second waves of the COVID-19 pandemic in Africa: a cross-sectional study. Lancet **2021;** 397:1265–75. https://doi.org/10.1016/S0140-6736(21)00632-2
22. Ritchie H, Mathieu E, Rodés-Guirao L, et al. Coronavirus pandemic (COVID-19). Available at: https://ourworldindata.org/coronavirus.
23. Jassat W, Cohen C, Tempia S, et al. Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study. Lancet HIV **2021;** 8:e554–67.
24. Minchella P, Chanda D, Hines J, et al. The first four COVID-19 waves in Zambia: comparison of epidemiologic and clinical characteristics among persons hospitalized for COVID-19.
25. World Health Organization. COVID-19 case definition. **2020**. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2022.1.
26. Chanda D, Minchella PA, Kampamba D, et al. COVID-19 severity and COVID-19–associated deaths among hospitalized patients with HIV infection —Zambia, March–December 2020. MMWR Morb Mortal Wkly Rep **2021;** 70: 807–10.
27. GISAID—EpiCov. Available at: https://www.epicov.org/epi3/frontend#220b8c. Accessed February 18, 2022.
28. World Health Organization. The WHO global clinical platform for COVID-19. **2020**. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical-2022.2.
29. Harris PA, Taylor R, Minor BL, et al. The REDCap Consortium: building an international community of software platform partners. J Biomed Inform **2019;** 95: 103208.
30. World Health Organization. COVID-19 clinical management; living guidance. **2021**. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1.
31. Mwenda-Chimfwembe M, Saasa N, Bridges D. Genomic epidemiology of novel coronavirus—Africa_Zambia-focused subsampling. Available at: https://nextstrain.org/groups/SC2ZamPub/ncov/africa/zambia. Accessed February 16, 2022.
32. UNAIDS. AIDSinfo: people living with HIV (all ages). Available at: http://aidsinfo.unaids.org/.
33. Thompson MG, Natarajan K, Irving SA. Effectiveness of a third dose of mRNA vaccines against COVID-19–associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant predominance—VISION network, 10 states, August 2021. Morb Mortal Wkly Rep **2022**; 71:139–45.
34. Lin D-Y, Gu Y, Wheeler B, et al. Effectiveness of COVID-19 vaccines over a 9-month period in North Carolina. N Engl J Med **2022;** 386:933–41.
35. Polinski JM, Weckstein AR, Batech M, et al. Durability of the single-dose Ad26.COV2.S vaccine in the prevention of COVID-19 infections and hospitalizations in the US before and during the Delta variant surge. JAMA Netw Open **2022;** 5:e222959.
36. Lewis NM, Self WH, Gaglani M, et al. Effectiveness of the Ad26.COV2.S (Johnson & Johnson) COVID-19 vaccine for preventing COVID-19 hospitalizations and progression to high disease severity in the United States. Clin Infect Dis. **In press**.
37. Modes ME, Directo MP, Melgar M, et al. Clinical characteristics and outcomes among adults hospitalized with laboratory-confirmed SARS-CoV-2 infection during periods of B.1.617.2 (Delta) and B.1.1.529 (Omicron) variant predominance—one hospital, California, July 15–September 23, 2021, and December 21, 2021–January 27, 2022. MMWR Morb Mortal Wkly Rep **2022;** 71:217–23.
38. Hui KPY, Ho JCW, Cheung M-C, et al. SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo. Nature **2022;** 603:715–20.
39. Shinde V, Bhikha S, Hoosain Z, et al. Efficacy of NVX-CoV2373 COVID-19 vaccine against the B.1.351 variant. N Engl J Med **2021;** 384:1899–1909.
40. Alcorn K. AIDSmap: COVID-19 vaccines in people with HIV. Available at: https://www.aidsmap.com/about-hiv/covid-19-vaccines-people-hiv. Accessed April 26, 2022.
41. Gushchin VA, Tsyganova E V, Ogarkova DA, et al. Sputnik V protection from COVID-19 in people living with HIV under antiretroviral therapy. EClinicalMedicine **2022;** 46:101360.
42. World Health Organization. Leaders make urgent call to accelerate vaccination globally and in Africa. Available at: https://www.who.int/news/item/14-09-2021-leaders-make-urgent-call-to-accelerate-vaccination-globally-and-in-africa.
43. World Health Organization. Strategic Advisory Group of Experts (SAGE) on immunization: interim statement on hybrid immunity and increasing population seroprevalence rates. Available at: https://www.who.int/news/item/01-06-2022-interim-statement-on-hybrid-immunity-and-increasing-population-seroprevalence-rates. Accessed June 27, 2022.
44. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis **2022;** 22:1293–302.