

Safety and Efficacy of COVID-19 Vaccine in Africa: Systematic Review

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Background: Coronavirus disease 2019 (COVID-19) pandemic scared the whole world at the end of 2019, which is a communicable respiratory disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). In South Africa and other African countries, the COVID-19 vaccines were subsequently approved for emergency use by the respective national regulatory authorities. There is a paucity of aggregated data that revealed the safety and efficacy of COVID-19 vaccines in Africa.

Objective: The aim of this systematic review was to synthesize the literature on the safety and efficacy of the COVID-19 vaccine which was given in Africa.

Methods: A systematic search was conducted on Science Direct, PubMed, EMBASE, Google Scholar, CINAHL, Cochrane Library, and direct Google searches. Only studies written in English and published articles from 2019 to October 30, 2022, which comprise nine randomized clinical trials (RCT), and four different studies including a single-arm implementation trials, prospective study, retrospective cohort study, and test-negative designs were included.

Results: A total of 13 studies were included which contain 810,466 participants from Africa. Of these, 62.18% of the participants were female. The efficacy of COVID-19 vaccine in Africa ranges from 41.7% to 100%. Moreover, vaccine efficacy against COVID-19 variants ranges from -5.7% to 100%. In general, systemic and local adverse events following vaccination in most trials were reported with a similar pattern between the placebo and vaccine groups. Out of the total reported adverse events, most of them were mild to moderate, whereas a few were serious.

Conclusion: Almost all current COVID-19 vaccines appear to be safe for African study participants. Regarding efficacy, the protein subunit vaccine and mRNA vaccine exhibited high efficacy (100%) in this group of participants. However, Ad26. COV2.S and ChAdOx1 nCoV-19 COVID-19 vaccines are not effective against the delta variant and B.1.351 variant, respectively.

Keywords: safety, immunogenicity, efficacy, COVID-19 vaccine, Africa

Background

Coronavirus disease 2019 (COVID-19) pandemic scared the whole world at the end of 2019, which is a communicable respiratory disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) part of single-stranded RNA viruses having spike-like projections of glycoprotein. The first cases of COVID-19 were reported in Wuhan, China, during late-December 2019.¹ The WHO declared COVID-19 as a public health emergency of global concern on 30 January 2020.² On the continent of Africa, the initial case of SARS-CoV-2 was reported in Egypt on 14 February 2020.³ Last updated on January 2023, in Africa, total number of cases are 12,741,465, deaths: 258,344.⁴

During the COVID-19 pandemic, across the globe, vaccination is the greatest hope of reducing the burden of COVID-19 outbreak with the widespread effect. Subsequently, in South Africa and other African countries, the COVID-19 vaccines were approved or authorized for emergency use.⁵

Polymorphisms in major histocompatibility complex (MHC) genes are one mechanism causing variations in vaccine response. Several study findings show that the immunogenicity of influenza A vaccines has demonstrated and this, in particular, to modulate anti-influenza antibody repertoires have been demonstrated by polymorphisms in the Immunoglobulin Heavy Variable 1-69 (IGHV1-69 gene). This gene is responsible for producing antibodies and it exists in 14 variations, with specific

polymorphisms being more effective in generating a response to the influenza A virus in contrast to others; with those from African, Asian and European descent showing marked differences about their ethnicity that is resulting in varying frequency of various polymorphisms. This is one of the key variables to take into account during clinical trials in the study development as well as during post-study data analysis of the potential differences between ethnicities. This may lead which vaccines may be more appropriate for different patient cohorts.⁶

Indeed, different clinical trials conducted on COVID-19 vaccine in Africa; however, there is a paucity of aggregated data that revealed the safety and efficacy of COVID-19 vaccines in Africa.

In public health and medical care system, obstacles to vaccination coverage include individuals’ and parents’ concerns or fears about vaccine efficacy and safety, thus side effect profiles are the core vaccines competencies. To this effect, pooled evidence regarding the safety and efficacy of COVID-19 vaccines among African’s population will create confidence to physicians, vaccinees, families and policy makers. Thus, this systematic review aimed to synthesize the literature/ evidence(s) of the safety and efficacy of COVID-19 vaccines which were conducted in Africa (Figure 1 and Table 1).⁷

Africa CDC COVID-19 Vaccination Overview Latest Update on April 3, 2023

The total number of populations in Africa in 2022 is 1,401,646,166. Total vaccine dose received in the continent was 1,005,968,458; from this, only 69% doses were utilized, 23.3% of the population was partially vaccinated and 23.2% of the population was fully vaccinated⁸ (Figures 2 and 3).

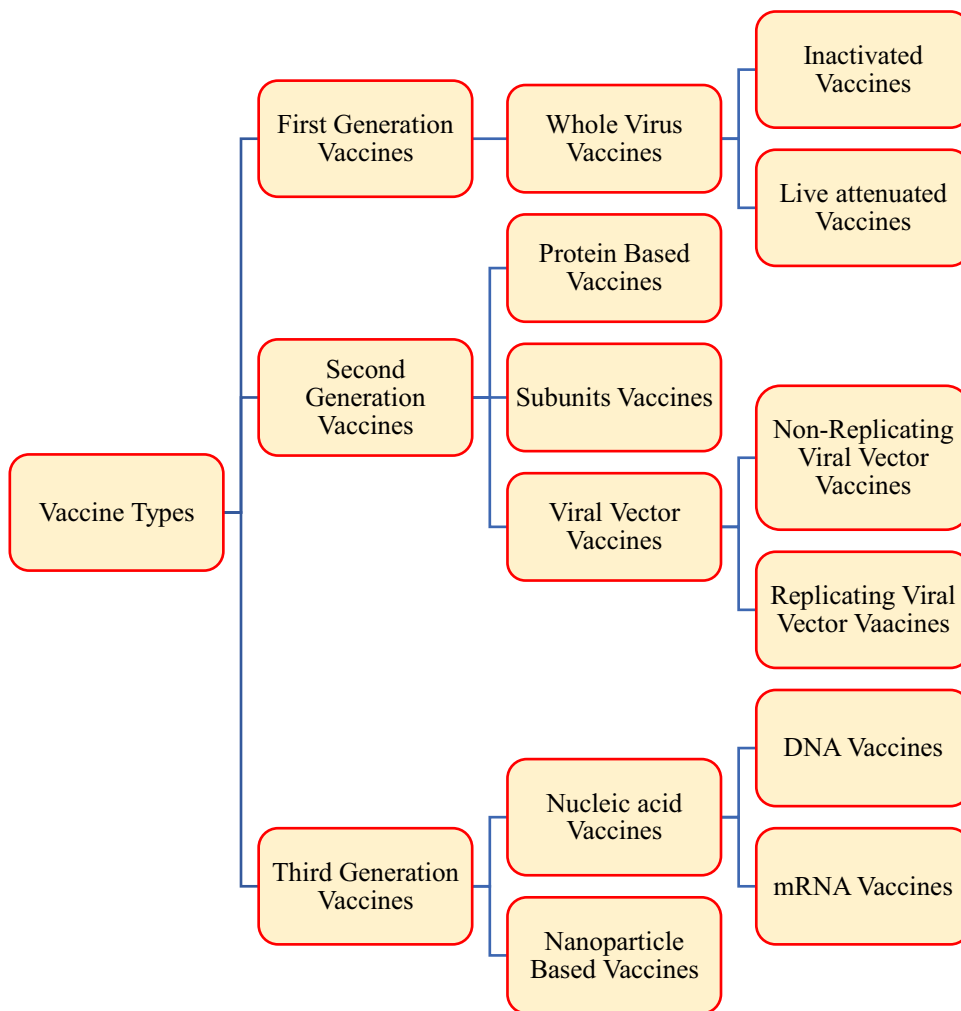


Figure 1 Main vaccines types and platforms for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
Notes: Reproduced with permission from Acosta-Coley I, Cervantes-Ceballos L, Tejada-Benitez L, et al. Vaccines platforms and COVID-19: what you need to know. *Trop Dis Travel Med Vaccines*. 2022;8:20. <https://doi.org/10.1186/s40794-022-00176-4> (<https://creativecommons.org/licenses/by/4.0/>).⁷

Table 1 Types of COVID-19 Vaccines Platform and Vaccine Characteristics

S. No.	Vaccine Manufacturer (Vaccine Name)	Platform	Vaccine Characteristics	Clinical Trial Regime
1.	Sinopharm (BBIBP-CorV)	Inactivated virus	Inactivated vaccine made of virus particles	2 doses (21 days apart)
2.	Sinovac Biotech (CoronaVac)	Inactivated virus	Inactivated SARS-CoV-2 alum Adjuvant	2 doses (14 days apart; 14 or 28 days apart in Chile)
3.	Bharat Biotech (BBV152/ Covaxin)	Inactivated virus	Inactivated whole virion	2 doses (28 days apart)
4.	Novavax (NVX-CoV2373)	Protein subunit	Full-length recombinant SARS-CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	2 doses (21 days apart)
5.	VECTOR (EpiVacCorona)	Protein subunit	A peptide-based vaccine that are conjugated to a large carrier protein	2 doses (21–28 days apart)
6.	AstraZeneca University of Oxford (ChAdOx1nCoV19/ AZD1222/Covishield)	Non-replicating viral vector	Chimpanzee adenovirus containing the genetic sequence of the SARS-CoV-2 surface spike protein	2 doses (<6 weeks apart)
7.	Gamaleya (Sputnik V)	Non-replicating viral vector	Recombinant adenovirus type 26 (rAd26) and type 5 (rAd5) vectors carrying the gene for SARS-CoV-2 spike glycoprotein (rAd26-S and rAd5-S)	2 doses (21 days apart)
8.	Johnson & Johnson (Ad26.COV2.S)	Non-replicating viral vector	Ad26 vector	2 doses (28 days apart)
9.	Pfizer–BioNTech (BNT162b2)	mRNA	Lipid nanoparticles (LNP) nucleoside-modified mRNA encoding an optimized SARS-CoV-2 Receptor-binding domain (RBD) antigen	2 doses (21 days apart)
10.	Moderna/NIAID (mRNA-1273)	mRNA	LNP-encapsulated mRNA encoding the surface spike protein	2 doses (28 days apart)
11.	Inovio Pharmaceuticals (INO-4800)	DNA	DNA plasmid encoding S protein delivered by electroporation	2 doses (28 days apart)

Note: Data from Acosta-Coley et al.⁷

Methods and Materials

Search Strategy

This systematic review was conducted through a database searching for literature and identified relevant studies; those were considered included to summarize the safety and efficacy of COVID-19 vaccines which were conducted in Africa were used.

The review followed the steps recommendation based on the criteria of preferred reporting items for systematic reviews and meta-analyses (PRISMA)⁹ (Figure 4). We independently searched electronic databases such as PubMed, Science Direct, Google Scholar, Cochrane Library, EMBASE, CINAHL and direct Google searches were performed. Electronic databases were searched using the combinations of the following key terms along with the Boolean operators (“OR, AND”): “safety, immunogenicity, efficacy, effect, COVID-19 vaccine, Africa, South Africa and Sub-Saharan Africa” from October 1 to 30, 2022.

The PubMed search detail was as ((((((safety) OR (immunogenicity)) AND (efficacy)) OR (effectiveness)) OR (effect)) AND (COVID-19 vaccine)) AND (Africa)) OR (South Africa)). (((“safety”[MeSH Terms] OR “safety”[All

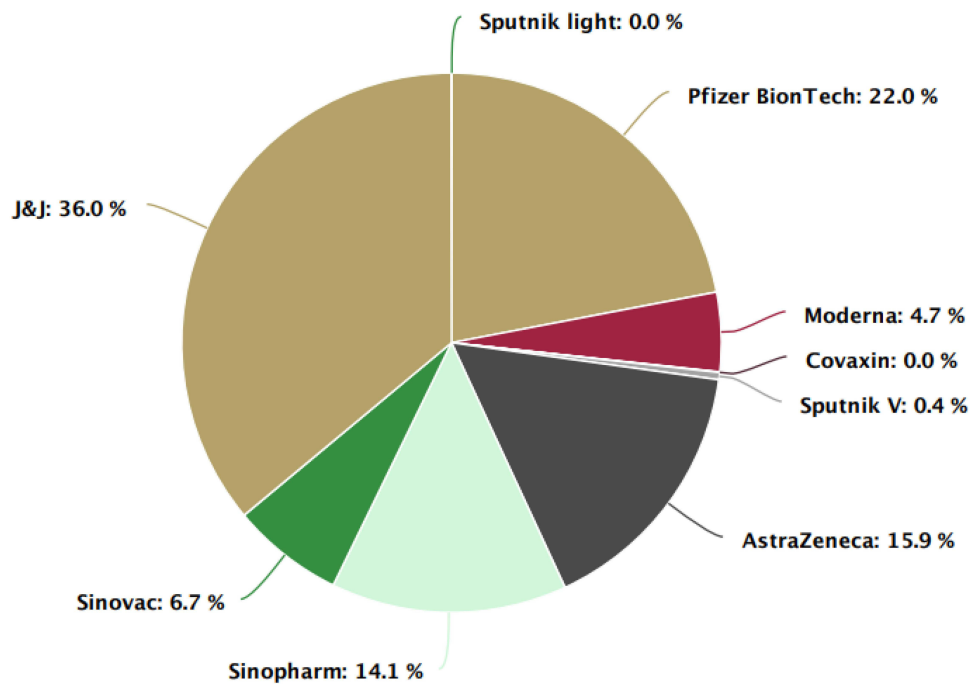


Figure 2 Proportion of vaccine type in Africa.

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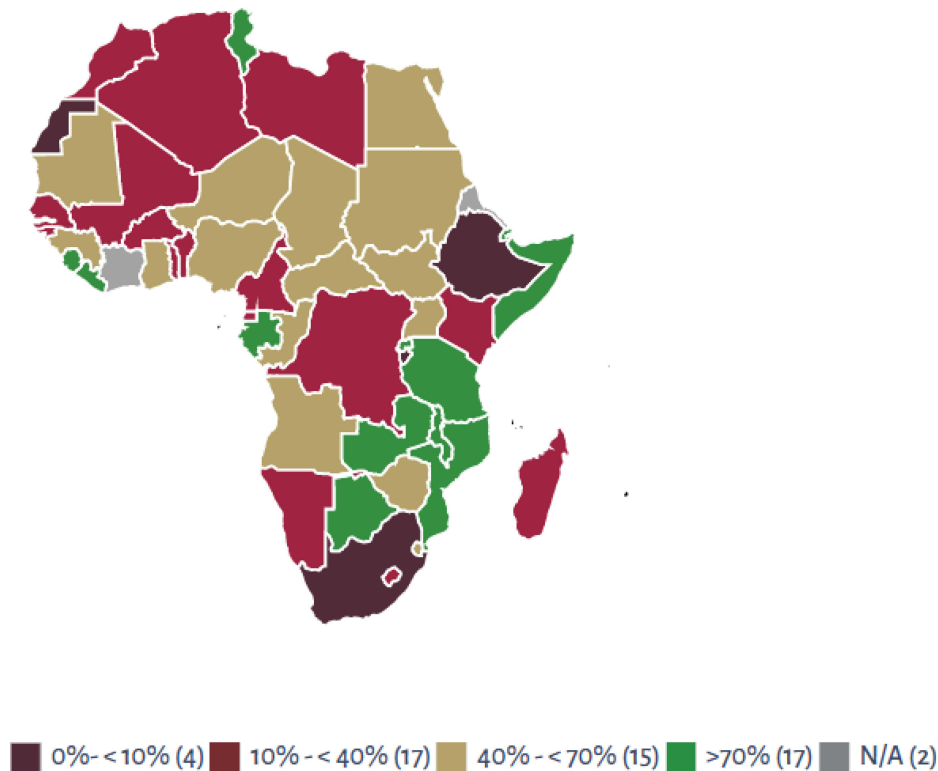


Figure 3 Vaccine coverage by member state in Africa.

Notes: Copyright © Africa CDC 2023. Reproduced with permission from africacdc.org. Africa CDC COVID-19 Vaccine Dashboard [webpage on the Internet]. Addis Ababa: Africa Centres for Disease Control and Prevention; 2022. Available from: <https://africacdc.org/covid-19-vaccination/>. Accessed October 30, 2022.⁸

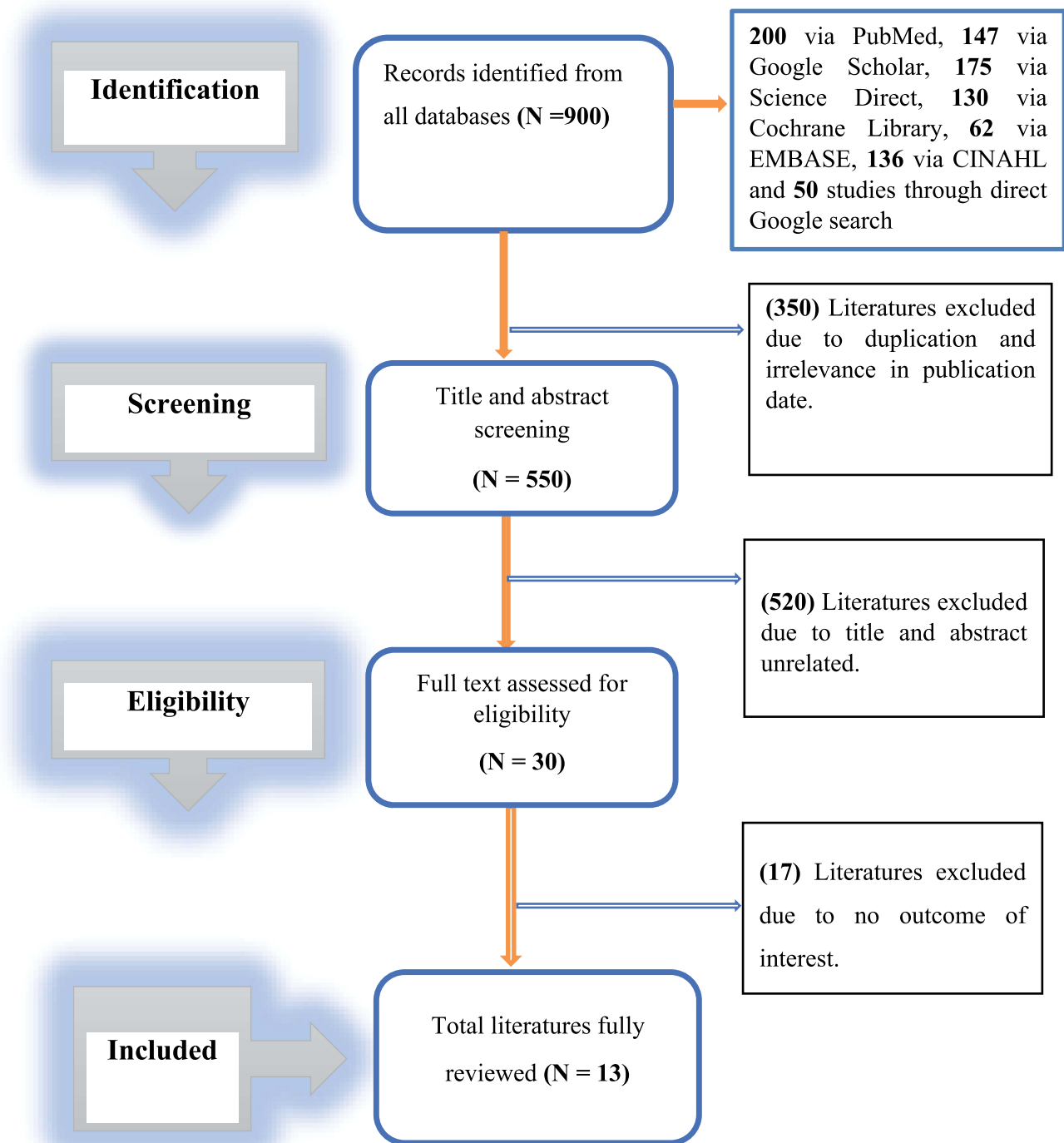


Figure 4 Flow diagram of included studies based on the criteria of PRISMA.

Notes: PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71. Creative Commons.¹⁰

Fields] OR “safeties”[All Fields] OR (“antigens”[MeSH Terms] OR “antigens”[All Fields] OR “immunogen”[All Fields] OR “immunogens”[All Fields] OR “immunogene”[All Fields] OR “immunogenes”[All Fields] OR “immunogenic”[All Fields] OR “immunogenically”[All Fields] OR “immunogenicities”[All Fields] OR “immunogenicity”[All Fields] OR “immunogenity”[All Fields])) AND (“efficacies”[All Fields] OR “efficacious”[All Fields] OR “efficaciously”[All Fields] OR “efficaciousness”[All Fields] OR “efficacy”[All Fields])) OR (“effect”[All Fields] OR “effecting”[All Fields] OR

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Inclusion and Exclusion Criteria

This review included studies written in English and published from 2019 up to recently published articles in 2022, which contains randomized clinical trials (RCTs), single-arm implementation trials, prospective studies, retrospective cohort studies and test-negative designs were included. However, researches published before 2019, articles that could not contain the full text, and research articles that were not written in English were excluded.

Methodological Quality Assessment

Selected studies were evaluated for validity by using Joanna Briggs Institute (JBI) critical appraisal checklist before inclusion in the review. Any difference that might bring disagreement for the summarization of the safety and efficacy of COVID-19 vaccine was fixed through critical evaluation (see [Supplementary Material](#)).

Data Extraction

Data extraction protocol was designed by the second author. Data were extracted by the name of the first author and approved after critically reviewed by the second author. Both authors were arranged the data by year of publication, study design, age, sex, COVID-19 vaccine name, placebo name, total sample size, sample size in Africa, dose, and treatment duration.

Result

Study Selection

A total of 900 papers were selected through the initial electronic database search (200 via PubMed, 200 via Google Scholar, 200 via Science Direct, 150 via Cochrane Library, 50 via EMBASE, 50 via CINAHL). Through direct Google search, 50 articles were identified through reference citations and other different guide searches. The total number of screened studies was 900, and after initial screening of titles and abstracts, 350 studies were excluded. After step-wise selection, only 13 studies were fully reviewed.

Characteristics of the Included Studies

A total of 13 studies were included in this systematic review (810,466 participants from Africa) and overall, 62.18% participants were female. From these included studies, the majority were conducted in South Africa except Zhang et al and Hammad et al; which were conducted in Morocco¹¹ and Egypt,¹² respectively. Five of the included studies were multinational trials. Nine studies out of 13 were a randomized clinical trial (RCT) and the other included studies were a single-arm implementation trial, retrospective cohort study, prospective study and test negative case-control study by Takuva et al,¹³ Zhang et al,¹¹ Hammad et al,¹² and Gray et al,¹⁴ respectively. In all studies, the minimum participant age was 18 years except studies done by Thomas et al¹⁵ in South Africa and Hammad et al¹² study in Egypt which were 12 and 20 years, respectively.

In the 13 included studies, different COVID-19 vaccines were used to assess and evaluate either the safety or efficacy to assess and evaluate both the safety and efficacy of COVID-19 vaccine; the vaccines used in the studies were SCB-2019 vaccine, BNT162b2 mRNA vaccine, Ad26.COV2.S Vaccine, a booster regimen of Ad26.COV2.S vaccine, NVX-CoV2373 vaccine, ChAdOx1 nCoV-19 vaccine and BBIBP-CorV vaccine. Moreover, the efficacy of NVX-CoV2373 and ChAdOx1 nCoV-19 vaccines was evaluated against the B.1.351 variant. Additionally, effectiveness of Ad26.COV2.S and BNT162b2 vaccines with Omicron variant was evaluated¹⁵⁻²⁷ (Table 2 and Table 3).

Table 2 Baseline Socio-Demographic and Clinical Characteristics of the Included Studies (N=13)

S. No.	Authors (Year)	Study Design	Study Area	Age	Sex		COVID-19 Vaccine Name	Placebo Name	Total Sample Size	Sample Size in Africa		Dose and Treatment Duration
					M	F						
1	Bravo et al ²⁸ (2022)	RCT	31 sites in five countries (Belgium, Brazil, Colombia, Philippines, and South Africa)	≥18 years	16,009 (53.1%)	14,119 (46.9%)	SCB-2019 (30 µg, adjuvanted with 1.50 mg CpG-1018 and 0.75 mg alum)	0.9% saline (sodium chloride)	N=30,128 SCB-2019 (N=15,064) Placebo (N=15,064)	N=1100 (3.7%) SCB-2019; N=555 (3.7%) Placebo; N=545 (3.6%)	Two 0.5 mL IM doses 21 days apart.	
2	Thomas et al ¹⁵ (2021)	RCT	152 sites (4 sites in South Africa)	≥12 years	22,420 (50.9)	21,627 (49.1)	BNT162b2	Saline	N = 44,047 BNT162b2 (N = 22,026) Placebo (N = 22,021)	N=4216 (9.6) BNT162b2; N=2098 (9.5) Placebo; N=2118 (9.6)	Two 30-µg doses, at 21 days apart, IM	
3	Moreira Jr et al ¹⁶ (2022)	RCT	123 sites in the USA, South Africa, and Brazil	≥16 years	4975 (49.1)	5150 (50.9)	BNT162b2	Saline	N = 10,125 BNT162b2 (N = 5081) Placebo (N = 5044)	N=932 (9.2) BNT162b2; N=472 (9.3) Placebo; N=460 (9.1)	Administered 7 to 9 months after the primary two-dose	
4	Sadoff et al ¹⁷ (2022)	RCT	Argentina, Brazil, Chile, Colombia, Mexico, Peru, USA, and South Africa	≥18 years	24,053 (54.9)	19,722 (45.0)	Ad26.COVS.2.S	Saline 0.5 mL IM	N = 43,783 Ad26.COVS.2.S (N = 21,895) Placebo (N = 21,888)	N=8515 (19.4) Ad26.COVS.2.S; 4251 (19.4) Placebo; 4264 (19.5)	A single IM dose of 5×10 ¹⁰ viral particles	
5	Takuva et al ¹³ (2022)	Single-arm implementation trial	South Africa	≥18 years	119,753	357,481	Ad26.COVS.2.S	—————	—————	N=477,234	A single IM dose of 5×10 ¹⁰ viral particles	
6	Hardt et al ¹⁹ 2022	RCT	Belgium, Brazil, Colombia, France, Germany, Philippines, South Africa, Spain, the UK, and the USA	≥18 years	16,474	14,820	A booster regimen of Ad26.COVS.2.S	Saline	N=31,300 Ad26.COVS.2.S (N=15,708) Placebo (N=15,592)	N=2554 Ad26.COVS.2.S; 1309 (8.3%) Placebo; 1245 (8.0%)	Two IM doses of 5×10 ¹⁰ viral particles 56 days apart	
7	Madhi et al ²⁰ (2022)	RCT	South Africa	18–84 years	2522 (57.2%)	1886 (42.8%)	NVX-CoV2373	0.9% Saline 0.5 mL IM	—————	HIV -ve N=4164 NVX-CoV2373 (N=2089) Placebo (N=2075)	HIV +ve N=244 NVX-CoV2373 (N=122) Placebo (N=122)	Two IM dose (5 µg recombinant spike protein with 50 µg Matrix-M adjuvant; 21 days apart

(Continued)

Table 2 (Continued).

S. No.	Authors (Year)	Study Design	Study Area	Age	Sex		COVID-19 Vaccine Name	Placebo Name	Total Sample Size	Sample Size in Africa		Dose and Treatment Duration
					M	F						
8	Madhi et al ²¹ (2021)	RCT	South Africa	18–65 years	63 (39%)	98 (61%)	ChAdOx1nCoV-19 (AZD1222)	0.9% Saline	—————	HIV -ve N=58 ChAdOx1nCoV-19 (N=29) Placebo (N=29)	HIV +ve N=103 ChAdOx1nCoV-19 (N=52) Placebo (N=51)	Two IM dose of 5×10 ¹⁰ virus particles; 28 days apart
9	Zhang et al ¹¹ (2022)	Retrospective cohort study	Morocco	18–99 years	82,608	59,437	BBIBP-CorV (Sinopharm)	—————	—————	Fully Vaccinated N = 140,892	Booster-vaccinated N = 1149	Two IM dose 21 to 28 days apart and booster dose
10	Hammad et al ¹² (2022)	Prospective Study	Egypt	20–80 years	111	144	Oxford/AstraZeneca (ChAdOx1/nCoV-19)	—————	—————	N = 255		Two IM dose of 5×10 ¹⁰ virus particles; 12-week interval
11	Madhi et al ²² (2021)	RCT	South Africa	18–65 years	1142 (56.5)	—————	ChAdOx1nCoV-19 (AZD1222)	0.9% Saline	—————	N= 2026 HIV -ve ChAdOx1nCoV-19 (N = 1011) Placebo (N = 1010)		Two IM dose of 5×10 ¹⁰ virus particles; 21 to 35 days apart
12	Shinde et al ²⁹ (2021)	RCT	South Africa	18–84 years	2518 (57.4)	1869 (42.6)	NVX-CoV2373	0.9% Saline 0.5 mL IM	—————	N = 4387 NVX-CoV2373 (N = 2199) Placebo (N = 2188)		Two IM dose 21 days apart
13	Gray et al ¹⁴ (2022)	Test negative case-control study	South Africa	≥18 years	67,629 (41.6)	95,008 (58.4)	Ad26.COV2.S and BNT162b2	Controls with a negative test	—————	The results of 162,637 PCR tests (of which 93,854 (57.7%) were obtained from participants who had received two doses of BNT162b2 vaccine or two doses of the Ad26.COV2.S vaccine)		Two-dose of BNT162b2; at least 42 days apart and (booster) dose of the Ad26.COV2.S; 4 to 6 months apart
Total No. of participants in these 13 studies									952,532			
Total No. of African participants in these 13 studies											810,466	

Notes: HIV -ve: HIV test negative participants; HIV +ve: HIV test positive participants; Fully vaccinated: if at least 14 days had passed since the administration of a second dose of BBIBP-CorV vaccine. Booster-vaccinated: who received three doses of BBIBP-CorV vaccine.

Abbreviations: N, number; USA, United States of America; UK, United Kingdom.

Table 3 The Safety and Efficacy of COVID-19 Vaccines of the Included Studies

S. No.	Authors (Year)	COVID-19 Vaccine Used in the Study	Outcome
1	Bravo et al ²⁸ (2022)	SCB-2019 vaccine	Safe and effective
2	Thomas et al ¹⁵ (2021)	BNT162b2 Vaccine through 6 months	Safe and effective
3	Moreira et al ¹⁶ (2022)	Third dose of BNT162b2 vaccine	Safe and effective
4	Sadoff et al ¹⁷ (2022)	Single-dose Ad26.COVS vaccine	Safe and effective but not effective against delta variant was (VE=-5.7%)
5	Takuva et al ¹³ (2022)	Single-dose Ad26.COVS vaccine	Safe and effective
6	Hardt et al ¹⁹ (2022)	A booster regimen of Ad26.COVS	Safe and effective
7	Madhi et al ²⁰ (2022)	NVX-CoV2373 vaccine	Favorable safety and immunogenicity
8	Madhi et al ²¹ (2021)	ChAdOx1nCoV-19 (AZD1222) in people living with and without HIV	Favorable safety and immunogenicity
9	Zhang et al ¹¹ (2022)	BBIBP-CoV (Sinopharm)	Safe and effective
10	Hammad et al ¹² (2022)	Oxford/AstraZeneca (ChAdOx1nCoV-19) during Delta and Omicron Variants Pandemic	Safe and effective
11	Madhi et al ²² (2021)	ChAdOx1nCoV-19 (AZD1222) vaccine against the B.1.351 Variant	Not-effective against B.1.351 variant (VE=10.4%)
12	Shinde et al ²⁹ (2021)	NVX-CoV2373 vaccine against the B.1.351 Variant	Safe and effective
13	Gray et al ¹⁴ (2022)	Ad26.COVS and BNT162b2 vaccines against Omicron Variant	Both vaccines were equally effective

COVID-19 Vaccine Efficacy of the Included Studies

Efficacy of Protein Subunit COVID-19 Vaccines

Three published studies were pooled evaluating the efficacy vs immunogenicity of protein subunit COVID-19 vaccines in adults aged 18 years and older. They were all conducted in South Africa; from the three studies, one was conducted at 31 sites in five countries (Belgium, Brazil, Colombia, Philippines, and South Africa)²⁸ and the other two were conducted only in South Africa.²⁰ The inactivated vaccine they contained; two studies on the NVX-CoV2373 vaccine and one study on the SCB-2019 vaccine.

According to Bravo et al²⁸ study of SCB-2019 vaccine, the efficacy of the SCB-2019 vaccine was not reported specific to the South Africa participants; however, it was reported that the overall vaccine efficacy of all participants against any severity COVID-19 was 67.2% (95% CI, 54.3–76.8), against moderate-to-severe COVID-19 accounted for 83.7% (95% CI, 55.9–95.4), and against severe COVID-19 was 100% (95% CI, 25.3–100.0).²⁸ Based on Madhi et al²⁰ study on the immunogenicity and safety of NVX-CoV2373 vaccine, which was conducted in people living with and without HIV-1 infection. Among participants in the NVX-CoV2373 group who were SARS-CoV-2 negative at baseline, the anti-spike IgG geometric mean titers (GMTs) and seroconversion rates (SCRs) were in people living with HIV-1 lower than (n=62) in HIV-negative people (n=1234) after the first vaccination (GMT: 508.6 vs 1195.3 ELISA units [EU]/mL; SCR: 51.6% vs 81.3%); and similarly, 14 days after the second vaccination for GMTs (14420.5 vs 31631.8 EU/mL), while the SCR was similar at this time point (100.0% vs 99.3%).²⁰ Moreover, study done by Shinde et al²⁹ on NVX-CoV2373 vaccine against the B.1.351(beta) variant, the vaccine efficacy was 51.0% (95% CI, -0.6 to 76.2) among the HIV-negative participants.

Efficacy of mRNA COVID-19 Vaccines

Three published studies evaluated the safety and efficacy vs effectiveness of mRNA vaccines against COVID-19. They were all conducted in South Africa; from the three studies, one was conducted at 152 sites (130 sites in the United States, 1 site in Argentina, 2 sites in Brazil, 4 sites in South Africa, 6 sites in Germany, and 9 sites in Turkey),¹⁵ the other one was conducted at 123 sites (in the United States, South Africa, and Brazil)¹⁶ and the remaining one was conducted only in South Africa.¹⁴ The inactivated vaccines they used for the vaccine group were BNT162b2 vaccine.

Of the three studies of BNT162b2 vaccine; Thomas et al study in South Africa, where the SARS-CoV-2 variant of concern B.1.351 was prevalent, a vaccine with 100% efficacy (95% CI, 53.5 to 100) was observed.¹⁵ A study done by Moreira et al on results of a third dose of the BNT162b2 vaccine; relative vaccine efficacy of South Africa participants; it was 100.0% (95% CI, -554.9 to 100.0), but in white race participants; which was 95.2% (95% CI, 88.4 to 98.5).¹⁶ In accordant with Gray et al study, the vaccine effectiveness against Omicron variant was 81% (95% CI, 41 to 94) during 13 days after the second dose, 88% (95% CI, 62 to 96) at 14 to 27 days, 70% (95% CI, 64 to 76) at 1 to 2 months, 71% (95% CI, 68 to 74) at 3 to 4 months, and 67% (95% CI, 63 to 71) at 5 months or longer.¹⁴

Efficacy of Non-Replicating Viral Vector COVID-19 Vaccines

Seven published studies were included in this article to evaluate either the safety and efficacy or immunogenicity of non-replicating viral vector COVID-19 vaccines; almost in all studies, the targeted participants were aged 18 and above years old. From the seven studies, two of them were multinational study,^{17,19} four of them were conducted only in South Africa^{13,14,21,22} and the remaining one was conducted in Egypt,¹² which contained four studies on Ad26.COV2.S vaccine and three studies on Oxford–AstraZeneca vaccine (ChAdOx1/nCoV-19).

Two studies were conducted on single-dose Ad26. COV2.S vaccine and the other two were conducted with the second dose or booster regimen. As reported by Sadoff et al¹⁷ multinational study of single-dose Ad26. COV2.S vaccine in South Africa; vaccine efficacy against moderate to severe–critical disease was 49.3 (95% CI, 26.9 to 65.3). Moreover, during this study, the vaccine efficacy against delta variant was -5.7% (95% CI, -177.7 to 59.2) and against the beta variant accounted for 51.9% (95% CI, 19.1 to 72.2).¹⁷ Another a single-dose Ad26. COV2.S vaccine was conducted by Takuva et al¹³ study in South Africa. The efficacy of the vaccine was 83% (95% CI, 75–89) to prevent COVID-19-related deaths, 75% (69–82) to prevent COVID-19-related hospitalizations requiring intensive care or critical care, and 67% (95% CI, 62–71) to prevent hospitalizations related to COVID-19. The vaccine effectiveness was maintained in older health-care workers and those with comorbidities including HIV infection. In addition, during Takuva et al¹³ study in South Africa, the vaccine effectiveness against COVID-19-related hospital admission during the beta wave was 62% [95% CI, 42–76] and during the delta wave was 67% [95% CI, 62–71], and vaccine effectiveness against COVID-19-related death during beta wave was 86% [95% CI, 57–100] and during delta wave was 82% [95% CI, 74–89]. In accordant with Gray et al¹⁴ study on the second dose of Ad26. COV2.S vaccine, effectiveness against Omicron variant for hospitalization of COVID-19 was 55% (95% CI, 22 to 74) within 13 days after the second dose, 74% (95% CI, 57 to 84) at 14 to 27 days, and 72% (95% CI, 59 to 81) within 1 to 2 months. Additionally, with Hardt et al¹⁹ multinational study on a booster regimen of Ad26.COV2.S vaccine in South Africa; vaccine efficacy was 60.0% (95% CI, -144.5 to 96.2).

As specified by Madhi et al²¹ study on the ChAdOx1 nCoV-19 (AZD1222) vaccine evaluation of immunogenicity in people living with and without HIV in South Africa. In this study, for SARS-CoV-2 antigen seronegative participants at baseline, full-length spike geometric mean concentration (GMC) at day 28 was 163.7 binding antibody units (BAU)/mL (95% CI, 89.9–298.1) for people living with HIV (n=36), and 112.3 BAU/mL (95% CI, 61.7–204.4) for participants of HIV-negative (n=23), whereas, with a rising day 42 GMC booster response in both groups. As expressed by Hammad et al¹² study on the Oxford–AstraZeneca vaccine (ChAdOx1/nCoV-19) in Egypt, compared to the baseline level, the anti-spike IgG serum level was significantly elevated at 12 weeks and 24 weeks. Among these, 88.2% participants were seropositive after the first dose, while the seropositivity reached 95.7% after the second dose. In patients with past COVID-19 infection, anti-spike IgG serum level was significantly higher after the first dose (mean: 348.8±140.5 IU/mL) and the second dose (mean: 309.8±120.9 IU/mL) of vaccination when compared to level after the first (mean: 199.5±164.4 IU/mL) and second dose (mean: 258.5 ±136. IU/mL) in those who gave a negative history of past infection. Nearly two-thirds (64.8%) of the seronegative

Table 4 Summary of the Efficacy Range of COVID-19 Vaccine Type for the Included Studies

S. No.	COVID-19 Vaccine Type	Efficacy Range
1	Protein subunit COVID-19 vaccines	51.0 to 100%
2	mRNA COVID-19 vaccines	67.0 to 100%
3	Non-replicating viral vector COVID-19 vaccines	-5.7 to 86%
4	Inactivated virus COVID-19 vaccines	90.2%

healthcare workers (HCWs) showed seroconversion rates of 81.8% and 93.3% after the first and second vaccination doses, respectively.¹² In consistent with Madhi et al²² study in South Africa, ChAdOx1 nCoV-19 COVID-19 vaccine efficacy against B.1.351 variant was 10.4% (95% CI, -76.8 to 54.8). A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate COVID-19 due to the B.1.351 variant.

Efficacy of Inactivated Virus COVID-19 Vaccines

One published study from Morocco was included in this article. This is a real-world, retrospective cohort study of the effectiveness of BBIBP-CorV (Sinopharm) COVID-19 vaccine among adults aged 18–99 years.

As declared by Zhang et al¹¹ study on BBIBP-CorV (Sinopharm) COVID-19 vaccine, unadjusted, full-series, unboosted BBIBP-CorV vaccine efficacy (VE) against hospitalization for serious or critical illness was 90.2% (95% CI, 87.8–92.0%). There were no serious or critical illnesses among BBIBPCorV-boosted individuals (Table 4).

COVID-19 Vaccine Safety of the Included Studies

Protein subunit COVID-19 vaccine showed a safety profile as follows: upon Bravo et al²⁸ study SCB-2019 vaccine elicited higher rates of mainly mild-to-moderate injection site pain than the placebo after the first (35.7% vs 10.3%) and second (26.9% vs 7.4%) doses, but systemic adverse events were similar between the groups. Serious adverse events have been reported by 0.3% vaccinees and 0.4% placebo recipients. Vaccine-related cases were rare; only five participants were considered to have treatment-related events. Of the reported deaths, there were 3 in the vaccine group and 13 in the placebo group; nothing is mentioned in the study whether the death is related to the vaccine or placebo. This study concluded that SCB-2019 vaccine has a favorable safety and reactogenicity profile. The results of Madhi et al²⁰ study in the NVX-CoV2373 group reported solicited local and systemic adverse events were more common in HIV-negative participants (30.6% local and 28.7% systemic) vs people living with HIV-1 (25.3% local and 25.3% systemic). In both Madhi et al²⁰ and Shinde et al²⁹ studies, the result shows that, of the serious adverse events that occurred, none of them were assessed as related to the NVX-CoV2373 vaccine by the study investigators.

The mRNA COVID-19 vaccine safety results demonstrated that, as a result of Thomas et al¹⁵ study, BNT162b2 vaccine on participants had adverse events leading to withdrawal from the trial 0.1%. Moreover, more participants in the BNT162b2 group than in the placebo group reported systemic events, the most common one was fatigue. Systemic events were mostly mild to moderate in severity, but there were occasional severe events and severe adverse events were 1.2%. During the study, death was reported, but none of the deaths were considered related to BNT162b2 by the investigators. According to Moreira et al¹⁶ study, serious adverse events were reported by slightly more participants in the placebo group than in the vaccine group (0.5% vs 0.3%). No new safety signals were identified, and no cases of myocarditis or pericarditis were reported. Generally, both studies concluded that BNT162b2 vaccines were safe and have an acceptable adverse-event profile.

Non-replicating viral vector vaccine (Ad26.COVS. S) safety result indicates that Sadoff et al¹⁷ reported that serious adverse events were reported by more participants in the vaccine group than in the placebo group (19 vs 2); which were considered by the investigator to be related to vaccination. Of the very rare events occurring after vaccination that were identified after marketing began, one case of VITT (vaccine-induced immune thrombotic thrombocytopenia). Ad26.COVS.S was mainly associated with mild-to-moderate adverse events (AEs), and no new safety concerns were identified. Deaths had been reported (28 in the vaccine group and 55 in the placebo group). All deaths were considered by the investigators to be unrelated to the vaccine or placebo.¹⁷ As stated by Takuva et al,¹³ 1.3% serious adverse events (AEs) were reported or AEs of

special interest. Two cases of thrombosis with thrombocytopenia syndrome and 4 cases of Guillain–Barre' Syndrome were reported post-vaccination. One death was related to thrombotic thrombocytopenic purpura (TTP) reported after Ad26.COVID.2.S vaccination. According to Hardt et al¹⁹ study reported that serious adverse events considered related to the study vaccine (0.1% of them in the booster regimen of Ad26.COVID.2.S group and <0.1% in the placebo group). Seventeen deaths were reported in the entire double-blind phase, and none of these deaths were considered related to the study vaccine. Solicited adverse events were transient and mostly grade 1–2 in severity. No participant in the vaccine group reported an event of thrombosis with thrombocytopenia syndrome like the above two studies. However, three of these studies concluded that the most serious adverse events (SAEs) occurred below the expected rates. The single-dose and booster regimen of Ad26.COVID.2.S vaccine showed an acceptable safety profile.^{13,17,19}

Non-replicating viral vector vaccine (ChAdOx1 nCoV-19 vaccine) safety result indicates that; in accordance with Madhi et al²¹ study on the ChAdOx1 nCoV-19 (AZD1222) vaccine with serious adverse events, one severe fever (body temperature above 40°C) in a HIV-negative participant was definitely related to trial intervention and one severely elevated alanine aminotransferase in a participant with HIV was unlikely related. One person with HIV died (unlikely related). As per Hammad et al,¹² safety report demonstrated that the most common adverse reactions were pain and malaise. No serious adverse event was reported. Both Madhi et al²⁰ and Hammad et al¹¹ conclude that the Oxford–AstraZenecavaccine is generally safe and well tolerated. As claimed by Madhi et al,²² the only serious adverse event attributed to the ChAdOx1 nCoV-19 vaccine was a body temperature above 40°C after the first dose; but, the fever subsided within 24 hours.

BBIBP-CorV is an inactivated virus COVID-19 vaccine, based on Zhang et al¹¹ study. The result shows that there were no serious or critical illnesses among BBIBP-CorV-boosted individuals.

Discussion

To develop new vaccine, clinical trials are the mainstay of clinical research, along with for product licensing extensions and marketing authorization for existing therapies. To ensure that pharmaceutical products including vaccines are safe and effective in the different groups of population who would benefit from these products, in particular vaccines, clinical trials should be conducted in varied populations including Africa.^{23,24} Hence, this systematic review discusses the synthesis literatures/evidences of the safety and efficacy of COVID-19 vaccine in Africa.

Efficacy, which is measured under RCTs, which means that the vaccine has the ability to protect vaccinated individuals. All COVID-19 vaccines approved by WHO for emergency use listing have been used through RCTs to test their quality, safety and efficacy. To be approved, vaccines are required to have a high efficacy rate of 50% or above.²⁵ Due to the limited number of studies that were conducted in Africa, this article only explored the efficacy of six vaccines against COVID-19 conducted in Africa.

Subunit vaccines are containing part of the pathogen proteins or glycoproteins and are considered to be the safest and effective vaccine. Currently, there are so many subunit vaccines on the market,²⁶ of them, SCB-2019 vaccine and NVX-CoV2373 (developed by Novavax) were included in this systematic review. A previous systematic review and meta-analysis of RCT studies showed that the first and second doses of protein subunit vaccines provided 79–87.3% efficacy on protection against COVID-19.²⁷ In this systematic review, in terms of efficacy, the investigated protein subunit vaccine was found to be 51.0–100% efficacious in preventing COVID-19 among Africa participants. Here, the efficacy of 51.0–100% is wide range, this may be due to the presence of beta variant in South Africa, and this one could be a possible reason for the wide range of efficacy. This result compared to the above previous study is somehow different; this may be due to the presence of beta variant in South Africa or the presence of genetic difference in Africa as compared to other nations (the efficacy of the vaccines may vary between individuals and populations), geographical location variation could be some possible reason for this difference in efficacy result. Antibody responses are an important part of immunity after COVID-19 vaccination. SARS-CoV-2 envelopes contain the spike protein (SP) on its surface, which is highly immunogenic and is a primary target for neutralizing antibodies.³⁰ Serology testing for SARS-CoV-2 antibodies has been recognized as a useful tool for diagnosing both previous and active infection in both symptomatic and asymptomatic individuals.³¹ Madhi et al study conducted on safety and immunogenicity of NVX-CoV2373 vaccine in South Africa. Of the total participants who took NVX-CoV2373 vaccine group with baseline SARS-CoV-2 negative, the seroconversion rates (SCRs) and anti-spike

IgG geometric mean titers (GMTs) were higher in HIV-negative people than in people living with HIV-1 following the first vaccination. This may be due to the fact that people living with HIV either have previous and active SARS-CoV-2 infection, compared to the general population, or those who are immunocompromised subjects should be considered a vulnerable group because they could have a higher risk of getting SARS-CoV-2. Moreover, the lower SCR in HIV-1 participants may indicate that immune mechanisms like innate immune response, CD4⁺ T-cell responses, and B-cell memory response contribute to protection of COVID-19.

mRNA vaccines are a nucleotide-based novel vaccine platform that contains viral genetic material (mRNA) which provides instructions for making viral proteins.⁷ Only BNT162b2 mRNA vaccine was included in this systematic review. A previous systematic review and meta-analysis of RCT studies showed that the mRNA vaccine provided 94.6% efficacy on protection against COVID-19 (30). In this systematic review, in terms of efficacy, the investigated mRNA vaccine was found to be 67.0–100% efficacious in preventing COVID-19 among Africa participants. This result compared to the above previous study is somehow different; this may be due to the same reason as mentioned in the protein subunit vaccines (the presence of beta variant in South Africa or presence of genetic difference in Africa compared to other nations), geographical location variation might contribute to this difference. Another possible reason may be due to the use of different types/platform of COVID-19 vaccine since in this systematic review only BNT162b2 mRNA vaccine was included or it may be due to the difference in the time interval of the study of vaccine efficacy after injection (previous study 4 weeks after injection vs this systematic review 5 months or longer).

Non-replicating viral vector vaccine contains genetically modified viruses that are made replication non-competent and do not cause the disease.⁷ Two non-replicating viral vector vaccines were included in this systematic review, Ad26.COV2.S and ChAdOx1 nCoV-19 (AZD1222) vaccine. A previous systematic review and meta-analysis of RCT studies showed that adenovirus-vectored COVID-19 vaccine provided 80.2% efficacy on protection against COVID-19 (30). In this systematic review, in terms of efficacy, the investigated non-replicating viral vector vaccine was found to be –5.7 to 86% efficacious in preventing COVID-19 among Africa participants. A negative vaccine efficacy reflects a higher infection rate among the vaccinated population than non-vaccinated people. It has been suggested that vaccines amplified the biological susceptibility, but in this case, the virus evolved to spread rapidly among vaccinated subjects.³² Moreover, COVID-19 vaccines are strongly recommended as safe, effective, and life-saving in preventing serious illness or death. In general, all vaccines do not provide full (100%) protection for those who are vaccinated, and yet it is not known how well they can prevent people from transmitting the virus to others.²⁵ So, as a suggestion as well as getting vaccinated, we must also continue with other measures to fight the pandemic, such as covering coughs and sneezes, coughing with a bent elbow or tissue, washing and sanitizing hands, physical distancing, wearing face masks, keeping room ventilated, and avoiding crowds. Get tested if they are sick, even if they have been vaccinated.

Vaccine effectiveness is a measure of its ability to reduce disease cases in a vaccinated group of people compared to an unvaccinated group under real-life conditions.³³ Upon Zhang et al the study provided real-world evidence of the effectiveness of BBIBP-CorV vaccine under conditions of widespread use in Morocco. The efficacy of unadjusted, full-series, unboosted BBIBP-CorV vaccine against hospitalization for serious or critical illness was 90.2%. This result is different from Nadeem et al study in the elderly population of Pakistan; the result shows that the efficacy of Sinopharm vaccine (BBIBP-CorV) 14 days after the second dose was efficient in 66.1% reduction in intensive care unit (ICU) admissions in the vaccinated group.³⁴ This difference may be due to Sinopharm (BBIBP-CorV) vaccine efficacy may vary between individuals and populations (could be affected by genetic variability). This result shows that BBIBP-CorV vaccine has better efficacy in African population, and this may be due to immunization history for other infection, and other factors like the presence of aged participants (aged 60 and above) and presence of comorbidity in Pakistan study, geographical location variation might contribute to this difference.

Vaccination is one of the greatest achievements of public health in human history. Vaccines are considered as safe and effective when used correctly during the national immunization programs (NIPs). Likewise, other medicines, vaccines are not free from risk and adverse events following immunization. To the success of the vaccination program hinges strongly on the trust people have about the safety and efficacy of vaccines.³⁵ In general, the systemic and local vaccine adverse events following immunization reported in most trials were similar between the vaccine and placebo groups. Most of the adverse events reported were mild to moderate, whereas a few were severe. The common adverse events were injection site pain and

fatigue. Few clinical trials reported serious adverse events and death, but most of them were unrelated to vaccination. From the serious adverse events reported with SCB-2019 vaccine, only five participants were considered to have treatment-related events. Of the very rare events occurring after Ad26.COV2. S (Johnson & Johnson) vaccination vaccine-induced immune thrombotic thrombocytopenia (VITT) was reported and one death was related to this. Generally, almost all studies concluded that COVID-19 vaccines were safe and have an acceptable adverse-event profile.^{11–17,19–22,28,29} This safety result is almost similar to a previous systematic review and meta-analysis of RCT study.³⁶ Except in this previous study, death was not reported, and given the very recent emergence, the meta-study does not include an analysis of VITT. This similarity may be due to COVID-19 vaccine safety may not be altered by genetic variability.

Strengths and Limitations of This Review

The strength of this systematic review was use of high-quality RCTs and other study designs that were conducted on the safety and efficacy of COVID-19 in the focus of African population. However, this review also has some limitations. The major limitation of this review is the heterogeneity in the three included studies since the immunogenicity of the vaccine was assessed rather than direct efficacy measurement of the COVID-19 vaccine, the inclusion of poor-quality study designs (the single-arm design), the inclusion of studies limited to a few geographic locations that is because of the limited number of studies were conducted in Africa. Moreover, one study done by Bravo et al, the efficacy of the SCB-2019 vaccine was reported in various continents which was not specific to the South Africa participants. The majority of the studies were conducted in South Africa; since South Africa is a multinational country with a variety of ethnicity, but in all included studies, the efficacy of only African participants (Blacks) was not reported, and these are some of the shortcomings of this review.

Conclusion

In this systematic review, almost all current COVID-19 vaccines included in the review had an acceptable safety profile for African study participants. Regarding efficacy, the protein subunit vaccine and mRNA vaccine exhibited high efficacy (100%) in this group of participants. However, Ad26. COV2.S and ChAdOx1 nCoV-19 COVID-19 vaccines are not effective against delta variant and B.1.351 variant, respectively. Future studies with longer follow-up are warranted to monitor the long-term efficacy and safety of various COVID-19 vaccines.

Abbreviations

ACIP, Advisory Committee on Immunization Practices; AEs, adverse effects; SAEs, serious adverse effects; Alum, aluminum hydroxide; B.1.1.7, Alpha variant; B.1.1.529, Omicron variant; B.1.351, Beta variant; BAU, binding antibody units; Anti-spike (S) IgG, severe acute respiratory syndrome coronavirus-2 antibody (immunoglobulin G); BLA, Biologics License Application; CpG, cytosine phosphoguanine; ELISA, enzyme-linked immunosorbent assay; EU, ELISA Units; EUA, Emergency Use Authorization; FDA, Food and Drug Administration; GMTs, geometric mean titers; HCWs, healthcare workers; HIV, human immunodeficiency virus; ICU, intensive care unit; IGHV1-69 gene, Immunoglobulin heavy variable 1-69 gene; LNP, lipid nanoparticles; MHC, major histocompatibility complex; NIAID, National Institute of Allergy and Infectious Disease; NIPs, National Immunization Programs; P.1, Gamma variant; PCR, polymerase chain reaction; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RBD, receptor-binding domain; RCT, randomized clinical trial; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome-coronavirus-2; SCRs, seroconversion rates; VE, vaccine efficacy; WHO, World Health Organization.

Data Sharing Statement

All data generated during the study were included in this systematic review.

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