

# Efficacy of Covid-19 Vaccines in Ethnically Diverse Population (BAME): A Systematic Review

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## ABSTRACT

**Background:** The Black, Asian, and minority ethnic (BAME) groups are more prone to covid-19 disease severity and its associated mortality. The research has reported that the response of vaccines against different viral infections has varied among different groups of populations such as age, gender, race, and comorbidities. Therefore, the present study aimed to evaluate the efficacy of covid-19 vaccines of Emergency Use License (EUL) in BAME ethnicities.

**Method:** We conducted a systematic review by using different names of EUL vaccines in Cochrane Covid-19 Study Register (CCSR) and WHO Covid-19 global literature and exported the retrieved results to EndNote X8 to eliminate the duplicate records. The study followed PRISMA (Preferred Items for Reporting Systematic Reviews and Meta-analysis) guidelines for reporting systematic reviews. We descriptively reviewed the included studies and performed data synthesis for randomized controlled trials (RCTs).

**Results:** A total of 4799 retrieved records were filtered down to 13 studies for inclusion which comprised nine RCTs, three case-control studies, and one retrospective cohort. The RCTs included in the data synthesis covered mRNA-1273, BNT162b2, NVX-CoV2373, AZD1222, and Ad26.COV2.S vaccines and reported 603 total events out of 125,874 participants in the interventional group and 3115 total events out of 109,093 participants in placebo groups. Compared to White participants, one RCT showed higher efficacy of mRNA-1237 in communities of color, whereas another RCT showed higher efficacy in Asians. Two RCTs showed that BNT162b2 had the highest efficacy (100%) in Black ethnicity. Similarly, one RCT of each NVX-CoV2373 and AZD1222 reported the highest efficacies of the respective vaccine in Black individuals. Among different vaccines, the Asian obtained the highest efficacy with mRNA-1273 but the lowest with BNT162b2. However, the data synthesis revealed a statistically significant favor for the efficacy of all vaccines over placebo across all subgroups of ethnicities.

**Conclusion:** The covid-19 vaccines have non-inferior efficacy in different ethnicities. Nonetheless, the mRNA vaccines might be comparatively suitable for Black and Asian individuals in terms of efficacy than other vaccines. However, more studies with substantial representation of the BAME population are warranted to increase the magnitude of evidence in this regard.

**Keywords:** Covid-19, vaccines, efficacy, BAME

## INTRODUCTION

In December 2019, there has been an outbreak of pneumonia in Wuhan, China. The origin of this disease was undetermined initially. Later, Chinese scientists isolated a novel coronavirus namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from patients in Wuhan.<sup>1</sup> By March 2020, the virus spread to more than 110 countries with a count of over 118,000 cases throughout the globe and the World Health Organization (WHO) declared SARS-CoV-2 as a covid-19 pandemic.<sup>2</sup> The majority of the covid-19 patients presented respiratory infection causing fever of 37.5 °C or higher, cough, chills, fatigue, difficulty in breathing, and lack of appetite.<sup>3,4</sup> whereas the severe covid-19 infection required ventilation support and caused multi-organ damage and death.<sup>5</sup>

The therapeutic strategies against covid-19 are currently focused on the prevention through vaccine. Despite that supportive therapies have been established and antiviral drugs have been approved, the role of vaccines remains pivotal in the prevention of covid-19-associated damage to public health.<sup>6</sup> Even when the vaccine-provided protection declined and waned during the emergence of the Delta variant, the Covid-19-associated hospitalization rate and deaths remained low in the vaccinated population compared to the unvaccinated population.<sup>7</sup>

Since the SARS-CoV-2 outbreak has prompted the generation of a vast data including the efficacy studies of covid-19 vaccines, the synthesis of evidence has been attempted in different subgroups of general and patient populations such as gender,<sup>8</sup> age groups,<sup>9,10</sup> pregnant and lactating women,<sup>11</sup> immune compromised patients,<sup>12-3</sup> renal diseases,<sup>14</sup> and mental disorders.<sup>15</sup> However, the evidence yet has not been synthesized for the efficacy of covid-19 vaccines in the BAME population. As this population has low representation in clinical trials,<sup>16-7</sup> is more vulnerable to the severity of covid-19 disease and has low levels of trust in covid-19 vaccines which can further worsen the situation, a need is identified to synthesize the data for covid-19 vaccine efficacy (VE) in BAME population.

Therefore, the present study aimed to systematically review the covid-19 VE in the BAME population. To the best of our knowledge, the present study is the first systematic review of VE in the BAME population, and its results could help to identify the differences in VE across different communities of color. The evidence from the present systematic review may play a role to inform evidence-based practices regarding vaccination in people from ethnic minorities. Moreover, the results of the present systematic review may impact the trust level among people of color leading to enhanced uptake of covid-19 vaccination.

**Research Objective:** The research objective of the present study was to systematically review the efficacy of Emergency Use License (EUL) vaccines in ethnically diverse BAME populations against SARS-CoV-2 and its variants.

## METHODOLOGY

Systematic review was done in concordance with the guidelines presented by the Cochrane Collaboration and conforms to PRISMA (Preferred Items for Reporting Systematic Reviews and Meta-analysis) guideline for reporting systematic reviews.<sup>17</sup>

The PICO (population, intervention, control, and outcomes) format was utilized to frame the research question (Tovey 2020). The ethnically diverse BAME population of any age, gender, and geographic location was taken as the population of interest while vaccines listed by WHO (2022) as emergency-use vaccines against covid-19 (as of January 12, 2022) were included as intervention. Any vaccine from the WHO EUL list other than interventional vaccine, placebo, or no vaccine (control group) was accounted for as a comparison. The efficacy of the vaccine was seen in terms of preventing covid-19 infection, reducing the post-vaccine frequency of infection, and the rate of post-vaccine seroconversion. The impact of vaccination on hospitalization and the need for mechanical ventilation were secondary outcomes. The PICO of the present systematic review is summarized in Table 4.1.

**Search Method:** Two databases were searched: 1) Cochrane COVID-19 Study Register (CCSR) and 2) WHO covid-19 global literature.

The names of the vaccines listed as WHO (2022) EUL vaccines were utilized as search strings. Table 4.2. Provides the list of vaccines that obtained EUL status as of January 12, 2022. Three filters were applied in CCSR: Report Results, Prevention, and Efficacy whereas two filters were applied in WHO covid-19 global literature: covid-19 vaccines as the main subject and English as the language of publication.

Table 1: PICO format for the research question.

P	Population of interest	Ethnically diverse (BAME) persons
I	Intervention	Covid-19 vaccine
C	Control	Any vaccine other than intervention, placebo, or unvaccinated individuals as control
O	Outcome (s)	Efficacy of vaccine Postvaccine reduction in infection Rate of postvaccine hospitalization

Table 2: EUL vaccines as-listed on WHO (2022) website.

S. No.	Vaccine	Date of EUL status
1	Pfizer/BioNTech Comirnaty vaccine	31 December 2020
2	SII/COVISHIELD and AstraZeneca/AZD1222 vaccines	16 February 2021
3	Janssen/Ad26.COV 2.S vaccine developed by Johnson & Johnson	12 March 2021
4	Moderna COVID-19 vaccine (mRNA 1273)	30 April 2021
5	Sinopharm COVID-19 vaccine	7 May 2021
6	Sinovac-CoronaVac vaccine	1 June 2021
7	Bharat Biotech BBV152 COVAXIN vaccine	3 November 2021
8	Covovax (NVX-CoV2373) vaccine	17 December 2021
9	Nuvaxovid (NVX-CoV2373) vaccine	20 December 2021

Table 1: Data synthesis for pooled effect.

Author (year of publication)	Study design	Intervention	Comparator	White				Black				Asian			
				Vaccine		Comparator		Vaccine		Comparator		Vaccine		Comparator	
				Events	Total	Events	Total	Events	Total	Events	Total	Events	Total	Events	Total
Baden et al. (2020)	Clinical trial	mRNA-1273	Placebo	10	9023	144	8916								
El Sahly et al. (2021)	Clinical trial	mRNA-1273	Placebo	48	1139	631	1127	4	1391	41	1352	1	628	29	700
Moreira et al. (2022)	Clinical trial	Pfizer-BioNTech	Placebo	5	3727	100	3709	0	363	13	364	1	272	3	255
Polack et al. (2020)	Clinical trial	Pfizer-BioNTech	Placebo	7	1450	146	1467	0	1502	7	1486				
Thomas et al. (2021)	Clinical trial	Pfizer-BioNTech	Placebo	67	1718	747	1725	4	1737	48	1737	3	946	23	934
Dunkle et al. (2021)	Clinical trial	NVX-CoV2373	Placebo	12	1314	48	6184	0	1893	7	905				
Heath et al. (2021)	Clinical trial	NVX-CoV2373	Placebo	8	6625	85	6635								
Falsey et al. (2021)	Clinical trial	AZD1222	Placebo	58	1401	99	6755	2	1401	12	706				
Sadoff et al. (2022)	Clinical trial	Ad26.COV2.S	Placebo	237	1207	574	1207	62	3330	139	3324	12	701	17	641

The retrieved results were exported to EndNote X8 which removed the duplicates, then remaining studies were manually screened by reading their title and abstract and later, evaluated through full-text articles. The studies that were found eligible following full-text screening were critically appraised by employing Joanna Briggs Institute (JBI) Critical Appraisal Tool Checklist (Tufanaru et al. 2017).

**Inclusion criteria:** Clinical trials randomized clinical trials, prospective and retrospective studies, and cohorts published in English with the objective to determine the efficacy of the EUL vaccine with participants from black and/or Asian ethnicities of any age and gender group.

**Exclusion criteria:** The studies in a language other than English, having a population with chronic and/or inflammatory diseases, articles that did not provide the ethnicity-wise result of efficacy, and non-clinical studies were excluded. Moreover, a study was also excluded if it could not obtain a  $\geq 75\%$  score on EBL critical appraisal tool (Glynn 2006).

## RESULTS

As of 5<sup>th</sup> April 2022, there were 135,039 covid-19-related references available on CCSR and 558,348 records on WHO covid-19 global literature. After applying filters, a total of 3823 records were retrieved from CCSR. In WHO covid-19 global literature, we got 976 records. After removal of duplicates (2936) by EndNote X8, the remaining 1863 records were manually screened by reading their title and abstract to determine their relevancy. After initial screening, 179 records were held for full-text screening. Among these, 13 articles were included in the present study. Search results are presented in a flowchart (Fig. 5.1) according to the PRISMA flowchart for the identification of studies via databases and registers.<sup>17</sup>Figure 5.1. PRISMA flowchart for identification of studies via databases.

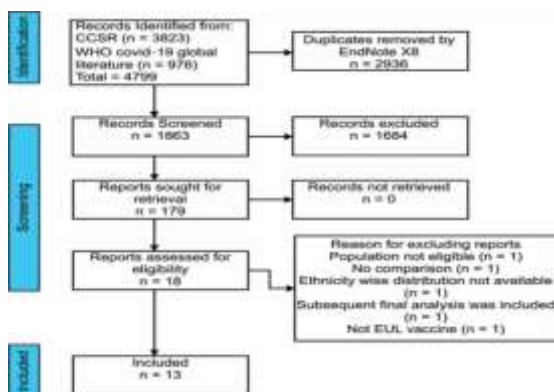


Figure 1:

The data was pooled by using RevMan to create different blobbograms (Forest plots) for subgroup analysis. The data from all included clinical trials for vaccines were combined and compared to placebo across various ethnic subgroups. Figure 5.2 shows a statistically significant difference in favor of vaccines in White (RR 0.16, 95% CI 0.15 to 0.18,  $p < 0.00001$ ), Black (RR 0.26, 95% CI 0.20 to 0.34,  $p < 0.00001$ ), Asian (RR 0.23, 95% CI 0.13 to 0.39,  $p < 0.00001$ ), multiracial (RR 0.42, 95% CI 0.31 to 0.57,  $p < 0.00001$ ), and "other" (RR 0.09, 95% CI 0.04 to 0.20,  $p < 0.00001$ ). The overall effect in Figure 5.2 also indicates a statistically significant favor for vaccines among all ethnic groups in comparison to placebo (RR 0.18, 95% CI 0.17 to 0.20,  $p < 0.00001$ ). The forest plot of all vaccines against placebo showed high heterogeneity in all groups except in the "other" subgroup ( $I^2 = 38\%$ ,  $p < 0.00001$ ).

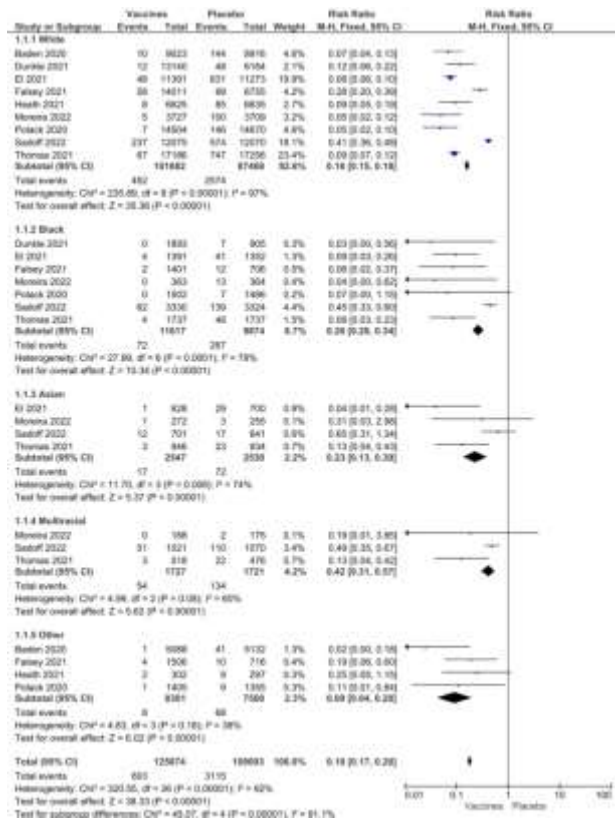


Figure 2: Efficacy of vaccines by ethnicity subgroups.

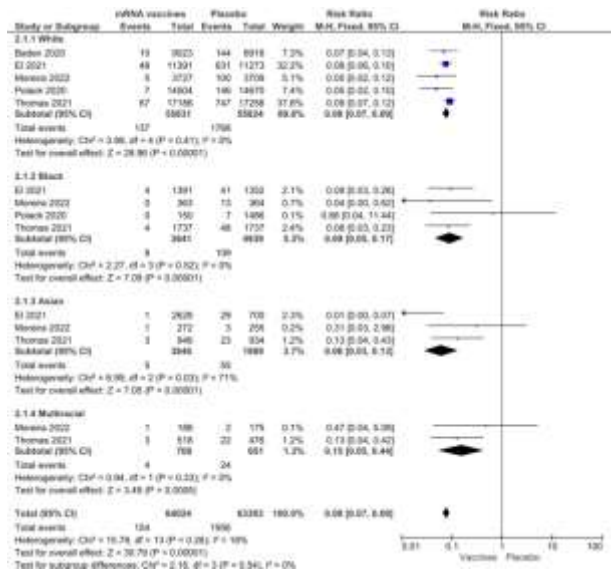


Figure 3: Efficacy of mRNA vaccines by ethnicity subgroups.

**DISCUSSION**

The present study systematically reviewed the efficacy of EUL vaccines in BAME population. The CCSR and WHO covid-19 global literature collectively had more than 69 thousand references (As of 5<sup>th</sup> April 2022) for studies on covid-19 related topics, indicating a need for evidence synthesis for various aspects of the covid-19 pandemic.

Previously, systematic reviews of the efficacy of covid-19 vaccines were done for immunogenicity, and safety in children and adolescents<sup>9</sup> and also Falsaperla did it in pregnant and lactating

females and their newborns. Safety and efficacy of covid vaccine was evaluated in Systematic review and meta-analysis for age difference by Wang and coworkers and in men and women by Zhu and colleagues. A systematic review was conducted to identify the factors that influenced the covid-19 vaccine hesitancy in lesbian, gay, bisexual, transgender, and queer people.<sup>18</sup>

Another important aspect of study subjects to correlate the efficacy of vaccines is the diversity of participants with reference to various races and ethnicities. Even more important is the fact that the race-related variations in antibody responses to several vaccines have been reported in the literature.<sup>19-24</sup> The substantial number of systematic reviews regarding covid-19-related different aspects of the population highlight the need for evidence synthesis for covid-19 VE in different groups of the public. However, no evidence was yet synthesized for the efficacy of covid-19 vaccines in the BAME population. The present study attempted to fill this gap by systematically reviewing the trials and other clinical studies.

The pooled effect of included studies in the present systematic review showed that VE in ethnic minority groups was non-inferior to that in the White group. However, the synthesized data also shows that the BAME population could hardly represent 20% of participants in clinical trials. Besides socio-demographic characteristics, low trust in covid-19 vaccines has been reported as an important factor for hesitancy among Black.<sup>25-7</sup> The trust in the vaccines thereby has been associated with greater levels of willingness to get vaccinated.<sup>28</sup> Therefore, the findings of the present systematic review may contribute as a piece of evidence to enhance the trust of people of color in covid-19 vaccines. Although their participation is underrepresented in clinical trials, the pooled effect reveals statistically significant favor of vaccines' efficacy in individuals from Black, Asian, and multiracial ethnicities.

Various reports have highlighted a higher vulnerability of individuals from black and Asian ancestries to elevated rate of covid-19-associated hospitalization and increased mortality in comparison to Caucasian counterparts.<sup>29,30</sup> Additionally, the race-related variations in antibody responses to a number of vaccines have also been reported in the literature.<sup>19-24</sup> Considering these data, the present systematic review highlights the efficacy of vaccines in people of color and could suggest that mRNA-1273, BNT162b2, NVX-CoV2373, and AZD1222 vaccines could potentially reduce the rate of covid-19 infection and associated severe disease, hospitalization, intensive care, and need of urgent care in people from communities of color.

Being the first systematic review of covid-19 VE in the BAME population—to the best of our knowledge, the present study fills the gap in synthesized evidence regarding mRNA-1273, BNT162b2, NVX-CoV2373, AZD1222, and Ad26.COV2.S vaccines in ethnically diverse communities. The other strengths of the present systematic review included the range of searched sources of information as the CCSR and WHO covid-19 global literature not only covered all subject-relevant well-known databases and clinical trial registries but also included references from grey literature. All of the randomized controlled clinical trials that were included in the present systematic review were published in the New England Journal of Medicine and all of the included studies represented a low risk of bias on quality appraisal tools. Another strength of the present systematic review could be the potential of its results for meta-analysis. The low heterogeneity values calculated for mRNA vaccines and the BNT162b2 vaccine indicate that obtained data can be processed for a meta-analysis of the efficacy of covid-19 vaccines in the BAME population.

Considering the question of the present research, only the efficacy of the covid-19 vaccines was evaluated. More than a limitation, this can be seen as an opportunity to synthesize further evidence regarding the safety of covid-19 vaccines in the BAME population. The inclusion of the BAME population with comorbid diseases could further advance the knowledge regarding the role of covid-19 vaccines in this population. Since the controlled trials included in the present systematic review generally had an efficacy follow-up of two to six months, a crucial need is identified to fill the

gaps in long-term follow-up data. The majority of the included RCTs incorporated observer-blinding rather than double-blinding which could lead to selection bias. Another limitation of the present study may be the language bias. However, as the major differences between summary treatment effects have not been found in English language-restricted and English language-nonrestricted studies,<sup>31</sup> the studies included in the present study could reasonably cover most of the knowledge generated up to now.

## CONCLUSION

The data synthesis from RCTs further revealed a statistically significant favor to the covid-19 vaccines versus placebo in Black, Asian, and multiracial ethnicities. The results of the present systematic review attempt to fill the gap in the literature regarding the covid-19 VE in different ethnicities and may be helpful to increase the trust level of covid-19 vaccines in people of color. More well-designed studies such as meta-analyses may be warranted to support the results of the present systematic review

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