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COMPARATIVE EVALUATION OF DIFFERENT COVID-19 VACCINES: EFFICACY AND SAFETY PROFILES

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ABSTRACT

The global response to the COVID-19 pandemic has seen the development and deployment of several vaccines aimed at controlling the spread of the virus. Each vaccine has unique characteristics regarding efficacy, safety, and immune response. A comparative evaluation of these vaccines is essential to guide public health decisions and improve vaccination strategies.

To compare the efficacy and safety profiles of different COVID-19 vaccines currently in use, including mRNA, viral vector, and protein subunit vaccines.

A systematic review and meta-analysis were conducted to evaluate data from clinical trials and real-world studies on the efficacy and safety of various COVID-19 vaccines. The vaccines included in the analysis were Pfizer-BioNTech, Moderna, AstraZeneca, Johnson & Johnson, and Sinovac. Efficacy was assessed in terms of prevention of symptomatic COVID-19, severe disease, and hospitalization. Safety profiles were examined through the incidence of common and severe adverse events.

The analysis revealed that mRNA vaccines (Pfizer-BioNTech and Moderna) demonstrated the highest efficacy in preventing symptomatic infection and severe outcomes, with efficacy rates exceeding 90% in early trials. Viral vector vaccines (AstraZeneca and Johnson & Johnson) showed slightly lower efficacy, ranging from 60% to 80%, but still provided significant protection against severe disease and hospitalization. The protein subunit vaccine (Sinovac) had a lower efficacy rate in preventing symptomatic infection (around 50%), but still contributed to reduced severity and hospitalizations. Safety profiles indicated that mRNA vaccines were generally well-tolerated, with mild to moderate side effects such as sore arms, fatigue, and fever. Rare severe adverse events, including myocarditis and thrombosis, were observed in some vaccines but remained infrequent.

All the vaccines analyzed showed high efficacy in preventing severe COVID-19 outcomes, though mRNA vaccines demonstrated superior efficacy in preventing symptomatic infection. Safety profiles were generally favorable, with most adverse events being mild and transient. Continued monitoring and comparative studies are necessary to evaluate the long-term efficacy and safety of these vaccines, particularly in diverse populations.

Keywords: COVID-19 vaccines, efficacy, safety profiles, mRNA vaccines, viral vector vaccines, protein subunit vaccines..

I. INTRODUCTION

Wuhan, China, reported the first detection of a new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December 2019. As a result, the extremely contagious Coronavirus Disease 2019 (COVID-19) spreads over the globe and turns into a pandemic.

Despite almost two years of international efforts to contain the pandemic, SARS-CoV-2 is still spreading, upsetting daily routines, and causing very high rates of morbidity (more than 225 million confirmed cases) and mortality (more than 4.5 million fatalities) globally as of September 15, 20212. It quickly became evident that the best method to combat the present pandemic is to provide effective treatment for patients with severe COVID-19 and to limit the spread of SARS-Cov-2 by immunising the general public. Global efforts have been concentrated on creating effective and safe vaccinations to prevent COVID-19 since the start of the epidemic. Up until recently, the process of developing a vaccine was thought to be drawn out and complex, taking decades before the product was approved for clinical use3. Scientists were rushing to create a safe and effective vaccination against SARS-CoV-2 based on both new and outdated vaccine technology shortly after the pandemic began. More than 300 vaccine candidates have been identified worldwide in less than two years, and 117 vaccines are in various clinical phases of development, including 30 in phase 35. As of the middle of 2021, seven COVID-19 vaccines have been granted emergency use authorisation (EUA) in several nations, including the US, UK, and EU. The World Health Organisation (WHO) Emergency Use Listing provides a summary of these emergency authorisations of use: Sinopharm and Sinovac (National Medical Products Administration (NMPA), China); Pfzer/BioNTech (US, EU, UK, WHO); Moderna (US, EU, UK); AstraZeneca (EU, UK); Janssen (US, EU); and Gamaleya (Russian Ministry of Health).5. Adjuvanted recombinant protein nanoparticles11, viral vectors8–10, and mRNA6–7 are some of the vaccine technologies used in EUA vaccines. Every technology has benefits and drawbacks. The most recent mRNA vaccine generations are mRNA-12737 and BNT162b26. The genetic information for the antigen is delivered via mRNA vaccines instead of the actual antigen, and the vaccinated person produces antigens in the host cells13. Since chemical synthesis is used to create every component of this technology, development may proceed more quickly in the case of a pandemic. High effectiveness and very little side effects are two benefits of mRNA vaccines. Prior to the current pandemic, mRNA vaccine technology seemed promise in treating a number of illnesses, including Zika and cytomegalovirus14; but, prior to the SARS-Cov-2 pandemic15, mRNA vaccines were not authorised for use in humans. However, COVID-19 mRNA vaccines have comparatively short-term effectiveness and safety evidence, including newly released short-term real-world studies6,7,16–20. A recombinant full-length wild-type SARS-CoV2 spike glycoprotein21 and Matrix-M1 adjuvant are both included in the adjuvanted recombinant protein vaccine known as NVX-CoV2373. The newly licensed Janssen Ebola vaccine22 by the EU made use of the same technical platform. Vaccines based on viral vectors include ChAdOx1, Ad26CoV2.S, and Gam-COVID-Vac8–10. Cloned antigen is used in the technology to create a viral vector that is incapable of reproducing. Compared to the recombinant protein vaccine, the viral vector may elicit stronger cellular immune responses by mimicking the disease state of viral infection. The safety of adenoviral vector vaccines has been well investigated, and clinical practice uses therapeutic medications based on adenoviral vectors23. Three novel whole-virus inactivated vaccines were shown to be effective in a newly published RCT, which coincided with the introduction of new technology. The effectiveness statistics for the majority of newly developed SARS-CoV-2 vaccines are derived from a single phase 3 RCT, with some of them also include recently released real-world data.6–

11, 17, 19, 24, 25. Numerous nations have started widespread immunisation campaigns, although there is little evidence of the COVID-19 vaccines' long-term effectiveness. Based on data from phase 3 randomised controlled trials (RCTs), a recent meta-analysis of eight COVID-19 vaccinations revealed outstanding effectiveness (pooled Risk Ratio (RR) to avoid symptomatic illness of 0.17; 95% Confdence Interval (CI): 0.09–0.32)26. No research examined the effectiveness of different COVID-19 vaccinations, despite the fact that all of the new ones were proven to be very effective in preventing symptoms of the illness when compared to a control group. Only two therapies may be compared at a time using the traditional meta-analysis method. It is possible to evaluate many therapies in a single study by using the network approaches. An indirect comparison may be made when there isn't a study that directly contrasts two different therapies. The evidence gathered using a common comparator27 is referred to as indirect evidence. A March 2021 network meta-analysis that included information on four COVID-19 vaccinations gave the following effectiveness ranking: mRNA-1273>Gam-COVID-Vac> > ChAdOx128 ≈ BNT162b2. In order to give an indirect comparison of the clinical effectiveness of several COVID-19 vaccines in preventing symptomatic and severe illness, we used network meta-analysis to include updated published data from phase 3 RCTs. Our findings could provide more evidence-based data to assist in selecting the optimal course of action to produce the greatest possible public health benefit.

II. METHODS

DATA SOURCES AND SEARCH STRATEGY

We conducted a thorough database search using the following keywords: COVID-19, severe acute respiratory syndrome coronavirus, Coronaviridae Infections, coronavirus, sudden acute respiratory syndrome, vaccines, vaccine, randomised controlled trial, controlled clinical trial, clinical trial, phase II/III, phase III. Our search included PubMed/Medline, Embase, including Mesh/Emtree terms search, Clinical Trials Registry Clinicaltrials.gov, and Te Cochrane Library. For the search ideas, the search tactics included text words and index terms (Mesh). Supplements available exclusively online provide specifics on the search terms. Databases were searched without regard to date or language until August 30, 2021. The vaccine's clinical effectiveness against laboratory-confirmed COVID-19 symptoms was one of the main results. The effectiveness of the aged vaccination and its ability to prevent severe COVID-19 infection were secondary results. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 framework guidelines29 were followed in the execution of the systematic review and network meta-analysis. On February 5, 2021, the protocol was added to the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021235364).

criterion for inclusion and exclusion.

To assess the effectiveness of the vaccination in preventing symptomatic COVID-19, we used published phase 3 RCTs. Phase 1 and phase 2 RCTs, non-randomized trials, observational studies, duplicate reports, pharmacokinetic studies in healthy individuals, reviews, expert opinions, editorials, letters to the editor, and comments were among the publications that were not included in the analysis.

Table 1. Characteristics of included studies

Data extraction.

The studies were identified by one reviewer (V.R.). Using the Rayyan online software for systematic reviews30, two reviewers (V.R., B.H.R.) separately looked over the abstracts, the list of titles, and finally the full-text publications to determine their eligibility. Consensus was used to settle disagreements.

Data collection.

The following data were extracted by two independent reviewers: study details (identifer, study design, geographical location, study period, publication year, length of follow up), participant details (number of participants, study population, age and gender, co-morbidities, SARS-Cov-2 variants), intervention details (vaccine name, vaccine platform, vaccine regimen), details about efficacy outcomes: number of cases of symptomatic disease, number of cases of severe disease, number of cases of symptomatic disease in participants above the age of 60 years (raw data). Disagreements between reviewers were resolved through consensus.

Quality assessment and risk of bias.

The risk of bias of the randomized control trials was assessed by two independent reviewers using the Cochrane tool for assessing the risk of bias for randomized control trials (RCT)31.

Statistical analysis

In compliance with PRISMA-NMA 201532, we conducted a network meta-analysis. Using a random-effects model33–36, we conducted a pairwise network meta-analysis to examine the variations in effectiveness across different vaccinations. Only indirect comparisons between two vaccinations have been carried out since there are no studies that directly compare them. Each included study's raw data on vaccination effectiveness in comparison to control was included into the network. The paired technique was used to compute RRs and 95% CIs for indirect comparisons of various vaccinations with respect to their relative effectiveness. P-scores obtained from network point estimates were used to rate the effectiveness of vaccines. The Bayesian network surface under the cumulative ranking curve is the frequentist counterpart of the P-score. On a scale of 0 (worst) to 1 (best), the P-score of an intervention may be used to rate it among a range of interventions. It can be seen as the mean degree of confidence that one intervention is superior than another37. We included raw data of severe cases among the vaccinated and control groups, as reported in each trial, in order to examine the effectiveness of vaccinations in preventing severe illness. The paired technique was used to compute RRs and 95% CIs for indirect comparisons of various vaccinations with respect to their relative effectiveness. P-scores obtained from network point estimates were used to rate the vaccine's effectiveness in preventing severe illness. We compared the effectiveness of vaccinations in preventing symptomatic illness in the elderly using a random-effects model and pairwise network meta-analysis. From each included trial, the network integrated raw data on vaccination effectiveness in patients over 60 years old as compared to control. P-scores obtained from network point estimates were used to rate the effectiveness of vaccines in preventing symptomatic illness in the elderly. R 3.4.3 and the "netmeta" package Version 0.9–838 were used for the analysis.

III. RESULTS

Using contributing data from nine articles (6–11,24,25,39), we identified eight phase-3 RCTs that showed main or preliminary CODIV-19 vaccination efficacy. Figure 1 shows the search and selection procedures. Table 1 provides a summary of the features of the included studies. Our network has data from more than two hundred thousand individuals.

Vaccine	P-Score ranking[a]		
	Symptomatic disease	Severe disease	Symptomatic disease in elderly[b]
BNT162b2	0.953	0.499	0.815
mRNA-1273	0.844	0.816	0.573
Gam-COVID-Vac	0.782	0.899	0.722
NVX-CoV2373	0.701	0.531	0.623
CoronaVac	0.570		
HB02	0.428	0.384	
WIV04	0.327	0.384	
Ad26.COV2.S	0.198	0.434	0.262
ChAdOx1	0.199		

Table 2. A P-score, which is based on network point estimates and standard errors, indicates the likelihood that each intervention will outperform all competing therapies in terms of preventing COVID-19. bsubjects who are older than 60.

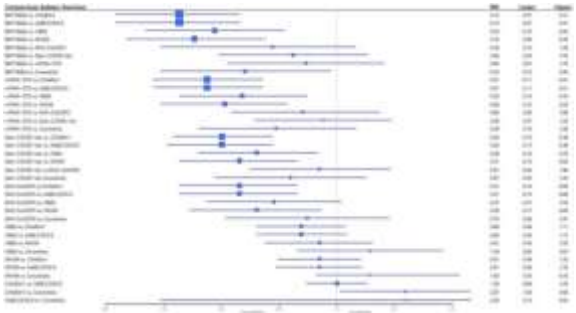

Figure 1. Risk Ratio (RR) for indirect comparison between the vaccinations or vaccine vs. placebo, and 95% confidence intervals are the outcomes of a random-effects network meta-analysis for the effectiveness of preventing symptomatic COVID-19 (seven trials included). meta-analysis. Of those who got the intervention (active COVID-19 vaccination), 114,247 (52%) are adults under 60 years of age. Over 70% of the participants are adults. There were 24,252 (±9,877) participants on average per trial. The included studies reported a total of 1,419 instances of the main outcome (eTable 1).

Indirect Analogy.

illness with symptoms. Information about the effectiveness of nine novel vaccines to prevent symptomatic COVID-19 was found during our search (Table 1). The BNT162b2 and mRNA-1273 vaccines were found to have the highest probability of effectiveness against symptomatic COVID-19 (P-scores of 0.952 and 0.843, respectively) when the indirect comparison of the vaccines was conducted. These were followed by Gam-COVID-Vac (P-score of 0.782), NVX-CoV23730 (P-score of 0.700), CoronaVac (P-score of 0.570), BN02 (P-score of 0.428), WIV04 (P-score of 0.327), ChAdOx1 (P-score of 0.199), and Ad26.COV2.S (P-score of 0. 0.198) (Table 2). The NVX-CoV23730, Gam-COVID-Vac, mRNA-1273, and BNT162b2 vaccinations were all statistically significantly linked to a lower probability of developing symptoms of COVID-19 (Fig. 1). Comparison of BNT162b2 with ChAdOx1 and Ad26.COV2.S: RR 0.15, 95% CI: 0.07–0.31; 0.23 (0.10–0.53) vs. HB02; 0.18 (0.08–0.42) vs. WIV04. mRNA-1273 is compared to ChAdOx1 and Ad26.COV2.S at 0.21 (0.11–0.41), HB02 at 0.32 (0.15–0.70), and WIV04 at 0.26 (0.12–0.55). Comparison of Gam-COVID-Vac with ChAdOx1 and Ad26.COV2.S: 0.25 (0.14–0.46); 0.38 (0.19–0.79) vs HB02; 0.31

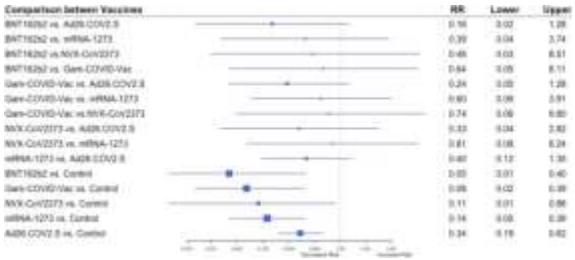

Figure 2. Findings from a random-effects network meta-analysis on the effectiveness of preventing COVID-19 symptoms in individuals aged 60 and above: 95% confidence intervals and the Risk Ratio (RR) for indirect comparisons between the vaccinations or vaccines vs placebos (four trials included).

60 years of age or older. The effectiveness of vaccinations in preventing symptomatic illness in the elderly population (60 years and older) was documented in five trials =6,7,9–11. According to each research, the network included 128 instances of symptomatic illness among individuals over 60 in the vaccination and control groups (eTable 1). BNT162b2 was shown to have the best efficacy against symptomatic COVID-19 (P-score 0.815) when the vaccinations were compared indirectly. Gam-COVID-Vac (P-score 0.722), NVX-CoV23730 (P-score 0.623), mRNA-1273 (P-score 0.573), and Ad26.COV2.S (P-score 0.263) were next in line (Table 2). But when compared to other vaccinations, none of them was statistically significantly linked to a lower risk (Fig. 2). onset of a serious illness. We also assessed the vaccinations' effectiveness in preventing clinically significant severe COVID-19. There were 107 instances of severe illness in all, according to data from five investigations (Table 1)6,7,9–11,24. Severe COVID-19 definitions as found in the included studies are summarised in Table 2. The Gam-COVID-Vac and mRNA-1273 vaccines were found to be the most effective at preventing a severe case of COVID-19 when an indirect comparison of the seven vaccines was conducted. These were followed by NVX-CoV23730 (P-score 0.531), BNT162b2 (P-score 0.500), Ad26.COV2.S (P-score 0.34), WIV04, and HB02 (P-score 0.384) (Table 2). Although there was a tendency towards a reduced risk for serious sickness with the mRNA1273 and Gam-COVID-Vac vaccinations when compared to the other vaccines, neither vaccine was statistically significantly linked to a lower risk (Fig. 3). Bias risk. Every published study's risk of bias was assessed. Four research (6–8,11) classified it as having some concerns, while other studies (9,10,24,25) classified it as moderate (eFigure 2).

IV. DISCUSSION

According to phase 3 RCT data, we have seen the development and clinical launch of very effective COVID-19 vaccines throughout the last year. Two vaccines based on novel mRNA technology, BNT162b2 and mRNA-1273 mRNA, provide very effective protection against COVID-19 with a two-dose regimen of 95% and 94.1%, respectively.6, 7. To prevent symptomatic COVID-19, several viral-vector vaccination regimens that expressed the SARC-CoV-2 S protein, such as GamCOVID-Vac, Ad26.COV2.S, and ChAdOx1, were very effective (91.6%, 66.9%, and 66.7%, respectively).8–10. Adult subjects who received a two-dose course of the recombinant S-protein vaccination NVX-CoV2373 showed 89.7% protection against SARS-CoV-2 infection.11. Three inactivated vaccines made from several SARS-CoV-2 strains have just been published, and the findings show that they are very effective at avoiding COVID-19 symptoms (83.5% CoronaVac, 78.1% HB02, and 72.8% WIV04).24, 25. When compared to control, the combined data from phase 3 RCTs showed that eight COVID-19 vaccinations were very effective at preventing symptoms (RR 0.17; 95% CI 0.09–0.32).26. Four treatments were included in the first network meta-analysis to examine the clinical efficacy of novel COVID-19 vaccines, which was released in March 2021: Gam-COVID-Vac, mRNA-1273, BNT162b2, and ChAdOx128. The present study compares the effectiveness of nine novel COVID-19 vaccines in preventing symptomatic and severe illness in the adult population in the most thorough network meta-analysis to date.

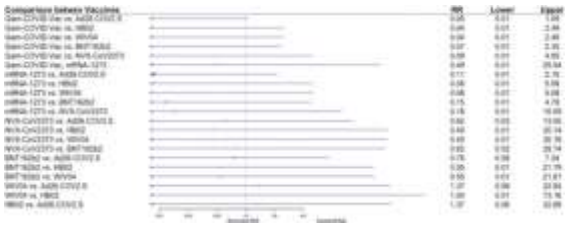

Figure 3. Results of a random-effects network meta-analysis on the effectiveness of vaccinations in preventing severe COVID-19: 95% confidence intervals and the Risk Ratio (RR) for an indirect comparison of the vaccines or vaccine vs. placebo (five studies included).

Our indirect evaluation of the novel vaccinations revealed that, in contrast to existing vaccines, mRNA vaccines (mRNA-1273 and BNT162b2) were linked to a more significant reduction in the risk of symptomatic COVID-19. Additionally, we discovered a tendency towards mRNA vaccinations being more effective for preventing severe COVID-19. However, due to the very low prevalence of serious illness, the findings did not achieve statistical significance. There are a few drawbacks to this indirect comparison, however. First, one trial is included for each intervention arm in our network meta-analysis. Furthermore, the two studies' findings have not undergone peer review, while the data that was provided came from reports and press releases that were sent to the FDA43,44. There are a number of notable variations in the procedures used in the various trials, which might account for some of the variations in vaccination efficacies. As previously stated, the effectiveness of Ad26.COV2.S is predicated on a single dosage regimen, but other vaccines, such as the ChAdOx1 (AZD1222) vaccine, were delivered in a two-dose regimen. The protocol for this vaccine was modified to a two-dose regimen after the trial had begun45. Additionally, vaccinations were tested in non-equivalent settings, including as nations with dissimilar socioeconomic circumstances, different COVID-19 epidemic phases, distinct seasons, and distinct SARS-CoV-2 strains. All of the aforementioned might affect how effective immunisations are. The UK strain of B.1.1.17 is sensitive to the immunity generated by the BNT162b2 and mRNA-1273 vaccines, according to recently published data46,47. The B.1.351 variety, which was mostly discovered in South Africa, is less vulnerable to neutralising antibodies produced by the mRNA-1273 vaccination, though47. Whether the drop in antibody susceptibility will be linked to a decline in vaccination effectiveness is still up in the air. Additionally, there's a good chance that the virus may develop new mutations that alter its vulnerability to vaccinations, and certain vaccines may be more affected than others. The effectiveness of the various vaccinations is thus anticipated to be impacted. Furthermore, the effectiveness and duration of immunity of various vaccinations cannot be compared since the available data on vaccine efficacy is based on short-term data. Which vaccination will elicit prolonged immunological responses is yet unknown. Additionally, booster doses may be necessary every few years to maintain protection, as is the case with other vaccinations. Second, without using data from observational studies, our meta-analysis analyses the effectiveness of the examined vaccinations in two hundred thousand participants of phase 3 RCTs. Millions of individuals worldwide have received vaccinations so far. The effectiveness of the BNT162b2 mRNA vaccine in over 600,000 vaccinated individuals is compared to that of a comparable size group of unvaccinated controls in one research from Clalit Health Services, a large health maintenance organisation in Israel48. The BNT162b2 mRNA vaccine's effectiveness in this investigation was comparable to that shown in the phase 3 RCT7. Lastly, the present network meta-analysis did not intend to address the safety consequences of the vaccinations. There has been relatively little evidence of serious adverse effects in the short term, and the safety outcomes that are now available are based on short-duration follow-up. Real-world data will be required to evaluate the safety of potential vaccinations since mRNA vaccine technology is still in its infancy and it is

still unknown which problems may surface in the long run.

V. CONCLUSION

In our indirect comparison, we found that the mRNA-based BNT162b2 and mRNA-1273 vaccines were the most effective for preventing symptomatic COVID-19. There was no difference in the efficiency of the compared immunisations in preventing severe disease. Our results showed no differences in the efficacy of vaccines to prevent symptomatic COVID-19 in the elderly.

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