Efficacy of COVID-19 vaccine

Review Article

EFFICACY OF COVID-19 VACCINE

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ABSTRACT

With the onset of the novel coronavirus, scientists and medical professionals worked tirelessly to develop an effective clinically approved vaccine for the same. Initially what seemed impossible is now a reality and not only have experts manufactured COVID vaccines in such a short span of time, but they have also developed different types and versions of it too. Equitable access to safe and effective vaccines is critical to ending the COVID-19 pandemic, so it is hugely encouraging to see so many vaccines proving and going into development. WHO is working tirelessly with partners to develop, manufacture and deploy safe and effective vaccines. Safe and effective vaccines are a game-changing tool. Being vaccinated does not mean that we can throw caution to the wind and put ourselves and others at risk, particularly because research is still ongoing into how much vaccines protect not only against disease but also against infection and transmission. But it’s not vaccines that will stop the pandemic, rather it’s vaccination with proper efficacy. Out of more than 100 research articles on COVID-19 and SARS-CoV-2 vaccines 41 articles were included in the present study. As of 1 May 2021, there have been 152 661 445 Covid-19 cases with 3 202 256 deaths globally. This pandemic led to the race to discover a safe and effective vaccine to achieve herd immunity and curtail the damaging effects of Covid-19. This study aims to discuss the most recent WHO-approved Covid-19 vaccine subtypes, their trials, doses and efficacy. As of 16 May 2021, the number of countries that have approved the use of the following vaccines is Pfizer in 85, Moderna in 46, Oxford/AstraZeneca in 101, and Janssen in 41.

Keywords: COVID-19, SARS-CoV-2, Pandemic, Vaccine, Efficacy.

INTRODUCTION

2020 has been a difficult year for all, but has seen 58 vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) be developed and in clinical trials, with some vaccines reportedly having more than 90% efficacy against COVID-19 in clinical trials. This remarkable achievement was much-needed good news as COVID-19 cases were at their highest daily levels globally during that period. New vaccine efficacy results were reported in The Lancet: investigators of four randomized, controlled trials conducted in the UK, South Africa, and Brazil report pooled results of an interim analysis of safety and efficacy against COVID-19 of the Oxford–AstraZeneca chimpanzee adenovirus vectored vaccine ChAdOx1 nCoV-19 (AZD1222) in adults aged 18 years and older. This was the first report of efficacy against COVID-19 for a non-profit vaccine aiming for global supply, equity, and commitment to low-income and middle-income countries (LMICs), and as such its publication was very welcomed. Currently, the efforts to develop a vaccine are paying off. Some vaccine candidates have shown worthy results and roll-outs have begun across nations. On 31 December 2020, the Pfizer COVID-19 vaccine (BNT162b2) was issued for emergency use listing by WHO. This was followed by the AstraZeneca/Oxford COVID-19 vaccine, manufactured by the Serum Institute of India and SKBio on 15 February 2021, and most recently, on 12 March 2021, the Ad26.COV2.S, developed by Janssen (Johnson & Johnson) and Moderna on 30 April, COVAX, coordinated by WHO, Gavi: The Vaccine Alliance, the Coalition for Epidemic Preparedness Innovations (CEPI), acts as a programme that supports the development of COVID-19 vaccine candidates and negotiates their pricing to ensure low-and-middle-income countries have a fair shot at receiving vaccines. Efficacy of a vaccines measured by looking at how well the vaccine works in the study, for example how well the vaccine prevents symptomatic disease. These efficacy measures are called ‘endpoints’. Efficacy endpoints are required because
COVID-19 is a new disease and because there are no known indicators (such as the levels of antibodies in the blood) that can predict protection.7

METHODS

The efficacy of a COVID-19 vaccine was defined as the relative reduction in SARS-CoV-2 infection risk following vaccination, as determined by previously published randomized placebo-controlled clinical trials. The study included observational, randomized and non-randomized studies. Positive reverse transcriptase PCR (RT-PCR) results for COVID-19 were considered as laboratory confirmed cases. Different electronic websites, databases and journals including Web of Science, The Lancet, The New England Journal of Medicine (NEJM), BBC News Online were searched to detect published articles on types, doses and efficacy of different COVID-19 vaccines. The study used the following heading as search terms: COVID-19, SARS-CoV-2, vaccine, types, doses, efficacy, clinical trials, observational study, randomized controlled study, mRNA, viral vector, subunit vaccine etc. Total 41 studies were reviewed in this article.

FINDINGS (BASED ON LITERATURE REVIEW)

The study found more than 100 research articles on COVID-19 and SARS-CoV-2 vaccines by using different search terms. From the searched articles 41 studies were included. In late 2019, COVID-19's caused virus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), was first isolated.8 Its genetic sequence was published on 11 January 2020, triggering an urgent international response to prepare COVID-19 vaccine.9,10 Since 2020, vaccine development has been expedited via unprecedented collaboration in the multinational pharmaceutical industry and between governments.12 By June 2020, tens of billions of dollars were invested by different health organizations, and research groups to develop dozens of vaccine candidates to immunize against COVID-19 infection.10,13,14,15 According to the Coalition for Epidemic Preparedness Innovations (CEPI), the geographic distribution of COVID-19 vaccine development shows North American entities to have about 40% of the activity, compared to 30% in Asia and Australia, 26% in Europe, and a few projects in South America and Africa.9,12 In February 2020, the World Health Organization (WHO) said it did not expect a vaccine against SARS-CoV-2 to become available in less than 18 months.16 Virologist Paul Offit commented that, in hindsight, the development of a safe and effective vaccine within 11 months was a remarkable feat.17 On 24 June 2020, China approved the CanSino vaccine for limited use in the military, and two inactivated virus vaccines for emergency use in high-risk occupations.18 On 11 August 2020, Russia announced the approval of its Sputnik V vaccine for emergency use, though one month later only small amounts of the vaccine had been distributed for use outside of the phase 3 trial.19 The Pfizer–BioNTech partnership submitted an Emergency Use Authorization (EUA) request to the U.S. Food and Drug Administration (FDA) for the mRNA vaccine BNT162b2 20 November 2020.20,21 On 2 December 2020, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) gave temporary regulatory approval for the Pfizer–BioNTech vaccine,22,23 becoming the first country to approve the vaccine and the first country in the Western world to approve the use of any COVID-19 vaccine.24,25 As of 21 December 2020, many countries and the European Union had authorized or approved the Pfizer–BioNTech COVID-19 vaccine.26,27 Bahrain and the United Arab Emirates granted emergency marketing authorization for BBIBP-CorV, manufactured by Sinopharm.28,29 On 11 December 2020, the FDA granted an EUA for the Pfizer–BioNTech COVID-19 vaccine.30 A week later, they granted an EUA for mRNA-1273 (active ingredient elasomeran), the Moderna vaccine.31–34

Table1. Difference between advantage and disadvantage of main types of COVID-19 vaccines

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Example</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| mRNA           | Pfizer-BioNTech, Moderna | a. Immune response involves B cells and T cells  
b. No risk of the vaccine triggering disease  
c. Easy to manufacture | a. Require ultra-cold storage  
b. Booster shots may be required |
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<table>
<thead>
<tr>
<th>Viral Vector</th>
<th>Johnson &amp; Johnson’s Janssen, AstraZeneca, Gamaleya (Sputnik-V)</th>
<th>a. Well-established technology</th>
<th>a. Previous exposure to the vector could reduce effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>b. Strong immune response &amp; involves B cells and T cells</td>
<td>b. Relatively complex to manufacture</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protein subunit vaccine</th>
<th>Novavax</th>
<th>a. Well-established technology</th>
<th>a. Relatively complex to manufacture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>b. Suitable for immuno compromised people</td>
<td>b. Adjuvants and booster shots may be required</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c. Relatively stable</td>
<td>c. Determining the best antigen combination takes time</td>
</tr>
</tbody>
</table>


Under normal circumstances, during which the stages of vaccine development occur sequentially, a vaccine takes 8-15 years on average to get from the laboratory into the hands of health-care providers. The fastest a vaccine had ever been developed before this pandemic was four years. Following the emergence of COVID-19, however, researchers around the globe accelerated the process by carrying out stages of development simultaneously and by looking to new vaccine technologies.35

The U.S. Operation Warp Speed timeline hinged on overlapping stages of development; mass production started for strong candidates even while clinical trials were ongoing. Another way researchers have quickened the process is by focusing on new vaccine approaches. RNA and DNA based vaccines can be developed far faster than conventional vaccines, which require months at a time of growing antigens in animal or insect cells.35

### Table 2. Distinction between doses COVID-19 vaccines

<table>
<thead>
<tr>
<th>Vaccine brand name</th>
<th>Eligible age of vaccination</th>
<th>No of doses</th>
<th>Dose interval</th>
<th>Fully vaccination time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech</td>
<td>12 years &amp; above</td>
<td>02</td>
<td>03 weeks</td>
<td>02 weeks after 2nd dose</td>
</tr>
<tr>
<td>Moderna</td>
<td>18 years &amp; above</td>
<td>02</td>
<td>04 weeks</td>
<td>02 weeks after 2nd dose</td>
</tr>
<tr>
<td>Johnson &amp; Johnson’s Janssen</td>
<td>18 years &amp; above</td>
<td>01</td>
<td>-</td>
<td>02 weeks after single dose</td>
</tr>
</tbody>
</table>


Clinical trials of vaccine normally conducted in three to four phases. When candidate vaccines make it to human clinical trials, they first go through phase 1 trials primarily to test the vaccine’s safety, determine dosages and identify any potential side effects in a small number of people. Phase 2 trials further explore safety and start to investigate efficacy on larger groups. Phase 3 trials, which few vaccines ever make it to, are much larger, involving thousands or tens of thousands of people, to confirm and assess the effectiveness of the vaccine and test whether there are any rare side effects that only show up in large groups. The final stage, phase 4 trials, is conducted after national regulatory approval and involves further monitoring in a wide population over a longer timeframe as a form of post-marketing surveillance. However, not all vaccines that have been approved for domestic are in phase 4 trials. Regulators in many countries have their own individual procedures and timelines for providing emergency use authorisations, relying on various types of evidence at different clinical trial phases.36
**Table 3. Difference between clinical trials and efficacy of some leading COVID-19 vaccine**

<table>
<thead>
<tr>
<th>Developer</th>
<th>Country</th>
<th>Clinical phase/trial</th>
<th>Efficacy (%)</th>
<th>Doses</th>
<th>Approved in at least one country</th>
</tr>
</thead>
<tbody>
<tr>
<td>CanSino</td>
<td>China</td>
<td>3</td>
<td>66</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>SinoPharm</td>
<td>China</td>
<td>3</td>
<td>78</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Sinovac</td>
<td>China</td>
<td>3</td>
<td>71-91</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Bharat</td>
<td>India</td>
<td>3</td>
<td>78</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Gamaleya (Sputnik-V)</td>
<td>Russia</td>
<td>3</td>
<td>92</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Vector Institute</td>
<td>Russia</td>
<td>3</td>
<td>-</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxford-AstraZeneca</td>
<td>United Kingdom, Sweden</td>
<td>2 and 3</td>
<td>76</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Pfizer-BioNTech</td>
<td>United States, Germany</td>
<td>2 and 3</td>
<td>91</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>United States</td>
<td>3</td>
<td>64-72</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>Moderna</td>
<td>United States</td>
<td>3</td>
<td>&gt;90</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Novavax</td>
<td>United States</td>
<td>3</td>
<td>90</td>
<td>2</td>
<td>Yes</td>
</tr>
</tbody>
</table>


There was an unprecedented global collaboration amongst scientists and governments in COVID-19 vaccine development. This has improved the speed of its development and the launch of clinical trials around the world. Researchers were able to use their knowledge of other coronaviruses and vaccine development to give them a head start. Clinical trials were also able to recruit large numbers of volunteers faster than usual because of the worldwide interest and concern about COVID-19. Some clinical trials could be done at the same time instead of one after the other. This meant they could quickly determine whether the vaccine was effective in a short amount of time – under normal circumstance this could take many months or even years. Large manufacturing plants have been developed, so vaccines can be produced faster and on a larger scale than was previously possible. The vaccines have been developed very quickly but without taking any shortcuts in the necessary processes or compromising safety.\(^{37}\)

Clinical trials for a COVID-19 vaccine are designed to assess the safety and efficacy of the vaccine. The Pfizer vaccine has been assessed in global studies across three phases. Phase one and two assessed the safety and immunogenicity (the immune response after each dose) of different dose levels of the vaccine in a small population. Phases two and three assessed the safety and efficacy of the vaccine against symptomatic COVID-19 after two doses of the chosen level, given 21 days apart, in a larger population. In addition, early findings from a small number of well-designed studies show that an extended gap of 6 weeks or more between doses of the Pfizer vaccine gives at least an equally robust immune response.

On June 30, 2021, Medsafe published its provisional approval of the Pfizer/BioNTech vaccine for 12-15 year-olds in New Zealand. Medsafe’s experts only grant consent for a vaccine to be used in New Zealand/Aotearoa once they are satisfied it has passed required levels of safety and effectiveness. The Pfizer/BioNTech vaccine has already been approved for 12-15 year-olds in Canada, the USA, Europe and Japan. Pfizer’s study in 12-15 year-olds looked for signs of a strong immune response to the vaccine. Pfizer reported 100% efficacy in this age group. The process used to assess the safety of the vaccine is the same robust process used to assess other vaccine. Ongoing clinical trials, safety monitoring, and real-world data from COVID-19 vaccination programmes worldwide provide useful information. This includes the long-term safety and benefits of the vaccine.\(^{37}\)

RNA and DNA vaccines use genetically engineered RNA or DNA to generate a protein that itself safely prompts an immune response. Viral vector vaccines use a safe virus that cannot cause disease but serves as a platform to produce coronavirus proteins to generate an immune response. Protein-based vaccines use harmless fragments of proteins or protein shells that mimic the COVID-19 virus to safely generate an immune response.  

**DISCUSSION**

The study was conducted to find out the efficacy of COVID-19 vaccines. Total 41 articles from different web sites and journals were included for the present study. All those articles were studied and reviewed thoroughly to know the exact efficacy of different COVID-19 vaccines which are commonly available.

Francis AI et al in their study revealed that, the Pfizer COVID-19 vaccine (BNT162b2) was issued first for emergency use listing by WHO on 31 December 2020 followed by the AstraZeneca/Oxford COVID-19 vaccine on 15 February 2021 and most recently, on 12 March 2021, the Ad26.COV2.S, developed by Janssen (Johnson & Johnson) and Moderna on 30 April. COVAX, coordinated by WHO. On 2 December 2020 United Kingdom became the first country in the western world to give temporary regulatory approval for the use of Pfizer–BioNTech as COVID-19 vaccine.

According to the study on “Different types of COVID-19 vaccines: how they work” - Pfizer-BioNTech and Moderna have better immune response & no risk of the vaccine triggering disease but require ultra-cold storage for preservation. On the other hand, Johnson & Johnson’s Janssen, AstraZeneca, and Sputnik-V have strong immune response, well-established technology but previous exposure to the vector could reduce effectiveness relatively complex to manufacture. Novavax, a protein subunit vaccine is suitable for immunocompromised people and relatively stable but relatively complex to manufacture and booster shots may be required.

Another study on “Different COVID-19 Vaccines” showed that Moderna and Johnson & Johnson’s Janssen vaccines were indicated for the age of 18 years & above whereas Pfizer-BioNTech was applicable for persons at and above 12 years of age. To vaccinate a person fully two doses are required of Pfizer-BioNTech and Moderna but only single dose is required for Johnson & Johnson’s Janssen vaccines.

Regarding clinical trial, almost all the vaccines completed phase three clinical trials before final application. Felter C in his article mentioned efficacy of different COVID-19 vaccines which include Sputnik-V 92%, Pfizer-BioNTech-91%, Moderna >90%, Novavax-90%, Sinovac 71-91%, SinoPharm-78%, Oxford-AstraZeneka-76%, Johnson & Johnson-64-72% and canSino 66%. Study carried out by Francis AI et al found the efficacies of Pfizer—95%, Moderna—94.1%, AstraZeneca—70.4% and Janssen—66.9%, proving that these vaccines are effective at reducing the incidence and severity of SARS-CoV-2 infection among the study populations.

Another study revealed that both Moderna and Pfizer vaccines have impressive efficacy and the degree of efficacy of these two vaccines is somewhat equivalent. At two doses, Pfizer showed 95% efficacy at the prevention of symptoms that were consistent with infection of Covid-19. After the second dose of Moderna showed 94.1% efficiency at preventing the symptoms consistent with Covid-19 infection.

Johnson & Johnson has committed 500 million doses of this vaccine to the COVAX initiative for distribution worldwide. In January, the company announced that the vaccine had an efficacy of 66% in Latin America, 57% in South Africa and 72% in the United States, with 100% efficacy against severe disease in all trials. In June 2021, the company launched a phase 4 trial in the Netherlands. Johnson & Johnson is among the vaccines in the COVAX portfolio. So, it is understood that the efficacy of same vaccine varies from country to country depending on clinical trials.

**CONCLUSION**

A number of international studies have shown that vaccination leads to a significant reduction in the rate of transmission of SARS-CoV-2. A reduction in the number of community cases following vaccination gives an indication that vaccination is contributing towards lowering the spread of the virus. Overall, the vaccine’s efficacy varies by the dosing interval. In an interim study, the efficacy of two doses of the vaccine was 70.4% and protection of 64.1% after at least one standard dose, against symptomatic disease. Based on this study, the vaccine was authorised for emergency use in the UK on a regimen of two standard doses administered 4–12 weeks apart for adults aged 18 years and older. Many other countries also use the same dose interval to get the desired efficacy of COVID-19 vaccines. The process used to assess the
Efficacy of COVID-19 vaccine

The safety of the vaccine is the same robust process used to assess other vaccines. Ongoing clinical trials, safety monitoring, and real-world data from COVID-19 vaccination programmes worldwide provide useful information. This includes the long-term safety and benefits of the vaccine.

REFERENCES


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