The effectiveness of selected SARS-CoV-2 vaccines

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Abstract

The Coronavirus Disease 2019 (COVID-19) was first detected in Wuhan, China in 2019 and set off a global pandemic. Millions of people got affected worldwide imposing a huge burden on healthcare system. There were no therapies available to reduce the morbidity and mortality rate. There was an urgent demand for treatment strategies to defeat the pandemic. Scientists around the world led a race to create a vaccine to achieve herd immunity. More than 200 possible vaccines were designed and 20 reached phase III-trials.

The aim of this rapport is to evaluate the effectiveness of the four major Covid-19 vaccines used in Europe: BNT162b2 (Pfizer/BioNTec), mRNA-1273 (Moderna), ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Janssen). The results are based on a literature search regarding the efficacy/effectiveness of the SARS-CoV-2 vaccines. Based on the available evidence, the evaluated vaccines prove to be effective and safe, demonstrating a high effectiveness also in real-life studies.

Background

The Coronavirus Disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in December 2019 in Wuhan, China. The disease has had a significant negative influence globally on both public health, lives and the world economy.[1] As of May 2022, SARS-CoV-2 has caused more than 520.102.852 million infections, contributing to more than 6.268.956 million deaths.[2]

Coronaviruses are a great family of viruses that can result in various diseases in both humans and animals. Previous coronavirus outbreaks occurred in 2002-2003 (SARS-CoV) with 8096 cases and in 2012 (Middle East Respiratory Syndrome, MERS) with 2519 cases, however the incidences were sporadic and geographically restricted. [3]

Symptoms of COVID-19 disease, caused by SARS-CoV-2, are in most cases mild, including fever, coughing and breathlessness; however, in older adults and those with chronic diseases, severe symptoms such as pneumonia and organ dysfunction may occur. The mortality rate has been reported to be 1-3%, and higher among elderly patients, especially in men.[1] So far, there is no definitive treatment, and the strategy is to reduce the symptoms and prevent progression. [4]

Infectious diseases can be controlled by the development of vaccines. Thus, the global increase in mortality caused by the COVID-19 pandemic made the development of an effective SARS-CoV-2 vaccine critical. [5] Development of vaccines is typically a complex and lengthy process taking up to decades. For the first time in medical history, vaccines were developed and tested in clinical trials in a very short span of time.[6,7]

In December 2020, the Pfizer/BioNTech mRNA vaccine was the first to be approved for emergency use, followed by mainly BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Janssen) in Europe.[8] This is considered as one of the greatest successes in the history of medicine.

Problem statement

The aim of this report is to investigate the effectiveness of the four major Covid-19 vaccines used in Europe based on the available literature. The selected vaccines are the following

- two mRNA vaccines: BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna)
- two vector based vaccines: ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Janssen)

Methods

The report is a literature study using pre-existing literature on the mRNA and viral vector Covid-19 vaccines and their efficacy and effectiveness. The literature has been searched using PubMed for studies published since April 2020 by searching for “efficacy of different Covid-19 vaccines “effectiveness of Covid-19 vaccines “, “Covid-19 mRNA vaccines “ and “Covid-19 viral vector vaccines“.

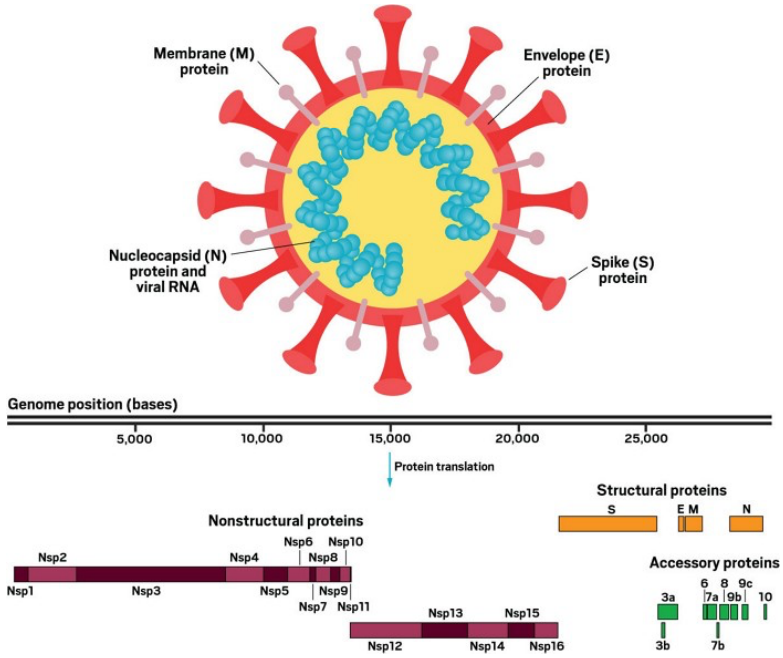
The screening included studies that examined the efficacy and effectiveness of different covid vaccines. A search including the keywords “the effectiveness of covid 19 vaccine” gave 10621 results. These were further restricted to clinical studies, which resulted in 194 studies. From these studies, only those investigating the mRNA vaccines (Pfizer-BioNTech, Moderna) and viral-vector vaccines (specifically AstraZeneca and Janssen) were selected, in total 194 results. These were screened, and the final selection was based upon study design and population size.

Introduction

Specific features of the SARS-CoV-2 virus

SARS-CoV-2 is a positive-sense single-stranded RNA virus with a genome-size of 29,700 nucleotides and approximately 80% sequence similarity with SARS-CoV. One-third of the genome encodes the structural proteins of the virus; the four mains being membrane glycoprotein (M), spike protein (S), nucleocapsid protein (N), and envelope protein (E). Protein S, E and M make up the virus's structure, whereas protein N contains the RNA-genome (**Figure 1)**. [1] The S-protein is the major coat glycoprotein expressed on the virus’ surface. It is the target point for the vaccine as it facilitates the virus's interaction with the host cell and consists of two subunits. The S1 subunit is involved in receptor binding, while the S2 subunit is facilitates the cell membrane fusion.[1] The virus uses the S protein to target the Angiotensin-converting enzyme 2 (ACE2) receptor on the host cells; this provides an entry point for covid -19 virus resulting in the release of viral RNA into the cytosol. The S-protein is therefore the most promising source of antigens for SARS-CoV-2 vaccine development, as an effective vaccine must target this protein.[9]

Fig.1: Genome Organization of the SARS-CoV-2 virus



The viral genome is organized into a minimum of 11 open reading frames (ORFs). The viral genome is polyadenylated at the 3'ends and capped at the 5'end. The ORF1a and ORF1b regions encode the non-structural proteins, where the structural genes encode the four structural proteins: spike (S), envelope (E), membrane (M) and nucleocapsid (N) and accessory proteins.
Source: [10]

Development of vaccine – considerations and challenges

Herd immunity can only be established through development of effective vaccines that provide long-term immunity. Many companies in many nations have made significant progress in developing vaccines in this regard.[11]

A number of vaccines, Nucleic acid (RNA/DNA), whole pathogen, viral vector and protein subunit vaccines have been widely studied. They all rely on SARS- CoV-2's viral spike protein (S) to induce neutralizing antibodies, but how this antigen is delivered to the immune system varies significantly between vaccination types.[12]

Different types of vaccines

Globally, different types of vaccines have been developed during the COVID-19 pandemic. In this report, we will focus on covid-19 vaccines widely used in Europe (mRNA and vector-based), whereas the protein-based and inactivated vaccines will not be discussed. (Figure 2).

mRNA vaccines

The mRNA vaccine technology has been studied for several years for a variety of viruses, including rabies, influenza and Zika virus. The COVID-19 vaccines are the first to be licensed and used on people. The technique is advanced but requires less time and has lower manufacturing costs.[9] Single-stranded, modified-nucleoside, manufactured mRNA is utilized to transmit genetic information to host cells. During this method, encapsulated mRNA is delivered to human cells.

Encapsulation preserves and stabilizes mRNA, which is significant because of its fragility. [13] The mRNA molecules persist in the human cells for less than two days. They are considered safe, as they do not cross the nucleus, eliminating the risk of unintended long-term expression and genetic integration. The mRNA vaccines contain mRNA encoding the full-length, transmembrane anchored protein S, in which the amino acid sequence is changed at two places to proline (a secondary amine), "locking" the S protein in a prefusion-state.[13] The production of S protein elicits an adaptive immune response; consisting of both cell-mediated immune responses and humoral immunological responses. This leads to that the S-protein is unable to interact with the ACE2 receptor on the host cells due to neutralizing antibodies released during immune response. The killer T-cells then recognize and destruct the infected cells. Among the approved mRNA vaccines are Pfizer–BioNTech Vaccine (PBV) and Moderna Vaccine (MV), both with huge similarities.[13,14] The main difference is the amount of mRNA used per dose, 100 μg and 30 μg in Moderna and Pfizer, respectively.[15]

Pfizer–BioNTech vaccine (BNT162b2)

The Pfizer–BioNTech vaccine was the quickest vaccine to be developed and was approved for emergency use in December 2020.[16] The vaccine is given in two doses separated by 3 weeks. It can only be stored at − 70 °C, limiting its use in remote settings and certain countries.

Moderna (mRNA-1273)

The Moderna is also given in two doses 4 weeks apart and can be stored at -20°C, allowing for utilization in remote and rural areas.[15]

Vector-based vaccines

There are two types of viral vector-based vaccines: replicating and non-replicating. Adenoviruses (Ads) are an example of vectors with both traits. The mostly common viral vector vaccines against COVID-19 used in Europe are the ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Janssen). Both use an adenovirus as a vector and encode the S protein of the SARS-CoV-2 virus.[17] Adenoviruses are used extensively in the transportation and delivery of a specific plasmid. The adenovirus vectors contain the human Ad26 and Ad5 adenoviruses and a chimpanzee adenovirus ChAdOx1. The S-protein is encoded by a double-stranded DNA component of the SARS-CoV-2 RNA on the plasmid.

After injection, the vectors are able to enter the body cells without replicating intracellularly. The genetic material from the vectors is delivered to the nucleus for transcription and translation to S-protein. Once the S-protein interacts with cells in the immune system, specific neutralizing antibodies are synthetized followed by T cell activation. The activated T cells eliminate the S protein.

The immune system is normally active after immunization as the surface spike protein is produced, and capable of attacking the SARS-CoV-2 virus if it is detected. [9]

Oxford AstraZeneca/ChAdOx1/AZD1222

This vaccine is a non-replicating chimpanzee viral vector vaccine and was produced in a collaboration between the University of Oxford and the pharmaceutical company AstraZeneca.[17] Following the first dose, humoral and cell-mediated immune responses are activated. The memory B- and T-cells s result in a long-term immune response, which later fights against the virus on exposure.[18]
One of the challenges of this technology may be a pre-existing immunity to adenoviruses, which can have an impact of the effectiveness of the vaccine. The AstraZeneca vaccine overcomes this by using Chimpanzee adenovirus (ChAdOx1), as preexisting immunity against this is not present in humans.[17]

Janssen vaccine/Ad26.COV2.

This vaccine is a non-replicating, recombinant vaccine using human adenovirus-26-CoV2 for delivery of the gene encoding the S-protein. This vaccine only requires one dose, and can be kept at 2–8 °C for up to 3 months or at -20°C for a period of 2 years. [9]

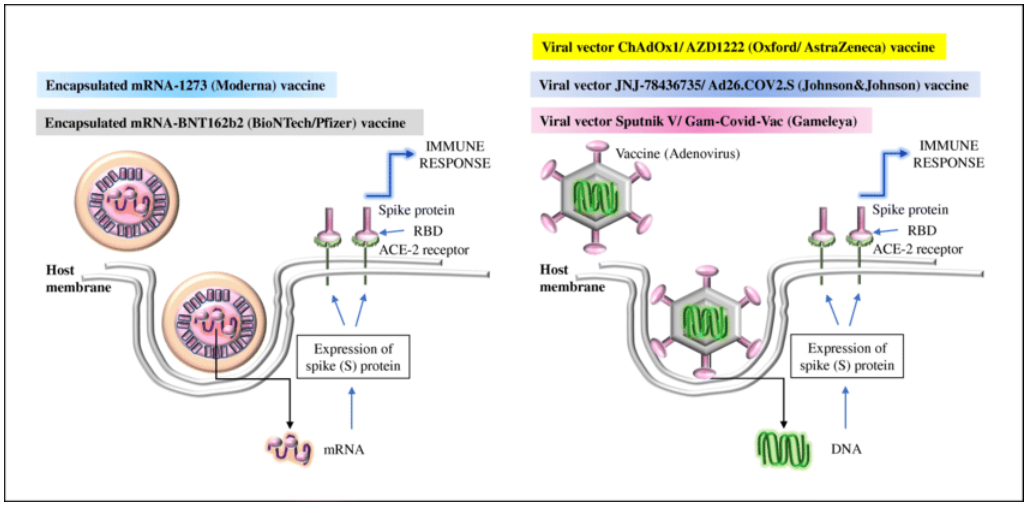


Fig. 2. An overview of the mode of action of mRNA and viral vector vaccines (Pfizer–BioNTech vaccine, Moderna, Oxford/AstraZeneca, Jannsen). Source:[19]

RESULTS

The immunological responses of the SARS-CoV-2 vaccination are critical for controlling and preventing this infection. Several covid-vaccines have been approved globally based on preliminary high efficacy and safety.

In this report, the available data from selected clinical trials and real-life studies for mRNA vaccines (Pfizer-BioNTech, Moderna) and viral vector vaccines (Oxford/AstraZeneca, Janssen) will be reviewed. An overview of the main results from both clinical and real-life studies are shown in **Table 1-2**. In real life studies, studies from different countries around the world are chosen, in order to compare outcomes in different areas. Though it is important to note that a comparison of these vaccines is not easy, as there is no set standard for measuring neutralization.

Pfizer–BioNTech vaccine (BNT162b2)

In august 2021, the FDA approved the first COVID-19 vaccine, known as Pfizer-BioNTech, for individuals aged above 16. Before that it was authorized by the Medicines & Healthcare Products Regulatory Agency (MHRA) in the UK for emergency use following a worldwide Phase III randomized controlled trial. [7,20]

The Phase III clinical trial was conducted as a multinational, placebo-controlled, observer-blinded, pivotal efficacy trial (**Table 1)**, where individuals above 16 years, who were healthy or had stable chronic medical conditions, were randomly assigned in a 1:1 order to receive two doses of either placebo or the BNT162b2 vaccine candidate. [20] Patients with immunocompromising disorders, previous COVID-19 infection or in immunosuppressive therapy were excluded. A total of 43,548 individuals were included, of whom 21,728 received either placebo (n=21,728) or BNT162b2 (n=21,720). Number of covid-cases with an onset at least 7 days after the second dose were 8 in the BNT162b2-group and 162 in the placebo-groups. Number of serious covid-19 cases with onset after the first dose were 1 in the BNT162b2-group and 9 in the placebo-group. The efficacy of BNT162b2 in preventing Covid-19 was reported as 95% (95% confidence interval (CI), 90.3-97.6%), and was reported to be similar across subgroups defined by age, sex, race, baseline body-mass index and existing comorbidities. The protecting effect occurred after approximately 12 days. Main adverse events reported during a median of 2 months were mild-to-moderate pain at the injection site, fatigue, and headache. These were 3-4 times more frequent after second dose. The number of serious adverse events was low and was similar in the vaccine and placebo groups.[20]

In order to evaluate the long-term response and variant-specific effectiveness, a retrospective cohort study by Tartof et al. was conducted.[21] The study included 3,436,957 individuals. Among

the fully vaccinated, effectiveness against SARS-CoV-2 infection was 73% (95% CI 72-74) and against COVID-19 related hospital admissions was 90% (89-92%). The effectiveness against the infection declined from 88% (95% CI 86-89) during the first month after vaccination to 47% (43-51%) after 5 months. The effectiveness against delta-variant infections was 93% (85-97%) in the first month after vaccination but declined to 53% (39-65%) 4 months post-vaccination. The effectiveness against delta-related hospital admissions was 93% (84-96%) up to 6 months. Thus, the results provided evidence for high effectiveness of the BNT162b2 vaccine against hospital admissions up till 6 months post-vaccination. The decline in effectiveness over time was suggested to be due to waning immunity rather than spread of new variants escaping vaccine protection.[21]
Other real-life studies from Israel[22], Sweden[23], Scotland[24] and US[25] have also reported an efficacy of 86-92% against infection and 87% against hospitalization due to COVID (**Table 2)**. Furthermore, a Danish study has investigated the impact of age on effectiveness and indicated an age-related difference with lower effectiveness among elderly (+80 years).[26]

Moderna

In January 2021, Moderna, an mRNA-based vaccine, was also issued an emergency use authorization.[27] The effectiveness was investigated in the Coronavirus Efficacy (COVE) phase III trial: a randomized, observer-blinded, placebo-controlled clinical trial.[28] The study included 30,420 medically stable individuals with no known history of COVID-19 or increased risk of severe infection (mean age 51.4 years). 96% of the participants received both injections of either the Moderna/mRNA-1273 vaccine (n=15.210) or placebo (n=15.210). The main outcome was protection against infection, at least 14 days after the second injection, and against severe COVID-infection. Number of symptomatic covid-19 cases were 185 in the placebo group and 11 in the mRNA-1273 group. The efficacy of the vaccine was reported to be 94.1% (95% CI, 89.3.96.8%) at least 14 days after the second injection. Similar findings were reported in sub analyses including an assessment 14 days after the first dose and analyses among participants 65 years of age or older. Number of severe covid-19 cases was 30 with one fatality, all in the placebo-group. Systemic adverse events occurred more often in the Moderna group than the placebo-groups, both after first dose (54.9% vs. 42.2%) and the second dose (79.4% vs. 36.5%) and lasted a mean of 2.9 and 3.1 days after first and second doses. The number of adverse events in the Moderna group was not affected by age and did not have any permanent damage. Serious adverse events were rare with a similar incidence across the two groups.[28]

The effectiveness was further investigated in a real-life study from US, conducted as a controlled cohort study with 1:1 matching of vaccinated and unvaccinated participants.[25] More than 30.000 patients above >18 years were included. Patients were either vaccinated with Pfizer-BioNTech or Moderna (2 doses). The effectiveness against prevention of infection and COVID-related hospitalization was assessed. The study reported an effectiveness of 89% after two doses of either Pfizer or Moderna.

Oxford AstraZeneca/ChAdOx1/AZD1222

A double-blinded, randomized, phase 3 III clinical trial was conducted to investigate the efficacy and safety of two doses of AstraZeneca among 32,451 individuals, including older adults (**Table 1)**.[29] The primary efficacy end point was the first occurrence of SARS-CoV-2 , with onset 15 days or more after the second dose of vaccine or placebo among participants who had been seronegative for Covid-19 at baseline. The overall estimated vaccine efficacy was 74% (95% CI: 65.3-80.5). In individuals above 65 years of age, the estimated vaccine efficacy was 83.5% (95% CI: 54.2-94.1). There were not observed any severe or critical symptomatic Covid-19 cases among the 17,662 participants in the AstraZeneca group, whereas 8 cases were present in the placebo group. In this trial both SARS-CoV-2 spike protein binding and neutralizing antibodies were increased in all age groups after the first dose of AZD1222, and further increased from baseline when monitored 28 days after the second dose.[29]

In a real-world study, conducted in Scotland, the effectiveness of one dose of AstraZeneca was also investigated.[24] The study included both vaccinated and unvaccinated individuals above 15 years of age and was further adjusted for e.g. age, sex, comorbidities. The study found an effectiveness of 94% (95% CI: 73-99%) at 28-34 days after first dose of the vaccine (**Table 2)**.[24]

In regard to safety, there was a concern regarding the risk of thromboembolic events following the AstraZeneca vaccine. A nationwide registry-based study was conducted in Denmark and Norway to assess the occurrence of thromboembolic events as serious adverse events.[30] More than 250.000 individuals, who had received the first dose, were included (median age 44 years, >70% women). The general population was used as comparator cohorts. Among the vaccinated individuals, increased rates of venous thromboembolic events, including cerebral venous thrombosis, were detected. However, the study group concluded, that the absolute risk was only slightly increased, and that more evidence was needed.[30]

Janssen:

A multinational, randomized, placebo-controlled trial was conducted, including 43,788 participants, who received a single-dose of Janssen (Ad26.COV2.S) or placebo.[31] Individuals participating in the trial were >18 years in good or stable health. The primary end point was the vaccine efficacy against moderate to severe Covid-19 with onset minimum 14 days after administration. A single dose of Janssen provided 56.3% (95% CI: 51.3-60.8) protection against moderate to severe–critical Covid-19 at least 14 days after administration. The efficacy against COVID-19 with onset minimum 28 days after administration, that led to medical intervention (including hospitalization) was 75.6% (95% CI: 54.3-88.0) and lasted 6 months or longer. The efficacy against severe-critical Covid-19 with the need of hospitalization, was initially approximately 90% and tapered to 70% by almost 6 weeks, remaining at that level for up to 6 months.[31]

In order to assess the effectiveness and long-term stability of the Janssen vaccine in real-life, a multi-center cohort study in US was performed.[32] More than 350,000 vaccinated and approx. 1,500,000 matched unvaccinated individuals were included. The effectiveness of the vaccine was 79% (95% CI, 77-80%) for COVID-19 infection and 81% (79-84%) for COVID-19 related hospitalization; though higher among individuals <50 years (83%; 81-85%) and lower among immunocompromised patients (64%: 57-70%). The effectiveness against the Delta variant was 78% (73-82%) for infections and 85% (73-91%) for hospitalizations.[32]

TABLE 1: CLINICAL TRIALS

Study	Vaccine	Study design	Study population	Study endpoints	Vaccine effectiveness on selected measures (95% CI)
Polack et al.[20]	Pfizer-BioNTech	Phase III randomized double-blinded controlled trial	43,448 participants (median age 52)	Efficacy against COVID-19 infection	95% (90-98)
Baden et al.[28]	Moderna (mRNA-1273)	Phase III randomized double-blinded controlled trial	30,420 individuals (mean age: 51)	Efficacy against COVID-19 infection	94.1% (89.3-96.8)
Falsey et al.[29]	AstraZeneca	Phase III randomized double-blinded controlled trial	32,451 individuals	Efficacy against COVID-19 infection	Overall: 74% (65.3-80.5) In participants > 65 years: 83.5% (54.2-94.1)
Sadoff J. et al.[31]	Janssen	Phase III randomized double-blinded controlled trial	43,778 individuals	Efficacy against COVID-19 infection	75,6 % (54.3-88.0)

TABLE 2: REAL-LIFE STUDIES

Study	Vaccine	Study design	Study population	Study endpoints	Confounder adjustments	Vaccine effectiveness (selected measures) (95% CI)	Viral variants of concern
Dagan et al. 2021[22] (Israel)	Pfizer-BioNTech	Target trial emulation using 1:1 individually matched unvaccinated and vaccinated study participants	596 618 vaccinated; 596 618 matched unvaccinated controls above >16 years	Infections (10, 561); hospitalizations (369); deaths (41)	1:1 matched on seven factors: age, sex, place, ethnicity, past influenza vaccine, pregnancy, number of comorbidities	Day 7+ after second dose: infection 92% (88–95%); hospitalization, 87% (55–100%)	Alpha variant was most dominant during the study
Bjork et.al 2021[23] (Sweden)	Pfizer-BioNTech	Controlled cohort study	26 587 vaccinated, 779 154 unvaccinated in the age group 18-64 years	Infections (4228); deaths (36)	Age- and gender adjustment	Day 7+ after second dose: infection, 86% (72–94%); death not calculated.	Alpha variant was most dominant during the study
Moutsen-Helms et.al 2021[26] (Denmark)	Pfizer-BioNTech	Observational cohort study	39,040 long-term care facility residents (median age 84 years); 95.2% received first dose and 86.0% received second dose. 331,039 health-care workers (median age 47 years), 27.8% received first dose and 24.4% received second dose	Infections	Adjusted for calendar time Adjusted for age, sex and comorbidities in a sensitivity analysis with no significant difference of results	Day 7+ after second dose: vaccine effectiveness was 64% (14-84%) among LTCF residents and 90% (82-95%) among health-care workers	Variant not mentioned
Vasileiou et al.2021[24] (Scotland)	Pfizer-BioNTech or AstraZeneca (1 dose)	Controlled cohort study	Aged ≥ 15 years: 1 137 775 vaccinated; 3 271 836 unvaccinated	Hospitalization (7914)	Adjusted for age, sex, deprivation score, number of prior SARS-CoV-2 PCR tests, comorbidities	Days 28–34 (Pfizer-BioNTech): hospitalization 86% (76-91%) Days 28–34 (AstraZeneca): hospitalization 94% (73–99%)	Alpha variant was most dominant during the study

Pawlowski et al. 2021[25] (US)	Pfizer-BioNTech or Moderna (2 doses)	Controlled cohort study with 1:1 individually matched vaccinated and unvaccinated study participants	31 069 vaccinated; 31 069 unvaccinated >18 years old	Infections (924); hospitalizations (224)	Propensity-matched according gender, age, ethnicity, location and number of previous SARSCoV-2 PCR test	Day 36+ (2 doses only); infection 89% (68–97%)	Variant not mentioned
Polinski et al.2021[32] **(US)**	Janssen/ Ad26.COV2.S	Cohort study of vaccinated and matched unvaccinated study participants	390,517 vaccinated 1,524,153 matched unvaccinated individuals >18 years old	Infections Hospitalizations	Propensity-matched by age, gender, date, location, comorbidity index plus 17 COVID-19 risk factors	79% (95% CI, 77-80%) for infection 81% (79-84%) for hospitalization; among individuals <50 years (83%; 81-85%) among immunocompromised patients (64%: 57-70%). 78% (73-82%) for infections with Delta variant 85% (73-91%) for Delta hospitalizations.	Variant not mentioned

Discussion

More than 11.5 billion doses of covid-19 vaccines have been given, in a minimum of 197 countries worldwide.[33] However, the evidence regarding effectiveness and safety remains limited.

The efficacy is determined by the ability of the vaccine to prevent a certain disease under ideal and controlled conditions and is a measure used in clinical studies. The effectiveness describes, how well it performs in the real-world studies, where the study population is more heterogenous, and other viral variants may be present.[34] In this report, we therefore include both clinical trials and real-life studies investigating the two types of COVID-vaccines: the mRNA (Pfizer, Moderna) and the vector-based vaccines (AstraZeneca and Janssen-Johnson).

Main findings for the two different types of COVID-vaccines were as following: 1) Pfizer-BioNTech had an efficacy of 95% in the clinical study, whereas the effectiveness in real-life studies was in a range of 74-92% against infection with a decline to 47% after 5 months. In regard to hospitalization, the effectiveness was 87-90% across studies. 2) Moderna had efficacy of 94% and real-life effectiveness of 89% against infection and hospitalization. 3) AstraZeneca was reported to have an efficacy of 74-84% against infection, higher among elderly, and real-world study showed 94% after first dose. However, there were data indicating increased safety risks 4) Janssen had an efficacy of 76% lasting 6-7 months against infection and 90% against hospitalization, whereas real-life effectiveness was approximately 80% for infection and hospitalization, lower among elderly.

Based on the above investigated, all vaccines proved to be highly effective in preventing severe cases of COVID-19 requiring hospitalizing, but the mRNA vaccines tended to have a higher efficacy/effectiveness in both clinical and real-life settings. The efficacies ranged from 64% to 95%, but it is important to note that a head-to-head comparison between the different vaccines are difficult due to differences in trial design, end point measured, trial location, study population, and prevalence of SARS-CoV-2 variants at the time of the trial. [35] It is also important to consider that the exact level of reported effectiveness also varies based on the country – as it is different how countries detect, treat and categorize COVID-19 cases. Another important factor is the timing of the clinical trials. The vaccine trials were all conducted at different times of the year and at a different geographical location. It may therefore be expected that trials during the summer will have a different outcome than those in winters with a higher exposure to Covid-19 infection.

The initial randomized clinical trials provided unbiased evidence of vaccine efficacy. These were conducted in selected patient groups – mainly excluding older and high-risk patients with underlying medical conditions. Real-world studies may help fill in the knowledge gaps regarding heterogenous patient groups (e.g. elderly frail patients, patients taking immunosuppressive

medication) and long-term effectiveness. Also, data from real-life may provide information regarding the effectiveness against other variants, than those studied in the RCTs

The virus itself has evolved due to mutations, and some variants became more transmissible than the earlier strains of the virus, which the vaccines were designed for. E.g. data from a Qatar study indicated a difference in effectiveness of the Pfizer-BioNTec vaccine depending on variants; with 90% effectiveness in preventing infection from the alpha variant, but 75% from the beta variant at least 14 days after the 2nd dose.[36] On the other hand, some studies have reported a 93% effectiveness of Pfizer against the Delta-variant and related hospitalization. Similar findings were reported in a study from UK, that little impact of variants on the effectiveness of Pfizer or the AstraZeneca vaccine; both were found to have comparable effectiveness against the Delta variant as the Alpha variant.[37]

In regard to safety, the viral vector-based COVID-19 vaccines developed by AstraZeneca and Johnson & Johnson have been linked to an extremely rare and potentially life-threatening blood-clotting syndrome called vaccine-induced thrombotic thrombocytopenia (VITT) – which is the combination of low platelet counts with blood clots. A Scandinavian study found a slight increased absolute risk of thromboembolic events among individuals vaccinated with AstraZeneca.[30] On the other hand, a multi-national clinical trial conducted in US, Chile and Peru, did not find any evidence of serious adverse events, and concluded the vaccine to be effective.[29] There is therefore a need for further studies, and some countries have taken their precautions by not using the AstraZeneca as first choice or among risk groups.

Despite a wide-spread use, there are still concerns among both healthcare professionals and the population regarding long-term effectiveness and safety. As more data emerges, our knowledge regarding the impacts of the vaccines will increase and help choose the ideal vaccination. This may vary globally, as there are also other considerations when choosing an ideal vaccination for a certain country or area, as several socioeconomic and logistic factors play a role – e.g. the storage of vaccines (temperatures), manufacturing costs, single dose as for Janssen-vaccine or two dosages for the rest.[17]

Conclusion

Based on our findings, we can conclude that Covid-19 vaccines have shown a high efficacy/effectiveness, especially against severe cases, both in clinical trials as well as in real life settings. Data indicated a slightly higher effectiveness of mRNA vaccines; however, a head-to-head comparison is difficult due to the various factors. There is a need for more research both regarding long-effectiveness and safety.

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