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## A review on COVID-19 vaccines: stages of clinical trials, mode of actions and efficacy

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### ABSTRACT

Coronavirus disease (COVID-19) is a communicable disease caused by a recently discovered coronavirus. The disease was first reported in Wuhan, China at the end of 2019 and has resulted in 1.71 million global deaths and over 77 million infections. Common symptoms of the disease include fever, dry cough, and fatigue. This literature review aims to summarize the following topics: review the clinical trials conducted on nine COVID-19 vaccines and follow their efficacy and modes of action through the three stages of the vaccine clinical development process. The analysis follows the individual vaccines through the three trials, examining and analysing drawn results to identify their capacity to contain severe acute respiratory syndrome (SARS-CoV-2). Four COVID-19 vaccines have been approved for use in different parts of the world and many other vaccines are under clinical trials 1, 2 and 3. In conclusion, these vaccines which are under clinical trials provide a great hope to fight against COVID-19 in near future.

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COVID-19; COVID-19 vaccine; Phase 3 clinical trials; SARS-CoV-2

### Introduction

World Health Organization (WHO's) official definition of COVID-19 is that it is a viral disease caused by a new coronavirus. It was first reported on the 31<sup>st</sup> of December 2019 in the Wuhan Province of China. First recognized in the mid-1960s, COVID-19 belongs to a larger family of respiratory viruses called Coronaviridae and affects both humans and animals (Demeco et al., 2020) and are also known to cause severe respiratory infections such as severe acute respiratory syndrome (SARS-CoV), middle east respiratory syndrome (MERS-CoV), and now globally famous novel coronavirus severe acute respiratory syndrome (SARS-Cov-2) and the disease is named as COVID-19 by WHO.

The disease infects the upper respiratory and gastrointestinal tract of birds and mammals. Owing to its slow mutation, the virus poses a treatment and control challenge. It manifests anywhere between 2 and 14 days of infection with the virus prevailing even after 27 days in some cases (Ali & Alharbi, 2020) and has an average incubation period of 5.2 days (Li et al., 2020). The disease has an average mortality duration of 6-24 days depending on prevailing clinical conditions of patients, their health, and age as well. Common infection symptoms include respiratory complications, high fever, dry

cough, sore throat, sneezing, muscle pain, and fatigue.

According to the WHO, COVID-19 can be transmitted from an infected person to one who is not infected upon contact, cough droplets, and sneezing where the virus enters the body through eyes, nose, or mouth (Center for Disease Control (CDC), 2020). COVID-19 droplets can land at a distance of up to 1.8M and survive upwards of 2 hours to two days. Traces of the virus have also been found on infected people's stool but no infection through stool has been confirmed yet. The virus can be prevented and controlled through a variety of measures against daily routines, with the most effective one being the avoidance of touching one's mouth, nose, and eyes (Center for Disease Control (CDC), 2020). Other measures include avoiding close contact with infected people, remaining at home if infected, regularly cleaning and disinfecting surfaces, maintaining proper hygiene practices especially when coughing or sneezing, using facial covering equipment like face masks and face shields when in crowded places and regularly washing your hands with soap and plenty of water or hand sanitizers.

Treatment for COVID-19 remains in the realm of uncertainties and the only care that patients of the virus have been getting is supportive. Experts for example argue that perhaps the best approach to

treat COVID-19 is through proper prevention and management measures (Ali & Alharbi, 2020). However, scientists from all over the world have been working very hard towards finding a treatment for the disease or even better, a vaccine. It is in this spirit that numerous research laboratories from every corner of the world have invested so much in resources towards developing and manufacturing a vaccine that will hopefully help flatten the COVID-19 curve for all humanity's sake.

### COVID-19 vaccine

As earlier mentioned, countless laboratories are working towards finding a COVID-19 vaccine. Customarily, vaccine development and in particular COVID-19 vaccine development is assuming a 5-stage process. This is especially following WHO's guidelines on clinical evaluation of vaccines which is so lengthy that it forces vaccine development to take months if not years. All this is however done in good faith seeing that a matter as delicate as human lives should not have any chances taken on it. At the moment, the World Health Organization requires vaccine developers to follow these guidelines (World Health Organization (WHO)):

- Good Clinical Practice (GCP) for trials on pharmaceutical products.
- Good Manufacturing Practice (GMP) for pharmaceuticals.
- Good Manufacturing Practice (GMP) for biologicals.
- Guidelines for state establishments on quality assurance for biological products.
- Biological products licensing and regulation in countries with emerging regulatory authorities.
- Guidelines that manufacture and control WHO defined vaccines are reviewed in detail by WHO reviewing bodies.

Following these regulations, any COVID-19 vaccine developing institution is required to conduct all operations by the book which has seen vaccine development follow this order; Preclinical stage, Phases 1, 2a & 2b, Phase 3, regulatory approval & licensing, and finally phase 4. These five stages will be covered in the discussions that follow but will be focused on the COVID-19 vaccine phase 3.

### The preclinical stage

This stage is usually aimed at finding synthetic or natural antigens that trigger a reaction similar to that triggered by the actual virus. This process is known for its notoriety for it can even take upwards

of four years which might spark the question of how the quest for the COVID-19 vaccine had the right antigen identified in just a couple of months.

### Phases 1, 2a and 2b

This stage essentially seeks to identify whether the vaccine is safe and what the right dose of it is safe for human administration. Initial testing of the vaccine is conducted in phase 1, is aimed at measuring its generated immune response, assessing the vaccine's safety, and involves a small group of test subjects, usually between 20 and 80 (Levine, 2020). Phase 2a not only seeks to broaden the safety scope of the vaccine but also find its correct dosage although they are said to be pilot trials since clinical trials at phase 2b are pivotal studies aimed at affirming phase 2a findings. Phase 2a trials are conducted on 100–300 subjects while phase 2b trials are done on a larger number of subjects.

### Phase 3

Phase 3 trials usually involve upwards of 3000 subjects and usually employ a randomized placebo-controlled approach to administer the vaccine in the trial. In this case, half the subjects receive the vaccine while the other half receive a placebo (control) but without knowledge of who gets what. The trial is meant to analyse the performance of the vaccine compared to already existing vaccines.

### Regulatory approval and licensing

After phase 3 trials, the vaccine manufacturing institute is required to submit the trial results to their relevant regulatory authority like the USA's Food and Drug Administration (FDA) or the European Commission. Should the trial have been a success, the regulating body approves and licenses it for manufacturing with the requirement that enough of the vaccine be manufactured for anyone who might need it.

### Phase 4

Even after the regulatory body's approval and licensing, they still follow up to ensure the vaccine's long-term effectiveness and safety.

The purpose of this study is to review the 3<sup>rd</sup> phase clinical trials of the various COVID-19 vaccines, their mechanism of action, and efficacy.

**Table 1.** Number of vaccines used in each clinical trial.

Clinical trial	Vaccines no.
1	43 vaccines
2	21 vaccines
3	18 Vaccines

## Materials and methods

### Search strategy

Research materials were identified by searching the U.S. National Library of Medicine. For the search strategy, each vaccine candidate's clinical trial was searched as an individual search item using its official name to broaden the search accuracy range. As such, the search strategy was based on these terms; mRNA-1273, BNT162b2, AZD1222, NVX-CoV2373, Sinopharm, Ad5-nCoV, CoronaVac, JNJ-78436735, Sputnik V. Each of these terms were then combined with the phrase 'phase 3 clinical trial' to form a high yielding search string that provided all the materials used in this study. Online search forums like PubMed, The Lancet and Google Scholar were also searched to confirm the results of initial searches. Since this is a study on the current SARS-CoV-2 outbreak, the search strategy was limited to the virus, related studies, and years of publication as well. All searches were also limited to the English language. The search strategy was improved with every search through the addition of relevant terms as the search process transitioned from one database to the other.

### Study selection

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) meta-analysis guidelines were used to warrant a disciplined and thorough literature search. Following the set of PRISMA guidelines, it was resolved that the meta-analysis would follow a Participant, Interventions, Comparators, Outcomes, and Study Design (PICOS) approach to provide a clear statement of questions being addressed. Study materials were selected on a multi-level screening basis and had to follow this inclusion criterion:

- Only randomized and placebo-controlled trials were included.
- Only phase 3 clinical trials on COVID-19 vaccines were included.
- All studies prior to the COVID-19 outbreak were excluded.

### Data collection

Pre-established outcomes were re-evaluated and used to guide the data extraction process which was conducted by two independent reviewers. The

reviewers were also responsible for resolving all outcome disparities that may have ensued during the extraction process. A dataset was then extracted from each study whose variables were the author/year published, subject, vaccine, duration of each trial, and outcomes. A meta-analysis for collective estimates of all collected data was then done.

## Results

Table 1 shows the number of vaccines involved in clinical trials 1, 2 and 3 of the COVID-19 vaccine development process. Clinical trial 1 is seen to have involved 43 vaccines, trial 2 involves 21 vaccines and trial 3 involves 18 vaccines (Xia et al., 2020).

### Sinopharm

#### Mechanism of action

This vaccine is being developed by a Chinese state-owned company called Sinopharm. It is an inactivated vaccine that gets introduced into the body as a dead copy of SARS-CoV-2. Its dead antigens are then used to produce antibodies that prime the immunity system against future attacks by the virus.

#### Results in trials 1 and 2

The phase 1 trial included 96 individuals which were provided one of three doses i.e. 2.5, 5, and 10 µg/dose and one group of an aluminium hydroxide (alum) adjuvant. There were 24 participants in each group who received three doses at day 0, 28 and 56. There were 224 participants in phase 2 trial who received two doses of vaccine at day 0 and 14 (Xia et al., 2020).

Trial 1 and 2 of the same vaccine were completed in August 2020 and showed that the vaccine triggered a COVID-19 neutralizing antibody response with a low rate of adverse reactions. The most common adverse reactions were pain at the site of injection and fever, but all these were mild and self-limiting, moreover, no treatment was required for any side effect (Xia et al., 2020).

#### Results in trial 3

Two Arab nations (Bahrain and UAE) were among the first to conduct phase three clinical trials of the vaccine. Interim results from the vaccine's phase 3 trials in the UAE and Bahrain found the vaccine to have an 86% efficacy rate (Reuters, 2020). The UAE Ministry of Health also reported the vaccine to be 100% effective in the prevention of mild and severe COVID-19 cases (Reuters, 2020). Official phase 3 results were however not out at the time of writing this paper. The National Health Regulatory Authority (NHRA) on 13th of December released an official

**Table 2.** Analysis of COVID-19 vaccines.

Trial Ref No.	Vaccine Type	Company	Institute	Number of participants	Storage	Trial Outcome (Efficiency %)
NCT04053010	Sinopharm (Inactivated)	China National Pharmaceuticals Group	Wuhan Institute of Virology	45,000	Regular Fridge temperature	79
NCT04283461	mRNA-1273	Moderna Inc	National Institute of Allergy and Infectious Diseases	30,000	-20°C for up to 6 months	94.1
NCT04649021	BNT162b2 (mRNA)	BioNTech & Pfizer	East-West Medical Research Institute	43,538	-70°C	95
NCT04516746	AZD1222 (Viral Vector)	AstraZeneca	Jenner Institute and Oxford Vaccine Group	40,000	Regular Fridge temperature	70
NCT04611802	NVX-CoV2373 (Recombinant spike protein)	Novavax	Serum Institute of India Private Limited	15,000	Regular Fridge temperature	89.3
NCT04341389	Ad5-nCoV (genetically engineered viral vector)	Cansino Biologics	Cansino and Beijing Institute of biotechnology	40,000	Regular Fridge temperature	65.7
NCT04352608	CoronaVac (Inactivated)	Sinovac	Butantan Institute	9,000	Regular Fridge temperature	In process
NCT04436276	JNJ-78436735 (recombinant vector)	Jansen Pharmaceuticals companies	National Institute of Allergy and Infectious Disease	40,000	Regular Fridge temperature	85
NCT04656613	Sputnik V (Viral vector)	UAE Health Services	The Gamaleya National Center of Epidemiology and Microbiology	40,000	Regular Fridge temperature	95

statement granting the vaccine's full approval based on data from trials conducted across several countries. Recently, China has also approved this vaccine and they claimed that the efficacy of this vaccine is 79%, although we do not have any published data available for this. The vaccine has been approved in various countries like the UAE and Bahrain where phase 3 trials were conducted as well as China where the vaccine is approved for general use. UAE had administered over 2 million doses of the vaccine while Bahrain had administered 97,000 doses as of mid-January.

### **Predicted availability**

Sinopharm predicted the vaccine to be available at the end of 2020 and they did it. In both the UAE and Bahrain, the vaccine was approved for emergency usage in September and registered for mass usage in early December. Bahrain followed shortly after also approving the use of the vaccine based on its 86% efficacy results. More than 7700 participants from Bahraini volunteered for the trial (The Daily Tribune, 2020).

### **mRNA-1273 (Moderna)**

#### **Mechanism of action**

Moderna's mRNA-1273 vaccine is an mRNA vaccine which is essentially strands of mRNA carrying instructions for the cell guiding it on how to produce a spike protein that is distinct to SARS-CoV-2 which then stimulates the immune response/produces antibodies to fight the virus. mRNA-1273 encodes for the full-length spike (S) protein of SARS-CoV-2,

modified to introduce 2 proline residues to stabilize the S protein (S2P) in a prefusion conformation. The CoV S protein mediates attachment and entry of the virus into host cells (by fusion), making it a primary target for neutralizing antibodies that prevent infection (ModernaTX, 2020).

#### **Results in trials 1 and 2**

Results from phase 1 and 2 trials of mRNA-1273 showed that the vaccine-induced anti-SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. They used 45 participants in trial 1 and 600 participants in trial 2. The vaccine was tolerated well and safe in general. mRNA-1273 showed very mild adverse effects and no serious adverse effect was recorded, moreover, all adverse events were for a short period and self-limiting (Moderna, 2020).

#### **Results in trial 3**

Phase 3 clinical trial for the mRNA-1273 vaccine by Moderna showed an efficacy rate of 94.1% against COVID-19; mRNA-1273 had efficacy against severe COVID-19 of 100% and continues to be generally well tolerated. No serious safety concerns have been reported so far (Moderna, 2020). The vaccine has been approved for use across the EU following a recommendation by the European Medicines Agency (EMA) and has had 17 million doses of the vaccine ordered in the UK (Mahase, 2021).

#### **Predicted availability**

The vaccine is expected to be ready upon approval for usage by the U.S Food and Drug Administration

(FDA) and the European Medicines Agency. Moderna says vaccinations can begin within one or two days of approval. The vaccine was expected to be ready for production by the end of the year 2020.

### **BNT162b2 (BioNTech & Pfizer)**

#### **Mechanism of action**

Just like mRNA-1273, BNT162b2 is an mRNA vaccine that passes instructions to human cells that do not make spike proteins on their own. The cells read the mRNA instructions of the BNT162b2 vaccine and instruct it to produce the spike protein responsible for triggering the immune system to initiate defensive responses against SARS-CoV-2.

#### **Results in trials 1 and 2**

Results from 37 participants vaccinated with BNT162b2 showed the vaccine produced an immune response with SARS-CoV-2 counterbalancing antibodies and T-cell responses specific to the SARS-CoV-2 protein. Vaccine showed consistent efficacy in all ages, gender, race and presence of any chronic condition. Main adverse effects were pain at the site of injection, fever, headache, chills, diarrhoea, vomiting, and muscle pain but all were transient and self-limiting (Pfizer, 2020).

#### **Results in trial 3**

Phase 3 clinical trial for the BNT162b2 vaccine by BioNTech showed consistent efficacy against gender, age, and ethnicity, and race demographics with an overall efficacy rate of 95%. Data from the trial showed that the vaccine was generally tolerated across the entire sample and no serious safety concerns were seen. The vaccine recorded a 2.0% headache frequency and 3.8% fatigue results (Jackson et al., 2020). Following these results, BNT162b2 has been approved by both the FDA and EMA for use in the US and EU. The vaccine has also been approved in countries like Israel, the UAE, Italy, Spain, Russia, Germany, Turkey, and China.

#### **Predicted availability**

BNT162b2 is currently in its approval stage with the FDA and most countries like Mexico have approved the vaccine for emergency usage. Pfizer is confident that they will ship millions of the vaccine's doses with the approval of relevant authorities. The vaccine has been available for emergency usage since the third week of November. The vaccine's availability for mass usage however remains dependent on the decisions of the various regulatory bodies. Based on their projections, Pfizer expects to produce 50 million doses of the vaccine by the time 2020 ends and up to 1.3 billion doses in 2021 (Pfizer, 2020).

### **AZD1222 (AstraZeneca/University of Oxford)**

#### **Mechanism of action**

Consists of a replication-deficient chimpanzee adenoviral vector ChAdOx1, containing the SARS-CoV-2 structural surface glycoprotein antigen (spike protein; nCoV-19) gene. AZD1222 uses a replication-deficient chimpanzee adenovirus as vector. It has within it an encoded genetic sequence of SARS-CoV-2 and works by instructing cells to produce the spike protein of COVID-19 that triggers the immune response that prepares the body against future attacks of the virus.

#### **Results in trials 1 and 2**

In phase 1 & 2 trials, the vaccine triggered neutralizing activity (strong immune response) – including increased antibodies and responses from T-cells – with subjects only experiencing minor side effects such as fatigue and headache. The interim analysis showed the vaccine to have an acceptable safety profile and very efficacious against symptomatic COVID-19 (Voysey et al., 2021). The vaccine showed a satisfactory safety profile. There was a case of haemolytic anaemia in a control group while another case of transverse myelitis was reported 14 days after first dose, but overall, vaccine showed very mild adverse effects.

#### **Results in trial 3**

When half the dosage was administered and a full dose after one month, the vaccine was seen to have a 90% efficacy rate and a 62% efficacy rate when administered as two full doses over the same duration. The combined analysis from both approaches showed an efficacy rate of 70%. No serious safety concerns related to the vaccine were reported and AZD1222 was well tolerated in both dosing procedures (Voysey et al., 2021). Following the results, the European Medicines Agency approved the vaccine in January for use in the EU across all age groups, including older adults with the UK ordering 100 million doses of the vaccine – enough to vaccinate 50 million people.

#### **Predicted availability**

The Oxford Vaccine Group and AstraZeneca project the AZD1222 to be available in the first half of 2021.

### **NVX-CoV2373**

#### **Mechanism of action**

The vaccine combines spike proteins into a knuckle-bone-shaped nanoparticle that can be injected along with its proprietary Matrix-M adjuvant which has demonstrated a potent and well-tolerated effect by stimulating the entry of antigen-presenting cells into the injection site and enhancing antigen

presentation in local lymph nodes, boosting immune response (Keech, 2020).

### **Results in trials 1 and 2**

From phase 1 & 2 trials, the vaccine was found to be safe and produced coronavirus antibodies at a higher level than is seen among those who have recovered from COVID-19. The vaccine also stimulated T cells, another arm of the human immune response (Keech, 2020).

### **Results in trial 3**

Phase 3 results for the clinical trial of NVX-CoV2373 (Novavax) found the vaccine to have met its primary endpoint with an efficacy rate of 89.3% (NOVAVAX, 2021).

### **Predicted availability**

The vaccine's availability depends on its approval by relevant regulatory bodies but Novavax projects its availability to the middle of 2021.

## **Ad5-nCoV (CanSino Biologics)**

### **Mechanism of action**

CanSino Biologics, the developers of Ad5-nCoV use the same technology they used for their globally innovative vaccine against the Ebola virus. The vaccine is a genetically engineered viral vector vaccine that contains the replication-defective adenovirus type- as its vector to express COVID-19 spike protein. Just like AZD1222, the vaccine uses a weakened adenovirus (common cold virus) to deliver genetic instructions about SARS-CoV-2 so that the cells can produce the spike protein that triggers an immune response where SARS-CoV-2 specific antibodies are produced (Zhu et al., 2020).

### **Results in trials 1 and 2**

Phase 1 & 2 clinical trials of the vaccine showed that it produces 'significant immune responses in the majority of subjects after single dosing. There were no serious adverse reactions documented (Zhu et al., 2020).

### **Results in trial 3**

Official phase 3 trial data released in February 2021 found Ad5-nCoV to have an efficacy rate of 65.7% at preventing moderate cases of COVID-19 and 90.98% effective at preventing severe cases (Peshimam & Farooq, 2021).

### **Predicted availability**

The vaccine has been available with the Chinese government's clearance for military usage since June 2020.

## **CoronaVac (Sinovac)**

### **Mechanism of action**

CoronaVac is an inactivated vaccine where the specific virus is contained with heat or chemicals and its dead cells introduced to the subject's body. The immune system then learns from the dead antigens how to deal with live versions of it should the subject happen to get infected with the virus in the future. In CoronaVac's case, the coronavirus was inactivated with beta-propiolactone and contained inactivated SARS-CoV-2 of course (Zhang et al., 2020).

### **Results in trials 1 and 2**

Results from stage 1 & 2 trial of the vaccine to produce antibodies that neutralized 10 strains of SARS-CoV-2. The vaccine produced antibodies with no severe adverse reactions with a 3 µg dose of CoronaVac being the suggested dosage for phase 3 trials (Zhang et al., 2020).

### **Results in trial 3**

Official results are yet to be published since the trial is still in process.

### **Predicted availability**

Sinovac expects the vaccine to be cleared for usage and in full production by the end of 2020.

## **JNJ-78436735**

### **Mechanism of action**

The vaccine uses Jansen's AdVac and PER.C6 technologies to develop the JNJ-78436735 vaccine (Johnson & Johnson, 2020). The vaccine is a recombinant vector vaccine that uses a human adenoviral vector to express the COVID-19 spike protein within cells. It introduces a piece of DNA from SARS-CoV-2 into the common cold-causing adenovirus that has been genetically changed so that it can't replicate in the body.

### **Results in trials 1 and 2**

A single dose of JNJ-78436735 induced a strong neutralizing antibody response in nearly all participants aged 18 years and older and was generally well-tolerated with immune responses remaining constant across the studied age groups including older adults. Phase 1/2a trials proved the vaccine's safety and efficacy after just a single dose and cleared it for further development (Johnson & Johnson, 2020).

### **Results in trial 3**

Johnson and Johnson reported their vaccine to have an overall efficacy rate of 85% in Preventing Severe Disease and Demonstrated Complete Protection

Against COVID-19 related Hospitalization and Death as of the 28<sup>th</sup> day of vaccination (Johnson & Johnson, 2021).

### **Predicted availability**

Johnson and Johnson predicts the vaccine availability to early 2021.

### **Sputnik V**

#### **Mechanism of action**

Sputnik V is a two adenoviral vector vaccine that gets gene encoding of SARS-CoV-2 S protein added into each vector (Clinical Trials, 2020). During the first vaccination, the initial gene-containing vector (rAd26) which carries instructions on SARS-CoV-2 S protein gets into the cells which after synthesis triggers an immune response. Another vector (rAd5) is introduced to the body through second vaccination which boosts the immune response and provides long-term immunity.

#### **Results in trials 1 and 2**

The Gamaleya Research Institute still has not published results from initial vaccine trials.

#### **Results in trial 3**

Secondary analysis of the Sputnik V phase 3 clinical trial showed a 91.4% efficacy rate 28 days after first dosing and 95% on the 42nd day after first dosing (Clinical Trials, 2020). Sputnik V reported no unexpected adverse events during the trials (SputnikV, 2020).

### **Predicted availability**

The expected availability date for the vaccine was December 2020 and large-scale usage has already begun with Russia having vaccinated over 100,000 high-risk individuals. The country however seems to be having problems with manufacturing large quantities of the vaccine.

### **Discussion**

Nine COVID-19 vaccines were evaluated for safety and efficacy through three successive trials. Phases 1 and 2 clinical trials sought to evaluate the safety of the vaccines and what dose was fit for human administration while phase 3 trials analysed the performance, immunogenicity, and efficacy of the vaccines. All the vaccines involved upwards of 30,000 apart from Sinovac's CoronaVac which had 9,000 participants.

In phase 1 & 2 trials, all nine passed and proceeded to phase 3. The vaccines were found to trigger a strong immune response and were all safe for

administration since no adverse reactions to the vaccine were reported. The vaccines used various mechanisms of action to trigger immune responses. mRNA-1273 and BNT162b2 used a messenger RNA (mRNA) to instruct cells on how to make a protein specific to that of SARS-CoV-2. Sinopharm was an inactivated vaccine that worked by introducing 'killed' copies of SARS-CoV-2 into the body to trigger the production of SARS-CoV-2 specific antibodies while others like Ad5-nCoV were viral vector vaccines that used a weakened adenovirus for genetic instructions delivery. The nine vaccines used fully effective delivery mechanisms which warrants their exceptional efficacy rates.

Results of the trials were very promising with some of the vaccines showing efficacy rates as high as 95%. mRNA-1273 was for example found to trigger an immune response to SARS-CoV-2 in all the trial's participants and reported an efficacy rate of 94.1% while BNT162b2 produced antibodies and T-cell responses specific to the SARS-CoV-2 protein with an efficacy rate of 95%. Of the 9, no vaccine reported any case of severe reactions to the virus with some like AZD1222 showing mild side effects like headaches and fatigue. This meant that the respective vaccines had passed phase 3 trials and only needed the approval of their respective regulatory bodies for mass usage approval.

The US FDA has set a 50% efficacy threshold for a vaccine to be considered for SARS-CoV-2 and experts even consider 90% effective vaccines as extraordinary given that a vaccine against a virus such as that of COVID-19 only needs to reach the lowest efficacy rate for approval (BioNTech & Pfizer, 2020). Results from some of the complete phase 3 trials show excellent numbers with vaccines like Pfizer's BNT162b2 having 95% effectiveness rates. The lowest recorded efficacy rate was that from AstraZeneca's AZD1222 that got 70% which is still well beyond par. These are all great numbers because the primary concern is never effectiveness but safety. Some vaccines have recorded sub-50 efficacy and some like the flu shot staggered at 30s for years. For the case of COVID-19, WHO recognizes that a vaccine should at the very least be 70% on a population basis with durability for at least a year for reactive use in an outbreak and/or protection for those with high ongoing risk (Gamaleya Research Institute, 2020). With efficacy out of question, all the published results are inclined towards maximum safety. No vaccine reported any case of severe side effects to the doses and is scheduled to be approved by the relevant regulatory bodies.

Several vaccines have been approved for general or emergency use in many countries including Bahrain, China, Russia, the United Kingdom, and the



United States. As of February 2021, over 131.5 million doses had been administered worldwide. The share of the total population that have received all doses prescribed by the vaccination protocol described Bahrain has vaccinated more than 11% of the population which is a key step towards herd immunity. Many other countries like the United Arab Emirates, the United States, Denmark, Italy, and Spain have vaccinated around 1% to 3% of their population (Oxford University, 2021).

As world will have to deal with the resistance against vaccines, current data have shown some very interesting study where they asked a question that who will get a COVID-19 vaccine if it is available to them this week. The survey shows that 71.3% population of the United Kingdom agreed to take the vaccine. In Bahrain, a study showed this acceptance rate at around 65%. The lowest acceptance of vaccine has been shown in France where only 29.8% people accepted to take vaccine (Oxford University, 2021).

## Conclusion

After the results drawn from phase 3 trials of the various vaccines against SARS-CoV-2, it can be concluded that very helpful interventions have been developed to fight the Coronavirus pandemic. At this rate, the world will not only have one vaccine but a dozen full of them if not more. In addition to the positive results, research from the whole vaccine development operation will provide very useful insights in future quests for a vaccine.

## Author contributions

Conceptualization M.Z.; methodology, M.Z., M.S., S.P.; formal analysis, M.S., M.Z., E.B.B.; investigation, M.S.; resources, M.Z., S.P.; data curation, M.S., M.Z.; writing – original draft preparation, M.S. and M.Z.; writing – review and editing, M.Z., S.P. E.B.B.; visualization, M.Z.; supervision, M.Z.

## Disclosure statement

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