J Appl Biotechnol Rep. 2022 December;9(4):790-798

Journal of
Applied Biotechnology Reports

doi 10.30491/JABR.2022.354528.1553

Review Article

# Efficacy and Adverse Effects of the Most Common COVID-19 Vaccines: a Rapid Review Study

**Alireza Soleymanitabar [1], Mohammad Amin Gharekhanloo [1], Mohammad Parsa Khalaj [1], Mohammad Mahdi Radfar [1], Danial Mnasour Kiaei [1], Alireza Bolouriyan [1], Mohammad Ali Abyazi [2], Hamed Gholizadeh [3], Mohammad Heiat [2*]**

[1] Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran
[2] Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL), Baqiyatallah University of Medical Sciences, Tehran, Iran
[3] Department of Surgery, Trauma Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

**Corresponding Author:** Mohammad Heiat, PhD, Assistant Professor, Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL), Baqiyatallah University of Medical Sciences, Tehran, Iran. Tel: +98-9366876929, E-mail: Mohamad.heiat@gmail.com

**Received** August 2, 2022; **Accepted** October 4, 2022; **Online Published** December 31, 2022

**Abstract**
COVID-19 raised a flood of events all through the world in multiple fields. Reaching an agreement to generate and use vaccines against SARS-CoV-2 (the cause of COVID-19) was likely the most controversial topic among different communities. Being new developed and lack of longitudinal characterization of these vaccines, the growing concerns were expectable. Now, regarding the conduction of large global studies, it is more possible to figure out the ambiguous characteristics of common anti-COVID-19 vaccines. The aim of the present study was to make a rapid overview on the efficacy and side effects of eight common COVID-19 vaccines used in Iran (Sinopharm, Oxford-AstraZeneca, BIV1-CovIran (COVIran Barekat), Pastocovac, Sputnik V, Covaxin (Bharat), Noora, and Pfizer-BioNTech). Using the designed search syntax, composed of MeSh terms, the published records were searched in PubMed database. The high-quality articles, meeting the inclusion criteria, were exploited to extract the interesting data. The final data pool, minded for all eight vaccines, was summarized, categorized, arranged, and presented separately. The trimmed findings demonstrated that all approved vaccines have several mild to moderate side effects. The final results of the present study depicted a big picture of commonly used vaccines and rapidly overviewed their efficacies and side effects.

**Keywords:** Efficacy, COVID-19 Vaccines, Safety, SARS-CoV-2 Virus, Side Effects
**Citation:** Soleymanitabar A, Gharekhanloo MA, Khalaj MP, Radfar MM, Masour Kiaei D, Bolouriyan A, et al. Efficacy and Adverse Effects of the Most Common COVID-19 Vaccines: a Rapid Review Study. J Appl Biotechnol Rep. 2022;9(4):790-8. doi:10.30491/JABR.2022.354528.1553

## Introduction

Overcoming the COVID-19 crisis is a hot topic which has involved scientific societies. Regarding no causal treatment is currently introduced; vaccination has been taken into account as the most robust confronting strategy against SARS-CoV-2 virus. There are three headings over an ideal vaccine. i) Safety and efficacy as the main features, ii) Immune response consistency, iii) Achievable approaches for vaccine development. Low cost, ease of administration, shelf stability, and multivalency are other characteristics of an ideal vaccine.[1] Numerous vaccines have been developed to prevent COVID-19.[2,3] Following the information published by COVID-19 vaccine trials and approvals database, led by the department of epidemiology and biostatistics in the school of population and global health at McGill university,[4] there are 230 COVID-19 vaccine candidates (89 vaccines in phase III, 71 vaccines in phase II, 58 vaccine in phase I and 12 vaccines no longer progressed) out of which 47 vaccines received approval for use (Table 1). Currently available vaccines against SARS-CoV-2 have shown significant immunity and have actually raised the antibody-mediated responses.[5] However, there are large differences among the developed vaccines in terms of the platform (Figure 1), efficacy, and side effects, which have made experts and different scientific communities hesitant to choose the right option.

Various studies on these vaccines demonstrated that the vaccination induces humoral and cellular immune responses.[6] These induced responses must have neutralizing properties and, on the other side, must not cause adverse effects. Locally or globally, a mass of studies have been conducted to determine the efficacy and side effects of COVID-19 vaccines. However, the reported data are not sufficient enough to make a firm decision for all individuals.

Apart from the vaccine technology, the host factors (immune-senescence, diet, microbiota, comorbidities, ageing, gender, etc.) play significant roles in the vaccine's effects.[7] Nevertheless, different platforms and technologies used for the development of COVID-19 vaccine[8] have undeniable roles

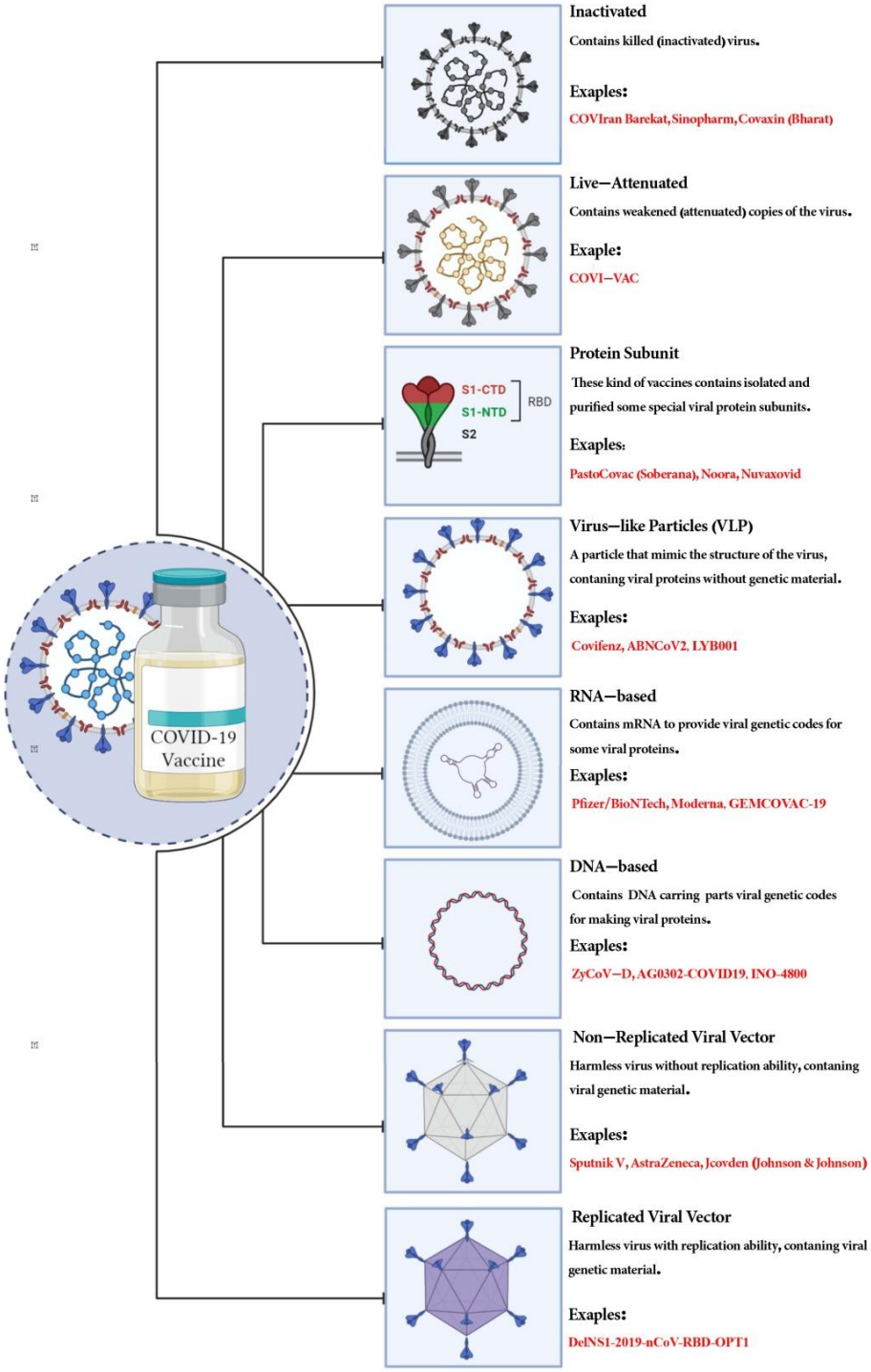


**Figure 1.** Platforms Recruited to Develop Vaccine Against COVID-19.

roles in their efficacy and adverse effects.[9]

Although extensive data have been published in the form of Randomized Clinical Trials (RCT), observational, and review studies on the efficacy and side effects of vaccines, the present study has tried to conduct a narrative review study on the characteristics of the most common vaccines.

## Materials and Methods

The present study was conducted to provide a rapid review on the efficacy and adverse effects of the most common COVID-19 vaccines, through which we discussed the main characteristics of the top eight frequent vaccines including Sinopharm, Oxford-AstraZeneca, BIV1-CovIran (COVIran Barekat), Pastocovac, Sputnik V, Covaxin (Bharat), Noora and Pfizer-BioNTech. To achieve this goal, every author was assigned to one or two vaccines and searched through the literature to find the most related publications. Studies were identified by mining within the electronic database of

**Table 1.** List of 47 Approved Vaccines

| No | Company: Symbol | Platform | Trials No. / countries No. | Countries with approval |
|---|---|---|---|---|
| 1 | Bharat Biotech: iNCOVACC | Non-Replicating Viral Vector | 4 / 1 | 1 |
| 2 | CanSino: Ad5-nCoV-IH | Non-Replicating Viral Vector | 5 / 4 | 1 |
| 3 | Gamaleya: Sputnik V | Non-Replicating Viral Vector | 25 / 8 | 74 |
| 4 | Janssen (Johnson & Johnson): Jcovden | Non-Replicating Viral Vector | 26 / 25 | 113 |
| 5 | Oxford/AstraZeneca: Vaxzevria | Non-Replicating Viral Vector | 71 / 33 | 149 |
| 6 | Serum Institute of India: Covishield (Oxford/ AstraZeneca formulation) | Non-Replicating Viral Vector | 6 / 1 | 49 |
| 7 | Gamaleya: Gam-COVID-Vac | Non-Replicating Viral Vector | 2 / 0 | 1 |
| 8 | CanSino: Convidecia | Non-Replicating Viral Vector | 14 / 6 | 6 |
| 9 | Gamaleya: Sputnik Light | Non-Replicating Viral Vector | 7 / 3 | 26 |
| 10 | Sinopharm (Beijing): Covilo | Inactivated | 38 / 16 | 93 |
| 11 | Sinopharm (Wuhan): Inactivated (Vero Cells) | Inactivated | 9 / 7 | 2 |
| 12 | Sinovac: CoronaVac | Inactivated | 40 / 10 | 56 |
| 13 | Bharat Biotech: Covaxin | Inactivated | 16 / 2 | 14 |
| 14 | Chumakov Center: KoviVac | Inactivated | 3 / 1 | 3 |
| 15 | Health Institutes of Turkey: Turkovac | Inactivated | 8 / 1 | 1 |
| 16 | Shenzhen Kangtai Biological Products Co: KCONVAC | Inactivated | 7 / 1 | 2 |
| 17 | Shifa Pharmed Industrial Co: COVIran Barekat | Inactivated | 6 / 1 | 1 |
| 18 | Valneva: VLA2001 | Inactivated | 9 / 4 | 33 |
| 19 | Research Institute for Biological Safety Problems (RIBSP): QazVac | Inactivated | 3 / 1 | 2 |
| 20 | Organization of Defensive Innovation and Research: FAKHRAVAC (MIVAC) | Inactivated | 3 / 1 | 1 |
| 21 | Bagheiat-allah University of Medical Sciences: Noora vaccine | Protein Subunit | 3 / 1 | 1 |
| 22 | Instituto Finlay de Vacunas Cuba: Soberana 02 | Protein Subunit | 7 / 2 | 4 |
| 23 | Instituto Finlay de Vacunas Cuba: Soberana Plus | Protein Subunit | 5 / 1 | 2 |
| 24 | Anhui Zhifei Longcom: Zifivax | Protein Subunit | 20 / 5 | 4 |
| 25 | Biological E Limited: Corbevax | Protein Subunit | 7 / 1 | 2 |
| 26 | Center for Genetic Engineering and Biotechnology (CIGB): Abdala | Protein Subunit | 5 / 1 | 6 |
| 27 | Medigen: MVC-COV1901 | Protein Subunit | 15 / 4 | 3 |
| 28 | Livzon Mabpharm Inc: V-01 | Protein Subunit | 7 / 3 | 1 |
| 29 | National Vaccine and Serum Institute: Recombinant SARS-CoV-2 Vaccine (CHO Cell) | Protein Subunit | 3 / 2 | 1 |
| 30 | Novavax: Nuvaxovid | Protein Subunit | 22 / 14 | 40 |
| 31 | Razi Vaccine and Serum Research Institute: Razi Cov Pars | Protein Subunit | 5 / 1 | 1 |
| 32 | SK Bioscience Co Ltd: SKYCovione | Protein Subunit | 7 / 6 | 1 |
| 33 | Takeda: TAK-019 (Novavax formulation) | Protein Subunit | 3 / 1 | 1 |
| 34 | Serum Institute of India: COVOVAX (Novavax formulation) | Protein Subunit | 7 / 3 | 6 |
| 35 | Vaxine/CinnaGen Co.: SpikoGen | Protein Subunit | 8 / 2 | 1 |
| 36 | Vector State Research Center of Virology and Biotechnology: Aurora-CoV | Protein Subunit | 2 / 1 | 1 |
| 37 | Vector State Research Center of Virology and Biotechnology: EpiVacCorona | Protein Subunit | 4 / 1 | 4 |
| 38 | Pfizer/BioNTech: Comirnaty | RNA | 97 / 31 | 149 |
| 39 | Moderna: Spikevax | RNA | 74 / 24 | 88 |
| 40 | Gennova Biopharmaceuticals Limited: GEMCOVAC-19 | RNA | 2 / 1 | 1 |
| 41 | Moderna: Spikevax Bivalent Original/Omicron BA.1 | RNA | 3 / 3 | 38 |
| 42 | Moderna: Spikevax Bivalent Original/Omicron BA.4/BA.5 | RNA | 2 / 1 | 1 |
| 43 | Takeda: TAK-919 (Moderna formulation) | RNA | 2 / 1 | 1 |
| 44 | Pfizer/BioNTech: Comirnaty Bivalent Original/Omicron BA.1 | RNA | 3 / 5 | 32 |
| 45 | Pfizer/BioNTech: Comirnaty Bivalent Original/Omicron BA.4/BA.5 | RNA | 3 / 1 | 32 |
| 46 | Medicago: Covifenz | Virus-like Particles (VLP) | 6 / 6 | 1 |
| 47 | Zydus Cadila: ZyCoV-D | DNA | 6 / 1 | 1 |

PubMed. All those discussed the different aspects of COVID-19 vaccines were considered to complete data.

The used search script was as follows: (safety OR efficacy OR efficiency OR side effects OR adverse effects OR authorization) AND (COVID-19 OR SARS-CoV-2) AND (vaccine OR "preclinical study" OR "clinical trial") to address all papers related to the topic.

The articles' eligibility factors considered as inclusion criteria were: the most updated and relevant original articles under reputable publishers, full-text accessibility, comprehensiveness in results, those with high sample size and citations and those focusing on safety and adverse effects of anti-COVID-19 vaccine as the study scope. Findings have been categorized and discussed in detail in the result sections (Table 2).

## Results

### *Oxford-AstraZeneca (ChAdOx1 nCoV-19; Codenamed AZD1222)*

After negotiation with multiple companies about financial and distribution aspects, the Oxford-AstraZeneca vaccine (ChAdOx1 nCoV-19; codenamed AZD1222) was manufactured by the cooperation of Oxford University with AstraZeneca Pharmaceutical and Biotechnology Company[10] and revived its Emergency Use Authorization (EUA) approval at December 8, 2021.[11]

**Table 2.** Summary of Efficacy and Adverse Effects of the Most Common COVID-19 Vaccines used in Iran

| Vaccine | Platform | Country | Time of accessibility | Vaccine doses No. | Age Range | Efficacy (%) | Main Side effects | Approval | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| Sinopharm (BBIBP_corv) | Inactivated | China | May 2021 | 2 | > 18 | 79.6 | ➢ Fatigue<br>➢ Chill<br>➢ Fever<br>➢ Dizziness<br>➢ Headache<br>➢ Local reactions | WHO | (19, 40) |
| Oxford-astrazeneca | Non-Replicated Viral Vector | UK-Sweden | February 2021 | 2 | >18 | 70.6 | ➢ Pain at injection site<br>➢ Tenderness<br>➢ Hyperthermia<br>➢ Redness<br>➢ Swelling<br>➢ Induration<br>➢ Itching<br>➢ Malaise<br>➢ Muscle ache<br>➢ Joint pain<br>➢ Fatigue<br>➢ Nausea<br>➢ Headache<br>➢ Chills<br>➢ Feverishness | FDA | (12) |
| Barekat vaccine | Inactivated | Iran | March 2021 | 2 | 18-75 | 82.5 | ➢ Fever<br>➢ Headache<br>➢ Fatigue<br>➢ Myalgia<br>➢ Pain<br>➢ Redness<br>➢ Swelling | Iran food and drug association | (33) |
| Sputnik V | Non-Replicated Viral Vector | Russia | August 2020 | 2 | >18 | 91.6 | ➢ Headache<br>➢ Asthenia<br>➢ Hyperthermia<br>➢ Myalgia<br>➢ Joint<br>➢ Pain at injection site | Russian ministry of health | (26) |
| Covaxin (Bharat) | Inactivated | India | November 2021 | 2 | >18 | 81% | ➢ Pain<br>➢ Swelling at injection site<br>➢ Fever<br>➢ Weakness<br>➢ Fatigue<br>➢ Muscle aches<br>➢ Body aches<br>➢ Headaches<br>➢ Nausea<br>➢ Vomiting<br>➢ Loss of appetite<br>➢ Chills<br>➢ Systemic rash<br>➢ Diarrhea | WHO | (21, 24) |
| Pfizer–BioNTech | mRNA vaccine | USA & Germany | December 2020 | 2 | >16 | 95 | ➢ Fatigue<br>➢ Headache<br>➢ Muscle pain<br>➢ Chills<br>➢ Injection pain<br>➢ Allergic reaction | FDA | (30) |
| Pastocovac | Protein Subunit | Cuba | March 2021 | 2 | >18 | 71 | ➢ Pain at injection site<br>➢ Swelling at injection site<br>➢ Erythema<br>➢ Induration and<br>➢ Local temperature<br>➢ Fever<br>➢ General discomfort | Iran food and drug association | (36) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Noora Vaccine | Protein Subunit | Iran | March 2022 | - | - | - | ➢ Local pain<br>➢ Induration<br>➢ Redness | Iran food and drug association | (38, 39) |

The Oxford–AstraZeneca vaccine (ChAdOx1 nCoV-19) has been produced from a common cold adenovirus, derived from the stool of chimpanzees, which is no longer hazardous for cells. After injection, it produces the SARS-CoV-2 spike protein which is a target for human immune systems.[10]

Following the studies on 11636 participants (18-55 year-olds (10218 [87.8%]), whites (9625 [82.7%]), and women (7045 [60.5%])) through four RCT conducted in the United Kingdom, South Africa, and Brazil, no hospital admission related to COVID-19 in people who had been vaccinated was shown.[12] The primary analysis showed an efficacy of 70.4% for vaccine against COVID-19 after the second dose.[12] The serological findings revealed that the ChAdOx1 nCoV-19 vaccine induced a specific antibody response to the SARS-CoV-2 spike glycoprotein Receptor Binding Domain (RBD) after a single dose administration.[10]

In a previous study, it was declared that AstraZeneca's COVID-19 vaccine provides protection against the Delta (B.1.617.2) and Kappa (B1.617.1) variants.[13]

According to the WHO announcement, pregnant women should be aware of vaccination complications. Nevertheless, it declares that the vaccine is unlikely to pose a risk to breastfeeding and doesn't advise delaying or terminating pregnancy because of vaccination.

Two doses of this vaccine with an interval of 8 to 12 weeks are proposed. There is a recommendation for an extra dose for immunocompromised individuals. Some adverse effects at the injection site including: pain, tenderness, warmth, redness, swelling, induration, and itching and some systemic adverse effects such as malaise, myalgia, joint pain, fatigue, nausea, headache, chills, and feverishness have been reported.[10]

In a study, it has been indicated that this vaccine was safe and greatly tolerated with a lower reactogenicity profile in old individuals compared to younger ones.[10]

Desalegn et al., reported that the prevalence of side effects after the first dose was higher than the second one (90% vs. 69.7%). The most prevalent side effect was injection site pain after both first and second dose of vaccine (63.8% vs. 50.4%) preceded by headache (48.8% vs. 33.5%), fever (38.8% vs. 20.9%), muscle pain (38.8% vs. 21.7%), fatigue (26% vs. 28.7%), tenderness at the site (27.6% vs. 21.7%), and joint pain (27.6% vs. 20.9%).[14]

European countries put a stop to vaccination after some reports of a blood clot which eventually turned out not to be more than an occurrence among a population with other vaccinations.[15] In accordance with Knoll's study, some delayed onset side effects of Oxford–AstraZeneca have been transverse myelitis, haemolytic anemia, and fever higher than 40 °C.[12]

A study on the Iranian population revealed that 29.4% of Oxford–AstraZeneca vaccine recipients showed no adverse effects after vaccination. However, chill/fever (45% vs. 7.5%), skeletal pain (27.7% vs. 8.8%), and fatigue (24.2% vs. 15%) were the most frequent adverse effects in first *vs* second doses. Elders showed fewer symptoms in comparison with younger recipients. Females also showed more symptoms compared to males.[16]

### *Sinopharm*

BBIBP-CorV (Sinopharm) is another type of COVID-19 vaccine manufactured by China National Biotec Group (CNBG). It contains chemically (Beta-propiolactone) inactivated coronavirus and has been successfully tested on mammalian species (rabbits, mice and primates). For instance, vaccination with BBIBP-CorV effectively protects rhesus macaques (*Macaca mulatta*).[17]

Sinopharm was tested in humans through a RCT setting for prophylaxis against COVID-19. Results obtained from phase I/II showed that the vaccine could be safe and well-tolerated.[13] Phase III results, in the UAE showed that the two-dose- administration of this vaccine creates 78% effectiveness in preventing COVID-19.[18] Sinopharm received the WHO emergency use listing (EUL) on May 7, 2021.

Following the study on 3,147,869 adults, conducted by Al Kaabi et al., two doses of Sinopharm vaccine demonstrated 79.6%, 86%, and 84.1% effectiveness in preventing hospitalization, intensive care need, and death in SARS-CoV-2 infected patients, respectively.[19]

Most adverse effects associated with Sinopharm have been reported to be mild. The most prevalent complications over injection sites were mild self-limiting pain, itching, and swelling. The systemic types of adverse effects were general complications such as fever, fatigue, inappetence, nausea, constipation, mucocutaneous abnormalities, headache, diarrhea, vomiting, itching, and joint pain.[20] However, few serious adverse effects have been observed.

According to a report by Babaee et al., 62.6% of the individuals receiving Sinopharm vaccination did not show any adverse effects after both doses. However, fatigue (14.5%, vs. 8.9%), chill/fever (6.5%, vs. 2.6%), dizziness/ headache (4.1%, vs. 2.6%), and local reactions (3.5%, vs. 2.7%) were the most frequent adverse effects in first *vs* second doses.

They also tracked the most frequent adverse effects between different age ranges. They reported that chill/fever among 30-50, dizziness/headache and skeletal pain among 50-60 year-olds participants were the most common symptoms.

Other age ranges were prevalently involved with fatigue.[16]

### *Covaxin (Bharat)*

In May 2020, the Indian Council of Medical Research (ICMR) approved a virus strain for developing a fully indigenous COVID-19 vaccine named Covaxin BBV152 (manufactured by Bharat Biotech). It is a whole virion β-propiolactone inactivated SARS-CoV-2 absorbed to alum (Algel-IMDG) needing a cold-chain (+2 °C to +8 °C) preservation. This vaccine was administered to people over the age of 18. To reach a full cell-mediated response, it is advised to inject two doses (0.5 ml/dose) of Covaxin intramuscularly into the deltoid muscle within 28 days apart.[21-23]

This vaccine has successfully completed three phases of RCT. Phase III with 25,800 members indicated an 81% efficacy for this vaccine. Pain and swelling at the injection site were mentioned as local side effects. However, fever, weakness, fatigue, myalgia, headaches, nausea, vomiting, loss of appetite, chills, systemic rash, and diarrhea were cited as systemic side effects.[21,24]

Covaxin was added to the WHO EUL on November 3, 2021.[20] This vaccine showed 100 and 90% neutralizing effects against the Delta and Omicron strains, respectively.[25]

### *Sputnik V*

Russia launched Sputnik V as an adenovirus-based vaccine against SARS-CoV-2 on August 11, 2020. This vaccine carries two different recombinant adenoviral vectors (rAd26 and rAd5), encoding genes for SARS-CoV-2 spike glycoprotein.[26]

Over this vaccine, an RCT was conducted on 21,977 adults who were randomly assigned to the vaccine (n = 16,501) or placebo group (n = 5476) between September 7 to November 24, 2020. Ultimately, 19,866 individuals received two doses of vaccine or placebo and were included in the primary outcome analysis. From day 21 after the first vaccination, 16 of 14,964 participants (0.1%) in the vaccine and 62 (1.3%) of 4902 in the placebo group showed positive test results for COVID-19. Therefore, the vaccine efficacy was 91.6% (95% CI: 85.6-95.2).[26]

This vaccine was recommended to be administered to individuals over the age of 18.[27] It has been revealed that Sputnik V is well tolerated and elicits a humoral and cell-mediated immune response in healthy adults. The literature published by Sapkal et al., demonstrated that COVID-19-recovered patients vaccinated by Sputnik V had very high neutralizing antibody titer in comparison with the COVID-19 naïve vaccinated subjects (180.2 [95% CI 84.43-384.6] vs. 4601 [95% CI 2429-8717] for Delta variant).[28]

Sputnik V received its approval for administration in 74 countries on June 14, 2022. No serious or long-lasting complication was seen after vaccination. However, some mild adverse systemic and local reactions as well as changes in laboratory variables have been reported.

The most frequently reported adverse effects (often after receiving the second dose) were injection-site pain (58%), hyperthermia (50%), headache (42%), asthenia (28%), and joint pain (24%).[26]

Babaee et al., reported that 17.3% of the individuals receiving Sputnik V vaccine, did not show any side effects after both doses. However, fatigue (44.3% vs. 24.8%), local reactions (20.7% vs. 18.6%), and chill/fever (29.9% vs. 22.1%) were the most frequent adverse effects in first vs second doses. They also reported that elders and males showed fewer adverse effects rather than other recipients.[16]

### *Pfizer–BioNTech*

The United States Food and Drug Administration (FDA) approved Pfizer–BioNTech (BNT162b2) vaccine against SARS-CoV-2 to be used in two doses within a 21 days interval. Advisory Committee on Immunization Practices (ACIP) advised using Pfizer–BioNTech COVID-19 vaccines on 12 December, 2020 in the emergency situation.[29]

Pfizer_BioNTech COVID-19 vaccine is a lipid non-particle formulated modified mRNA vaccine encoding the spike glycoprotein of SARS-CoV-2. Every dose should be injected intramuscularly and used in people who are 16 years or older. Pfizer_BioNTech vaccine's efficacy is about 94.5%, and its immunity is persistent for at least four months.[29]

Through a randomized clinical trial (phase II/II), 43545 individuals aged 16 or older were randomly divided into two groups (placebo and vaccine groups). Of them, 21720 individuals were injected with Pfizer and 21728 individuals with a placebo.

A week after receiving the second dose, eight individuals in the vaccine and 162 in the placebo group showed COVID-19 positive test. The results of this clinical trial revealed that the BNT162b2 vaccine is 95% (95% CI 90.3-97.6) effective in protecting humans from COVID-19.[30]

In accordance with the study by Oliver et al., the observed side effects after BNT162b2 vaccination have been mild to moderate. Grade three side effects which occurred in 8.8% of individuals were fatigue (4.2%), headache (2.4%), muscle pain (1.8%), chills (1.7%), and pain at the injection site (1.4%).[29] Kadali et al., reported that 64.5% of participants experienced one or more symptoms, and among them, only 0.62% needed emergency help, and 0.25% needed hospitalization.[31]

### *BIV1-CovIran (COVIran Barekat)*

BIV1-CovIran (COVIran Barekat) is an inactivated whole virus particle vaccine which has been produced by Shifa Pharmed Industrial Group in Iran. The protection and immunogenicity of COVIran Barekat have been evaluated through a preclinical research in mice, rabbits and non-human primates.[32]

In a single-center, double-blind randomized clinical trial (phase I/II), 332 patients (52 in phase I and 280 in phase II) with no history of COVID-19, with an age range of 18-75 year olds were enrolled into the study. The initial safety assessment was checked in phase I. Fifty-six volunteers in phase I were divided into three groups. The first group (24 participants) received 3 µg, the second (24 participants) received 5 µg of the vaccine, and the third one (8 participants) received placebo on days 0 and 14. After safety validation, 280 participants enrolled in phase II for more evaluation of safety and efficacy. On day 42, through the conventional virus neutralization test (cVNT), 82.5% of vaccinated participants neutralized SARS-CoV-2 at 1/64 times serum dilution.[33]

Accordingly, 152 (54.0%) of the participants who had enrolled in phase II experienced side effects. No serious adverse event was found in vaccinated patients in phase I/II. However, some mild to moderate side effects such as pain at the injection site, weakness, and headache were observed.

RCT Phase III on COVIran Barekat has been started in March 2021, in which 20000 volunteers received 5 µg of BIV1-CovIran on days 0 and 28 (IRCT registration number: IRCT20201202049567N3).

In a historical cohort study, conducted by Mirahmadizadeh et al., the data of 72162 participants who received two doses of BIV1-CovIran was analyzed. There was a 2.64 incidence density of confirmed COVID-19 per 100000 person-days. The effectiveness of the BIV1-CovIran vaccine in the prevention of infection (positive RT-PCR), hospital admission (suspicious/definite), hospital admission (definite), death (suspicious/definite), and death (definite) were 87.1%, 85.5%, 86.4%, 97.7%, and 98.3%, respectively.[34]

### *PastoCovac (SOBERANA 02/FINLAY-FR-2)*

SOBERANA 02 vaccine has been made by the Finlay Institute of Vaccines in Cuba. It is the first conjugated vaccine developed for SARS-CoV-2 in which the recombinant Receptor Binding Domain (RBD) protein has been conjugated to Tetanus Toxoid (TT). This vaccine was administered to people aged over 18 and has successfully completed three phases of clinical trials. It received emergency use authorization in Iran in June 2021.

In the meantime, the evaluation consequences have indicated that SOBERANA 02 efficacy is 71% for the prevention of COVID-19.[35-37] The results showed an increase to 92.4% after adding a dose of SOBERANA Plus as a third booster.[36] Pain and swelling at the injection site, erythema, induration, and local temperature were mentioned as its local side effects, and fever and general discomfort were cited as systemic side effects.[35-37]

In the first phase, the solicited adverse effect of local pain and the unsolicited adverse effect of high blood pressure were reported.

In the second phase, the solicited side effect of pain at the injection site and unsolicited adverse effect of headache were reported. In terms of immunogenicity, the first and second phases were almost similar to each other and were reported to be over 75%. In the third phase, the immunegenicity of this vaccine was about 70%, and the solicited adverse effects of local pain and reaction at the injection site and unsolicited side effects of high blood pressure and headache have been reported.[37]

### *Noora Vaccine*

Noora is a new recombinant COVID-19 vaccine candidate developed in Iran. It is composed of three truncated recombinant proteins (truncated spike protein, receptor-binding domain (RBD), and nucleoprotein (N)). Up to now, a pre-clinical study and a randomized double-blind placebo-controlled Phase I trial (RCT phase I) have been published on this vaccine candidate through which its safety and immunegenicity have been evaluated in mice, rabbits, primates, and human beings.

Through the pre-clinical study, the researchers scheduled an immunization program with different compositions of active agents and adjuvants to investigate all features of their vaccine in animals. The results showed that at the best condition, the candidate vaccine generates a high titer IgG at doses of 80 and 120 µg. The results also revealed that Alum, AS03, and Montanide adjuvants caused the immune system to raise a higher titer of antibodies. However, the highest neutralization rate was observed over immunization with Alum adjuvant. The Noora candidate did not show cytotoxicity and pathologic effects in animals.[38]

Conducting phase I RCT, Salimian et al., evaluated the safety and immunogenicity of Noora vaccine in adults. Totally 70 cases were included in their study, out of which 60 individuals completed the trial. They reported no severe adverse effects for Noora. However, local pain, induration, and redness at the injection site were observed as mild to moderate adverse effects for this recombinant vaccine. In comparison with the placebo group, significant levels of Anti-RBD and neutralizing antibody were detected in test individuals. The authors stated that this trial has demonstrated an acceptable safety and significant seroconversion rate in human beings.[39]

## Conclusion

Nowadays, it has been proved that vaccination is the most effective way to encounter the COVID-19 pandemic and decrease its morbidity and mortality. Hitherto, several vaccines have been used in Iran. Nevertheless, Pfizer was the alleged most efficient vaccine in literature, Sinopharm had been the most frequent with the least adverse effect vaccine used in Iran. In addition, all features of these two vaccines summarized in this rapid report were obtained

mainly from non-Iranian studies. Therefore, some meritorious studies are needed to evaluate the efficacy and safety of these vaccines exclusively for the Iranian population. Perhaps our key limitation in this study was the lack of access to all data related to vaccines due to lack of publication or incomplete data.

## Authors' Contributions

Idea design and research supervision by MH. All other authors had equal contribution.

## Conflict of Interest Disclosures

The authors declare that they have no conflicts interest.

## Acknowledgment

The authors would like to thank the Clinical Research Development Unit of Baqiyatallah Hospital, Tehran, Iran, for their guidance and support.

## References

1. Ada GL. The ideal vaccine. World J Microbiol Biotechnol. 1991;7(2):105-9. doi:10.1007/BF00328978
2. Ahmed S, Khan S, Imran I, Al Mughairbi F, Sheikh FS, Hussain J, et al. Vaccine development against COVID-19: study from pre-clinical phases to clinical trials and global use. Vaccines. 2021;9(8):836. doi:10.3390/vaccines9080836
3. Kudlay D, Svistunov A. COVID-19 vaccines: an overview of different platforms. Bioengineering. 2022;9(2):72. doi:10.3390/bioengineering9020072
4. COVID19 vaccine tracker. Available from: https://covid19.trackvaccines.org
5. Lopera TJ, Chvatal-Medina M, Florez-Alvarez L, Zapata-Cardona MI, Taborda NA, Rugeles MT, et al. Humoral Response to BNT162b2 Vaccine Against SARS-CoV-2 Variants Decays After Six Months. Front Immunol. 2022:13:879036. doi:10.3389/fimmu.2022.879036
6. Oyaert M, De Scheerder MA, Van Herrewege S, Laureys G, Van Assche S, Cambron M, et al. Evaluation of humoral and cellular responses in SARS-CoV-2 mRNA vaccinated immunocompromised patients. Front Immunol. 2022;13:858399. doi:10.3389/fimmu.2022.858399
7. Falahi S, Kenarkoohi A. Host factors and vaccine efficacy: Implications for COVID-19 vaccines. J Med Virol. 2022;94(4):1330-5. doi:10.1002/jmv.27485
8. Romero JR, Bernstein HH. COVID-19 vaccines: a primer for clinicians. Pediatr Ann. 2020;49(12):e532-6. doi:10.3928/19382359-20201116-01
9. Xing K, Tu XY, Liu M, Liang ZW, Chen JN, Li JJ, et al. Efficacy and safety of COVID-19 vaccines: a systematic review. Zhongguo Dang Dai Er Ke Za Zhi. 2021 Mar 15;23(3):221-8. doi:10.7499/j.issn.1008-8830.2101133
10. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet. 2020;396(10267):1979-93. doi:10.1016/S0140-6736(20)32466-1
11. Nagy A, Alhatlani B. An overview of current COVID-19 vaccine platforms. Comput Struct Biotechnol J. 2021;19:2508-17. doi:10.1016/j.csbj.2021.04.061
12. Knoll MD, Wonodi C. Oxford–AstraZeneca COVID-19 vaccine efficacy. Lancet. 2021;397(10269):72-4. doi:10.1016/S0140-6736(20)32623-4
13. Supasa P, Zhou D, Dejnirattisai W, Liu C, Mentzer AJ, Ginn HM, et al. Reduced neutralization of SARS-CoV-2 B. 1.1. 7 variant by convalescent and vaccine sera. Cell. 2021;184(8):2201-11. doi:10.1016/j.cell.2021.02.033
14. Desalegn M, Garoma G, Tamrat H, Desta A, Prakash A. The prevalence of AstraZeneca COVID-19 vaccine side effects among Nigist Eleni Mohammed memorial comprehensive specialized hospital health workers. Cross sectional survey. Plos One. 2022;17(6):e0265140. doi:10.1371/journal.pone.0265140
15. Wise J. Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. BMJ. 2021;372:n699. doi:10.1136/bmj.n699
16. Babaee E, Amirkafi A, Tehrani-Banihashemi A, Soleiman vandiAzar N, Eshrati B, Rampisheh Z, et al. Adverse effects following COVID-19 vaccination in Iran. BMC Infect Dis. 2022;22(1):476. doi:10.1186/s12879-022-07411-5
17. Wang H, Zhang Y, Huang B, Deng W, Quan Y, Wang W, et al. Development of an inactivated vaccine candidate, BBIBP-CorV, with potent protection against SARS-CoV-2. Cell. 2020;182(3):713-21. doi:10.1016/j.cell.2020.06.008
18. Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: a randomized clinical trial. Jama. 2021;326(1):35-45. doi:10.1001/jama.2021.8565
19. Al Kaabi N, Oulhaj A, Ganesan S, Al Hosani FI, Najim O, Ibrahim H, Acuna J, Alsuwaidi AR, Kamour AM, Alzaabi A, Al Shehhi BA. Effectiveness of BBIBP-CorV vaccine against severe outcomes of COVID-19 in Abu Dhabi, United Arab Emirates. Nat Commun. 2022;13(1):3215. doi:10.1038/s41467-022-30835-1
20. Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF, et al. Safety and immunogenicity of an inactivated COVID-19 vaccine, BBIBP-CorV, in people younger than 18 years: a randomised, double-blind, controlled, phase 1/2 trial. Lancet Infect Dis. 2022;22(2):196-208. doi:10.1016/S1473-3099(21)00462-X
21. Ella R, Reddy S, Blackwelder W, Potdar V, Yadav P, Sarangi V, et al. Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomised, double-blind, controlled, phase 3 trial. Lancet. 2021;398(10317):2173-84. doi:10.1016/S0140-6736(21)02000-6
22. Ella R, Reddy S, Jogdand H, Sarangi V, Ganneru B, Prasad S, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: interim results from a double-blind, randomised, multicentre, phase 2 trial, and 3-month follow-up of a double-blind, randomised phase 1 trial. Lancet Infect Dis. 2021;21(7):950-61. doi:10.1016/S1473-3099(21)00070-0
23. Ella R, Vadrevu KM, Jogdand H, Prasad S, Reddy S, Sarangi V, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. Lancet Infect Dis. 2021;21(5):637-46. doi:10.1016/S1473-3099(20)30942-7
24. Shrestha Y, Venkataraman R, Moktan JB, Chitti R, Yadav SK. COVID-19 vaccine authorized in India-a mini review. Available at SSRN 3836545. 2021. doi:10.2139/ssrn.3836545
25. Edara VV, Patel M, Suthar MS. Covaxin (BBV152) vaccine neutralizes SARS-CoV-2 Delta and Omicron variants. medRxiv. 2022.
26. Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, et al. Safety and

efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. Lancet. 2021;397(10275):671-81. doi:10.1016/S01406736(21)00234-8
27. Vanaparthy R, Mohan G, Vasireddy D, Atluri P. Review of COVID-19 viral vector-based vaccines and COVID-19 variants. Infez Med. 2021;29(3):328-38. doi:10.53854/liim-2903-3
28. Sapkal G, Deshpande GR, Tilekar B, Yadav P, Abraham P, Salunke A, et al. Antibody responses to Sputnik Vaccination in naıve and COVID 19-recovered vaccine recipients, India. J Travel Med. 2022;29(3):taac040. doi:10.1093/jtm/taac040
29. Oliver SE, Gargano JW, Marin M, Wallace M, Curran KG, Chamberland M, et al. The advisory committee on immunization practices' interim recommendation for use of Pfizer-BioNTech COVID-19 vaccine—United States, December 2020. MMWR Morb Mortal Wkly Rep. 2020;69(50):1922-4. doi:10.15585/mmwr.mm6950e2
30. Mahase E. Covid-19: Pfizer vaccine efficacy was 52% after first dose and 95% after second dose, paper shows. BMJ. 2020;371:m4826. doi:10.1136/bmj.m4826
31. Kadali RA, Janagama R, Peruru S, Malayala SV. Side effects of BNT162b2 mRNA COVID-19 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers. Int J Infect Dis. 2021;106:376-81. doi:10.1016/j.ijid.2021.04.047
32. Abdoli A, Aalizadeh R, Aminianfar H, Kianmehr Z, Teimoori A, Azimi E, et al. Safety and potency of BIV1-CovIran inactivated vaccine candidate for SARS-CoV-2: A preclinical study. Rev Med Virol. 2021:e2305. doi:10.1002/rmv.2305
33. Mohraz M, Salehi M, Tabarsi P, Abbasi-Kangevari M, Ghamari SH, Ghasemi E, et al. Safety and immunogenicity of an inactivated virus particle vaccine for SARS-CoV-2, BIV1-CovIran: findings from double-blind, randomised, placebo-controlled, phase I and II clinical trials among healthy adults. BMJ Open. 2022;12(4):e056872. doi:10.1136/bmjopen-2021-056872
34. Mirahmadizadeh A, Heiran A, Bagheri Lankarani K, Serati M, Habibi M, Eilami O, Heiran F, Moghadami M. Effectiveness of Coronavirus Disease 2019 Vaccines in Preventing Infection, Hospital Admission, and Death: A Historical Cohort Study Using Iranian Registration Data During Vaccination Program. InOpen forum infectious diseases 2022;9(6):ofac177. doi:10.1093/ofid/ofac177
35. Eugenia-Toledo-Romaní M, Verdecia-Sánchez L, Rodríguez-González M, Rodríguez-Noda L, Valenzuela-Silva C, Paredes-Moreno B, et al. Safety and immune genicity of anti-SARS CoV-2 vaccine SOBERANA 02 in homologous or heterologous scheme: Open label phase I and phase IIa clinical trials. Vaccine. 2022;40(31):4220-30. doi:10.1016/j.vaccine.2022.05.082
36. Toledo-Romani ME, Garcia-Carmenate M, Silva CV, Baldoquin-Rodriguez W, Perez MM, Gonzalez MC, et al. Efficacy and Safety of SOBERANA 02, a COVID-19 conjugate vaccine in heterologous three doses combination. MedRxiv. 2021.
37. Toledo-Romani ME, García-Carmenate M, Verdecia-Sánchez L, Pérez-Rodríguez S, Rodriguez-González M, Valenzuela-Silva C, et al. Safety and immunogenicity of anti-SARS-CoV-2 heterologous scheme with SOBERANA 02 and SOBERANA Plus vaccines: Phase IIb clinical trial in adults. Med. 2022;3(11):760-73.e5. doi:10.1016/j.medj.2022.08.001
38. Nazarian S, Olad G, Abdolhamidi R, Motamedi MJ, Kazemi R, Kordbacheh E, et al. Preclinical study of formulated recombinant nucleocapsid protein, the receptor binding domain of the spike protein, and truncated spike (S1) protein as vaccine candidates against COVID-19 in animal models. Mol Immunol. 2022;149:107-18. doi:10.1016/j.molimm.2022.06.007
39. Salimian J, Ahmadi A, Amani J, Olad G, Halabian R, Saffaei A, et al. Safety and immunogenicity of a recombinant receptor-binding domain-based protein subunit vaccine (Noora vaccine™) against COVID-19 in adults: A randomized, double-blind, placebo-controlled, Phase 1 trial. J Med Virol. 2022. doi:10.1002/jmv.28097
40. Babaee E, Amirkafi A, Tehrani-Banihashemi A, Soleiman vandiAzar N, Eshrati B, Rampisheh Z, et al. Adverse effects following COVID-19 vaccination in Iran. BMC Infect Dis. 2022;22(1):476. doi:10.1186/s12879-022-07411-5