Comparative Review on Major SARS-CoV-2 Vaccines

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.)

Department of Pharmacy
Brac University
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Declaration

It is hereby declared that

1. The thesis submitted is my original work while completing my degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material that has been accepted or submitted, for any other degree or diploma at a university or other institution.
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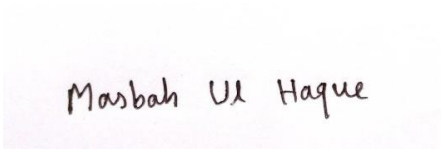

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Approval

The thesis/project titled “Comparative Review on Major SARS-CoV-2 Vaccines” Submitted by Masbah Ul Haque Zihad (17346030) of Summer, 2017 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.) on [Date-of-Defense].

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Ethics Statement

This study comprises no human or animal trial.

Abstracts

In December 2019, a transmittable disease widely known as Coronavirus-2 infection broke out in Wuhan, Hubei Province, China, due to severe acute respiratory syndrome (SARS), and became malignant throughout the world. Coronaviruses (CoVs) are structured as single-stranded RNA viruses (ssRNA) that contain club-like spikes on their outer layer which consequently causes lung diseases in humans and leads toward death. The main target of the vaccination program is to ensure the production of antibodies against the spike glycoprotein, which has been implicated in protection against SARS-CoV in animal studies that further identified in SARS-COV and set the goal of most early candidate vaccines. There are several vaccination possibilities are currently under development through clinical trials, and some of them are prepared for human use, such as inactivated vaccines, recombinant protein vaccines, live-attenuated vaccinations, viral vector vaccines, nucleic acid-based vaccines, which differ in terms of many parameters. This review article purposes to deliberate the comparison between vaccines and the current update.

Keywords: SARS-CoV-2; Effectiveness; Coronavirus Variants; Inactivated virus vaccine; Viral vector vaccine; RNA based vaccine

Dedication

This review article is dedicated to my beloved parents and my respected supervisor Dr. Afrina Afrose Madam.

Acknowledgment

To begin with, I am indebted to Almighty Allah for giving me the opportunity, well-being, and strength to complete the project within the allocated time in a sound and healthy condition.

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Lastly, I am grateful to my family and friends for their constant support and love which encouraged me throughout the difficult times.

In the end, I emphasize that the limitations of this project are completely my sole responsibility.

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List of Acronyms

WHO	World Health Organization
ACE	Angiotensin-Converting Enzyme
RNA	Ribonucleic Acid
Nsps	Non-structural proteins
ER	Endoplasmic Reticulum
CD	Cluster of Differentiation
Kb	Kilobase
MERS	Middle East Respiratory Syndrome
RTC	Replication-Transcription Complex
Nabs	Neutralizing Antibodies
cGMP	Current Good Manufacturing Practice
VLP	Virus-like Particles
DNA	Deoxyribonucleic Acid
CDC	Centers for Disease Control and Prevention
NCT	National Clinical Trial number
mRNA	Messenger RNA
FDA	Food and Drug Administration

BBIBP	Beijing Bio-Institute of Biological products
TLR	Toll-like Receptors
LNP	Lipid Nanoparticles
MHRA	Medicines and Healthcare Products Regulatory Agency
Ig	Immunoglobin
Ad26	Adenovirus Types 26
TGA	Therapeutic Goods Administration
SMQ	Standardized MedDRA Queries
VOC	Variants of Concern
VOI	Variants of Interest

Chapter 01 Introduction

Coronavirus 2 infections through the RNA virus first appeared in Wuhan, Hubei Province (China) in December 2019 and immediately transmitted throughout the country and beyond (Zu et al., 2020). This infection is globally termed SARS-CoV-2, a new type of coronavirus that develops coronavirus infection which became deadlier over time (Chen & Chen, 2020). Coronaviruses are a kind of positive-sense RNA virus with a single strand that induces gastrointestinal, pulmonary, hepatic, neurological illnesses in humans and other animal species. (Zumla et al., 2016). According to WHO, there have been 213,050,725 confirmed cases till August 26, 2021, where almost 4,448,352 died due to COVID-19. As of now, overall 4,619,976,274 Vaccine shots have been distributed around the world (*WHO – COVID19 Vaccine Tracker*, n.d.). After researching through different technologies and coating of distinctive trials, over 90 vaccine candidates against coronavirus are already being created all around the world to build adaptive immunity that can identify the invading pathogens of SARS-CoV-2. (Callaway, 2020). The life span of coronavirus-2 starts with binding of virus-cell with host cell by attaching with membrane receptor ACE2. The RNA genome is released after endocytosis when virions enter the host cell. The viral polymerase protein, which is further split into numerous non-structural proteins (Nsps) and an RNA-dependent polymerase, converts plus-strand RNA into pp1a and pp1ab (Nsp12). Following RNA replication, the RNA-dependent polymerase is utilized as a template to generate new positive-stranded genomic and sub-genomic RNA, which is then translated into key proteins including Spike (S), Nucleocapsid (N), Envelop (E), and Membrane (M) proteins. These proteins are key structural proteins that combine with positive-strand genomic RNA to generate mature virions inside the endoplasmic reticulum (ER). Then, the whole mature virion leaves the cell through exocytosis (Li et al., 2020). Coronavirus vaccines usually help a host body to develop immunity against the virus.

After receiving the coronavirus vaccine it takes some weeks to produce T-lymphocytes and B-lymphocytes that will remain inside a host cell as "memory" to remember how to fight coronavirus in the future (*Understanding How COVID-19 Vaccines Work | CDC*, n.d.). Clinical studies for a number of vaccines have already begun and some of them are still under development. Earlier in the 2000s, a deadly outbreak took place correspondingly to the development of the SARS-CoV vaccine (Chen & Chen, 2020). For such an understanding, primary stage is the ability to quantify the virus-specific CD4+ and CD8+ T cells to accumulate information on cellular response and the etiology of SARS-CoV-2 infection; such knowledge will also aid in vaccine creation and evaluation of potential candidates for vaccinations. Evaluating immunity is also necessary for optimizing epidemiological models for potential pandemic prevention and control associated with social isolation (Kissler et al., 2020). *Table 1* shows the latest global data of coronavirus cases and vaccination.

Table 1: Latest update on Coronavirus cases and vaccination (Kant Sahu et al., 2020)

Latest Global Coronavirus Data by October 24, 2021	
Total Cases: 243,857,028	New Daily cases: 295,432
Total deaths: 4,953,246	New Daily deaths: 5,999
Total vaccination: 6,697,607,393	New Daily Vaccination: 24.2m

The primary goal of this review article is to give a preview of such approved coronavirus vaccines, their stages of clinical trials, their impact on variants of concern, as well as their comparison.

1.1 Research Gap

As the effectiveness and risk factors linked with coronavirus vaccinations have not been studied in pregnant women, children, or infants, however, the effectiveness and risk factors are still unclear. Although the creation of coronavirus vaccines is recognized as one of public health medicine's greatest triumphs, the knowledge and information acquired from the study article are insufficient to acquire comprehensive acknowledgment of the coronavirus vaccine's future implications. Furthermore, there is a lot of misinformation out there regarding the benefits, medical composition, and adverse effects of the worldwide vaccination program, which might lead to a section of the population not getting vaccinated thus creating vaccine hesitancy. In addition to this, new variants are arising as the gene of Coronavirus is frequently mutating based on demographic separation over time thus the efficacy and mode of action of distinctive vaccines cannot be ensured.

1.2 Objective

The objective of this review article on SARS-CoV-2 vaccines is to compare and contrast the authorized vaccines by addressing their features, characteristics, clinical trial stage, efficacy, adverse reactions, anaphylaxis reactions, safety, cost-effectiveness, storage condition, and variants responses to different vaccines. Moreover, the purpose of the current study is to convey latest update on developing vaccines for novel coronavirus SARS-CoV-2.

To specify the main objectives of this review is as follows:

1. To comprehend distinctive major vaccines principles, characteristics, and mode of action.

2. To deliberate the risk factors associated with vaccines such as contraindication, anaphylaxis reaction, etc.
3. To know the effectiveness of different vaccine candidates against idiosyncratic variants.

1.3 Rationale

Coronavirus vaccines are designed to induce protective immunity against coronavirus infection. This study includes all the necessary information which is important to know to understand the different parameters associated with distinctive vaccination strategies. Moreover, healthcare practitioners and researchers will be able to design efficient and successful immunization programs with the aid of this information.

Chapter 2 Mechanism of Action

The mechanism of action starts with the viral entry through the receptor and packing of RNA inside the human host genome occurs. Coronavirus cell outer layer contains spike protein (S) which attaches to ACE2 receptors and enters inside the host cell. Following that, the S protein participates in proteolytic cleavage, S1, and S2, both sites on the borderline, respectively containing two subunits (associated with the release of synthesis peptide); initiated Furin and trypsin, two host proteases. Coronavirus then enters into the cytoplasm by a process known as endocytosis which includes a three-step process to cell fusion that includes receptor attachment as well as alterations in the membrane S protein's structure (Boopathi et al., 2020). Proteasomes which can typically hydrolyze endogenous proteins, uncoating of viral nucleocapsid occurs right after endosome opens to release coronavirus into cytoplasm that can also degrade SARS nucleocapsid protein is an exogenous protein (Q. Wang et al., 2010). Finally, the genetic material of the coronavirus is entirely disseminated into the cytoplasm. Following that, replication-transcription complex (RTC) initiates processes like transcription and replication that are encoded inside viral genome, composed of Nsps. Inside cytoplasm, bi-membrane structure of the cell is assumed to be induced within an infected cell by RTC as, over past few decades, it is found that RTCs are habitually associated with virus-induced membrane structure (Hemert et al., 2008). The cytoplasm produces M, S, and E structural viral proteins, afterward transported into Endoplasmic reticulum-Golgi intermediate compartment through the rough ER. Then virions are started to assemble from nucleocapsid, which is produced in cytoplasm by the N-protein encapsidation of replicated genomes. Finally, virion results in the production from vesicles through a process known as exocytosis, allowing it to infect surrounding cells. (Masters, 2006). A schematic diagram has shown below in Figure 1 (Li et al., 2020).

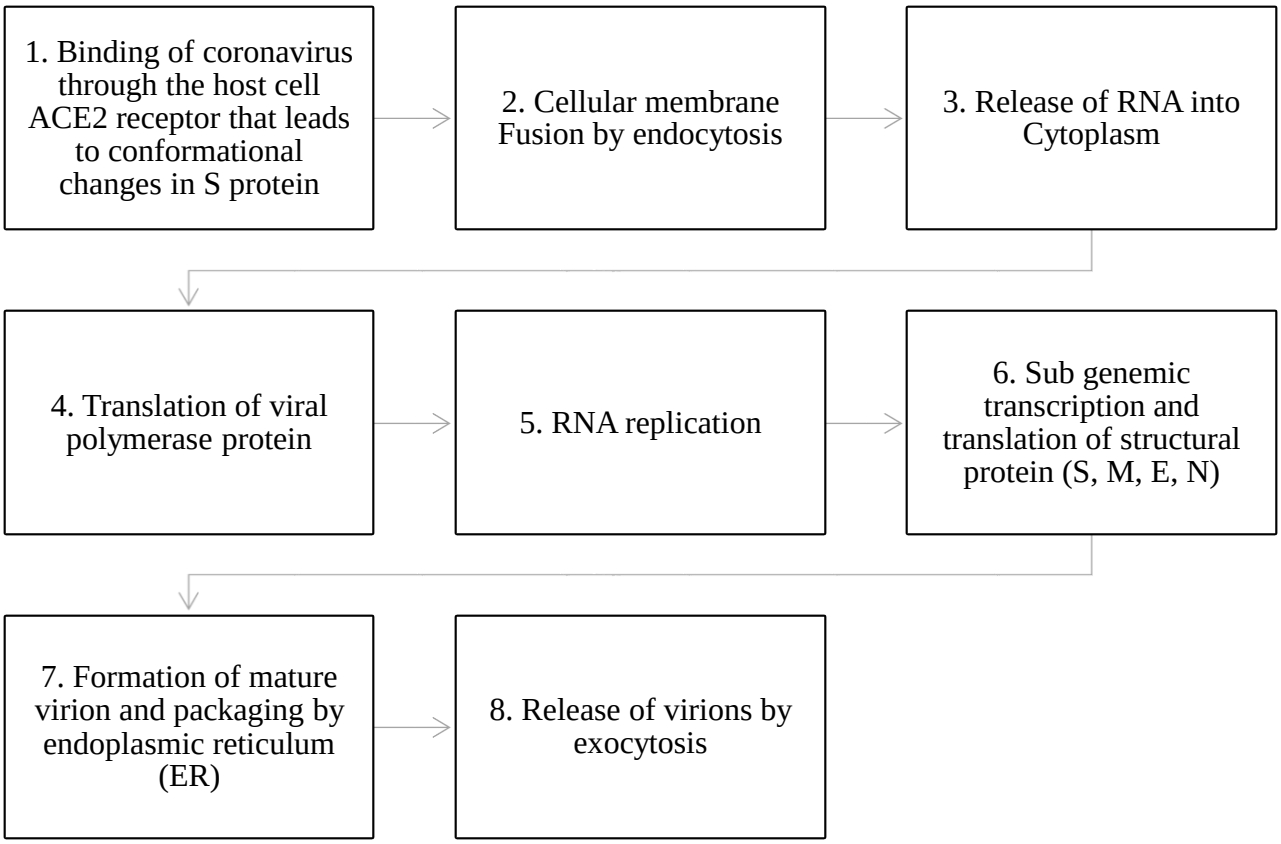

Figure 1: The schematic diagram of the mechanism of action of Coronavirus inside a host cell

Chapter 3 An Overview of Coronavirus Vaccine

Vaccines have always been the most efficient and affordable option to limit and control contagious diseases and viral outbreaks (Remy et al., 2014). More than 120 vaccines, including protein subunit, DNA-based and RNA-based vaccines, Virus-like particles (VLP), Viral vector, and whole virus vaccines such as inactivated, live-attenuated virus vaccines with distinctive mode of action and properties are now being evaluated in preclinical study, and phase 1 to 3 clinical studies worldwide to provide individual protection and increase population-level herd immunity (Poland et al., 2020). There are currently widespread immunization programs against Covid-19 taking place in several countries (Ritchie et al., 2020). Despite being the gold standard for evaluating vaccine effectiveness, phase 3 clinical studies have certain drawbacks, such as tight inclusion criteria and execution under strict experimental settings that may not be representative of a mass immunization campaign (Doshi, 2020). S protein among the other three proteins is targeted mostly to develop the vaccine of coronavirus (Amanat & Krammer, 2020). S is the most important protective antigen, eliciting an extremely powerful antibody neutralizer (Nabs), several auxiliary proteins, and 16 nonstructural proteins (nsp1 to nsp16) (Wu et al., 2020). Many vaccines are presently under advancement to combat COVID-19 such as the whole virus vaccine, nucleic acid vaccine, adenovirus-based vector vaccine, and recombinant subunits vaccine (Roper & Rehm, 2014). Among these vaccines, most of them protected animals against SARS-CoV-1 infection but cannot provide sterilizing immunity. In a mouse model, immunization with the live virus can cause consequences such as lung injury and eosinophil infiltration (Tseng et al., 2012) (Bolles et al., 2011a). Another factor to consider while developing a coronavirus vaccine is the fading of antibody responses. Human coronavirus infection may not necessarily result in long-lasting

antibody reactions, and a participant's re-infection with the same virus after a longer duration is conceivable (although the fewer percentage of people has shown minor or no symptoms), as demonstrated in the human trial (Callow et al., 1990). It can take years to develop a vaccine for general use, particularly if novel technologies are utilized that haven't been thoroughly tested for safety or expanded for industrial implementation, although no coronavirus vaccine exists with large-scale manufacturing capability in the market (Amanat & Krammer, 2020). In these circumstances, questions may arise regarding the duration of vaccine development that requires a significant amount of time even though many vaccine candidates are being researched after S protein has been detected on the cell wall that is believed to play a vital role by altering its pharmacological activity. Following that, two critical phases must be accomplished before a vaccine may be evaluated in clinical trials. To begin with, the vaccination is tested in animal models to check its effectiveness parameter. Another essential aspect to remember is that sufficient manufacturing capacity for cGMP-quality vaccination is available (*Bao: The Pathogenicity of 2019 Novel Coronavirus… - Google Scholar*, n.d.).

3.1 Principle of SARS-CoV-2 vaccine

A vaccine is designed to strengthen the body's immune system to invading pathogens like viruses, providing long-term protection (L, 2020). When a vaccine is introduced into antigen-presenting cells in the host to the structure and biological agents of a particular virus, which further ingest it and transmit parts of it to activate helper T (Th) cells (

Figure *2*). Then the helper T cells trigger additional immunological responses such as B cell activation and cytotoxic T cell (Tc) activation. Tc cells detect as well as destroy virus-infected cells, which helps the body's surveillance cells monitor the virus for lengthy periods. In the case of B cell activation, it generates antibodies against SARS-CoV-2 preventing from infecting host cells, while Tc cells identify and kill virus-infected cells as well as preventing the virus from infecting cells (F, 2010).

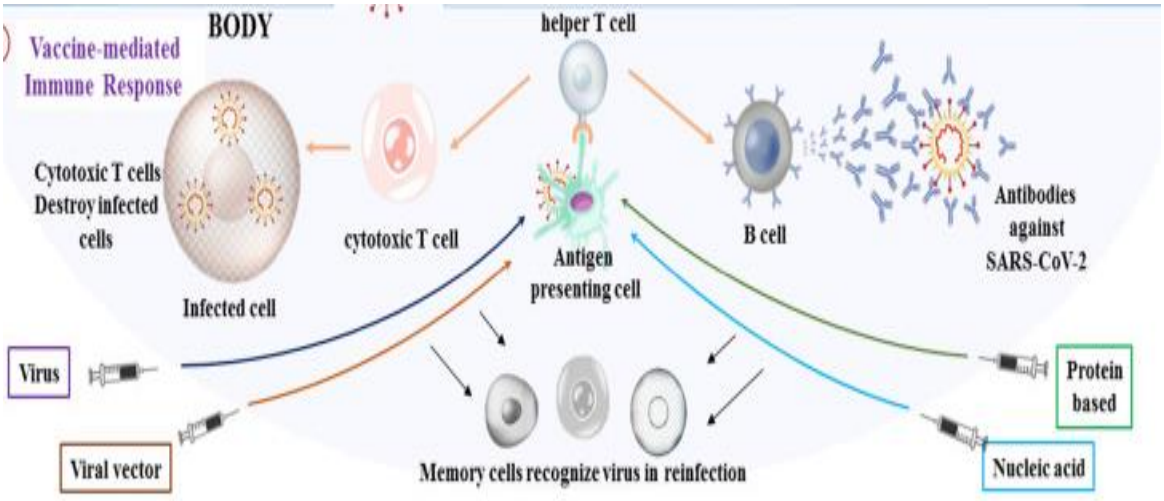

Figure 2: Basic principle of vaccine-mediated immune response (Haidere et al., 2021)

3.2 Vaccine Types

The vaccine advancement process has employed a variety of technologies and platforms over the years. The most prevalent vaccines approved for human use in history are viral live-attenuated or protein-conjugated subunits, virus-like particles (polysaccharides), or inactivated viruses. In the preceding decade, nucleic acid (DNA or RNA) and viral vector vaccines were introduced, both of which provide improved technological platforms for vaccine production. (Chakraborty, Sharma, et al., 2021). When it comes to coronavirus vaccine development, there are two main approaches: using the whole virus such as inactivated or live-attenuated forms vaccines (Figure 3), another option is using genetically modified vaccine antigens that can be administered in a variety of ways (See et al., 2006), (Graham et al., 2012). Entire virus vaccines, in general, can generate a strong immune response and protect from coronavirus infections (Gao et al., 2020). Vaccines that have been genetically engineered to target particular coronavirus antigens are frequently utilized to increase immunity, safety, and efficacy. Antigens from the plasma proteins of coronaviruses can be used in recombinant DNA vaccines and viral vector vaccines. (Ong et al., 2020).

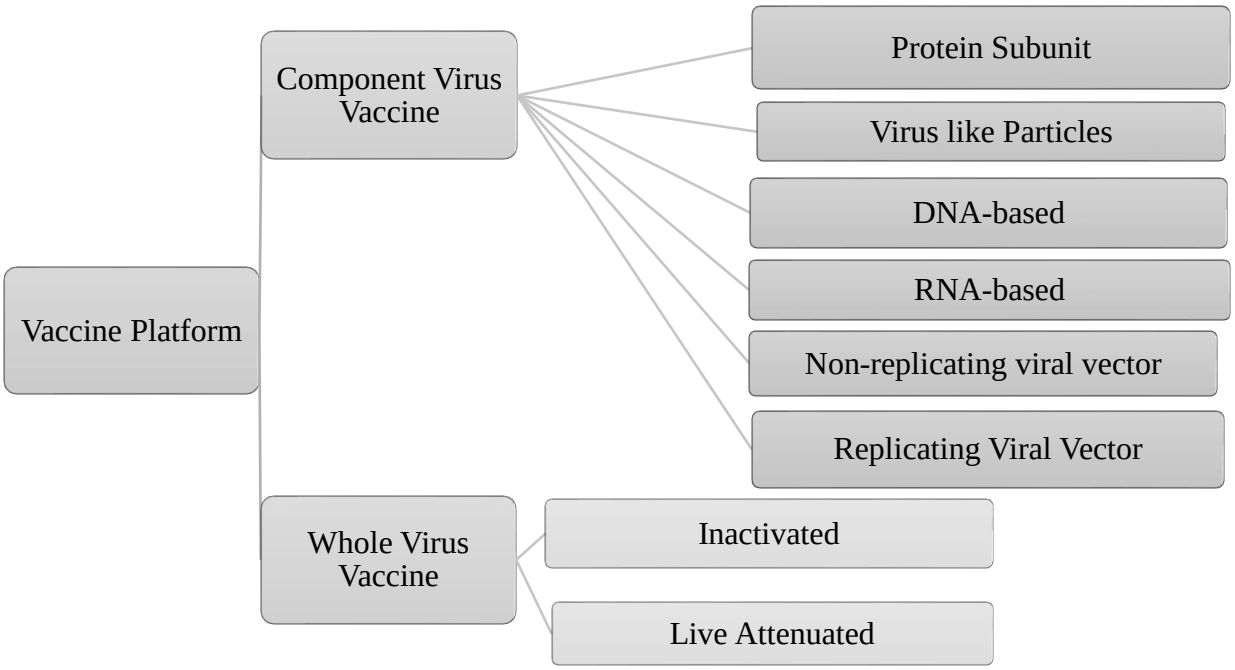

Figure 3: Types of Vaccines (Types of Vaccines – COVID19 Vaccine Tracker, n.d.)

3.3 Update of Clinical Trial of Distinctive Coronavirus Vaccines

According to CDC, there are approximately 150 vaccine candidates in development worldwide. Several vaccines are now undergoing preclinical testing, while others are currently under clinical trials (Chakraborty, Sharma, et al., 2021). Table 2 shows that as of 11 November 2020, various vaccines are being tested and designed upon acceptance under different phases of clinical trial. Among them, there are 9 inactivated or live-attenuated vaccine candidates, 18 DNA and RNA vaccines, There are eight non-replicating viral vectors and two replicating viral vectors, 11 protein subunits, and three additional vaccine candidates (Haidere et al., 2021). According to CEPI (September 2020), the majority of the leading vaccines in clinical research have highlighted variations of coronavirus's spike protein because principal antigen is responsible for infection caused by coronavirus. In contrast, CEPI stated that 11 potential vaccine candidates in current trials are using adjuvants to increase immunogenicity (TT et al., 2020).

Table 2: Ongoing Clinical Trial on SARS-CoV-2 Vaccine Candidates and their types. (Home - ClinicalTrials.Gov, n.d.) (Haidere et al., 2021) (Chinese Clinical Trial Register (ChiCTR) n.d.) (Imperial: LNP-NCoVsaRNA – COVID19 Vaccine Tracker, n.d.) (CTRI, n.d.)

Vaccine Candidates and NCT Identifier	Study Design	Phases	Vaccine Type	Country
Aivita AV-COVID-19 NCT04386252	Randomized, double-blind	phase II	Dendritic Cell Vaccine	United States
AnGes AG0301-COVID19 NCT04463472	Non-randomized, open-label, non-controlled single-center trial	Phase I/II	DNA Vaccine	Japan
Arcturus ARCT-021 NCT04480957	A randomly selected, double-blind trial	Phase I or II	RNA	Singapore
AZLB protein subunit vaccine NCT04466085	Placebo-controlled, randomized, blinded study Trial	Phase II	Protein subunit	China

AZLB protein subunit vaccine NCT04445194	Randomized, double-blind, placebo Controlled	Phase I	Protein Subunit	China
Bharat Covaxin BBV152 NCT04471519	Multicenter, randomized, double-blind study	Phase I/II	Inactivated	India
BIBP/ Sinopharm BBIBP-CorV (Vero cell) NCT04560881	A randomized, double-blind, placebo-controlled study	Phase III	Inactivated SARS-CoV-2 vaccine	Argentina
BioNTech BNT162 NCT04368728	Randomized, placebo-controlled	Phase III	RNA	USA, Argentina, Brazil, others
BioNTech BNT162 NCT04380701	Non-randomized	Phase I Phase II	RNA	USA, Argentina, Brazil, others
BioNTech BNT162b1	Randomized, Placebo-controlled	Phase I	RNA	China

NCT04523571				
CAMS vaccine NCT04412538	Randomized, Placebo-controlled, Double-blind	Phase I Phase II	Inactivated	China
CAMS vaccine NCT04470609	Randomized, Placebo-controlled, Double-blind	Phase I Phase II	Inactivated	China
Cansino Ad5-nCoV NCT04526990	Randomized, double-blind, placebo-controlled multicenter study	Phase III	Non-replicating viral vector	Pakistan
Cansino Ad5-nCoV NCT04398147	Randomized	Phase I or II	Same	Canada
Cansino Ad5-nCoV NCT04313127	A non-randomized, single-center study	Phase I	Non-replicating viral vector	China

Clover SCB-2019 NCT04405908	A placebo-controlled, randomized, double-blind study	Phase I	Protein Subunit	Australia
Curevac CVnCoV NCT04515147	Randomized, Multicenter controlled study	Phase II	RNA	Panama, Peru
Curevac CVnCoV NCT04449276	A randomized and placebo-controlled study	Phase I	RNA	Belgium, Germany
Gamaleya Gam-COVID-Vac (Lyo) NCT04437875	Non-randomized	Phase I Phase II	Non-replicating viral vector	Russia
Genexine GX-19 NCT04445389	Randomized, Multi-center, double-blind study	Phase I Phase II	DNA	Republic of Korea
Imperial LNP-nCoVsaRNA ISRCTN17072692	A non-randomized, open-label study	Phase I	RNA	England, United Kingdom

Inovio INO-4800 NCT04447781	Randomized	Phase I Phase II	DNA	Republic of Korea
Inovio INO-4800 NCT04336410	Non-randomized open trial	Phase I	DNA	United States
KBP-COVID-19 NCT04473690	A randomized, positive-controlled study	Phase I, II	Protein Subunit	United States
Medicago CoVLP NCT04450004	Randomized	Phase I	Virus-like particle	Canada
Medigen MVC-COV1901 NCT04487210	A non-experimental, open-label clinical trial	Phase I	Protein Subunit	Taiwan
Moderna mRNA-1273 NCT04470427	Randomized, Placebo-controlled, observer-blind study	Phase III	RNA	USA
Novavax NVX-CoV2373 NCT04611802	A randomized, placebo-controlled study	Phase III	Protein subunit	USA, Mexico, Puerto Rico

Novavax NVX-CoV2373 NCT04533399	Randomized, placebo-controlled, observer-blind study	Phase II	Protein subunit	South Africa
Novavax NVX-CoV2373 NCT04368988	Randomized, placebo-controlled, observer-blind study	Phase I Phase II	Protein Subunit	Australia, USA
Oxford ChAdOx1-S NCT04516746	Randomized, placebo-controlled, double-blinded study	Phase III	Non-replicating viral vector	USA, Chile, Peru
Oxford ChAdOx1-S NCT04400838	Randomized	Phase II Phase III	Non-replicating viral vector	UK
Oxford ChAdOx1-S NCT04444674	RCT, double-blinded study	Phase I/II	Non-replicating viral vector	South Africa
Oxford ChAdOx1-S NCT04324606	RCT (Randomized Control Trial), single-blinded, multi-centered study	Phase I Phase II	Viral vector	UK

PLA-AMS ARCoV **ChiCTR2000034112**	Parallel study	Phase I	RNA	China
SGMI aAPC **NCT04299724**	Not applicable	Phase I	T cell vaccine	China
SGMI LV-SMENP-DC **NCT04276896**	Not applicable	Phase I Phase II	cytotoxic T cell vaccines that target particular antigens	China
Sinovac Coronavac **NCT04383574**	RCT placebo-controlled, double-blind trial	Phase I Phase II	Inactivated	China
Sinovac CoronaVac **NCT04456595**	An experimental placebo-controlled, double-blind study	Phase III	Inactivated Virus Vaccine	Brazil
Sinovac CoronaVac	Randomized, placebo-controlled,	Phase I Phase II	Inactivated	China

NCT04352608	double-blinded study			
Symvivo bacTRL-Spike NCT04334980	Randomized, placebo-controlled, study	Phase I	DNA	Australia
Themis V591 NCT04498247	A randomized, placebo-controlled, double-blind study	Phase I Phase II	Replicating viral vector	USA, Austria, Belgium
Themis V591 NCT04497298	Randomized, placebo-controlled trial	Phase I	Replicating viral vector	Belgium, France
University of Queensland vaccine NCT04495933	A randomized placebo-controlled, double-masked study	Phase I	Protein Subunit	Australia
Protein subunit vaccine NCT04453852	Randomized	Phase 1	Protein Subunit	Australia

WIBP vaccine NCT04510207	Randomized, Parallel placebo-controlled, double-blind study	Phase III	Inactivated Virus Vaccine	Middle East countries	
WIBP vaccine ChiCTR2000031809	Randomized, placebo parallel-controlled, double-blind study	Phase I/II	Inactivated	China	
Zydus Cadila ZyCoV-D CTRI/2020/07/026352	Randomized study	Phase I and II	DNA	India	

Chapter 4 Approved Coronavirus Vaccines

According to Coronavirus Vaccine Tracker as of September 17, 2021; In a human clinical study, researchers are now evaluating 104 vaccinations. Phase 1 has been reached by 55 of them, 45 reached phase 2 trial and 34 candidates reached the final stage for large-scale efficacy test. After that, 13 vaccine candidates got authorization, and 8 got approval for full use as shown in Figure 4 (Walsh et al., 2020).

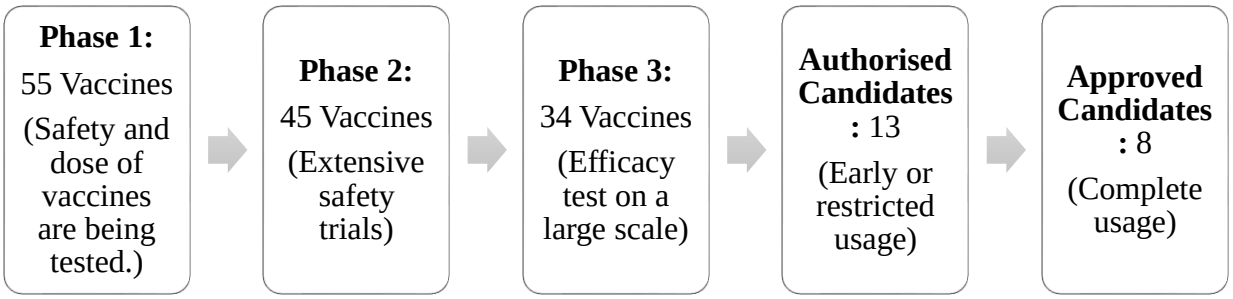

Figure 4: Recent Updates on vaccine testing process (Corum et al., n.d.)

Currently, FDA has approved three major vaccines intended for emergency use: Comirnaty and Pfizer, Moderna, and Janssen. (*COVID-19 Vaccines | FDA*, n.d.). Furthermore, World Health Organization (WHO) has approved 7 vaccines for administration which are mRNA-1273, BNT162b2, Ad26.COV2.S, AZD1222, Covishield, BBIBP-CorV, and Sinovac/CoronaVac. Furthermore, 22 vaccines have been approved, authorized, licensed by a regulatory agency, a

national authority, or another entity in at least one country. (*WHO – COVID19 Vaccine Tracker*, n.d.).

4.1 Inactivated Virus Vaccine

Inactivated viral vaccines, also known as WKV vaccines usually are intriguing for their easy manufacturing properties (at least in theory) that provide an antigenic fraction comparable to those found in infecting virus particles. Furthermore, the surface of these vaccines contains several proteins that help in immune detection (JP et al., 2004). Microorganisms that have been destroyed physically or chemically are used to make inactivated vaccines. Moreover, these vaccines are often not successful in eliciting an immune response, and even when they do, the reaction may be short-lived. As a result, many vaccination doses may be required to elicit a sufficient immunological response (Venkatesh, n.d.). According to research, SARS-CoV can produce Th2 immunopathological alterations in mice, suggesting that SARS-CoV components might cause hypersensitive responses. Subsequent research has revealed that viral nucleoproteins have such a role in the immunopathology that leads to eosinophilia (Bolles et al., 2011b). Additionally, after a viral infection, oligomeric immunization with the SARS-CoV S protein causes an increase in eosinophils in several animal experimental systems (Zhou et al., 2021). Inactivated vaccine development is a well-established technology that is frequently utilized to prevent and control new infectious illnesses such as influenza and poliovirus (Gao et al., 2020). VeroCell is an ideal instance of an inactivated coronavirus vaccine that stimulates the immune system without causing infection. Inactivated viruses stimulate the production of antibodies and prepare the body's way of

responding to a live infection when given to immune system. This vaccine has been adjuvanted (with aluminum hydroxide) to improve immune system response (Aryal et al., 2021).

4.1.1 Sinopharm (BBIBP-CorV)

Sinopharm was assessed as an inactivated viral vaccine by the Wuhan Institute of Biological Products in conjunction with the Beijing Institute of Vaccine (H. Wang et al., 2020). It produced antibodies in participants in the Phase 1/2 trials, and while some of them got fevers as well as other adverse effects. The Wuhan vaccine was then put into a global Phase 3 study by Sinopharm (Walsh et al., 2020). It has a 79% success rate in preventing hospitalization and symptomatic treatment of COVID-19. The WHO noted most frequent adverse effects of the Sinopharm/BBIBP COVID-19 vaccine are dizziness, fever, tiredness, headache, vomiting, nausea, and allergic dermatitis (Saeed et al., 2021).

4.1.2 Sinovac (CoronaVac)

Sinovac Biotech, a Chinese pharmaceutical company based in Beijing, has developed CoronaVac Vaccine. The exclusive emphasis of the company is the research and manufacture of vaccines that target highly infectious diseases (Halim et al., 2021). Since mid-2020, it has been in phase 3 research in many South American countries. It is approved to administer in 40 nations for emergency usage as of September 22, 2021 (*Sinovac: CoronaVac – COVID19 Vaccine Tracker*,

n.d.). It has been administered in moderate- and intermediate-income countries as part of mass immunization efforts as a result of Coronavirus-2 strains of concern triggering outbreaks in several of them. The results of two-dose Sinovac vaccine in contrast to symptomatic infection on healthcare personnel and general public shows inconsistent efficacy in randomized controlled trials (51% to 84%) (Tanriover et al., 2021), (Palacios et al., 2021). Comparison between major Inactivated virus vaccines has shown in Table 3 including their route of administration, efficacy, cost per dose, storage condition, shelf life, and risk factor.

Table 3: Comparison between two WHO-approved Inactivated Virus Vaccines. (Jara et al., 2021), (Jahromi & Al Sheikh, 2021), (Sinovac Vaccine in 12 Easy Questions, n.d.), (Ledford, 2021), (Covid-19 Vaccine Characteristics | ViewHub, n.d.), (Antal et al., 2021).

Characteristics	**Sinopharm (BBIBP-CorV)**	**Sinovac (CoronaVac)**
Route of Administration	Intramuscular-deltoid muscle	Intramuscular-deltoid muscle
Booster dose	After Six month	After 6-8 months
Efficacy (%)	79	83.5
Cost per dose	$19-$36	$29.75
Storage Condition	Stored between 2-8 ℃	Stored between 2-8 ℃
Shelf life	3 years	3 Years

Characteristics	Sinopharm (BBIBP-CorV)	Sinovac (CoronaVac)
Adverse effect	Commonly occurring adverse reaction include pain around administration spot, exhaustion, lethargy, headache also discomfort.	Pain around administration site, headaches, exhaustion are highly common.
Anaphylaxis Reaction	It can occur within 4 hours after vaccination, causing symptoms such as hives, swelling, and wheezing (respiratory discomfort)	(0.1-1%) people may have uncommon side effects as an allergic reaction. And 0.01%-0.1% of people can have rare side effects. For such conditions, seeking healthcare professionals' opinions is necessary.
Risk in pregnant, infant and children	COVID-19 prevention and clinical study are not addressed in pre-adolescents, children, or pregnant women. So that, the risk is still unknown.	Pregnant, infants and children cannot be administered the Sinovac vaccine as it contains Aluminium Hydroxide as an adjuvant and no trial has been done till now.
Contraindication	Anaphylaxis or an immediate allergic response can be seen	Anaphylaxis or an immediate allergic reaction (even if

Characteristics	Sinopharm (BBIBP-CorV)	Sinovac (CoronaVac)
	after the first shot (even if mild)	mild) after first dose of vaccination is also one of the reasons not to be vaccinated.

4.2 Live-Attenuated Whole Virus Vaccine

One of the preferred common vaccine preparation methods is inactivated whole viral vaccines. According to a manufacturing publication, among a few multinational companies, Johnson & Johnson is working on vaccine development for coronavirus using their adenoviral vector in their cell line technology (PER.C6®) (Mutua et al., 2019). The present research is centered on this method based on a 2′O MTase enzyme (Züst et al., 2011). Previous research with SARS-CoV, murine hepatitis virus, and MERS-CoV showed an attenuated strain of NSP16, responsive to IFN-stimulated IFIT1 (Menachery et al., 2017). Particularly stimulating TLRs 3, 7, 8, and 9, is a significant benefit over fragmented vaccinations. However, to confirm the safety of live virus vaccinations, more study is typically necessary (Jiang et al., 2014). The majority of live-attenuated vaccines are given intranasally and are attenuated by deleting one or more genes, such as M2-2, NS2, SH, and G (Verdijk et al., 2020) (McFarland et al., 2020). On ClinicalTrials.gov, there are nine active early-stage trials are ongoing that employ live-attenuated RSV vaccinations, with only one, is registered for the phase 2 clinical trial (Billard & Bont, 2021).

4.3 RNA based Vaccine

An RNA-based vaccination platform developed by Moderna and Pfizer/BioNTech is now in phase 3 clinical studies. Moderna and Pfizer are both working on potential vaccines based on lipid nanoparticles encapsulated with mRNA (LNP) (Triggle et al., 2020). Spike protein and multiple doses are the antigens that both of these treatment options are aiming to neutralize. They'll also set

off immune responses on the humoral and cell-mediated responses. They have the advantage of not requiring cell culture because they are made using genetic sequencing (Sabati et al., n.d.). In mRNA vaccines, the antigen genome is contained, and after vaccination, it can be translated into the host cell. There are currently two types of mRNA vaccinations being established, traditional and self-amplifying vaccines are among them (Zhang et al., 2019). The processes in the creation of mRNA vaccine include immunogen identification, arrangement enhancement, visualization of changed bases, delivery platform improvement, and immunological function and safety testing (Jahanafrooz et al., 2020). An mRNA vaccine developed by Moderna, Inc. and the National Institute of Allergy and Infectious Diseases is formerly in phase 3 clinical trials. Vaccines technologically advanced by Moderna, Inc. are formulated in silico rather than in cell culture systems, allowing for a quicker time to development and testing. (Sumirtanurdin & Barliana, 2021).

4.3.1 Moderna (mRNA-1273)

The Moderna vaccine has been commonly administered in the United States since December 2020 (Jackson et al., 2020). The MHRA approved a two-dose regimen of this vaccine with an interval of 28 days of period for second dose administration after the first shot (Banoun, n.d.). According to a preliminary review of phase III of Moderna, effectiveness of the vaccine after 14 days of the second shot was 94.5%. It was announced after the United Kingdom said that earlier licensed

vaccines from AstraZeneca and Pfizer can be administered with an interval period of 12 weeks. (Elisabeth Mahase, 2021a). Adverse effects arose seven days after vaccination in clinical studies; however, the severity of these side effects was typically mild to moderate. Myalgia, chills, malaise, and headache are some common effects seen after the second dose. Only a few people had major side effects that need close monitoring or even hospitalization (LR et al., 2021).

4.3.2 Pfizer/BionTech (BNT162b2)

BNT162b2 is an mRNA vaccine of two-dose regimen given 21 days apart provided approximately 94%-95% effective against coronavirus infection (Polack et al., 2020). The FDA approved the approval for the Pfizer vaccine for emergency usage on December 10th, according to an authorized panel of specialists (Tanne, 2020). BNT162b2 vaccine contains messenger RNA that helps to encode spike protein IgM or IgG either before vaccination or infection (Dooling et al., 2021). Some common adverse effects are injection spot soreness, fever, flu-like symptoms, headaches, and exhaustion. Additionally side effects like a racing heart, generalized aches, difficulty breathing, joint discomfort, cold, and tiredness are new among participants (El-Shitany et al., 2021). More comparisons between major RNA-based vaccines; Pfizer and Moderna has shown in Table 4.

Table 4: Comparison between RNA-based Vaccines (Meo et al., n.d.)

Characteristics	Pfizer/BioNTech Vaccine	Moderna Vaccine
Route of Administration	Intramuscular-deltoid muscle	Intramuscular-deltoid muscle
Booster dose	After Six month	After 6-8 months
Efficacy (%)	95	94.5
Cost per dose	$19.50 per dose excluding taxes	$32-37 per dose excluding taxes
Storage Condition	Stored between -80ºC and -60ºC	Stored between -25ºC and -15ºC
Shelf life	6 Month	6 Month
Adverse effect	Discomfort, swelling, redness, fever, shoulder injury, exhaustion, headache, shivering, nausea, upset stomach, muscle pain, joint pain, lymphadenopathy, and right axillary lymphadenopathy, etc.	Pain, edema, and redness at the injection site, fever, arthralgia, myalgia, tiredness, headache, chills, vomiting, and urticaria

Characteristics	Pfizer/BioNTech Vaccine	Moderna Vaccine
Anaphylaxis Reaction	The CDC has found six cases of anaphylaxis reaction caused by the Pfizer-BioNTech vaccine.	There were no similar reports in the peer-reviewed medical literature, and the same was true in the trial.
Risk in pregnant, infant and children	Unknown: not administered in infants, children, teenagers, and pregnant women.	Unknown.
Contraindication	Patients having previous severe allergic reactions, such as anaphylaxis, those with weaker immune systems, and people who are using immunosuppressive drugs.	Patients having a history of severe hypersensitive reactions, such as anaphylaxis and persons with weaker immune systems, and those who are using immunosuppressive medications are also at risk.

4.4 Non-replicating Viral Vector

Virus vectors are usually used for transmitting vaccine antigens into tissues or cells. There are two types of vectors – replicating viral vector and non-replicating viral vector (Robert-Guroff, 2007). Ads are the most frequently used vector in the development of vaccines. According to statistics of WHO, various organizations depend on non-replicating Ads to produce the COVID-19 vaccine. Non-replicating vector-like Ads can infect DCs as well as dividing and non-dividing cells, has an insert capacity of 7–8 kb, is physically and genetically safe and stable, and can infect both cells. Furthermore, it is used in gene therapy and not merged within itself. on the other hand, Ad vectors need substantial dosages to boost immunity (Sumirtanurdin & Barliana, 2021). Clinical trials are ongoing for five non-replicating viral vectors that are non-replicating, all of which are based on adenoviral vectors. The E1A and E1B genes are missing from the replication-deficient adenoviral vectors; these are the first genes required for virus replication and antigen gene transfer in a vaccinated host. (S.M. Wold & Toth, n.d.).

4.4.1 Janssen (Ad26.COV2.S)

Ad26 vector is a recombinant, replication-incompetent type of vector that carries a prefusion-stabilized spike protein on the plasma membrane of coronavirus (Bos et al., 2020). Janssen is based on current technology and involves the adenovirus virus, which is a common cause of respiratory diseases. The adenovirus's DNA is altered to produce a critical component of the coronavirus particle, and the body generates an immunological response. The adenovirus that contains the

SARS-CoV-2 DNA particle is incapable of reproducing and so does not induce infection (Livingston et al., 2021). The most typically reported adverse effects include discomfort at administered spot, weariness, muscular soreness, headache, and vomiting. Most of the side effects developed after 1-2 days following the vaccine shot and ranged in intensity from mild to moderate, lasting for another 2-3 days (*Janssen COVID-19 Vaccine | FDA*, n.d.). According to clinical research, Janssen vaccine shows approximately 66.3% effectiveness in preventing laboratory-confirmed infections. Infection with COVID-19 in patients (Table 5) (Shay et al., 2021).

4.4.2 AstraZeneca (AZD1222)/ Vaxzervria

The AZD1222 was formed at Oxford University (Voysey et al., 2021). It creates virus S protein genetic material based on the replication-deficient chimp. The surface spike protein is created after vaccination, preparing the immune system to fight coronavirus if it infects the body later (Elisabeth Mahase, 2021b). According to trials conducted in 2020, after the first dose, the vaccine has a 63.09% efficiency in avoiding symptomatic infection and an 81.3% effectiveness after the second dose (Table 5) (Voysey et al., 2021). Vomiting, diarrhea, fever, edema, soreness at the injection spot, and low blood platelet levels have been documented in less than one out of every ten people. As illustrated in Table 5, less than one out of every hundred people might develop lymph nodes enlargement, less hunger, nausea, tiredness, perspiring, stomachache, and rash (Solomon et al., 2021).

Table 5: Comparison between non-replicating viral vector vaccines (Crommelin et al., 2021), (Covid-19 Vaccine Characteristics | ViewHub, n.d.)

Characteristics	**Janssen (Ad26.COV2.S)**	**AstraZeneca (AZD1222)/ Vaxzervria**
Route of Administration	Intramuscular-deltoid muscle	Intramuscular-deltoid muscle
Booster dose	6 months after the single shot	AstraZeneca administrators have cautioned against rushing to provide boosters
Efficacy (%)	66	70
Cost per dose	$10 per dose excluding taxes	$2.15 - $5.25 (USD) varies in countries
Storage Condition	Stored frozen 2 years at -25ºC to -15ºC Stored between 2ºC to 8ºC	Stored between 2ºC to 8ºC
Shelf life	4.5 Month	6 Month
Adverse effect	The most frequent symptoms include discomfort at the injection site, headache, weariness, muscular soreness, nausea, and exhaustion.	vomiting, diarrhea, fever, edema, tenderness at the injection spot, and decreased blood platelet counts. Fewer common symptoms include enlarged

Characteristics	Janssen (Ad26.COV2.S)	AstraZeneca (AZD1222)/ Vaxzervria
		lymph nodes, no or less appetite, nausea, tiredness, sweating, stomach pain, and rash.
Anaphylaxis Reaction	Serious adverse events are recorded after the injection of the Janssen vaccine in widespread vaccination. Adverse events (AEs) classified as 'anaphylactic response' in the wide Standardized MedDRA Queries (SMQ) were uncommon (0.1 percent) in both the Ad26 and the SMQ.	No evidence of increased anaphylaxis reaction has not been recorded according to Therapeutic Goods Administration (TGA).
Risk in pregnant, infant and children	Unknown: clinical trial is not addressed on younger teens, children, or pregnant women.	Unknown.
Contraindication	Patients have severe allergic responses, including anaphylaxis, people with	Patients with severe allergic responses, including anaphylaxis, people with weakened immune

Characteristics	Janssen (Ad26.COV2.S)	AstraZeneca (AZD1222)/ Vaxzervria
	weakened immune systems, and those on immunosuppressive treatment.	systems, and those on immunosuppressive treatment.

4.5 Effectiveness and Dosage of Coronavirus Vaccines

Vaccine Effectiveness measures how well vaccines do their job in the real world. Clinical trials include a diverse group of participants, including people of various ages, genders, ethnicities, and medical conditions (Evans & Jewell, 2021). Clinical trial efficacy refers to a study's ability to produce a successful objective. Vaccine effectiveness is measured by how successfully they protect significant number of individuals at once. Because we cannot foresee how successful vaccination will be for a much bigger and more varied population that gets vaccinated in much more genuine life conditions, an effective vaccine may vary from an effective vaccine in test. (*Vaccine Efficacy, Effectiveness, and Protection*, n.d.). The effectiveness against symptomatic disease and hospitalization of approved coronavirus vaccines has shown below in Table 6. Table 6 also includes other parameters such as dosage, age limit, and number, of approved countries.

Table 6: Approved Vaccines effectiveness against symptomatic and hospitalization parameter, dosage, number of approved countries for trial and age limit (Krishna Raju Sagiraju et al., 2021), (COVISHIELD FAQs - Serum Institute Of India., n.d.), (Coudeville et al., 2016)

Vaccine	**Dosage**	**Effectiveness**	**Age limit**	**Number of Approved Country**
Moderna (mRNA-1273)	2 shots/28 days apart	94.1% effective against symptomatic disease 95% effective in severe cases	Adults 18 and older	72
Pfizer (BNT162b2)	2 Shots/21 days apart	88% effective against symptomatic disease 96% effective against hospitalization	12 years or older	99
Janssen (Ad26.COV2.S)	Single Shot	71% effective against hospitalization 95% effective against death	Adults 18 and older	65

AstraZeneca (AZD1222)	2 doses/ 4-12 weeks apart	60% effective against symptomatic disease and 93% effective against hospitalization	Adults 18 and older	121
Covishield	2 shots/ 12-16 weeks apart	81.3% effective against symptomatic disease after 12 weeks	18 years of age and above	45
Sinopharm BBIBP-CorV	2 shots/ 21-28 days apart	79% effective against symptomatic infection and hospitalization	18 years of age and above	64
Sinovac/CoronaVac		51% effective against symptomatic infection 100% against hospitalization	18 years of age and above	40

Chapter 05: Coronavirus Variants and Vaccine Response

Several SARS-CoV-2 variations have emerged as a worldwide concern, raising several important issues among scientists and researchers regarding the nature of the variants and their implications such as transmissibility, infectibility, and impact on vaccine activity (Challen et al., 2021). To assume enhanced transmissibility of novel variations, many strategies have been introduced. Moreover, to determine transmissibility, scientists compute the fundamental reproduction number (R0), as well as the peak viral load and viral shedding time (Volz et al., n.d.). According to WHO, variants of Concern that have been found so far include Alpha - the United Kingdom, Beta - South Africa, Gamma - Brazil, and Delta - India. Table 7 demonstrates the efficiency of major coronavirus vaccines in terms of new VOC. Furthermore, current Variants of Interest are Lambda (C.37) and Mu (B.1.621). 14 additional versions are presently being tracked (Parums, 2021). Garcia-Beltran showed that due to various changes in RBD (K417T/N, E484K, and N501Y), coronavirus variants might outflow several vaccines like Moderna and Pfizer. But many vaccines show significant activity and effectiveness to protect against new variants. Immune responses capable of neutralizing Coronavirus are induced by the vaccination. Nonetheless, further monitoring revealed the emergence of variants with spike mutations, which are the primary target of neutralizing antibodies (Garcia-Beltran et al., 2021).

Table 7: Major Vaccine efficacy by significant Variants of Concern (Chakraborty, Bhattacharya, et al., 2021), (Abu-Raddad et al., 2021)

	Concern and Vaccine Efficacy			
Vaccines	**Alpha (α) variants**	**Beta (β) variant**	**Gamma (γ) variant**	**Delta (δ) variant**
Moderna (mRNA-1273)	(81-90) % effectiveness against infection	(71-90) % effectiveness against infection (Require booster shot)	More data needed	76% effective at preventing infection
Pfizer (BNT162b2)	Efficacy was 90–95%, with 81.5% vaccine efficacy in cases with B.1.1.7 prevalence.	100% efficacy	Efficacy has dropped by 6.7%.	Previously, lowered antibody levels showed 70-75 % effectiveness, but now the effectiveness has dropped to 42%

Concern and Vaccine Efficacy

Vaccines	Alpha (α) variants	Beta (β) variant	Gamma (γ) variant	Delta (δ) variant
Janssen (Ad26.COV2.S)	Same efficacy as original virus 72%	The effectiveness against intermediate disease is 52%, while it is 72% against severe disease.	Reduced efficacy shows in Latin America trials)	67% effective against delta variants
AstraZeneca (AZD1222)	The vaccine's efficacy against B.1.1.7 was reported earlier to be 81%, but it has now dropped to 70%.	100% efficacy has shown	More data needed	67% protection against infection

Concern and Vaccine Efficacy

Vaccines	Alpha (α) variants	Beta (β) variant	Gamma (γ) variant	Delta (δ) variant
Covishield	Reduced by 2.5 times in case of alpha variants	Efficacy against beta variants is lower	More data needed	It may range from 70% to 90%
Novavax NVX-CoV2373	vaccine effectiveness was lowered from 95.6% to 85.6%.	Effectiveness shows 51%	Highly effective against North America variants trial	More data needed
Sinovac/CoronaVac & Sinopharm BBIBP-CorV	Same efficacy	Decreased in antibody levels	51% efficacy has shown against symptomatic infection	70% effectiveness against delta variants

Concern and Vaccine Efficacy

Vaccines	Alpha (α) variants	Beta (β) variant	Gamma (γ) variant	Delta (δ) variant
References	(Emary et al., n.d.), (Dagan et al., 2021), (E Mahase, 2021)	(Madhi et al., 2021), (E Mahase, 2021), (EUA & Agnihothram, 2020), (Boehm et al., n.d.)	(Boehm et al., n.d.), (Abdool Karim & de Oliveira, 2021)	(Evans & Jewell, 2021), (J et al., 2021)

Chapter 06: Limitations and Future Recommendations

6.1 Limitations

As elaborated earlier, Coronavirus-2 is a whole new dimension of research to the researchers and new variants are being discovered, so the availability of accurate and reliable data is insufficient for this study. Also, information regarding coronavirus infection and vaccine effectiveness that are included in this paper may vary depending on particular demographic and geographic efficacy parameter. In contrary to this, vaccine development and manufacturing companies, as well as researchers, has focused on specific demographic participants which is why information included and discussed in this article are limited to a particular vaccine candidate. Separate modes of action of the particular vaccine on candidates have not elaborated rather general MOA of vaccines is discussed here. Moreover, post-vaccination reactions discussed here cannot be distinguished separately also, in most cases, similar or different adverse reactions can be noticed and the intensity of side effects is not included here as information regarding this is still unclear.

6.2 Future Recommendations

Although the study regarding Coronavirus is not complete, scientists are still researching the fact that more new strains of this virus can be discovered in the nearer future as the gene of coronavirus has mutated itself previously. For this reason, scientists and researchers need to be more alert for future possibilities. Thus, a universal Coronavirus vaccine can be developed and globally approved which can fight against all types of existing and new variants. As of now, most of the preventive measure was taken by using microneedle in intramuscular-deltoid muscle, no other dosage form is

available. So that, a good portion of people became vaccine-hesitant and resist to take the vaccine. Developing other dosage forms is necessary to ensure maximum immunization rate. The vaccination process already took almost two and half years worldwide, but except for few developed countries other countries' people are still lacking behind. So, enabling diversified vaccine manufacturing companies and technological advancement must be established to ensure rapid vaccine production and vaccination globally. However, Coronavirus infection can not be prevented permanently and we have to co-live with this virus as previous viruses so, necessary precautions must be maintained along with the dependency on vaccines as vaccines cannot ensure 100% effectiveness against coronavirus infection.

Chapter 07: Conclusion

As of September 2020, 150 vaccine candidates have been developed. But after completion of the preclinical and clinical-stage, only a few advanced candidates got approval which includes mRNA-1273 (Moderna), Sinopharm (BBIBP-CorV), Pfizer (BNT162b2), Janssen (Ad26.COV2.S), AstraZeneca (AZD1222), etc. The fundamental method of action of several vaccines is developing antibodies contrary to the spike glycoprotein. Identifying, quantifying, and weighing known and theoretical safety concerns against possible benefits is an important component of creating any vaccine that can be acknowledged by knowing different vaccine properties and effectiveness. The pandemic's global demand for vaccines and the pandemic's broad regional variety requires more than one successful vaccine strategy. Collaboration among biotechnology and pharmaceutical organizations, many of which are developing a range of vaccination methods, will be critical. Moreover, there are different variants have been found in different countries. So that, it is obvious that not every vaccine can show the same effectiveness against different variants. Thus, we need to know which vaccine is effective in what conditions and what are the possible risk factors associated with this. Being vaccinated is necessary even if you do get COVID-19, vaccines can prevent you from becoming very sick. Getting vaccinated will help protect individuals as well people having the higher threat of getting infected with the virus.

To conclude, Vaccines have been given to billions of people across the globe, and the evidence is unambiguous that they provide life-saving protection against a disease that has killed millions of people worldwide. They are our greatest hope for remaining safe while the pandemic continues.

References:

Abdool Karim, S. S., & de Oliveira, T. (2021). New SARS-CoV-2 Variants — Clinical, Public Health, and Vaccine Implications. *New England Journal of Medicine*, *384*(19), 1866–1868. https://doi.org/10.1056/NEJMC2100362

Abu-Raddad, L. J., Chemaitelly, H., & Butt, A. A. (2021). Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. *New England Journal of Medicine*, *385*(2), 187–189. https://doi.org/10.1056/NEJMC2104974

Amanat, F., & Krammer, F. (2020). SARS-CoV-2 Vaccines: Status Report. *Immunity*, *52*(4), 583–589. https://doi.org/10.1016/J.IMMUNI.2020.03.007

Antal, C., Cioara, T., Antal, M., & Anghel, I. (2021). Blockchain Platform For COVID-19 Vaccine Supply Management. *IEEE Open Journal of the Computer Society*, *2*, 164–178. https://doi.org/10.1109/OJCS.2021.3067450

Aryal, S., Devbhandari, R. P., Shrestha, A., Rajbhandari, P., Shakya, T., Tuladhar, S., Maharjan, S., Bashyal, R., Suwal, R., Mishra, D., Kumar Jha, R., Shrestha, S., & Prof, A. (2021). Adverse events following Immunization with Sinopharm (Vero Cell) inactivated COVID-19 vaccine. *Journal of Patan Academy of Health Sciences*, *8*(2), 18–24. https://doi.org/10.3126/JPAHS.V8I2.31099

Banoun, H. (n.d.). *Clinical trials of Covid vaccines in adolescents: do the EMA and FDA have access to the same data? Immunology and theory of evolution View project*. https://doi.org/10.32388/KP77NW

Bao: The pathogenicity of 2019 novel coronavirus... - Google Scholar. (n.d.). Retrieved

September 14, 2021, from https://scholar.google.com/scholar_lookup?title=The Pathogenicity of 2019 Novel Coronavirus in hACE2 Transgenic Mice&publication_year=2020&author=L. Bao&author=W. Deng&author=B. Huang&author=H. Gao&author=L. Ren&author=Q. Wei&author=P. Yu&author=Y. Xu&author=J. Liu&author=F. Qi

Billard, M.-N., & Bont, L. J. (2021). Live-attenuated Respiratory Syncytial Virus Vaccines: Time for the Next Step. *Https://Doi.Org/10.1164/Rccm.202009-3431ED*, *203*(5), 538–539. https://doi.org/10.1164/RCCM.202009-3431ED

Boehm, E., Kronig, I., Neher, R., Eckerle, I., … P. V.-C. M., & 2021, undefined. (n.d.). Novel SARS-CoV-2 variants: the pandemics within the pandemic. *Elsevier*. Retrieved September 30, 2021, from https://www.sciencedirect.com/science/article/pii/S1198743X21002627

Bolles, M., Deming, D., Long, K., Agnihothram, S., Whitmore, A., Ferris, M., Funkhouser, W., Gralinski, L., Totura, A., Heise, M., & Baric, R. S. (2011a). A Double-Inactivated Severe Acute Respiratory Syndrome Coronavirus Vaccine Provides Incomplete Protection in Mice and Induces Increased Eosinophilic Proinflammatory Pulmonary Response upon Challenge. *Journal of Virology*, *85*(23), 12201–12215. https://doi.org/10.1128/JVI.06048-11/ASSET/01F31744-F8F4-492C-9956-4ECC10CF8B4C/ASSETS/GRAPHIC/ZJV9990952940001.JPEG

Bolles, M., Deming, D., Long, K., Agnihothram, S., Whitmore, A., Ferris, M., Funkhouser, W., Gralinski, L., Totura, A., Heise, M., & Baric, R. S. (2011b). A Double-Inactivated Severe Acute Respiratory Syndrome Coronavirus Vaccine Provides Incomplete Protection in Mice and Induces Increased Eosinophilic Proinflammatory Pulmonary Response upon Challenge.

Journal of Virology, *85*(23), 12201–12215. https://doi.org/10.1128/JVI.06048-11

Boopathi, S., Poma, A. B., & Kolandaivel, P. (2020). Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment. *Https://Doi.Org/10.1080/07391102.2020.1758788*, 1–10. https://doi.org/10.1080/07391102.2020.1758788

Bos, R., Rutten, L., van der Lubbe, J. E. M., Bakkers, M. J. G., Hardenberg, G., Wegmann, F., Zuijdgeest, D., de Wilde, A. H., Koornneef, A., Verwilligen, A., van Manen, D., Kwaks, T., Vogels, R., Dalebout, T. J., Myeni, S. K., Kikkert, M., Snijder, E. J., Li, Z., Barouch, D. H., … Schuitemaker, H. (2020). Ad26 vector-based COVID-19 vaccine encoding a prefusion-stabilized SARS-CoV-2 Spike immunogen induces potent humoral and cellular immune responses. *Npj Vaccines 2020 5:1*, *5*(1), 1–11. https://doi.org/10.1038/s41541-020-00243-x

Callaway, E. (2020). The race for coronavirus vaccines: a graphical guide. *Nature*, *580*(7805), 576–577. https://doi.org/10.1038/D41586-020-01221-Y

Callow, K. A., Parry, H. F., Sergeant, M., & Tyrrell, D. A. J. (1990). The time course of the immune response to experimental coronavirus infection of man. *Epidemiology & Infection*, *105*(2), 435–446. https://doi.org/10.1017/S0950268800048019

Chakraborty, C., Bhattacharya, M., & Sharma, A. R. (2021). Present variants of concern and variants of interest of severe acute respiratory syndrome coronavirus 2: Their significant mutations in S-glycoprotein, infectivity, re-infectivity, immune escape and vaccines activity. *Reviews in Medical Virology*, e2270. https://doi.org/10.1002/RMV.2270

Chakraborty, C., Sharma, A. R., Bhattacharya, M., Sharma, G., Saha, R. P., & Lee, S.-S. (2021). Ongoing Clinical Trials of Vaccines to Fight against COVID-19 Pandemic. *Immune*

Network, *21*(1), 1–22. https://doi.org/10.4110/IN.2021.21.E5

Challen, R., Brooks-Pollock, E., Read, J. M., Dyson, L., Tsaneva-Atanasova, K., & Danon, L. (2021). Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study. *BMJ*, *372*. https://doi.org/10.1136/BMJ.N579

Chen, J.-W., & Chen, J.-M. (2020). Potential of live pathogen vaccines for defeating the COVID-19 pandemic: History and mechanism. *Journal of Medical Virology*, *92*(9), 1469–1474. https://doi.org/10.1002/JMV.25920

Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. (n.d.). Retrieved September 16, 2021, from https://www.chictr.org.cn/showprojen.aspx?proj=55524

Corum, J., Wee, S.-L., & Zimmer, C. (n.d.). *Coronavirus Vaccine Tracker*.

Coudeville, L., Baurin, N., & Vergu, E. (2016). Estimation of parameters related to vaccine efficacy and dengue transmission from two large phases III studies. *Vaccine*, *34*(50), 6417–6425. https://doi.org/10.1016/J.VACCINE.2015.11.023

Covid-19 Vaccine Characteristics | ViewHub. (n.d.). Retrieved September 22, 2021, from https://view-hub.org/covid-19/characteristics/

COVID-19 Vaccines | FDA. (n.d.). Retrieved September 21, 2021, from https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines

COVISHIELD FAQs - Serum Institute Of India. (n.d.). Retrieved September 22, 2021, from https://www.seruminstitute.com/health_faq_covishield.php

Crommelin, D. J. A., Volkin, D. B., Hoogendoorn, K. H., Lubiniecki, A. S., & Jiskoot, W. (2021). The Science is There: Key Considerations for Stabilizing Viral Vector-Based Covid-19 Vaccines. *Journal of Pharmaceutical Sciences*, *110*(2), 627–634. https://doi.org/10.1016/J.XPHS.2020.11.015

CTRI. (n.d.). Retrieved September 16, 2021, from http://ctri.nic.in/Clinicaltrials/showallp.php?mid1=45306&EncHid=&userName=Zydus

Dagan, N., Barda, N., Kepten, E., Miron, O., Perchik, S., Katz, M. A., Hernán, M. A., Lipsitch, M., Reis, B., & Balicer, R. D. (2021). BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. *New England Journal of Medicine*, *384*(15), 1412–1423. https://doi.org/10.1056/NEJMOA2101765

Dooling, K., Gargano, J. W., Moulia, D., Wallace, M., Rosenblum, H. G., Blain, A. E., Hadler, S. C., Plumb, I. D., Moline, H., Gerstein, J., Collins, J. P., Godfrey, M., Campos-Outcalt, D., Morgan, R. L., Brooks, O., Talbot, H. K., Lee, G. M., Daley, M. F., & Oliver, S. E. (2021). Use of Pfizer-BioNTech COVID-19 Vaccine in Persons Aged ≥16 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, September 2021. *Morbidity and Mortality Weekly Report*, *70*(38), 1344. https://doi.org/10.15585/MMWR.MM7038E2

Doshi, P. (2020). Will covid-19 vaccines save lives? Current trials aren't designed to tell us. *BMJ*, *371*. https://doi.org/10.1136/BMJ.M4037

El-Shitany, N. A., Harakeh, S., Badr-Eldin, S. M., Bagher, A. M., Eid, B., Almukadi, H., Alghamdi, B. S., Alahmadi, A. A., Hassan, N. A., Sindi, N., Alghamdi, S. A., Almohaimeed, H. M., Mohammedsaleh, Z. M., Al-Shaikh, T. M., Almuhayawi, M. S., Ali,

S. S., & El-Hamamsy, M. (2021). Minor to Moderate Side Effects of Pfizer-BioNTech COVID-19 Vaccine Among Saudi Residents: A Retrospective Cross-Sectional Study. *International Journal of General Medicine*, *14*, 1389. https://doi.org/10.2147/IJGM.S310497

Emary, K., Golubchik, T., Aley, P., Ariani, C., Lancet, B. A.-T., & 2021, undefined. (n.d.). Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B. 1.1. 7): an exploratory analysis of a randomised. *Elsevier*. Retrieved September 30, 2021, from https://www.sciencedirect.com/science/article/pii/S0140673621006280

EUA, A., & Agnihothram, S. (2020). *Emergency use authorization (EUA) for an unapproved product review memorandum identifying information*. https://www.ncbi.nlm.nih.gov/books/NBK570900/bin/fdacovideuas_146338.pdf

Evans, S. J. W., & Jewell, N. P. (2021). Vaccine Effectiveness Studies in the Field. *Https://Doi.Org/10.1056/NEJMe2110605*, *385*(7), 650–651. https://doi.org/10.1056/NEJME2110605

F, Z. (2010). Principles of vaccine design-Lessons from nature. *Vaccine*, *28 Suppl 3*(SUPPL. 3). https://doi.org/10.1016/J.VACCINE.2010.07.020

Gao, Q., Bao, L., Mao, H., Wang, L., Xu, K., Yang, M., Li, Y., Zhu, L., Wang, N., Lv, Z., Gao, H., Ge, X., Kan, B., Hu, Y., Liu, J., Cai, F., Jiang, D., Yin, Y., Qin, C., … Qin, C. (2020). Development of an inactivated vaccine candidate for SARS-CoV-2. *Science*, *369*(6499), 77–81. https://doi.org/10.1126/SCIENCE.ABC1932

Garcia-Beltran, W. F., Lam, E. C., St. Denis, K., Nitido, A. D., Garcia, Z. H., Hauser, B. M.,

Feldman, J., Pavlovic, M. N., Gregory, D. J., Poznansky, M. C., Sigal, A., Schmidt, A. G., Iafrate, A. J., Naranbhai, V., & Balazs, A. B. (2021). Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity. *Cell*, *184*(9), 2372-2383.e9. https://doi.org/10.1016/J.CELL.2021.03.013

Graham, R. L., Becker, M. M., Eckerle, L. D., Bolles, M., Denison, M. R., & Baric, R. S. (2012). A live, impaired-fidelity coronavirus vaccine protects in an aged, immunocompromised mouse model of lethal disease. *Nature Medicine 2012 18:12*, *18*(12), 1820–1826. https://doi.org/10.1038/nm.2972

Haidere, M. F., Ratan, Z. A., Nowroz, S., Zaman, S. Bin, Jung, Y.-J., Hosseinzadeh, H., & Cho, J. Y. (2021). COVID-19 Vaccine: Critical Questions with Complicated Answers. *Biomolecules & Therapeutics*, *29*(1), 1. https://doi.org/10.4062/BIOMOLTHER.2020.178

Halim, M. | ;, Halim, A., Tjhin, Y., & Halim, M. (2021). COVID-19 Vaccination Efficacy and Safety Literature Review. *J Clin MedRes Research Article Halim M |*, *3*(1), 1–10. https://doi.org/10.37191/Mapsci-2582-4333-3(1)-058

Hemert, M. J. van, Worm, S. H. E. van den, Knoops, K., Mommaas, A. M., Gorbalenya, A. E., & Snijder, E. J. (2008). SARS-Coronavirus Replication/Transcription Complexes Are Membrane-Protected and Need a Host Factor for Activity In Vitro. *PLOS Pathogens*, *4*(5), e1000054. https://doi.org/10.1371/JOURNAL.PPAT.1000054

Home - ClinicalTrials.gov. (n.d.). Retrieved September 16, 2021, from https://clinicaltrials.gov/ct2/home

Imperial: LNP-nCoVsaRNA – COVID19 Vaccine Tracker. (n.d.). Retrieved September 16, 2021, from https://covid19.trackvaccines.org/vaccines/19/

J, L. B., N, A., C, G., E, G., R, S., S, T., J, S., E, T., N, G., G, D., R, M., CNJ, C., G, A., M, E., M, Z., KE, B., S, H., M, C., & M, R. (2021). Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. *The New England Journal of Medicine*, *385*(7), 585–594. https://doi.org/10.1056/NEJMOA2108891

Jackson, L. A., Anderson, E. J., Rouphael, N. G., Roberts, P. C., Makhene, M., Coler, R. N., McCullough, M. P., Chappell, J. D., Denison, M. R., Stevens, L. J., Pruijssers, A. J., McDermott, A., Flach, B., Doria-Rose, N. A., Corbett, K. S., Morabito, K. M., O'Dell, S., Schmidt, S. D., II, P. A. S., … Beigel, J. H. (2020). An mRNA Vaccine against SARS-CoV-2 — Preliminary Report. *Https://Doi.Org/10.1056/NEJMoa2022483*, *383*(20), 1920–1931. https://doi.org/10.1056/NEJMOA2022483

Jahanafrooz, Z., Baradaran, B., Mosafer, J., Hashemzaei, M., Rezaei, T., Mokhtarzadeh, A., & Hamblin, M. R. (2020). Comparison of DNA and mRNA vaccines against cancer. *Drug Discovery Today*, *25*(3), 552–560. https://doi.org/10.1016/J.DRUDIS.2019.12.003

Jahromi, M., & Al Sheikh, M. H. (2021). Partial protection of Sinopharm vaccine against SARS COV2 during recent outbreak in Bahrain. *Microbial Pathogenesis*, *158*, 105086. https://doi.org/10.1016/J.MICPATH.2021.105086

Janssen COVID-19 Vaccine | FDA. (n.d.). Retrieved September 20, 2021, from https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine

Jara, A., Undurraga, E. A., González, C., Paredes, F., Fontecilla, T., Jara, G., Pizarro, A., Acevedo, J., Leo, K., Leon, F., Sans, C., Leighton, P., Suárez, P., García-Escorza, H., & Araos, R. (2021). Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. *New*

England Journal of Medicine, *385*(10), 875–884. https://doi.org/10.1056/NEJMOA2107715

Jiang, S., Bottazzi, M. E., Du, L., Lustigman, S., Tseng, C.-T. K., Curti, E., Jones, K., Zhan, B., & Hotez, P. J. (2014). Roadmap to developing a recombinant coronavirus S protein receptor-binding domain vaccine for severe acute respiratory syndrome. *Http://Dx.Doi.Org/10.1586/Erv.12.126*, *11*(12), 1405–1413. https://doi.org/10.1586/ERV.12.126

JP, G., M, P., W, C., & PL, M. (2004). SARS corona virus peptides recognized by antibodies in the sera of convalescent cases. *Virology*, *324*(2), 251–256. https://doi.org/10.1016/J.VIROL.2004.04.017

Kant Sahu, K., Mishra, A. K., & Lal, A. (2020). Comprehensive update on current outbreak of novel coronavirus infection (2019-nCoV). *Ann Transl Med*, *8*(6), 393. https://doi.org/10.21037/atm.2020.02.92

Kissler, S. M., Tedijanto, C., Goldstein, E., Grad, Y. H., & Lipsitch, M. (2020). Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science*, *368*(6493), 860–868. https://doi.org/10.1126/SCIENCE.ABB5793

Krishna Raju Sagiraju, H., Elavarasi, A., Gupta, N., Kumar Garg, R., Sekhar Paul, S., Vig, S., Sirohiya, P., Ratre, B., Garg, R., Pandit, A., Nalwa, R., Kumar, B., Prakash Meena, V., Wig, N., Mittal, S., Pahuja, S., Madan, K., Das, N., Dwivedi, T., … Bhatnagar Head, S. (2021). The effectiveness of SARS-CoV-2 vaccination in preventing severe illness and death – real-world data from a cohort of patients hospitalized with COVID-19. *MedRxiv*, 2021.08.26.21262705. https://doi.org/10.1101/2021.08.26.21262705

L, P. (2020). News Feature: Avoiding pitfalls in the pursuit of a COVID-19 vaccine.

Proceedings of the National Academy of Sciences of the United States of America, *117*(15), 8218–8221. https://doi.org/10.1073/PNAS.2005456117

Ledford, H. (2021). Should children get COVID vaccines? What the science says. *Nature*, *595*(7869), 638–639. https://doi.org/10.1038/D41586-021-01898-9

Li, Y.-D., Chi, W.-Y., Su, J.-H., Ferrall, L., Hung, C.-F., & Wu, T.-C. (2020). Coronavirus vaccine development: from SARS and MERS to COVID-19. *Journal of Biomedical Science 2020 27:1*, *27*(1), 1–23. https://doi.org/10.1186/S12929-020-00695-2

Livingston, E. H., Malani, P. N., & Creech, C. B. (2021). The Johnson & Johnson Vaccine for COVID-19. *JAMA*, *325*(15), 1575–1575. https://doi.org/10.1001/JAMA.2021.2927

LR, B., HM, E. S., B, E., K, K., S, F., R, N., D, D., SA, S., N, R., CB, C., J, M., S, K., N, S., J, S., A, B., C, F., H, S., K, N., L, C., … T, Z. (2021). Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *The New England Journal of Medicine*, *384*(5), 403–416. https://doi.org/10.1056/NEJMOA2035389

Madhi, S. A., Baillie, V., Cutland, C. L., Voysey, M., Koen, A. L., Fairlie, L., Padayachee, S. D., Dheda, K., Barnabas, S. L., Bhorat, Q. E., Briner, C., Kwatra, G., Ahmed, K., Aley, P., Bhikha, S., Bhiman, J. N., Bhorat, A. E., du Plessis, J., Esmail, A., … Izu, A. (2021). Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. *New England Journal of Medicine*, *384*(20), 1885–1898. https://doi.org/10.1056/NEJMOA2102214

Mahase, E. (2021). *Covid-19: Novavax vaccine efficacy is 86% against UK variant and 60% against South African variant*. https://www.bmj.com/content/372/bmj.n296

Mahase, Elisabeth. (2021a). Covid-19: UK approves Moderna vaccine to be given as two doses 28 days apart. *BMJ*, *372*, n74. https://doi.org/10.1136/BMJ.N74

Mahase, Elisabeth. (2021b). AstraZeneca vaccine: Blood clots are "extremely rare" and benefits outweigh risks, regulators conclude. *BMJ*, *373*, n931. https://doi.org/10.1136/BMJ.N931

Masters, P. S. (2006). The Molecular Biology of Coronaviruses. *Advances in Virus Research*, *66*, 193–292. https://doi.org/10.1016/S0065-3527(06)66005-3

McFarland, E. J., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Karron, R. A., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Muresan, P., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Cunningham, C. K., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Perlowski, C., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Libous, J., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Oliva, J., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Jean-Philippe, P., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Moye, J., Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S., Schappell, E., … Team, the I. M. P. A. A. C. T. (IMPAACT) 2013 S. (2020). Live-Attenuated Respiratory Syncytial Virus Vaccine With M2-2 Deletion and With Small Hydrophobic Noncoding Region Is Highly Immunogenic in Children. *The Journal of Infectious Diseases*, *221*(12), 2050–2059. https://doi.org/10.1093/INFDIS/JIAA049

Menachery, V. D., Gralinski, L. E., Mitchell, H. D., Dinnon, K. H., Leist, S. R., Yount, B. L., Graham, R. L., McAnarney, E. T., Stratton, K. G., Cockrell, A. S., Debbink, K., Sims, A. C., Waters, K. M., & Baric, R. S. (2017). Middle East Respiratory Syndrome Coronavirus Nonstructural Protein 16 Is Necessary for Interferon Resistance and Viral Pathogenesis. *MSphere*, *2*(6). https://doi.org/10.1128/MSPHERE.00346-17

Meo, S., Bukhari, I., Akram, J., … A. M.-E. R. M., & 2021, undefined. (n.d.). COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines. *Europeanreview.Org*. Retrieved September 24, 2021, from https://www.europeanreview.org/wp/wp-content/uploads/1663-1669.pdf

Mutua, G., Anzala, O., Luhn, K., Robinson, C., Bockstal, V., Anumendem, D., & Douoguih, M. (2019). Safety and Immunogenicity of a 2-Dose Heterologous Vaccine Regimen With Ad26.ZEBOV and MVA-BN-Filo Ebola Vaccines: 12-Month Data From a Phase 1 Randomized Clinical Trial in Nairobi, Kenya. *The Journal of Infectious Diseases*, *220*(1), 57–67. https://doi.org/10.1093/INFDIS/JIZ071

Ong, E., Wong, M. U., Huffman, A., & He, Y. (2020). COVID-19 Coronavirus Vaccine Design Using Reverse Vaccinology and Machine Learning. *Frontiers in Immunology*, *0*, 1581. https://doi.org/10.3389/FIMMU.2020.01581

Palacios, R., Batista, A. P., Albuquerque, C. S. N., Patiño, E. G., Santos, J. do P., Tilli Reis Pessoa Conde, M., Piorelli, R. de O., Pereira Júnior, L. C., Raboni, S. M., Ramos, F., Sierra Romero, G. A., Leal, F. E., Camargo, L. F. A., Aoki, F. H., Coelho, E. B., Oliveira, D. S., Fontes, C. J. F., Pileggi, G. C. S., Oliveira, A. L. L. de, … Kallas, E. G. (2021). Efficacy and Safety of a COVID-19 Inactivated Vaccine in Healthcare Professionals in Brazil: The PROFISCOV Study. *SSRN Electronic Journal*. https://doi.org/10.2139/SSRN.3822780

Parums, D. V. (2021). Editorial: Revised World Health Organization (WHO) Terminology for Variants of Concern and Variants of Interest of SARS-CoV-2. *Medical Science Monitor : International Medical Journal of Experimental and Clinical Research*, *27*, e933622-1. https://doi.org/10.12659/MSM.933622

Polack, F. P., Thomas, S. J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J. L., Marc, G. P., Moreira, E. D., Zerbini, C., Bailey, R., Swanson, K. A., Roychoudhury, S., Koury, K., Li, P., Kalina, W. V., Cooper, D., Robert W. Frenck, J., Hammitt, L. L., … Gruber, W. C. (2020). Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *Https://Doi.Org/10.1056/NEJMoa2034577*, *383*(27), 2603–2615. https://doi.org/10.1056/NEJMOA2034577

Poland, G. A., Ovsyannikova, I. G., Crooke, S. N., & Kennedy, R. B. (2020). SARS-CoV-2 Vaccine Development: Current Status. *Mayo Clinic Proceedings*, *95*(10), 2172–2188. https://doi.org/10.1016/J.MAYOCP.2020.07.021

Remy, V., Largeron, N., Quilici, S., & Carroll, S. (2014). The Economic Value of Vaccination: Why Prevention Is Wealth. *Value in Health*, *17*(7), A450. https://doi.org/10.1016/J.JVAL.2014.08.1211

Ritchie, H., Mathieu, E., Rodés-Guirao, L., Appel, C., Giattino, C., Ortiz-Ospina, E., Hasell, J., Macdonald, B., Beltekian, D., & Roser, M. (2020). Coronavirus Pandemic (COVID-19). *Our World in Data*. https://ourworldindata.org/coronavirus

Robert-Guroff, M. (2007). Replicating and non-replicating viral vectors for vaccine development. *Current Opinion in Biotechnology*, *18*(6), 546–556. https://doi.org/10.1016/J.COPBIO.2007.10.010

Roper, R. L., & Rehm, K. E. (2014). SARS vaccines: where are we? *Http://Dx.Doi.Org/10.1586/Erv.09.43*, *8*(7), 887–898. https://doi.org/10.1586/ERV.09.43

S.M. Wold, W., & Toth, K. (n.d.). *Adenovirus Vectors for Gene Therapy, Vaccination and Cancer Gene Therapy*.

Sabati, H., Abed, H. M., Dizaji, P. P., Hekmatnezhad, H., & Zare, D. (n.d.). *A mini-review of the validity, quality and efficacy of candidate vaccines in controlling the COVID-19*. *2*(1), 2021. https://doi.org/10.52547/JCBioR.2.1.3

Saeed, B. Q., Al-Shahrabi, R., Alhaj, S. S., Alkokhardi, Z. M., & Adrees, A. O. (2021). Side effects and perceptions following Sinopharm COVID-19 vaccination. *International Journal of Infectious Diseases*, *111*, 219–226. https://doi.org/10.1016/J.IJID.2021.08.013

See, R. H., Zakhartchouk, A. N., Petric, M., Lawrence, D. J., Mok, C. P. Y., Hogan, R. J., Rowe, T., Zitzow, L. A., Karunakaran, K. P., Hitt, M. M., Graham, F. L., Prevec, L., Mahony, J. B., Sharon, C., Auperin, T. C., Rini, J. M., Tingle, A. J., Scheifele, D. W., Skowronski, D. M., … Finlay, B. B. (2006). Comparative evaluation of two severe acute respiratory syndrome (SARS) vaccine candidates in mice challenged with SARS coronavirus. *Journal of General Virology*, *87*(3), 641–650. https://doi.org/10.1099/VIR.0.81579-0

Shay, D. K., Gee, J., Su, J. R., Myers, T. R., Marquez, P., Liu, R., Zhang, B., Licata, C., Clark, T. A., & Shimabukuro, T. T. (2021). Safety Monitoring of the Janssen (Johnson & Johnson) COVID-19 Vaccine — United States, March–April 2021. *MMWR. Morbidity and Mortality Weekly Report*, *70*(18), 680–684. https://doi.org/10.15585/MMWR.MM7018E2

Sinovac: CoronaVac – COVID19 Vaccine Tracker. (n.d.). Retrieved September 22, 2021, from https://covid19.trackvaccines.org/vaccines/7/

Sinovac Vaccine in 12 easy questions. (n.d.). Retrieved September 22, 2021, from https://www.otandp.com/blog/sinovac-vaccine-faq

Solomon, Y., Eshete, T., Mekasha, B., & Assefa, W. (2021). COVID-19 Vaccine: Side Effects After the First Dose of the Oxford AstraZeneca Vaccine Among Health Professionals in

Low-Income Country: Ethiopia. *Journal of Multidisciplinary Healthcare*, *14*, 2577. https://doi.org/10.2147/JMDH.S331140

Sumirtanurdin, R., & Barliana, M. I. (2021). Coronavirus Disease 2019 Vaccine Development: An Overview. *Https://Home.Liebertpub.Com/Vim*, *34*(3), 134–144. https://doi.org/10.1089/VIM.2020.0119

Tanne, J. H. (2020). Covid-19: FDA panel votes to authorise Pfizer BioNTech vaccine. *BMJ*, *371*, m4799. https://doi.org/10.1136/BMJ.M4799

Tanriover, M. D., Doğanay, H. L., Akova, M., Güner, H. R., Azap, A., Akhan, S., Köse, Ş., Erdinç, F. Ş., Akalın, E. H., Tabak, Ö. F., Pullukçu, H., Batum, Ö., Şimşek Yavuz, S., Turhan, Ö., Yıldırmak, M. T., Köksal, İ., Taşova, Y., Korten, V., Yılmaz, G., … Aksu, K. (2021). Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. *The Lancet*, *398*(10296), 213–222. https://doi.org/10.1016/S0140-6736(21)01429-X

Triggle, C. R., Bansal, D., Farag, E. A. B. A., Ding, H., & Sultan, A. A. (2020). COVID-19: Learning from Lessons To Guide Treatment and Prevention Interventions. *MSphere*, *5*(3). https://doi.org/10.1128/MSPHERE.00317-20

Tseng, C.-T., Sbrana, E., Iwata-Yoshikawa, N., Newman, P. C., Garron, T., Atmar, R. L., Peters, C. J., & Couch, R. B. (2012). Immunization with SARS Coronavirus Vaccines Leads to Pulmonary Immunopathology on Challenge with the SARS Virus. *PLOS ONE*, *7*(4), e35421. https://doi.org/10.1371/JOURNAL.PONE.0035421

TT, L., JP, C., R, C., & S, M. (2020). Evolution of the COVID-19 vaccine development

landscape. *Nature Reviews. Drug Discovery*, *19*(10), 667–668. https://doi.org/10.1038/D41573-020-00151-8

Types of Vaccines – COVID19 Vaccine Tracker. (n.d.). Retrieved September 21, 2021, from https://covid19.trackvaccines.org/types-of-vaccines/

Understanding How COVID-19 Vaccines Work | CDC. (n.d.). Retrieved August 30, 2021, from https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/how-they-work.html

Vaccine efficacy, effectiveness and protection. (n.d.). Retrieved September 22, 2021, from https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection

Venkatesh, N. D. (n.d.). *Clinical Evaluation of Vaccines*.

Verdijk, P., van der Plas, J. L., van Brummelen, E. M. J., Jeeninga, R. E., de Haan, C. A. M., Roestenberg, M., Burggraaf, J., & Kamerling, I. M. C. (2020). First-in-human administration of a live-attenuated RSV vaccine lacking the G-protein assessing safety, tolerability, shedding and immunogenicity: a randomized controlled trial. *Vaccine*, *38*(39), 6088–6095. https://doi.org/10.1016/J.VACCINE.2020.07.029

Volz, E., Hill, V., McCrone, J., Price, A., Cell, D. J.-, & 2021, undefined. (n.d.). Evaluating the effects of SARS-CoV-2 spike mutation D614G on transmissibility and pathogenicity. *Elsevier*. Retrieved September 30, 2021, from https://www.sciencedirect.com/science/article/pii/S0092867420315373

Voysey, M., Clemens, S. A. C., Madhi, S. A., Weckx, L. Y., Folegatti, P. M., Aley, P. K.,

Angus, B., Baillie, V. L., Barnabas, S. L., Bhorat, Q. E., Bibi, S., Briner, C., Cicconi, P., Collins, A. M., Colin-Jones, R., Cutland, C. L., Darton, T. C., Dheda, K., Duncan, C. J. A., … Zuidewind, P. (2021). Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *The Lancet*, *397*(10269), 99–111. https://doi.org/10.1016/S0140-6736(20)32661-1

Walsh, E. E., Frenck, R. W., Falsey, A. R., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Neuzil, K., Mulligan, M. J., Bailey, R., Swanson, K. A., Li, P., Koury, K., Kalina, W., Cooper, D., Fontes-Garfias, C., Shi, P.-Y., Türeci, Ö., Tompkins, K. R., … Gruber, W. C. (2020). Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. *New England Journal of Medicine*, *383*(25), 2439–2450. https://doi.org/10.1056/NEJMOA2027906

Wang, H., Zhang, Y., Huang, B., Deng, W., Quan, Y., Wang, W., Xu, W., Zhao, Y., Li, N., Zhang, J., Liang, H., Bao, L., Xu, Y., Ding, L., Zhou, W., Gao, H., Liu, J., Niu, P., Zhao, L., … Yang, X. (2020). Development of an Inactivated Vaccine Candidate, BBIBP-CorV, with Potent Protection against SARS-CoV-2. *Cell*, *182*(3), 713-721.e9. https://doi.org/10.1016/J.CELL.2020.06.008

Wang, Q., Li, C., Zhang, Q., Wang, T., Li, J., Guan, W., Yu, J., Liang, M., & Li, D. (2010). Interactions of SARS Coronavirus Nucleocapsid Protein with the host cell proteasome subunit p42. *Virology Journal 2010 7:1*, *7*(1), 1–8. https://doi.org/10.1186/1743-422X-7-99

WHO – COVID19 Vaccine Tracker. (n.d.). Retrieved September 21, 2021, from https://covid19.trackvaccines.org/agency/who/

Wu, A., Peng, Y., Huang, B., Ding, X., Wang, X., Niu, P., Meng, J., Zhu, Z., Zhang, Z., Wang, J., Sheng, J., Quan, L., Xia, Z., Tan, W., Cheng, G., & Jiang, T. (2020). Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. *Cell Host & Microbe*, *27*(3), 325–328. https://doi.org/10.1016/J.CHOM.2020.02.001

Zhang, C., Maruggi, G., Shan, H., & Li, J. (2019). Advances in mRNA Vaccines for Infectious Diseases. *Frontiers in Immunology*, *0*(MAR), 594. https://doi.org/10.3389/FIMMU.2019.00594

Zhou, P., Li, Z., Xie, L., An, D., Fan, Y., Wang, X., Li, Y., Liu, X., Wu, J., Li, G., & Li, Q. (2021). Research progress and challenges to coronavirus vaccine development. *Journal of Medical Virology*, *93*(2), 741–754. https://doi.org/10.1002/JMV.26517

Zu, Z. Y., Jiang, M. Di, Xu, P. P., Chen, W., Ni, Q. Q., Lu, G. M., & Zhang, L. J. (2020). Coronavirus Disease 2019 (COVID-19): A Perspective from China. *Https://Doi.Org/10.1148/Radiol.2020200490*, *296*(2), E15–E25. https://doi.org/10.1148/RADIOL.2020200490

Zumla, A., Chan, J. F. W., Azhar, E. I., Hui, D. S. C., & Yuen, K. Y. (2016). Coronaviruses-drug discovery and therapeutic options. *Nature Reviews Drug Discovery*, *15*(5), 327–347. https://doi.org/10.1038/NRD.2015.37

Züst, R., Cervantes-Barragan, L., Habjan, M., Maier, R., Neuman, B. W., Ziebuhr, J., Szretter, K. J., Baker, S. C., Barchet, W., Diamond, M. S., Siddell, S. G., Ludewig, B., & Thiel, V. (2011). Ribose 2′-O-methylation provides a molecular signature for the distinction of self and non-self mRNA dependent on the RNA sensor Mda5. *Nature Immunology 2011 12:2*, *12*(2), 137–143. https://doi.org/10.1038/ni.1979