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Review Article

A Critical Review for COVID-19 Vaccines: Contents, Technologies Used, Mode of Actions and Efficacies -

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ABSTRACT

The only effective way to provide people with an immunity against Severely Acute Respiratory Syndrome Coronavirus 2 (SARS CoV 2) is to discover and produce an appropriate vaccine for developing herd immunity thus to prevent the current pandemics of Covid-19. Due to sharing of the SARS CoV 2 genetic sequence data on January 10, 2020 by GISAID, leading global pharmaceutical companies, in turn, vocalized their commitment to produce vaccines for Covid-19 by Mar 19, 2020 [1]. After almost one year of that, somewhere in February 2021, 66 pharmaceutical companies were found undertaking clinical research [2]. Their valuable efforts brought them to different phases of the trials; Phase First - 17, Phase Second - 23 in Phase First Second- 23, Phase Second- 6, and Phase Third - 20. Moreover, the clinical trials for the four vaccines had already been terminated. Many Covid - 19 vaccines under the Phase III trials have claimed to demonstrate their efficacy upto 95% against the infection due to Covid - 19. However, some challenges are encountered by these candidate vaccines due to 501.V2 (South Africa) and B.1.1.7 (United Kingdom) Variants of Covid - 19 Virus [3].

Among all the vaccines candidates, 11 have already got approved by at least one national regulatory authority and are ready to use by February 2021 in accordance with all the safety and efficacy criteria propounded by WHO and other authorities. These included RNA vaccines - 2 (the Pfizer - BioNTech and the Moderna), Inactivated Conventional vaccines - 4 (the BIBP - CorV, Covexin, CoronaVac, & CoviVac), Viral Vector vaccines- 4 (the Sputnik Vaccine, the Oxford - AstraZeneca vaccine, the Convidicea &the Johnson & Johnson vaccine), and Peptide vaccine- 1 (the Epi Vac Corona) [4].

Based on priorities for the high risk groups of infection and transmission; elderliness, healthcare workers, taskforce, distribution Phase plans were devised and adopted by many countries to implement the vaccination program in parts [5].

According to the reports from various national agencies, nearly 275.84 million doses (AstraZeneca - Oxford - 3 billion, Pfizer BioNTech - 1.3 billion, Sputnik V - 1 billion, Sinopharm - 1 billion, Sinovac - 1 billion, Johnson & Johnson - 1 billion) of the Covid - 19 vaccines have already been administered worldwide till March 3, 2021. The Moderna has targeted producing 6 billion doses and the Convidicea 5 billion doses by 2021. The production of more than 10 billion doses had already been done by December 2020 by different countries. First word countries harboring 15% of the population of the world had already placed their orders for procurement of about half of the doses [6].

Keywords: Pandemic; Outbreak; Critical review; Report ; Covid-19; Vaccines; Vaccine contents; Vaccine technologies; Mode of action; Efficacy

INTRODUCTION

Isolation of the genetic sequences of a coronavirus in December 2019 published on 11 January 2020 had triggered an urgent international response to prepare for the outbreak and hastened the development of various Covid-19 vaccines. Therefore, after a longtime invested in R&D, firstly the Medicines and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom granted a temporary regulatory approval for the Pfizer - BioNTech vaccine on December 2, 2020 [7]. Whereas the other nine among all the vaccines candidates with their respective technologies are still continuously under the research and development to bring up an effective vaccine for Covid – 19 [7]. Some of them have successfully completed their clinical trials while many of them under their clinical trials [7].

The main focus of these vaccines is the primary antigen of Covid - 19 that is the spike protein and its variants [8]. Recently a few vaccines producing organizations, somewhere in 2020, seemed aggressively focusing on the mRNA (nucleoside-modified) & DNA technologies, viral vectors (non-replicating), proteomics (peptides and recombinant proteins), live attenuated viruses and inactivated viruses [9].

Recently many vaccine technologies are being developed for Covid - 19 that are entirely different from the technologies which were already in use to prevent viral flu and other respiratory infections. In fact, these newly developed technologies (next generation) are aimed at more precision on controlling the mechanism of the Covid - 19 infections [10].

Thus, the new generation vaccines has more antigen manipulation flexibility thus may improve the effectiveness of the vaccines. These can effectively targete all different variants of the virus prevailing in different subpopulations of the world. Moreover, these can provide different types of vaccine variants for different subgroups like healthcare workers, the elderly, children, pregnant women and people with co-existing weakened immune systems and comorbidities [11].

METHODOLOGY

There are various types of research designs and methodologies are available to choose according to the objectives of the planned study. Some of the research designs are like general structure and writing style, action research design, case study design, cohort design, cross sectional design, descriptive design, experimental, design, exploratory design, historical design, longitudinal design, observational design, philosophical design, sequential design, etc. Whereas, some of the research methodologies are like qualitative research methodologies, qualitative research methodologies, mixed type, emerging, systems, operational, etc. Under these different approaches are planned like randomized, stratified, etc. Since this research paper was a literature review (from December 2019 to February 2021) on the Covid – 19 that has extracted the facts and figures &/ information out from the preexisting research studies. Hence, there was nothing to employ any other statistical tools to bring something new out but the compilation of the significant systematic information [12].

This research paper included the review of many independent but small research studies (small or medium sample size) on different ethnic groups and different geographical locations with different climatic zones and nutritional and health hygiene status. So the results discussed and the information compiled cannot be generalized &/ extrapolated to the whole globe population but have significance for general and overall understanding about the available options of the effective Covid – 19 vaccines to cope up with the pandemics. The efficacy and safety issues of the vaccines (for all ethnicities of the world) have been very crucial to combat Covid - 19 safely. It has its very high infectivity, virulence, morbidity and mortality involving almost all systems & organs systems and leading to multi system failure in patients [13].

These information are valuable enough for contemporary actions to develop a benchmark data required for the scientists engaged effectively to bring a novel and a completely effective solution, as per the exigency of the time, for the Covid - 19.

COMPARATIVE CONTENTS AND MODE OF ACTIONS OF DIFFERENT COVID-19 VACCINES

RNA Vaccines

On introduction to a tissue, RNA in the vaccines act as a messenger RNA (mRNA) upon ribosomes of the cells to translate the proteins in sequence (forensic) which, in turn, adaptive immune response mechanism is initiated that induces a cognition to the body for identifying and destroying the incidental foreign belies like pathogen or virus or cancer cells [14].

However, nonetheless, in these messenger RNA, it's pieces called nucleotides are highly prone to modify to achieve the target proteins production. The delivery of the mRNA to the tissues is done through a coformulation of the molecules into nano particles made up of lipid that safeguard the mRNA in the vaccine while getting absorbed into the cells thus, the desirable immunological properties with an outstanding safety profile is achieved with the unmet flexibility of such genetic vaccines [15]. Moreover, the mRNA vaccines are capable of inducing a balanced immune response comprising both cellular and humoral immunity while not subject to MHC haplotype restriction according to in situ protein expression. Further, the foreign mRNA in vaccines seems to be an intrinsically safe vector as it carries a minimal and only transient genetic information that may not interact with the genome. Because any protein may be expressed from mRNA without the need to adjust the natural production process, mRNA vaccines also may offer a maximum flexibility with respect to development [16]. Taken together, mRNA presents a promising vector that may well become the basis of a game-changing vaccine technology platform [15].

Adenovirus Vector Vaccines

These viral vector vaccines (non-replicating) use an adenovirus shell containing DNA as a vector that encodes for a spike protein of the Covid - 19 virus. These vectors in the vaccines, however, remain non-replicating, it means that they do not give rise to new viruses, but indeed only manufacture the antigen protein that provokes an immune response as the virus does [17].

However, Adenovirus-based HIV vaccine Trivalent AdHu5 vector expressing three HIV antigens, gag, pol, and nef, is the most widely studied HIV vaccine worldwide but this vaccine fails to reduce viral load clinically and increases the risk of HIV in AdHu5 seropositive males. Hence, it catches least attraction for the development of an effective vaccine against covid-19 [18].

However, Covishield or AZD - 1222 vaccine also makes use of a viral vector made using a weakened strain of the common cold virus (adenovirus), which contains genetic material similar to that of SARS CoV 2. Upon administration, the body's defences recognize the spike protein and prepare antibodies to evade out the infection [19].

Inactivated Virus Vaccines

Certain virus particles grown in culture media are killed through either heat or radiation or chemicals or formaldehyde and used in these vaccines. Hence, these inactivated virus fragments can't manifest as the disease but stimulate or trigger a systemic immune response [20].

COVAXIN, India's indigenous Covid - 19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). The indigenous, inactivated vaccine is developed and manufactured in Bharat Biotech's BSL-3 (Bio - Safety Level 3) high containment facility [21].

The vaccine is developed using Whole Virion Inactivated Vero Cell derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects [21]. Conventionally, inactivated vaccines have been around for decades [21]. Numerous vaccines for diseases such as Seasonal Influenza, Polio, Pertussis, Rabies, and Japanese Encephalitis use the same technology to develop inactivated vaccines with a safe track record of > 300 million doses of supplies to date. It is the well-established, and time-tested platform in the world of vaccine technology [22].

Inactive vaccines have been used by a lot of vaccine makers and have been used since years to fight out viruses and pathogens - meaning that to an extent, inactive vaccines are safer and reliable [23].

Subunit Vaccines

The word "subunit" simply means the epitopes of the antigen is a fragment of the pathogen. Subunit vaccines consist of one or more desired antigens instead of involving a complete pathogen/virus. These fragments or subunits (i.e. antigens) are most of the time proteinaceous while sometimes they are made up of some other biomolecules [23].

Multiple DNA Plasmid Vaccines

Plasmids are circular deoxyribonucleic acid (DNA) vectors that can be used as vaccines to prevent various types of diseases. These plasmids are DNA junctions that are usually composed of a viral promoter gene, a gene coding resistance to antibiotics, a bacterial origin of replication gene and a multiple cloning site (MCS) for a transgenic region, where one or several genes of antigenic interest can be inserted [24]. Immunization with these recombinant vectors allows intracellular expression of the encoded antigens by molecular and cellular machinery of transfected cells, stimulating an antigen-specific immune response. This process provides an effective protection against diverse types of pathogens, tumor cells and even allergy and autoimmune diseases [24]. Protective efficacy is achieved by the induction of a strong humoral and cellular immune response dependent on B and T cells [24]. The immunity induced by these DNA vaccines, added to the ease of production, administration, genetic stability, and safety, has transformed plasmid-based immunization into a safe strategy in prevention of various diseases [24].

Other Miscellaneous Types

These vaccines are also under the clinical trials for the Covid - 19 include (1) lentivirus vector vaccines (at least two), based on this, types of cancer vaccines using have been investigated: dendritic cell vaccines and cancer cell vaccines. Dendritic cells loaded with peptide from a tumor antigen can be used as a vaccine against cancers expressing that antigen [25] (2) conjugate vaccine, it is a vaccine type that combines a weak antigen with a strong antigen as a carrier so that

the immune system has a stronger response to the weak antigen [26] and (3) vesicular stomatitis virus (displaying the spike protein of the Covid - 19 virus) vaccine [27].

Process Of Authorized and Approved Vaccines

On the onset of the Covid - 19 pandemics, in absence of an effective treatment for combating the disease, all leading researchers and scientists has started investigating if any of the existing vaccines could work for preventing the Covid - 19. Although the mode of action of the BCG vaccine is well known to generate non-specific impaction on the body's immune system, no evidence yet validates that this vaccine is effective against Covid - 19.

Any newly developed vaccine firstly needs proven safe and effective to be authorized prior to its public use. Therefore, clinical trials entail peer-reviews and publications pave way to their approval and authorization.

The First Phase of the clinical trials are primarily meant for the patient safety as well as for the preliminary dose calibration upon a few dozens of the healthy subjects [28].

The First - Second Phase of the clinical trials are meant for the preliminary safety concerns (histocompatibility) and as well as the testing for immunogenicity. These trials follow a typical randomized research design with the controlled placebo effects thus these are more precisely done than the first ones for calibrating more effective doses [28, 29].

The Second Phase of the clinical trials are meant for the evaluation of the success achieved during the First Phase. It evaluates

Table 1: Covid-19 vaccines are the day by day enriching WHO emergency use listening.

S.No.	Vaccine	Type	Prepared By	Authorized In
1	Comirnaty (BNT162b2)	mRNA based vaccine	Pfizer, BioNTech; Fosun Pharma (Multinational)	Albania, Andorra, Argentina, Aruba, Australia, Bahrain, Brazil, Canada, Caribbean, Chile, Colombia, Costa Rica, Ecuador, European Union, Faroe Islands, Greenland, Hong Kong, Iceland, Iraq, Israel, Japan, Jordan, Kuwait, Liechtenstein, Malaysia, Mexico, Monaco, New Zealand, North Macedonia, Norway, Oman, Panama, Philippines, Qatar, Saint Vincent, the Grenadines, Saudi Arabia, Serbia, Singapore, Suriname, Switzerland, United Arab Emirates, United Kingdom, United States, Vatican City, and World Health Organization
2	Moderna Covid - 19 Vaccine	mRNA - 1273): mRNA - based vaccine	Moderna, BARDA, NIAID (United States)	Canada, European Union, Faroe Islands, Greenland, Iceland, Israel, Liechtenstein, Norway, Qatar, Saint Vincent, the Grenadines, Singapore, Switzerland, UK, USA, and Vietnam
3	Covid - 19 Vaccine AstraZeneca (AZD1222); also known as Covishield	Adenovirus vaccine	BARDA, OWS (UK)	Argentina, Bahrain, Bangladesh, Barbados, Brazil, Canada, Chile, Dominican Republic, Ecuador, El Salvador, Egypt, EU, Guyana, Hungary, India, Iraq, Malaysia, Maldives, Mauritius, Mexico, Morocco, Myanmar, Nepal, Nigeria, Pakistan, Philippines, Saint Vincent and the Grenadines, South Africa, South Korea, Sri Lanka, Taiwan, Thailand, UK, and Vietnam
4	JNJ - 78436735 (formerly Ad26COV2S)	Non-replicating viral vector vaccine	Janssen Vaccines (Johnson & Johnson) (The Netherlands, US)	Bahrain, Saint Vincent and the Grenadines, and US
5	Sputnik V)	Recombinant adenovirus vaccine (rAd26 and rAd5)	Gamaleya Research Institute, Acellena Contract Drug Research and Development (Russia	Algeria, Angola, Argentina, Armenia, Bahrain, Belarus, Bolivia, Congo, Djibouti, Egypt, Gabon, Ghana, Guatemala, Guinea, Guyana, Honduras, Hungary, Iran, Kazakhstan, Kyrgyzstan, Lebanon, Mexico, Moldova, Mongolia, Montenegro, Myanmar, Nicaragua, Pakistan, Palestine, Paraguay, Republika-Srpska, Russia, Saint Vincent, the Grenadines, San Marino, Serbia, Slovakia, Syria, Tunisia, Turkmenistan, USE, Uzbekistan, and Venezuela
6	EpiVacCorona	Peptide vaccine	Federal Budgetary Research Institution State Research Center of Virology and Biotechnology (Russia)	Russia, and Turkmenistan
7	CoviVac	Inactivated vaccine	Chumakov Federal Scientific Center for Research and Development of Immune and Biological Products (Russia)	Russia
8	Covaxin	Inactivated vaccine	Bharat Biotech, ICMR (India)	India
9	ZF2001	Recombinant vaccine	Anhui Zhifei Longcom Biopharmaceutical, Institute of Microbiology of the Chinese Academy of Sciences (China & Uzbekistan)	Uzbekistan
10	CoronaVac	Inactivated vaccine (formalin with alum adjuvant)	Sinovac (China)	Azerbaijan, Bolivia, Brazil, Cambodia, China, Chile, Colombia, Ecuador, Hong Kong, Indonesia, Laos, Malaysia, Mexico, Thailand, Turkey, Philippines, and Uruguay

Source: WHO Website

Table 2: Authorized and approved vaccines have shown the following efficacies against symptomatic Covid-19.

S.No.	Vaccine	Efficacy Details
1	Moderna vaccine	89 - 97% (no severe cases in United States was tested)
2	Pfizer–BioNTech vaccine	90 - 97% (no cases were reported in multinational scenarios)
3	Sputnik Vaccine	86 - 95% (94 - 100% cases in Russia were tested)
4	Oxford - AstraZeneca vaccine	62 - 90% [citation needed]
5	Novavax vaccine	75 - 95% (no cases in United Kingdom and 20 - 80% cases in South Africa were tested)
6	BIBP – CorV	(1) 78% - 100% (unreliable medical source?)
7	CoronaVac	(1) 78% - 100% (unreliable medical source?)
8	Johnson & Johnson vaccinea	55 - 75% (moderate), 54 - 97% (multinational), 58 - 82% (moderate cases) 9 - 100% in United States, 49 - 81% (moderate cases), 8 - 100% in Brazil, 41 - 79% (moderate cases) and 46 - 95% in South Africa
9	Covaxin	81% in India

Source: Wikipedia

the immunogenicity, dose levels (efficacy based on biomarkers) and adverse effects of the vaccine, typically using a few hundreds of the subjects [29].

The Third Phase of the clinical trials are meant for engaging more participants than the previous ones at many locations. It includes both a control group and test group to evaluate the effectiveness of the vaccine if it can prevent the disease. These trials are also known as interventional or pivotal trial. These trials also aim at monitoring for adverse effects, if any arises, at the optimal dose [28,29].

Standards and parameters like defining the degree of the side effects, infection of the Covid - 19, and severity for the vaccine safety, efficacy, and the trials termination point, during the Third Phase of the clinical trials, may differ from company to company [30].

Moreover, the design of the ongoing clinical trial can be altered to be an "adaptive design" if the contemporary data suggest to do so. It all depends on the early insights of either positive or negative efficacy of the trial.

Adaptive design is often adopted during the First - Second Phase of the clinical trial. It may lessen the duration of the trial and needs fewer subjects, hopefully disburses early termination or success, shortens research efforts, and amplifies design changers coordination across its multiple/ international locations for the Solidarity of the trial [31]. As per exigency of the time, the National Regulatory Authorities had granted their authority for the emergency use of the eleven vaccines. Six of them had been approved for the full use by the WHO recognized (at least one) stringent regulatory authorities [32].

Who Emergency Use Listing (EUL) of COVID-19 Vaccines

The emergency use listing (EUL) procedure assesses the suitability of novel health products during public health emergencies. The objective is to make medicines, vaccines and diagnostics available as rapidly as possible to address the emergency, while adhering to stringent criteria of safety, efficacy and quality. The assessment weighs the threat posed by the emergency as well as the benefit that would accrue from the use of the product against any potential risks [33].

The EUL pathway involves a rigorous assessment of late phase II and phase III clinical trial data as well as substantial additional data on safety, efficacy, quality and a risk management plan. These data are reviewed by independent experts and WHO teams who consider the current body of evidence on the vaccine under consideration, the plans for monitoring its use, and plans for further studies [33,34].

As part of the EUL process, the company producing the vaccine must commit to continue to generate data to enable full licensure and WHO prequalification of the vaccine. The WHO prequalification process will assess additional clinical data generated from vaccine trials and deployment on a rolling basis to ensure the vaccine meets the necessary standards of quality, safety and efficacy for broader availability [32,33].

DISCUSSION

The efficacy which is proven through the research is the percentage of the risk reduced or chances of not getting the disease after vaccination. Subjects in the clinical trial are examined for the disease after the vaccine incubation period and their signs are compared with the unvaccinated subjects. Out of total vaccinated subjects, how many have not developed the signs & symptoms of the disease, these numbers are converted to the percentage of the efficacy.

Since the clinical trials of the Covid - 19 vaccines produced by different companies at different locations of the world were made on different populations, they cannot directly be compared for their relative efficacies due to variations in ethnicities as well as variants of the virus.

As per some experts' opinions, in this case, a vaccine efficacy of 67% is enough to slow down the spread of the pandemic if the vaccine is able to confers sufficient immunity for its sterilization and transmission, Although the vaccine efficacy is mainly concerned with the disease prevention, it is a poor indicator of transmissibility because asymptomatic people can highly be infectious [35]. However, the United States of America's Food and Drug Administration (FDA) as well as the European Medicines Agency (EMA) has set a cutoff of 50% for the efficacy to approve a Covid - 19 vaccine [36].

In efficacy calculations, the symptomatic Covid - 19 patients with a (+) rT PCR test and those who have at least one or two defined symptoms of the Covid - 19, were included though the exact specifications varied between trials ranging below 95% confidence intervals [37].

A clinical trial on 820 volunteers owing to a mixe - match approach was conducted to evaluate the efficacy of the results achieved after combined two different vaccines administration to these volunteers. The ultimate goal of the trial was to find out if the mix - match method was just as or more effective than the conventional ones. The trial

Table 3: Authorized and approved vaccines have shown the following efficacies against symptomatic Covid-19.

Key	Vaccine	Efficacy (CI*)	Data
1	Tozinameran (BNT/Pfizer)	95% (90-98%)	>43k people (half on placebo) *Reviewed & detailed reports public*; *protocol public* Evidence: **strong**
			Most common systemic adverse event: fatigue (56%) Most commonly severe: fatigue (4%)
2	Moderna	94% (89-97%)	>30k people (half on placebo) *Reviewed & detailed reports public*; *protocol public* Evidence: **strong**
			Most common systemic adverse event: fatigue (65%) Most commonly severe: fatigue (10%)
3	Sputnik V (Gamaleya)	92% (86-95%)	>22k people (3:1 placebo) *Reviewed & detailed report public*; *protocol not public* Evidence: **strong** (with reservations about methodology); adverse event data used from very small early phase trial, as adverse events not routinely solicited in a representative group in phase 3
			Most common systemic adverse event: feverishness/mild fever (95%) None severe.
4	Oxford/AstraZeneca	63% (52-72) 76% (59-86) *(delayed 2nd dose)* *(Standard dose, February data, includes "UK", "SA" strains)*	>17k people (half in control group, half on varied vaccine regimens) *Reviewed & detailed reports public*; *protocol public* Evidence: **weak to moderate**, from group of trials with reservations about methodology (but a strong trial in progress); adverse event data from MHRA
			Most common systemic adverse event: fatigue (62%) Most commonly severe: malaise (4%)
5	Sinopharm – Beijing	79% (?)	Up to 30k people (half on placebo) *Reviewed, negligible details public*; *protocol not public* Adverse event data from earlier phase trial Evidence: **potentially strong** (too little known) (Other trials in progress)
			Most common systemic adverse event: fever (4%) None severe
6	CoronaVac (Sinovac)	50% (35-62%) *(Anvisa, Brazil)* 84% (?) *(Turkey)*	Brazil >12k people (half on placebo) *Reviewed, basic details public*; *protocol public* Turkey >10k people (half on placebo) *Press announcement only; protocol not public* Evidence: **moderate** (further trials in progress)
			Most common systemic adverse event: fatigue (<2%) No severe event reached 1%.
7	Novavax	90% (80-95%) *(UK trial only, including "UK" strain)* 96% *(Original strain only)* (74-99.5)	>14k people (half on placebo) (UK trial) *Press release only; protocol public* Evidence: **moderate**; adverse event data only available for small early phase trial (large trial in progress) Note: the results from a small phase 2b trial in SA showed it worked, but with much lower efficacy because of the "SA" strain (perhaps 49% or 60%). However the evidence was very **weak**.
			Most common systemic adverse event: fatigue (36%) Most commonly severe: fatigue (3%)
8	J&J	66% at 28 days *(Including "SA" strain)* (55-75) ~70% after 56 days; 72% at 28 days USA (58-82)	>43k people (half on placebo) *Reviewed, detailed report; protocol public* Evidence: **strong** (further large trial on 2 shots in progress)
			Most common systemic adverse event: fatigue (38%) Most commonly severe: fatigue (1%)
9	CanSino	69% at 14 days (?) 65% at 28 days (?)	ca 40k people (half on placebo) *Press release only; protocol not public* Adverse event data only available for small early phase trial Evidence: **potentially strong** (too little known)

			Most common systemic adverse event: fatigue (34%) None severe reached 1%
10	Sinopharm – Wuhan	73% (?) *2nd trial stopped for lack of efficacy*	Up to 30k people (half on placebo) *Reviewed, negligible details public*; *protocol not public* 2nd trial 6k people (half on placebo) *No data released* Adverse event data from earlier phase trial Evidence: **potentially strong** (too little known)
			Most common systemic adverse event: fever (5%) None severe
11	Covaxin	81% (?)	Under 26k people (half on placebo) *Press release of interim results only*; *protocol not public* Adverse event data from earlier phase trial Evidence: **potentially strong** (too little known)
			Most common systemic adverse event: fatigue (3%) None severe

Sources: My tagged public Zotero collection *(detailed below this post). * 95% confidence or* credible interval: A measure of the uncertainty of the estimate. ** *Unofficial: I calculated this from the data in press release-official statistical method may have different result.* MHRA = UK drug regulator; Anvisa = Brazil's drug regulator; EMA = European drug regulator.

would use the vaccine developed by Pfizer and BioNTech with the University of Oxford and the vaccine developed by AstraZeneca, both relied on different methods to deliver information to the recipient cells. However, this trial was opposed by some people like Ugur Sahin stating that the trial "will use up doses that people who need them could profit from, I am not happy about this," though Pfizer and AstraZeneca have supported the trials [38].

A preliminary study by Pfizer, Inc. has indicated that there is, at most, there was only a minor reduction in the effectiveness of mRNA vaccine of the company against the different variants of the SARS CoV 2. According to the most of experts from the CDC of the United States, the emergent variants could completely escape from the immune response due to the nature of the virus because the response of both natural virus and vaccine induced mRNA was unlikely [39].

Moreover, the T-cell immunity is under investigation to bring out a potential solution to the problem of the reduced effectiveness of vaccines against the emergent variants. As the majority of genetic variation noted were in the spike protein of the virus, T-cells are able to - target multiple pieces of the virus by attacking on it to recognise new variants. Both viral - vector and mRNA based vaccines are believed to elicit the strongest t-cell response. That is why the vaccine developed for yellow fever was a RNA based vaccine [40].

The virus like SARS CoV 2 has remained active for such a long period because of its antigen spike protein found on the surface of the virus. The vaccines attempted to target the antigen. It is unaffected by the majority of mutations. Companies including Emergex, Osivax and eTheRNA are also targeting some internal antigens in the hope of creating a "universal" SARS CoV 2 vaccine. Gritstone, a Biotech firm is also experimenting to develop an effective vaccine which aimed specifically at creating T-cell immunity against the Covid - 19 virus in healthy people [41].

Researchers of the University of Oxford have, as of commencement of 2021, begun enrolling volunteers for the achievement of the goal of the study that would find whether the mix - match method would just be as or more effective than the currently used methods in practice [42].

CHALLENGES DUE TO NEWLY EMERGENT

Variants

Darya Besedina, the deputy to the Moscow City Duma, has requested on January 29, 2021 the Russian Minister of Health to fund the research study of the new variants for the effectiveness of Russian vaccines against these variants [43]. Moreover, the European Medicines Agency has made a similar appeal to vaccine manufacturers on February 10, 2021, Russian President Vladimir Putin had also instructed the Russian government to deploy the sequencing of the genomes of Russian SARS CoV 2 variants within a month, allocate funds for these studies and also check for if the Russian vaccines are effective against the new strains [44].

(United Kingdom) variant

A newly emerged SARS-CoV-2 variant known as B.1.1.7, was identified in the UK in December 2020. Early results of the trials made for the UK - variant suggested that both the Pfizer and the Moderna vaccines could prevent the UK - variant infections. Another study of the effectiveness of the same Comirnaty's vaccine against the B.1.1.7 variant has also confirmed the statement. Moreover, the preliminary results presented from the biorxiv have also shown that the Covaxin is effective against this variant [45].

(South Africa) variant

However, both the Pfizer and the Moderna vaccines are said to be less effective against the South Africa variant. The Moderna has reported that the current vaccine trials had produced only one-sixth of the total antibodies in response to the South African variant compared to the original virus [46].

They have already launched another trial of a new vaccine to tackle the South African 501.V2 variant (also known as B.1.351). Pfizer announced that in the new vaccine, the neutralization activity was reduced by two thirds for the 501.V2 variant, but no claim was made about the efficacy of the new vaccine in preventing illness for this variant on February 17, 2021. Johnson & Johnson, which held trials for its Ad26.COV2.S vaccine in South Africa during January 2021, had reported the level of protection moderate to severe against Covid - 19 infection that was 72% in the United States and 57% in South Africa [47,48].

The Financial Times acclaimed on February 6, 2021 that the contemporary data from the trial (the study undertaken by South Africa's University of the Witwatersrand in conjunction with Oxford University) illustrated a reduced efficacy of the Oxford - AstraZeneca Covid - 19 vaccine against the 501.V2 variant [49,50].

The results from the study stated that in a sample size of 2,000 subjects, the AZD 1222 vaccine, provided only with the minimal protection in all but the most severe cases of Covid - 19 could not. The Minister for Health for South Africa suspended the planned deployment of around 1 million doses of the vaccine on February 7, 2021 when they examine the data and await advice on how to proceed [51].

All the eleven of the vaccine producers, during the clinical development they used adjuvants to enhance immunogenicity during September 2020. An immunological adjuvant is a chemical substance in a vaccine to elevate the immune response to an antigen of the Covid - 19 virus. An adjuvant may specifically be used during the formulation of the Covid - 19 vaccine to enhance its immunogenicity and efficacy and to reduce or prevent Covid - 19 infection in vaccinated populations. Adjuvants used in Covid - 19 vaccine formulation may particularly be effective for the technologies using the inactivated Covid - 19 viruses and recombinant protein based or vector based vaccines [52].

Alum (Aluminum salts), were the first adjuvant substance which was used for the licensed vaccines, and are still the adjuvant of choice in some 80% of adjuvanted vaccines. The alum adjuvant induce a diversed molecular and cellular mechanisms to amplify immunogenicity, including release of proinflammatory interleukins and cytokines [53].

CONCLUSION

Since Different vaccines employ different technology, each type of Covid-19 vaccine has its own merits and demerits as discussed above and the clinical trials of the Covid - 19 vaccines produced by different companies at different locations of the world were made on different populations and subpopulations, they cannot directly be compared for their relative efficacies and safety issues due to variations in ethnicities as well as variants of the virus. However, both the efficacy and safety can be established following the directive and proper clinical trials for each Covid-19 vaccine type but it would take a long time. Nonetheless, as per the exigency of the time, since we are facing pandemics, we need to adopt vaccines which have already been authorized for the public use by the competent authorities.

RECOMMENDATIONS

- Wear a mask to protect yourself and others and stop the spread of COVID-19.
- Stay at least 6 feet (about 2 arm lengths) from others who don't live with you.
- Avoid crowds. The more people you are in contact with, the more likely you are to be exposed to COVID-19
- Keep checking your rapid RTPCR results if you COVID-19 signs and symptoms
- Get vaccinated with the authorized vaccines available in your area with all safety precautions and measures

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