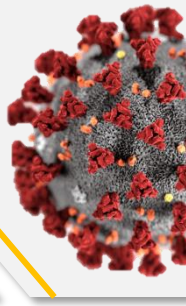
COVID-19 VACCINES

Based on available evidence up to 16 November 2020



INTRODUCTION

COVID-19 is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which responsible for the outbreak began in Wuhan, China, in December 2019 and progressively became pandemic affecting more than 120 countries globally.[1] As to 15 November 2020, confirmed cases of COVID-19 accumulated to 53 million people worldwide, with confirmed death cases of 1,308,975 people.[2]

SARS-CoV-2 is highly transmissible and pathogenic virus and bats are considered as the natural hosts.[3] The virus mainly infect lower respiratory tract and can cause severe pneumonia, which leads to fatal acute lung injury and acute respiratory distress syndrome, resulting in high morbidity and mortality. Currently, the efforts to prevent the spread of COVID-19 is by primary intervention which include physical distancing, practicing proper hand hygiene and routine cleaning of high-touched surfaces with disinfectants.

The sudden emergence and rapid spread of SARS-CoV-2 virus does not only endangering life but has disrupted the social and economic equilibrium, Therefore the development of vaccine are urgently needed as an effort to fight against COVID-19. To date, no vaccines against any human-infecting coronaviruses have been approved for general population.[4] On 22 October 2020, the U.S. Food and Drug Administration approved the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization.[5] The aim of vaccines is to induce neutralising antibodies and there could be an advantage of inducing cytotoxic T-lymphocytes.[6] These neutralising antibodies will be targeting S1 receptor-binding-domain (RBD), S1 N-terminal domain, or the S2 region; these antibodies block binding of the RBD to the ACE2 receptor and prevent S2-mediated membrane fusion or entry into the host cell, thus inhibiting viral infection.[7]

Structurally, there are several targets for vaccination on the surface of SARS-CoV-2 which includes the envelope spike protein S, the small envelope protein E, the matrix protein M and the unexposed nucleocapsid protein N.[4] However, the spike protein is the antigen of choice for the vaccine due to its association with strong (neutralizing) antibody response proven pre-clinically against Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV).[4,6] Since the SARS-CoV-2 virus shares striking structural similarity and sequence conservation with these two lethal coronaviruses, the immunization strategies exploited against SARS and MERS viruses have been adopted in guiding the design of new SARS-CoV-2 vaccines.[4]

As to date, there are more than 170 candidate vaccines for COVID-19 have been developed.[8] The candidate vaccines were developed based on one of the following technology platform:[6,9]

- Virus: live-attenuated or inactivated viral vaccine
- Viral vector: replicating or non-replicating viral vector vaccine
- Nucleic acid: DNA or RNA vaccine
- Protein-based: protein subunit or virus-like particles vaccine

Live attenuated vaccines (LAV) or weakened vaccine employ viruses that are conventionally weakened or rendered replication-incompetent through different passages in culture that make it mutated and less able to cause diseases. Whereas, inactivated vaccines employ pathogens which have been killed throughout exposure to chemicals and heat to make it non-infectious. Many existing vaccines are made in this way, such as those against measles and polio, but they require extensive safety testing.

Viral vector protein vaccine uses other virus such as measles or adenovirus which is genetically engineered[10] so that it can produces coronavirus proteins in the body. There are two types of viral-vector vaccines; those that can still replicate within cells and those that cannot because key genes have been disabled. The replicating viral vector vaccine replicates within cells and provokes a strong immune response. However, existing immunity to the vector could blunt the vaccine's effectiveness. The non-replicating viral vector vaccines might need booster shots to induce long-lasting immunity.[9] There was concern that the use of an Ad5 vector for immunisation against SARS-CoV-2 infection could increase the risk of HIV-1 acquisition among men based on a few studies on Ad5 vector-based vaccines developed against HIV-infection.[11]

Nucleic-acid vaccines use genetic instructions in the form of deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). The nucleic acid which encodes the virus spike protein is inserted into human cells, which then churn out copies of the virus protein to induce immune responses. Nucleic-acid vaccines are theoretically safe and easy to develop which involves making genetic materials only, not the virus. However, there are no licensed vaccines using this technology.[9]

Protein subunit vaccines are produced in vitro by employing antigenic proteins (virus' spike protein or a key part of it called the receptor binding domain) that induce a protective immune response.[9,10] These vaccines might require multiple doses to make it work and might require adjuvants which is immune-stimulating molecules delivered with the vaccine.

Forty-one candidate vaccines are being evaluated clinically with six of the products have passed to phase III clinical trials.[12] Two vaccines candidate has received Fast-track Designation by U.S Food and Drug Administration (FDA). As to date, six vaccines have received emergency approval for usage to certain groups of people.[8]

Table 1: WHO List of candidate vaccines with its on-going clinical trials.[12]

No	Name	Developer	Vaccine Platform	Clinical Stage
1.	ChAdOx1-S	University of Oxford/AstraZeneca	Non-Replicating Viral Vector	Phase 3 ISRCTN89951424

2.	Coronavac	Sinovac	Inactivated	Phase 3 NCT04456595
3.	Inactivated vaccine	Sinopharm/Wuhan	Inactivated	Phase 3 ChiCTR2000034780
4.	Inactivated vaccine	Sinopharm/Beijing	Inactivated	Phase 3 ChiCTR2000034780
5.	mRNA-1273	Moderna	mRNA	Phase 3 NCT04470427
6.	BNT162 (BNT162b1 & BNT162b2)	BioNTech/Pfizer/Fosun Pharma	mRNA	Phase 3 NCT04368728
7.	Ad5-nCOV	CanSino Biologic	Non-Replicating Viral Vector	Phase 3 NCT04540419
8.	Sputnik V	Gamaleya Research Institute	Non-Replicating Viral Vector	Phase 3 NCT04564716
9.	NVX-CoV2373	Novavax	Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	Phase 3 2020-004123-16
10.	Ad26COVS1	Janssen Pharmaceutical Companies	Non-Replicating Viral Vector	Phase 3 NCT04505722
11.	Adjuvanted recombinant protein	Anhui Zhifei Longcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences	Adjuvanted recombinant protein (RBD-Dimer)	Phase 2 NCT04466085
12.	mRNA	Curevac	mRNA	Phase 2 NCT04515147
13.	DNA plasmid vaccine + Adjuvant	Osaka University/ AnGes/ Takara Bio	DNA plasmid vaccine + Adjuvant	Phase 1 / 2 NCT04463472
14.	DNA plasmid vaccine	Cadila Healthcare Limited	DNA plasmid vaccine	Phase 1 / 2 CTRI/2020/07/026352

15.	DNA Vaccine (GX-19)	Genexine Consortium	DNA Vaccine (GX-19)	Phase 1 / 2 NCT04445389
16.	Whole-Virion Inactivated	Bharat Biotech	Whole-Virion Inactivated	Phase 1 / 2 NCT04471519
17.	INO-4700	Inovio Pharmaceuticals/ International Vaccine Institute	DNA plasmid vaccine with electroporation	Phase 1 / 2 NCT04447781
18.	RBD-based	Kentucky Bioprocessing, Inc	RBD-based	Phase 1 / 2 NCT04473690
19.	mRNA	Arcturus/Duke-NUS	mRNA	Phase 1 / 2 NCT04480957
20.	Inactivated	Research Institute for Biological Safety Problems, Rep of Kazakhstan	Inactivated	Phase 1 / 2 NCT04530357
21.	CovidVax	Institute of Medical Biology, Chinese Academy of Medical Sciences	Inactivated	Phase 1 / 2 NCT04470609
22.	S protein (baculovirus production)	Sanofi Pasteur/GSK	Protein Subunit	Phase 1 / 2 NCT04537208
23.	RBD-HBsAg VLPs	SpyBiotech/Serum Institute of India	VLP	Phase 1 / 2 ACTRN12620000817943
24.	Protein Subunit	Clover Biopharmaceuticals Inc./GSK/Dynavax	Native like Trimeric subunit Spike Protein vaccine	Phase 1 NCT04405908
25.	Protein Subunit	Vaxine Pty Ltd/Medytox	Recombinant spike protein with Advax™ adjuvant	Phase 1 NCT04453852
26.	Protein Subunit	University of Queensland/CSL/Seqirus	Molecular clamp stabilized Spike protein with MF59 adjuvant	Phase 1 ACTRN12620000674932p ISRCTN51232965
27.	Measles-vector based	Institute Pasteur/Themis/Univ. of Pittsburg CVR/Merck Sharp & Dohme	Replicating Viral Vector	Phase 1 NCT04497298

28.	LNP-nCoVsaRNA	Imperial College London	mRNA	Phase 1 ISRCTN17072692
29.	mRNA	People's Liberation Army (PLA) Academy of Military Sciences/Walvax Biotech.	mRNA	Phase 1 ChiCTR2000034112
30.	VLP	Medicago Inc.	Plant-derived VLP adjuvanted with GSK or Dynavax adjs.	Phase 1 NCT04450004
31.	S-2P protein + CpG 1018	Medigen Vaccine Biologics Corporation/NIAID/Dynavax	Protein subunit	Phase 1 NCT04487210
32.	Replication defective Simian Adenovirus (GRAd) encoding S	ReiThera/LEUKOCARE/ Univercells	Non-Replicating Viral Vector	Phase 1 NCT04528641
33.	Ad5-nCoV	Institute of Biotechnology, Academy of Military Medical Sciences, PLA of China	Non-Replicating Viral Vector	Phase 1 NCT04552366
34.	Ad5 adjuvanted Oral Vaccine platform	Vaxart	Non-Replicating Viral Vector	Phase 1 NCT04563702
35.	MVA-SARS-2-S	Ludwig-Maximilians - University of Munich	Non-Replicating Viral Vector	Phase 1 NCT04569383
36.	RBD + Adjuvant	Instituto Finlay de Vacunas, Cuba	Protein Subunit	Phase 1 IFV/COR/04
37.	Peptide	FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo	Protein Subunit	Phase 1 NCT04527575
38.	RBD (baculovirus production expressed in Sf9 cells)	West China Hospital, Sichuan University	Protein Subunit	Phase 1 ChiCTR2000037518

39.	SARS-CoV-2 HLA-DR peptides	University Hospital Tuebingen	Protein Subunit	Phase 1 NCT04546841
40.	S1-RBD-protein	COVAXX	Protein Subunit	Phase 1 NCT04545749
41.	Intranasal flu-based-RBD	Beijing Wantai Biological Pharmacy/ Xiamen University	Replicating Viral Vector	Phase 1 ChiCTR2000037782

EVIDENCE ON EFFECTIVENESS AND SAFETY

There were eight articles retrieved from the scientific databases such as Medline, EBM Reviews, EMBASE via OVID, PubMed and from the general search engines [Google Scholar and US Food and Drug Administration (USFDA)] on the effectiveness and safety of COVID-19 vaccines.

Table 2 Summary Of Evidence Retrieved On Candidate Vaccines.

Name of technology & Developer	Summary of Technology	Clinical trials	Remarks
mRNA-1273 by: Moderna	Using mRNA technology It is a lipid nanoparticle (LNP)-encapsulated mRNA based vaccine that encodes full-length, perfusion stabilized spike protein of SARS-COV-2. IM 0.5ml Day 1 & Day 29 (on Deltoid)	**Phase 1 study** (NCT04283461)[13] -open-label trial -Days 1 and days-29 vaccination schedule across 3 dose levels (25, 100, 250 µg) n= 45 healthy adults (18 to 55 years old) with n=15 participant for each dosage group. *Participants were not screened for SARS-CoV-2 infection by serology or polymerase chain reaction before enrollment. <u>Safety profile</u> AEs were generally transient and mild to moderate in severity. No serious AEs. -One participant in the 25-µg group developed transient urticaria at day 5 post-vaccination. The most commonly reported AE : pain at the injection site (100%), fatigue (80%), chills (80%), headache (60%) &myalgia (53%).	Received Fast Track Designation by US FDA.[15] Phase 3 study of mRNA-1273 being conducted in collaboration with the NIH and BARDA (started on 25 July 2020)

		Efficacy -neutralizing antibody titers were detected at Day 43 in all participants in all dose cohorts after second vaccinations. -after 1st vaccination, seroconversion in all participants by day 15 -geometric mean titers of antibody titers were 2.1-fold higher than those seen in convalescent sera (n=38) among 25-µg group and the titer is higher among higher dosage group. **Phase 3 COVE Study (press)[14]** N=30,000 participants in the U.S. Efficacy First interim analysis was based on 95 cases, of which 90 cases of COVID-19 were observed in the placebo group versus 5 cases observed in the mRNA-1273 group, resulting in a point estimate of vaccine efficacy of 94.5% (p <0.0001).[14] However, there was no specification defining its efficacy either neutralising antibody titer or seroconversion in the statement above. Safety The majority of adverse events were mild or moderate in severity. Grade 3 (severe) events greater than or equal to 2% in frequency after the first dose included injection site pain (2.7%), and after the second dose included fatigue (9.7%), myalgia (8.9%), arthralgia (5.2%), headache (4.5%), pain (4.1%) and erythema/redness at the injection site (2.0%). These solicited adverse events were generally short-lived. These data are subject to change based on ongoing analysis of further Phase 3 COVE study data and final analysis.	

BNT162 (BNT162b1& BNT162b2) by: BioNTech, Pfizer & Fosun Pharma -USA & Germany	Using mRNA technology. It encodes an optimized SARS-CoV-2 full length spike glycoprotein (S).	**Phase 1/2 study** (NCT04368728)[16] **(BNT162b1)** -n= 45 healthy adults age 18 to 55 years old 30 µg dose level in a 2 dose regimen (21 days apart) <u>Safety</u> No serious adverse events were reported. severe AE: 1 fever post-vaccine and 1 sleep disturbance <u>Efficacy</u> RBD-binding IgG concentrations and SARS-CoV-2 neutralizing titers in sera increased with dose level and after a second dose. Geometric mean neutralizing titers reached 1.8- to 2.8-fold that of a panel of COVID-19 convalescent human sera. **Phase 3 (press)[17]** N=43,538 participants Vaccine candidates versus placebo. Analysis evaluated 94 confirmed cases of COVID-19 in trial participants, vaccine candidate was found to be more than 90% effective (at 7 days after the second dose) in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection in the first interim efficacy analysis.[17] However, there was no specification defining its efficacy either neutralising antibody titer or seroconversion in the statement above.	Both vaccines have received Fast-Track Designation from US FDA.[18] On 27th July 2020, phase 2/3 study, n=30,000 (aged 18 – 85 years old) started in the U.S. and expected to include approximately 120 sites globally . On 12th September 2020, phase 3 pivotal COVID-19 vaccine trial expanded up to approximately 44,000 participants, increases the study's population diversity, and include adolescents as young as 16 years of age and people with chronic, stable HIV, Hepatitis C, or Hepatitis B infection. The vaccine is planned to be distributed by end of 2020.
NVX-CoV2373 by: Novavax -USA	Using recombinant nanoparticle technology to generate antigen derived from the coronavirus spike (S) protein and contains	**Phase 1/2** (NCT04368988)[19] evaluated two doses (5 and 25 µg) n= 131 healthy adults ages 18-59 years old. (vaccine with adjuvant= 83, without adjuvant= 25, and placebo =23). <u>Safety</u> - No serious adverse events (SAEs) were reported <u>Efficacy</u> -The vaccine induced neutralization titers in 100% of participants -Both 5 µg and 25 µg adjuvanted doses	To start pivotal Phase 3 clinical trial by end of 2020.

	Novavax' patented saponin-based Matrix-M™ adjuvant to enhance the immune response and stimulate high levels of neutralizing antibodies.	generated peak geometric mean titer (GMT) greater than 1:3,300 . -Matrix-M™ adjuvant induced robust polyfunctional CD4+ T cell responses.	
Coronavac by: Sinovac Biotech Ltd (Sinovac Life Sciences) - China	Inactivated strain of SARS-CoV-2 vaccine -2 doses 14 days apart -0.5 ml injection	**Phase 1/2 in China**[20] **(press)** -n = 743 (143 phase I & 600 phase II healthy volunteers aged 18-59 years old) <u>efficacy</u> -Induces neutralizing antibodies 14 days after vaccination. -Seroconversion rate was 90% <u>Safety</u> -no serious adverse event after vaccination	-Late August 2020, CoronaVac was **approved** for emergency use as part of a program in China to vaccinate high-risk groups such as medical staff.[21] -To start phase III trial in Brazil partnering with Butantan Institute, Sao Paolo -Reported on 3/6/2020 -Will recruit 9,000 individuals (doctors & HCWs) -Vaccine expected to be ready & distributed by June 2021
COVID-19 vaccine by: Sinopharm Group (China National Biotec Group – CNBG) – China	Inactivated virus received 3 intramuscular injections at days 0, 28, and 56.	**Phase 1 / 2** (ChiCTR2000031809)[22] Phase 1 recruited 96 participants (aged 18-59 years old) - 3 doses group (2.5, 5, and 10 μg/dose) and adjuvant-only group (n=24 each group) Phase 2 recruited 224 adults -were randomized to • 5 μg/dose in 2 schedule groups (injections on days 0 &14 [n = 84] vs alum only [n = 28]	-United Arab Emirates (UAE) **approved** the vaccine for emergency use, making China's Sinopharm the first vaccine maker to receive approval to deploy a COVID-19 candidate in a foreign country. -Phase III trial ongoing in UAE in partnership

		• 5 μg/dose in day 0 & 21 [n = 84] vs alum only [n = 28] <u>Efficacy</u> -Induces antibodies in 28 days -100% seroconversion rate <u>Safety</u> -The most common AEs: injection site pain, followed by fever, which were mild and self-limiting -no serious adverse reactions were noted	with Abu Dhabi's G42 Healthcare -Reported on 16/7/20 -Will recruit 15,000 volunteers
Ad5-nCOV By: CanSino Biologics - China	Using Adenovirus-based viral vector vaccine technology -cloned optimised full-length spike gene based on Wuhan-Hu-1 with tissue plasminogen activator signal peptide gene into E1 and E3 deleted ad5 vector	**Phase 1** n=108, (healthy, age 18-60 years old) <u>Safety:</u> No severe AEs reported <u>Efficacy:</u> -ELISA antibodies and neutralising antibodies increased significantly at day 14 and peaked at day 28 post-vaccine. -Specific T-cell response peaked at Day 14. **Phase 2 (NCT04341389)[23]** -randomised, double-blind, placebo-controlled -Total of 508 participants receive the vaccine at a dose of • 1×10^{11} viral particles per mL (n=253) • 5×10^{10} viral particles per mL (n=129) • Placebo (n=126) <u>Efficacy</u> Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2, with GMTs of 19.5 (95% CI 16.8–22.7) and 18.3 (14.4–23.3) in participants receiving 1×10^{11} and 5×10^{10} viral particles, respectively. **Seroconversion at D28** • The vaccine induced seroconversion of the neutralising antibodies in 59% and 47% of participants,and	China **approved** limited use of CanSino's vaccine for its military in June 2020. Starting September 2020, phase 3 trial of Ad5-nCoV vaccine candidate is being tested on 40,000 participants in Russia, Saudi Arabia, Pakistan and Mexico.

		seroconversion of binding antibody in 96% and 97% of participants, in the 1 × 10^{11} and 5 × 10^{10} viral particles dose groups, respectively. **Tcell responses** -At Day 28, vaccine induced significant SARS-CoV-2 spike glycoprotein-specific IFNγ-ELISpot responses in 90% patients (95% CI 85–93) receiving the 1 × 10^{11} viral particles dose, and 88% (95% CI 81–92) receiving the 5 × 10^{10} viral particles dose. <u>Safety</u> Most common systematic AEs reported: fatigue, fever, headache, injection site pain. No serious AEs reported.	
ChAdOx1 nCoV-19 By: AstraZeneca - UK	Using chimpanzee adenovirus-vectored vaccine expressing the SARS-CoV-2 spike protein (ChAdOx1)	**Phase 1/2 (NCT04324606)[24]** Single-blind, RCT, multicenter n= 1077 participants (aged 18–55 years old) were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or meningococcal conjugate vaccine MenACWY (n=534) 10 participants assigned to a non-randomised, unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. <u>Safety (at day 28)</u> -most reported AE: pain, feeling feverish, chills, muscle ache, headache, and malaise -no serious AEs reported <u>Efficacy</u> - Neutralising antibody responses detected 91% after a single dose when measured in MNA_{80} and in 100% participants when measured in $PRNT_{50}$. -After a booster dose, all participants had neutralising activity -T-cell response that peaked by day 14 and maintained two months after injection was observed in all subjects	Aim for approval by the end of this year.

Sputnik V **By: Gamaleya Research Institute, Russia**	recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein (rAd26-S and rAd5-S)	**Phase 1/2 studies** (NCT04436471 and NCT04437875)[7] **non-randomised, multi-center, testing on vaccine with two formulations (frozen [Gam-COVID-Vac] and lyo-philised [Gam-COVID-Vac-Lyo]).** n= 76 , healthy adult age: 18–60y.o Phase 1 (n=38) IM on day 0 either rAd26 or rAd5, safety assessed at day 28. Phase 2 (n=38) IM rAd26-S given on day 0 and rAd5-S on day 21. <u>Safety</u> Most common AE: pain at injection site (44 [58%] hyperthermia (38 [50%]) headache (32 [42%]), asthenia (21 [28%]) muscle & joint pain (18 [24%]) There was no serious AE detected. <u>Efficacy</u> -Antigen-specific IgGs: Seroconversion rate of 100% on day 28 and day 42. -Cellular immune responses showed formation of antigen-specific cells of both T-helper ($CD4^+$) and T-killer ($CD8^+$) and an increase in the concentration of interferon-γ secretion in peripheral blood mononuclear cells, in 100% of volunteers at day 28 post-vaccination.	- On 11th August 2020, Sputnik V was **approved** for usage in Russia -Currently, phase 3 trial has been launched.
Ad26.COV2.S **By: Janssen Vaccines & Prevention B.V.**	Non-replicating adenovirus 26 vector expressing the stabilized pre-fusion spike (S) protein of SARS-CoV-2.	**Phase 1/2a (NCT04436276)[25]** **randomized, double-blinded, placebo-controlled** cohort 1a & cohort 1b (aged 18-55 years old, n= 402) cohort 3 (aged 65–75years old, n=394). Ad26.COV2.S were given $5x10^{10}$ or $1x10^{11}$ vp or placebo (0.9% saline) administered intramuscularly (IM) as single-dose or two-dose schedules, 8 weeks apart.	

		Safety -most frequent local AE : injection site pain -most frequent systematic –AE: fatigue, headache and myalgia -two serious AEs: • one hypotension judged 211 by the investigator to not be vaccine related because of a past history of recurrent hypotension • one participant with fever :judged by the investigator to be vaccine-related Efficacy **S-binding antibody titers** By Day 29 after vaccination, GMTs had increased to respectively 528 (95% CI: 442-630) and 695 (95% CI: 596- 810), with 99% seroconversion in each dose group. **Neutralizing antibodies** Similarly, high response rates were observed in a wtVNA. 29 days post vaccination, 98% of the participants had detectable neutralizing antibodies. 92% of cohort 1a participants and respectively 6 out of 6, and 5 out of 6 recipients of the $5x10^{10}$ vp and $1x10^{11}$ vp dose level in cohort 3, seroconverted for SARS-CoV-2 neutralizing antibodies.	
EpiVacCorona **By:** **Vektor State Research Center of Virology and Biotechnology in Russia**	peptide vaccine	**Phase 1 / 2 (press)**[26] Participants: 57 volunteers, while 43 received a placebo two injections administered 14 to 21 days apart. -No details of the clinical trials mentioned.	EpiVacCorona received **approval** before a Phase 3 trial to demonstrate that it was safe and effective.

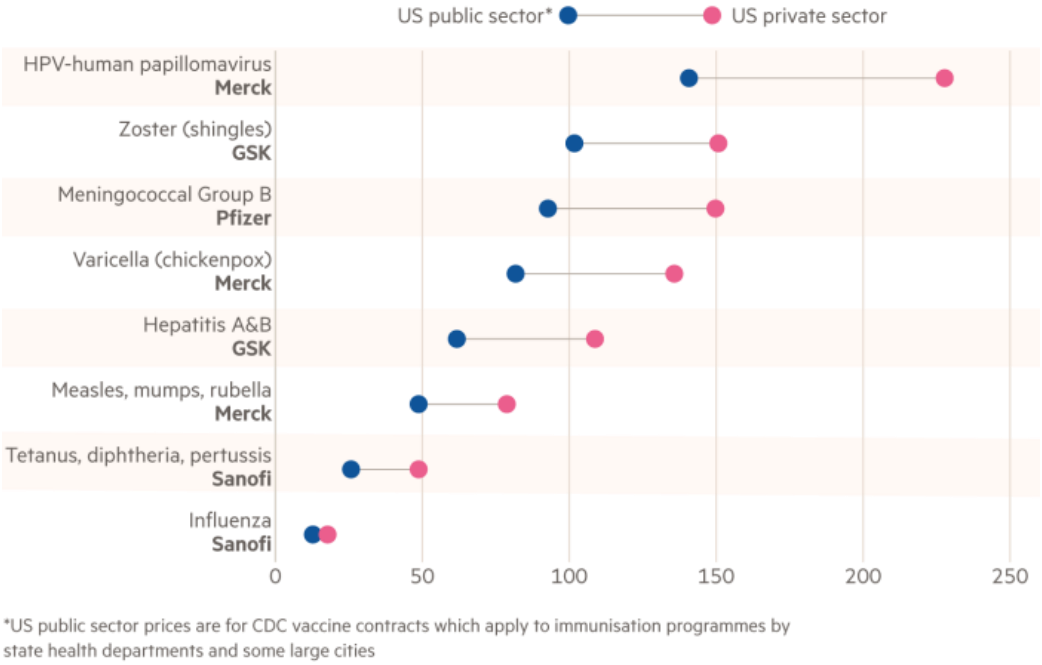
Cost

There were no retrievable evidences on the cost-effectiveness of the above-mentioned candidate vaccines. The price range of COVID-19 candidate vaccines ranges from USD 3 to 30 per dose which equivalent to RM 12.30 to RM123.00. [27]

AstraZeneca expected to sell its ChAdOx1-S vaccine at about USD 3 to USD 4 per dose, whereas Moderna's mRNA-1273 was sought to sell at about USD 50 to USD 60 for its course of two injections. Meanwhile Sinovac, has began selling its vaccine in select cities at USD 60 (~RM 246.15) for two shots as part of an emergency use programme with hundreds of thousands of participants.[27]

The price range of currently available vaccines is shown below. (Figure 1)

Figure 1 Price Range of Existing Vaccines



*US public sector prices are for CDC vaccine contracts which apply to immunisation programmes by state health departments and some large cities

Source: Financial times

Other issue

The government has to provide effective vaccine cold chain to maintain its potency from the time of manufacture until the point of administration. The key procedures must be observed (as recommended by WHO) include:[28]

- store vaccines and diluents within the required temperature range at all sites
- pack and transport vaccines to and from outreach sites according to recommended procedures
- keep vaccines and diluents within recommended cold chain conditions during immunization sessions.

CONCLUSION

According to interim data and phase 1 / 2 clinical data retrieved above, the listed COVID vaccines produce neutralising antibodies which indicate potential efficacy against COVID-19 infection and not associated with severe adverse events. However, few other factors need consideration including how long the protection would last for each vaccine and the cost of the vaccine. The on-going Phase 3 results are very much required to determine the safety and efficacy of the vaccines for larger population.

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Disclaimer: This rapid assessment was prepared to provide urgent evidence-based input during COVID-19 pandemic. The report is prepared based on information available at the time of research and a limited literature. It is not a definitive statement on the safety, effectiveness or cost effectiveness of the health technology covered. Additionally, other relevant scientific findings may have been reported since completion of this report.

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