

**Research Article,**

# **Evaluation of the Moderna, Pfizer/Biotech, Astrazeneca/Oxford and Sputnik V Vaccines for Covid-19**

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**Abstract:**

The SARs-CoV-2 (COVID-19) virus, which was first identified in December 2019, in Wuhan China, is a respiratory virus that induces respiratory distress and a systemic inflammatory reaction in the vasculature mediated by a cytokine storm. Currently, 72 million people have been infected with 1.6 million deaths giving a mortality rate of 2.2% despite the best post-infective medical intervention available. Due to the rapid spread of the COVID virus and the worldwide pandemic that has developed, the rush for the development of a vaccine has become a priority amongst health care official's world-wide. In this review, we discuss what is currently known about the mechanism of action, efficacy, and toxicity of three of the most promising vaccines mRNA-1273 (Moderna), BNT162b2 (Pfizer/BioNtech), ChAdOx1 nCoV-19 (Astrazenac/Oxford), and rAd26)/rAd5 (Sputnik V) against COVID-19.

**Key words:** COVID-19, SARs-Cov-2, vaccine, ChAdOx1 nCoV-19, AstraZeneca, Oxford, Moderna, mRNA-1273, Gamaleya, Sputnik V, Pfizer, BNT162b2

## **INTRODUCTION**

In December 2019, a cluster of patients with a form of respiratory distress syndrome were linked to a seafood wholesale market in Wuhan, China. Samples from these patients allowed for the isolation of a new virus SARS-CoV-2 (COVID-19)<sup>1</sup>. Since that report over 72 million individuals have become infected with 1.6 million related deaths.<sup>2</sup> The deaths follow a cytokine storm that creates not only pulmonary edema but a systemic hyperinflammatory state.<sup>3</sup> This results in vascular damage, altered blood flow and hypercoagulability of blood with systemic organ damage often inclusive of cardiomyopathy and associated sudden death.<sup>4</sup> Those most at risk for severe COVID are those over the age of 60, and those with chronic disease. In both cases, the adaptive immune system is impaired and fails to

suppress the innate immune system which is responsible for the cytokine storm.<sup>5</sup>

The COVID-19 virus is a messenger RNA virus that is similar to the common cold virus. The COVID-19 virus enters lung type II alveolar cells, enterocytes of the small intestine, arterial and venous endothelial cells, and smooth muscle cells of the vasculature via its S spike protein binding the ACE2 receptor of the target cells. Variances in the expression of the ACE2 receptor may be partly responsible for difference susceptibility to infections by sex and ethnic group.<sup>6</sup> Mutations in the S-Spike protein have been associated with differences in the virulence of COVID-19 subtypes.<sup>7</sup> It is against this S protein that current vaccines have been developed against to target. There is little knowledge of post-infection

immunity to SARS-CoV-2 with cases being reported of reinfection. This finding may be a result of the rapid mutation of the COVID -19 virus implying the potential need for continuous vaccine development yearly as is the case of flu vaccine.<sup>8,9</sup> Among the three most promising vaccines are the novel mRNA vaccines BNT162b2 (Pfizer/BioNtech), mRNA-1273 (Moderna) and the DNA vaccines ChAdOx1 nCoV-19 (AstraZeneca/Oxford), rAd26/rAd5 (Sputnik V) vaccines. Here we outline the mechanism of action of these vaccines and compare their safety and efficacy.

### VACCINE MECHANISM OF ACTION

The Moderna and Pfizer/BioNtech vaccines are both delivered by lipid nanoparticles which phospholipid membranes are surrounding the mRNA those codes for the S protein of the COVID-19 virus. Once the lipid nanoparticle is injected, the phospholipid membrane of the nanoparticle will fuse with the host membrane and release the mRNA into the cytoplasm of the target cell. The mRNA of the S protein is then translated at the rough endoplasmic reticulum producing the S protein within the cytoplasm. The S protein is then degraded and expressed by Major Histocompatibility Complex I (MHC I) and II (MHC II). MHC II is found on antigen presenting immune cells such as macrophages, dendritic cells, and B-cells. A T-helper cell binds to the S protein fragment presented by the MHC II molecule with its TCR protein while it also binds with the MHC II molecule itself with its CD4 receptor. The T-helper cell then releases interleukins which cause B cells to proliferate and differentiate into plasma cells. These plasma cells then release specific antibodies to the S protein fragment. These same interleukins cause the original T-helper to proliferate and form T-helper memory cells.

(Fig.1).

Cytotoxic T cells also play a part by binding to S protein fragments that are expressed by non-immune cells through the MHC I complex. The CD8 molecule of the cytotoxic T cell will bind to MHC I while the cytotoxic T cell TCR will bind the S protein fragment. The cytotoxic T cell will then release cytokines that will amplify the T-Helper cells own stimulation of B cell differentiation into plasma cell proliferation. In addition, the cytotoxic T cell will be primed to kill any infected cells that later present with the S protein of the COVID-19 virus.

The AstraZeneca/Oxford vaccine is composed of DNA that codes for the S protein and is encased in a capsid from a chimpanzee adenovirus. The adenovirus with the accompanying DNA is brought into the cell by endocytosis. Once, inside the cytoplasm the DNA is released into the cytoplasm. This DNA migrates to the cell nucleus where it is transcribed creating mRNA that codes for the S protein. This mRNA is translated at the rough endoplasmic reticulum where it creates the S protein in the cytoplasm. As is the case with the S protein made by the mRNA vaccines above the S protein is processed and presented by the MHC I and MHC II complexes by non-immune and immune antigen presenting cells, respectively.

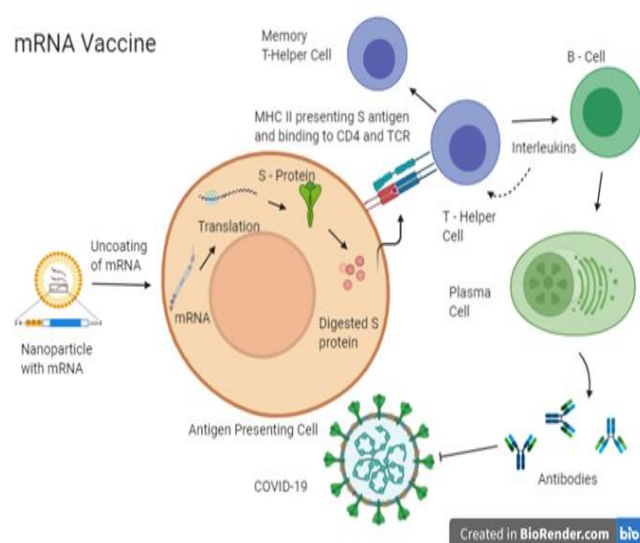


Fig1. The mRNA is delivered via a nano particle to the target cell. The phospholipid membrane of the nanoparticle fuses with the cell membrane releasing the mRNA which is translated by the

cell's machinery. An S protein is made and degraded into fragments which are present by MHC II molecules to T- Helper cells. The T Helper cells then release Interleukins which stimulate the creation of memory T – Helper Cells and Plasma cells which produce antibodies against parts of the S protein on SARs-CoV-2.

**EFFICACY**


The approach to developing vaccines against COVID-19 has followed two pathways, a more traditional utilizing DNA inserted into a viral capsid and the newer technology of mRNA placed within a phospholipid membrane forming a nanoparticle. The advantages of mRNA vaccines are thought to include the use of animal cells or the need for mRNA to enter the nucleus of the cell and potentially integrate into the host DNA.<sup>10</sup> Disadvantages include the lower stability of mRNA as indicated by the need to store these vaccines and very low temperatures and a theoretically lesser ability to stimulate the cellular manufacturing of S protein antigen.

The Moderna vaccine was given to 30,000 individuals with a placebo and non-placebo group (vaccinated). Both groups were given injections at day 0 and day 28. At 14 days, after the second injection both the placebo and the vaccinated groups were evaluated for clinical symptoms. In the non-placebo group, 185 individuals showed clinical symptoms while among the vaccinated group 11 individuals showed clinical symptoms. Of the 185 individuals in the placebo group there were 30 severe cases while of those who received the vaccine there were 0 severe cases.<sup>11</sup> this gives a maximum efficacy of 94.5% against the development of clinical symptoms and a maximum efficacy of 100% against severe disease.

The Pfizer/BioNtech vaccine was given to 43,000 individuals broken up into placebo and vaccinated groups with injections given at day 0 and day 21. Seven days after the second dose was given the

trial was unmasked and those with clinical symptoms categorized. In the placebo, group 162 individuals presented with clinical symptoms and 8 in the vaccinated group. This gives an efficacy against clinical symptoms of 95%. Of the 162 symptomatic patients in the Placebo group, 9 went on to develop severe disease while 1 in the vaccine group developed severe disease. This gives an efficacy against severe disease about 87% for those who developed clinical symptoms. The AstraZeneca/Oxford DNA vaccine or the meningococcal vaccine serving as the baseline was given at day 0 and again at day 28 with a PCR test looking for infection and not clinical symptoms as earlier discussed at 14 days after the second dose. The size of the study was 12,000 individuals with an efficacy to prevent infection at 70% and an efficacy to prevent severe disease at 100%.<sup>12</sup> The Sputnik V vaccine produced by the Russian Federation is a DNA vaccine that used two different types of adenovirus vectors (rAd26) and rAd5. The vaccine was administered as follows initially either the rAd26 or rAd5 adenovector was administered. This was followed 5 days later by administration of rAd26 and 21 days later of rAd5.<sup>13</sup> PCR was then completed to determine the efficacy by evaluating positive PCR cases between the treatment and placebo groups. The vaccine had an efficacy of 91.4 % in preventing infection however the ability of the vaccine to prevent serious disease was not reported<sup>13</sup> See Table I.

**Table 1 Comparative Efficacy Vaccines**

	Study Size	Prevention of Symptoms	Prevention of Infection	Prevention of Severe Disease
ChAdOx1nCoV-19(AstraZeneca/Oxford)	12,000	unknown	70%	100%
mRNA-1273 (Moderna)	30,000	94.5%	unknown	100%
Sputnik V Gamaleya/Russian Federation	19,000	unknown	91.4%-95%	unknown
BNT162b2 (Pfizer/BioNtech)	43,000	95.0%	unknown	87%

## SIDE EFFECTS

Among the most important and common side effects of vaccines are anaphylaxis, febrile seizures and autoimmune disease with anaphylaxis generally being the most prevalent of the side effects that are life threatening.<sup>14</sup> Other side effects that are common with vaccines are fever, pain, headache and muscle/joint pain. The side effects are generally graded as follows:

**Grade 1** are mild adverse events. (e.g., minor event requiring no specific medical

Intervention; asymptomatic laboratory findings only; marginal clinical relevance)

**Grades 2** are moderate adverse events (e.g., minimal intervention, local intervention.

Non-invasive intervention; transfusion; elective interventional radiological procedure.

Therapeutic endoscopy or operation).

**Grades 3** are severe and undesirable adverse events (e.g., significant symptoms requiring

Hospitalization or invasive intervention; transfusion; elective interventional radiological

Procedure; therapeutic endoscopy or operation).

**Grades 4** are life threatening or disabling adverse events (e.g., complicated by acute, life threatening metabolic or cardiovascular complications such as circulatory failure,

Hemorrhage, sepsis; life-threatening physiologic consequences; need for intensive care or

Emergent invasive procedure; emergent interventional radiological procedure, therapeutic

Endoscopy or operation).

**Grade 5** death.

The Pfizer/BioNtech side effects were categorized by those from the ages of 16 – 55 and those over the age of 55. For those under the age of 55 headache 42%, fever 4%, muscle/joint pain 33% and fatigue 47%. In those over the age of 55 headache 39% fever 11% muscle/joint pain 48% and fatigue 51%.<sup>15</sup> The Pfizer/BioNtech vaccine


has been associated with rare anaphylaxis reactions of 0.63% of those who have taken the vaccine. However, 0.51% of those who did not have the vaccine also had an allergic reaction implying that most of the allergic reactions were not associated with the vaccine. As most of the individuals had a history of severe allergic reactions prior to being enrolled to the study it is safe to assume that the actual number of those who had allergic reactions directly due to the vaccine was actually around 0.12% while, 0.51% were most likely exposed around the time of vaccination to an allergen not related to vaccination.

The side effects due to the Moderna vaccine were potentially skewed upwards as all the participants were over the age of 56. The side effects were also classified at the respective dosages of 25 µg and 100 µg. The reported number of side effects after the second dose was administered at the reported low and high disease were as follows 40% 84% headaches; 18% 20% fever; 60% 84% muscle/joint pain and 50% 83% for fatigue.<sup>11</sup> There were no serious adverse side effects reported. The side effects of the AstraZeneca/BioNtech vaccine were evaluated with and without the administration of Tylenol. In the group without Tylenol headaches were 42%, fever 51%, muscle/joint pain 60% and fatigue 70%.<sup>12</sup> the group that received Tylenol is not reported here as this can mask side effects. Severe adverse events were at 0.3% and revolved around a case of hemolytic anemia.

The Sputnik V vaccines come in two forms frozen and lyophilized. The frozen form was associated with a much higher reporting of side effects with 100% reporting hyperthermia, 55% headache and 25% muscle/joint pain, this compared with 35%, 25% and 30% for the lyophilized form. Most significantly there were no severe reactions (Grade 3) reported. Interestingly, despite the theoretical advantage of mRNA vaccines to have fewer side effects than DNA vaccines this was not observed when comparing these vaccines except for a modestly higher risk of a fever with the

DNA vaccines. It should also be noted that the trials thus far are limited by the exceptionally short time frame of reporting side effects. Additionally, no information on the side effects towards children or pregnant women is reported. The side effects are summarized on

**Table 2.**

	Head ache Grad e 1-2	Fev er Gr ade 1-2	Muscle/ Joint Pain Grade 1-2	Fatig ue Grad e 1-3	Seve re Adv erse
ChAdOx1nCoV-19 (AstraZeneca/Oxford) c/o Tylenol	42%	51%	60%	70%	0.3%
mRNA-1273 (Moderna) <i>All over the age of 56</i> Dosage 25 µg - 100 µg	40%-84%	18%-20%	60% - 84%	50 - 83%	0%
Sputnik V (Phase Gamaleya/Russian Federation Frozen)	55%	100%	25%	Not Reported	0%
Sputnik V (Phase Gamaleya/Russian Federation Lyophilized)	25%	35%	30%	Not Reported	0%
BNT162b2 (Pfizer/BioNtech) (16-55) – (55 or older)	42%-39%	4% - 11%	33-48%	47-51%	0.6%

## DISCUSSION

The 4 vaccines evaluated and compared here all have the ability to minimize infections or the presentation of clinical symptoms. Perhaps, more importantly the Moderna, AstraZeneca/Oxford, and Pfizer/BioNtech vaccines all seem to be effective in preventing serious disease with statistically no difference. The short time frame of

evaluation however may skew the effectiveness of the vaccines upwards. The short time frame was most likely due to the rush to find a vaccine and the intense competition to influence one's market share. It is currently unknown how long the antibody response will last against the S protein of the COVID-19 virus. COVID-19 an RNA virus has a very unstable genome and hence like the common cold of which the virus is related it mutates very rapidly. At this time, there are at least 6 major subtypes which seem to be aggregating geographically. Type I in China and Southeast Asia, Type II in Western Europe, Type III is prevalent in the United States, Type IV in Japan, Type V in Australia, and Type VI in South America.<sup>16</sup> This means that vaccines developed in one part of the World may not be as efficacious elsewhere. The best estimate is 6-8 months meaning that these vaccines will need to be administered every year in a similar fashion that the flu shot is given. The efficacy of the vaccines did not seem to be dependent on the technology used as the mRNA vaccines and the DNA based vaccines seem equally efficacious.

The side effects were relatively minor but quite common. Surprisingly, the side effects of the mRNA vaccines had a similar rate as the DNA vaccines excluding fever where the DNA based vaccines were more common. Most importantly serious adverse effects were relatively rare with the caveat there has only been a relatively short time frame. Indeed, the safeties of these vaccines or their efficacy in those under the age of 16 and in pregnant women are unknown. The risk for those with a history of allergies may also be elevated. The Moderna vaccine must be stored at -4 F (-20 C), the Pfizer/BioNtech vaccine at -94 F (-70 C), and the AstraZeneca/Oxford vaccine at 36 – 46 F (2.2 – 7.8C). The ability of the AstraZeneca/Oxford and Sputnik V vaccines to be stored at normal refrigeration temperature may play a large role in the ability to distribute this vaccine over the others to rural areas and poorer countries.<sup>17</sup>



In time it is expected that the virulence of COVID virus in terms of its ability to cause serious disease will decrease. This is due to a fundamental principle in microbiology that the more prevalent a microbe becomes the less deadly it becomes, this with the proven ability of these vaccines to limit serious disease means the end of this Pandemic is in sight.

## SUMMARY

All four of the vaccines evaluated here seem to be effective in either preventing infection or the symptoms of infection. Most importantly the Moderna, AstraZeneca/Oxford, and Pfizer/BioNtech vaccines seem effective and nearly equivalent in preventing serious disease due to COVID-19. Evidence, for the ability of the Sputnik V vaccine to prevent serious disease has yet to be published though it is effective in preventing infection. All four vaccines seem relatively safe with the greatest risk being anaphylaxis, though rare can be life threatening. Though these vaccines will more and likely be approved following the completion of their phase III clinical trials one should consider a benefit cost analysis. Those at high risk such as those over the age of 60 or with moderate to severe chronic health problems should be the first to receive these vaccines. Those at moderate risk such as health care workers or in a gray area 40 years and above or with mild chronic disease may also seek to be vaccinated. Those who are healthy and under 40 might want to take a watch and wait approach as the full nature of the efficacy and side effects generally are not completely known until sometime after both phase III clinical trials and drug approval have occurred. Due to regional subtypes of COVID-19, vaccines created in one part of the World may not be as efficacious elsewhere. The vaccine efficacy and side effects in those under the age of 16 or in pregnant women is unknown.

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## REFERENCES

1. Zhu N., Zhang D, Wang W, Li X, M.D., Yang B et al.. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020; 382:727-733 DOI: 10.1056/NEJMoa2001017.
2. Sutcliffe E. Global Data Epidemiologist Report: Global Covid cases pass 72.3 million – deaths exceed 1.6 million. *Pharmaceutical Technology* accessed 14 Dec 2020. <https://www.pharmaceutical-technology.com/special-focus/covid-19/globaldata-epidemiologist-report-global-covid-cases-pass-72-3-million-deaths-exceed-1-6-million/>
3. Fajgenbaum DC, June CH. Cytokine Storm. *NEJM* 2020; 383:2255-73. DOI: 10.1056/NEJMra2026131.
4. Ahmed S, Zimba O, Gasparyan AY. Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. *Clin Rheumatol.* 2020 Sep; 39 (9):2529-2543. Doi: 10.1007/s10067-020-05275-1.
5. Zhao J, Yang X, Auh SL, Kim KD, Tang H et al. . . . Do adaptive immune cells suppress or activate innate immunity? *Trends Immunol.* 2009 Jan; 30 (1):8-12. doi: 10.1016/j.it.2008.10.003
6. Li Q, Cao, Rahman P. Genetic variability of human angiotensin-converting enzyme 2 (hACE2) among various ethnic population, *Mol Genet Genomic Med* 2020 Aug;8(8):e1344. doi: 10.1002/mgg3.1344.
7. Wu S, Tian C, Liu P, Guo D, Zheng W et al.. Effects of SARS-CoV-2 mutations on protein structures and intraviral protein-protein interactions. *J Med Virol.* 2020 Oct 14;10.1002/jmv.26597. Doi: 10.1002/jmv.26597.
8. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A et al. (2020) Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *NEJM* DOI: 10.1056/NEJMoa2034577.

9. Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N et al.. Genomic evidence for reinfection with SARS-CoV-2: a case study. *Lancet Infectious Disease* Oct 20, 2020. DOI: [https://doi.org/10.1016/S1473-3099\(20\)30764-7](https://doi.org/10.1016/S1473-3099(20)30764-7).
10. Liu MA. A Comparison of Plasmid DNA and mRNA as Vaccine Technologies. *Vaccines (Basel)*. 2019 Jun; 7(2): 37. Doi: 10.3390/vaccines7020037.
11. Anderson EJ, Roupheal NJ, Widge AT, Jackson LA, Roberts PC et al. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. *N Engl J Med* 2020 Sep 29; NEJMoa2028436. Doi: 10.1056/NEJMoa2028436.
13. Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomized controlled trial. *Lancet*. 2020 Aug 15; 396(10249):467-478. Doi: 10.1016/S0140-6736(20)31604-4.
14. Logunov DY, Dolzhikova IV, Zubkova OV, Tukhvatullin AI, Shcheblyakov DV et al. . . .Safety and immunogenicity of a rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. *The Lancet* 2020 Sep 26; 396(10255):887-897.
15. Destefano F, Offit PA, Fisher A. Vaccine Safety. *Plotkin's Vaccines*. 2018:1584–1600.e10. Doi: 10.1016/B978-0-323-35761-6.00082-1.
16. Poland GA, Ovsyannikova IG, Kennedy RB. SARS-CoV-2 immunity: review and applications to faze 3 vaccine candidates. *Lancet* 2020; 396: 1595–606.
17. Morais IJ, Polveiro RC, Souza GM, Bortolin DI, Sassaki FT et al. The global population of SARS-CoV-2 is composed of six major subtypes. *Nature Research* 2020 10:18289.
18. Mishraa SK, Tripathib Y. One year update on the COVID-19 pandemic: Where are we now? *Acta Trop*. 2021 Feb; 214: 105778. Doi: 10.1016/j.actatropica.2020.105778.