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Research/Review

Review on Post Market Surveillance of Covid-19 Vaccines in Clinical Trials

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Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a type of coronavirus that causes the Coronavirus Disease 2019 (COVID-19), which has been the most challenging pandemic in this century. We discussed about the post marketing surveillance of the given vaccines like Pfizer, Sputnik, AstraZeneca, Covaxin and Sinopharm and also that the trials tested two slightly different viral vector vaccines which use genetically engineered adenoviruses to produce corona virus proteins in the body on 76 volunteers. We outline the essential Vaccines antibodies to fight against the COVID-19 in addition we summarize the countries which are denied to use the vaccines. And also the approval of the countries and mainly the Covaxin is yet to introduce the vaccines through nasal route is the upcoming vaccination process. And finally we discussed about the public responses of the vaccinations during the pandemic situations.

Keywords: Covid-19, Covaxin, Pfizer – BioNTech, Sinopharm, Sputnik-V

INTRODUCTION

The COVID-19 infection caused by severe acute respiratory syndrome coronavirus-2 (SARS- CoV-2) has posed a severe unprecedented social, economic, healthcare crisis across the globe. It was declared as a pandemic by World Health Organization (WHO), on March 2020 following its spread outside of China. Being a healthcare challenge itself, it has led to prevalence of other conditions, directly or indirectly as well, such as depression and anxiety endemics, and hindrance to vaccine dissemination and elective surgeries. As of February 17th 2023, about 756,581,850 confirmed cases and 6,844,267 associated deaths have been reported worldwide.

Vaccine, as an effective way to prevent and control disease infection, stimulate the human immune system to produce antibodies, thus increases immunity to the disease and generating protection for the immunized individual . Vaccination aims to curb the spread of disease and helps to achieve herd immunity.

Less than 18 months since the onset of the pandemic, there have also been massive efforts geared towards finding safe and effective vaccines. By July 2021 there were 184 COVID-19 vaccine candidates in pre-clinical

development, 105 in clinical development, and 18 vaccines approved for emergency use by at least one regulatory authority. These vaccines include whole virus live attenuated or inactivated, protein-based, viral vector, and nucleic acid vaccines. Several International organization and countries have been also developed guidelines for different aspects of covid-19 vaccination, including vaccination of special population, management of adverse reaction and causes for vaccination. However experts have been raising concerns about the logistical issue linked to the distribution of this vaccine, which needs to store at particular temperature. Most vaccines in India can be stored at temperature between 2-8 degrees.

As of February 13th 2023, a total of 12,195,832,385 vaccine doses have been administered around the world according to World health organization (WHO). COVID-19 vaccination provides hope for an end to the pandemic, if and only if there would be equal access and optimal uptake in all countries around the world.

mRNA vaccines, adenoviral vector vaccines and recombinant nanoparticles and also considered the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants and their impact on the effectiveness of the most widely implemented vaccines. Recent findings General properties, efficacy, safety and global uptake of Pfizer/BioNTech's Comirnaty (BNT162b2), Moderna's Spikevax (mRNA-1273), Oxford/AstraZeneca's ChAdOx1 nCoV-19, J&J/Janssen's Ad26.COV2.S and Novavax's NVX-CoV2373 vaccines at the end of the year 2021 were presented. Summarized the information on the effectiveness against COVID-19 infection, severe disease and death. Then focused on important missense mutations in the five variants of concern (VoC): Alpha, Beta, Gamma, Delta and Omicron. We explored the evidence for the effectiveness of the vaccines against those five VoC. Summary It is difficult to predict the further development of the COVID-19 pandemic. The development of vaccines of an increasingly broad spectrum against coronaviruses, more easily deliverable and conferring more durable immune protection is likely. However, the very large number of infections may lead to new mutations with unpredictable impacts. Interventions that would control COVID-19 more effectively and enable a safer coexistence with the SARS-CoV-2 virus and its emerging variants are still needed in early 2022.

Here, We analyzing and reviewing of some of the Covid-19 vaccine's mechanism of action, efficacy, adverse events and approval organization etc. The vaccines we are used are Covaxin, Sinopharm, Sputnik-V, Pfizer BioNTech and Oxford/AstraZeneca.

COVAXIN

Covaxin is a vaccine granted approval for restricted use in emergency situation that may prevent COVID-19. The Central Licensing Authority (CDSCO) has granted permission for the sale or distribution of COVAXIN for restricted use in emergency situation in public interest as an abundant precaution, in clinical trial mode [13]. In phase 1 and phase 2 clinical trials, Covaxin has demonstrated the ability to produce antibodies against COVID-19. It is a 2-dose vaccination regimen given 28 days apart. It is a vaccine with no sub-zero storage, no reconstitution requirement, and ready to use liquid presentation in multi-dose vials, stable at 2-8oC. A total of 375 subjects have been enrolled in the Phase 1 study and generated excellent safety data without any reactogenicity. Vaccine-induced neutralizing antibody titers were observed with two divergent SARS-CoV-2 strains.

Percentage of all the side-effects combined was only 15% in vaccine recipients. In Phase 2 study, 380 participants of 12-65 years were enrolled. COVAXIN led to tolerable Safety outcomes and enhanced humoral and cell-mediated immune responses. SAGE recommends the use of BBV152 vaccine as 2 doses (0.5 ml) given intramuscularly. India's first domestic COVID-19 vaccine, Covaxin developed and manufactured by Bharat Biotech International Limited, in collaboration with the National Institute of Virology of ICMR, is one of the two vaccines of the company, undergoing clinical trials, and is being stockpiled under an "at-risk manufacturing and stockpiling license".

Covaxin is an inactivated-virus vaccine, developed in Vero cells. The inactivated virus is combined with Alhydroxiquim-II (Algel-IMDG), chemosorbed imidazoquinoline onto aluminum hydroxide gel, as an adjuvant to boost immune response and longer-lasting immunity. This technology is being used under a licensing agreement with Kansas-based ViroVax. The use of the Imidazoquinoline class of adjuvants (TLR7/8 agonists), shifts the T-cell response towards Th1, a T- Helper 1 phenotype (which is considered safer than Th2 responses against SARS-CoV-2) and reduces the risk of immunopathologically mediated enhanced disease.

DOSES

There is no change between the 2 vaccines in terms of amount. Both of them are administered as 0.5ml in the upper arm region. But, the dosing schedule for both vaccines however varies. The second dose of Covaxin is scheduled after 4-6 weeks after the first dose, while for Covishield vaccines it is 84 days or 12-16weeks after the 1st dose.

STORAGE GUIDELINES

Both Covishield and Covaxin can be stored at 2-8° Centigrade, which is a household refrigerator temperature. This makes both the vaccines most suited for Indian conditions as most of the vaccines here are kept at the same temperature range. This also makes the transportation and storage of both vaccines easier.

STRUCTURE

Covaxin showed promising efficacy and immunogenicity towards SARS-CoV-2, which is available in a double dose. Covaxin is included along with immune-potentiators, also known as vaccine adjuvants, which are added to the vaccine to also known as vaccine adjuvants, which are added to the vaccine to increase and boost its increase and boost its immunogenicity. The manufacturer developed a formulation containing the whole virion containing inactivated SARS- CoV-2 antigen (strain: NIV-2020-770), adjuvant aluminium hydroxide gel, immune stimulatory imidazoquinolinone, and the preservative 2-phenoxyethanol (2-PE) (Figure 1) (Figure 1) Imidazoquinoline (IMDG) molecule is also a toll-like receptor (TLR) 7/8 like receptor (TLR) 7/8 agonist and thus can have an immunomodulatory effect agonist and thus can have an immunomodulatory effect. On 3 November 2021, the technical advisory group for emergency use listing, WHO listed the Covaxin vaccine against COVID-19 for emergency use.

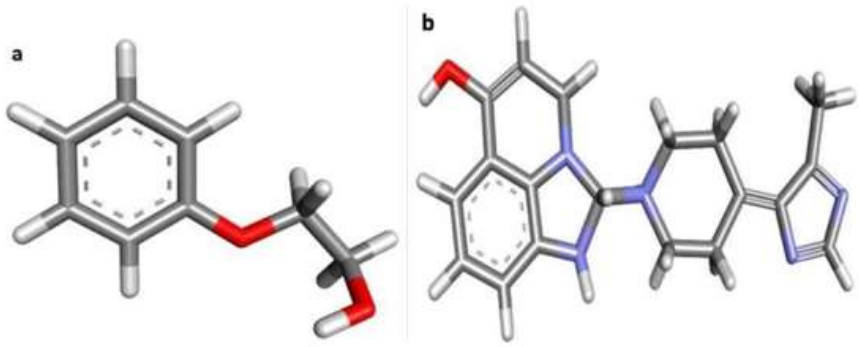


Fig 1: Structure of (a) 2-phenoxyethanol and (b) imidazoquinolinone

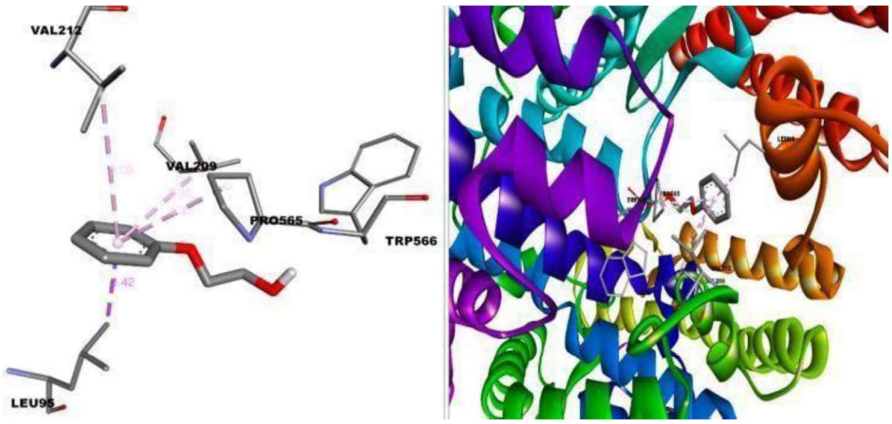


Fig 2: Docked pose of 2-phenoxyethanol in the binding pocket of ACE
This figure was produced using Discovery Studio Visualizer

MECHANISM OF ACTION

The vaccine works by stimulating the immune system to produce antibodies against the inactivated SARS-CoV-2 strain. The vaccine is used, along with immune stimulants commonly known as vaccine adjuvants (Alhydroxiquim-II), to improve the immune response and provide longer-lasting immunity. The vaccine candidate is produced through the formulation of the inactivated virus with Kansas-based Viro Vax's Alhydroxiquim-II adjuvant.

COVAXIN contains 6µg of whole-virion inactivated SARS-CoV-2 antigen (Strain: NIV-2020-770). Other inactive components include 250µg aluminium hydroxide gel, 15µg TLR 7/8 agonist (imidazoquinolinone), 2.5mg TM 2-phenoxyethanol and up to 0.5ml of phosphate buffer saline.

The vaccine does not require sub-zero storage or reconstitution and is available for use in multi-dose vials, which are stable at 2˚ to 8˚C.

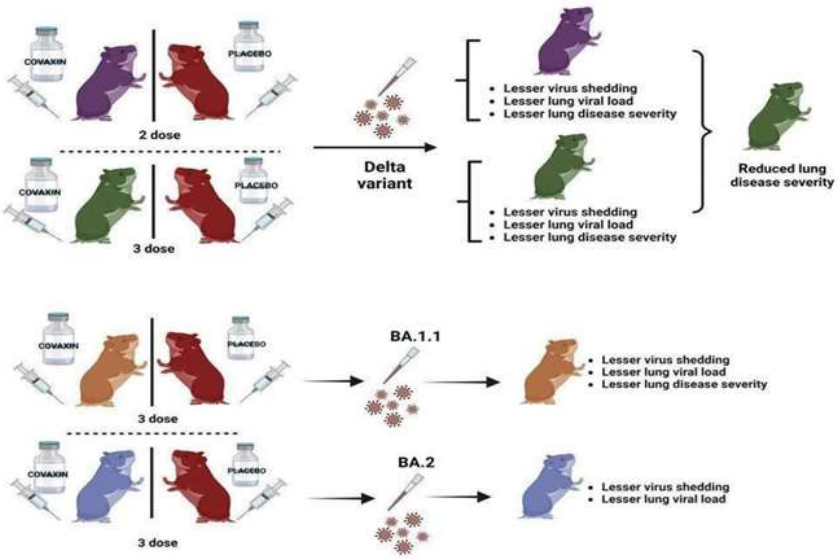
EFFICACY

Vaccine efficacy against COVID-19 of any severity, 14 or more days post dose 2, was 78%. Vaccine efficacy against severe disease is 93%. In adults aged less than 60 years, efficacy was 79%; and in those aged 60 years and over it was 68%. The efficacy of Covaxin against SARS-CoV-2 variants was evaluated in India from January to April 2021. The UK variant B.1.617 was found to have various mutations on the spike receptor-binding domain (RBD), which aid its attachment to the angiotensin-converting enzyme 2 (ACE2) receptor on the surface of human cells. The median ratio of 50% neutralization of sera was found to be 0.8, indicating that sera from the BBV152 vaccine recipients could possibly neutralize the UK-variant strains. The B.1.1.2 variant, also known as the delta variant, was found to be more deadly and wide spread due to higher transmissibility and potential immune escape. A study assessed the neutralization capacity of COVID-19 recovered (n=20) and vaccinated individuals era (n=17) against the particular variant of concern compared to the prototype strain B1 (D614G).

The GMT ratio was 1.95 for D614G vs. 1.84 for B.617. The neutralizing capacity of the BBV152 vaccine (Covaxin) against the variant is the same for sera of vaccines and recovered cases, indicating the potential protective efficacy of the vaccine. A study assessed the neutralization capacity of COVID-19 recovered and vaccinated individuals against the B.1.351 variant of concern compared to the D614G (B.1.1) strain. The results showed a 3.3 fold and 3.0 fold reduction in neutralization titers. The IgG immune response against the P2 variant was 794.8 and 4627 for the S1- RBD and the N.

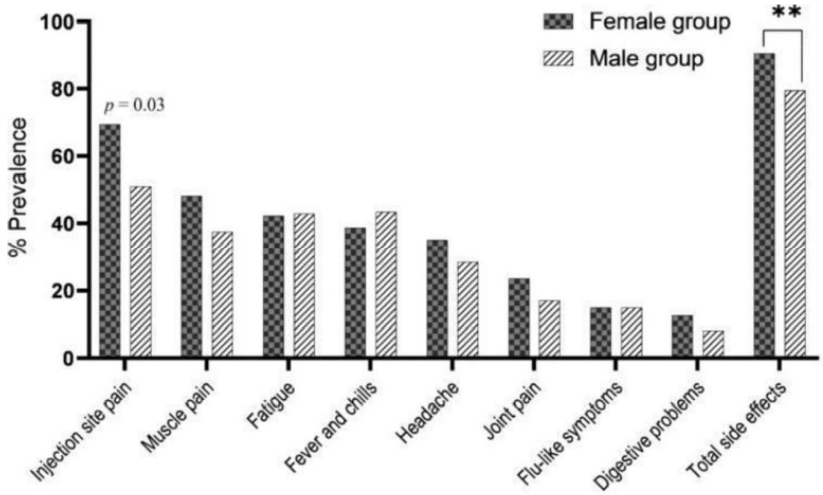
Schematic representation

Protective efficacy of COVAXIN against Delta and Omicron variants in Hamster model.



ADVERSE EVENTS

Effect frequency was higher in the female group (90.6%) than the male group (79.5%) Moreover, the prevalence and frequency of these side effects were different in female and male groups, which was shown and Fig. 1. Among the reported side effects, only injection site pain was significantly different between female (69.5 %) and male (51.1 %) groups (p = 0.03), while the prevalence of other side effects was not significantly different between female and male group.



Prevalence of different side effects among male and females. The difference in the prevalence and frequency of injection site pain between the two gender group (female and male) was examined by Chi-square test, *pValue* <0.05 was considered as a significant level.

AEs	Covaxin (*n*=290)[5]
Fever	48.3%
Bodyache	33.8%
Headache	30.7%
Pain at injection site	24.5%
Flue like syndrome	16.2%
Join pain	16.2%
Cough	12.8%
-	-

Covaxin (Bharat)	Inactivated	India	November 2021	2	>18	81%	➢ Pain ➢ Swelling at injection site ➢ Fever ➢ Weakness ➢ Fatigue ➢ Muscle aches ➢ Body aches ➢ Headaches ➢ Nausea ➢ Vomiting ➢ Loss of appetite ➢ Chills ➢ Systemic rash ➢ Diarrhea	WHO	(21, 24)

SINOPHARM

The SARS-CoV-2 Vaccine (VeroCell) is an inactivated vaccine against coronavirus disease 2019 (COVID-19) which stimulates the body's immune system without risk of causing disease. Once inactivated viruses get presented to the body's immune system, they stimulate the production of antibodies and make the body ready to respond to an infection with live SARS-CoV-2. This vaccine is adjuvant (with aluminum hydroxide), to boost the response of the immune system.

Phase III clinical trials conducted in Argentina, Bahrain, Egypt, Morocco, Pakistan, Peru, and the United Arab Emirates (UAE), have shown 79.34% efficacy of the vaccine. Following clinical trials, the vaccine was approved for emergency use in May by WHO. As per the guidance of WHO, two doses of vaccine are required to

be administered with 3-4 weeks interval. Data available on the side effects of the vaccine shows milder side effects like headache, fever, and pain on injection site, etc. The required storage condition is +2°C to 8°C

As of August 2022, the Sinopharm COVID-19 Vaccine is authorized/approved in about 90 countries and Listed by the WHO. In Thailand, the vaccine is known as COVILO. Separately, Sinopharm (Wuhan) Inactivated (Vero Cells) vaccine is approved, and the UK authorized it for international visitors, as did Australia. In June 2021, a vaccination drive resumed in parts of Bangladesh with the China-donated Sinopharm vaccines. World Health Organization approved this vaccine as Emergency use listing (EUL) and also approved by Africa Regulatory Taskforce Endorsed and Caribbean Regulatory System Emergency Use Recommendation.

COMPOSITION

It is prepared by inoculating African green monkey kidney cells (Vero cells) with SARS-CoV-2 WIV04 strain, followed by culturing, harvesting, virus inactivation, concentration, purification, and adding aluminum hydroxide adjuvant. It doesn't contain any antibiotic or preservative. Active ingredient: inactivated antigen of SARS-CoV-2 WIV04 strain. Adjuvant: aluminum hydroxide. Auxiliary materials: sodium chloride, disodium hydrogen phosphate, sodium di hydrogen phosphate.

MECHANISM OF ACTION

A Vaccine Made From Coronaviruses

BBIBP-CorV works by teaching the immune system to make antibodies against the SARS-CoV-2 coronavirus. The antibodies attach to viral proteins, such as the so-called spike proteins that stud its surface. To create BBIBP-CorV, the Beijing Institute researchers obtained three variants of the coronavirus from patients in Chinese hospitals. They picked one of the variants because it was able to multiply quickly in monkey kidney cells grown in bioreactor tanks.

Killing the Virus

Once the researchers produced large stocks of the coronaviruses, they doused them with a chemical called beta-propiolactone. The compound disabled the coronaviruses by bonding to their genes. The inactivated coronaviruses could no longer replicate. But their proteins, including spike, remained intact. The researchers then drew off the inactivated viruses and mixed them with a tiny amount of an aluminum-based compound called an adjuvant. Adjuvants stimulate the immune system to boost its response to a vaccine. Inactivated viruses have been used for over a century. Jonas Salk used them to create his polio.

Prompting an Immune Response

Because the coronaviruses in BBIBP-CorV are dead, they can be injected into the arm without causing Covid-19. Once inside the body, some of the inactivated viruses are swallowed up by a type of immune cell called an antigen-presenting cell. The antigen-presenting cell tears the coronavirus apart and displays some of its fragments on its surface. A so-called helper T cell may detect the fragment. If the fragment fits into one of its surface proteins, the T cell becomes activated and can help recruit other immune cells to respond to the vaccine.

Making Antibodies

Another type of immune cell, called a B cell, may also encounter the inactivated coronavirus. B cells have surface proteins in a huge variety of shapes, and a few might have the right shape to latch onto the coronavirus. When a B cell locks on, it can pull part or all of the virus inside and present coronavirus fragments on its surface.

A helper T cell activated against the coronavirus can latch onto the same fragment. When that happens, the B cell gets activated, too. It proliferates and pours out antibodies that have the same shape as their surface proteins.

Stopping the Virus

Once vaccinated with BBIBP-CorV, the immune system can respond to an infection of live coronaviruses. B cells produce antibodies that stick to the invaders. Antibodies that target the spike protein can prevent the virus from entering cells. Other kinds of antibodies may block the virus by other means.

EFFICACY

Vaccine is efficient in reducing the risk of symptomatic COVID-19 infection by 94.3% at CI of 92.2% to 95.9% with significant p value of 0.001 as compared with non-vaccinated individuals in this age group. Hospital admission after COVID-19 is reduced by 60.5% at CI of 7.9% to 82.9% among vaccinated individuals at a significant p value of 0.001 as compared with non-vaccinated individuals. Intensive care unit (ICU) admission due to COVID-19 was reduced by 66.1% but with a non-significant p value (0.19)

Sinopharm vaccine was effective in preventing mortality from COVID-19 by 98.6% at CI of 94.2%-99.6% with significant p value of 0.001. Only 0.5% of vaccinated individuals reported adverse effect (AE)

following immunization after first dose, and 0.36% after the second dose. Nine out of 2066 who replied, reported mild fever after first dose of vaccine, two reported pain at injection site and only one person reported fatigue and headache. The most common AE after the second dose was fever which settled within 1 day of onset.

Sr. no	Parameter		Non-vaccinated (%)	Fully vaccinated (%)	P value	Vaccine effectiveness (%)	Vaccine effectiveness at 95% CI (min-max)
1	COVID-19 status	Not detected	983 (72.3)	2022 (97.9)	0.001	94.3	92.2 to 95.9
		Detected	377 (27.7)	44 (2.1)			
2	Hospital admission after COVID-19	Not admitted	255 (67.6)	37 (84.1)	0.001	60.5	7.9 to 82.9
		Admitted	122 (32.4)	7 (15.9)			
3	ICU admission after COVID-19	Not admitted	38 (31.1)	4 (57.1)	0.19	66.1	–
		Admitted	84 (68.9)	3 (38.9)			
4	Dead or alive	Alive	1274 (93.7)	2064 (99.9)	0.001	98.6	94.2 to 99.6
		Dead	86 (6.3)	2 (0.1)			

The phase 3 trial of BBIBP-CorV, which lead to its subsequent WHO-granted emergency use licence, 18 included 40411 individuals and showed a VE of 78.1% against infection with COVID-19. Notably, only 1.5% of these participants were aged >60years, and few had comorbidities. This study provides new and reassuring data on the VE of BBIBP-CorV in the older, comorbid cohort. A total of 3246 adults aged 60 years and above in a large Pakistani district were studied. The results showed a vaccine effectiveness (VE) of 94.3% (95% CI 92.2% to 95.9%) for two doses of the BBIBP-CorV Sinopharm vaccine in the prevention of symptomatic SARS-CoV-2 infection, 60.5% (95% CI 7.9% to 82.9%) in reducing hospitalization with SARS-CoV-2% and 98.6% (95% CI 94.2% to 99.6%) in preventing death from SARS-CoV-2 as compared with unvaccinated individuals. The prevention of ICU admission was not a primary or secondary outcome of the study, and our study was not powered to detect a statistically significant result in this domain. We noted a 66.1% reduction in ICU admissions in the vaccinated group however. The percentage individuals with comorbidities in the vaccinated group was greater than the unvaccinated group (89% vs 36%). This may have been because those with known comorbidities had a greater anxiety about COVID-19 infection and sought vaccination sooner. The high level of VE in this high-risk age group is therefore reassuring and shows that vaccine works equally well in vulnerable group and lessens the severity of disease in comorbid cohort. Eighty-six individuals (39 female and 47 male) died in unvaccinated group. Two patients (one male and one female) died in vaccinated group. The mean age of those who died was 75 years and both had multiple comorbidities. It should be noted that the average life expectancy of individuals (male, female) in Pakistans per 2022 is 67 years.

ADVERSE EVENT

In this cross-sectional study, four-hundred and fourteen (414) people participated, all of whom were vaccinated with both doses of Sinopharm, and where the majority of respondents were males at 85.7% (355), and 14.3% (59) were females. A total of 96.4% (399) of the vaccine recipients belonged to the age group between 18 and 25 years, 2.2% (9) fell in the range of 26─35 years, 0.2% (1) in the 46─55 years. Range, and 1.2% (5) were between 56 and 65 years. Out of the 414 vaccine recipients, 16.7% (69) of people had a history of allergies. The most reported comorbidity was asthma at 5.07% (21) followed by hypertension at 1.69% (7), ischemic heart disease at 0.72% (3), and diabetes mellitus at 0.48% (2). No one reported a history of tuberculosis.

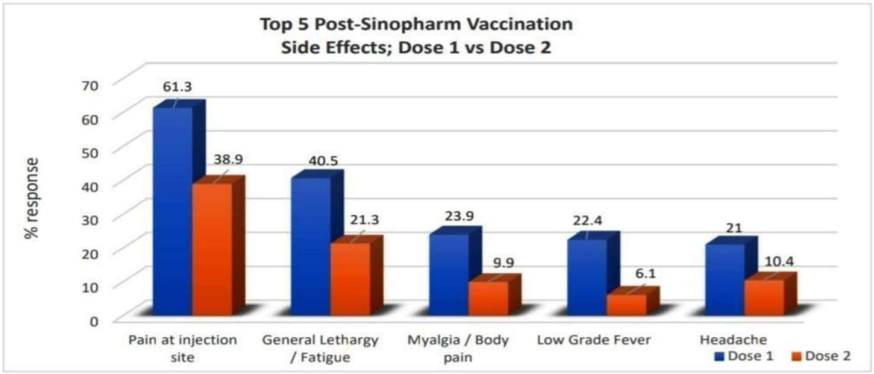
Parameter	Frequency (#)	Frequency (%)
Gender		
Male	355	85.7
Females	59	14.3
Age (years)		
18–25	399	96.4
26–35	9	2.2
36–45	0	0
46–55	1	0.2
56–65	5	1.2
Comorbidities		
Allergies	69	16.70
Asthma	21	5.07
Hypertension	7	1.69
Ischemic Heart Disease	3	0.72
Diabetes Mellitus	2	0.48
Tuberculosis	0	0
History of COVID-19		
Positive	85	20.5
Negative	329	79.5
If positive, was COVID-19 contracted before or after vaccination		
Before vaccination	70	82.4
After vaccination	15	17.6

When the COVID-19 history was taken, 79.5% (329) of the participants had no previous COVID-19 history while 20.5% (85) people had contracted the virus in the past. Amongst those who had been infected

previously, 82.4% of these eighty-five individuals (70) contracted it before getting socio demographic data are summarized along with their history of COVID-19 infections in a given table. Out of the twenty-five potential adverse events that were listed for each dose, After first dose, No side effects were encountered at all in 19.3% (80) of participants and after second dose no side effects were seen in 54.3% (225). In total, no overall vaccinated with sinopharm while 17.6% (15) contracted in after getting vaccinated. The respondents' side effects from any dose were reported in 13.8% of the respondents (57).

DOSE 1		DOSE 2	
Top 5 Symptoms	**Percentage/Frequency**	**Top 5 Symptoms**	**Percentage/Frequency**
1. Pain at the injection site	61.3% (253)	1. Pain at the injection site	38.9% (161)
2. General lethargy	40.6% (168)	2. General lethargy	21.3% (88)
3. Myalgia/body aches	23.9% (99)	3. Headache	10.4% (43)
4. Low-grade fever	22.4% (93)	4. Myalgia/body aches	9.9% (41)
5. Headache	21% (87)	5. Low-grade fever	6.1% (25)

When the results of dose one and dose two were compared, it was noted that most of the participants experienced a greater number of symptoms in the form of a larger total number of post vaccine symptoms (out of 25 symptoms) for dose one than they did for dose two. Moreover, each side effect was reported by a greater number of participants for dose one compared to dose two, as pictorially represented in the bar graph below



COUNTRIES THAT DENIED THE USAGE OF SINOPHARM VACCINE

In the United States, until now, the country has authorized the use of Pfizer/BioNTech, Moderna, and Johnson and Johnson vaccines for use. Nonetheless, since the US has been closed for international travellers it is still unclear whether the country will allow entry to those who have been immunized with another vaccine in early November, when the entry ban on 33 world countries, including the UK, Ireland and the Schengen Area countries, is set to end. In regards to this, several universities, including Harvard, Colombia, Yale University, and several others, have announced that they would allow students who have been vaccinated with Sinopharm to follow their studies there. The United Kingdom hasn't approved the Sinopharm vaccine for use. This means that all persons who have been immunized with this type of vaccine are subject to restrictions when entering the UK's territory. Currently, the UK recognizes only the vaccines that EMA has approved.

SPUTNIK-V VACCINE

The Sputnik V COVID-19 vaccine or Gam-COVID-Vaccine has been developed by the Gamaleya National Center of Epidemiology and Microbiology in Russia. It is a two-part adenovirus (Ad) viral vector vaccine designed to trigger the production of antibodies against the spike protein (S). Ads serve as the delivery vehicle for the DNA instructions to produce the S of the SARS-CoV-2 virus in the body. They are engineered to be able to invade cells but not replicate. Sputnik V is made up of two different Ads, Ad26 and Ad5, both carriers of the gene for the SARS-CoV-2 glycoprotein S, which are given separately, three weeks apart. Ad26 is used in the first dose and Ad5 is used in the second to boost manufacturer's information states that only developing antibodies to Ad after the first dose, which could make the second dose ineffective. The non-replicating Ad vectors of type E1 and E3, which are developed and produced on HEK293 cells, are used in Sputnik V vaccine production. Deletion of the E1 gene prevents the virus from replicating, while deletion of the E3 gene prevents it from interacting with the immune system. On 12 April 2021, India approved the use of Sputnik V vaccine for emergency use against COVID-19 based on strong immunogenicity data. However World health organization is the vaccine's effect. The use of two different vectors is designed to reduce the chance of the body not yet approved the Sputnik-V vaccine.

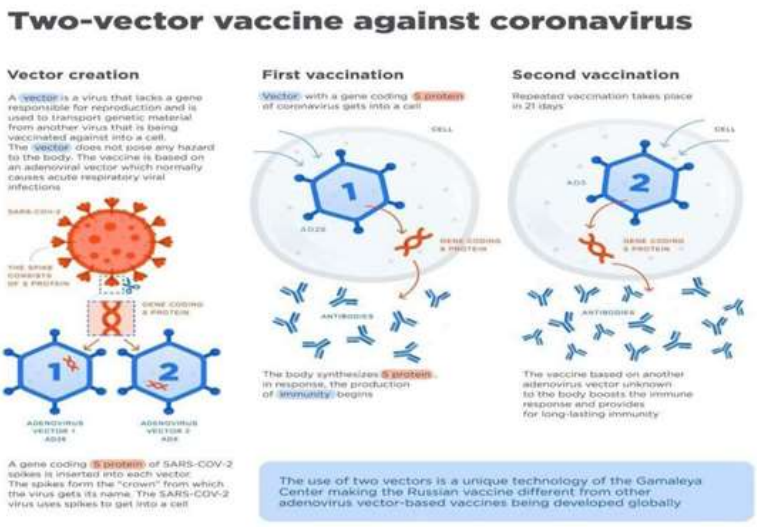
For the prevention of the novel Coronavirus infection (COVID-19) in adults aged over 18, when given in two separate doses three weeks apart.

Day 0: Component I (0.5 ml) & Day 21: Component II (0.5 ml.)
Sputnik V vaccination course consists of two separate doses of 0.5 ml each. The vaccination is carried out in two stages: first with component I, then 3 weeks later with component II. The product is administered intramuscularly. First component I at a dose of 0.5 ml, then after 3 weeks component II at a dose of 0.5 ml. After the vaccine is administered, the patient should be monitored by a healthcare professional for 30 minutes.

COMPOSITION
Composition per dose contains (0.5 ml)

Component I contains
Active substance: Recombinant adenovirus serotype 26 particles containing the SARS-CoV-2 protein S gene 1.0±0.5 x 1011 Particles.
Excipients: Tris (hydroxymethyl) aminomethane-1.21mg, sodium chloride-2.19mg, sucrose-25.0 mg, magnesium chloride hexahydrate-102.0µg, EDTA disodium salt dehydrate-19.0µg, polysorbate 80-250.0µg, 95% ethanol-2.50µl, water for injection q.s to 0.5 ml.

Component II contains
Active substance: Recombinant adenovirus serotype 5 particles containing the SARS-CoV-2 protein S gene 1.0±0.5 x 1011 Particles.
Excipients: Tris (hydroxymethyl) aminomethane-1.21mg, sodium chloride-2.19mg, sucrose-25.0 mg, magnesium chloride hexahydrate-l02.0µg, EDTA disodium salt dehydrate-19.0µg polysorbate 80-250.0µg, 95% ethanol-2.50µl, water for injection q.s to 0.5 ml.



MECHANISM OF ACTION

The vaccine induces the formation of humoral and cellular immunity against coronavirus infection caused by the SARS-CoV-2 virus. The mechanism of the drug's action is based on the ability of Ad26 and Ad5-based recombinant viral particles carrying the SARS-CoV-2 S protein gene to transduce efficiently the cells of the vaccinated body; in this case, genetic sequences which code the antigen is delivered to the cells, so the transduced cells start to produce the antigen.

When the first dose (component 1) is administered (intramuscularly), the rAd26-based vector enters the cells of the body leading to the expression of SARS-CoV-2 S protein thus triggering the development of specific SARS-CoV-2 immunity. When the second dose (component 2) is administered (intramuscularly), the rAd5-based vector enters the cells of the body leading to the expression of SARS-CoV-2 S protein thus boosting efficiently the immune response to ensure a pronounced long-lasting immunity against SARS-CoV-2.

Results in trials 1 and 2

The Gamaleya Research Institute still has not published results from initial vaccine trials.

Results in trial 3

Secondary analysis of the Sputnik V phase 3 clinical trial showed a 91.4% efficacy rate 28 days after first dosing and 95% on the 42nd day after first dosing (Clinical Trials, 2020). Sputnik V reported no unexpected adverse events during the trials (SputnikV, 2020).

EFFICACY

Phase I/II Clinical Trial in Russia (NCT04436471)

38 volunteers were recruited in this trial, of which 9 each received either component 1 or 2 and were observed for 28 days thereafter as part of Phase I study. Another 20 volunteers received component 1 followed by 2 at interval of 21 days and were followed up till day 42 (3 weeks after the second dose) as part of Phase II study. Phase I study indicated that both components of the vaccines were highly immunogenic and safe in the volunteers. Phase II indicated that humoral immunogenicity parameters s-glycoprotein (spike protein) specific antibodies and virus neutralizing antibodies increased over the observations at days, 14, 21, 28 and 42 with significantly superior titres to the convalescent plasma for the earlier parameter on days 28 and 42 as well as 100 seroconversion for both parameters by day 42.

Cellular immunogenicity parameters of CD4/CD8 lymphocyte proliferation and interferon gamma secretion also increased over days 14 and 28 with 100% volunteers showing response in these parameters on day 28.

Phase III Clinical Trial in Russia (RESIST, NCT04530396)

As per the recent interim analysis, 33,771 volunteers [25,321 received Gam-COVID-Vac combined vector vaccine and 8,450 received placebo in 1:3 proportion] were enrolled in the study, which included subjects aged 18 to 92 years old (43.9±12 years), 33.6% females, 8.9% subjects > 60 years of age and 22.8% subjects with comorbidities.

Earlier interim analysis, which was published in Lancet. indicated that amongst 18,695 volunteers receiving both vaccine doses, there were 78 cases of COVID-19 reported [16 in vaccine arm and 62 in Placebo arm] from day 21 onwards with efficacy calculated at 91.6% (95% Confidence interval 85.6% - 95.2%). There were no significant differences in the efficacy across age groups or genders. In terms of moderate to severe COVID-19 cases, all 20 cases were reported in placebo arm indicating 100% protection against such disease. While considering the 60 COVID-19 cases reported from day 28 onwards (1 week after the second dose), the efficacy was calculated at 91.1% (95% confidence interval 83.8% to 95.1%).

In terms of humoral immunogenicity, s-glycoprotein (spike protein) specific antibody data from 980 volunteers (733 from the vaccine arm and 247 from the placebo arm), indicates that by day 42 (3 weeks after the second shot), 98.64% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 9818 fold) as compared to 12.55% ($P<0.001$) volunteers in placebo arm. As per earlier interim analysis, based on 100 volunteers (72 from the vaccine arm and 28 from the placebo arm), indicates that by day 42 (3 weeks after the second shot), 95.83% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 44.5 fold) as compared to 7.14% ($P<0.001$) volunteers in placebo arm. Further, on day 28 (1 week after the second dose) vaccinated arm reported significant proliferation of CD4 lymphocytes compared to CD8 lymphocytes and significant increase in interferon gamma secretion compared to placebo arm.

India Phase II/III adaptive study (NCT04640233)

Phase II part of the India study enrolled 100 subjects (75 in vaccine arm and 25 in placebo arm) and tested the immunogenicity as well as safety of the vaccine in Indian population. The immunogenicity trends in the Phase II population closely correlated with Russia Phase II results as indicated by serial increase in immunogenicity parameters and similar seroconversion. Based on the same, go-ahead was given to Phase III part by the Drug Controller General (India).

Phase III part of the India study enrolled 1500 subjects (1125 in vaccine arm and 375 in placebo arm), of which 284 subjects are being evaluated for immunogenicity parameters. In terms of humoral immunogenicity, s-glycoprotein (spike protein) specific antibody data from 284 volunteers (213 from the vaccine arm and 71 from the placebo arm), indicates that by day 42 (3 weeks after the second shot), 99.5% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 8327.99 fold). For Viral neutralizing Antibody (VNA) - based on 284 volunteers (213 from the vaccine arm and 71 from the placebo arm), indicates that by day 42 (3week after the second shot), 81.1% of volunteers in vaccine arm achieved seroconversion (with a geometric mean titre of 88.5 fold). Further, on day 28 (1 week after the second dose) vaccinated arm reported significant proliferation of CD4 lymphocytes compared to CD8 lymphocytes and significant increase in interferon gamma secretion compared to placebo arm. These results indicate the Gam-COVID-Vac vaccine is highly immunogenic in Indian subjects in line with the results of Russia study.

Another reports from Lancet shows that results of the phase 3 Gam-COVID-Vac trials how that the vaccine is 91·6% (95% CI 85·6–95·2) efficacious against COVID-19 (from day 21 after first dose, the day of

receiving second dose). Our results also showed that the vaccine was 100% (95% CI 94·4-100) efficacious against severe COVID-19, although this was a secondary outcome so the results are preliminary. The vaccine was well tolerated, with 45 (0·3%) of 16 427 participants in the vaccine group reporting serious adverse events, all of which were considered not related to the vaccine. According to the study design, the starting point for counting COVID-19 cases for estimation of vaccine efficacy was 21 days after dose 1 (day of dose 2 administration). Although the study was not designed to assess the efficacy of a single-dose regimen, our early starting point allows us to observe a possible partial protective effect of a single dose. The cumulative COVID-19 incidence curves of COVID-19 cases among the placebo and vaccine groups begin to diverge 16–18 days after the first immunization, showing early onset of a partially protective effect after a single-dose immunization; however, the study design does not allow us to draw conclusions from these observations.

ADVERSE EVENTS

We investigated an adverse effects of Sputnik V vaccines on the basis of following age groups. The study included 1751 participants who had received both the dose of the vaccine which includes 664 Male and 1087 Female.

AGE	18-30	31-40	41-50	51-60	61-70	>70
NUMBER	233	362	533	436	122	65

Male	664 participants
Female	1087 participants

Number of participants with specific adverse effects and respective percentage to the whole recipients.

For first 72 Hour, 1st Dose

Local Reaction	363 (20.7%)
General Fatigue	776 (44.3%)
Chills and Fever	524 (29.9%)
Dizziness and Headache	240 (13.7%)
Skeletal pain	603 (34.4%)
Nausea	86 (4.91%)
Diarrhea	35 (2%)
Sleepiness	28 (1.6%)
Loss of appetite	11 (0.62%)
Chest Pain and Dyspnea	6 (0.34%)
Abdominal Pain	13 (0.74%)
Severe neurological	0
No adverse effects	489 (28%)

For first 72 Hour, 2nd Dose

Local Reaction	326 (18.6%)
General Fatigue	435 (24.8%)
Chills and Fever	387 (22.1%)
Dizziness and Headache	126 (7.2%)
Skeletal pain	439 (25.1%)
Nausea	33 (1.88%)
Diarrhea	8 (0.45%)
Sleepiness	18 (1.02%)
Loss of appetite	3 (0.17%)
Chest Pain and Dyspnea	2 (0.11%)
Abdominal Pain	13 (0.74%)
Severe neurological	2 (0/11%)
No adverse effects	719 (41.06%)

Most common adverse effects of the first dose of the Sputnik V vaccine in participants. Three hundred and three individuals (17.3%) of the Sputnik V vaccine recipients did not have any adverse effects after both doses. Fatigue (1st dose: 44.3%, 2nd dose: 24.8%), local reactions (1st dose: 20.7%, 2nd dose: 18.6%), and chill/fever (1st dose: 29.9%, 2nd dose: 22.1%), were the most common adverse effects after the first and second dose of the

vaccine. Younger recipients reported more adverse effects than the older age groups (86.4% in participants younger than 50 vs 76% in younger ones). Female participants reported more adverse effects per participant compared to males (87.1% vs 75.6%, P=0.001). Occurrence of adverse effects per participant was higher (P=0.001) after the first dose (mean=1.69, median=2, max=10) compared to the second dose (mean=1.1, median=1, max=6).

Pfizer - BioNTech

Pfizer–BioNTech were the first vaccines to get authorization for emergency use in December 2020, and have reported an efficacy of 95% following the phase III clinical trials. Both these vaccines use lipid nanoparticle delivery system or modified mRNA system. In the latter system, modified mRNA is used to encode the COVID spike proteins, adding mutant mRNA to lock them in a three-dimensional structure which is required to induce an interaction between spike proteins and viral neutralizing antibodies. These RNA vaccines have a potent effect and can be manufactured rapidly at a very low cost. Since, they are not developed with actual pathogens and are not incorporated into host DNA as is the case with other viral vaccines, they show a better safety profile. However, due to their unstable mRNA, they require extreme refrigeration for storage. Refrigerating temperatures required for Pfizer and Moderna are -60°C to -80°C and -15°C to -25°C, respectively. Since ultra-cold temperatures are required for their refrigeration, they are not available in Pakistan. Both vaccines have shown localized side effects like vomiting, pain, nausea, fever, headache, and muscle aches. In rare cases, these vaccines have also been found to cause anaphylactic reactions.

For all persons aged 12 years and above, SAGE recommends two doses (30 µg, 0.3 ml each), 4-8 weeks apart given intramuscularly into the deltoid muscle. For children aged 5 to 11 years SAGE recommends two doses (10µg, 0.2ml each) given intramuscularly into the deltoid muscle and provided 4-8 weeks apart, preferentially 8 weeks. For infants and children aged 6 months to 4 years, the recommended schedule is three doses (3µg, 0.2 ml each): a schedule of two doses 3 weeks apart followed by a third dose at least 8 weeks after the second dose are recommended according to the label. However, countries could consider extending the interval between the first and second dose up to 8 weeks. Compliance with the full schedule is recommended and the same product can be used for both doses.

SAGE (Strategic Advisory group of Experts) recommends that severe and moderately immune compromised persons, including children, should be offered an additional dose of vaccine, as part of the primary series. This is due to the fact that this group is less likely to respond adequately to vaccination following a standard primary vaccination series and are at higher risk of severe COVID-19 disease.

COMPOSITION

The full list of ingredients for the Pfizer vaccine is: mRNA, lipids ((4- hydroxybutyl)azanediyl) bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]- N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose. The Pfizer vaccine does not contain eggs, preservatives, or latex.

MECHANISM OF ACTION

Entering a Cell

After injection, the vaccine particles bump into cells and fuse to them, releasing mRNA. The cell's molecules read its sequence and build spike proteins. The mRNA from the vaccine is eventually destroyed by the cell, leaving no permanent trace. Some of the spike proteins form spikes that migrate to the surface of the cell and stick out their tips. The vaccinated cells also break up some of the proteins into fragments, which they present on their surface. These protruding spikes and spike protein fragments can then be recognized by the immune system.

Spotting the Intruder

When a vaccinated cell dies, the debris will contain many spike proteins and protein fragments, which can then be taken up by a type of immune cell called an antigen-presenting cell. The cell presents fragments of the spike protein on its surface. When other cells called helper T cells detect these fragments, the helper T cells can raise the alarm and help marshal other immune cells to fight the infection.

Making Antibodies

Other immune cells, called B cells, may bump into the coronavirus spikes on the surface of vaccinated cells, or free-floating spike protein fragments. A few of the B cells may be able to lock onto the spike proteins. If these B cells are then activated by helper T cells, they will start to proliferate and pour out antibodies that target the spike protein.

Stopping the Virus

The antibodies can latch onto coronavirus spikes, mark the virus for destruction and prevent infection by

blocking the spikes from attaching to other cells.

Killing Infected Cells

The antigen-presenting cells can also activate another type of immune cell called a killer T cell to seek out and destroy any coronavirus-infected cells that display the spike protein fragments on their surfaces.

EFFICACY

Effectiveness of BNT162b2 against infections caused by the delta variant, which became the predominant strain in KPSC by July, 2021, was 75% (95% CI 71─78) over the study period. Effectiveness against delta infections at 1 month after being fully vaccinated was high at 93% (85─97) but fell to 53% (39─65) up to 5 months after being fully vaccinated. Effectiveness against other (non- delta) variants within 1 month of being fully vaccinated was also high at 97% (95─99) and also waned, to 67% (45─80) up to 5 months after being fully vaccinated. Effectiveness against delta-related hospital admissions over the entire study period was high, at 93% (84─96) and was similar to effectiveness against hospital admissions for other (non-delta) variants. These findings are consistent with reports from the USA and Qatar Our variant specific analyses suggest that reductions in vaccine effectiveness over time are likely to be primarily due to waning vaccine effectiveness rather than the delta variant escaping vaccine protection given that vaccine effectiveness against delta infections was more than 90% soon after vaccination, vaccine effectiveness against delta and other variants for hospital admissions was very high over the entire study period, and reductions in vaccine effectiveness against infection by time since being fully vaccinated were observed irrespective of the variant. We did not observe a difference in waning between variant types; however, the number of events at 3─4 months was low for analyses by variant. As such, analyses with longer follow-up to measure the rate of waning for the delta versus other variants are warranted. Related to our findings, studies from Canada and the UK have shown high effectiveness of BNT162b2 against symptomatic COVID-19 caused by the delta variant in a vaccine schedule that separates the first and second doses by 2─3 months instead of 3 weeks. This longer interval between doses could lead to higher immunological responses; however, duration of follow-up in these studies (<3 months) was insufficient to establish the effects of waning. Moreover, given the lower effectiveness after only one dose observed in our study and in other reports of one-dose effectiveness against variants of concern like beta or delta, delaying the second dose is not without risk.

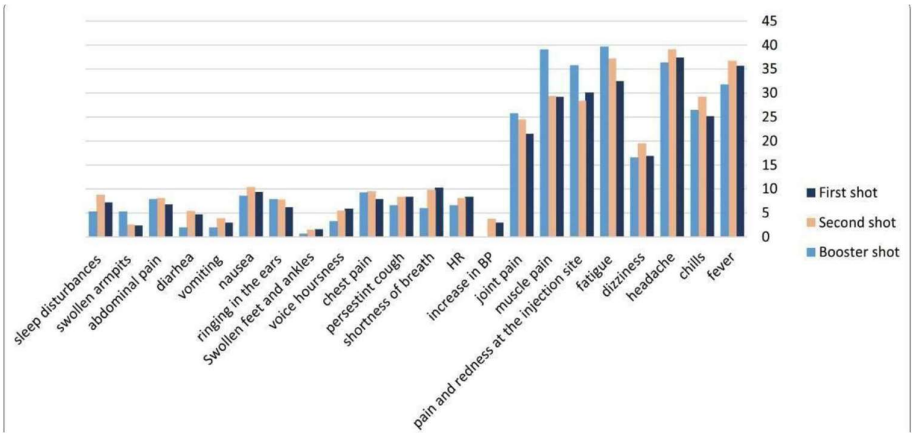
Our results reiterate in a real-world US setting that vaccination with BNT162b2 remains an essential tool for preventing COVID-19, especially COVID-19-associated hospital admissions, caused by all current variants of concern. Along with other emerging evidence, our results suggest that despite early effectiveness of BNT162b2 against delta and other variants of concern, effectiveness against infection erodes steadily in the months after receipt of the second dose. Waning effectiveness and an increased number of infections 6─12 months after the second dose along with the potential need for booster doses was expected given that lower neutralizing antibody titres during this time period have been observed in immunogenicity studies.

ADVERSE EVENT

Tis study included 1137 participants from Birzeit University in Palestine. All participants received at least one dose of the Pfzer-BioNTech COVID-19 Vaccine. The mean age of the participants was 21.163 years±5.361, with 63.2% older than 20 years. In addition, 66.8% were females, 91.8% were healthy without chronic diseases, 7% were smokers, and 14.4% had drug/food allergies.

Variable	Category	n (%)
Gender	Male	378 (33.2%)
	Female	759 (66.8%)
Age	(mean ± SD)	21.163 ± 5.361
	Less than 20	418 (36.8%)
	20 and more	719 (63.2%)
Participants	University employee	55 (4.8%)
	Student	1082 (95.2%)
BMI	Underweight (< 18.5)	92 (8.1%)
	Normal (18.5–24.9)	735 (65.1%)
	Overweight (25.0–29.9)	236 (20.9%)
	Obese (≥ 30)	66 (5.8%)
Smoking	Smoker	304 (26.7%)
Comorbidities	Yes	93(8.2%)
Allergies	Drug / food	164 (14.4%)
	Post-Pfizer Vaccine	144 (13%)
Number of vaccine doses	One dose	110 (9.7%)
	Two doses	876 (77.0%)
	Three doses	151 (13.30%)
Vaccine Side effects Counseling	Received Counsel by Health care provider	583 (51%)

Approximately one-third of participants reported no adverse effects after receiving the first, second, or third dose of the Pfizer vaccine, with 34%, 33.6%, and 32.5%, respectively. Participants who received more than one dose experienced more side effects. The most commonly reported adverse effects were fever, chills, headache, fatigue, pain and swelling at the injection site, muscle pain, and joint pain. Allergic reactions following vaccination, such as allergic skin reactions (itching, burning, and rash), angioedema, shortness of breath, coughing, and significant swelling of the tongue or lips, were reported by 144 (12.7%) participants



As shown in above table, McNemar's test results revealed that the proportion of respondents who reported systemic adverse events after the second vaccine dose and did not report after the first dose was statistically significantly increased (p-value<0.05). These adverse events include; chills (14.2%), Chest pain (6%), Dizziness (9.9%), Ringing in the ears (Tinnitus) (4.9%), tiredness and fatigue (12.5%), Joint pain (10%), over sleepiness, and decreased sleep quality (4%), and (9.5%) of females reported menstrual cycle changes after the second dose only. Te onset and duration of side effects vary among vaccine doses. The onset of side effects was reported within 12 h of vaccination by 50.70%, 43.20%, and 41.10% of participants for the first, second, and third doses. Furthermore, side effects persisted from 1 to 3 days in 41.10%, 39.20%, and 39.10% for the first, second, and third vaccine doses (Fig. 4). The onset and duration of symptoms were not affected by age or gender in the three doses.

Adverse event	Reported after 1st dose	Reported after 2nd dose		P- value
		Yes	No	
No symptoms	Yes	216 (21.0)	133 (13.0)	0.853
	No	129 (12.6)	549 (53.5)	
Local adverse events				
Pain or swelling at the injection site	Yes	232 (22.6)	84 (8.2)	0.068
	No	61 (5.9)	650 (63.3)	
Swollen armpit glands	Yes	11 (1.1)	11 (1.1)	0.441
	No	41.6 (1.6)	989 (96.3)	
Systemic adverse events				
Fever	Yes	214 (20.8)	150 (14.6)	0.498
	No	163 (15.9)	500 (48.7)	
Chills	Yes	154 (15.0)	101 (9.8)	0.005
	No	146 (14.2)	626 (61.0)	
Headache	Yes	245 (23.9)	136 (13.2)	0.221
	No	158 (15.4)	488 (47.5)	
Increase in blood pressure	Yes	11 (1.1)	18 (1.8)	0.185
	No	28 (2.7)	970 (94.4)	
Increase in heart rate	Yes	29 (2.8)	50 (4.9)	0.769
	No	54 (5.3)	894 (87.0)	
Shortness of breath	Yes	37 (3.6)	55 (5.4)	0.463
	No	64 (6.2)	871 (84.8)	
Persistent Cough	Yes	34 (3.3)	44 (4.3)	0.475
	No	52 (5.1)	897 (87.3)	
Chest pain	Yes	36 (3.5)	37 (3.6)	0.016
	No	62 (6.0)	892 (86.9)	
Voice hoarseness	Yes	19 (1.9)	38 (3.7)	1.000
	No	37 (3.6)	933 (90.8)	
Dizziness	Yes	98 (9.5)	71 (6.9)	0.023
	No	102 (9.9)	756 (73.6)	
Ringing in the ears (Tinnitus)	Yes	30 (2.9)	28 (2.7)	0.017
	No	50 (4.9)	919 (89.5)	
Nausea	Yes	53 (5.2)	36 (3.5)	0.073
	No	54 (5.3)	884 (86.1)	
Vomiting	Yes	9 (0.9)	17 (1.7)	0.061
	No	31 (3.0)	970 (94.4)	
Diarrhea	Yes	25 (2.4)	21 (2.0)	0.263
	No	30 (2.9)	951 (92.6)	
Abdominal pain	Yes	41 (4.0)	27 (2.6)	0.091
	No	42 (4.1)	917 (89.3)	
Tiredness and fatigue	Yes	254 (24.7)	82 (8.0)	0.002
	No	128 (12.5)	563 (54.8)	
Muscle pain (myalgia)	Yes	191 (18.6)	105 (10.2)	0.734
	No	111 (10.8)	620 (60.4)	
Joint pain	Yes	148 (14.4)	70 (6.8)	0.012
	No	104 (10.1)	705 (68.6)	
Swollen ankles and feet	Yes	4 (0.4)	11 (1.1)	1.000
	No	11 (1.1)	1001 (97.5)	
Sleep disturbances	Yes	49 (4.8)	20 (1.9)	0.010
	No	41 (4.0)	917 (89.3)	
Menstrual cycle changes	Yes	60 (8.6)	20 (2.9)	<0.001
	No	66 (9.5)	548 (79.0)	

*McNemar's test

Oxford/AstraZeneca

The AstraZeneca developed by Oxford University and British-Swedish Company AstraZeneca manufactured in India by serum institute and it's also called as Covishield. The AstraZeneca covid-19 vaccine, now called as a viral vector vaccine ,just like the Johnson and Johnson vaccine it uses as chimpanzee adenovirus to carry spike proteins from the corona virus into your body create an immune response.

CHIMPANZEE ADENOVIRUS

Adenovirus is a very common virus usually causing mild illness like the common cold. Adenovirus are wide spread and efficient there are more than 50 types of adenovirus that causes respiratory infection A chimpanzee adenovirus is an adenovirus that causes these infections in chimpanzees. When modified for use in vaccines these viruses are very efficient at helping to produce immune responses these type of vaccines like the AstraZeneca

vaccines are known as viral vector vaccines.

DOSAGE

One dose 0.5ml contains $5x10^{10}$ chadoxl-s (recombinant) viral particles, this product is also contains the excipients L-histidine, magnesium chloride hexahydrate and water for injection. The excipients are well established for pharmaceutical products Vaxzevria is given as two injection, usually into the muscle of the upper arm. The second dose should be given 4 and 12 weeks after the first dose. A booster dose may be given at least 3 months after the second dose. A booster dose of vaxzevria can also be given to adults who have had two doses of an authorized mRNA covid- 19 vaccines.

STORAGE

Temperature needed for storing AstraZeneca/vaxzevria vaccine +2° to 8°C.

APPROVAL

Vaxzevria vaccine may also be referred to as AzD1222, ChAdox1 nCoV-19 it's a non-replicating viral vector was approved in 149 countries including United Kingdom, Brazil, Canada, Australia, European Union, India and other countries. In some countries, the vaccine is distributed under the name vaxzevria. It's recommended for adults 18 years and older.

MECHANISMS OF ACTION

Vaxzevria works by preparing the body to defend itself against covid-19. It is made up of another virus (Adenovirus) that has been modified to contain the gene for making the SARS-COV-2 spike protein. This is a protein on the surface of the SARS-COV-2 virus which the virus needs to enter the body's cells. Once it has been given, the vaccine delivers the SARS-COV-2 gene into cells in the body. The cell will use the gene to produce the spike protein the person's immune system will then recognize this protein as foreign and produce antibodies and activate T-cells (white blood cells) to attack it. The adenovirus in the vaccine cannot reproduce and does not cause disease.

ADVERSE EVENT

Most common side effects are tenderness pain and bruising at the injection site, headache, tiredness, muscle pain, general feeling of being unwell, chills, fever, joint pain and nausea, they may affect more than 1 in 10 people. Thrombosis [formation of blood clots in the blood vessels] in combination with thrombocytopenia [low level of blood platelets] May affect upto 1 in 10,000 people. A very small number of cases of immune thrombocytopenia [a condition in which the immune system mistakenly Targets blood platelets, reducing the level and affecting normal blood clotting]

EFFICIENCY

Combined results from 4 clinical trials in the United Kingdom, Brazil and South Africa showed that vaxzevria was safe and effective at preventing covid-19 in people 18 years 28 age these studies involved around 24,000 people standard dose

- Cov001,a phase ½ trial in UK,
- Cov002,a phase trial in UK
- Cov003,a phase 3 trial in Brazil
- Cov005,a phase ½ trial in South Africa
- One dosing regimen (n=2,741) showed vaccine efficacy of 90% when AZD1222 was given as a half dose, followed by full dose at least one month apart, and another design regimen (n=8,895) showed 62% efficacy when given as two full dose at least one month apart. The combined analysis from both design regimens (n=11,636) resulted in average efficacy of 70% Report of blood clots, after administering the AstraZeneca covid-19 vaccine. The clots that are linked to this vaccine have very specific characteristics:
- The occur less common areas of the body, like the abdomen (or) brain.
- People affected also have low platelets levels.
- It was found that people with these blood clots showed some symptoms similar to a condition called heparin induced thrombotic thrombocytopenia (HITT).
- HITT is a rare side effect sometime seen in people who have used heparin, an anti-coagulant medication but the people vaccinated had never taken this drug. Researches after to this new condition as VITT [vaccine-induced thrombotic thrombocytopenia].
- Over 20 million doses of AstraZeneca vaccine have been given in the United Kingdom. The risk of a serious blood clot is about 1 in 250,000 people (or) 4 in 1 million.

Administration of the vaccine was paused in passed in many parts of the world as regulators investigated the clots

despite the initial pause about it safety regarding blood clots. Vaxzevria vaccine has been deemed safe by the European medicines agency (EMA) and is still recommended by WHO but some countries restricted its use to older adults.

CONCLUSION

Health care workers responded differently to the vaccine as compared to the general public. If they were better educated about which narrow population underwent the adverse reactions and fatalities upon being administered the vaccine, more number of them would accept the vaccine. Easy accessibility played a very big role in the general public saying yes to the vaccine, and the government could help in propagating easy accessibility in every corner of the country. The following steps may be taken by the government to address this issue: (1) standardizing a lower price for the vaccine across the country, (2) declaring small clinics around the block opened for the administration of the vaccine, (3) imbursing the further production and release of vaccine as there is a glaring shortage, (4) calling interns and medical students closer to graduation for vaccine administration duty. The general public had few concerns, and the biggest concern was the development of fever and myalgia post administration. However, even though the long-term effects of the vaccine are unclear and the efficacy of neither vaccine has been precisely determined and made public, the vaccines are surely more beneficial than not. The limitation of this survey was that we could not reach the rural areas to understand their perception, and the survey was filled by where to focus while educating health-care professionals and the general public that taking the vaccine is a better choice. Furthermore, the government must ensure adequate preparedness to vaccinate large numbers.

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