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Development and Interventions on Vaccines and Complications of Coronavirus

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Abstract

The advent of coronavirus disease has prompted the production of a COVID-19 vaccine. The COVID-19 vaccines, which over 12.7 billion doses worldwide, have been reported to have some complications. Out of the various COVID-19 vaccines, the three most common were studied to analyze their complications. The objectives of the research were (i) evaluation and systematic review of articles based on COVID-19 vaccines, (ii) assessment of complications of variants of COVID-19 vaccines, and (iii) intervention on complications of COVID-19 vaccines from different studies. Adenovirus vector, nucleic acid (mRNA), and protein subunit COVID-19 vaccines complications were assessed and studied using related articles. A systematic review was used to synthesize qualitative findings on COVID-19 vaccine complications. Seventy-five (75) articles were identified and screened from Google, PubMed, Web of Science, and Embase; only 26 articles met the inclusion criteria and were used for the qualitative synthesis. The qualitative findings on COVID-19 vaccine complications were neurological, cerebrovascular, cardiovascular, systemic, and local adverse events.

Keywords: Coronavirus (COVID-19) (C19); Complication of COVID-19 (CCV); Adenovirus vector (VVnr); Nucleic acid (RNA); Protein subunit (PS).

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1. Introduction

The coronavirus disease, popularly called COVID-19 (C19), is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), caused by a family of viruses called Coronavirus. The recent pandemic prompted the development of vaccines called COVID-19 vaccines. The fight against COVID-19 has facilitated the development of vaccines moving at record speed, with more than 170 different vaccines in trials [1].

The outbreak of pandemic diseases is substantially impactful on a global scale, and in most cases, it is highly impactful. The outbreak of coronavirus in 2019 has set the human race to develop vaccines, and some are still underdeveloped development. These COVID-19 vaccines (CV) have been reported recently to cause medical complications, namely uveitis and ocular complications [2], cerebrovascular complications [3], neurological complications [4] and even carditis in children and adolescents [5] just to mention a few.

Currently, 12.7 billion COVID-19 vaccine (CV) doses have been administered worldwide [6, 7], with 67.9 percent of the global population having received at least one dose [6]. Additionally, the United Kingdom has administered 53.8 million doses of vaccine, having utilized 50.9% as of April 2023 [6]. Furthermore, this study will focus on the commonly used vaccines mentioned above, mainly in the form of products, namely Pfizer/BioNTech (RNA) (over 600 million doses administered) [6, 7], Moderna (RNA) (over 200 million doses administered), Oxford-AstraZeneca (Adenovirus vector) (over 100 million doses administered), Janseen/Johnson & Johnson (Adenovirus vector), Novavax (Protein subunit), and Sanofi-GSK (Protein subunit) [6-8].

The complication of COVID-19 vaccines (CCV) is a concern for researchers, microbiologists, and medical experts. This research focuses on three types of COVID-19, namely adenovirus vector (non-replicating viral vector) (VVnr), nucleic acid (RNA), and protein subunit (PS), out of the 183 vaccines that have been clinically developed [9]. These COVID-19 vaccines were selected based on prevalence and their number of candidate vaccines which are in clinical development, namely protein subunit (32%), adenovirus vector (14%), and RNA (24%) [9]. Consequently, these popularly used vaccines and publications in which their complications have been established are the area of focus for this study.

Prominently, scholars have established that neurological complications [4, 10, 11], cerebrovascular complications [3], cardiovascular complications [12, 13] and uvetis & other ocular complications [2] are associated with the dosage of COVID-19 vaccines. These complications are ambiguously established, and it is therefore a research gap that this proposed study is willing to provide answers and establish facts by analyzing these complications of COVID-19 vaccines using a systematic approach.

This research is to assess the study of these side effects and complications using a systematic approach in evaluating and assessing different studies on complications and interventions of COVID-19 vaccines.

The objectives of the proposed research are:

- Evaluation and systematic review of articles based on COVID-19 vaccines.

- Assessment of complications of variants of COVID-19 vaccines
- Intervention on complications of COVID-19 vaccines from different studies.

2. Evaluation of Studies on COVID-19 Vaccines

Since its emergence in 2019, C19 has rapidly spread globally, leading to a pandemic, or an epidemiology. It has affected countries worldwide, with varying degrees of transmission rates and impacts on healthcare systems [14]. The pandemic of C19 was a result of various implications. The mode of transmission of C19 is the primary reason for the spread of C19 through respiratory droplets when an infected person coughs, sneezes, talks, or breathes [15, 16]. It can also spread by touching surfaces contaminated with the virus and then touching the face, particularly the mouth, nose, or eyes. The incubation period for COVID-19 is typically around 2 to 14 days, during which an infected person may not show any symptoms but can still transmit the virus to others [17].

COVID-19 vaccines are vaccines that are created to provide acquired immunity against SARS-CoV-2, the virus that causes COVID-19. The C19 vaccines are widely credited for their role in reducing the spread of C19 and reducing the severity and death caused by C19 [18]. According to Watson and his colleagues [19] C19 vaccines prevented an additional 14.4 to 19.8 million deaths in 185 countries and territories from 8 December 2020 to 8 December 2021

By December 2020, more than 10 billion vaccine doses had been preordered by countries, with about half of the doses purchased by high-income countries comprising 14% of the world's population [20]. Evidence from the use of vaccines during the pandemic shows that vaccination can reduce infection and is most effective at preventing severe COVID-19 symptoms and death, but is less effective at preventing mild COVID-19. In 2021, the CDC reported that unvaccinated people were 10 times more likely to be hospitalized and 11 times more likely to die than fully vaccinated people [21, 22].

Adenovector virus vaccines are the type of non-replicating viral vector vaccine, using an adenovirus shell containing DNA that encodes a SARS-CoV-2 protein [23]. The viral vector-based vaccines against COVID-19 are non-replicating, which means that they do not make new virus particles, but rather produce only the antigen, which activates a systemic immune response [23].

An RNA vaccine, also established as a messenger RNA (mRNA) vaccine, is a type of immunization that uses a replica of pre-existing mRNA to elicit an immune response. Pursuing immunization, RNA is transfected into immune cells and transformed into mRNA, allowing the host cells to produce extracellular protein [24].

Protein subunit vaccines contain pieces (proteins) of the virus that causes COVID-19. The pieces of the virus that cause COVID-19 are the spike protein. The vaccine also contains another ingredient that is known as an adjuvant, which helps the immune system respond to the spike protein in the future. Protein subunit vaccines are generally made through protein production, manipulating the gene expression of an organism so that it expresses large amounts of a recombinant gene [25]. A variety of approaches can be used for development depending on the vaccine involved. Yeast, baculovirus, or mammalian cell cultures can be used to produce large amounts of

proteins in vitro [26].

The complications of COVID-19 vaccines (CCV) are a major concern in the medical field and natural sciences. The vaccines administered to people have been reported to have one or two complications. This study critically and systematically reviews the complications of three major vaccines published by the World Health Organisation, namely adenovirus vector CVs, nucleic acid CVs, and protein subunit CVs.

Adverse reaction following immunization is defined as a post-vaccination event of CV that is either life-threatening, requires hospitalization, or results in severe disability. The World Health Organization listed Guillain-Barré syndrome (GBS), seizures, anaphylaxis, syncope, encephalitis, thrombocytopenia, vasculitis, and Bell's palsy as serious neurologic adverse events. The most devastating neurological post-vaccination complication of CV is cerebral venous sinus thrombosis (CVST). Cerebral venous sinus is frequently reported in females of childbearing age, generally following adenovector-based vaccination. Another major neurological complication of concern is Bell's palsy, which was reported dominantly following mRNA vaccine administration. Acute transverse myelitis (ATM), acute disseminated encephalomyelitis (ADE), and acute demyelinating polyneuropathy (ADP) are other unexpected neurological adverse events that occur as a result of the phenomenon of molecular mimicry [9].

Bolletta and his colleagues [2] conducted a research study on uveitis and other ocular complications following C19 vaccinations on 42 eyes of 34 patients with a mean age of 49.8 years (range 18-83 years) in 2021 at the Ocular Immunology Reggio Emilia, Italy. They reported that the mean time between the vaccination given to the patients and ocular complication onset was 9.4 days, which ranged from 1 to 30 days. It was concluded that uveitis and other ocular complications may develop after the administration of the CV to the patients.

De Michele and his colleagues [3] carried out a research study on cerebrovascular complications (CCs) of C19 and C19 vaccination disease infection. De Michele and his colleagues [3] stated that the novel DNA and mRNA vaccines offered great flexibility in terms of antigen production. It was concluded that the risk of stroke and other prespecified outcomes established by WHO following a SARS-CoV-2 infection was significantly higher than following vaccination with either the Oxford-AstraZeneca or Pfizer vaccines.

Fazlollahi and his colleagues [12] reviewed case reports on cardiac complications to identify the clinical profile, investigations, and management of reported cardiac complications post-mRNA COVID-19 vaccines. Fazlollahi and his colleagues [12] reported myocarditis as the most commonly reported adverse cardiac event associated with mRNA CV, which presented as chest pain with a rise in cardiac biomarkers.

Patone and his colleagues [11] performed an investigation on neurological complications after the first dose of CV and SARS-CoV-2 infection. A self-controlled case series study was conducted to investigate hospital admissions from neurological complications within 28 days after a first dose of ChAdOx1nCoV-19 (n = 20,417,752) or BNT162b2 (n = 12,134,782), and after a SARS-CoV-2-positive test (n = 2,005,280). Patoneand his colleagues [11] reported that, even though an increased risk of neurological complications in those who received CV was found, the risk of these complications is greater following a positive SARS-CoV-2

test.

Liu and his colleagues [13] performed a research study on the complications of cardiovascular on CV. Liu and his colleagues [13] established that "vaccination against SARS-CoV-2 has proven to be the most effective measure to suppress the pandemic". The first four applications of vaccines that have several adverse effects include ChAdOx1, Ad26.COV2.S, BNT162b2, and mRNA-1273.2. Significantly, the most serious type of complication is cardiovascular-related related which includes myocarditis, immune thrombocytopenia (ITP), and CSVT, among others. Thus, the incidence rate of mRNA vaccine-related ITP is almost the same as that of the baseline incidence rate for the population [13].

Fragkou and Dimopoulou [27] performed a study on the complications of C19 vaccines. The common mild side effects of the authorized vaccines, as reported by Fragkou and Dimopoulou [27] were increasingly reported worldwide during the post-marketing surveillance phase of vaccines' circulation, such as anaphylaxis, VITT, myopericarditis, and GBS. Fragkou and Dimopoulou [27] claimed that rare cases with complications from CV and the net benefit-risk ratio showed a favorable balance towards CVs for all age and sex groups. Furthermore, Fragkou and Dimopoulou [27] established that there were rare cases of severe vaccine complications and concluded that the complications should not constitute a reason for changes in the vaccine policy in order to alleviate concerns and reluctance to C19 vaccinations.

Oudjedi and his colleagues [28] carried out a report on CV side effects among Algerian athletes in 2022, in comparison between adenoviral vector and mRNA COVID-19 vaccines. It was reported that a cross-sectional survey-based validated questionnaire was used. A total of 273 athletes completed the survey, with over 54.6% of the athletes reporting at least one local side effect, while 46.9% reported at least one systemic side effect, which were more prevalent among the adenoviral vector group compared to the mRNA groups. The most common local side effect was injection site pain (29.9%), while fever (30.8%) was the most prevalent systemic side effect. The age group of 31–40 years, allergy, previous infection with C19, and the first dose of vaccines were associated with an increased risk of side effects for all groups of CV.

Aghabaklou and his colleagues [29] performed a study on cerebral coagulation complications of VVnr on CV. More than 2 billion doses of the vaccines against COVID-19 were administered worldwide by June 2021, resulting in a reduced number of severe cases and mortality. Similar to other vaccines, the CV caused benign complications such as headache, fever, diarrhea, and pain at the injection site. The administration of millions of doses containing adenoviral vector vaccines (e.g., Oxford-AstraZeneca (ChAdOx1 nCoV-19) and Janssen/Johnson & Johnson (Ad26.COV2. S)) has helped control the disease. Numerous cases of CVST with thrombocytopenia have been reported in vaccinated individuals, following the age of the patients ranging from 18 to 60. Among CVST cases following COVID vaccination, 44% succumbed to death. It was confirmed that early diagnosis and treatment of CVST play a fundamental role in decreasing morbidity and mortality, and the benefit of vaccination outweighs the potential harm.

Greinacher and his colleagues [30] reported observations on 11 patients from Germany and Austria in whom a diagnosis of thrombosis or thrombocytopenia after vaccination with the AstraZeneca. Approximately half of the

entire thrombotic events diagnosed were located in the cerebral veins (9/19, 47.4%), and splanchnic vein thrombosis and pulmonary embolism were each detected in three patients (3/19, 15.8%). Interestingly, a total of 19 thrombotic events were identified in only 11 patients, leading to the conclusion of a frequent appearance of multilocular thrombosis.

Hosseini and Askari [31] carried out a study on the neurological side effects of C19 vaccination. According to these reports, vaccination has adverse effects, especially on the nervous system. The most important and common complications are cerebrovascular disorders including CVST, transient ischemic attack (TIA), intracerebral hemorrhage (IH), ischemic stroke (IS), and demyelinating disorders (DD) including transverse myelitis (TM), first manifestation of multiple sclerosis (MS), and neuromyelitis optica (NO). These effects are often acute and transient, but they can be severe and even fatal in a few cases.

Kroumpouzos and his colleagues [32] conducted a study on cutaneous complications of mRNA and AZD1222 C19 vaccines. Kroumpouzos and his colleagues [32] established that cutaneous reactions were more prevalent in females (81.6%) while delayed large local reactions were the most common complication (40.4%), followed by local injection site reactions (16.5%), zoster (9.5%), and urticarial eruptions (UE) (9.0%). Moreover, injection site and delayed large local reactions were predominantly caused by the mRNA-1273 vaccine (79.5% and 72.0%, respectively). Conclusively, appropriate patient counseling regarding cutaneous reactions to COVID-19 vaccines is crucial and prevents generating concerns disproportionate to potential complications.

Malayala and his colleagues [33] reported that, upon receiving the first dose of the Novavax vaccine, a 60-year-old African-American man developed the symptoms of low-grade fever, chills, followed by the appearance of a severe generalized rash on his skin that quickly spread throughout his body [33]. From mid-February to mid-March, nearly 5 million people in Israel were vaccinated with the BNT162b2 mRNA vaccine, and four patients were diagnosed with acquired thrombotic thrombocytopenic purpura (ATTP) [34].

Dadras and his colleagues [35] conducted a research study on the safety and adverse events related to Novavax. Dadras and his colleagues [35] reported that the most common local side effects included injection site pain and swelling, redness, and pruritus. Also, fatigue, headache, muscle pain, fever, and gastrointestinal symptoms, including abdominal pain and diarrhea, were among the most common systemic adverse effects. Dadrasand his colleagues [35] concluded that C19 vaccines, which include Novavax, were considered safe choices due to having milder side effects and fewer severe, life-threatening adverse events.

Kim and his colleagues [36] conducted an assessment on the safety surveillance of the NVX-CoV2373 CV among Koreans aged 18 years and above. Kim and his colleagues [36] carried out the study using the COVID-19 vaccination management system (CVMS) and the text-message survey (TMS) to analyze the national safety data. Kim and his colleagues [36] reported that CVMS identified that the rate of adverse events per 100,000 doses were lower after booster doses (84.0) than after dose 1 (254.6) or dose 2 (272.9); and in 65-year-olds and over (83.4) than in 18- to 64-year-olds (168.1) while the TMS found that local and systemic adverse events were lower in 65-year-olds and over than in 18- to 64-year-olds. Conclusively, no major safety issues and fewer adverse events were identified following the Novavax COVID-19 vaccination among 65-year-olds and above in

Korea.

Yasmin and his colleagues [37] carried out a study on the adverse events of cardiovascular complications, thrombosis, and thrombocytopenia on C19 mRNA vaccines. Yasmin and his colleagues [37] stated that the mRNA vaccines on cardiovascular complications, first and second dose, include pericarditis/myopericarditis, myocarditis, hypotension, arrhythmia, cardiogenic shock, stroke, myocardial infarction (MI)/STEMI, IH, thrombosis, and pulmonary embolism (PE). Thrombotic events were the most common complication analyzed for both vaccines overall, and which affected individuals with displayed symptoms such as severe headache, dizziness, visual disturbances, fever, and shortness of breath.

Li and Wu [38] analyzed C19 RNA-based vaccines. RNA-based vaccines were the first to be created and approved for use in humans, and they continue to play a crucial role in the global effort to fight the illness. Also, RNA vaccines have recently achieved significant success in the fight against COVID-19, with high protection rates above 90% for the Pfizer and Moderna vaccine candidates in the United States.

Kim and his colleagues [39] conducted a research case study on acute myopericarditis after NVX-CoV2373 (Novavax) COVID-19 vaccination. Kim and his colleagues [39] reported that a 30-year-old man was referred to the emergency department with complaints of chest pain and a mild febrile sense for two days after he had received the second dose of Novavax CV. Furthermore, acute myopericarditis by the vaccination was diagnosed by cardiac endomyocardial biopsy and was treated with corticosteroids. Kim and his colleagues [39] concluded that the present case suggests acute myopericarditis as a vaccination complication by Novavax in Korea.

Underwood and his colleagues [40] conducted a research study on the safety, efficacy, and immunogenicity of the NVX-CoV2373 vaccine in adults and adolescents aged ≥12 years in the US. Underwood and his colleagues [40] carried out the research using the clinical trials method, where NVX-CoV2373. Underwoodand his colleagues [40] reported that NVX-CoV2373 vaccination was associated with complete protection against severe disease and a high (90%) rate of protection against symptomatic disease in adults. Conclusively, the NVX-CoV2373 adjuvanted recombinant protein platform offers a means to address issues of COVID-19 vaccination hesitancy and global vaccine equity.

El Sahly and his colleagues (2021) experimented on the efficacy of the MRNA-1273 SARS-CoV-2 vaccine after the blinded phase on 30,415 participants. The study was analysed using observer-blinded, placebo-controlled clinical trial techniques to determine the level of efficacy in preventing COVID-19. They reported that over 96% of participants received both injections, while 2.3% of the participants had evidence of SARS-CoV-2 infection at baseline, and the median follow-up was 5.3 months in the blinded phase. The results indicated that 1.8% of placebo recipients and 2.2% in vaccines were recorded for hypersensitivity reactions, anaphylaxis occur in 2 participants (<0.1%), dermal filler reactions were reported in 14 placebo recipients (<0.1%) and 20 mRNA-1273 recipients, thromboembolic events were observed in in 43 placebo recipients (0.3%) and 47 mRNA-1273 recipients, and pericarditis events occurred in 2 participants each.

Ali and his colleagues (2021) evaluated the mRNA-1273 SARS-CoV-2 vaccine on the incidence of COVID-19

among adolescents between 12 and 17 years of age in 3732 participants. Ali and his colleagues (2021) carried out the research using a placebo-controlled trial method to randomly assign healthy adolescents to receive two injections of the mRNA-1273 vaccine or placebo. They reported that the most common solicited adverse reactions after the first or second injections were injection-site pain (in 93.1% and 92.4%, respectively), headache (in 44.6% and 70.2%, respectively), and fatigue (in 47.9% and 67.8%, respectively. Also, it was reported that no cases of COVID-19 with an onset of 14 days after the second injection were indicated in the mRNA-1273 group. Ali and his colleagues (2021) concluded that the mRNA-1273 vaccine was efficacious in preventing COVID-19 due to its similarity in young adults.

Sadoff and his colleagues (2021) researched the safety and efficacy of single-dose Ad26.COV2.S vaccine against COVID-19, ,630 SARS-CoV-2 negative participants. The research was carried out using a randomized double-blind placebo-controlled clinical trial. Sadoff and his colleagues reported that vaccine efficacy was higher against severe–critical C19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥14 days and 85.4% [adjusted 95% CI, 54.2 to 96.9] for onset at ≥28 days). Also, it was reported that injection-site pain was the most common local adverse reaction, while headache, fatigue, myalgia, and nausea were systemic adverse reactions.

Polack and his colleagues (2020) carried out a research study on the safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine on 43,548 participants who underwent randomization. The study was conducted using a placebo-controlled, observer-blinded, pivotal efficacy trial method to randomly assign people to receive vaccine doses. Polack and his colleagues (2020) reported that safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site (1% of participants), pain (78% participants) in local adverse reaction, while fatigue (59% of the participants), headache (52% of the participants). It was also reported that the incidence of serious adverse events was low. Conclusively, a two-dose regimen of the BNT162b2 vaccine conferred 95% protection against COVID-19 in persons 16 years of age or older.

Malayala and his colleagues [33] reported that, upon receiving the first dose of the Novavax vaccine, a 60-year-old African-American man developed the symptoms of low-grade fever, chills, followed by the appearance of a severe generalized rash on his skin that quickly spread throughout his body [33]. From mid-February to mid-March, nearly 5 million people in Israel were vaccinated with the BNT162b2 mRNA vaccine, and four patients were diagnosed with acquired thrombotic thrombocytopenic purpura (ATTP) [34].

3. Qualitative Synthesis on Complications of COVID-19 Vaccines

This study was performed and reported based on the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and as conducted by prominent scholars. [29, 32, 41, 42]**.** A concise literature search was executed for the three featured vaccines, namely Adenovirus vector, RNA, and protein subunit, on Google Scholar, ResearchGate, PubMed, Embase, and Web of Science databases. Using the following key terms

1. COVID-19 vaccine complications “AstraZeneca” or Oxford-AstraZeneca” and “ChAdOx1 nCoV-19 COVID-19 vaccine”)

2. "Janssen" or "Johnson & Johnson COVID vaccine complication" or"Ad26.COV2 COVID vaccine"
3. mRNA COVID-19 vaccine and nucleic COVID-19 vaccine complications, Moderna and Pfizer BioNTech
4. protein subunit COVID vaccine complication, Novavax vaccine complication, and Nanocovax vaccine complication

All the relevant articles on COVID-19 complications, namely ocular, neurological, cerebrovascular, cardiovascular, and so on, were captured. More than fifty complications were gathered from the eligible articles. These complications were analyzed and grouped accordingly. Figures 1 and 2 present the complications of CV. These complications are perceived from vaccines which include AstraZeneca-Oxford, Johnson Johnson, nucleic (Moderna and Pfizer-BioNTech), and protein subunit (Novavax). Tables 1 and 2 present CV complications with the referenced COVID-19 vaccines. The table indicates that nucleic (Moderna and Pfizer-BioNTech) and adenoviral (AstraZeneca-Oxford, Johnson & Johnson) vaccines appeared as the most used vaccines and have several COVID-19 complications and side effects.

Figure 1 shows that cardiovascular complications are the most common adverse side effects among COVID-19 patients, while Figure 4 shows that the most common reaction (complications) among patients with COVID-19 is systemic adverse events. Also, Table 1 indicated that pericarditis/myopericarditis side effects (cardiovascular complications) is the most reference side effects by the authors in accordance to the gathered articles, while Table 2 shows that fever side effects (systemic adverse events) is the most common disease among COVID-19 patients in accordance to the gathered articles by the authors.

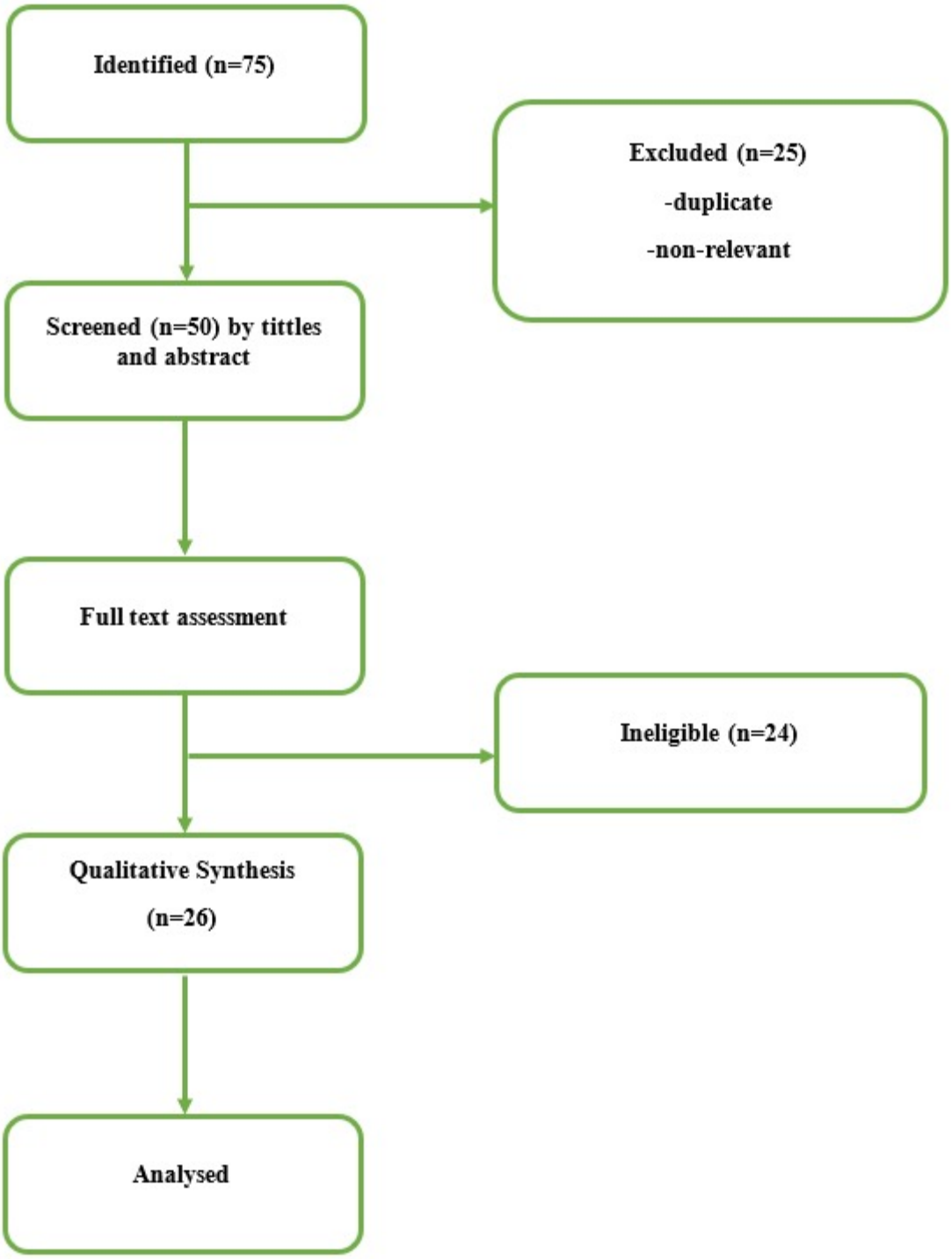

Figure 1: Analysis chart of COVID-19 vaccine complication articles

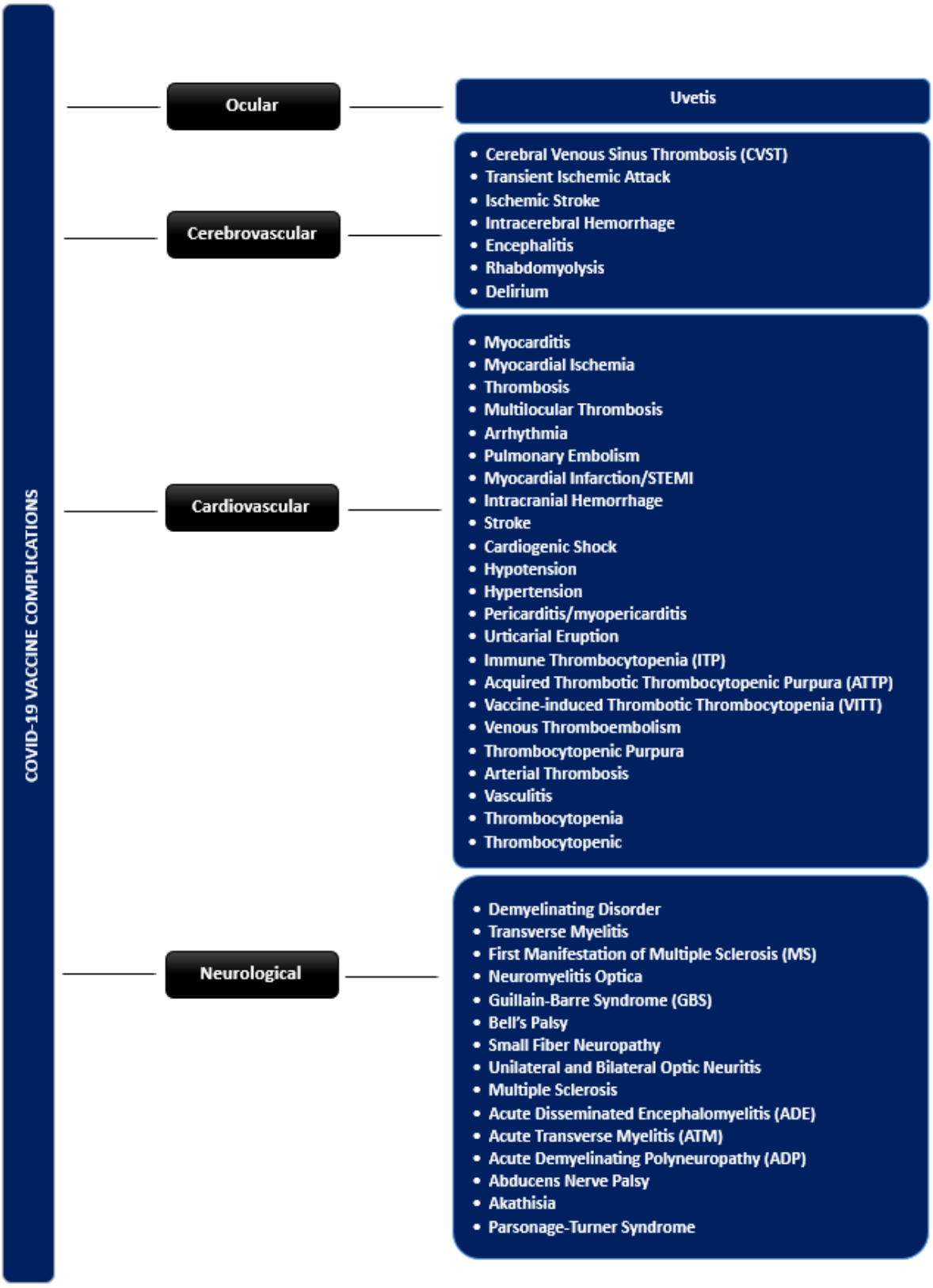

Figure 1: Categorize COVID-19 vaccine complications

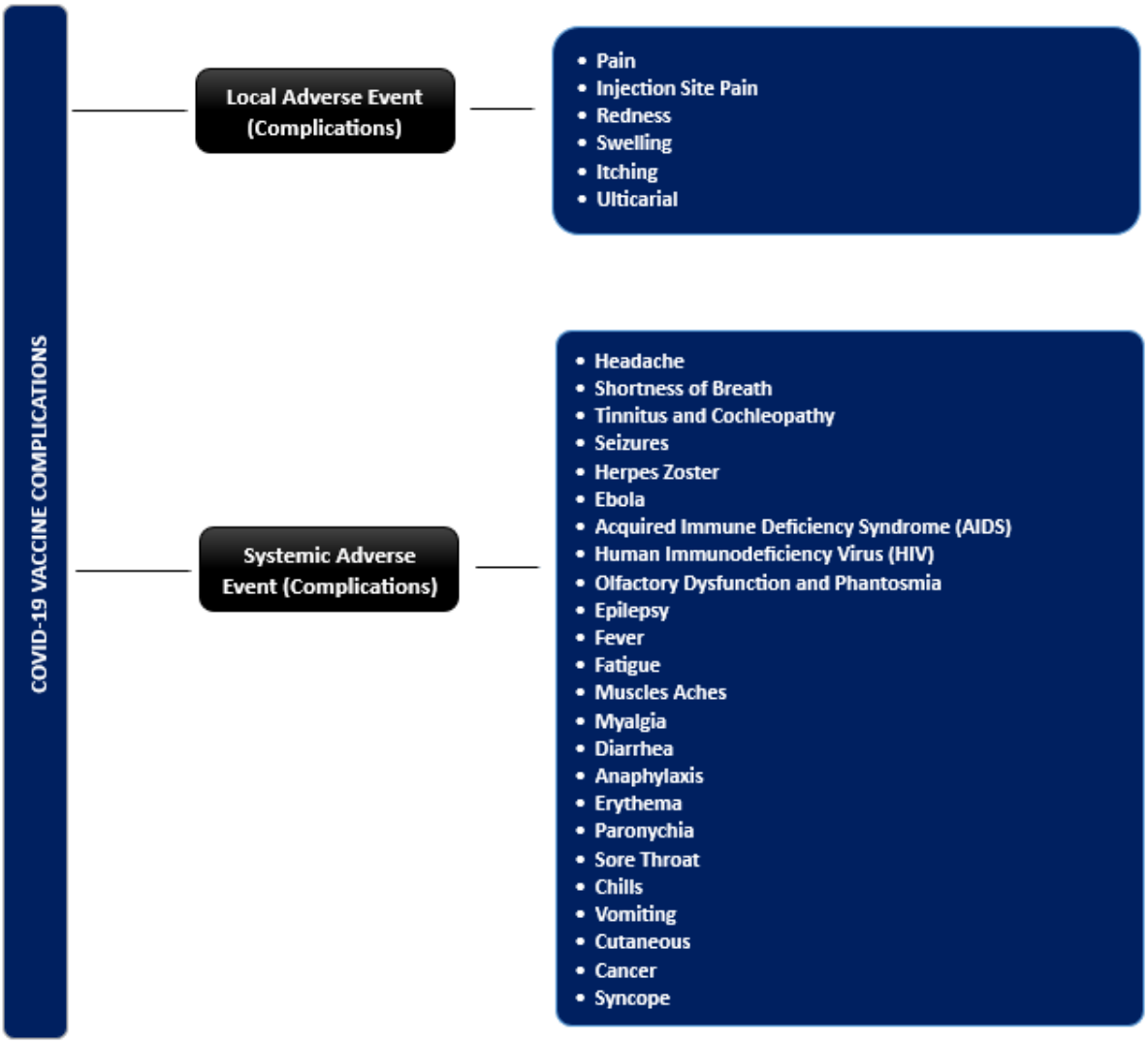

Figure 2: Categorized COVID-19 vaccine complications

Table 1. a: Categorized CV complications with the C19 vaccine responsible

N	CV Complication	Side Effects	Vaccine	Vaccine Brand
1	Ocular	Uveitis [2, 37]		
2	Cerebrovascular	Cerebral venous sinus thrombosis (CVST) [3, 29, 31, 38]	VV	AstraZeneca, Johnson & Johnson
		Transient ischemic attack[31]	VV, mRNA	Johnson & Johnson, Pfizer
		Ischemic stroke [12, 31]	VV, mRNA	AstraZeneca, Pfizer
		Intracerebral hemorrhage [31]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Encephalitis [9]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Rhabdomyolysis	mRNA, VV	Pfizer, AstraZeneca
		Delirium	mRNA	Pfizer
3	Cardiovascular[17]	Myocarditis [12, 13, 37, 43-46]	mRNA	Pfizer, Moderna
		Myocardial Ischemia [12]	mRNA	Moderna
		Thrombosis [3, 37]	mRNA, VV	Pfizer, AstraZeneca
		Arrhythmia [37]	mRNA	Pfizer, Moderna
		Pulmonary embolism [37]	mRNA	Moderna, Pfizer
		Myocardial infarction/STEMI [3],[37]	mRNA	Moderna, Pfizer
		Intracranial hemorrhage [41],[37]	mRNA	Moderna, Pfizer
		Stroke[3],[37]	mRNA	Moderna, Pfizer
		Cardiogenic shock [37]	mRNA	Moderna, Pfizer
		Hypotension [37]	mRNA	Moderna, Pfizer
		Hypertension [37]	mRNA	Moderna, Pfizer
		Pericarditis/myopericarditis [12, 37, 39, 45, 46]	mRNA	Moderna, Pfizer
		Immune Thrombocytopenia ITP [13, 41, 47]	mRNA	Pfizer
		Acquired Thrombotic Thrombocytopenic Purpura (ATTP) [33]	mRNA	Pfizer
		Vaccine-induced Thrombotic Thrombocytopenia (VITT) [27, 47, 48]	VV	AstraZeneca, Johnson & Johnson
		Thrombocytopenic purpura	mRNA, VV	Moderna, AstraZeneca, Johnson & Johnson
		Arterial Thrombosis [3, 49]	mRNA	Moderna
		Thrombocytopenia [3, 29, 37, 48]	mRNA	Moderna

Table 1b: Categorized CV complications with the C19 vaccine responsible

N	CV Complication	Side Effects	Vaccine	Vaccine Brand
4	Neurological [11, 31]	Transverse myelitis [31]	VV, mRNA	AstraZeneca, Johnson & Johnson, Pfizer, Moderna
		First manifestation of Multiple Sclerosis (MS)	VV, mRNA	Sputnik, Pfizer, Moderna
		Neuromyelitis optica [31]	mRNA	Pfizer
		Guillain-Barré syndrome (GBS) [9, 27]	VV	AstraZeneca, Johnson & Johnson
		Bell's palsy [9]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Small fiber neuropathy	mRNA	Pfizer, Moderna
		Unilateral and bilateral optic neuritis	VV	AstraZeneca
		Acute disseminated encephalomyelitis (ADE)	VV, mRNA	AstraZeneca, Pfizer
		Acute Transverse Myelitis (ATM)	VV	AstraZeneca
		Acute Demyelinating Polyneuropathy (ADP) [9]	mRNA	Pfizer
		Abducens nerve palsy	mRNA	Pfizer
		Akathisia	mRNA	Pfizer
		Parsonage-Turner syndrome	VV, mRNA	AstraZeneca, Pfizer
5	Local Adverse Events (Complications)	Pain [36]	VV, mRNA	AstraZeneca, Moderna
		Injection Site Pain [28, 32, 44, 45]	VV, mRNA	AstraZeneca, Pfizer
		Redness [36]	VV, mRNA	AstraZeneca, Pfizer
		Swelling [36]	VV, mRNA	AstraZeneca, Pfizer
		Itching [36]	VV, mRNA	AstraZeneca, Moderna
		Urticarial [36]	VV, mRNA	AstraZeneca, Pfizer
6	Systemic Adverse Event (Complications)	Headache [35, 37, 44, 45]	VV, mRNA	AstraZeneca, Sputnik, Pfizer
		Shortness of Breath [37]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Tinnitus and cochleopathy	VV, mRNA	AstraZeneca, Pfizer
		Seizures [9]	VV, mRNA	AstraZeneca, Pfizer
		Herpes zoster [32]	VV, mRNA	AstraZeneca, Pfizer, Moderna

Table 1c: Categorized CV complications with the C19 vaccine responsible

N	CV Complication	Side Effects	Vaccine	Vaccine Brand
6	Systemic Adverse Event (Complications)	Epilepsy	mRNA	Moderna
		Fever [28, 33, 35, 37, 44]	mRNA	Moderna
		Fatigue [35, 44, 45]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Muscle Aches [44]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Myalgia [45]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Diarrhea [35, 50]	VV	AstraZeneca
		Anaphylaxis [9, 27, 44, 51]	mRNA	Moderna, Pfizer
		Erythema [51]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Paronychia [45]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Sore Throat [50]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Chills [45]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Vomiting [50]	VV, mRNA	AstraZeneca, Pfizer, Moderna
		Cutaneous [32]	VV, mRNA	Moderna, AstraZeneca

4. Discussion

The systematic review employed in this research is based on qualitative synthesis. The qualitative findings are extracted from relevant articles, which are categorized and related to each COVID-19 vaccine. Qualitatively, ocular complication was analyzed. Ocular complications are one of the rare findings synthesized from an article established by Bolletta and his colleagues [2]. Bolletta and his colleagues [2] claimed that adults between the ages of 18-83 years experienced ocular complications, which were mainly uveitis, after administration of COVID-19 vaccines.

From eligible studies, neurological complications are one of the common complications of COVID-19 vaccines that occur after vaccination. Neurological complications are comorbidities of COVID-19 disease. These neurological complications gathered from eligible studies are transverse myelitis [31], first manifestation of multiple sclerosis (MS) [31], neuromyelitis optica (Hosseini and Askari, 2023), Guillain-Barré syndrome (GBS) [14, 27], Bell's palsy ([14] and so on.

Several articles claimed that neurological complications are perceived and experienced after receiving a dose of the COVID-19 vaccines. Patone and his colleagues [11] established that neurological complications after the first dose of CV and SARS-CoV-2 infection have an increased risk of neurological complications in those who received Covid-19 vaccines, and the risk of these complications is greater following a positive SARS-CoV-2 test. These neurological complications were confirmed by Hosseini and Askari [31], who stated that the neurological side effects of COVID-19 vaccination are experienced as cerebrovascular disorders, which include

demyelinating disorders, including transverse myelitis, the first manifestation of MS, and neuromyelitis optica. Hosseini and Askari [31] also highlighted that COVID-19 vaccines induced complications after vaccination.

The CVs responsible for these neurological complications are AstraZeneca-Oxford, Johnson &Johnson, Pfizer, and Moderna; only Novavax has not been reported to have neurological complications.

From eligible studies, cerebrovascular complications are the least common complication of COVID-19 vaccines, which occur after vaccination. Although cerebrovascular complications are closely related to neurological and cardiovascular complications. Cerebrovascular complications are a subgroup of cardiovascular morbidities according to WHO [52]. The cerebrovascular complications established so far are transient ischaemic stroke, cerebral venous sinus thrombosis (CVST), ischaemic stroke, intracerebral hemorrhage, and others. Also, AstraZeneca-Oxford is the vaccine responsible for this complication, and rarely, Pfizer and Moderna have been named to cause cerebrovascular complications. Liu and his colleagues [13] established that the most serious type of complication is cerebrovascular-related, which also includes cerebral venous sinus thrombosis for CV complications. Hosseini and Askari [31] confirmed in their study that COVID-19 vaccination causes cerebral venous sinus thrombosis, which was an important and one of the common complication. Hosseini and Askari [31] also identified other cerebrovascular disorders, namely transient ischemic attack, intracerebral hemorrhage, and ischemic stroke.

Cardiovascular complications are one of the most common after-vaccination complications. Also, cardiovascular complications are comorbidities of COVID-19 disease. These cardiovascular complications, gathered from eligible studies, are myocarditis [12, 13, 53], myocardial ischemia [12], thrombosis [3, 37, 48], arrhythmia [37], pulmonary embolism [37], myocardial infarction/ STEMI [3, 37], intracranial hemorrhage [37, 41], stroke [3, 37], cardiogenic shock [37], hypotension [37], hypertension [37], pericarditis/myopericarditis [12, 37, 54], immune thrombocytopenia [13, 41, 47], acquired thrombotic thrombocytopenic purpura (ATTP) [33], vaccine-induced thrombotic thrombocytopenia (VITT) [27, 47, 48], arterial thrombosis [3], vasculitis [14], thrombocytopenia [29, 48]. All the COVID-19 vaccines except Novavax are responsible for one or more complications. The vaccines responsible for most of these complications are Moderna (mRNA) and AstraZeneca-Oxford (Adenovirus).

Fazlollahi and his colleagues [12] established that myocarditis is the most commonly reported adverse cardiac event associated with the mRNA COVID-19 vaccine. De Michele and his colleagues (2022) established that the risk of stroke and other prespecified outcomes of interest (thrombocytopenia, venous thromboembolism, arterial thrombosis, CVST, and myocardial infarction) following a SARS-CoV-2 infection was significantly higher than following vaccination with either the Oxford-AstraZeneca or Pfizer vaccines. Liu and his colleagues [13] listed four vaccine applications, namely, ChAdOx1, Ad26.COV2.S, BNT162b2, and mRNA-1273.2 that induce cardiovascular complications. Significantly, the most serious type of complication is cardiovascular-related, which include myocarditis and immune thrombocytopenia (ITP). Fragkou and Dimopoulou [27]established that increased complications of C19 vaccines during the post-marketing surveillance phase of vaccine' circulation, namely vaccine-induced thrombotic thrombocytopenia, myopericarditis, and Guillain-Barré syndrome (GBS) and Guetl and his colleagues [48] confirmed the occurrence of thrombotic events at unusual sites, namely the

venous vascular system, which are in association with concomitant thrombocytopenia.

Greinacher and his colleagues [30] claimed that diagnosis of thrombosis or thrombocytopenia after vaccination with the AstraZeneca adenovirus vector vaccine ChAdOx1 nCov-19 among patients. Bidari and his colleagues [41], also claimed that mRNA-based COVID-19 vaccines, namely BNT16B2b2 and mRNA-1273, induce ITP after the first dose of COVID-19 vaccination, just like AstraZeneca-Oxford, within 12 days after vaccination. This is further validated in Yasminand his colleagues [37] who claimed that adverse events of cardiovascular complications, namely thrombosis and thrombocytopenia, are induced by COVID-19 mRNA vaccines. Moreover, the second dose of mRNA vaccines induces cardiovascular complications pericarditis/myopericarditis, myocarditis, hypertension, cardiogenic shock, stroke, myocardial infarction, intracranial hemorrhage, thrombosis (of various types), and pulmonary embolism.

Abdulla and his colleagues (2021) established that in rare cases, protein subunit COVID-19 vaccines induce serious side effects such as myocarditis (inflammation of the heart muscle), however, these side effects are very rare. Maayan and his colleagues [34] claimed that out of 5 million people in Israel who were vaccinated with the BNT162b2 (Pfizer) mRNA vaccine, some patients were diagnosed with acquired thrombotic thrombocytopenic purpura (ATTP). Twentyman and his colleagues [54] stated that myocarditis/pericarditis complication was experienced by patients administered protein subunit-based Novavax COVID-19 vaccine. El Sahlyand his colleagues [51] stated that patients who received the mRNA-1273 vaccine developed common adverse reactions, namely thromboembolic events. Kim and his colleagues [36] established that among serious adverse events, acute cardiovascular injury, including myocarditis, is experienced by some vaccine recipients.

Systemic complications are also one of the most common after-vaccination complications. The various complications gathered from the eligible studies are headache [35, 37, 44, 45], shortness of breath [37], seizures [9], herpes zoster [32], fever [28, 33, 35, 37, 44], fatigue [35, 44, 45], muscle aches [44], myalgia [45], diarrhea [35, 50], anaphylaxis [9, 27, 35, 44], erythema [51], paronychia [45], sore throat [50], chills [45], vomiting [50], and cutaneous [32]Systemic complications are the most common reaction event, established by several authors. These systemic include fever, headache, chills, sore throat, seizures, and many more. Systemic complications have a large effect size, a negative one associated with the dosage of the vaccine.

Aghabaklou and his colleagues [29] established that the COVID-19 vaccine causes benign complications such as headache, fever, and diarrhea. El Sahlyand his colleagues [51] stated that patients who received the mRNA-1273 vaccine developed common adverse reactions, namely hypersensitivity reactions, anaphylaxis, and dermal filler reactions. Oudjedi and his colleagues [28] claimed that vaccine side effects among Algerian athletes who experienced at least one systemic side effect (fever) were more prevalent among the adenoviral vector group compared to the mRNA groups. Yasmin and his colleagues [37], went further and established that although thrombotic events were the most common complication perceived by individuals after vaccination yet individuals still display symptoms such as severe headache, dizziness, visual disturbances, fever, and shortness of breath. Abdulla and his colleagues [44], stated that the most common side effects of protein subunit COVID-19 vaccines are mild and include fever, fatigue, headache, muscle aches, and chills, and these side effects usually go away on their own within a few days and in rare cases protein subunit COVID-19 vaccines can cause

more serious side effects such as anaphylaxis.

Malayala and his colleagues [33] established that, upon receiving the first dose of the Novavax vaccine, a man developed the symptoms of fever, chills, followed by the appearance of a severe generalized rash on his skin that quickly spread throughout his body. Fragkou and Dimopoulou [27], attested that increased complications of C19 vaccines during the post-marketing surveillance phase of vaccine circulation induce anaphylaxis. Aliand his colleagues [55], **e**stablished individuals who received mRNA-1273 experienced the most common solicited systemic adverse reactions after the first or second injections were headache and fatigue. Chu and his colleagues [56] stated that the most frequently solicited systemic AR corrected after the first vaccination were headache, fatigue, which are prevalent among older individuals. Furthermore, incidences of myalgia, arthralgia, nausea/vomiting, and chills are increased after the second vaccination in the mRNA-1273 cohort. The majority of solicited adverse reactions (AR) were mild and moderate in severity. Twentyman and his colleagues [54] extended their claim, and added that among vaccine recipients aged ≥16 years within both precrossover and postcrossover vaccine. The most common reactions associated with any vaccine dose included tenderness, fatigue, muscle pain, and headache, while cases of myocarditis or pericarditis were also detected in Novavax clinical trials [54].

Kim and his colleagues [36] established vaccine recipients aged 18 years and over who received the Novavax COVID-19 vaccination reported the most common systemic adverse event symptoms, namely myalgia, headache, dizziness, chest pain, and allergic reactions. Walter and his colleagues [57], already been established that children who received BNT162b2 experienced fatigue, headache, chills and muscle pain, and fever. The same year, Sablerollesand his colleagues [58] established that patients who received Ad26.COV2.S vaccine experienced the most common adverse reactions, namely fatigue, chills, fever, nausea, headache, muscle aches, and joint. Kroumpouzos and his colleagues [32] specified that common complications include zoster and urticarial eruptions in patients vaccinated with Moderna vaccines. Sadoff and his colleagues [59] claimed that participants in the vaccine group experienced headache, fatigue, myalgia, and nausea as systemic reactions.

Local complications are also one of the most common after-vaccination complications. The various complications gathered from the eligible studies are injection site pain [28, 32, 44, 45], redness [36], swelling [36], itching [36], and urticarial [36]. From eligible studies, neurological complication is the fourth common complication of COVID-19 vaccines, which occur after vaccination. Neurological complications are comorbidities of COVID-19 disease. These neurological complications gathered from eligible studies are transverse myelitis. The local complications or simply local reactions experienced by vaccine recipients include injection site pain, redness, swelling, and itching. Walter and his colleagues [57], already been established that children who receive BNT162b2 experience a common reaction, namely injection-site pain. Twentyman and his colleagues [54] confirmed that one of the local the most common reactions associated with any vaccine dose included injection site pain. Ali and his colleagues [55], **e**stablished individuals who received mRNA-1273 experienced the most common solicited systemic adverse reactions after the first or second injections, that is, injection-site pain. Aghabaklou and his colleagues [29] established that the COVID-19 vaccine causes benign complications such as pain at the injection site.

Oudjedi and his colleagues [28] claimed that COVID-19 vaccine side effects experienced among Algerian athletes include at least one local side effect (injection site pain), which was more prevalent among the adenoviral vector group compared to the mRNA groups. Kroumpouzosand his colleagues [32], stated that cutaneous reactions were more prevalent in females among local reactions that are experienced among vaccinated persons. Injection site and delayed large local reactions were predominantly caused by the mRNA-1273 vaccine [32]. Abdullaand his colleagues [44], claimed that the most common side effects of protein subunit COVID-19 vaccines are mild and these are mainly local reactions, namely pain and swelling at the injection site, and these side effects usually go away on their own within a few days. Dadrasand his colleagues [35] established that the protein subunit vaccines (Novavax) are considered safe choices due to having milder side effects and fewer severe life-threatening adverse events; these side effects are local reactions. Falseyand his colleagues [60] has a different finding; they established that AZD1222 (Johnson and Johnson) is safer, that is, the most common adverse events are general pain, injection-site pain, which are mild in nature. Polack and his colleagues [61], established that the safety profile of BNT162b2 is characterized by short-term, mild-to-moderate pain at the injection site and Sadoffand his colleagues [59] claimed that participants in the vaccine group experienced injection-site pain as the most common local reaction.

5. Conclusion

In conclusion, this systematic review has provided valuable findings on complications associated with COVID-19 vaccines. The findings presented a concise overview of various COVID-19 vaccines and their potential adverse effects. Overall, the evidence indicates that mRNA vaccines have the highest record of complications, which include all the categories outlined in this research, namely ocular, cardiovascular, cerebrovascular, neurological, systemic, and local complications. Moderna mRNA accounts for 80% of these complications. Adenovirus vector vaccines also have a record of cardiovascular, cerebrovascular, neurological, local, and systemic complications. Overall, systemic complications are the adverse events commonly experienced after the vaccination from any of the vaccines, be it adenovirus vector, nucleic acid, or protein subunit.

This study has gathered qualitative findings on complications of COVID-19 vaccines, which categorically can be neurological, cerebrovascular, cardiovascular, local, or systemic. These findings are deemed to have important implications for clinical practice and future research in addressing and managing these complications effectively. However, further studies and investigations are needed to validate and strengthen these results. Hence, the complication of COVID-19 vaccines is real and substantially affecting the vaccine recipients.

Key Findings:

1. The analyzed data showed that the most common side effects of COVID-19 vaccines are systemic or local, which are mild and self-limiting, such as fever, pain at the injection site, fatigue, and headache.

2. Serious complications, such as anaphylaxis, thrombosis, and carditis, are rare but notable.

3. Nucleic acid vaccine mRNA has the highest dosage worldwide and the highest record of vaccine complications.

6. List of Abbreviations

Table 4

ADE	Acute Disseminated Encephalomyelitis
ADP	Acute Demyelinating Polyneuropathy
AR	Adverse Reaction
ATM	Acute Transverse Myelitis
ATTP	Acquired Thrombotic Thrombocytopenic Purpura
C19	COVID-19
CCs	Cerebrovascular Complications
CCV	Complication of COVID-19 Vaccines
CI	Confidence Interval
CV	COVID-19 Vaccines
CVC	COVID-19 Vaccines Complication
CVMS	COVID-19 Vaccination Management System
CVST	Cerebral Venous Sinus Thrombosis
DD	Demyelinating Disorders
GBS	Guillain-Barré syndrome
IH	Intracerebral Hemorrhage
IS	Ischemic Stroke
ITP	Immune Thrombocytopenia
MS	Multiple Sclerosis
NO	Neuromyelitis Optica
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PS	Protein Subunit
SE	Standard Error
TIA	Transient Ischemic Attack
TM	Transverse Myelitis
TMS	Text-Message Survey
UE	Urticarial Eruptions
VITT	Vaccine-induced Immune Thrombotic Thrombocytopenia

References

[1] G. Staff, "There are four types of COVID-19 vaccines: here is how they work," ed, 2020.

[2] E. Bolletta *et al.*, "Uveitis and other ocular complications following COVID-19 vaccination," *Journal of clinical medicine,* vol. 10, no. 24, p. 5960, 2021.

[3] M. De Michele *et al.*, "Cerebrovascular complications of COVID-19 and COVID-19 vaccination," *Circulation Research,* vol. 130, no. 8, pp. 1187-1203, 2022.

[4] A. L. Goss, R. D. Samudralwar, R. R. Das, and A. Nath, "ANA investigates: neurological complications of COVID-19 vaccines," *Annals of neurology,* vol. 89, no. 5, p. 856, 2021.

[5] O. H. I. Chou *et al.*, "COVID-19 vaccination and carditis in children and adolescents: A systematic review and meta-analysis," *Clinical Research in Cardiology,* vol. 111, no. 10, pp. 1161-1173, 2022.

[6] H. Ritchie *et al.*, "Coronavirus pandemic (COVID-19)," *Our world in data,* 2020.

[7] E. Mathieu *et al.*, "A global database of COVID-19 vaccinations," *Nature human behaviour,* vol. 5, no. 7, pp. 947-953, 2021.

[8] H. Wang, B. Yu, X. Chen, and H. Yan, "Global pattern and determinants of coronavirus disease 2019 (COVID-19) vaccine coverage and progression: a global ecological study," *Global Health Journal,* vol. 7, no. 1, pp. 18-23, 2023.

[9] WHO, "COVID-19 vaccine tracker and landscape," ed, 2023.

[10] S. Waheed, A. Bayas, F. Hindi, Z. Rizvi, and P. S. Espinosa, "Neurological complications of COVID-19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine," *Cureus,* vol. 13, no. 2, 2021.

[11] M. Patone *et al.*, "Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection," *Nature medicine,* vol. 27, no. 12, pp. 2144-2153, 2021.

[12] A. Fazlollahi *et al.*, "Cardiac complications following mRNA COVID-19 vaccines: A systematic review of case reports and case series," *Reviews in medical virology,* vol. 32, no. 4, p. e2318, 2022.

[13] R. Liu, J. Pan, C. Zhang, and X. Sun, "Cardiovascular complications of COVID-19 vaccines," *Frontiers in Cardiovascular Medicine,* vol. 9, 2022.

[14] WHO. Coronavirus disease (COVID-19)-Strategy and planning [Online] Available: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/strategies-and-plans

[15] C. Novel, "The epidemiological attributes of a flare-up of 2019 novel Covid sicknesses (Coronavirus) in china," *Zhonghualiuxingbingxuezazhi= Zhonghualiuxingbingxuezazhi,* vol. 41, no. 2, p. 145, 2020.

[16] C. Bulut and Y. Kato, "Epidemiology of COVID-19," *Turkish journal of medical sciences,* vol. 50, no. 9, pp. 563-570, 2020.

[17] S. D. Chowdhury and A. M. Oommen, "Epidemiology of COVID-19," *Journal of digestive endoscopy*, vol. 11, no. 01, pp. 03-07, 2020.

[18] D. Ndwandwe and C. S. Wiysonge, "COVID-19 vaccines," *Current opinion in immunology*, vol. 71, pp. 111-116, 2021.

[19] O. J. Watson, G. Barnsley, J. Toor, A. B. Hogan, P. Winskill, and A. C. Ghani, "Global impact of the first year of COVID-19 vaccination: a mathematical modelling study," *The Lancet Infectious Diseases*, vol. 22, no. 9, pp. 1293-1302, 2022.

[20] A. Mullard, "How COVID vaccines are being divvied up around the world," *Nature*, vol. 30, no. 10.1038, 2020.

[21] N. Chauhan, B. Manjunath, V. Yadav, A. Kumar, B. Sabbarwal, and J. S. Kumar, "COVID-19 vaccine development in India during Janaury 2021-December 2021: A narrative review," *Saudi J Med*, vol. 7, no. 2, pp. 118-126, 2022.

[22] H. M. Scobie *et al.*, "Monitoring incidence of COVID-19 cases, hospitalizations, and deaths, by vaccination status—13 US jurisdictions, April 4–July 17, 2021," *Morbidity and Mortality Weekly Report*, vol. 70, no. 37, p. 1284, 2021.

[23] E. Lamptey, "Post-vaccination COVID-19 deaths: a review of available evidence and recommendations for the global population," *Clinical and Experimental Vaccine Research*, vol. 10, no. 3, p. 264, 2021.

[24] C. L. Jackson, J. B. Ward, D. A. Johnson, M. Sims, J. Wilson, and S. Redline, "Concordance between self-reported and actigraphy-assessed sleep duration among African-American adults: findings from the Jackson Heart Sleep Study," *Sleep*, vol. 43, no. 3, p. zsz246, 2020.

[25] H. Ledford, "News in focus," *Nature*, vol. 592, p. 495, 2021.

[26] D. McGonagle, G. De Marco, and C. Bridgewood, "Mechanisms of immunothrombosis in vaccine-induced thrombotic thrombocytopenia (VITT) compared to natural SARS-CoV-2 infection," *Journal of autoimmunity*, vol. 121, p. 102662, 2021.

[27] P. C. Fragkou and D. Dimopoulou, "Serious complications of COVID-19 vaccines: A mini-review," *Metabolism open*, vol. 12, p. 100145, 2021.

[28] A. Oudjedi, A. Allali, A. Bekli, M. Lounis, H. Ben Saad, and M. Boukoufa, "Reported COVID-19 vaccines side effects among Algerian athletes: a comparison between inactivated virus, adenoviral vector, and mRNA COVID-19 vaccines," *The Physician and Sportsmedicine*, pp. 1-13, 2023.

[29] S. Aghabaklou, S.-M. Razavi, P. Mohammadi, S. Gholamin, and A. Mowla, "Cerebral coagulation complications following COVID-19 adenoviral vector vaccines: a systematic review," *Journal of*

Neurology Research, vol. 11, no. 5, p. 69, 2021.

[30] A. Greinacher, T. Thiele, T. E. Warkentin, K. Weisser, P. A. Kyrle, and S. Eichinger, "Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination," *New England Journal of Medicine,* vol. 384, no. 22, pp. 2092-2101, 2021.

[31] R. Hosseini and N. Askari, "A review of neurological side effects of COVID-19 vaccination," *European Journal of Medical Research,* vol. 28, no. 1, pp. 1-8, 2023.

[32] G. Kroumpouzos, M. E. Paroikaki, S. Yumeen, S. Bhargava, and E. Mylonakis, "Cutaneous complications of mRNA and AZD1222 COVID-19 vaccines: a worldwide review," *Microorganisms,* vol. 10, no. 3, p. 624, 2022.

[33] S. V. Malayala, G. Mohan, D. Vasireddy, and P. Atluri, "Purpuric rash and thrombocytopenia after the mRNA-1273 (Moderna) COVID-19 vaccine," *Cureus,* vol. 13, no. 3, 2021.

[34] H. Maayan *et al.,* "Acquired thrombotic thrombocytopenic purpura: a rare disease associated with BNT162b2 vaccine," *Journal of Thrombosis and Haemostasis,* vol. 19, no. 9, pp. 2314-2317, 2021.

[35] O. Dadras *et al.,* "Safety and adverse events related to inactivated COVID-19 vaccines and Novavax; a systematic review," *Archives of Academic Emergency Medicine,* vol. 10, no. 1, 2022.

[36] S. Kim *et al.,* "Safety surveillance of the NVX-CoV2373 COVID-19 vaccine among Koreans aged 18 years and over," *Vaccine,* 2023.

[37] F. Yasmin *et al.,* "Adverse events following COVID-19 mRNA vaccines: A systematic review of cardiovascular complication, thrombosis, and thrombocytopenia," *Immunity, inflammation and disease,* vol. 11, no. 3, p. e807, 2023.

[38] Q. Li and J. Wu, "The Focused Analysis of COVID-19 RNA-based vaccines," *Highlights in Science, Engineering and Technology,* vol. 36, pp. 866-870, 2023.

[39] H. Y. Kim *et al.,* "A case report for acute myopericarditis after NVX-CoV2373 (Novavax®) COVID-19 vaccination," *J Korean Med Sci,* vol. 37, no. 34, p. e265, 2022.

[40] E. Underwood *et al.,* "Safety, efficacy, and immunogenicity of the NVX-CoV2373 vaccine," *Expert Review of Vaccines,* no. just-accepted, 2023.

[41] A. Bidari *et al.,* "Immune thrombocytopenic purpura secondary to COVID-19 vaccination: A systematic review," *European Journal of Haematology,* vol. 110, no. 4, pp. 335-353, 2023.

[42] M. Lounis *et al.,* "Side effects of COVID-19 inactivated virus vs. adenoviral vector vaccines: experience of Algerian healthcare workers," *Frontiers in public health,* vol. 10, 2022.

[43] C. Jacob-Dolan and D. H. Barouch, "COVID-19 vaccines: adenoviral vectors," *Annual review of medicine*, vol. 73, pp. 41-54, 2022.

[44] Z. A. Abdulla, S. M. Al-Bashir, N. S. Al-Salih, A. A. Aldamen, and M. Z. Abdulazeez, "A summary of the SARS-CoV-2 vaccines and technologies available or under development," *Pathogens*, vol. 10, no. 7, p. 788, 2021.

[45] J. L. Andresen and O. S. Fenton, "Nucleic acid delivery and nanoparticle design for COVID vaccines," *Mrs Bulletin*, pp. 1-8, 2021.

[46] E. Twentyman *et al.*, "Interim Recommendation of the Advisory Committee on Immunization Practices for Use of the Novavax COVID-19 Vaccine in Persons Aged≥ 18 years—United States, July 2022," *Morbidity and Mortality Weekly Report*, vol. 71, no. 31, p. 988, 2022.

[47] I. P. Trougakos *et al.*, "Adverse effects of COVID-19 mRNA vaccines: the spike hypothesis," *Trends in Molecular Medicine*, 2022.

[48] K. Guetl, R. B. Raggam, and T. Gary, "Thrombotic Complications after COVID-19 Vaccination: Diagnosis and Treatment Options," *Biomedicines*, vol. 10, no. 6, p. 1246, 2022.

[49] L. Dai *et al.*, "A universal design of betacoronavirus vaccines against COVID-19, MERS, and SARS," *Cell*, vol. 182, no. 3, pp. 722-733. e11, 2020.

[50] F. Sakurai, M. Tachibana, and H. Mizuguchi, "Adenovirus vector-based vaccine for infectious diseases," *Drug Metabolism and Pharmacokinetics*, vol. 42, p. 100432, 2022.

[51] H. M. El Sahly *et al.*, "Efficacy of the mRNA-1273 SARS-CoV-2 vaccine at completion of blinded phase," *New England Journal of Medicine*, vol. 385, no. 19, pp. 1774-1785, 2021.

[52] WHO. "Cardiovascular diseases." World Health Organization. https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1 (accessed August 2, 2023).

[53] E. J. Anderson *et al.*, "Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults," *New England Journal of Medicine*, vol. 383, no. 25, pp. 2427-2438, 2020.

[54] E. Twentyman *et al.*, "Interim Recommendation of the Advisory Committee on Immunization Practices for Use of the Novavax COVID-19 Vaccine in Persons Aged ≥18 years - United States, July 2022," (in eng), *MMWR Morb Mortal Wkly Rep*, vol. 71, no. 31, pp. 988-992, Aug 5 2022, doi: 10.15585/mmwr.mm7131a2.

[55] K. Ali *et al.*, "Evaluation of mRNA-1273 SARS-CoV-2 vaccine in adolescents," *New England Journal of Medicine*, vol. 385, no. 24, pp. 2241-2251, 2021.

[56] L. Chu *et al.*, "A preliminary report of a randomized controlled phase 2 trial of the safety and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine," *Vaccine*, vol. 39, no. 20, pp. 2791-2799, 2021.

[57] E. B. Walter *et al.*, "Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age," *New England Journal of Medicine*, vol. 386, no. 1, pp. 35-46, 2022.

[58] R. S. Sablerolles *et al.*, "Immunogenicity and reactogenicity of vaccine boosters after Ad26. COV2. S priming," *New England Journal of Medicine*, vol. 386, no. 10, pp. 951-963, 2022.

[59] J. Sadoff *et al.*, "Safety and efficacy of single-dose Ad26. COV2. S vaccine against Covid-19," *New England Journal of Medicine*, vol. 384, no. 23, pp. 2187-2201, 2021.

[60] A. R. Falsey *et al.*, "Phase 3 safety and efficacy of AZD1222 (ChAdOx1 nCoV-19) Covid-19 vaccine," *New England Journal of Medicine*, vol. 385, no. 25, pp. 2348-2360, 2021.

[61] F. P. Polack *et al.*, "Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine," *New England journal of medicine*, vol. 383, no. 27, pp. 2603-2615, 2020.