



Research Paper

## Cardiovascular Side Effects of COVID- 19 Vaccination

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### ABSTRACT :

**Background:** The COVID-19 pandemic has had a profound impact on global health, with vaccination playing a crucial role in mitigating the spread of the virus and reducing the severity of illness. However, the potential cardiovascular side effects associated with COVID-19 vaccination have raised concerns. Myocarditis, an inflammation of the heart muscle, is one of the most widely reported side effects, particularly among male adolescents and young adults, following the second dose of mRNA vaccines. The incidence of myocarditis post-vaccination ranges from 150 to 4,000 cases per 100,000 individuals, higher than the pre-pandemic estimate of 1-10 cases per 100,000. Other cardiovascular complications such as pericarditis and stroke have also been reported in a small subset of vaccine recipients. Although these side effects are often acute and transient, they can be severe and even fatal in some cases. Understanding the incidence, clinical presentation, and long-term outcomes of these cardiovascular side effects is crucial for informing healthcare professionals and the public about the potential risks and benefits of the COVID-19 vaccination. Ongoing research and surveillance are essential to better understand the underlying mechanisms, identify risk factors, and develop strategies for preventing and managing adverse events, while maintaining public trust in the safety and efficacy of COVID-19 vaccines. **Search Methods:** This review was conducted by searching the WHO database and other relevant medical literature for studies published from 2000 to 2024 that reported on cardiovascular side effects of COVID-19 vaccination. **Conclusion:** Several studies have investigated the incidence of myocarditis, pericarditis, and stroke in individuals who received the COVID - 19 vaccines. Although the overall risk appears relatively low, cardiovascular complications have been reported in a small subset of vaccine recipients, particularly among younger individuals. These effects are often acute and transient but can be severe and even fatal in a few cases. Herein, we have provided a comprehensive review of documents reporting cardiovascular side effects of COVID-19 vaccines in international databases from 2000 to 2024 and discussed the possible causes of these disorders.

**KEYWORDS:** COVID-19 Vaccination, Cardiovascular Side Effects, Myocarditis, Pericarditis, Deep Vein Thrombosis, Heart Attack, Arrhythmia

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### BACKGROUND OF THE COVID-19 PANDEMIC:

The COVID-19 pandemic has had a devastating impact on global health, leading to over six million deaths worldwide as of early 2023 (Arāja, 2022). The rapid development and deployment of several effective vaccines against SARS-CoV-2, the virus that causes COVID-19, have been instrumental in curbing and preventing the spread of the virus and reducing the severity of illness (Table 2). However, the potential cardiovascular side effects associated with COVID-19 vaccination have been a topic of growing concern among healthcare professionals, researchers, and the public (Figure 1).

One of the most widely reported cardiovascular side effects of COVID-19 vaccination is myocarditis, an inflammation of the heart muscle. Myocarditis has been reported as a rare adverse event following other vaccinations, such as smallpox, influenza, and hepatitis B. Prior to the COVID-19 pandemic, the incidence of myocarditis is estimated to be between 1 and 10 cases per 100,000 individuals (Bozkurt et al., 2021). However, studies have suggested that the risk of myocarditis may be higher in the context of COVID-19 vaccination, with incidence ranging from 150 to 4,000 cases per 100,000 individuals (Woo et al., 2021) (Rout et al., 2022) (Heymans & Cooper, 2021).

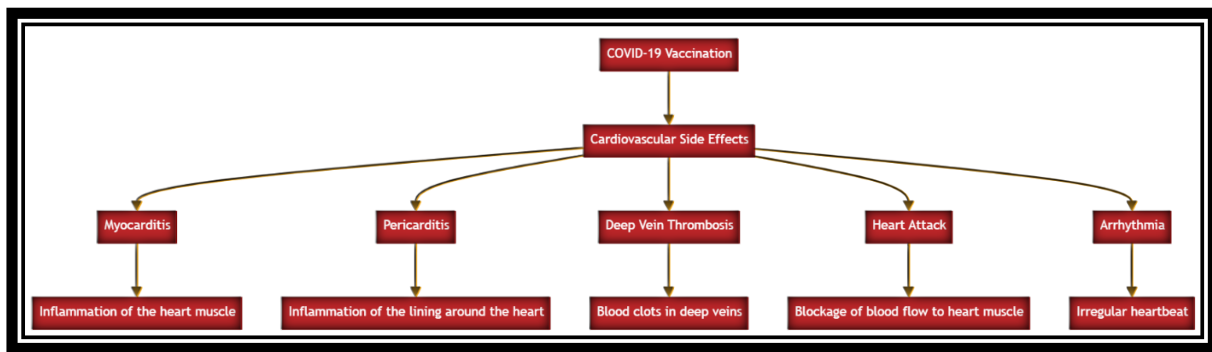


Figure 1 represents the side effects of COVID-19 vaccination itself which could be cardiovascular in nature like myocarditis which indicates inflammation of the heart muscles; pericarditis which indicates inflammation of the lining around the heart; Deep Vein Thrombosis which is blood clots in deep veins; heart attack representing blockage of blood flow to the heart muscle; and arrhythmia which is an irregular heartbeat.

Interestingly, the risk of myocarditis appears to be higher in younger individuals, particularly male adolescents and young adults, and is more commonly observed after the second dose of an mRNA COVID-19 vaccine(Sousa et al., 2024)(Rout et al., 2022).

In addition to myocarditis, other cardiovascular complications, such as pericarditis (inflammation of the protective sac surrounding the heart) and stroke, have also been reported in a small subset of COVID-19 vaccine recipients.(Sousa et al., 2024)These cardiovascular side effects can be acute and transient, but in some cases, they can be severe and even fatal.(Shiravi et al., 2021)

**IMPACT of Cardiovascular Side Effects:** The occurrence of cardiovascular side effects associated with COVID-19 vaccination, although relatively low, has raised concerns and prompted further investigation of the underlying mechanisms and potential risk factors. These adverse events have the potential to impact public confidence in the safety of COVID-19 vaccines, which could lead to vaccine hesitancy and undermine the overall success of vaccination programs.(Shiravi et al., 2021)

Understanding the incidence, clinical presentation, and long-term outcomes of these cardiovascular side effects is crucial for informing healthcare professionals, public health authorities, and the general public about the potential risks and benefits of COVID-19 vaccination.

**CONCLUSION:** The COVID-19 pandemic highlights the critical role of vaccination in mitigating the spread of the virus and reducing the severity of the illness. Although the overall risk of cardiovascular side effects associated with COVID-19 vaccination appears to be relatively low, conditions such as myocarditis, pericarditis, and stroke in a small subset of vaccine recipients, particularly younger individuals, have raised concerns and prompted further investigations.

Ongoing research and surveillance are essential to better understand the mechanisms underlying these cardiovascular side effects, identify potential risk factors, and develop effective strategies to prevent and manage adverse events. By addressing these concerns and maintaining public trust in the safety and efficacy of COVID-19 vaccines, healthcare professionals and public health authorities can ensure the continued success of vaccination programs and their crucial role in protecting global health.

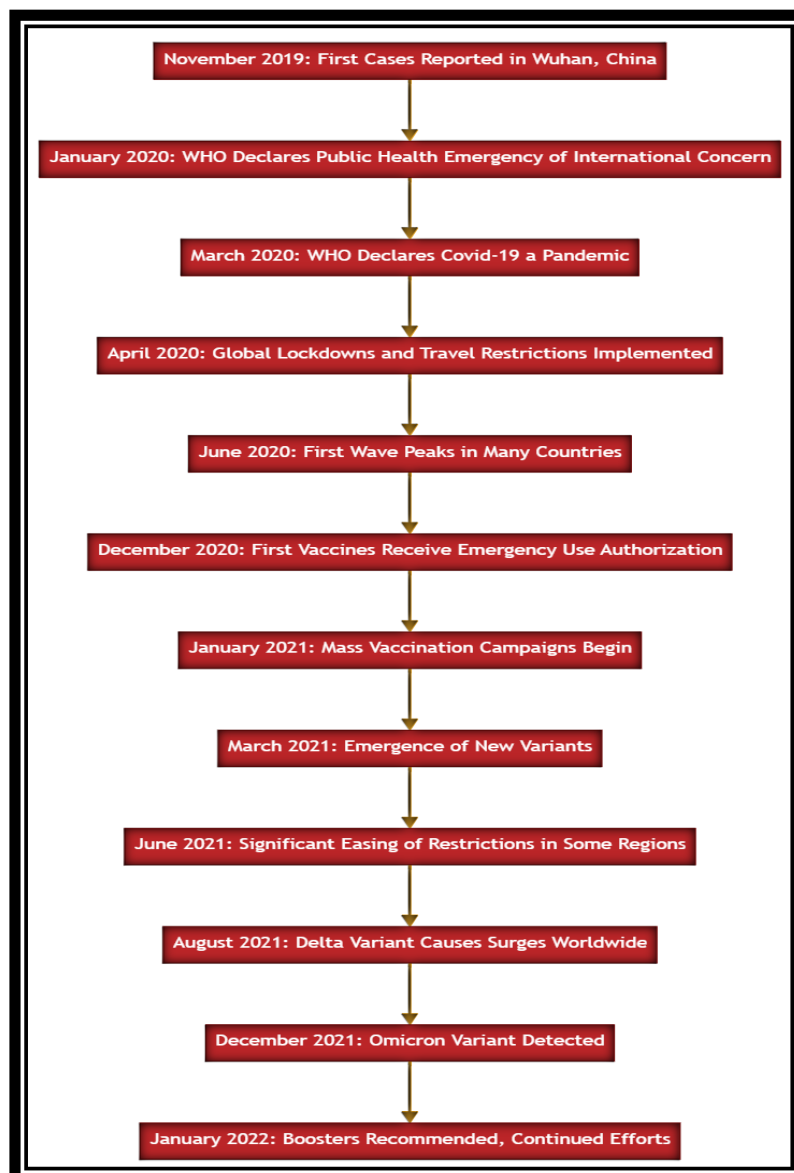


Figure 2-This visualises the key milestones and trends in the Covid-19 pandemic timeline.

### COVID-19 PANDEMIC TIMELINE AND IMPACT

The COVID-19 pandemic has had a devastating impact on global health since its emergence in late 2019 (Figure 2). The rapid spread of the SARS-CoV-2 virus has led to millions of infections and deaths worldwide, straining healthcare systems and disrupting social and economic activities.(The Committee for the Coordination of Statistical Activities (CCSA), n.d)(Sanyaolu et al., 2021)(Đenić, 2022) In response to this public health crisis, the development and distribution of safe and effective vaccines has been a top priority for governments and healthcare organizations globally.

### VACCINE DEVELOPMENT AND DEPLOYMENT

Since the beginning of the pandemic, the scientific community has made unprecedented progress in the development and deployment of COVID-19 vaccines at a remarkable pace. Several COVID-19 vaccines have been authorised for emergency use or granted full approval by regulatory agencies worldwide, including mRNA vaccines from Pfizer-BioNTech and Moderna, and viral vector vaccines from Astra Zeneca and Johnson & Johnson. These vaccines have demonstrated high efficacy in clinical trials and have been instrumental in reducing COVID-19 burden.

**SEARCH METHOD:**

This review was conducted by searching the WHO database and other relevant medical literature for studies published from 2020 to 2024 that reported on cardiovascular side effects of COVID-19 vaccination. Research, Review, and Case Report articles related to the adverse effects of COVID-19 vaccination from 2020 to July 2024 were searched and reviewed using the Google Scholar, PubMed, and NCBI databases. Many case reports were not considered because of the lack of a convincing link between the complications and vaccination. The keywords used for this search included COVID-19, SARS-CoV-2, vaccination, side effects, complications, vascular thrombosis, thrombocytopenia, myocarditis, pericarditis, stroke, cardiovascular disease, all types of mRNA vaccines, adenovirus vaccine, Pfizer, AstraZeneca, Johnson & Johnson, Moderna, Sinovac, Sinopharm, Sputnik, and Covaxin.

**MECHANISM OF ACTION**

SARS-CoV-2 has been shown to directly infect and impact the cardiovascular system, leading to a range of severe complications including myocarditis (inflammation of the heart muscle), pericarditis (inflammation of the protective sac surrounding the heart), arrhythmias (abnormal heart rhythms), acute coronary syndromes (such as heart attacks), and thromboembolic events (blood clots that can cause strokes or pulmonary embolisms).(Abrignani et al., 2022) Endothelial dysfunction, a hallmark pathological feature of COVID-19 infection, can contribute to the development of these cardiovascular complications by disrupting normal homeostasis and triggering harmful inflammatory cascades within the cardiovascular system.(Evans et al., 2020)(Jin et al., 2020)

**DISCUSSION**

Recent studies have highlighted the potential of COVID-19 vaccination to be associated with certain cardiovascular side effects, including myocarditis, pericarditis, thrombotic events such as deep vein thrombosis and pulmonary embolism, and a possible increased risk of stroke, particularly among younger individuals and those with preexisting cardiovascular conditions or risk factors. Although the overall incidence of these complications appears to be relatively low, healthcare providers should remain vigilant in monitoring vaccine recipients for any signs or symptoms of acute cardiovascular events in the weeks following vaccination.

**Myocarditis and Pericarditis**

Studies have reported an increased incidence of myocarditis, particularly in young males, following COVID-19 vaccination.(Kaur et al., 2021). The case definition of Myocarditis is given in Table 1. The risk of stroke appears to be higher after the second dose of mRNA vaccines.(Đenić, 2022)(Woo et al., 2021)(Rout et al., 2022). Most cases of vaccine-related myocarditis are mild, and patients recover with conservative care.(Woo et al., 2021)(Rout et al., 2022)

In addition to myocarditis, pericarditis, an inflammation of the pericardial sac surrounding the heart, has also been reported in a small number of vaccine recipients, although its incidence appears to be lower than that in myocarditis.(Kaur et al., 2021)(Shiravi et al., 2021)

**TABLE 1. CASE DEFINITIONS OF PROBABLE AND CONFIRMED MYOCARDITIS, PERICARDITIS, AND MYOPERICARDITIS**

Condit ion	Definition	
<b>Acute myocarditis</b>	<b>Probable case</b>	<b>Confirmed case</b>
	Presence of ≥1 new or worsening of the following clinical symptoms:*	Presence of ≥1 new or worsening of the following clinical symptoms:*
	• chest pain, pressure, or discomfort	• chest pain, pressure, or discomfort
	• dyspnea, shortness of breath, or pain with breathing	• dyspnea, shortness of breath, or pain with breathing
	• palpitations	• palpitations
	• syncope	• syncope
	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms:	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms:
	• irritability	• irritability
	• vomiting	• vomiting
	• poor feeding	• poor feeding
	• tachypnea	• tachypnea
	• lethargy	• lethargy
AND	AND	
≥1 new finding of	≥1 new finding of	
• troponin level above upper limit of normal (any type of troponin)	• Histopathologic confirmation of myocarditis <sup>†</sup>	
• abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis <sup>‡</sup>		

	<ul style="list-style-type: none"> <li>• abnormal cardiac function or wall motion abnormalities on echocardiogram</li> <li>• cMRI findings consistent with myocarditis<sup>‡</sup></li> </ul>	<ul style="list-style-type: none"> <li>• cMRI findings consistent with myocarditis<sup>‡</sup> in the presence of troponin level above upper limit of normal (any type of troponin)</li> </ul>
	AND	AND
	<ul style="list-style-type: none"> <li>• No other identifiable cause of the symptoms and findings</li> </ul>	<ul style="list-style-type: none"> <li>• No other identifiable cause of the symptoms and findings</li> </ul>
<b>Acute pericarditis**</b>	Presence of ≥2 new or worsening of the following clinical features:	
	<ul style="list-style-type: none"> <li>• acute chest pain<sup>††</sup></li> <li>• pericardial rub on exam</li> <li>• new ST-elevation or PR-depression on EKG</li> <li>• new or worsening pericardial effusion on echocardiogram or MRI</li> </ul>	
<b>Myopericarditis</b>	This term may be used for patients who meet criteria for both myocarditis and pericarditis.	

**Abbreviations:** AV, atrioventricular; cMRI, cardiac magnetic resonance imaging; ECG, electrocardiogram.  
 \* Persons who lack the listed symptoms but meet other criteria may be classified as having subclinical myocarditis (probable or confirmed).  
 † Using the Dallas criteria (Aretz, Billingham, Edwards, et al. Myocarditis. Histopathological definition and classification. Am J Cardiovasc Pathol 1987; 1:3–14). Autopsy cases may be classified as confirmed clinical myocarditis based on the basis of meeting histopathologic criteria if there is no other identifiable cause.  
 § To meet the ECG or rhythm monitoring criteria, a probable case must include at least one of 1) ST-segment or T-wave abnormalities; 2) paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias; or 3) AV nodal conduction delay or intraventricular conduction defect.  
 ¶ Using either the original or revised Lake Louise criteria.  
<https://www.sciencedirect.com/science/article/pii/S0735109718388430?via%3Dihub>  
 \*\* <https://academic.oup.com/eurheartj/article/36/42/2921/2293375>  
 †† Typically described as pain worsened by lying down, deep inspiration, or cough and relieved by sitting up or leaning forward, although other types of chest pain might occur.

TABLE 2. INDIVIDUAL-LEVEL ESTIMATED NUMBER OF COVID-19 CASES AND COVID-19-ASSOCIATED HOSPITALIZATIONS, INTENSIVE CARE UNIT ADMISSIONS, AND DEATHS PREVENTED AFTER USE OF 2-DOSE MRNA COVID-19 VACCINE FOR 120 DAYS AND NUMBER OF MYOCARDITIS CASES EXPECTED PER MILLION SECOND MRNA VACCINE DOSES ADMINISTERED, BY SEX AND AGE GROUP* — UNITED STATES, 2021					
Sex/Benefits and harms from mRNA vaccination	No. per million vaccine doses administered in each age group (yrs) <sup>†</sup>				
	12–29	12–17	18–24	25–29	≥ 30
<b>Male</b>					
<b>Benefit</b>					
COVID-19 cases prevented <sup>§</sup>	1,000	5,700	2,100	5,200	5,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	27	15	242
Deaths prevented	6	2	3	1	7
<b>Harms</b>					
Myocarditis cases expected <sup>¶</sup>	39–47	56–69	45–56	15–18	3–4
<b>Female</b>					
<b>Benefit</b>					
COVID-19 cases prevented <sup>§</sup>	2,500	8,500	4,300	4,700	4,900
Hospitalizations prevented	922	183	127	459	3,484
ICU admissions prevented	73	38	3	7	707
Deaths prevented	6	1	1	4	347
<b>Harm</b>					
Myocarditis cases expected <sup>¶</sup>	4–5	8–10	4–5	2	1

**Abbreviations:** ICU = intensive care unit; VAERS = Vaccine Adverse Event Reporting System.  
 \* This analysis evaluated the direct benefits and harms per million second doses of the mRNA COVID-19 vaccine administered in each age group over 120 days. The number of events per million people aged 12–29

years was the average number per million people aged 12–17, 18–24, and 25–29 years.  
† Receipt of two doses of the mRNA COVID-19 vaccine compared to no vaccination.  
§ Cases are rounded to the nearest hundred.  
¶ Ranges calculated as  $\pm 10\%$  of crude VAERS reporting rates. Estimates included myocarditis, pericarditis, and myopericarditis.

#### *Thrombotic Events:*

Thrombotic events, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have been reported in a minority of vaccine recipients, particularly with the AstraZeneca and Johnson–Johnson vaccines.(Abrignani et al., 2022)(Kaur et al., 2021)

#### *Stroke:*

Some studies have suggested a potential link between COVID-19 vaccination and increased risk of stroke, although the overall incidence remains low.(Yoshida et al., 2022) The underlying mechanisms are not fully understood, but it is hypothesized that the transient inflammatory response triggered by the vaccination may contribute to the development of cerebral thrombosis or ischemic stroke in individuals with pre-existing severe atherosclerosis or other cardiovascular risk factors. Although the absolute risk appears to be low, healthcare providers should closely monitor vaccine recipients, especially those with known cardiovascular diseases, for any signs or symptoms of acute neurological events in the weeks following vaccination. Further research is needed to better characterize the potential relationship and underlying pathophysiology.

#### *Thromboembolic Events:*

Thromboembolic events such as deep vein thrombosis and pulmonary embolism have also been reported following COVID-19 vaccination, particularly with certain vaccine types.(Abrignani et al., 2022)(Famularo, 2022)(Kakovan et al., 2022)

Thrombotic complications such as deep vein thrombosis and pulmonary embolism have also been reported in a subset of vaccine recipients, although the overall risk is low.(Abrignani et al., 2022)(Burn et al., 2022)

#### *Other Cardiovascular Events*

In addition to more serious cardiovascular complications such as myocarditis, pericarditis, and thrombotic events, other potential side effects of COVID-19 vaccination have been reported, including tachycardia (rapid heart rate), flushing, hypertension (high blood pressure), hypotension (low blood pressure), and peripheral coldness.(Bozkurt et al., 2021)(Famularo, 2022) These less severe but still concerning cardiovascular reactions have been observed in a small subset of vaccine recipients and warrant continued monitoring and reporting.

## **CONCLUSION**

The cardiovascular side effects of COVID-19 vaccination appear to be relatively infrequent, and the benefits of vaccination in preventing severe COVID-19 and its associated cardiovascular complications likely outweigh the risks in the vast majority of individuals.(Yasmin et al., 2023)Ongoing surveillance, reporting, and research are crucial to better understand the mechanisms behind these adverse events and to guide clinical management and risk mitigation strategies. Healthcare providers must be vigilant in monitoring potential cardiovascular complications following COVID-19 vaccination, and should be prepared to provide prompt and appropriate treatment when necessary.

In summary, although cardiovascular side effects of COVID-19 vaccination appear to be relatively uncommon, it is important for healthcare providers and the public to be aware of their potential risks, particularly in high-risk populations. The benefit-risk ratio of COVID-19 vaccination strongly favors vaccination for all age groups and both sexes, as the overall risk of severe COVID-19 and its complications far outweighs the potential risks of these rare cardiovascular events.(Đenić, 2022)(Harkin et al., 2010)(Kytö et al., 2013)

Ongoing surveillance, reporting, and further research are needed to better characterise the incidence, underlying mechanisms, and long-term outcomes of these cardiovascular complications associated with the COVID-19 vaccination.

## **SUMMARY**

*What is already known regarding this topic?*

An elevated risk of cardiovascular adverse events among COVID-19 vaccines was observed, particularly in males aged 12–29 years.

*What is added by this report?*

COVID-19 vaccination has been crucial in mitigating the spread and severity of the virus; however, potential cardiovascular side effects have raised concerns. Myocarditis, an inflammation of the heart muscle, is the most widely reported side effect, particularly among male adolescents and young adults, after the second dose of mRNA vaccines. The incidence of myocarditis post-vaccination was higher than that of the pre-pandemic estimates. Other cardiovascular complications such as pericarditis and stroke have also been reported in a small subset of vaccine recipients. Although these side effects are often acute and transient, they can be severe and even fatal in some cases. Understanding the incidence, clinical presentation, and long-term outcomes of these cardiovascular side effects is crucial for informing healthcare professionals and the public about the potential risks and benefits of the COVID-19 vaccination.

*What are the implications for public health practice?*

The continued use of COVID-19 vaccines in all recommended age groups will prevent morbidity and mortality from COVID-19, far exceeding the expected number of myocarditis cases. Information regarding the risk of myocarditis with mRNA COVID-19 vaccines should be disseminated to providers for sharing with the vaccine recipients.

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**Consent for publication**

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**Competing interests**

Not applicable.

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