

Stroke and Blood Clotting Disorders Rare After Monovalent and Bivalent COVID Vaccination

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Key Findings:

- Stroke, thrombocytopenia, or thrombosis in the 30 days after monovalent and bivalent COVID-19 vaccination are very uncommon, seen in less than 1% of patients.
- Patients that receive the monovalent or bivalent COVID-19 vaccine are about 9% less likely to develop a stroke, 20% less likely to develop thrombocytopenia, and 12% less likely to develop thrombosis than patients who receive the flu vaccination.
- The incidence of thrombocytopenia and thrombosis are more than twice as common after COVID-19 infection than after COVID-19 vaccination.

There have been some reports of ischemic stroke in patients after COVID-19 vaccination, but CDC and FDA have noted that these risks are small and continue to recommend COVID-19 vaccination for most patients.¹ Additionally, there have been contradictory observations around the risk of stroke and thrombosis related to receiving the COVID-19 vaccination.² Because both monovalent and bivalent COVID-19 vaccinations make use of pioneering mRNA design, we wanted to compare rates of different clotting conditions following COVID-19 mRNA vaccination with those following a non-mRNA vaccination, such as the influenza vaccine.

We evaluated the rate of new diagnoses of stroke, thrombocytopenia, and arterial and venous thrombosis after monovalent and bivalent COVID-19 vaccination and compared those to the rates of those conditions after influenza vaccination and COVID-19 infection.

We evaluated 16,687,080 patients that had an influenza vaccination, monovalent COVID-19 vaccination, bivalent COVID-19 vaccination, or COVID-19 infection. We matched these groups on age, sex, immunization or infection year, and number of previously diagnosed chronic conditions that increase cardiovascular risk. We then determined the rate of new diagnoses of stroke, thrombocytopenia, and arterial and venous thrombosis in the 30 days following the vaccine administration or COVID-19 infection.

We found that all four of the conditions were very rare for all the populations assessed, but were most common after COVID-19 infection, as shown in Figure 1. Stroke, thrombocytopenia, and thrombosis are more common after influenza vaccination than after the monovalent or bivalent COVID-19 vaccinations. Both COVID-19 vaccinations were nearly equivalent for all four of the cardiovascular diagnoses assessed.

Cardiovascular Diagnoses After Vaccination or Infection

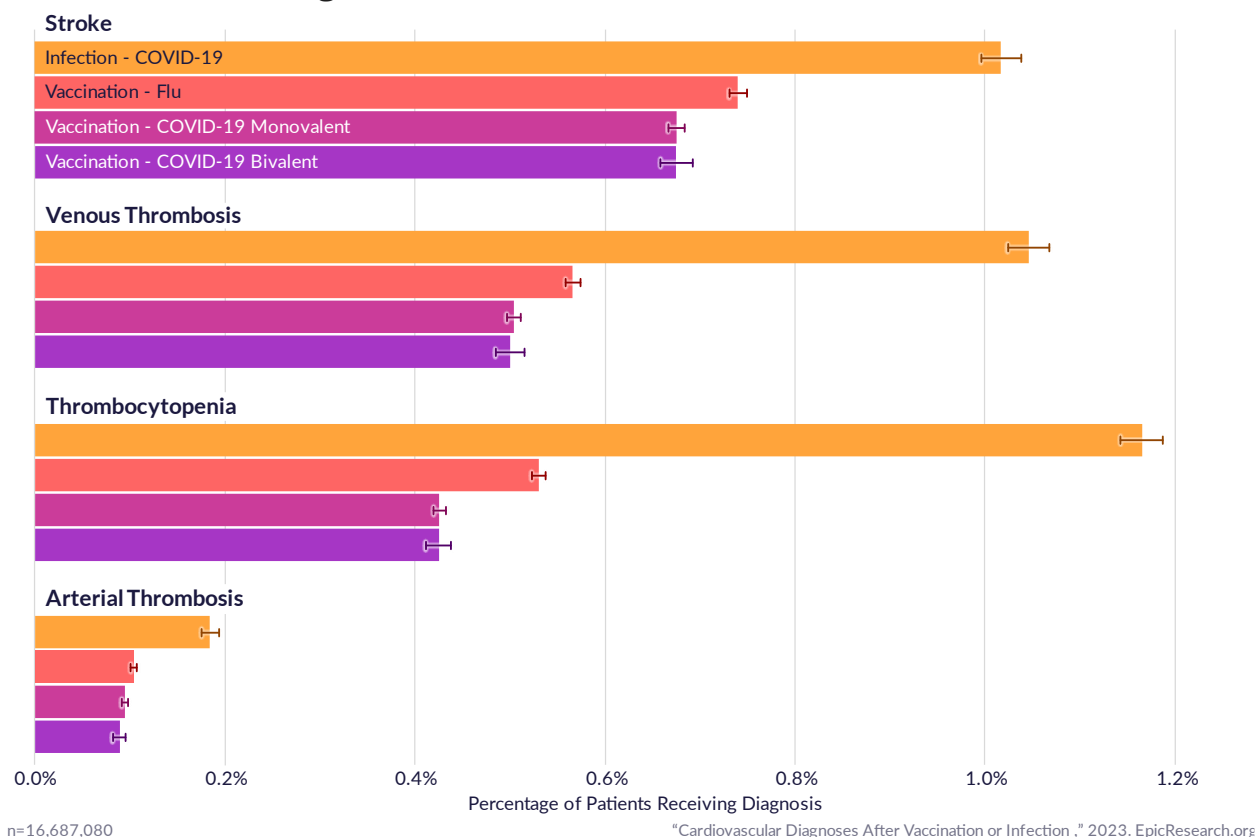


Figure 1. Unadjusted rates of diagnosis of cardiovascular conditions within the 30 days after vaccination or infection.

These findings align with CDC and FDA reports that these conditions after COVID-19 vaccination remain rare and suggest that bivalent and monovalent COVID-19 vaccinations have similar rates of these diagnoses after vaccination.¹

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 184 million patients from 199 Epic organizations including 1,141 hospitals and over 24,900 clinics, serving patients in all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions.

References

1. CDC. CDC & FDA identify preliminary COVID-19 vaccine safety signal for persons aged 65 years and older. Centers for Disease Control and Prevention. Published January 13, 2023. Accessed May 1, 2023. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/bivalent-boosters.html>
2. Kakovan M, Ghorbani Shirkouhi S, Zarei M, Andalib S. Stroke associated with COVID-19 vaccines. J Stroke Cerebrovasc Dis. 2022;31(6):106440. doi:10.1016/j.jstrokecerebrovasdis.2022.106440

Data Definitions

Term	Definition
Study period	1/1/2021 – 3/1/2023
Study population	Patients aged 18 or older

Number of comorbidities	The number of distinct diagnoses occurring prior to the event of interest from the following categories:	
	Category	Definition
	Peripheral Vascular disease	ICD-10-CM code I73*
	Prior Stroke	ICD-10-CM code I63* or G4[5-6]*
	Diabetes	ICD-10-CM code E1[0-1]*
	Hypertension	ICD-10-CM code I1*
	Factor 5 Leiden Mutation	ICD-10-CM code D68.51
	Prothrombin Gene Mutation	ICD-10-CM code D68.52
	Protein S/C Deficiency	ICD-10-CM code D68.59
	Antiphospholipid Syndrome	ICD-10-CM code D68.61
Lupus	ICD-10-CM code L93* or D68.62	
Event of interest	A single flu or COVID-19 vaccination or COVID-19 infection without another COVID-19 or flu vaccination in the 30 days prior to or following the first event of interest. Additionally, the patient must not have a COVID-19 infection in the 180 days prior to or 30 days following the event of interest. To ensure uniformity between our different events of interest, we used event matching.	
Flu vaccination	An event of Interest represented by a vaccination administration event with a CVX code of one of the following: 15, 16, 88, 111, 123, 125, 126, 127, 128, 135, 140, 141, 144, 149, 150, 151, 153, 155, 158, 160, 161, 166, 168, 171, 185, 186, 194, 197, 200, 201, 202, or 205	
COVID-19 vaccination	An event of Interest represented by a vaccination administration event with a CVX code of one of the following: Bivalent: 229, 230, 300, 301, 302, 519, or 520 Monovalent: 207, 208, 217, 218, 219, or 221	
COVID-19 infection	An event of interest represented by an encounter or billing diagnosis with ICD –10-CM code U07.1, J12.81, or J12.82 or a SNOMED CT code of 840539006	
Event matching	Flu vaccination, monovalent COVID-19 vaccination, bivalent COVID-19 vaccination, and COVID-19 Infection events were matched using a 4:4:1:1 ratio on sex, age group, number of comorbidities, and year of event. This left us with the following population sizes for each sub grouping: Flu vaccinated patients: 6,674,832 COVID-19 monovalent vaccinated patients: 6,674,832 COVID-19 bivalent vaccinated patients: 1,668,708 COVID-19 infection patients: 1,668,708	

Side effect	Side effects are measured as one of the following diagnoses occurring within the 30 days following the corresponding event of interest: Stroke: A diagnosis with ICD-10-CM code I63* or G4[5-6]* Thrombocytopenia: A diagnosis with ICD-10-CM code D69.[3-6]* Thrombosis – Arterial: A diagnosis with SNOMED CT code 65198009 Thrombosis – Venous: A diagnosis with SNOMED CT code 111293003
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Table 1a: Population Distribution of Flu Vaccinated Patients

Group	Subgroup	# Of Patients	Rates
Overall	Overall	6,674,832	100.000%
Sex	Female	4,004,832	59.999%
	Male	2,668,192	39.974%
	Other	1,808	0.027%
Age Group	18-35	735,176	11.014%
	36-50	996,524	14.930%
	51-65	1,977,644	29.628%
	66-75	1,736,908	26.022%
	76-85	933,240	13.981%
	86+	295,340	4.425%
Census Region	Midwest	2,217,013	33.215%
	West	730,791	10.948%
	Northeast	1,623,054	24.316%
	South	2,102,170	31.494%
	Unknown	1,804	0.027%
SVI Quartile	[0,.25]	1,677,539	25.132%
	(.25,.5]	1,669,732	25.015%
	(.5,.75]	1,585,296	23.750%
	(.75,1]	1,678,277	25.143%
	Unknown	63,988	0.959%
Race Ethnicity	White	4,937,918	73.978%
	Black	732,170	10.969%
	Hispanic	500,399	7.497%
	Other	504,345	7.556%
Side Effects	Stroke	49,448	0.741%
	Thrombocytopenia	35,388	0.530%
	Thrombosis	44,202	0.662%
	Arterial Thrombosis	6,961	0.104%
	Veinous Thrombosis	37,785	0.566%

Table 1b: Population Distribution of Covid Infection Patients

Group	Subgroup	# Of Patients	Rates
Overall	Overall	1,668,708	100.000%

Sex	Female	1,001,208	59.999%
	Male	667,048	39.974%
	Other	452	0.027%
Age Group	18-35	183,794	11.014%
	36-50	249,131	14.930%
	51-65	494,411	29.628%
	66-75	434,227	26.022%
	76-85	233,310	13.981%
	86+	73,835	4.425%
Census Region	Midwest	535,920	32.116%
	West	168,429	10.093%
	Northeast	430,776	25.815%
	South	531,983	31.880%
	Unknown	1,600	0.096%
SVI Quartile	[0,.25]	394,961	23.669%
	(.25,.5]	414,070	24.814%
	(.5,.75]	406,354	24.351%
	(.75,1]	432,862	25.940%
	Unknown	20,461	1.226%
Race Ethnicity	White	1,251,458	74.996%
	Black	186,773	11.193%
	Hispanic	122,469	7.339%
	Other	108,008	6.473%
Side Effects	Stroke	16,982	1.018%
	Thrombocytopenia	19,444	1.165%
	Thrombosis	20,218	1.212%
	Arterial Thrombosis	3,074	0.184%
	Veinous Thrombosis	17,456	1.046%

Table 1c: Population Distribution of Monovalent Vaccinated Patients

Group	Subgroup	# Of Patients	Rates
Overall	Overall	6,674,832	100.000%
Sex	Female	4,004,832	59.999%
	Male	2,668,192	39.974%
	Other	1,808	0.027%
Age Group	18-35	735,176	11.014%
	36-50	996,524	14.930%
	51-65	1,977,644	29.628%
	66-75	1,736,908	26.022%
	76-85	933,240	13.981%
	86+	295,340	4.425%
Census Region	Midwest	2,351,104	35.223%
	West	1,109,178	16.617%
	Northeast	1,646,086	24.661%

	South	1,566,967	23.476%
	Unknown	1,497	0.022%
SVI Quartile	[0,.25]	1,687,699	25.285%
	(.25,.5]	1,676,767	25.121%
	(.5,.75]	1,552,861	23.264%
	(.75,1]	1,708,733	25.600%
	Unknown	48,772	0.731%
Race Ethnicity	White	4,633,572	69.419%
	Black	873,906	13.093%
	Hispanic	567,555	8.503%
	Other	599,799	8.986%
Side Effects	Stroke	45,150	0.676%
	Thrombocytopenia	28,424	0.426%
	Thrombosis	39,541	0.592%
	Arterial Thrombosis	6,344	0.095%
	Veinous Thrombosis	33,648	0.504%

Table 1d: Population Distribution of Bivalent Vaccinated Patients

Group	Subgroup	# Of Patients	Rates
Overall	Overall	1,668,708	100.000%
Sex	Female	1,001,208	59.999%
	Male	667,048	39.974%
	Other	452	0.027%
Age Group	18-35	183,794	11.014%
	36-50	249,131	14.930%
	51-65	494,411	29.628%
	66-75	434,227	26.022%
	76-85	233,310	13.981%
	86+	73,835	4.425%
Census Region	Midwest	576,440	34.544%
	West	271,065	16.244%
	Northeast	431,719	25.871%
	South	389,165	23.321%
	Unknown	319	0.019%
SVI Quartile	[0,.25]	469,967	28.164%
	(.25,.5]	447,844	26.838%
	(.5,.75]	379,099	22.718%
	(.75,1]	360,752	21.619%
	Unknown	11,046	0.662%
Race Ethnicity	White	1,216,933	72.927%
	Black	185,022	11.088%
	Hispanic	100,289	6.010%
	Other	166,464	9.976%
Side Effects	Stroke	11,269	0.675%

	Thrombocytopenia	7,088	0.425%
	Thrombosis	9,711	0.582%
	Arterial Thrombosis	1,480	0.089%
	Veinous Thrombosis	8,340	0.500%

Table 2a: Side Effect Rates Among Flu Vaccinated Patients

Side Effect		# of Patients Affected	Incidence Rate
Stroke		49,448	0.741% (0.732%-0.750%)
Thrombocytopenia		35,388	0.530% (0.523%-0.538%)
Thrombosis	Combined	44,202	0.662% (0.654%-0.671%)
	Arterial	6,961	0.104% (0.101%-0.108%)
	Veinous	37,785	0.566% (0.558%-0.574%)

Table 2b: Side Effect Rates Among Covid Infection Patients

Side Effect		# of Patients Affected	Incidence Rate	Rate Ratio (Flu Control)
Stroke		16,982	1.018% (0.997%-1.039%)	1.374 (1.341-1.407)
Thrombocytopenia		19,444	1.165% (1.143%-1.188%)	2.198 (2.145-2.251)
Thrombosis	Combined	20,218	1.212% (1.189%-1.235%)	1.83 (1.788-1.872)
	Arterial	3,074	0.184% (0.175%-0.193%)	1.766 (1.666-1.873)
	Veinous	17,456	1.046% (1.025%-1.067%)	1.848 (1.803-1.894)

Table 2c: Side Effect Rates Among Monovalent Vaccinated Patients

Side Effect		# of Patients Affected	Incidence Rate	Rate Ratio (Flu Control)
Stroke		45,150	0.676% (0.668%-0.685%)	0.913 (0.897-0.929)
Thrombocytopenia		28,424	0.426% (0.419%-0.433%)	0.803 (0.786-0.821)
Thrombosis	Combined	39,541	0.592% (0.584%-0.600%)	0.895 (0.878-0.911)
	Arterial	6,344	0.095% (0.092%-0.098%)	0.911 (0.869-0.955)
	Veinous	33,648	0.504% (0.497%-0.512%)	0.891 (0.873-0.909)

Table 2d: Side Effect Rates Among Bivalent Vaccinated Patients

Side Effect		# of Patients Affected	Incidence Rate	Rate Ratio (Flu Control)
Stroke		11,269	0.675% (0.658%-0.693%)	0.912 (0.886-0.938)
Thrombocytopenia		7,088	0.425% (0.411%-0.438%)	0.801 (0.773-0.83)
Thrombosis	Combined	9,711	0.582% (0.566%-0.598%)	0.879 (0.853-0.906)
	Arterial	1,480	0.089% (0.082%-0.095%)	0.85 (0.787-0.919)
	Veinous	8,340	0.500% (0.485%-0.515%)	0.883 (0.854-0.912)