COVID-19

CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AGAINST COVID-19 AND OTHER UPDATES

Thirty-second report

WASHINGTON, DC

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PAHO Pan American Health Organization World Health Organization Americas

In partnership with Canada

CONTENTS

CANADA

- As of 7 January 2022, 48,639,064 doses of the Pfizer-BioNTech COVID-19 vaccine, 17,033,942 doses of the Moderna vaccine, and 2,804,327 doses of the AstraZeneca and Covishield vaccine (AstraZeneca vaccine manufactured by the Serum Institute of India) had been administered.
- For these three vaccines, there were 33,160 individual reports of one or more AEFI (0.048% of doses administered). Of these, 7,090 reports involved serious events (0.010% of doses administered).
- There were a total of 86,933 reports of AEFI (of which 33,387 involved one or more events associated with the three vaccines, with no indication of which specific vaccine was involved). The most frequently reported adverse events were non-serious events such as paresthesia, injection-site pain, headache, pruritus, dyspnea, fatigue, urticaria, chest pain, nausea, etc.

Number of reports and reporting rate of AEFI (per 100,000 doses administered), by vaccine, as of 7 January 2022

Vaccine	*Number of reports of non-serious AEFI*		*Number of reports of serious AEFI*		*Total number of reports of AEFI*	
	N	***Rate/100,000 doses administered***	***N***	***Rate/100,000 doses administered***	***N***	***Rate/100,000 doses administered***
Pfizer-BioNTech	14,784	30.40	4,937	10.15	19,721	40.55
Moderna	8,729	51.24	1,361	7.99	10,090	59.23
Covishield y AstraZeneca	2,557	91.18	792	28.34	3,349	119.42
Total	26,070	38.07	7,090	10.35	33,160	48.42

On 19 November 2021, the Pfizer-BioNTech Comirnaty vaccine was authorized for children between 5 and 11 years of age. Information regarding adverse events in this population and, more generally, in those under 18 years of age, already included in the above total for Pfizer-BioNTech, is broken down in the following table:

Number of reports and reporting rate of AEFI (per 100,000 doses administered) for the Pfizer-BioNTech vaccine in the under-18-year-old population, as of 7 January 2022

Age group (doses administered, ds)	***Number of reports of non-serious AEFI***		***Number of reports of serious AEFI***		***Total number of reports of AEFI***	
	N	***Rate/100,000 doses administered***	***N***	***Rate/100,000 doses administered***	***N***	***Rate/100,000 doses administered***
Ages 12 to 17 (4,318,162 ds)	812	18.80	281	6.50	1,093	25.30
Ages 5 to 11 (1,403,906 ds)	97	6.91	19	1.35	116	8.26

Number of reports and reporting rate of the main serious AEFI (per 100,000 doses administered), by vaccine, in the general population, as of 7 January 2022			
	Vaccine		
AESI	***Pfizer-BioNTech***	***Moderna***	***Covishield and AstraZeneca***
Anaphylaxis	552 (1.16/100,000)	159 (0.98/100,000)	27 (0.96/100,000)
Thrombosis with thrombocytopenia syndrome (TTS)	29 (0.06/100,000)	11 (0.07/100,000)	70 (2.50/100,000)
Guillain-Barré syndrome	51 (0.11/100,000)	23 (0.14/100,000)	39 (1.39/100,000)
Myocarditis/pericarditis	1009 (2.12/100,000)	556 (3.42/100,000)	29 (1.03/100,000)
Bell's palsy/facial paralysis	509 (1.07/100,000)	160 (0.99/100,000)	51 (1.82/100,000)
Category: Autoimmune disease	70 (0.15/100,000)	33 (0.20/100,000)	70 (2.50/100,000)
Category: Cardiovascular system	1125 (2.36/100,000)	603 (3.71/100,000)	46 (1.64/100,000)
Category: Circulatory system	580 (1.22/100,000)	204 (1.26/100,000)	373 (13.30/100,000)
Category: Central and peripheral nervous systems	645 (1.35/100,000)	211 (1.30/100,000)	92 (3.28/100,000)
Fatal events	261* post-vaccination deaths		
** Following a medical review of the 261 deaths, it was determined that 96 were not linked to administration of the COVID-19 vaccine; 42 remain under investigation and 123 could not be classified due to insufficient information.*			

Source: Public Health Agency of Canada. Canadian COVID-19 vaccine safety report. Ottawa: Public Health Agency of Canada; January 14, 2022. https://health-infobase.canada.ca/covid-19/vaccine-safety/. Data reproduced by PAHO/WHO.

UNITED STATES

Following is updated information from the U.S. Centers for Disease Control and Prevention (CDC) regarding serious adverse events of special interest:

Anaphylaxis, a severe type of allergic reaction following COVID-19 vaccination, is rare and has occurred in approximately five people per million people vaccinated in the United States. Anaphylaxis can occur after administration of any type of vaccine.

Thrombosis with thrombocytopenia syndrome (TSS) following vaccination with the Janssen (J&J/Janssen) COVID-19 vaccine is rare. TTS is a rare but serious adverse event that causes blood clots in large blood vessels, along with low platelet counts (blood cells that help form clots). As of 6 January 2022, more than 17.7 million doses of the J&J/Janssen COVID-19 vaccine had been administered in the United States. The CDC and FDA identified 57 confirmed reports of people who received this vaccine and later developed TTS. They also identified nine deaths caused by or directly attributable to TTS following vaccination with the J&J/Janssen COVID-19 vaccine. Women between the ages of 30 and 49, especially, should be made aware of the increased risk of this rare adverse event, and of the fact that there are other COVID-19 vaccine options available for which this risk has not been detected.

To date, three confirmed cases of TTS following vaccination with Moderna's COVID-19 mRNA vaccine have been reported to VAERS, after more than 496 million doses of mRNA-based vaccines (Moderna and Pfizer-BioNTech) had been administered in the United States. Based on the available data, there is no increased risk of TTS after vaccination against COVID-19 with mRNA vaccines.

Guillain-Barré syndrome (GBS) in people who received the J&J/Janssen COVID-19 vaccine is uncommon. GBS is a rare disorder in which the body's immune system attacks nerve cells, causing muscle weakness and, in some cases, paralysis. Most people recover fully from GBS, but some suffer permanent nerve cell damage. After administration of more than 17.7 million doses of the J&J/Janssen COVID-19 vaccine, VAERS had received approximately 294 preliminary reports of GBS as of 6 January 2022. The vast majority of these cases were reported approximately two weeks after vaccination, and mainly in men, many of whom were 50 years old or older.

Based on these data, the rate of GBS within the first 21 days after administration of the J&J/Janssen COVID-19 vaccine was 21 times higher than after administration of the Pfizer-BioNTech or Moderna COVID-19 mRNA vaccines; and in the 42 days following vaccination, the rate of GBS was 11 times higher

for the J&J/Janssen vaccine than for the mRNA vaccines. The analysis found no increased risk of GBS after vaccination with the Pfizer-BioNTech or Moderna COVID-19 mRNA vaccines.

Myocarditis and pericarditis following vaccination against COVID-19 are rare. Myocarditis is an inflammation of the heart muscle, while pericarditis is an inflammation of the lining surrounding the heart. Most patients in whom myocarditis or pericarditis occurs after vaccination against COVID-19 responded well to medication and rest, and recovered quickly. As of 6 January 2022, VAERS had received 2,077 preliminary reports of myocarditis or pericarditis among people 30 years of age or younger who had received one of the COVID-19 vaccines. Most reported cases were among people, particularly male adolescents and young adults, who received the Pfizer-BioNTech or Moderna COVID-19 mRNA vaccine. Through follow-up, including a review of medical records, the CDC and FDA verified 1,175 reported cases of myocarditis.

Reports of deaths following vaccination with COVID-19 vaccines are rare. The FDA requires health care providers to report to VAERS any deaths following COVID-19 vaccination, even if it is unclear whether the vaccine was the cause. Reports to VAERS of adverse events, including deaths, following vaccination, do not necessarily mean that a vaccine caused a health problem. More than 520 million doses of COVID-19 vaccines were administered in the United States between 14 December 2020 and 10 January 2022. During this time, VAERS received 11,225 reports of deaths (0.0022%) among people who had received a COVID-19 vaccine. Doctors at the CDC and FDA review deaths reported to VAERS, including death certificates, autopsies, and medical records.

Additional information on this update is available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

Consolidated adverse events of special interest (AESI) reported by countries in the Region, by vaccine, December 2021

As of 10 December 2021, 1,378,223,759 doses of COVID-19 vaccines had been administered in the Region of the Americas. The following tables provide information on number of vaccine doses administered per manufacturer, from countries that report these figures (Argentina, Bolivia, Brazil, Colombia, Ecuador, Honduras, Mexico, Paraguay, Peru, Saint Vincent and the Grenadines, Uruguay, and United States) and number of reports involving AESI in VigiBase (the WHO's Collaborating Centre for international drug monitoring in Uppsala, Sweden:

	Number of reports of the event/100,000 doses of vaccine administered (including US)																			
	ASTRAZENECA		GAMALEYA		SINOPHARM		PFIZER		SINOVAC		BHARAT BIOTECH		JANSSEN		CANSINO		MODERNA		TOTALS	
	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S
Anaphylaxis	0.002	0.026	0.003	0.013	0.003	0.002	0.006	0.016	0.002	0.001	0.000	0.000	0.000	0.000	0.000	0.350	0.000	0.006	0.003	0.013
Appendicitis	0.000	0.002	0.000	0.000	0.000	0.005	0.026	0.126	0.000	0.000	0.000	0.000	0.027	0.173	0.000	0.000	0.020	0.080	0.017	0.077
Seizures	0.012	0.071	0.000	0.003	0.016	0.071	0.688	0.376	0.002	0.003	0.000	0.000	2,267	0.780	0.000	0.146	0.616	0.260	0.490	0.252
Herpes Zoster	0.016	0.032	0.000	0.000	0.028	0.012	1,268	0.207	0.001	0.000	0.000	0.000	1,448	0.104	0.000	0.000	1,202	0.097	0.849	0.118
Lymphadenopathy	0.074	0.041	0.013	0.000	0.021	0.010	3,820	0.391	0.006	0.000	0.000	0.000	2,328	0.280	0.000	0.000	3,997	0.199	2.587	0.226
Myelitis	0.000	0.002	0.000	0.000	0.000	0.002	0.012	0.032	0.000	0.000	0.000	0.000	0.008	0.054	0.000	0.000	0.004	0.014	0.006	0.019
Transverse myelitis	0.000	0.009	0.000	0.000	0.000	0.005	0.008	0.037	0.000	0.000	0.000	0.000	0.023	0.154	0.000	0.000	0.008	0.030	0.006	0.027
Myocarditis	0.000	0.017	0.000	0.000	0.002	0.014	0.397	0.898	0.000	0.000	0.000	0.000	0.150	0.446	0.000	0.000	0.201	0.745	0.220	0.564
Pericarditis	0.003	0.032	0.000	0.000	0.002	0.023	0.462	0.416	0.000	0.000	0.000	0.000	0.284	0.257	0.000	0.000	0.214	0.272	0.255	0.251
Facial paralysis	0.009	0.071	0.007	0.000	0.012	0.050	3,689	0.869	0.003	0.000	0.513	0.000	1,291	0.960	0.000	0.029	0.879	0.248	1,836	0.468
Paresthesia	0.238	0.188	0.023	0.000	0.177	0.116	0.748	0.235	0.218	0.005	0.000	0.000	9,547	1,721	0.000	0.175	3,842	0.432	1,442	0.267
GBS	0.002	0.107	0.000	0.003	0.003	0.043	0.067	0.197	0.000	0.002	0.000	0.000	0.384	1,368	0.000	0.175	0.031	0.132	0.046	0.164
TTS	0.000	0.004	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.008	0.031	0.000	0.000	0.000	0.001	0.000	0.002
Thrombosis	0.008	0.156	0.000	0.000	0.000	0.049	0.497	0.391	0.000	0.000	0.000	0.000	2,305	2,032	0.000	0.029	0.374	0.276	0.355	0.301
CVT	0.001	0.017	0.000	0.000	0.000	0.005	0.003	0.033	0.000	0.000	0.000	0.000	0.004	0.146	0.000	0.000	0.001	0.014	0.002	0.024
Vertigo	0.055	0.028	0.010	0.000	0.061	0.023	0.921	0.192	0.033	0.000	0.513	0.000	2,320	0.411	0.000	0.029	1,374	0.199	0.766	0.141
Total events	13,897	3,840	3,446	0.132	9,965	4,830	96,992	23,658	8,659	0.098	30,283	51,840	236,797	42,820	0.204	1,810	140,500	16,502	81,412	15,669

	Number of reports of the event /100,000 doses of vaccine administered (excluding USA)																			
	ASTRAZENECA		GAMALEYA		SINOPHARM		PFIZER		SINOVAC		BHARAT BIOTECH		JANSSEN		CANSINO		MODERNA		TOTALS	
	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S
Anaphylaxis	0.002	0.026	0.003	0.013	0.003	0.002	0.021	0.058	0.002	0.001	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.133	0.007	0.028
Appendicitis	0.000	0.002	0.000	0.000	0.000	0.005	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
Seizures	0.012	0.071	0.000	0.003	0.016	0.071	0.046	0.077	0.002	0.003	0.000	0.000	0.012	0.058	0.000	0.146	0.000	0.000	0.018	0.052
Herpes Zoster	0.016	0.032	0.000	0.000	0.028	0.012	0.038	0.031	0.001	0.000	0.000	0.000	0.012	0.000	0.000	0.000	0.000	0.019	0.018	0.018
Lymphadenopathy	0.074	0.041	0.013	0.000	0.021	0.010	0.800	0.120	0.006	0.000	0.000	0.000	0.058	0.015	0.000	0.000	0.066	0.000	0.233	0.044
Myelitis	0.000	0.002	0.000	0.000	0.000	0.002	0.000	0.006	0.000	0.000	0.000	0.000	0.000	0.008	0.000	0.000	0.085	0.294	0.002	0.009
Transverse myelitis	0.000	0.009	0.000	0.000	0.000	0.005	0.000	0.006	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.000	0.000	0.000	0.000	0.005
Myocarditis	0.000	0.017	0.000	0.000	0.002	0.014	0.004	0.068	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.000	0.000	0.028	0.001	0.025
Pericarditis	0.003	0.032	0.000	0.000	0.002	0.023	0.006	0.030	0.000	0.000	0.000	0.000	0.000	0.004	0.000	0.000	0.000	0.000	0.002	0.019
Facial paralysis	0.009	0.071	0.007	0.000	0.012	0.050	0.027	0.059	0.003	0.000	0.513	0.000	0.012	0.038	0.000	0.029	0.000	0.038	0.012	0.043
Paresthesia	0.238	0.188	0.023	0.000	0.177	0.116	0.650	0.145	0.218	0.005	0.000	0.000	0.510	0.211	0.000	0.175	0.218	0.057	0.322	0.115
GBS	0.002	0.107	0.000	0.003	0.003	0.043	0.000	0.052	0.000	0.002	0.000	0.000	0.023	0.077	0.000	0.175	0.000	0.009	0.001	0.053
TTS	0.000	0.004	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
Thrombosis	0.008	0.156	0.000	0.000	0.000	0.049	0.002	0.043	0.000	0.000	0.000	0.000	0.000	0.058	0.000	0.029	0.000	0.000	0.003	0.061
CVT	0.001	0.017	0.000	0.000	0.000	0.005	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.000	0.000	0.000	0.000	0.006
Vertigo	0.055	0.028	0.010	0.000	0.061	0.023	0.169	0.030	0.033	0.000	0.513	0.000	0.070	0.019	0.000	0.029	0.095	0.009	0.078	0.019
Total events	13,897	3,840	3,446	0.132	9,965	4,830	27,957	2,666	8,659	0.098	30,283	51,840	16,907	5,172	0.204	1,810	22,191	0.825	15,259	2,442

NS: non-serious cases; S: serious cases;
GBS: Guillain-Barré syndrome;
TTS: Thrombosis with thrombocytopenia syndrome
CVT: cerebral venous thrombosis

Countries included in the table: Argentina, Bolivia, Brazil, Colombia, Ecuador, Honduras, Mexico, Paraguay, Peru, Saint Vincent and the Grenadines, Uruguay, United States. Source: Number of doses is taken from the Dashboard on COVID-19 Vaccination in the Americas. (https://ais.paho.org/imm/IM_DosisAdmin-Vacunacion.asp. Accessed 10 Dec. 2021); Cases reported to VigiBase as of 8 Dec. 2021.

Publications on potential safety signals identified in the use of COVID-19 vaccines

RECOVAC Immune-response Study: The Immunogenicity, Tolerability, and Safety of COVID-19 Vaccination in Patients with Chronic Kidney Disease, on Dialysis, or Living with a Kidney Transplant

On 9 November 2021, a prospective, controlled multicenter study was published, including 162 participants with chronic kidney disease (CKD) in stages G4/5 (eGFR < 30 mL/min/1.73m^2), 159 participants on dialysis, 288 kidney transplant recipients, and 191 controls. Participants received two doses of the mRNA-1273 COVID-19 vaccine (Moderna). The primary endpoint was seroconversion. Transplant recipients had a significantly lower seroconversion rate when compared with controls (56.9% versus 100%, p<0.001), especially with mycophenolic acid, but also, higher age, lower lymphocyte concentration, lower eGFR, and shorter time after transplantation. Transplant recipients also showed significantly lower titers of neutralizing antibodies and T-cell responses when compared with controls. Although a high seroconversion rate was observed for participants with CKD G4/5 (100%) and on dialysis (99.4%), mean antibody concentrations in the CKD G4/5 cohort and dialysis cohort were lower than in controls (2405 [interquartile interval 1287-4524] and 1650 [698-3024] versus 3186 [1896-4911] BAU [binding antibody units]/mL, p=0.06 and p<0.001, respectively). Dialysis patients and especially kidney transplant recipients experienced less systemic vaccination-related adverse events. No specific safety issues were noted. The authors conclude that the immune response following vaccination in patients with CKD G4/5 and on dialysis is almost comparable to controls. In contrast, kidney transplant recipients have a poor response. In this latter patient group, development of alternative vaccination strategies are warranted.

Source: Sanders JF, Bemelman FJ, Messchendorp AL, et al. The RECOVAC Immune-response Study: The Immunogenicity, Tolerability, and Safety of COVID-19 Vaccination in Patients with Chronic Kidney Disease, on Dialysis, or Living with a Kidney Transplant. Transplantation. 2021 Nov 9. Doi: 10.1097/TP.0000000000003983. Epub ahead of print. PMID: 34753894.

Immune thrombocytopenia following immunization with Vaxzevria ChadOx1-S (AstraZeneca) vaccine, Victoria, Australia

On 26 November 2021, a retrospective case series of immune thrombocytopenia (ITP) following vaccination with Vaxzevria ChadOx1-S (AstraZeneca) and mRNA Comirnaty BNT162b2 COVID-19 (Pfizer-BioNTech) vaccines, comparing the incidence to expected background rates for Victoria during the first six months of the Australian COVID-19 vaccination roll-out in 2021, was published. Cases were identified by reports to the Victorian state vaccine safety service. The selected reports were for individuals aged 18

years or older presenting with thrombocytopenia following COVID-19 vaccination without evidence of thrombosis. Twenty-one confirmed or probable cases of ITP were identified following receipt of AstraZeneca (n=17) or Pfizer-BioNTech (n=4) vaccines. This translates to an observed incidence of eight cases per million doses for AstraZeneca vaccine, twice the expected background rate of 4.1 per million. The observed rate for Pfizer-BioNTech was consistent with the expected background rate. The median time to onset for the cases post AstraZeneca vaccination was 10 days (range 1–78) and median platelet nadir 5×10^9/L (range 0–67×10^9/L). Hospital presentations or admissions for management of symptoms such as bleeding occurred in 18 (86%) of the cases. The majority of cases (n=11) required intervention with at least two therapy modalities. The authors observed a substantially higher than expected rate of ITP following AstraZeneca vaccination. ITP is the second hematological adverse event, distinct from that of thrombosis with thrombocytopenia syndrome (TTS), observed following AstraZeneca vaccination.

Source: Gordon SF, Clothier HJ, Morgan H, et al. Immune thrombocytopenia following immunization with Vaxzevria ChadOx1-S (AstraZeneca) vaccine, Victoria, Australia. Vaccine. 2021 Nov 26;39(48):7052–7057. 10.1016/j.vaccine.2021.10.030. Epub 2021 Oct 30. PMID: 34756770; PMCID: PMC 8556135. https://www.sciencedirect.com/science/article/pii/S0264410X21013505?via%3Dihub.

Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection

On 14 December 2021, a self-controlled case series was published, assessing cardiac adverse events following COVID-19 vaccination in England between 1 December 2020 and 24 August 2021. The objective was to investigate hospital admission or death from myocarditis, pericarditis, and cardiac arrhythmias in the 1–28 days following adenovirus (ChAdOx1, n=20,615,911) or messenger RNA-based (BNT162b2, n=16,993,389; mRNA-1273, n=1,006,191) vaccines or a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive test (n=3,028,867). The authors found an increased risk of myocarditis (including hospitalization or death) associated with the first dose of ChAdOx1 and BNT162b2 vaccines and the first and second doses of the mRNA-1273 vaccine over the 1–28 day postvaccination period, and after a SARS-CoV-2 positive test. They estimated an extra two (95% CI 0, 3), one (95% CI 0, 2), and six (95% CI 2, 8) myocarditis events per million people vaccinated with ChAdOx1, BNT162b2, and mRNA-1273, respectively, in the 28 days following a first dose, and an extra ten (95% CI 7, 11) myocarditis events per million vaccinated in the 28 days after a second dose of mRNA-1273. This compares with an extra 40 (95% CI 38, 41) myocarditis events per million patients in the 28 days following a SARS-CoV-2 positive test. The authors also observed increased risks of pericarditis and cardiac arrhythmias (hospitalization or death) following a positive SARS-CoV-2 test. There was an increased risk of cardiac arrhythmia following a second

dose of mRNA-1273 (IRR 1.93, 95% CI 1.25, 2.96 at 1–7 days). Subgroup analyses by age group showed that the increased risk of myocarditis associated with the two mRNA vaccines was present only in those under 40 years of age.

Source: Patone M, Mei XW, Handunnetthi L, et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nat Med; 2021 Dec 14; Doi: 10.1038/s41591-021-01630-0. Online ahead of print. PMID: 34907393. https://www.nature.com/articles/s41591-021-01630-0.

Incidence of Myopericarditis and Myocardial Injury in Coronavirus Disease 2019 Vaccinated Subjects

On 28 November 2021, a study was published comparing the gender-specific cumulative incidence of myopericarditis and myocardial injury in a cohort of COVID-19 vaccinated patients at a United States tertiary care center in 2021 versus the cumulative incidence of these conditions in the same subjects exactly two years earlier. The age-adjusted incidence rate of myopericarditis in men was higher in the vaccinated group than in the control group, rate ratio 9.7 (p=0.04). In women, however, the age-adjusted incidence rate of myopericarditis was no different between vaccinated patients and controls, rate ratio 1.28 (p=0.71). In addition, the rate of myocardial injury was found to be higher in both men and women in 2021 than in 2019 both before and after vaccination, suggesting that some of the apparent increase in the diagnosis of myopericarditis after vaccination may be attributable to factors unrelated to the COVID-19 vaccinations. The authors conclude that the study reaffirms the apparent increase in the diagnosis of myopericarditis in men after COVID-19 vaccination but not in women, although this finding may be confounded by increased rates of myocardial injury in 2021. The benefits of COVID-19 vaccination to individual and public health clearly outweigh the small potential increased risk of myopericarditis after vaccination.

Source: Farahmand R, Trottier CA, Kannam JP, Ho KKL. Incidence of Myopericarditis and Myocardial Injury in Coronavirus Disease 2019 Vaccinated Subjects. Am J Cardiol. 2022 Feb 1;164:123–130. Doi: 10.1016/j.vaccine.2021.10.022. Epub 28 Nov 2021. PMID: 34852929; PMCID: PMC8627580. https://linkinghub.elsevier.com/retrieve/pii/S0002-9149(21)01047-X.

Risk of venous thrombotic events and thrombocytopenia in sequential time periods after ChAdOx1 and BNT162b2 COVID-19 vaccines: A national cohort study in England

On 13 December 2021 a cohort study was published, assessing the risk of thrombosis with thrombocytopenia, or thrombocytopenia on its own, after ChAdOx1 adenovirus-vector and BNT162b2 mRNA vaccines in England. Its objective was to assess the risk of thrombosis with thrombocytopenia or thrombocytopenia alone after administration of the ChAdOx1 adenovirus vector and BNT162b2 mRNA vaccines in England. An analysis was conducted of hospital admissions to all hospitals in the National Health Services (NHS) for cerebral venous thrombosis (CVT), other venous thrombosis, or thrombocytopenia between 30 November 2020 and 18 April 2021, linked to the national Covid-19 immunization register (a total of 27,378,384 people had received at least one dose of a COVID-19 vaccine). The incidence of events by dose in pre-defined post-vaccination risk periods relative to the unvaccinated cohort was estimated after adjustment for age, gender, co-morbidities, care home residency, and health/social care worker status. Elevated relative incidence (RI) estimates with $p<0.001$ were considered strong evidence of an association. The RI for CVT after a first ChAdOx1 dose in 15-39 and 40-64-year-olds was 8.7 (95% confidence interval 5.8-13.0) and 2.2 (1.4-3.2), respectively, $p<0.001$. The elevated risk period in 15-39-year-olds was highest 4-13 days post-vaccination (16.3, 9.9-27.0). The attributable risk (AR) was 16.1 per million doses for 15-39-year-olds and 3.2 per million for 40-64-year-olds. RIs for other thrombosis admissions were elevated in these age groups with ARs of 36.3 and 16.4 per million, respectively, as were RIs for thrombocytopenia, with ARs of 11.3 and 10.1 per million, respectively. No elevated risks were found for people over 65 or after a second ChAdOx1 dose, nor for BNT162b2 vaccine recipients of any age. Based on this epidemiological study, the authors conclude that there is an increased risk of thrombotic episodes and thrombocytopenia in adults under 65 within a month of a first dose of ChAdOx1 vaccine but not after the BNT162b2 vaccine.

Source: Andrews NJ, Stowe J, Ramsay ME, Miller E. Risk of venous thrombotic events and thrombocytopenia in sequential time periods after ChAdOx1 and BNT162b2 COVID-19 vaccines: A national cohort study in England. Lancet Reg Health Eur. 2022 Feb;13:100260. Doi: 10.1016/j.lanepe.2021.100260. Epub 2021 Dec 13. PMID: 34927118; PMCID: PMC8668159. https://www.sciencedirect.com/science/article/pii/S2666776221002465?via%3Dihub.

SARS-CoV-2 infection and COVID-19 vaccination rates in pregnant women in Scotland

Population-level data on COVID-19 vaccine uptake in pregnancy and SARS-CoV-2 infection outcomes are lacking. COVID-19 vaccine uptake and SARS-CoV-2 infection in pregnant women in Scotland, using whole-population data from a national, prospective cohort. Between the start of a COVID-19 vaccine program in Scotland, on 8 December 2020 and 31 October 2021, 25,917 COVID-19 vaccinations were given to 18,457 pregnant women. Vaccine coverage was substantially lower in pregnant women than in the general female population ages 18 to 44. Of women giving birth in October 2021, 32.3% had two doses of vaccine compared to 77.4% in all women. The extended perinatal mortality rate for women who gave birth within 28 days of a COVID-19 diagnosis was 22.6 per 1,000 births (95% CI 12.9−38.5; pandemic background rate 5.6 per 1,000 births; 452 out of 80,456; 95% CI 5.1−6.2). Overall, 77.4% (3,833 out of 4,950; 95% CI 76.2−78.6) of SARS-CoV-2 infections, 90.9% (748 out of 823; 95% CI 88.7−92.7) of SARS-CoV-2 associated with hospital admission, and 98% (102 out of 104; 95% CI 92.5−99.7) of SARS-CoV-2 associated with critical care admission, as well as all baby deaths, occurred in pregnant women who were unvaccinated at the time of COVID-19 diagnosis. Addressing low vaccine uptake rates in pregnant women is imperative to protect the health of women and babies in the ongoing pandemic.

Source: Stock SJ, Carruthers J, Calvert C, et al. SARS-CoV-2 infection and COVID-19 vaccination rates in pregnant women in Scotland. Nat Med; 2022 Jan 13. Doi: 10.1038/s41591-021-01666-2. Online ahead of print.

The European Medicines Agency recommends Nuvaxovid for authorization in the EU

On 20 December 2021, the European Medicines Agency (EMA) recommended granting conditional marketing authorization for Novavax's Nuvaxovid COVID-19 vaccine (also known as NVX-CoV2373), to prevent COVID-19 in people age 18 and older. This recombinant protein-based vaccine is the fifth vaccine recommended in the European Union (EU) for preventing COVID-19.

After a thorough evaluation by the EMA, the Committee for Medicinal Products for Human Use (CHMP) concluded by consensus that the data on the vaccine were robust and met the EU criteria for efficacy, safety, and quality. The results of two major clinical trials, the first study conducted in Mexico and the United States and the second conducted in the United Kingdom, involved a total of more than 45,000 people. Taken together, the results of the two studies show a vaccine efficacy for Nuvaxovid of around 90%. The original strain of SARS-CoV-2 and some variants of concern such as Alpha and Beta were the most common viral strains circulating when the studies were ongoing. There is currently a limited amount of data on the efficacy of Nuvaxovid against other variants of concern (VOC), including Omicron.

The side effects observed with Nuvaxovid in the studies were usually mild or moderate and cleared within a couple of days after vaccination. The most common ones were tenderness or pain at the injection site, tiredness, muscle pain, headache, a general feeling of being unwell, joint pain, and nausea or vomiting. The safety and effectiveness of the vaccine will continue to be monitored as it is used across the EU, through the EU pharmacovigilance system and additional studies by the company and European authorities.

Additional information about this recommendation can be found at:
https://www.ema.europa.eu/en/news/ema-recommends-nuvaxovid-authorisation-eu.

Meeting highlights from the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency

The Pharmacovigilance Risk Assessment Committee (PRAC), of the European Medicines Agency (EMA), met from 10 to 13 January 2022. Highlights of the conclusions of this meeting are summarized below.

- **Vaxzevria and Janssen COVID-19 Vaccines: Update on very rare cases of transverse myelitis (TM):** The Committee has reviewed available information on globally reported cases, including those in the European database for suspected side effects (EudraVigilance) and data from the scientific literature, with both vaccines. The PRAC has concluded that a causal relationship between these two vaccines and TM is at least a reasonable possibility.

  TM is a rare neurological condition characterized by an inflammation of one or both sides of the spinal cord. It can cause weakness in the arms or legs, sensory symptoms (such as tingling, numbness, pain or loss of pain sensation) or problems with bladder or bowel function.

  The PRAC concluded that the benefit-risk profile of both vaccines remains unchanged. TM has also been added as an adverse reaction of unknown frequency. Product information is to include a warning indicating that healthcare professionals should be alert to signs and symptoms of TM, allowing for early diagnosis, supportive care and treatment, and recommending that people receiving any of these vaccines seek immediate medical attention if they develop symptoms of the condition. EMA will continue to closely monitor this issue and will communicate further if new information becomes available.

- **Vaxzevria: Fewer cases of thrombosis with thrombocytopenia syndrome reported after second dose.** The PRAC has recommended updating the product information for Vaxzevria on the very rare cases of thrombosis with thrombocytopenia (TTS). After reviewing 1,809 reported cases of thromboembolic with thrombocytopenia worldwide, the Committee found that 1,643 were reported after the first dose and 166 after the second dose. According to the current product information, the administration of a second dose of Vaxzevria is contraindicated in people who have experienced TTS following vaccination with this vaccine.

Additional information on this meeting can be found at:
https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-10-13-january-2022.

The U.S. Food and Drug Administration authorizes a second Moderna COVID-19 vaccine, Spikevax, for marketing in the United States.

On 31 January 2022, the U.S. Food and Drug Administration (FDA) authorized a second Moderna COVID-19 vaccine, Spikevax, for marketing in the U.S.; the Pfizer vaccine was the first COVID-19 vaccine to obtain an FDA marketing license.

Moderna's COVID-19 vaccine was granted emergency use authorization by the FDA on 18 December 2020 for use in people ages 18 and older. The FDA has now reported that Spikevax meets the safety, effectiveness, and manufacturing quality standards required for granting the license to market the vaccine.

Spikevax has the same formulation as the EUA Moderna COVID-19 vaccine, and can be used interchangeably with the Moderna COVID-19 vaccine to provide the COVID-19 vaccination series. The Moderna COVID-19 vaccine remains available under EUA as a two-dose primary series for individuals 18 years of age and older, as a third primary series dose for individuals 18 years of age and older who have been determined to have certain kinds of immunocompromise, and as a single booster dose for individuals 18 years of age and older at least five months after completing a primary series of the vaccine. Spikevax is also authorized for use as a heterologous single booster dose for individuals 18 years of age and older following completion of primary vaccination with a different COVID-19 vaccine available in the U.S.

Additional information can be found at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-key-action-approving-second-covid-19-vaccine.

CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

Update to the WHO interim statement of the Strategic Advisory Group of Experts on Immunization regarding booster doses for COVID-19 vaccination

On 22 December 2021, the Strategic Advisory Group of Experts (SAGE) on Immunization and its COVID-19 Vaccines Working Group updated the interim statement on booster doses for COVID-19 vaccines that have received Emergency Use Listing (EUL). This statement summarizes and contextualizes current evidence on booster vaccination, indicating that data are currently insufficient to assess the impact of this new SARS-CoV2 variant of concern, Omicron, on vaccine effectiveness. This information will therefore be updated as data become available. The statement presents the following conclusions:

- The focus of COVID-19 immunization efforts must remain on decreasing death and severe disease, and the protection of the health care system. In the context of ongoing global vaccine supply constraints and inequities, broad-based administration of booster doses risks exacerbating vaccine access by driving up demand in countries with substantial vaccine coverage and diverting supply, while priority populations in some countries, or in subnational settings, have not yet received a primary vaccination series

- Introducing booster doses should be firmly evidence-driven and targeted to the population groups at highest risk of serious disease and those necessary to protect the health system. To date, the evidence indicates a minimal to modest reduction of vaccine protection against severe disease over the six months after the primary series.

- More data will be needed to understand the potential impact of booster vaccination on the duration of protection against severe disease, but also against mild disease, infection, and transmission, particularly in the context of emerging SARS-CoV-2 variants. Over time, as vaccination programs effectively protect populations from severe disease and death, the protection against milder disease and the reduction of transmission become important additional considerations.

SAGE will further discuss policies to optimize the use of vaccines, including the consideration of booster vaccination at its forthcoming meeting.

Additional information can be found at: https://www.who.int/news/item/22-12-2021-interim-statement-on-booster-doses-for-covid-19-vaccination---update-22-december-2021.

Interim Statement on COVID-19 vaccines in the context of the circulation of the Omicron SARS-CoV-2 Variant of Concern (VOC) from the WHO Technical Advisory Group

On 11 January 2022, the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) issued an interim statement, which is summarized below:

The TAG-CO-VAC is developing a framework to analyze the evidence on emerging VOCs in the context of criteria that would trigger a recommendation to change COVID-19 vaccine strain composition, and will advise WHO on updated vaccine compositions, as required. This framework considers the global spread and transmissibility, clinical severity, genetic, antigenic and phenotypic characteristics of the VOC, including capacity for immune escape and assessments of vaccine effectiveness.

In the context of the circulation of Omicron SARS-CoV-2 Variant of Concern, the TAG-CO-VAC urges broader access globally to current COVID-19 vaccines for primary series and booster doses, in the hope that this also mitigates the emergence and impact of new VOCs, and encourages vaccine developers to gather data on a small scale on the breadth and magnitude of immune response for monovalent and multivalent vaccines against VOCs. This data would then be considered in a broader decision-making framework on vaccine composition by the TAG-CO-VAC.

In terms of the composition of COVID-19 vaccines, the TAG-CO-VAC considers that COVID-19 vaccines that have a high impact on prevention of infection and transmission, in addition to the prevention of severe disease and death, are needed and should be developed. Until such vaccines are available, and as the SARS-CoV-2 virus evolves, the composition of current COVID-19 vaccines may need to be updated, to ensure that COVID-19 vaccines continue to provide WHO-recommended levels of protection against infection and disease caused by VOCs, including Omicron and future variants.

To improve the protection induced by COVID-19 vaccines, options include:

- a monovalent vaccine that elicits an immune response against the predominant circulating variant(s), although this option faces the challenge of the rapid emergence of SARS-CoV-2 variants and the time needed to develop a modified or new vaccine;
- a multivalent vaccine containing antigens from different SARS-CoV-2 VOCs; and
- a pan-SARS-CoV-2 vaccine: a more sustainable long-term option that would effectively be variant-proof.

This statement and its conclusions will be updated by the TAG-CO-VAC as data become available.

Additional information can be found at: https://www.who.int/news/item/11-01-2022-interim-statement-on-covid-19-vaccines-in-the-context-of-the-circulation-of-the-omicron-sars-cov-2-variant-from-the-who-technical-advisory-group-on-covid-19-vaccine-composition.

The European Medicines Agency notes that COVID-19 vaccines remain effective against severe disease and hospitalizations caused by the Omicron variant

On 11 January 2022, the European Medicines Agency (EMA) stated that preliminary data on the effectiveness of COVID-19 vaccines, including against disease caused by the Omicron variant, indicate that licensed COVID-19 vaccines remain effective against severe disease and hospitalization.

They note that although Omicron appears to be more infectious than other variants, studies from South Africa, UK and some EU countries show a lower risk of being hospitalized after infection with Omicron; based on these studies, the risk is currently estimated to be between a third and half of the risk with the Delta variant. Results from recently published studies show that effectiveness of the AstraZeneca, Moderna, and Pfizer vaccines against symptomatic disease is lower for Omicron than for other variants, and tends to wane over time.

However, these studies also show that vaccination continues to provide a high level of protection against severe disease and hospitalization linked to the Omicron variant. The latest evidence, which includes real-world effectiveness data, also suggests that people who have had a booster dose are better protected than those who have only received their primary course. Data from South Africa indicate that people who have received two doses of a COVID-19 vaccine have up to 70% protection from hospitalization; similar data from the UK show that while protection declines a few months after vaccination, protection from hospitalization rises again to 90% after a booster shot.

The EMA emphasizes that vaccination remains an essential part of the approach to fighting the ongoing pandemic. In line with recommendations by national authorities, efforts should continue to increase full vaccination uptake in individuals who are currently unvaccinated or partially vaccinated, and to accelerate the roll-out of booster doses.

Additional information can be found at: https://www.ema.europa.eu/en/news/preliminary-data-indicate-covid-19-vaccines-remain-effective-against-severe-disease-hospitalisation.

According to the European Medicines Agency, the latest safety data provide reassurance about the use of mRNA COVID-19 vaccines during pregnancy

On 18 January 18 2022, the European Medicines Agency (EMA) indicated that its COVID-19 task force (ETF) conducted a detailed review of several studies involving around 65,000 pregnancies at different stages. Despite some limitations in the data, the results are consistent and found no sign of an increased risk of pregnancy complications, miscarriages, preterm births, or adverse effects in the unborn babies following mRNA COVID-19 vaccination.

In addition, the EMA indicates that these studies also showed that COVID-19 vaccines are as effective at reducing the risk of hospitalization and deaths in pregnant women as they are in non-pregnant women, and that side effects were similar and improve within a few days of vaccination.

Given that so far pregnancy has been associated with a higher risk of severe COVID-19 particularly in the second and third trimesters, women who are pregnant or might become pregnant in the near future are encouraged to get vaccinated in line with national recommendations.

Additional information can be found at: https://www.ema.europa.eu/en/news/covid-19-latest-safety-data-provide-reassurance-about-use-mrna-vaccines-during-pregnancy.

Inclusions in the WHO Emergency Use Listing (EUL)

On 23 December 2021, WHO added the following additional Moderna COVID-19 vaccine production sites to the Emergency Use Listing (EUL):

COVID-19 vaccine (EUL)	NRA of record	EUL holder	Authorized sites added to the Emergency Use Listing	
			Manufacturer	NRA of record
Vaxzevria COVID-19 vaccine (ChAdOx1-S [recombinant])	European Medicines Agency (EMA)	AstraZeneca	Active ingredient: mAbxience SAU, Argentina. Final product: Liomont, S.A. Mexico	COFEPRIS, Mexico; ANMAT, Argentina
Spikevax mRNA COVID-19 vaccine (nucleoside- modified)	European Medicines Agency (EMA)	Moderna Biotech	Samsung Biologics, Republic of Korea	Ministry of Food and Drug Safety (MFDS), Republic of Korea

NRA of record: The NRA that first authorized the vaccine and that is responsible for supervision of the vaccine.

Additional information can be found at: https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued.

Decisions of the Region's Regulatory Authorities

U.S. Food and Drug Administration (FDA):

- **Shortening the interval for booster doses of Moderna's COVID-19 vaccine:** On 7 January 2022, the U.S. Food and Drug Administration (FDA) amended the emergency use authorization (EUA) for the Moderna COVID-19 vaccine to shorten the time between the completion of a primary series of the vaccine and a booster dose from six months to at least five months for individuals 18 years of age and older.

  The most commonly reported side effects by individuals who received a booster dose of the Moderna COVID-19 vaccine after completion of a two-dose primary series were: pain, redness and swelling at the injection site, as well as fatigue, headache, muscle or joint pain, and chills. The fact sheets for recipients and caregivers and for healthcare providers include information about the potential side effects, as well as the risks of myocarditis and pericarditis.

  Additional information can be found at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-shortens-interval-booster-dose-moderna-covid-19-vaccine-five-months.

- **Multiple actions to expand use of the Pfizer-BioNTech COVID-19 vaccine:**

  On 3 January 2022, the FDA amended the Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine to:

  - Expand the use of a single booster dose to include use in individuals ages 12 through 15. The agency has determined that the protective health benefits of a single booster dose of the vaccine, to provide continued protection against COVID-19 and the associated serious consequences that can occur including hospitalization and death, outweigh the potential risks in individuals 12 through 15 years of age.
  - Shorten the time between the completion of primary vaccination and a booster dose to at least five months. Peer-reviewed data indicate that a booster dose of the Pfizer-BioNTech COVID-19 vaccine greatly improves an individual's antibody response to be able to counter the Omicron variant. Given the demonstrated safety and effectiveness of a

booster dose when administered five months after the primary vaccination series, and the fact that a booster dose may help provide better protection against the rapidly spreading Omicron variant, the FDA has determined that the known and potential benefits of administering a booster to individuals ages 12 and older at least five months following completion of the primary vaccination series, outweighs the known and potential risks.

- Allow for a third primary series dose for certain immunocompromised children 5 through 11 years of age who have undergone solid organ transplantation, or who have been diagnosed with conditions that are considered to have an equivalent level of immunocompromise, and who may not respond adequately to the two-dose primary vaccination series. Thus, a third primary series dose has now been authorized for this group.

Additional information can be found at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-multiple-actions-expand-use-pfizer-biontech-covid-19-vaccine.

Federal Commission for the Protection against Sanitary Risks (COFEPRIS), Mexico:

- Authorization for emergency use of the Abdala vaccine: On 29 December 2021, COFEPRIS granted emergency use authorization of the Abdala vaccine, with the distinctive designation "SARS-CoV-2 recombinant receptor-binding domain (RBD) protein."

The New Molecules Committee (known by its Spanish acronym CMN) met to consider the use of this biologic drug, which was given a favorable technical reception. After incorporating the opinion of the CMN and submitting the application for emergency use authorization to COFEPRIS, staff specializing in vaccines analyzed the dossier and certified that the biologic drug meets the appropriate quality, safety, and efficacy requirements.

Additional information can be found at: https://www.gob.mx/cofepris/articulos/cofepris-emite-autorizacion-para-uso-de-emergencia-de-vacuna-abdala?idiom=es.

Public Health Institute of Chile (ISP)

- **Safety review of AstraZeneca and Janssen COVID-19 Vaccines Following International Reports of Capillary Leak Syndrome:** On 30 December 2021, the ISP published a pharmacovigilance briefing note on the safety review of the AstraZeneca and Janssen COVID-19 vaccines, following international reports of capillary leak syndrome. The ISP states that while the available evidence indicates that an association cannot be ruled out, the benefits of these vaccines, like the other vaccines authorized in Chile, continue to outweigh the possible risks, due to their enormous potential for preventing infection and reducing mortality from the SARS-CoV-2 virus. Although a definitive causal relationship has not been established, the briefing note is intended to assist in the early identification of the clinical situation by both health professionals and the vaccinated population, in order to maximize the benefits of COVID-19 vaccination, given that the benefits outweigh the identified risks.

Additional information can be found at: https://www.ispch.cl/wp-content/uploads/2021/12/Scan30-12-2021-112108.pdf.