COVID-19

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

Twenty-fifth report

WASHINGTON, DC

Updated: 20 September 2021

CONTENTS

Doses administered, spontaneous reports of suspected cases of AEFI, and fatal outcomes in Europe, based on the EudraVigilance database as of 2 September 2021

Vaccine	Doses administered	Reports of AEFI	Reports of AEFI /100,000 doses	Fatal outcomes (cases)	Fatal outcomes /100,000 doses
Comirnaty	392 million	302,517	77.2	4,714	1.2
AstraZeneca	68.4 million	184,679	270.0	1,149	1.7
Spikevax	54.2 million	64,885	119.7	447	0.8
Janssen	13.8 million	20,206	146.4	138	1.0

Source: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/safety-covid-19-vaccines#latest-safety-information-section

BRAZIL

- As of 1 August 2021, in Brazil (not including the State of São Paulo), 100,379,140 doses of COVID-19 vaccines had been administered – 49,893,631 of the AstraZeneca/FioCruz vaccine, 36,062,724 of the Sinovac/Butantan vaccine, 11,440,705 of the Pfizer-BioNTech vaccine, and 2,982,080 of the Janssen vaccine.[1]
- During the first months of the vaccination campaign (from 18 January to 1 August 2021), 106,006 AEFI were reported, an incidence of 105/100,000 doses administered, with the AstraZeneca/FioCruz vaccine having the highest incidence of AEFI.
- The following table shows the total number of AEFI and the number of serious AEFI, along with incidence per 100,000 doses administered, for each of the four vaccines:

[1] The Epidemiological Bulletin No. 78, of 6 September 2021, does not include doses administered in the State of São Paulo, since the State uses its own AEFI reporting system.

AEFI	AstraZeneca/FioCruz	Sinovac/Butantan	Pfizer- BioNTech	Janssen	TOTAL
	Number per 100,000 doses administered	Number per 100,000 doses administered	Number per 100,000 doses administered	Number per 100,000 doses administered	Number per 100,000 doses administered
Serious	3,180 (6.4)	3,674 (10.2)	285 (2.5)	52 (1.7)	7,191
Non-serious	64,114 (128.5)	29,509 (81.8)	4,043 (35.3)	1,149 (38.5)	98,815
TOTAL	67,294 (134.9)	33,183 (92.0)	4,328 (37.8)	1,201 (40.3)	106,006

- For the four vaccines administered, AEFI with the highest incidence were headache, myalgia, and pyrexia.
- According to the System Organ Class (SOC), the reported occurrence of serious AEFI per 100,000 doses administered, by preferred term (PT), was as follows:

Preferred term	AstraZeneca/FioCruz (serious events per 100,000 doses administered)	Sinovac/Butantan (serious events per 100,000 doses administered)	Pfizer-BioNTech (serious events per 100,000 doses administered)	Janssen (serious events per 100,000 doses administered)
Thoracic or mediastinal disorders	2.6	5.8	0.92	0.80
General disorders and clinical manifestations at the injection site	1.5	3.4	0.52	0.23
Nervous system disorders	1.4	1.3	0.59	0.40
Gastrointestinal disorders	0.74	1.2	0.44	
Cardiac disorders	0.78	0.94	0.25	0.17
Vascular disorders	0.85	0.43	0.22	0.20
Immune system disorders	0.44	0.55	0.17	0.10
Metabolic and nutritional disorders		0.55		
Musculoskeletal and connective tissue disorders	0.44	0.43	0.23	
Disorders of the skin or subcutaneous tissues	0.46			0.03

- With regard to reports of serious events, by preferred term (PT), the following table shows incidence per 100,000 doses administered:

PT	AstraZeneca/FioCruz (serious events per 100,000 doses administered)	Sinovac/Butantan (serious events per 100,000 doses administered)	Pfizer- BioNTech (serious events per 100,000 doses administered)	Janssen (serious events per 100,000 doses administered)
Dyspnea	1.3	2.6	0.47	0.34
Pyrexia	0.60	1.2	0.25	0.10
Cough	0.39	0.88	0.19	
COVID-19	0.33	0.84		0.23
Severe acute respiratory syndrome (SARS)	0.27	0.56		0.13
Acute respiratory distress syndrome (ARDS)	0.19	0.38		
Low oxygen saturation	0.19	0.38		
Asthenia		0.34		0.10
Fatigue		0.33		
Myalgia	0.21		0.16	
Convulsion			0.08	0.07
Cerebral thrombosis				0.07
Mesenteric venous thrombosis				0.07
Facial paralysis			0.07	

- There were 7,944 reports of programmatic errors, as shown in the table below. Among these errors, 480 developed into adverse events, of which 25 resulted in serious events, including 9 deaths.

Vaccine	Number of errors	Number of errors per 100,000 doses administered	Total doses administered
Sinovac/Butantan	2,855	5.7	49,893,631
AstraZeneca/FioCruz	4,132	11.5	36,062,724
Pfizer- BioNTech	112	3.8	2,982,080
Janssen	845	7.4	11,440,705
TOTAL	7,944	7.9	100,379,140

Type of vaccination error	Number
Product switched/incorrect vaccine administered	3,415
Dosage, incorrect dose administered	1,355
Vaccine administered to person of inappropriate age	950
Incorrect interval	155
Incorrect administration site	28
Route of administration	96
Vaccination contraindicated	422
Inadvertent exposure to vaccine (pregnancy and lactation)	413
Use of expired vaccine	295
Other, not clearly defined	815
TOTAL	7,944

Source: MINISTÉRIO DA SAÚDE, Secretaria de Vigilância em Saúde. 78- BOLETIM EPIDEMIOLÓGICO ESPECIAL. Doença hair Novo Coronavírus – COVID-19. SE 34, 22/8 to 28/8/2021. https://www.gov.br/saude/pt-br/media/pdf/2021/setembro/14/boletim_epidemiologico_covid_78-1.pdf

CANADA

- As of 10 September 2021, 37,610,913 doses of the Pfizer-BioNTech COVID-19 vaccine, 13,202,225 doses of the Moderna vaccine, and 2,784,910 doses of the AstraZeneca and Covishield vaccine (AstraZeneca vaccine manufactured by the Serum Institute of India) had been administered.
- There were 15,326 individual reports of one or more adverse events (0.028% of doses administered). Of these, 4,195 reported events were considered serious (0.008% of doses administered).
- A total of 40,929 AEFI were reported (15.326 involving one or more events). Most reported adverse events were non-serious, such as injection-site reactions, paresthesia, headache, pruritus, dyspnea, fatigue, nausea, etc.

Number of reports and reporting rate (per 100,000 doses administered) of adverse events per vaccine, as of 10 September 2021

Vaccine	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
	N	Rate per 100,000 doses administered	N	Rate per 100,000 doses administered	N	Rate per 100,000 doses administered
Pfizer-BioNTech	5,764	15.33	2,724	7.24	8,488	22.57
Moderna	3,899	29.53	716	5.42	4,615	34.96
Covishield and AstraZeneca	1,431	51.38	604	21.69	2,035	73.07
Unknown	37	-	151	-	188	-
Total	11,131	20.56	4,195	7.75	15,326	28.31

Number of reports and reporting rate (per 100,000 doses administered) of the main severe AEFI, by vaccine, as of 10 September 2021			
Vaccine	**Pfizer-BioNTech**	**Moderna**	**Covishield and AstraZeneca**
Anaphylaxis	142 (0.38/100,000)	30 (0.22/100,000)	0
Thrombosis with thrombocytopenia syndrome (TTS)	16 (0.04/100,000)	4 (0.03/100,000)	61 (2.19/100,000)
Guillain-Barré syndrome	31 (0.08/100,000)	15 (0.11/100,000)	30 (1.08/100,000)
Capillary leak syndrome	-	-	2 (0.07/100,000)
Myocarditis/pericarditis	408 (1.08/100,000)	290 (2.17/100,000)	18 (0.65/100,000)
Bell's palsy/facial paralysis	325 (0.86/100,000)	105 (0.79/100,000)	43 (1.54/100,000)
Fatal events	189* post-vaccination deaths		
** Following a medical review, it was determined that, of the 189 deaths, 73 were not linked to administration of the COVID-19 vaccine, 39 are still under investigation, 6 (cases of TTS) are considered to be potentially attributable to vaccination, and 71 could not be classified due to insufficient information.*			

An analysis of 716 of the 718 cases of myocarditis/pericarditis, with indication of the vaccine administered, is detailed below:

Vaccine	Total number of cases (rate per 100,000 doses administered)	By sex (median age)		Number of reports, by doses administered		
		Number of women (median age)	Number of men (median age)	1st	2nd	Unknown
Pfizer-BioNTech*	408 (1.08)	146 (40 years)	258 (23 years)	176	193	49
Moderna**	290 (2.17)	75 (32 years)	211 (28 years)	59	199	32
Covishield and AstraZeneca	18 (0.65)	Not available	Not available	Not available	Not available	Not available

* In four cases, the sex of the individual was not specified.

** In three cases, the sex of the individual was not specified, and in one case the sex was given as "other."

Source: Public Health Agency of Canada. Canadian COVID-19 vaccine safety report. Ottawa: Public Health Agency of Canada; September 17, 2021. https://health-infobase.canada.ca/covid-19/vaccine-safety/. Data reproduced by PAHO/WHO.

UNITED STATES (data to 8 September)

Below are data reported by the United States for selected events as of 8 September:

Events	Vaccine	Doses administered	Cases/Incidence

Anaphylaxis	Any vaccine	More than 380 million doses	Approx. 2 to 5 cases per million people vaccinated
Thrombosis with thrombocytopenia syndrome (TTS)	J&J/Janssen	More than 14.5 million doses	46 confirmed cases of people who received the vaccine and were later diagnosed with TTS
	Moderna	More than 362 million doses of mRNA vaccine	Two cases. There is no increased risk of TTS after receiving this COVID-19 mRNA vaccine
Guillain-Barré syndrome	J&J/Janssen	More than 14.5 million doses	195 preliminary reports identified
Myocarditis/pericarditis	Moderna or Pfizer-BioNTech	362 million doses	1,413 reports, of which 854 were confirmed (pending evaluation of their link to vaccination)
Deaths	All vaccines	More than 380 million doses	7,653 deaths, reported to VAERS, of people who had received a COVID-19 vaccine (0.0020%), which does not necessarily mean that there is a causal relationship.

Source: Centers for Disease Control and Prevention. COVID-19. Some adverse reactions were reported after receiving a COVID-19 vaccination. Updated 14 September 2021. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html. Data reproduced by PAHO/WHO.

URUGUAY

- Between 27 February and 12 August 2021, 4,962,211 doses of SARS-CoV-2 vaccines were administered. A total of 1,157 reports of AEFI were received following administration of these vaccines, equivalent to a rate of 23.3 reports per 100,000 doses administered.
- The following table gives the number of vaccine doses administered, by type of vaccine, reports that resulted in closed cases (cases evaluated and cases for which causality was established), number of AEFI (taking into account that each report could involve more than one AEFI), and number of cases of AEFI that required or prolonged hospitalization. Rates per 100,000 doses administered are also given:

Vaccine	Doses administered	Number of reports resulting in closed cases/100,000 doses administered	Number of AEFI reported/100,000 doses administered	Cases of AEFI involving hospitalization/100,000 doses administered
AstraZeneca	85,858	24 (27.9)	53 (54.7)	6 (7.0)
CoronaVac	3,234,213	560 (17.3)	786 (24.3)	12 (0.37)
Pfizer-BioNTech	1,642,140.	543 (33.1)	976 (59.4)	21 (1.3)
Not indicated		18	47	
Total	4,962,211	1.145 (23.1)	1.862 (37.5)	39 (0.77)

- The 39 cases of AEFI that required or prolonged hospitalization were classified using the WHO-AEFI algorithm. Notable adverse events identified as "vaccine-related" (A1) included the following:
    - for the AstraZeneca vaccine: one case of deep vein thrombosis of the lower limbs;
    - for CoronaVac: one case of Guillain-Barré syndrome and one case of deep vein thrombosis of the lower limbs;
    - for Pfizer-BioNTech: two cases of autoimmune thrombocytopenic purpura, one case of Guillain-Barré syndrome, one case of myopericarditis, one case of aggravated bronchospasm, one case of dyspnea, one of facial paresthesia, one case of acute migraine, and one case of headache with loss of balance.

Source: https://www.gub.uy/ministerio-salud-publica/comunicacion/noticias/informe-vigilancia-seguridad-vacunas-contra-sars-cov-2-uruguay-actualizacion

WHO calls for moratorium on the use of COVID-19 vaccine booster doses

An international group of scientists, including staff from the World Health Organization (WHO), in a recent issue of the journal The Lancet, questioned the need for boosters to increase the immune response provided by COVID-19 vaccines. Their main point was that, to date, fully vaccinated people have been shown to remain highly protected against severe COVID-19 disease. Further, they recommend that the extra doses be used to vaccinate people who have not yet been vaccinated.

Even if it were shown that booster doses could potentially decrease the risk of severe disease, the amount of vaccine available at the moment would save more lives if used to vaccinate the unvaccinated population than if it were used as a booster for people already vaccinated. The authors also indicated that the booster might be advisable for people with immunodeficiencies or immunosuppression who had already received the full schedule of one or two doses of vaccine.

The evidence presented so far seems to show that efficacy against severe disease is maintained, and that humoral immunity appears to be waning, but the relation between neutralizing antibody titers and vaccine efficacy has not yet been established. The cell-mediated response, which is longer-lasting, also plays a role in protection.

The findings being presented to justify booster doses are from observational studies that, for various reasons, may be biased by patient characteristics, registry systems, differences between vaccinated and unvaccinated groups, social patterns of behavior, etc.

The authors also expressed concern about the impact that messages on boosters could have on the population, along with concern about the potential for adverse events resulting from a booster dose.

Most important, however, is the benefit that could be achieved globally if the vaccine were administered to a greater number of unvaccinated people, thereby hastening the end of the pandemic by reducing the chance for new variants to emerge.

WHO is calling for a moratorium on the use of booster doses until more people worldwide have received primary vaccination.

Source: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02046-8/fulltext

Surveillance of adverse events following administration of COVID-19 mRNA vaccines

On 3 September, JAMA published an interim analysis of safety surveillance data from the Vaccine Safety Datalink. Approximately 10,162,227 vaccine-eligible members of eight participating U.S. health plans were monitored, with administrative data updated weekly and supplemented with medical record review of selected outcomes from 14 December 2020 through 26 June 2021. The objective was to monitor 23 serious events weekly, following

administration of the BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccine, comparing those vaccinated with a risk interval of 21 days after vaccination with those vaccinated with the comparison interval of between 22 to 42 days.

A comparison was made of the incidence of serious events, including acute myocardial infarction, Bell's palsy, cerebral venous sinus thrombosis, Guillain-Barré syndrome, myocarditis/pericarditis, pulmonary embolism, stroke, and thrombosis with thrombocytopenia syndrome. For four serious events (acute respiratory distress syndrome, anaphylaxis, multisystem inflammatory syndrome in children and adults, and narcolepsy), only descriptive analyses were performed.

A total of 11,845,128 doses of COVID-19 mRNA vaccines (57% BNT162b2; 6,175,813 first doses and 5,669,315 second doses) were administered to 6.2 million people (mean age, 49 years; 54% women). The incidence of events in the studied population per million person-years during the risk versus comparison intervals for ischemic stroke was 1,612 versus 1,781 (RR, 0.97; 95% CI, 0.87-1.08); for appendicitis, 1,179 versus 1,345 (RR, 0.82; 95% CI, 0.73-0.93); and for acute myocardial infarction, 935 versus 1,030 (RR, 1.02; 95% CI, 0.89-1.18). No vaccine-outcome association met the pre-specified requirement for a signal. Incidence of confirmed anaphylaxis was 4.8 (95% CI, 3.2-6.9) per million doses of BNT162b2 and 5.1 (95% CI, 3.3-7.6) per million doses of mRNA-1273.

The authors conclude, based on this interim analysis of surveillance of mRNA COVID-19 vaccines, that the incidence of selected serious outcomes was not significantly higher one to 21 days postvaccination compared with 22 to 42 days postvaccination. While CIs were wide for many outcomes, surveillance is ongoing.

Source: Klein NP, Lewis N, Goddard K, et al. Surveillance for Adverse Events After COVID-19 mRNA Vaccination. JAMA. Published online 3 September 2021. doi: 10.1001/jama.2021.15072. Available at: https://jamanetwork.com/journals/jama/fullarticle/2784015

Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app

A study published on 1 September attempted to identify risk factors for post-vaccination SARS-CoV-2 infection and describe the characteristics of post-vaccination illness.

This prospective, community-based, nested, case-control study used self-reported data from UK-based adult (≥18 years) users of the COVID Symptom Study mobile phone app. For the risk factor analysis, cases had received a first or second dose of a COVID-19 vaccine between 8 Dec 2020 and 4 July 2021; had either a positive COVID-19 test at least 14 days after their first vaccination (but before their second; cases 1) or a positive test at least 7 days after their second vaccination (cases 2); and had no positive test before vaccination. Two control groups were selected (who also had not tested positive for SARS-CoV-2 before vaccination): users reporting a negative test at least 14 days after their first vaccination but before their second (controls 1) and users reporting a negative test at least 7 days after their second vaccination (controls 2). Controls 1 and controls 2 were matched (1:1) with cases 1 and cases 2,

respectively, by the date of the post-vaccination test, healthcare worker status, and sex. In the disease profile analysis, participants were sub-selected from cases 1 and cases 2 who had used the app for at least 14 consecutive days after testing positive for SARS-CoV-2 (cases 3 and cases 4, respectively). Controls 3 and controls 4 were unvaccinated participants reporting a positive SARS-CoV-2 test who had used the app for at least 14 consecutive days after the test, and were matched (1:1) with cases 3 and 4, respectively, by the date of the positive test, health-care worker status, sex, body-mass index (BMI), and age.

Between 8 Dec 2020, and 4 July 2021, 1,240,009 COVID Symptom Study app users reported a first vaccine dose; of these, 6,030 (0.5%) subsequently tested positive for SARS-CoV-2 (cases 1), and 971,504 reported a second dose, with 2,370 (0.2%) subsequently testing positive for SARS-CoV-2 (cases 2). In the risk factor analysis, frailty was associated with post-vaccination infection in older adults (≥60 years) after their first vaccine dose (odds ratio [OR] 1.93, 95% CI 1.50–2.48; p<0·0001), and individuals living in highly deprived areas had increased odds of post-vaccination infection following their first vaccine dose (OR 1·11, 95% CI 1·01–1·23; p=0·039). Individuals without obesity (BMI <30 kg/m^2) had lower odds of infection following their first vaccine dose (OR 0.84, 95% CI 0.75–0·94; p=0·0030).

For the disease profile analysis, 3,825 users from cases 1 were included in cases 3, and 906 users from cases 2 were included in cases 4. Vaccination (compared with no vaccination) was associated with reduced odds of hospitalization (OR 0.27, 95% CI 0.16 – 0.45; p = <0·001). and with having more than five symptoms in the first week of illness following the first or second dose (OR 0.69, 95% CI 0.51 – 0.94; p = <0·01), and long-duration (≥28 days) symptoms following the second dose (OR 0.51, 95% CI 0.32 – 0.82; p = <0·001). Almost all symptoms were reported less frequently in infected vaccinated individuals than in infected unvaccinated individuals, and vaccinated participants were more likely to be completely asymptomatic, especially if they were 60 years or older.

These findings might support caution around relaxing physical distancing and other personal protective measures in the post-vaccination era, particularly around frail older adults and individuals living in more deprived areas.

Source: Antonelli M, Penfold RS, Merino J. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. Lancet Infect Dis 2021; Published online 1 September. doi.org/10.1016/S1473-3099(21)00460-6.

Study on allergic reactions after administration of the Pfizer-BioNTech COVID-19 vaccine among adults with high allergy risk

On 31 August, a study was published analyzing the vaccination of patients at high risk for anaphylactic reactions with the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine. This was a prospective cohort study conducted from 27 December 2020 to 22 February 2021, which included 8,102 patients with a history of allergies who underwent a risk

assessment at a specialized referral center in Israel. High-risk patients considered "highly allergic" were identified (n = 429), and were immunized under medical supervision. Of the 429 people attended at the COVID-19 referral center and defined as highly allergic, 304 (70.9%) were women and the mean (SD) age was 52 (16) years. After the first dose of the BNT162b2 vaccine, 420 patients (97.9%) had no immediate allergic event, 6 (1.4%) developed minor allergic responses, and 3 (0.7%) had anaphylactic reactions. During the study period, 218 highly allergic patients (50.8%) received the second dose of the BNT162b2 vaccine; of these, 214 (98.2%) had no allergic reactions and 4 patients (1.8%) had minor allergic reactions. Other immediate and late reactions were comparable with those seen in the general population, except for delayed itch and skin eruption, which were more common among allergic patients.

The rate of allergic reactions to the BNT162b2 vaccine was higher among patients with allergies, particularly among a subgroup with a history of high-risk allergies. This study suggests that most patients with a history of allergic diseases and, particularly, highly allergic patients, can be safely immunized using an algorithm that can be implemented in different medical facilities and includes a referral center, a risk assessment questionnaire, and a setting for immunization under medical supervision of highly allergic patients. Further studies are required to define more specific risk factors for allergic reactions to the BNT162b2 vaccine.

Source: Shavit R, Maoz-Segal R, Iancovici-Kidon M, et al. Prevalence of Allergic Reactions After Pfizer-BioNTech COVID-19 Vaccination Among Adults With High Allergy Risk. JAMA Netw Open. 2021;4(8):e2122255.

doi:10.1001/jamanetworkopen.2021.22255. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783626

CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

The European Agency for Medicines and Medical Products updates information on the safety of COVID-19 vaccines

In line with the conclusions from the meeting of the Pharmacovigilance Risk Assessment Committee (PRAC) held from 31 August to 2 September 2021, the European Medicines Agency (EMA) updated safety information for the following vaccines, as summarized below:

- Pfizer-BioNTech Comirnaty Vaccine: The Pharmacovigilance Risk Assessment Committee (PRAC) evaluated safety data, including the latest report submitted by the manufacturer, and concluded that no updated product safety information was needed. In relation to the following events, PRAC indicated the following:
    - Myocarditis and pericarditis: These were added in July 2021 to the product information sections on side effects and warnings, and at present there are no updates.
    - Multisystem Inflammatory Syndrome (MIS) in children and adolescents coinciding chronologically with COVID-19 (MIS-C): PRAC is evaluating a possible relationship between this condition and administration of this vaccine, in light of the case, reported on 19 August 2021, of a 17-year-old in Denmark. To date, there are no safety updates related to this event.
- Janssen COVID-19 Vaccine: PRAC evaluated safety data, including the latest report submitted by the manufacturer, and noted the following:
    - Multisystem Inflammatory Syndrome (MIS) in children and adolescents coinciding chronologically with COVID-19 (MIS-C): No reports have been received for this vaccine.
    - Venous thromboembolism (VTE) (blood clots in the veins): This event is different from thrombosis with thrombocytopenia syndrome (TTS) (blood clots with low platelet levels). This was included, in Janssen's COVID-19 vaccine risk management plan, as a safety issue to be investigated, based on a higher proportion of VTE cases in the vaccinated group versus the placebo group in the clinical studies used to authorize this vaccine. PRAC will evaluate additional data from two large clinical trials currently in progress.
    - Lymphadenopathy (swollen lymph nodes): PRAC concluded that this should be added as a very low-frequency side effect (less than 1 in 1,000 people vaccinated) of the Janssen COVID-19 vaccine.
    - Paresthesia (unusual sensation in the skin, such as tingling) and hypoesthesia (decreased sensation or sensitivity, especially in the skin): These were added as side effects of the Janssen COVID-19 vaccine.

The frequency of paresthesia has been determined to be uncommon (less than 1 in 100 people vaccinated), and hypoesthesia as rare (less than 1 in 1,000 people vaccinated).

- Tinnitus (persistent ringing in the ear): This was added as a rare side effect of Janssen's rare COVID-19 vaccine (less than 1 in 1,000 vaccinated people). In addition, PRAC requested more information from the authorization holder, in order to better characterize the nature of the cases, symptoms, and duration.
- Diarrhea and vomiting: These were added as side effects of Janssen's COVID-19 vaccine; the frequency of diarrhea has been determined to be uncommon (less than 1 in 100 people vaccinated), with vomiting as rare (less than 1 in 1,000 people vaccinated).

- Moderna Spikevax COVID-19 Vaccine: PRAC evaluated safety data, including the latest report submitted by the manufacturer, and noted the following:
  - Myocarditis and pericarditis: These were added, in July 2021, to the product information sections on side effects and warnings, and at present there are no updates.
  - Multisystem Inflammatory Syndrome (MIS) in children and adolescents coinciding chronologically with COVID-19 (MIS-C): No reports have been received for this vaccine.
  - Anaphylaxis and other hypersensitivity reactions: This is a known side effect of the Spikevax COVID-19 vaccine, and is included in the product information, along with recommendations for the clinical management of anaphylaxis. There are no updates on this.
  - Delayed injection-site reactions: The information has been updated to include delayed injection-site reactions (rash, redness, or hives) as a common side effect (less than 1 in 10 people vaccinated). PRAC requested further information from the vaccine's authorization holder, in an effort to specify the characteristics of this side effect, including details such as time of onset, duration, and severity of the reaction.
  - Diarrhea: PRAC, continuing its May 2021 assessment, requested that the vaccine's authorization holder add diarrhea as a side effect of the vaccine, including information on frequency, based on data from the latest clinical trials.

- AstraZeneca Vaxzevria Vaccine: PRAC evaluated safety data, including the latest report submitted by the manufacturer, and noted the following:

- Guillain-Barré syndrome (GBS): PRAC, in consultation with experts in neurology, after evaluating the additional data requested from the vaccine's authorization holder and reviewing the scientific literature, concluded that there is at least a plausible possibility of a causal relationship between Vaxzevria and GBS, and determined that it should be added to the product information as a side effect of Vaxzevria, with the frequency of occurrence designated as "very rare" (less than 1 in 10,000 people vaccinated). In addition, PRAC recommended updating the warning included in the vaccine's package insert, so that patients can notify healthcare personnel if they contracted GBS after being vaccinated with the Vaxzevria vaccine, with the additional warning that people should seek immediate medical attention if they develop weakness and paralysis in the extremities, which can progress to the chest and face.

- Capillary leak syndrome (CLS): PRAC evaluated the available data and concluded that it was insufficient to definitively establish the mechanism involved. There is a continued warning remains in place that people with a previous diagnosis of CLS should not be vaccinated with Vaxzevria, and that people should seek immediate medical attention if they experience rapid swelling of the arms and legs, sudden weight gain, and feeling faint (low blood pressure) in the days following vaccination with the Vaxzevria vaccine.

- Thrombosis with thrombocytopenia syndrome (TTS): PRAC concluded that the product information should be updated, to remove the indication that cases occur primarily in women under the age of 60, since the most recent analysis indicates that 43% of TTS cases occurred in males, and 37% in vaccinated individuals over the age of 60, with no significant difference between men and women. The warning remains in place that people should seek immediate medical attention if they experience severe or persistent headache, blurred vision, confusion, seizure, shortness of breath, chest pain, swelling of the legs, persistent pain in the legs, abdominal pain, unusual bruising of the skin, or round dots outside of the vaccination site, within three weeks following vaccination.

- Cerebral venous sinus thrombosis (CVST) without thrombocytopenia: PRAC has asked the vaccine's authorization holder for more information on cases of CVST, so that it can conduct the necessary evaluation. CVST is a rare form of stroke, involving the formation of a blood clot in the bran's venous sinuses without thrombocytopenia (low levels of platelets in the blood), reported after vaccination with the Vaxzevria vaccine.

- Multisystem Inflammatory Syndrome (MIS) in children and adolescents coinciding chronologically with COVID-19 (MIS-C): No reports have been received for this vaccine.

- Menstrual disorders: PRAC concluded that there is no evidence of a causal relationship between this condition and administration of the Vaxzevria vaccine.

Source: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/safety-covid-19-vaccines#latest-safety-information-section

Brazilian Ministry of Health issues technical note on booster doses of COVID-19 vaccines

Brazil's Ministry of Health, in its Technical Note No. 27/2021-SECOVID/GAB/SECOVID/MS, highlighted major achievements in the number of COVID-19 vaccinations and the impact this has had on reducing severe cases of disease, as well as deaths. However, it also reported an increase in morbidity and mortality in recent weeks among the most vulnerable groups, such as people over 70 years of age and individuals with a high level of immunosuppression, for whom the current two-dose or single-dose vaccination schedule may provide lower levels of protection.

In light of this situation, the Ministry of Health has decided to increase the immune response in these groups with booster doses, and is therefore planning that, as of 15 September, a booster dose will be given to:

Adults over 70 years of age, to be administered six months after receiving their final scheduled dose of vaccine (two-dose or single-dose schedule), regardless of the particular vaccine administered previously.

A booster dose for people with a high level of immunosuppression (severe primary immunodeficiency); people receiving cancer chemotherapy; solid-organ transplant or hematopoietic stem cell transplant recipients using immunosuppressant drugs; people with HIV/AIDS whose CD4 is <200 cells/mm3; people using corticosteroids, such as ≥20 mg/day of prednisone or the equivalent, for ≥14 days; individuals using immunomodulating drugs; patients on hemodialysis; and patients with chronic immune-mediated inflammatory diseases (rheumatic, auto-inflammatory, and inflammatory bowel diseases).

For immunosuppressed individuals, the interval for administering the booster dose is 28 days from the last administered basic-schedule dose.

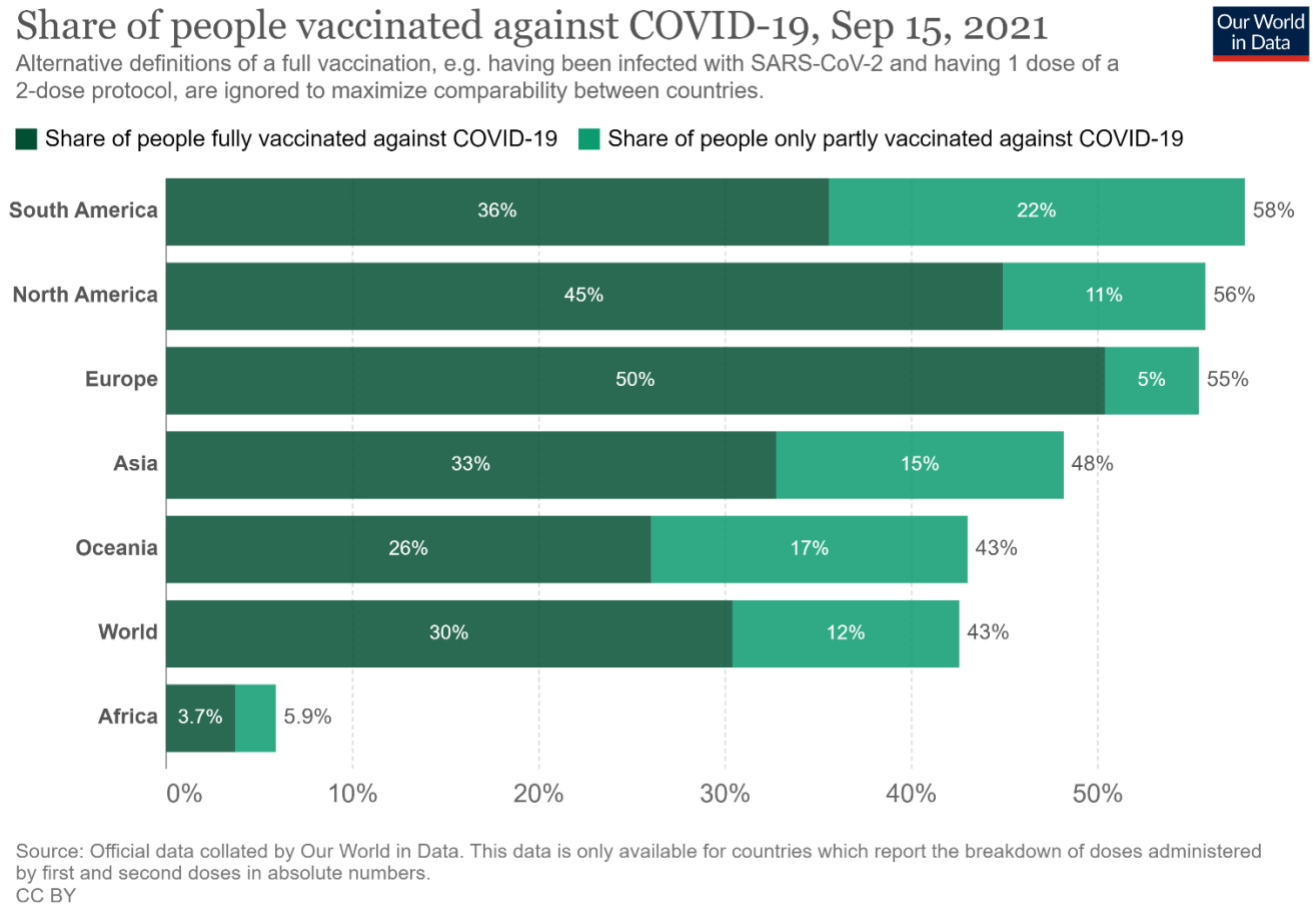
The vaccine used as a booster should preferably be an mRNA-platform vaccine (Pfizer-BioNTech); as an alternative, a viral vector vaccine (Janssen or AstraZeneca) could be administered.

As vaccinations progress, and as the epidemic in the country evolves and new evidence emerges, administering boosters to additional population groups could be considered.

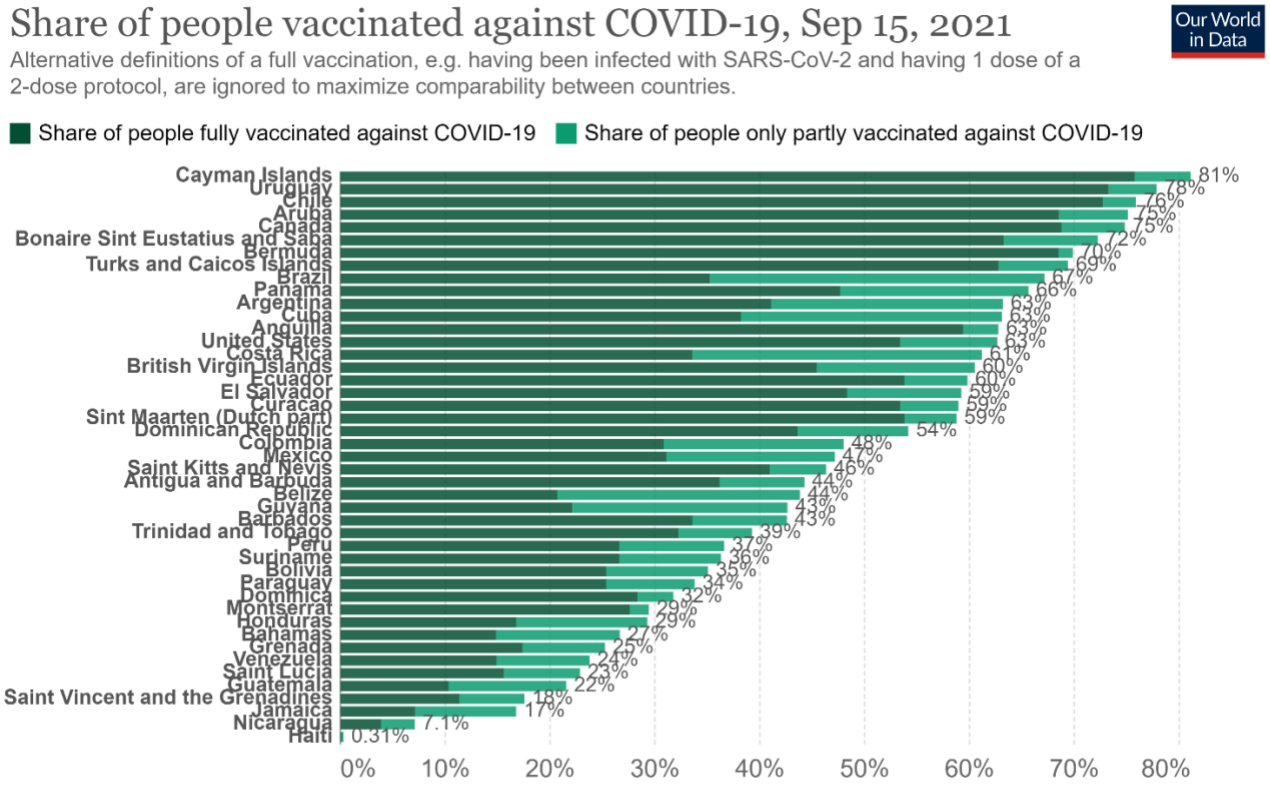
Source: https://www.gov.br/saude/pt-br/coronavirus/vacinas/NTDoseReforo.pdf

Use of COVID-19 vaccines worldwide and in the Region of the Americas as of 15 September 2021

Below are consolidated data on the percentage of people partially or completely vaccinated with COVID-19 vaccines in the different continents and in the countries of the Region of the Americas. As can be seen, there is a marked inequity in the administration of vaccines, both globally and within the Region of the Americas itself – a region notable for having the highest percentage of the population at least partially vaccinated.



Source: Our World in Data. https://ourworldindata.org/covid-vaccinations



Source: Our World in Data. https://ourworldindata.org/covid-vaccinations