COVID-19

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

WASHINGTON, DC
Update: 22 March 2021

ARGENTINA

- As of 15 March 2021, 1,181,292 doses of vaccine (951,722 of Sputnik V, 228,665 of Covishield, and 905 of Sinopharm) had been administered.
- A total of 23,642 adverse events following immunization (AEFI) were reported (2.0% of doses administered), of which 143 (0.60%) resulted in hospitalization for treatment of symptoms, with subsequent recovery.
- A total of 22,183 AEFI were linked to the Sputnik V vaccine (2.3% of Sputnik V doses administered) and 713 to the Covishield vaccine (0.3% of Covishield doses administered). The one report of an AEFI linked to the Sinopharm vaccine was due to a programmatic error.
- The most common events reported were: fever with headaches and/or myalgia, headaches with or without myalgia

Link: https://www.argentina.gob.ar/coronavirus/vacuna/equipos-salud/informes-seguridad

BRAZIL

- Vaccination against COVID-19 in Brazil began in the second half of January 2021, with the AstraZeneca/Fiocruz and Sinovac/Butantan vaccines. Between 18 January and 18 February 2021, 5,874,000 doses of vaccine were administered in the 27 federated units.
- In the same period, 20,612 suspected cases of ESAVI were reported, with 20,181 classified as non-serious and 430 as serious.
- 83% of the reported cases were among women. The age group most affected by non-serious ESAVI was between the ages of 30 and 39, while serious events most frequently occurred in the over-70 group, with the highest number of deaths occurring in the 80- to 84-year-old age group.
- The highest incidence of adverse events in terms of System Organ Classification (SOC) were: general disorders and clinical conditions at the injection site (3.32 per 1,000 doses administered), nervous system disorders (1.92 per 1,000 doses administered), and musculoskeletal disorders (1.58 per 1,000 doses administered).
- In the PT (MedDRA Preferred Terms) analysis, the highest incidence of events per 1,000 doses administered were headache (1.7), pain (1.4), myalgia (0.9), and pyrexia (fever) (0.8).
- Of the total serious adverse events reported, 139 reports (32.3%) involved deaths following COVID-19 vaccination, with 129 (92.8%) of these deaths among adults over 60 years old, most of whom resided in long-term care facilities for the elderly that include a highly vulnerable population with comorbidities.
- Of the 10 deaths in people under the age of 60, two were considered unclassifiable due to insufficient information, while eight were the result of diseases unconnected with the vaccine (six confirmed cases of

COVID-19, one due to acute myocardial infarction, and one, in an institutionalized individual with multiple comorbidities, due to pneumonia that predated the vaccination).

- With regard to deaths following vaccination (n=139), 70% (n=97) were attributable to pre-existing or emerging conditions caused by other factors, not by the vaccine, i.e. they were coincidental AEFI with no causal relationship to the vaccine, immunization errors, etc. The remaining 30% of cases (n=42) lack complete information, and are awaiting additional data for analysis.
- None of the deaths were considered causally related to COVID-19 vaccines. Of the deaths from other causes, 34 (35%) were diagnosed with COVID-19.
- With regard to deaths in the elderly population, the baseline mortality rate per 100,000 institutionalized older adults is between 325 and 916 deaths per month. As of 2/18/2021, 191,029 doses of COVID-19 vaccine had been administered to this population, and the observed death rate of approximately 72.7 per 100,000 doses administered was significantly lower than the expected baseline rate cited above.

Link: https://www.gov.br/saude/pt-br/media/pdf/2021/marco/15/boletim_epidemiologico_svs_9-1.pdf

CANADA

- As of 12 March 2021, 2,830,164 doses of Pfizer-BioNTech and Moderna COVID-19 vaccines had been administered.
- There were 2,209 individual reports of one or more adverse events (0.078% of doses administered). Of these, 287 were considered serious events (0.010 % of doses administered), with anaphylaxis being the most frequently reported.
- A total of 6,376 AEFI were reported (2,209 with one or more adverse events), most of which involved non-serious adverse events such as injection-site reactions, paraesthesia, itching, hives, headache, hypoesthesia, and nausea. Only 0.8% of cases of anaphylaxis were reported (54 cases, representing 19.1 per one million doses administered).
- Most adverse events reported were among women, and in people between the ages of 18 and 49, these being the groups prioritized for vaccination.
- A total of 22 reported adverse events involved post-vaccination deaths. Following a medical review, it was determined that 12 of these deaths were not linked to administration of the COVID-19 vaccine, while the other 10 are still under investigation.

Link: https://health-infobase.canada.ca/covid-19/vaccine-safety/

CHILE

- Between 24 December 2020 and 4 March 2021, 3,671,086 doses of vaccine were administered – 3,378,552 doses of the CoronaVac vaccine and 292,534 doses of the Pfizer-BioNTech vaccine.

- The National Pharmacovigilance Center received 4,677 AEFI reports (0.13% of doses administered), of which 2,553 were reported to the Pfizer-BioNTech vaccine and 1,911 to the CoronaVac vaccine, while 213 did not specify the vaccine.
- Of the total AEFI, 124 were serious (2.65%) and were mostly among women (92 cases; 74%), and in people over 65 years of age (79 cases; 64%).
- Reports of serious AEFI included 495 clinical manifestations -- construed to mean signs or symptoms -- among which anaphylaxis was the most common (62 clinical manifestations). The cumulative reporting rate for this event was 1.69 cases per 100,000 doses administered, and reports continue to be monitored.
- Of the reports of fatal outcomes analyzed (10 cases), nine had no causal association with the vaccine administered, while one case is awaiting further information for analysis.

Link: https://www.ispch.cl/wp-content/uploads/2021/03/20210319-Tercer-Informe-Estadistico-ESAVI-serias-VF-jrs-1.pdf

COSTA RICA

- As of March 15, 2021, the Directorate of Epidemiological Surveillance of the Costa Rican Social Security Fund reported 248,082 people vaccinated against COVID-19 with the Pfizer-BioNTech vaccine.
- From 24 December 2020 to 14 March 2021, 2,146 AEFI were reported, with the highest number of reports (459) occurring in the week from 8 to 14 February. Of the total reports, 2,093 AEFI have been analyzed.
- In the week of 7 to 12 March, 248 AEFI were analyzed, of which 72% were among women, and 36% in people between 30 to 39 years of age.
- All of the AEFI analyzed were classified as non-serious, with 96% of events categorized as mild. Of these, 20% of reported events were due to headache, 17% to pain at the injection site, 11% fever, 5% fatigue, 5% myalgia, 4% body pain, 3% diarrhea, 3% chills, 2% rash, 2% nausea, and 2% itching.
- For this period, there was no report of any case of anaphylactic reaction; however, the CNFV is remaining alert for any cases of this type of AEFI.

Source: Report of adverse events following immunization (AEFI) with the COVID-19 Pfizer-BioNtech vaccine, from 7 March to 14 March 2021. Directorate for Regulation of Health-related Products. National Pharmacovigilance Center (CNFV). Ministry of Health of Costa Rica.

MEXICO

- As of 21 March 2021, 5,612,291 doses of the Pfizer-BioNTech, AstraZeneca, Sinovac, and Sputnik V vaccines had been administered.
- As of that date, 12,308 cases of AEFI were reported (0.22% of doses administered), of which 11,696 were to the Pfizer-BioNTech vaccine, 419 to the AstraZeneca vaccine, 98 to the Sinovac vaccine, and 93 to the Sputnik V vaccine.

- Of these, 97 were for serious events, representing 0.79% of total events reported. Among serious events, 73 were reported to the Pfizer-BioNTech vaccine, 11 to the AstraZeneca vaccine, 10 to the Sinovac vaccine, and 3 to the Sputnik V vaccine.

Link: https://www.gob.mx/salud/acciones-y-programas/versiones-estenograficas-conferencia-de-prensa

UNITED KINGDOM

- As of 7 March 2021, in the United Kingdom, an estimated 10.7 million first doses of Pfizer/BioNTech vaccine had been administered; 11.7 million doses of the Oxford University/AstraZeneca vaccine; and approximately one million second doses, mostly of the Pfizer-BioNTech vaccine.
- As of that date, 35,325 Yellow Cards had been reported for the Pfizer/BioNTech vaccine, 61,304 for the Oxford University/AstraZeneca vaccine, and 251 that did not specify the vaccine. In both cases the reporting rate was about three to six cards per 1,000 doses administered. To be clear, Yellow Card data cannot be used to draw conclusions regarding adverse event rates or to compare the safety profile of vaccines, as more information is required.
- For both vaccines, the vast majority of reports were related to injection site reactions (arm pain) or general symptoms such as headaches, chills, fatigue, nausea, fever, weakness, muscle pain, tachycardia, or flu-like sensations. These events usually occurred shortly after vaccination, and were not associated with more serious or longer-lasting events.
- Reactions of this type are the body's normal response to vaccines. These reactions are seen with many other vaccines, and resolve within a day or two.
- Regarding anaphylactic reactions (severe allergic reactions), the Medicines and Healthcare Products Regulatory Agency (MHRA) has received 223 spontaneous reports of adverse events associated with anaphylaxis or anaphylactic reactions to the Pfizer/BioNTech vaccine. The nature and frequency of these reports are consistent with previous reports, and it can be concluded that severe allergic reactions to this vaccine are very rare. MHRA's recommendation continues to be that people with a previous history of allergic reaction to vaccine ingredients should not be vaccinated.
- For the AstraZeneca vaccine, 234 spontaneous reports of adverse events associated with anaphylaxis or anaphylactic reactions were reported. Although these events are very rare, a product-information update has been made, reflecting the fact that cases of anaphylaxis have been reported for the vaccine.
- Regarding Bell's Palsy (facial paralysis), MHRA continues to review reports of facial paralysis and compare them to cases that would occur randomly in the non-vaccinated population (natural rate). To date, the number of cases reported is similar to the natural rate, and there is no indication that it will increase with vaccination. These events continue to be monitored.

Link: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions

NEW STUDIES AND DEVELOPMENTS

New vaccines development

The emergence of variants with the ability to evade the immune system is driving a search for new development strategies and expanding the range of viral epitopes, which the new vaccines are designed to address. The first generation of vaccines targeted the virus's S protein, generating antibodies and T cells that recognize the receptor-binding domain (RBD), to prevent the virus from entering host epithelial cells.

Some of the new approaches to the development of COVID-19 vaccines are now undergoing clinical evaluation. For example, the RBD SARS-CoV-2 HBsAg VLP vaccine, which is in phase 1 and 2 clinical trials, is composed of protein subunits, virus-like particles (VLP), which are composed of the receptor binding domain (RBD) of the SARS-CoV-2 S protein, conjugated with hepatitis B surface antigen, obtained by recombinant DNA technology (rDNA).
Additional information on clinical trials of this vaccine is available at:
https://anzctr.org.au/Trial/Registration/TrialReview.aspx?id=380145&isReview=true

Another vaccine under development, based on VLP technology, called GBP-510, consists of computer-designed protein nanoparticles obtained using rDNA technology. The size of the nanoparticles seems to favor immune transit to the lymph nodes. This vaccine is in phase 1 and 2 clinical trials.
Additional information about the clinical trial is available at: https://clinicaltrials.gov/ct2/show/record/NCT04750343

For multivalent vaccines, the California Institute of Technology, in the United States, has reported promising immunogenicity data with an experimental multivalent vaccine using protein nanoparticles from different S protein receptors (RBD) from various human and animal coronaviruses. This vaccine appears to cause cross-reactive immune responses in mice, providing protection against strains that were not included in the experimental vaccine. In addition, protection against the B.1.351 lineage strain is being evaluated, with protection studies to be conducted in non-human primates

Source: Sheridan C. Innovators target vaccines for variants and shortages in global South. Nature Biotechnology. 3/17/2021.

Vaccination and patients with long-term symptoms

There are a number of patients with COVID-19 who develop long-term symptoms after infection with SARS-CoV-2, for which the term "Long COVID" has begun to be used. The symptoms vary, but the most common are fatigue, shortness of breath, myalgia, and insomnia.

In addition to the question of whether to vaccinate people who have been infected with COVID-19, there is concern about whether it is advisable to vaccinate people suffering from "Long COVID" or whether this could make their situation worse. There are reports that state that, in some cases, vaccination would have achieved significant improvements and a decrease in these symptoms.

A study was conducted with 44 participants suffering from "Long COVID," 82% of whom had symptoms that had persisted for as long as eight months. Half of the participants were vaccinated and were evaluated for a period of 32 days following vaccination, and were then compared with the control group. The study concluded that there was no negative effect on the symptoms and quality of life of participants who received the mRNA or adenoviral vaccine, and there had even been an improvement. Although the sample size was small, the results are of interest, and may indicate that people with "Long COVID" could be vaccinated.

Source: Arnold DT, Milne A, Samms E, Stadon L, Maskell NA, Hamilton FW. Are vaccines safe in patients with Long COVID? A prospective observational cohort study. MedRxiv 21253225. 3/11/2021.

Influenza-like illness after administration of COVID-19 vaccines

The Global Advisory Committee on Vaccine Safety (GACVS) of the World Health Organization (WHO) reviewed clinical trial data and a summary of reports of influenza-like illnesses following COVID-19 vaccination, drawn from the WHO Global Database of Individual Case Safety Reports (VigiBase). They report that symptoms of a flu-like illness can be expected, as generally occurs with the body's immune response to vaccines. Symptoms are usually mild to moderate, resolve within a few days, and may include headache, fatigue, muscle aches, fever, and chills.

These expected side effects of vaccination are more common in younger vaccine recipients (under age 55) than in older people.

In this respect, it is important to highlight the recommendation of GACVS regarding the possibility of short-term adverse events after vaccination, which should be taken into account when planning the appropriate timing for vaccinating health teams, and other workers who cover a specific type of service.

Source: GACVS COVID-19 Vaccine Safety subcommittee meeting to review reports on influenza-like illness in individuals vaccinated with COVID-19 vaccines (8 Mar 2021).

PROGRAMMATIC ERRORS, LOGISTICS, AND RELATED ISSUES

Recommendations for countries using the AstraZeneca vaccine

According to the latest recommendations of the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA), the following information is provided for the groups indicated:

Patients

- The AstraZeneca COVID-19 vaccine is not associated with an increased risk of blood clotting disorders.
- There have been very rare and unusual cases of blood clots, accompanied by low platelet levels, following vaccination. The reported cases have almost all been among women over the age of 55.
- Since COVID-19 can be extremely serious and is widespread, the benefits of vaccination to prevent COVID-19 outweigh the risk of adverse events.
- If you have any of the following symptoms after an AstraZeneca COVID-19 vaccination:
    - Shortness of breath
    - Chest or stomach pain
    - Swelling and cold in arms or legs
    - Severe headache or worsening of pain, or blurred vision after vaccination
    - Persistent bleeding
    - Multiple small bruises, reddish or purple spots, or blisters of blood under the skin, seek medical attention immediately and indicate that you were recently vaccinated.

Health Care Workers

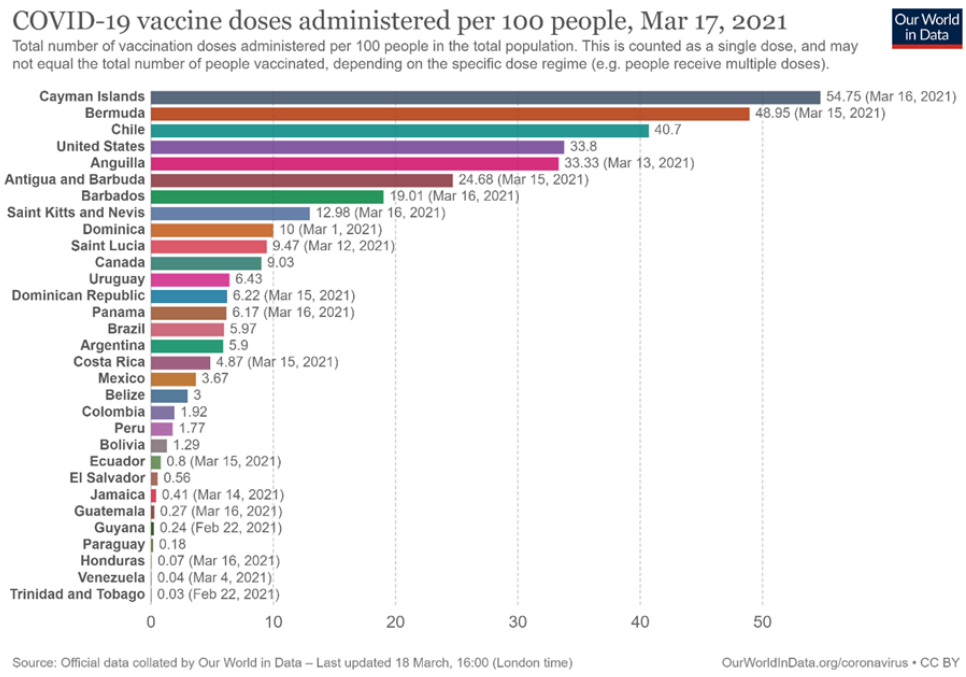
- Cases of thrombosis and thrombocytopenia, some presenting with mesenteric veins or cerebral vein/cerebral venous sinus thrombosis, have been reported in people who have received the AstraZeneca COVID-19 vaccine, most occurring within 14 days after vaccination. Most of the reports were among women under the age of 55. The higher exposure of this population group may be due to the fact that those individuals have been vaccinated at the highest rates, due to the countries' vaccination strategies.
- The number of reported events exceeds the number of expected events and expected causation, and although this cannot be confirmed, neither can it be excluded as a possibility. However, given the rarity of adverse events and the difficulty of establishing a baseline, since COVID-19 itself can result in hospitalizations with thromboembolic complications, the strength of the association is uncertain.

- The EMA believes that the benefit-risk balance of vaccination remains positive, and that there is no association, in general, with thromboembolic disorders.
- Health professionals are encouraged to be alert to possible cases of thromboembolism, DIC, or CVST occurring in vaccinated individuals.
- Vaccinated people should be advised to seek medical help if they have symptoms of thromboembolism, and, particularly, signs of thrombocytopenia or cerebral blood clots such as easily caused bleeding or bruising, and persistent headache, particularly after 3 days following vaccination.

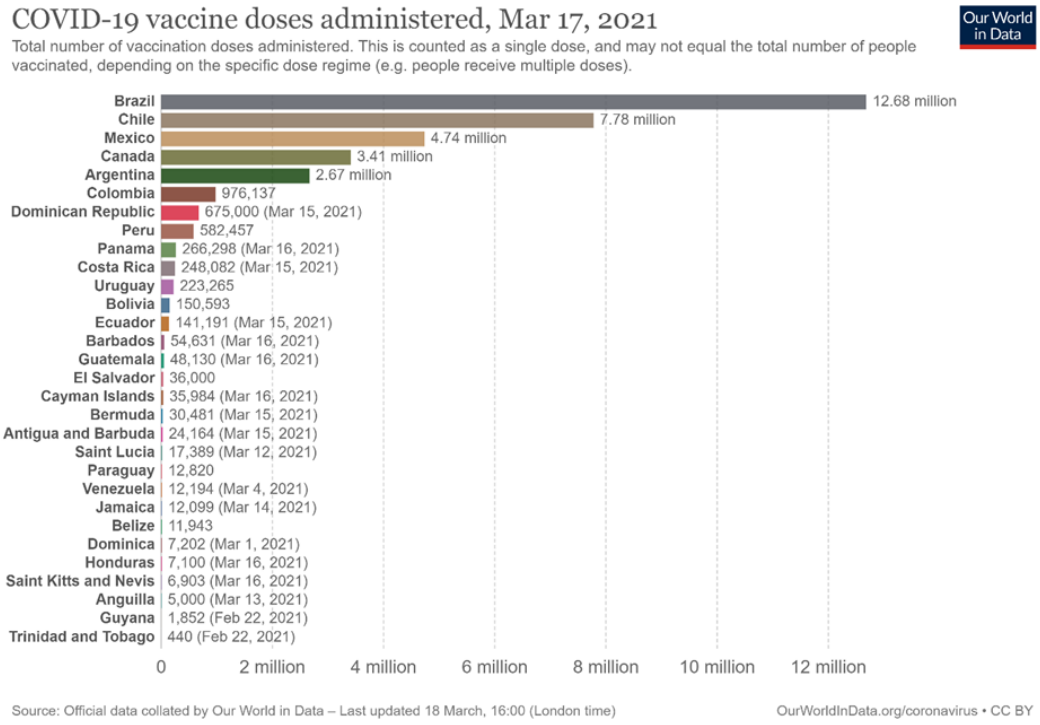
Link: https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-benefits-still-outweigh-risks-despite-possible-link-rare-blood-clots

Use of the COVID-19 vaccination in the Region of the Americas as of 17 March 2021

Below, there is consolidated data on doses administered per 100 people in the total population, by country and total doses administered, as of 17 March 2021. The figure is for single doses, and may not match the number of people vaccinated, depending on the specific dosing regimen (i.e. some people are receiving multiple doses).



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



The United States, with 113.04 million doses administered as of 17 March 2021, was excluded.

Source: Our World in Data.

Link: https://ourworldindata.org/covid-vaccinations

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