COVID-19

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

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OFFICIAL REPORTS ON PHARMACOVIGILANCE PROGRAMS

ARGENTINA

- As of 16 March 2021, 2,541,362 doses of Sputnik V, Covishield, and Sinopharm vaccines had been administered. A total of 26,721 adverse events following immunization (AEFI) were reported.
- More than 99% of AEFI were mild or moderate. Only 197 of these cases (0.73%) resulted in hospitalization.
- The most common adverse events were fever, headache, myalgia, and arthralgia.
- Two immune thrombocytopenia events were deemed to be related to the Sputnik V vaccine.
- Four deaths following administration of the Covishield vaccine, in patients with multiple comorbidities, were determined not to be linked to the vaccination, and were classified as coincidental.

Link: https://bancos.salud.gob.ar/recurso/10deg-informe-de-seguridad-en-vacunas

CANADA

- As of 26 March 2021, 4,800,931 doses of Pfizer-BioNTech, Moderna, and Covishield COVID-19 vaccines had been administered.
- There were 2,859 individual reports of one or more adverse events (0.060% of doses administered). Of these, 384 were considered serious (0.008% of doses administered), with anaphylaxis being the most frequently reported.
- A total of 8,409 AEFI were included in the 2,859 individual reports of one or more events. The most commonly reported events were reactions in the injection site, parestesia, itching, hives, headache, hypoesthesia, and nausea. Only 0.7% of cases of anaphylaxis were reported (60 cases, or 12.5 cases per million doses administered).
- Of adverse events reported, 82% were in women, and 50.9% were in people between the age of 18 and 49, both of these being groups prioritized for vaccination.
- A total of 26 reported cases of adverse events resulted in post-vaccination deaths. Following a medical review, it was determined that 14 of these deaths were not linked to administration of the COVID-19 vaccine. The other 12 are still under investigation.

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

FRANCE

- As of 18 March 2021, 8,163,000 doses of Comirnaty, Moderna, and Oxford-AstraZeneca COVID-19 vaccines had been administered. There were 17,104 reported cases of adverse events following immunization, of which 24% were serious and 76% non-serious.
- There were 10,963 reports of adverse events (22% serious and 78% non-serious) following administration of the Comirnaty vaccine (Pfizer-BioNTech), out of 6,282,000 doses administered since 27 December 2020. Of total adverse events reported, 74% were in women and 26% in men. Women accounted for 59% of the vaccinated population. Most of the adverse events associated with this vaccine are non-serious and are expected.
- A total of 458 adverse events (16% serious and 84% non-serious) following administration of the Moderna COVID-19 vaccine were reported, out of a total 441,000 doses administered between 19 January and 18 March 2021. Of total adverse events reported, 76% were in women and 24% in men. Women accounted for 55% of the vaccinated population. Most cases of adverse events associated with this vaccine involved non-serious delayed local reactions.
- There were 5,683 reports of adverse events (27% serious and 73% non-serious) following administration of the Oxford-AstraZeneca COVID-19 vaccine, out of a total 1,430,000 doses administered between 6 February and 18 March 2021. Of total adverse events reported, 76% were in women and 24% in men. Women accounted for 52% of the vaccinated population.
- Since the start of vaccination with the Oxford-AstraZeneca vaccine, 29 cases of thromboembolic events have been reported. Most of these have occurred within 15 days of vaccination, in patients with risk factors.
- Of the 29 thromboembolic events, nine cases of vein thrombosis were reported (mainly in cerebral and some intestinal veins) - which may be associated with thrombocytopenia or coagulation disorders – including two deaths –. These cases occurred within an average of 8.5 days after vaccination, in people for whom no specific history has been identified to date (seven patients were under age 55, while two were over age 55).
- The weekly monitoring committee of the National Agency for the Safety of Medicines and Health Products (ANSM) confirmed that people vaccinated with the Oxford-AstraZeneca vaccine were at risk of these very rare thrombotic events. The European Medicines Agency (EMA), which is continuing to investigate these events, confirms that the benefits of vaccination with the Oxford-AstraZeneca vaccine in preventing COVID-19 outweigh the risks.

Link: https://ansm.sante.fr/actualites/point-de-situation-sur-la-surveillance-des-vaccins-contre-la-covid-19-periode-du-12-03-2021-au-18-03-2021

MEXICO

- As of 7 April 2021, 10,089,420 doses of the Pfizer-BioNTech, Oxford-AstraZeneca, Sinovac, Sputnik V, and CanSino vaccines had been administered.
- To date, 14,218 cases of AEFI (0.14% of doses administered) have been reported, of which 12,911 were associated with the Pfizer-BioNTech vaccine, 545 with the Oxford-AstraZeneca vaccine, 530 with Sinovac, 189 with Sputnik V, and 37 with the CanSino vaccine.
- A total of 143 serious events have been reported, representing 1% of total events reported. Of these, 91 were associated with the Pfizer-BioNTech vaccine, 18 with the Oxford-AstraZeneca vaccine, 26 with Sinovac, 5 with Sputnik V, and 2 with the CanSino vaccine. Of these events, 85 were in women and 58 in men; 42 cases remain hospitalized.

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

UPDATE ON THE SAFETY OF AUTHORIZED VACCINES: EUROPEAN MEDICINES AGENCY (EMA)

- Comirnaty: On 25 March, the Pharmacovigilance Risk Assessment Committee (PRAC) evaluated the new vaccine safety data and identified swelling in the limbs, especially in the vaccinated arm, as a new adverse event for this vaccine. The event resolves within a couple of days after vaccination. With regard to the frequency of diarrhea and vomiting: diarrhea is very common (occurring in more than one in 10 people vaccinated), while vomiting is common (occurring in more than one in 100 people vaccinated).
- Vaxzevria (previously referred to as the Oxford-AstraZeneca COVID-19 vaccine): In EudraVigilance, PRAC evaluated 41 reported cases of anaphylaxis and other allergic reactions out of a total of nearly five million doses administered in the UK. The findings indicate that these events are now included as known adverse events.
- In regard to thrombotic events related to the Vaxzevria vaccine, on 7 April PRAC issued a new bulletin after evaluating 62 reported events of cerebral venous sinus thrombosis (CVST) and 24 of splenic vein thrombosis (SVT), based on spontaneous notification systems, out of a total of approximately 25 million people vaccinated with this product. To date, most reported cases had occurred in women under the age of 60 and occurred within two weeks of vaccination. Taking into account all of the evidence available at the time, PRAC decided that these very rare coagulation

events should be included in the information on Vaxzevria. As of 4 April, 169 cases of CVST and 53 cases of SVT had been reported in Europe, out of a total of 34 million vaccinations; however, PRAC confirms that the vaccine's overall benefit-risk ratio remains favorable.

- Information on the safety of Cominarty, Moderna, and Vaxzevria COVID-19 vaccines is consistent with the recognized benefit-risk ratio, i.e., the benefits outweigh the risks. No changes in the use of these vaccines have been recommended.

Link: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#safety-updates-for-authorised-covid-19-vaccines-section

Source: AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets. Available at: https://bit.ly/3gdtXLN

COVID-19 vaccination and children

Vaccinating children will have a significant impact on people returning to normal activities, since it will contribute to herd immunity.

To date, there are no published results from studies of currently available vaccines administered to children under the age of 17. However, several companies whose COVID-19 vaccines are being used in the countries of the Region are conducting clinical studies to assess the safety, immunogenicity, and effectiveness of their vaccines in children and adolescents.

- **AstraZeneca**: The company is proposing a Phase 2 study with 300 participants between the ages of 6 and 17; 240 participants will receive the vaccine and 60 will receive a meningococcal vaccine as a control.
- **Bharat Biotech**: This company is in the approval process for a Phase 3 study in children between the ages of 5 and 18.
- **Cansino:** The company indicates that Phase 2 clinical trials in a population of 6- to 18-year-olds have concluded.
- **Janssen**: Janssen plans to begin trials for 12- to 18-year-olds, followed by another trial for individuals from birth to 18 years of age. Safety, reactogenicity, and immunogenicity studies are in the planning stage.
- **Moderna:** The company is reporting Phase 2/3 studies for TeenCOVE, with approximately 3,000 children between ages 12 and 17 (100-microgram dose), and a Phase 2/3 study for KidCOVE, with 6,750 children between 6 months of age and 11 years, in which three different doses will be evaluated: 25 micrograms, 50 micrograms, and 100 micrograms.
- **Novavax**: EMA has approved a study plan for use of the vaccine in the pediatric population, consisting of three age groups: adolescents from ages 12 to 18, children ages 6 to 18, and individuals from birth to age 6.
- **Pfizer-BioNTech:** The company is planning a study, to begin in July 2020. Of 3,013 participants, 2,259 will be children between the ages of 12 and 15, while 754 will be 16- and 17-year-olds. In addition, the company will conduct a Phase 1/2/3 global study to assess safety, tolerability, and immunogenicity in three age groups: ages 5 to 11, ages 2 to 5, and 6 months to 2 years, for a total of 4,644 children, starting in March 2021. This study includes an evaluation of dosing.

- **Sinopharm**: The manufacturer has reported that its vaccine was shown to be safe according to clinical studies in three subgroups of children: ages 3 to 5, ages 5 to 12, and ages 12 to 17. This information should be evaluated by regulatory authorities.

- **Sinovac**: Studies have been conducted in approximately 500 children and adolescents, ages 3 to 17, including an evaluation of two possible doses—medium and low. Two children who received the lower dose were reported to have experienced high fever.

The hope is that the results of these studies will show that there are vaccines that are safe and effective in children and can be used to vaccinate the young population, once regulatory authorities authorize their use for this purpose. At the same time, the importance of maintaining high levels of vaccination coverage for all other childhood vaccines should be emphasized.

Sources:

Mahase E. Covid vaccine could be rolled out to children by autumn. BMJ 2021; 372:n723 doi:10.1136/bmj.n723.

Couzin-Frankel, J. Vaccine trials ramp up in children and adolescents. SCIENCE 26 FEB 2021: 874-875.

Pfizer-BioNTech announces positive results for study on COVID-19 vaccine in adolescents

The clinical trial included 2,260 adolescents ages 12 to 15 in the United States. In the placebo group, there were 18 cases of COVID-19 (n = 1,129), compared with no cases in the vaccinated group (n = 1,131). Vaccination with BNT162b2 demonstrated strong immunogenicity with high neutralizing antibody titers one month after the second dose. The geometric mean titer (GMT) of antibodies in this group was no lower than the GMT of participants ages 16 to 25 from an earlier study. There are plans to submit these results to the Regulatory Authorities (FDA, EMA, etc.) to seek an amendment to the Emergency Use Authorization, expanding use of the vaccine to adolescents ages 12 to 15 as soon as possible. Monitoring of participants will continue for an additional two years after the second dose.

Source: Pfizer-BioNTech announce positive topline results of pivotal COVID-19 vaccine study in adolescents. Pfizer website news. 3/31/2021

LOGISTICS AND RELATED ISSUES

Evaluation of the effectiveness of the COVID-19 vaccine

On 17 March 2021, the World Health Organization (WHO) published interim guidance on the Evaluation of COVID-19 vaccine effectiveness, available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-measurement-2021.1

The document presents different aspects to consider in developing and evaluating COVID-19 vaccine-effectiveness studies. It includes examples of vaccine-effectiveness protocols, sample size, and possible case definitions and inclusion/exclusion criteria. In addition, there is an Excel file to calculate the sample size for evaluation of COVID-19 vaccine effectiveness, available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-measurement_tool-2021.1

Protection against possible falsification of COVID-19 vaccines

In order to have an adequate system for tracking COVID-19 vaccines and detecting falsifications in a timely manner, it is important to consider the following:

- ✓ Ensure traceability of the vaccine, from the manufacturer to the locations where immunizations are being administered.
- ✓ Remember that all vaccine vials should be tracked, taking account of opened, unopened, and used vials.
- ✓ Have software that allows for information on the COVID-19 vaccines to be centralized, with registration of the corresponding barcode containing the manufacturer's information, lot number, and expiration date.
- ✓ If such software is not available, the existing registration systems should be used to collect the required information on the vaccines received, including lot numbers.
- ✓ Use the vaccine's QR code, which can be read with available cell phone apps, to verify that the vaccine is not a falsification.
- ✓ In terms of detecting falsified products or products of substandard quality, suspicious vials should be quarantined under appropriate conditions, but with a clear marking identifying them as "quarantined". They should be separated from other products in the cold chain to prevent shipping or inadvertent use, until a final determination is made.

- ✓ The national drug regulatory authority should be informed, so that investigations and corresponding actions can be taken in the event that product recalls, alerts, or rapid notifications are required.
- ✓ In the case of falsified products, there should be an official decision on their destruction and final disposal.
- ✓ It is important to remind health professionals and the general population that vaccines, like other medical products, must be obtained from authorized and reliable providers, and that the authenticity and physical condition of the products received must be carefully checked.
- ✓ Relevant health authorities are requested to immediately notify the national focal point (NFP) and the WHO Global Surveillance and Monitoring System if they discover falsified products in their country, through rapidalert@who.int.

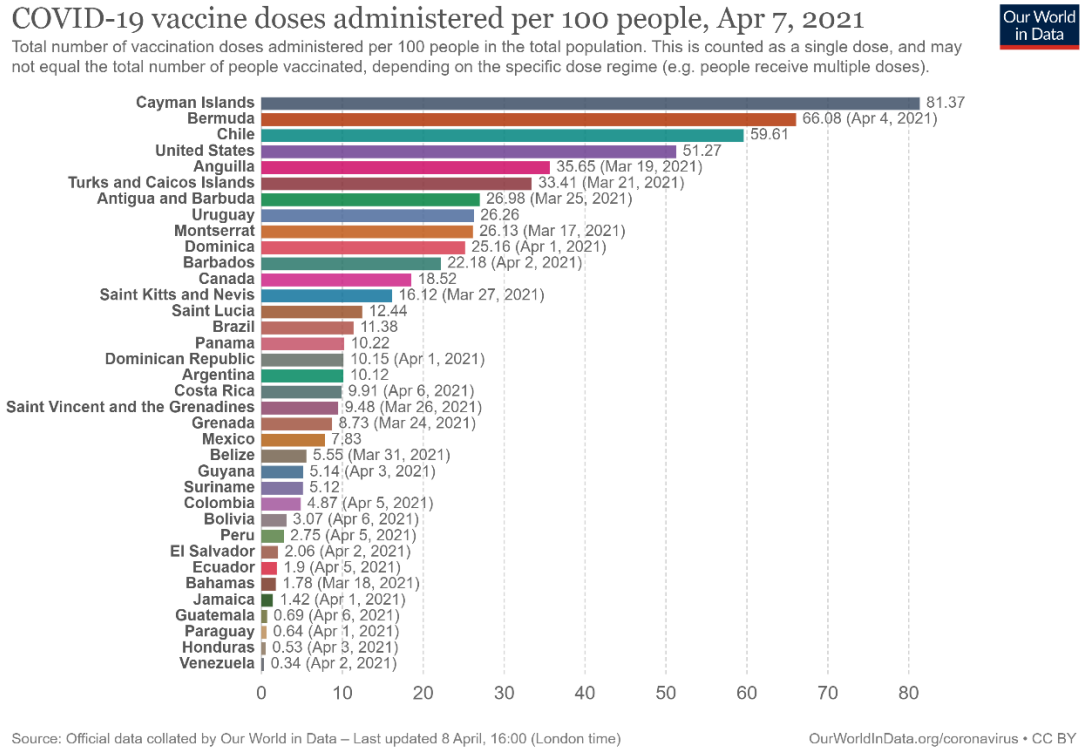
Sources:

WHO. Substandard and falsified medical products. Available at: https://www.who.int/health-topics/substandard-and-falsified-medical-products#tab=tab_1

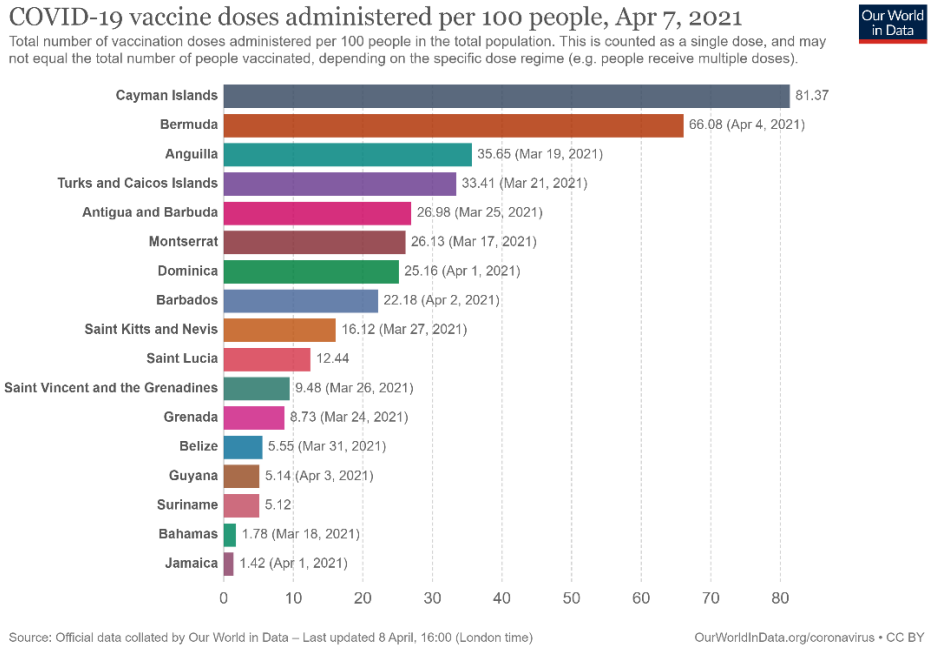
WHO. COVID-19 vaccination: supply and logistics guidance, interim guidance, 12 February 2021. Available at: https://apps.who.int/iris/handle/10665/339561

Use of the COVID-19 vaccine in the Region of the Americas as of 7 April 2021

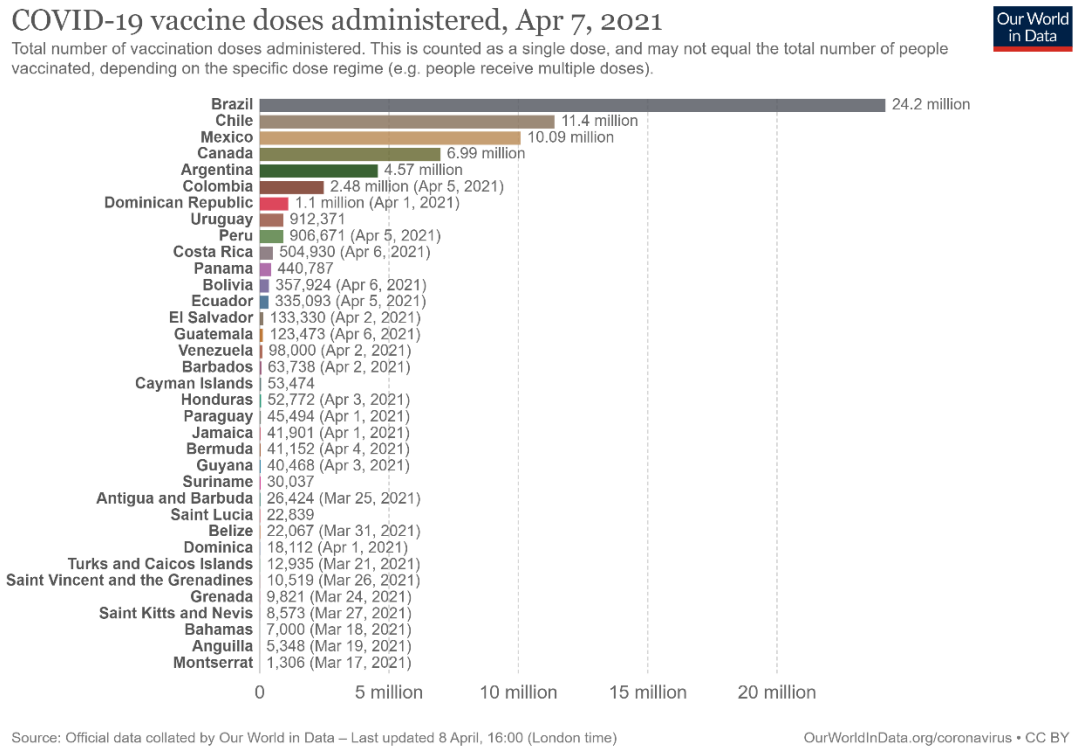
The following are consolidated data on doses administered per 100 people in the overall population, by country and total doses administered, as of 7 April 2021. The count corresponds to single doses and may not be the same as the number of people vaccinated, depending on the specific dosing regimen (i.e., some people receive multiple doses). The United States, with 171.48 million doses administered as of 7 April 7 2021, was excluded.



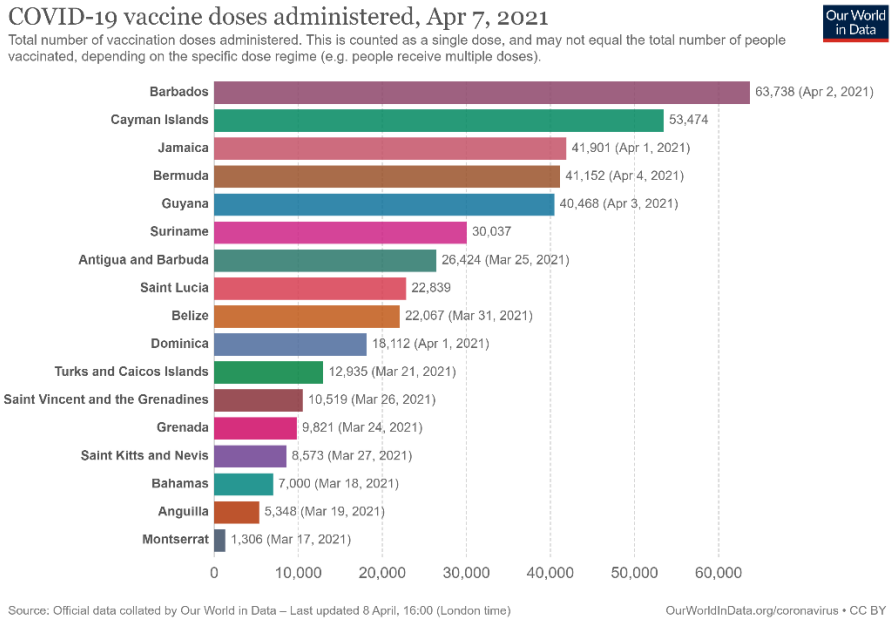
Source: Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations



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