COVID-19

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

Number 12

WASHINGTON, DC
Update: 5 May 2021

CANADA

- As of 23 April 2021, 11,526,938 doses of COVID-19 vaccines of Pfizer-BioNTech, Moderna, AstraZeneca, and Covishield (AstraZeneca manufactured by the Serum Institute of India) had been administered.
- A total of 4,128 individual reports of one or more adverse events (0.036% of doses administered) were received. Of these, 617 were considered serious events (0.005% of doses administered), with anaphylaxis being the most frequently reported.
- Of total reports, 1,928 non-serious events and 445 serious events were associated with the Pfizer-BioNTech vaccine. For the Moderna vaccine, 1,385 non-serious and 87 serious events were reported; for Covishield, 167 non-serious events and 46 serious events; and for AstraZeneca, 29 non-serious events and 32 serious events.
- A total of 12,140 adverse events following immunization (AEFI) were reported—equivalent to 0.1% of doses administered (4,128 with one or more events). The most frequently reported adverse events were injection-site reactions, parestesia, itching, hives, headache, hypoesthesia, and nausea. There were 60 reported cases of anaphylaxis.
- As of 23 April, there were six reports of thrombosis with thrombocytopenia syndrome following vaccination with Covishield/AstraZeneca.
- Most of the adverse events were reported in women (85%) and in people between the ages of 18 and 49 (47%), which are the groups prioritized for vaccination.
- A total of 40 reported adverse events resulted in deaths. Following medical review, it was determined that 21 of these deaths were not linked to administration of the COVID-19 vaccine. The other 19 cases are still under investigation.
- On 5 May, Health Canada authorized the use of the Pfizer-BioNTech vaccine in children between the ages of 12 and 15.

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

https://bit.ly/3uOsPmt

COSTA RICA

- As of 20 April 2021, the Epidemiological Sub-Surveillance Directorate, of the Costa Rican Social Security Fund, recorded a total of 698,327 people vaccinated against COVID-19 with the Pfizer-BioNTech vaccine.
- From 24 December 2020 to 18 April 2021, 3,164 AEFI were reported.
- From 11 April to 16 April, 216 AEFI were analyzed, of which 76% were in women and 35% were in people between the ages of 30 and 39. All of the AEFI analyzed during this period were classified as non-serious, with 95% of events categorized as mild, and the remaining 5% as moderate. Of the total, 23% of reported events involved pain at the vaccination site, 10% involved fever, and 10% headache.

Source: Reports of adverse events following immunization (AEFI) associated with the Pfizer-BioNTech COVID-19 vaccine between 11 April and 16 April 2021. Directorate for the Regulation of Healthcare Products of Interest. National Pharmacovigilance Center. Costa Rica Ministry of Health.

UNITED STATES

- Nearly 245 million doses of vaccines were administered between 14 December 2020 and 3 May 2021.
- The Vaccine Adverse Event Reporting System (VAERS) received 4,178 (0.0017%) reports of deaths among vaccinated individuals; tests failed to reveal a link between the deaths and vaccination.
- Anaphylaxis following vaccination against COVID-19 remains very rare, with approximately two to five cases per million people vaccinated in the United States. When this occurs, it is around 30 minutes after vaccination, and is immediately and effectively treatable.
- Johnson & Johnson's COVID-19 Janssen Vaccine: Since 23 April, the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) have recommended that the use of Johnson & Johnson's COVID-19 vaccine should be continued. However, women under the age of 50, in particular, should be informed that there is a very low risk of blood clots, accompanied by low platelet levels, after administration of this vaccine.

Source: https://cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html

FRANCE

- As of 22 April 2021, 18,749,000 doses of COVID-19 vaccines (Comirnaty, Moderna, and Vaxzevria) had been administered, with reports of 29,752 cases of AEFI (0.16% of doses administered), of which 25% were serious and 75% non-serious.
- Regarding the Comirnaty vaccine (Pfizer-BioNTech): 13,660,000 doses have been administered since the start of the vaccination program, with 16,030 reports of adverse events (25% serious and 75% non-serious). Of total adverse events, 73% were reported in women and 27% in men. Most of the adverse events associated with this vaccine were expected and were non-serious.
- To date, five cases of myocarditis have been identified after administration of the Comirnaty vaccine. However, based on the available data, there is no evidence to conclude that there is a causal link between the event and the vaccine. These effects do not call into question the benefit/risk ratio of the vaccine; however, they could constitute a possible vaccine safety signal and are continuing to be tracked.
- For The Moderna COVID-19 vaccine, with 1,483,000 doses administered as of 22 April, 1,283 adverse events (23% serious and 77% non-serious) had been reported. Of total adverse events reported, 75% were in women and 25% were in men. Most cases of adverse events with this vaccine involved delayed local non-serious reactions.
- Regarding the AstraZeneca COVID-19 vaccine: 3,605,000 doses have been administered, with 12,439 adverse events reported (25% serious and 75% non-serious). Of total adverse events reported, 71% were in women and 29% were in men.
- Most of these cases involved flu-like symptoms, often intense (such as high fever, body aches, and headaches). In France, use of this vaccine is restricted to people over 55 years of age.
- A new case of thrombosis of atypical location (total 28 cases, including 8 deaths), was analyzed.

Source: https://ansm.sante.fr/actualites/point-de-situation-sur-la-surveillance-des-vaccins-contre-la-covid-19-periode-du-16-04-2021-au-22-04-2021

MEXICO

- As of 30 April 2021, 17,718,806 doses of Pfizer-BioNTech, AstraZeneca, Sinovac, Sputnik V, and CanSino vaccines had been administered.

- A total of 17,027 cases of AEFI (0.1% of doses administered) had been reported as of that date, of which 14,183 were associated with the Pfizer-BioNTech vaccine, 1,591 with the AstraZeneca vaccine, 711 with Sinovac, 268 with Sputnik V, and 333 with the CanSino vaccine.
- A total of 280 serious events were reported, representing 1.6% of reported events. Of these serious events, 133 occurred with the Pfizer-BioNTech vaccine, 65 with the AstraZeneca vaccine, 51 with Sinovac, 9 with Sputnik V, and 20 with the CanSino vaccine. Among these, 156 occurred in women and 124 in men; 89 cases remain hospitalized.

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

UNITED KINGDOM

- As of 21 April 2021, an estimated 18 million doses of the Pfizer-BioNTech vaccine and 26.4 million doses of the Oxford-AstraZeneca vaccine had been administered in the United Kingdom. No information is available on the number of Moderna vaccine doses administered.
- As of the above date, there were 52,130 Yellow Card reports for the Pfizer-BioNTech vaccine, 153,098 for the Oxford-AstraZeneca vaccine, 228 for the Moderna vaccine, and 541 for which the vaccine was not specified. For the first two vaccines, the reporting rate was approximately three to six cards per 1,000 doses administered (0.3% to 0.6%). To be clear, Yellow Card data cannot be used to reach conclusions on adverse event rates, or to compare the safety profile of vaccines, since more information is required.
- For all of the vaccines, the vast majority of reports were related to injection-site reactions (arm pain) or to general symptoms such as headaches, chills, fatigue, nausea, fever, weakness, muscle pain, tachycardia, or flu-like symptoms. These events usually occur shortly after vaccination, and are not associated with more-serious or longer-lasting events.
- Regarding anaphylaxis (severe allergic reaction) events, the Medicines and Healthcare Products Regulatory Agency (MHRA) received 275 spontaneous reports for the Pfizer-BioNTech vaccine.
- For the AstraZeneca vaccine, 562 spontaneous reports of adverse events involving anaphylaxis or anaphylactic reactions have been reported. Although these events are very rare, a product information update has been issued, stating that cases of anaphylaxis have been reported for the vaccine.
- With regard to Bell's palsy (facial paralysis) events, the MHRA continues to review reports and compare these against the number of cases that would occur randomly in the unvaccinated population (baseline rate). The number of cases reported to date is similar to the baseline rate.

- In terms of thromboembolic events with thrombocytopenia, the MHRA received 209 Yellow Card reports following administration of the AstraZeneca vaccine (120 in women and 89 in men), with 41 deaths, a mortality rate of 19%.
- Of more than 20 million doses of the AstraZeneca vaccine administered, four cases of capillary filtration syndrome (a condition in which blood filters from small blood vessels to the body) have been reported. Current evidence does not suggest a causal link between this syndrome and the vaccine.

Source: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

Reports of recommendations from agencies in the Region of the Americas regarding some serious events following administration of COVID-19 vaccines

On 19 April 2021, the Chilean Institute of Public Health (ISP), through the National Medicines Agency, published recommendations on use of the AstraZeneca vaccine, following a review of the history presented by the European Medicines Agency (EMA) and other international regulatory authorities. They recommended, as a precautionary measure, that administration of the AstraZeneca vaccine be limited to women over 55 years of age and men 18 years of age and older.

The ISP indicated that, like the EMA, they believe that the benefit/risk balance of this vaccine remains positive, since the vaccine's benefit in preventing transmission and reducing the risk of hospitalization and death due to COVID-10 is greater than the risk of thrombosis with thrombocytopenia. In addition, they indicated that, in the case of Chile, there are no reports, to date, of thrombotic events with thrombocytopenia in the Phase three clinical studies of this vaccine.

Sources:

https://www.ispch.cl/noticia/el-isp-a-traves-de-su-agencia-nacional-de-medicamentos-entrega-recomendaciones-para-la-inoculacion-de-la-vacuna-de-astrazeneca-en-chile/

https://www.ispch.cl/wp-content/uploads/2021/04/20210419-INFORME-TECNICO-VACUNA-ASTRAZENECA-1.pdf

In the case of Argentina, the National Commission for Vaccine Safety (Conaseva) also issued recommendations regarding the diagnosis and management of COVID-19 thrombotic syndrome following vaccination, establishing that the definition of suspected cases of thrombotic phenomena and thrombocytopenia occurring between 3 and 28 days after vaccination should consider: (a) arterial or venous thrombosis based on clinical suspicion (intense or persistent headache of sudden onset that does not respond to painkillers, visual disturbances, severe abdominal pain, lower-limb pain or edema, dyspnea, or precordial pain), and imaging, depending on the location of the thrombus (CT angiography, MRI angiograph, Doppler ultrasound, VQ scan, etc.); and (b) thrombocytopenia, with platelet counts of less than 150,000/mm3, with peripheral blood smears that rule out other causes, and with no history of heparin use.

In the same report, Conaseva indicates that there is a concern about COVID-19 vaccination for people with a history of Guillain-Barre Syndrome (GBS), and therefore recommends, on an interim basis, that: (a) people with a history of non-vaccine-related GBS may receive the COVID-19 vaccine; (b) in people with a history of GBS related to vaccines in general, the benefit/risk of administering the COVID-19 vaccine should

be evaluated; and (c) in people with a history of GBS after receiving the COVID-19 vaccine, administration of a second dose of the COVID-19 vaccine is contraindicated.

Source: https://bancos.salud.gob.ar/recurso/informe-especial-comision-nacional-de-seguridad-en-vacunas-abril-2021

ANVISA authorizes FIOCRUZ to produce the active pharmaceutical ingredient (API) for the Oxford-AstraZeneca COVID-19 vaccine

On 30 April, the Brazilian National Health Surveillance Agency (ANVISA) approved the production of the active pharmaceutical ingredient (API) for the COVID-19 vaccine, as part of technology transfer agreements between AstraZeneca and the Institute of Technology in Immunobiologicals (Bio-Manguinhos), of the Oswaldo Cruz Foundation (Fiocruz).

Fiocruz will begin producing, on a commercial scale, pilot lots of COVID-19 vaccine based on ChAdOx1 chimpanzee adenovirus, which contains genes encoding the surface expression of the SARS-CoV-2 S protein. Following these tests, Fiocruz will be required to request the inclusion of the API produced in the current register, or request emergency use authorization. ANVISA previously conducted an inspection to verify that the production line was in compliance with good manufacturing practices.

This production, once authorized, will be provided to the Unified Health System (SUS).

Source: https://www.gov.br/pt-br/noticias/saude-e-vigilancia-sanitaria/2021/05/fiocruz-e-autorizada-a-produzir-o-insumo-da-vacina-astrazeneca

COVID-19 Variants of concern (VOC)

The World Health Organization (WHO), in the document "Weekly epidemiological update on COVID-19 – 13 April 2021," describes important information on troubling variants of SARS-CoV-2 and their possible impact on vaccination. The following table is an adaptation of the summary presented in the above-mentioned report.

SARS-CoV-2 Variants of concern*			
PANGO Lineage	B.1.1.7	B.1.351	P.1
Country of initial detection and date of samples	United Kingdom September 2020	South Africa August 2020	Brazil and Japan December 2020
Major mutations in the S protein	D614G / N501Y	D614G / N501Y / E484K / K417N	D614G / N501Y / E484K / K417T
Common mutation	S106/G107/F108 Deletion of non-structural protein 6 (NSP6)		
Transmissibility	Increased (43%-90%); increase in secondary attack rate, 11% (95% CI: 10.9-11.2%) among the closest contacts	Increased, 1.5 times (95% CI: 1.2-2.13) more transmissible than the previous circulating variant	Increased, more transmissible than the previous circulating variant
Severity	Possible increase in risk of hospitalization, severity, and mortality. Other studies show limited impact/mixed findings	Possible increase in the risk of inpatient mortality (20%)	Under investigation, limited impact
Risk of reinfection	Slight reduction in neutralization capacity, but levels remain above the level estimated to be protective	Reduced neutralization capacity, suggesting a potential increased risk of reinfection	Reduced neutralization capacity, reinfections reported
Potential impact on vaccines	Post-vaccination neutralization: - Zero or minimal impact for Moderna, Pfizer-BioNTech, Oxford-AstraZeneca, Novavax, Bharat, Gamaleya, and Sinopharm -There is some evidence of a more substantial loss for AstraZeneca. - In individual studies, no significant reduction in neutralization was reported for the Bharat, Gamaleya, Sinopharm, and Sinovac vaccines. Disease prevention: -No significant change for Oxford-AstraZeneca, Novavax, and Pfizer Prevention of infections: Limited evidence. Reduced effect reported for Oxford-AstraZeneca	Post-vaccination neutralization: -Several studies indicate reductions ranging from minimal to substantial with the Moderna and Pfizer vaccines Substantial reductions have been found with the Oxford-AstraZeneca vaccine -Minimal to modest reductions have been found for Sinopharm - A single study found a modest reduction for Sinovac -Single studies found a more substantial reduction for Novavax and Gamaleya Disease prevention: - In South Africa, efficacy against the disease remained, but was somewhat lower for the Novavax and Janssen vaccines when 501Y. V2 was dominant, compared to environments where this variant was not present - In a small study, the AstraZeneca vaccine was not shown to be effective against mild to moderate COVID-19 disease, with wide confidence intervals, while efficacy against serious disease was not evaluated and remains undetermined - There continues to be a gap in information regarding the impact of the vaccine on asymptomatic infection for 501Y.V2	Post-vaccination neutralization: -Limited to moderate reduction for the Oxford-AstraZeneca, Moderna, and Pfizer vaccines; however, there is some evidence of a more substantial reduction - Preliminary suggestion of loss of neutralization after vaccination with Sinovac - Preliminary effectiveness of the Sinovac vaccine in Brazil was assessed in the context of P.1
Number of countries where it is present	132	82	52

* Name used by WHO to refer to the variants indicated in this publication.

Source: WHO, COVID-19 Weekly Epidemiological Update, 13 April 2021. Available at: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---13-april-2021

CLARIFICATIONS, CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

At the moment there are no additional updates to the most recent note on conclusive analyses of the AEFI presented.

New vaccine included in WHO's Emergency Use Listing (EUL)

Name	COVID-19 mRNA vaccine (modified nucleoside)
Commercial name	N/A
Date of WHO recommendation	30 April 2021
Platform/vaccine type	mRNA
EUL holder	Moderna Biotech
Manufacturers	Active ingredient: Lonza, Switzerland Finished product: Rovi Pharma Industrial Services, Spain
Pharmaceutical form	Suspension for injection
Presentation	10-dose vial
Diluent	N/A
Dose/route of administration	0.5 mL / intramuscular
Storage temperature/shelf life	-20° ± 5° C for seven months Within its seven-month lifespan, the vaccine can be stored for up to 30 days at a temperature of 2° C to 8 ° C.
Open vial/in use	It is recommended that open vials of this vaccine be discarded six hours after being opened, or at the end of the immunization session, whichever comes first.

Source: https://extranet.who.int/pqweb/vaccines/covid-19-mrna-vaccine-nucleoside-modified

International Nonproprietary Names of COVID-19 vaccines

International Nonproprietary Names (INN) apply to vaccines with well-defined active ingredients, such as mRNA, DNA, viral vectors, and recombinant proteins. Some mRNA-based COVID-19 vaccines already have designated INNs, including abdavomeran, ganulameran, tozinameran, and zorecimeran. In each case the descriptions can be found at: https://www.who.int/publications/m/item/inn-pl-124-covid

With regard to possible modifications to current COVID-19 vaccines, aimed at providing better protection against new SARS-CoV-2 virus variants of concern, WHO indicated that the designation of a new INN may be required, if the modifications lead to changes in the structure of the active ingredient. The report can be found in the document "International Nonproprietary Names for Variant COVID-19 Vaccine Active Substances." The INN of the variant active substance will be linked to the INN of the initial vaccine when it has an assigned INN, by adding a short, random, two- or three-letter syllable as a prefix to the original INN.

In the event of a change in the structure of the active substance, or for other reasons, such as improved antigen stability, it will be assigned a new, unique, alternative INN, not necessarily related to the previous INN, in cases where one already exists.

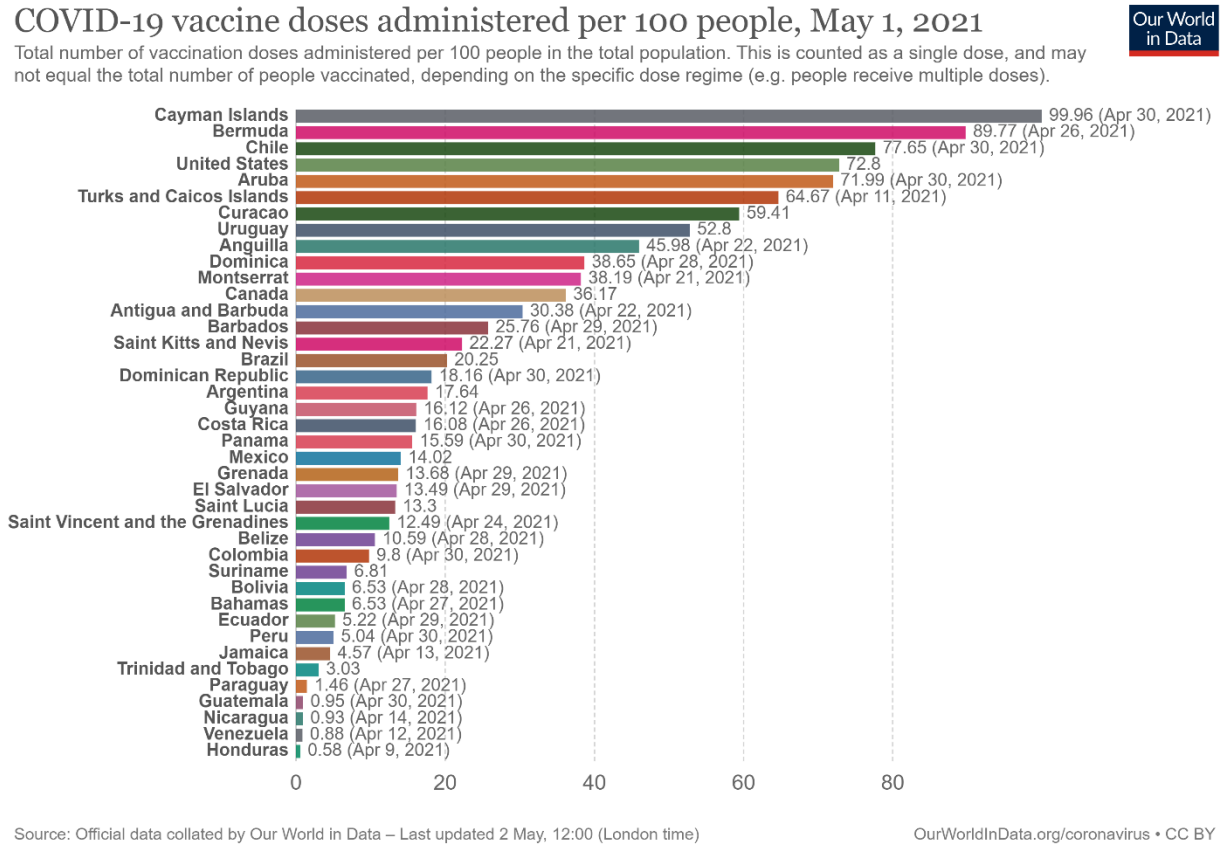
Sources:

https://cdn.who.int/media/docs/default-source/international-nonproprietary-names-(inn)/21-520_inn_for_vocs.pdf?sfvrsn-9b14f30_6&download-true

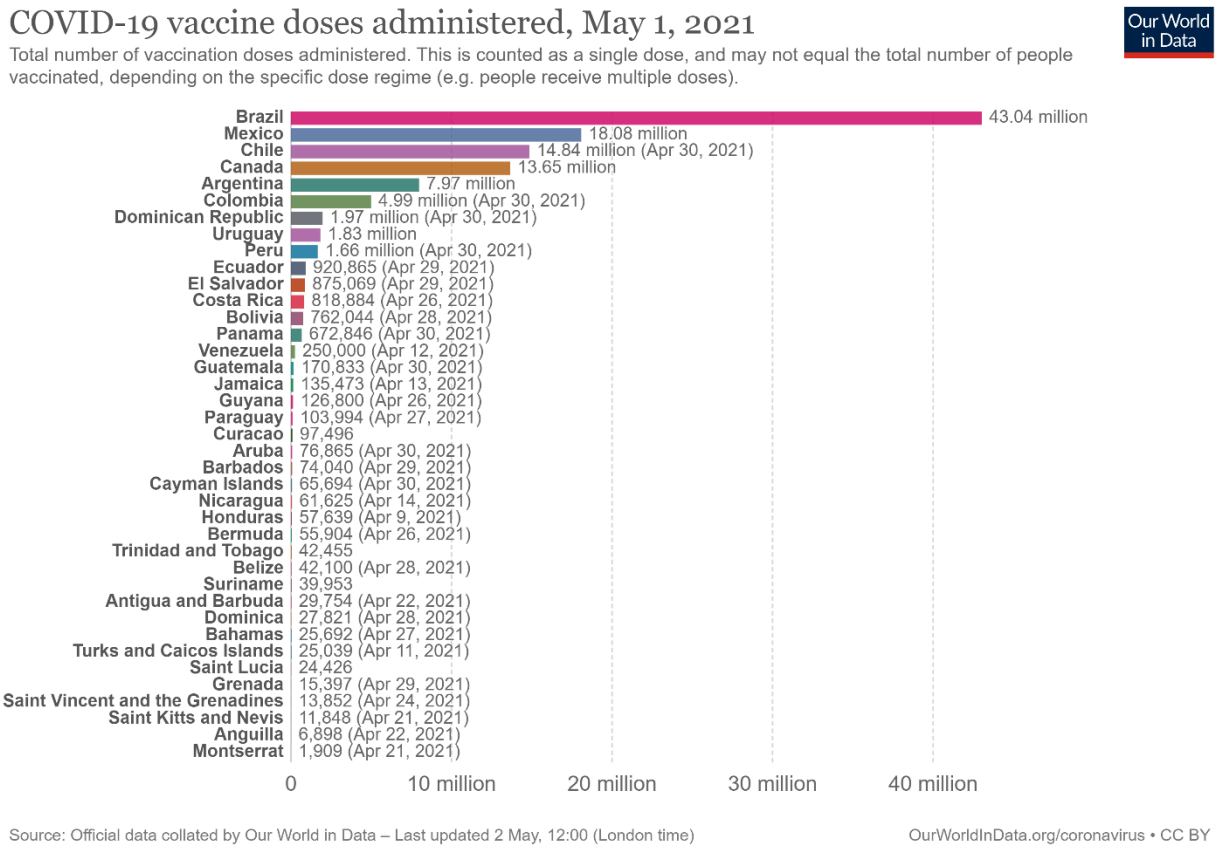
https://www.who.int/publications/m/item/inn-pl-124-covid

Use of the COVID-19 vaccine in the Region of the Americas as of 1 May 2021

Below are consolidated data on doses administered per 100 people in the overall population, by country, and total doses administered, as of 1 May 2021. To be clear, the count relates to single doses, and may not match the number of people vaccinated, depending on the specific dosing regimen (i.e. some people receive more than one dose). In the second graph, the United States, with 243.46 million doses administered as of 1 May 2021, was excluded.



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



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