IX Ad Hoc Meeting of the PAHO Technical Advisory Group (TAG) On Vaccine-Preventable Diseases

25 July 2022

Virtual

PAHO Pan American Health Organization World Health Organization Americas

IX Ad Hoc Meeting of the PAHO's Technical Advisory Group (TAG) On Vaccine-Preventable Diseases

25 July 2022

Virtual

Washington, D.C. 2022

IX Ad Hoc Meeting of the PAHO Technical Advisory Group (TAG) On Vaccine-Preventable Diseases, 25 July 2022 (Virtual)

PAHO/FPL/IM/COVID-19/22-0046

Contents

List of Tables

List of Figures

TAG Members

J. Peter Figueroa, *TAG Chair*
Professor of Public Health, Epidemiology & HIV/AIDS
University of the West Indies
Kingston, Jamaica

Jon K. Andrus
Adjunct Professor and Senior Investigator
Center for Global Health, Division of Vaccines, and Immunization
University of Colorado
Washington, D.C., United States of America

Pablo Bonvehi
Scientific Director
Fundación VACUNAR and CEMIC University Hospital
Buenos Aires, Argentina

Roger Glass*
Director
Fogarty International Center & Associate Director for International Research
NIH/JEFIC-National Institutes of Health
Bethesda, MD, United States of America

Arlene King
Adjunct Professor
Dalla Lana School of Public Health
University of Toronto
Ontario, Canada

Nancy Messonnier
Executive Director for Pandemic Prevention and Health Systems
Skoll Foundation
Palo Alto, CA, United States of America

José Ignacio Santos
Secretary
General Health Council
Government of Mexico
Mexico City, Mexico

Cristiana Toscano
Head of the Department of Collective Health

Institute of Tropical Pathology and Public Health,
Federal University of Goiás
Goiania, Brazil

Daniel Salas, *Ad hoc Secretary*
Unit Chief
Comprehensive Family Immunization
Pan American Health Organization
Washington, D.C., United States of America

*Not present at the meeting

Background

When the regional Technical Advisory Group (TAG) on Vaccine-Preventable Diseases last met on 31 May 2022, the focus was on the multi-country outbreak of monkeypox. At the time, 23 Member States across four WHO regions that were not endemic for monkeypox virus (MPXV) had reported at least one case. As of 7 July, 7,892 confirmed cases, including three deaths, have been reported from 63 Member States in five WHO regions. The three fatal cases were reported from Nigeria and the Central African Republic – both endemic countries.

In addition, the worldwide COVID-19 case count now stands at 565 million, of which 168 million (29.8%) were reported in the Americas. A growing proportion of cases are being caused by the Omicron BA.4 and BA.5 sub-lineages, and this is driving new infections across the Americas. Omicron BA.5 has been detected in at least 22 countries and territories and is likely to become predominant in all the subregions during the next weeks.

Finally, vaccination coverage rates for the Expanded Program on Immunization (EPI) continue to decline across the world. The 2021 WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) report that coverage with the third dose of the diphtheria, tetanus, and pertussis-containing vaccine (DTP3) in the Americas stands at 80%, down from 84% in 2019 and 94% in 2010. Coverage for all other EPI antigens continues to fall as well. More than 2.7 million children under the age of 1 year in the Americas – representing 19.7% of eligible children – did not receive all their vaccine doses, leaving them susceptible to diseases such as polio, tetanus, measles, and diphtheria. New evidence of these immunity gaps is emerging every day. In September 2022, the United States of America (USA) reported its first case of vaccine-derived poliovirus type 2 (VDPV2) since 2013. The measles outbreak in Brazil is entering its fourth year. Diphtheria is endemic in Haiti.

This confluence of epidemics, outbreaks, and declining vaccination rates is occurring while health services in all countries and territories have been deeply impacted by the pandemic and are still struggling with its effects. In July 2021, TAG stated that, “The Region is facing an impending crisis around routine vaccination.” One year later, the crisis is closer than ever. Member States must address multiple health emergencies at the same time, while entering the third year of socio-economic hardships.

Now more than ever, Member States must balance emergency vaccination operations with the urgent demands of the regular immunization program. Member States must prioritize response strategies in a context of finite financial and human resources and ensure the greatest benefit to the general public. The Pan American Health Organization (PAHO) must provide strong technical support to Member States as they rebuild their national immunization programs and essential care service systems, while building a wide-ranging coalition of global and regional organization, donors, and partners to close vaccination gaps and reclaim the Region’s primacy in immunization achievements.

Decreasing the Proportion of Children Susceptible to Poliovirus Type 2 (PV2) in the Americas

Question for the TAG

1. What can countries do to fill the immunity gaps against PV2?

Polio Epidemiological Update

In 2022, wild poliovirus type 1 (WPV1) remains endemic in only two countries: Afghanistan and Pakistan. As of 12 July 2022, 17 WPV1 cases have been reported in the previous 12 months (four in Afghanistan, 11 in Pakistan, one imported WPV1 case in Malawi, and one imported WPV1 case in Mozambique). In the same 12-month period, the World Health Organization (WHO) received notification of 12 circulating vaccine-derived poliovirus type 1 (cVDPV1) cases in Madagascar, 571 circulating vaccine-derived poliovirus type 2 (cVDPV2) cases in 18 countries, and one circulating vaccine-derived poliovirus type 3 (cVDPV3) case in Israel *(1)*. Additionally, by July 2022, a total of 124 cVDPV2 viruses have been isolated from different sources (44 from contacts and 80 from environmental surveillance) in 13 countries.

Background Information

The Global Polio Eradication Initiative (GPEI) proposed that all countries synchronously switch from using the trivalent oral poliovirus vaccine (tOPV) to the bivalent OPV (bOPV) in April 2016 *(2)*. Unlike tOPV, which contains all three poliovirus serotypes, bOPV contains only type 1 and 3. Therefore, to maintain immunity levels against poliovirus type 2 as well, the injectable polio vaccine (IPV) must be used in the schedule. In 2015, TAG recommended that all countries introduce at least one dose of IPV in their national vaccination schedule by the end of 2015. The goal was to minimize any immunity gap in poliovirus type 2 during the switch from tOPV to bOPV.

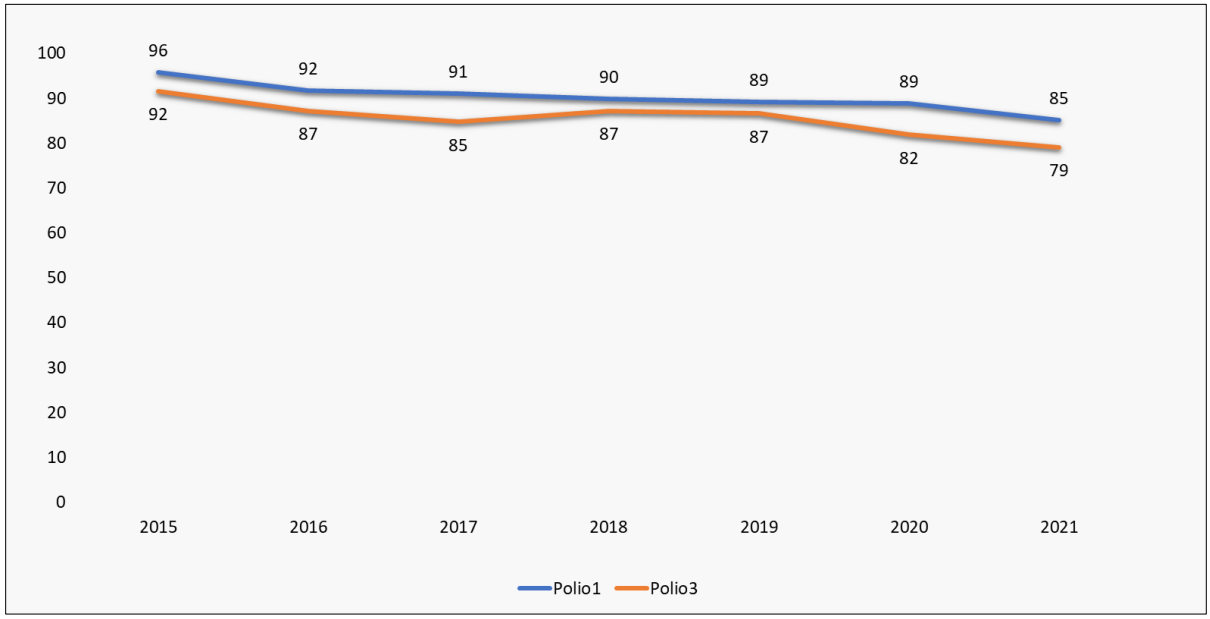
Even though this recommendation could not be implemented across the Region because of insufficient IPV supply, all countries introduced at least one dose of IPV in 2016. Also, the TAG recommended that all countries should be prepared to introduce a second dose of IPV as soon as supplies were sufficient *(3)*. As of May 2022, of 35 countries and 9 territories of the Americas, six have not introduced IPV2 (Haiti, Dominican Republic, Curaçao, Saint Kitts and Nevis, Saint Lucia, and Suriname). Also, ten countries (Belize, Bolivia, Dominica, Guatemala, Jamaica, Nicaragua, Paraguay, Trinidad and Tobago, British Virgin Islands, and Venezuela [Bolivarian Republic of]) introduced IPV2 between 2020 and April 2022 *(4)*.

Despite these efforts, gaps in immunity against PV2 emerged in many countries of the world. Indeed, both the number of emergences and incidences of cVDPV2 since the switch have been higher than anticipated, even exceeding the number of WPV cases *(5)*. In March 2021, WHO's Strategic Advisory Group of Experts (SAGE) on immunization expressed concern over the intensification of cVDPV2 transmission across Africa and the Middle East in 2020. It urged countries to implement IPV catch-up campaigns to provide type 2 immunity to the cohorts of children missed due to the earlier shortage of IPV supply *(6)*.

Following a 10-year trend, which has been exacerbated by the COVID-19 pandemic, regional polio vaccination coverage in the Americas has decreased, thus increasing the number of susceptible children to all polioviruses. Even in this context, susceptibility to PV2 should be analyzed separately – particularly for children born after the switch in April 2016 – because of the withdrawal of PV2 from the oral vaccine and the delay in the introduction of a second IPV dose in many countries.

In 2016, regional coverage for the first dose of the polio vaccine (polio1) was 92%, which includes first doses of tOPV/bOPV and IPV, in accordance with the national schedules that were used at the time *(4)*. The regional IPV1 coverage in 2020 was 89% *(4)*. The regional coverage with the third dose against polio (polio3), which includes both IPV or bOPV depending on the country schedule, also decreased from 87% in 2016 to 79% in 2021, and the number of countries that reported a polio3 coverage lower than 80% increased *(4)* **(Figures 1 and 2)**. Furthermore, the percentage of districts that reported polio3 vaccination coverage <80% increased from 27.5% in 2018 to 50% in 2021 (preliminary data as of 19 July 2022) *(4)*.

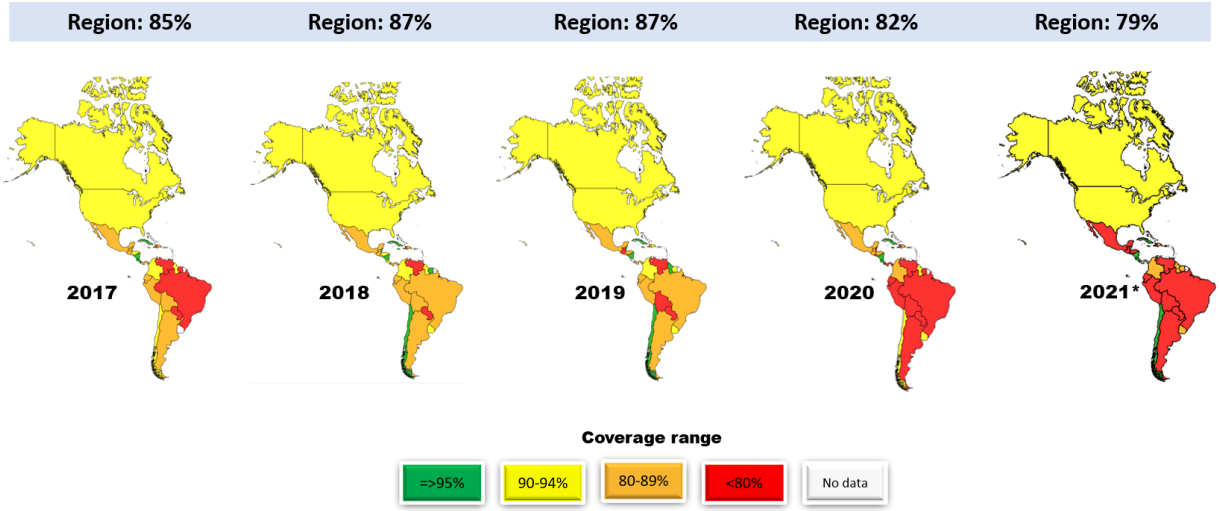
Figure 1. Regional polio vaccination coverage in children younger than 1 year old, Region of the Americas, 2016–2021*



*2021 preliminary data as of 19 July 2022.

Source: Country reports through the PAHO-WHO/UNICEF joint reporting form (JRF).

Figure 2. Polio3 vaccination coverage in children younger than 1 year old, Region of the Americas, 2017-2020*



*2021 preliminary data as of 19 July 2022.
Source: Country reports through the PAHO-WHO/UNICEF JRF.

Available studies show different seroconversion rates for each poliovirus type, depending on the vaccine used and the number of doses. For example, seroconversion can be as low as 50% against poliovirus type 2 when only one IPV dose is applied *(7)*. Therefore, the number of susceptible children to PV2 goes beyond the number of unvaccinated. Estimates must account for children who are fully vaccinated with bOPV (if they were born after the 2016 switch) but are under-immunized with IPV.

In 2013, TAG recommended that countries that do not achieve >95% coverage against poliovirus in every district or municipality must evaluate the accumulation of susceptible population and conduct catch-up vaccination campaigns *(8)*. Most campaigns employed OPV (tOPV before the switch and bOPV since 2016) because this vaccine stops transmission in the community and is easy to administer. However, bOPV doses do not provide protection against PV2. Using IPV will not interrupt poliovirus transmission in the community but will decrease the probability of a child having paralysis in case of an importation of WPV1/cVDPV or the emergence of a VDPV in the Region *(9)*.

The only vaccines against polio that are available for use in the Region of the Americas are bOPV and IPV. After the switch, the WHO maintains a stockpile of mOPV2 to respond to cVDPV2 outbreaks, but this vaccine is not deployed outside the context of a PV2 outbreak because of the risk of seeding additional cVDPV2 outbreaks *(10)*. Sabin OPVs are known to revert; therefore, a safer, more genetically stable novel OPV2 strain has been developed and is now available under WHO's Emergency Use Listing (EUL) for use in outbreak settings *(11)*. mOPV2 and nOPV2 are currently only authorized for outbreak control.

Analysis of Susceptible Children to Poliovirus by Type

PAHO conducted an analysis to estimate the susceptibility to poliovirus 1, 2, and 3 in children born between 2015 and 2020, by birth cohort, in 19 selected countries of Latin America and the

Caribbean (countries classified as high and very-high risk countries for polio by the Regional Certification Commission [RCC] in 2021, countries that are planning a measles/rubella campaign for 2022 or 2023, and countries that had not introduced IPV2 as of March 2022).

Methodology

To calculate the proportion of susceptible children, the following steps were followed:

1. The number of vaccinated children was calculated based on the vaccination coverage rates reported through the JRF.
2. From the vaccinated population, the proportion of protected children against each poliovirus type was calculated using seroconversion values from different studies and considering the country's vaccination schedule *(7, 12, 13, 14, 15, 16)* **(Table 1)**.
3. The number of protected children was subtracted from the "under 1" population for the corresponding year to determine the proportion of susceptible children by birth cohort and poliovirus serotype.

Table 1. Reported seroconversion rates by poliovirus type in the studies included in the analysis

Reference	Schedule in the study	Seroconversion for PV1	Seroconversion for PV2	Seroconversion for PV3
Study in Taiwan and Oman (1984, 1991)	tOPV-tOPV-tOPV	>90	>90	>90
Study in Guatemala (2007)	IPV-IPV-tOPV	98-100	98-100	98-100
Study in Chile (2015)	IPV-bOPV-bOPV	>98	>80	>98
WHO Meta-analysis (2021)	fIPV-fIPV	-	72.4	-
	IPV	-	46.7	-
	IPV-IPV	-	92.4	-
	IPV-IPV-IPV	98	94.6	98.7
Study in Ecuador (2022)	IPV	100	50	97.5
	fIPV-fIPV	99.4	83.2	92.5

Considerations

- United Nations (UN) population estimates were used as the source of denominator data for children younger than one year old.
- Official vaccination coverage rates were derived from the eJRF reports.
    - Doses administered as boosters[1] or during vaccination campaigns[2] were not included in these estimates.
    - If the country reported a coverage >100%, the coverage rate of 100% was used for the calculation.

[1] All the countries included in the analysis used either tOPV or bOPV as booster doses between 2015 and 2020 except for Argentina, which started using an only IPV schedule in June 2020.
[2] All the vaccination campaigns have been done with OPV (tOPV before the switch and bOPV after the switch).

- To calculate the size of the population susceptible to PV1 and PV3, the lower bound of the seroconversion value reported in each study was used.
- To calculate the number of children susceptible to PV, we used the reported vaccination coverage rate for polio3 (to estimate immunity against PV1 and PV3), as well as the reported vaccination coverage rate for the last IPV dose that was used (to estimate immunity against PV2). In countries that apply more than two IPV doses, polio3 coverage was used to estimate seroconversion against all poliovirus serotypes.
- When IPV was not introduced in January of a given year, the population was divided equally among the 12 months and coverage was assumed to be the equal across months. If IPV was introduced during or after the month of November, the new schedule was not considered to be active until the following year.

- The results of our analysis show the highest percentage of susceptible population from the different scenarios that were considered.

Results

1. In all countries, except for Panama and Peru, the proportion of children who are susceptible to PV1 and PV3 is lower than the percentage of children who remain susceptible to PV2. *The true proportion of PV1-PV3 susceptibility may be even lower because of booster doses and bOPV campaigns that were implemented in multiple countries since the switch*. The proportion of children that are susceptible to PV1 and 3 is higher in Panama and Peru because these countries introduced IPV2 before the switch but have a high drop-out rate from IPV2 to polio3.

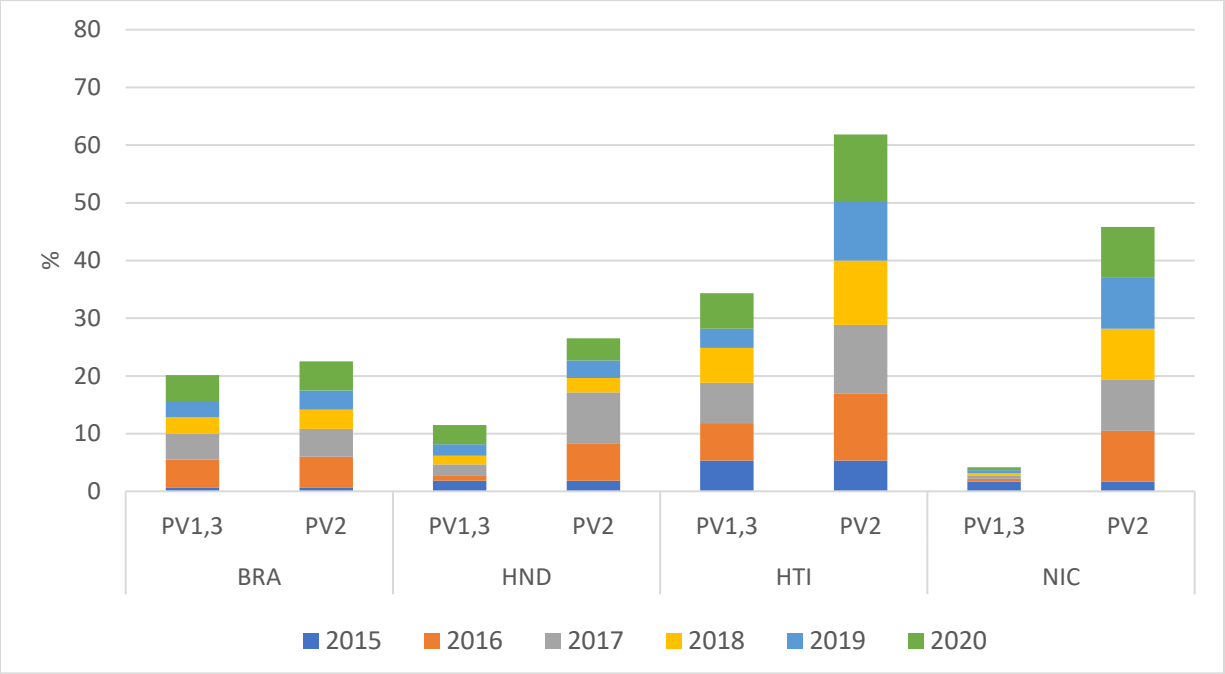
2. Even with high vaccination coverage for polio3, countries with a late introduction of IPV2 or that have not introduced IPV2 have a high proportion of children who are susceptible to PV2.

3. The introduction of IPV2 reduces the proportion of children who are susceptible to PV2, but cohorts who were born before the introduction of this second dose remain susceptible. The longer the period between the switch and the introduction of IPV2, the greater the proportion of susceptible children to poliovirus type 2.

Figure 3 shows the results for four different scenarios that summarize all country situations:

1. A country (BRA) that introduced IPV2 before the switch that has reported vaccination coverage with polio3 $\leq$85% since 2016.
2. A country (HND) that introduced IPV2 in 2018 and that has reported vaccination coverage $\leq$95% since 2018.
3. A country (HTI) that has not introduced IPV2 and that has reported vaccination coverage with polio3 $\leq$85%.
4. A country (NIC) that introduced IPV2 in 2022 and has reported vaccination coverage with polio3 >95%.

Figure 3. Percentage of children (born between 2015 and 2020) who are susceptible to polio, by country, poliovirus type, and year of birth for selected countries



Status of the Multi-Country Monkeypox Outbreak and Updates on the Availability and Deployment of Monkeypox Vaccines

Monkeypox (MPX) Epidemiological Update as of 14 July 2022

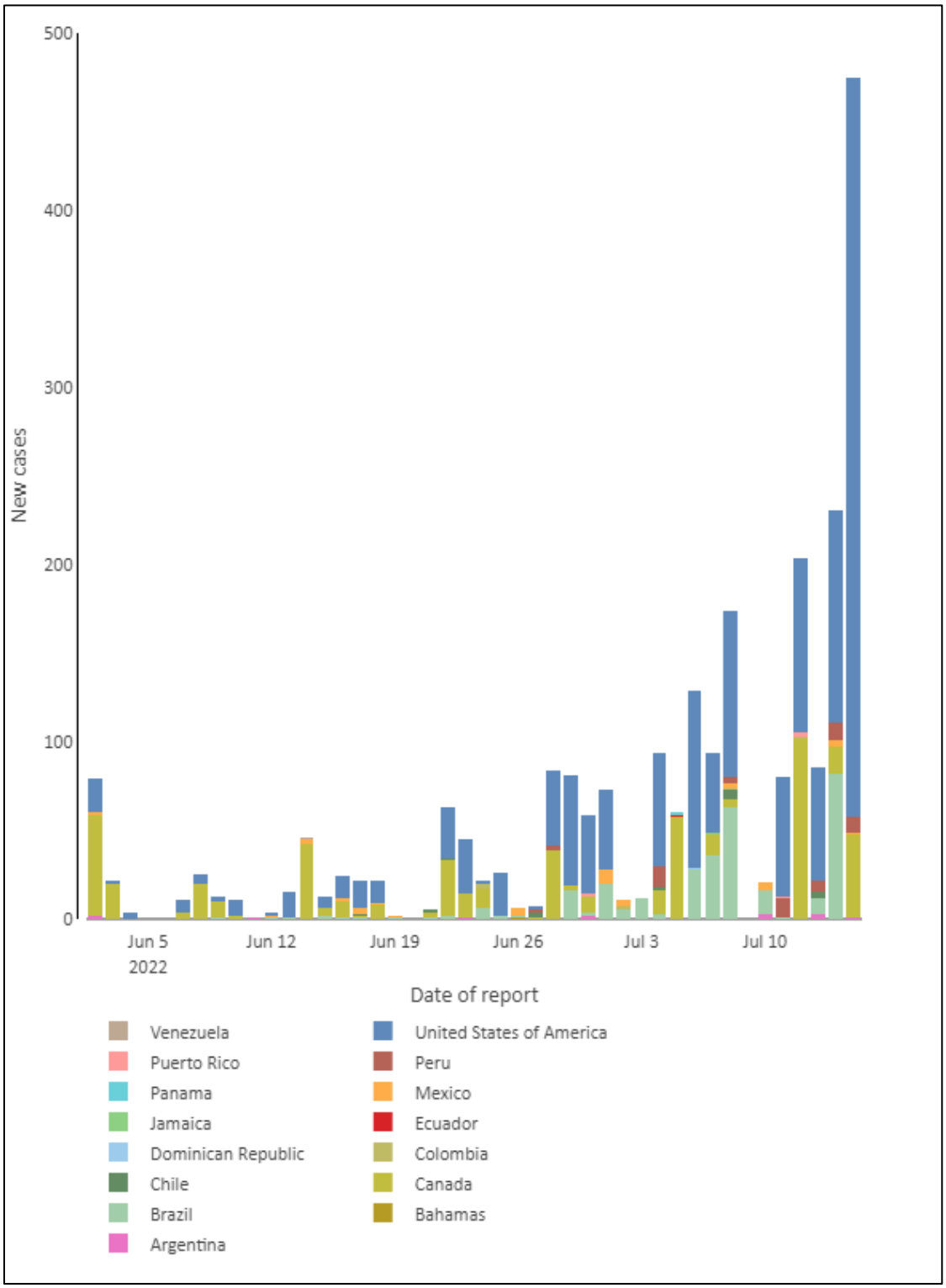
From 1 January to 14 July 2022, 11 188 laboratory-confirmed cases of monkeypox and five deaths (two in the Central African Republic and three in Nigeria) have been reported to WHO from 66 countries, areas, and territories in five WHO Regions. 80% in the European Region, 18% in the Region of the Americas, 2% in the Africa Region, <1% in the Eastern Mediterranean Region, and <1% in the Western Pacific Region *(17)*. In the Region of the Americas, as of July 15, there are 2456 confirmed cases and no deaths, in 15 countries *(18)* **(Table 2, Figure 4)**.

Table 2. Confirmed, probable, and suspected monkeypox cases by country/territory, 15 July 2022

Country	Confirmed	Probable	Suspected
United States of America	1466	0	0
Canada	539	71	0
Brazil	310	0	23
Peru	55	0	2
Mexico	40	0	0
Chile	16	0	0
Argentina	13	0	0
Colombia	7	0	0
Puerto Rico	4	0	0
Bahamas	1	0	1
Dominican Republic	1	0	0
Ecuador	1	0	0
Jamaica	1	0	0
Panama	1	0	0
Venezuela (Bolivarian Republic of)	1	0	0
Total	2456	71	26

Source: PAHO monkeypox dashboard *(18)*.

Figure 4. Confirmed monkeypox cases by country/territory, 15 July 2022



Source: PAHO monkeypox dashboard *(18)*.

In the Region of Americas, according to the information received from Member States, 1639 monkeypox cases have been confirmed. Of these, 758 cases had sex information available, of which 751 (99%) were male; 758 cases had age information, which ranged from 19 to 69 years old (median 35 years, mean 37 years). Of 554 cases with available information on the history of reported travel, 35% (n=196) reported having recently traveled. As of 14 July 2022, the global and regional risk assessment is moderate *(17)*.

The advice of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country monkeypox outbreak, held on 23 June 2022, does not determine that the event constitutes a Public Health Emergency of International Concern (PHEIC). The Committee noted that many aspects of the current multi-country outbreak are unusual, such as the occurrence of cases in countries where monkeypox virus circulation had not been previously documented, and the fact that most cases are observed among men who have sex with men, of young age, and not previously immunized against smallpox. Some Member States suggested that, given the low level of population immunity against pox virus infection, there is a risk of further sustained transmission into the wider population that should not be overlooked.

The Committee also noted that the response to the outbreak requires collaborative international efforts, and that such response activities have already started in several high-income countries experiencing outbreaks, although there has been insufficient time to have evaluated the effectiveness of these activities *(19)*. The IHR Emergency Committee for monkeypox was reconvened on 21 July 2022 to update on the current epidemiology and evolution of the outbreak and implementation of counter measures.

Monkeypox Vaccines

Smallpox vaccines held in national reserves and vaccines more recently developed would likely provide protection against monkeypox. This statement is based on experience with their use during the Smallpox Eradication Programme (SEP), as well as available pre-clinical and clinical studies for the newer products *(20)*.

The ACAM2000 and LC16 have been shown to be protective against monkeypox in animal models and immunogenic in human studies. Licensure for the prevention of monkeypox has not been sought to date for ACAM2000 or LC16 *(20)*.

The vaccine effectiveness of 85% of smallpox vaccines against MPXV reported is based on studies in the 1980s describing the protective effect of the smallpox vaccine against MPX infection *(21, 22)*. This data was generated with the first and second generations of the vaccine and cannot be directly extrapolated to the MVA-BN vaccine *(23)*.

In 2019, the MVA-BN vaccine was approved for the prevention of smallpox and monkeypox in the USA and in Canada. Pre-exposure phase III trials have demonstrated positive results for immunogenicity and efficacy, and a favorable safety profile was confirmed for healthy population groups, as well as for people with HIV, atopic dermatitis, and hematopoietic stem cell transplants. MVA-BN has shown protection in primate models challenged with lethal doses of MPXV *(23)*.

While there is limited clinical data on the use of vaccines to prevent monkeypox, the effectiveness of MVA-BN against monkeypox was extrapolated from human immunogenicity trials and efficacy data from pre-clinical studies in comparison with ACAM2000 *(20)*.

The only United States Food and Drug Administration (FDA) approved MVA-BN dosing regimen is two doses. People who receive MVA-BN are considered to reach maximum immunity 14 days after their second dose (~6 weeks from first dose). They should continue to take precautions against monkeypox during this time. There is no certainty if MVA-BN will fully protect against monkeypox virus infection in this outbreak *(24)*.

Vaccine antigens and replication capacity differ for MVA-BN and ACAM2000. The neutralizing antibody response that predicts protection is not established. Therefore, the demonstration of the efficacy of the vaccine in non-human primates (monkeypox challenge) was necessary in addition to the clinical immunological comparison of non-inferiority *(25)*.

People are considered fully vaccinated about two weeks after their second shot of MVA-BN and four weeks after receiving one dose of ACAM2000. However, people who get vaccinated should continue to take steps to protect themselves from infection by avoiding close, skin-to-skin contact, including intimate contact, with someone who has monkeypox *(24)*.

No data are available yet on the effectiveness of these vaccines to prevent monkeypox. Also, clinical efficacy of the first dose to prevent transmission is not known, neither efficacy of the two doses is well known. While there are good reasons to think these vaccines will be effective against monkeypox, there is no clinical data to support use in specific situations *(20)*.

Considering the vaccine's availability is limited at this time, some countries have defined a prioritization of the vaccination and taking also in consideration the epidemiological scenario.

The Superior Health Council of Belgium (SCH) *(23)* considers four possible scenarios for the deployment of monkeypox vaccine. Each one of them with different presuppositions and actions to be taken in the event of development **(Table 3)**.

Table 3. Scenarios for the deployment of monkeypox vaccine in the current outbreak

Scenario 1	Scenario 2	Scenario 3 (unlikely)	Scenario 4 (highly unlikely)
Very low vaccine supply	Low to moderate vaccine supply		
- Progressive reduction in the number of new cases - Some positive cases imported via travel	- Long and persistent chains of transmission - Emergence of several endogenous cases not linked to recent travel or to a known case	In the coming months, there is an exponential increase in cases.	In the coming months, there is an exponential increase in cases, hospitalizations, and deaths.

- Short transmission chains observed - No massive increase of cases in bordering countries	- Separate clusters not easily linked via contact tracing		
No systematic vaccination of very-high-risk contacts (VHRC) and high-risk contacts (HRC) Exceptions can be made on an individual basis and on medical recommendations.	**Systematic vaccination as post-exposure prophylaxis (PEP) of all:** • **Very high-risk contacts (VHRC)** - Sexual partner(s) - Person(s) with prolonged skin-to-skin contact while the patient had a rash, sore or scabs • **High-risk contacts (HRC):** - Person(s) living in same household - Person(s) sharing clothing, bedding, utensils while the patient had a rash - Co-passengers seated 1-2 seats distance around a case who was symptomatic in an airplane, bus, or train ≥3 hours. This period is set arbitrarily because there is no scientific evidence to guide the decision.	**Systematic vaccination of all risk groups with or without contact with a PCR+ case** - Healthcare workers (HCWs) - Persons with multiple sex partners - Sex workers - Sexual and gender minorities - Immunocompromised population - Children (off-label use, with close B/R balance evaluation and risk of contacts evaluation) - Pregnant women (off-label use, with close B/R balance evaluation and risk of contacts evaluation)	**Systematic vaccination of the entire Belgian population:** - Starting with people who have never been vaccinated against smallpox and the groups most at risk of death and hospitalization - One booster dose if people have been vaccinated against smallpox before 1976
Offer the vaccine to HCWs and occupational groups who have been exposed (as PEP), especially if they fall in these categories: - HCWs with contact with an MPX case (lesions or prolonged face-to-face contact)	**PEP vaccination of HCWs and occupational groups who have been exposed to the virus,** especially if they are in the following categories: - HCWs (caregivers) of a MPX case - HCW who had contact with MPX case (lesions		

without appropriate personal protection equipment (PPE) - HCWs or other persons who suffered a sharps injury or was exposed to MPX case body fluids or aerosol generating procedure without PPE - Laboratory staff suffering exposure to occupational accident with virus containing sample (splash, sharp or aerosol exposure, etc.) without PPE	or prolonged face-to-face contact) without appropriate PPE - HCW or other persons who suffered a sharps injury or was exposed to MPX case body fluids or aerosol generating procedure without PPE - Laboratory staff suffering exposure to occupational accident with virus-containing sample (splash, sharp or aerosol exposure) without PPE - Staff of the sexually transmitted diseases (STD) testing centers		

The SHC recommends that the responsibility for moving from one scenario to another be given to the case progress and tracing data. At this moment, the probability of further spread of MPX among the broader population in the coming months is assessed as very low leading to an overall low risk for the general population. Scenarios 3 and 4 are closer to mass vaccination. However, there is no sufficient data (vaccine effectiveness, safety, etc.) or vaccines to support strategies for scenarios 3 and 4 *(23)*.

If vaccine availability is limited, which is currently assumed to be the case, PEP should primarily be offered to exposed contacts. In addition, with respect to both PEP as well as the indication vaccination, individuals with an increased risk of severe illness (e.g., individuals with immunodeficiency) should be vaccinated preferentially *(26)*.

Smallpox vaccine can be considered for PEP of close contacts at increased risk for severe disease; however, careful benefit/risk assessment should be performed for the exposed individual. Important information on the use of currently available smallpox vaccines is missing for groups at increased risk for severe disease.

WHO Recommendations to Date on Vaccines

On 14 June 2022, WHO published its first interim recommendations on the use of (smallpox) vaccines against monkeypox. WHO recommended that any vaccination program should be accompanied by a strong information campaign, robust pharmacovigilance, and the implementation of vaccine effectiveness studies. Interim recommendations reported concerns with off-label use of vaccines *(20)*.

WHO encourages countries to use vaccines against monkeypox within a framework of collaborative research and randomized clinical trial (RCT) protocols with standardized data collection tools for clinical and outcome data, using standardized design methods and data collection tools for clinical and outcome data. This will allow the rapid generation of safety and effectiveness data for the use of vaccines for different purposes, in different at-risk groups and in different settings, and document their performance.

When the use of vaccines and antivirals for monkeypox in the context of collaborative research and RCT protocols is not possible, then consider their use under expanded access protocols, such as Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI) *(27)*.

In the current monkeypox outbreak, there is no clinical data supporting vaccine efficacy against monkeypox infection, nor clinical efficacy of the first dose of vaccine is known, neither efficacy of vaccine to prevent transmission. Also, the main goal of the monkeypox vaccination should be defined to prevent transmission, prevent severe disease (hospitalizations are rare), as well as the role of pre and post exposure prophylaxis.

In order to have better knowledge of monkeypox vaccination, countries are encouraging to use vaccines against monkeypox within a framework of collaborative clinical efficacy or observational studies using standardized design methods and data collection tools for clinical and outcome data to rapidly increase evidence generation on efficacy and safety.

In anticipation of a potential regional need and in response to inquiries from several PAHO Member States regarding vaccine access, PAHO initiated an early negotiation with the manufacturers of the second and third generations of the smallpox vaccine for the eventual supply through the PAHO Revolving Fund for Access to Vaccines.

Based on the TAG recommendation, negotiations with the manufacturer of the third-generation vaccine have continued. These discussions are ongoing and PAHO continues to analyze technical, regulatory, programmatic, legal, and ethical aspects of this matter, as well as logistics, price, and availability. PAHO notes that global availability currently depends on a single manufacturer and supply is extremely limited, even though vaccine demand continues to increase.

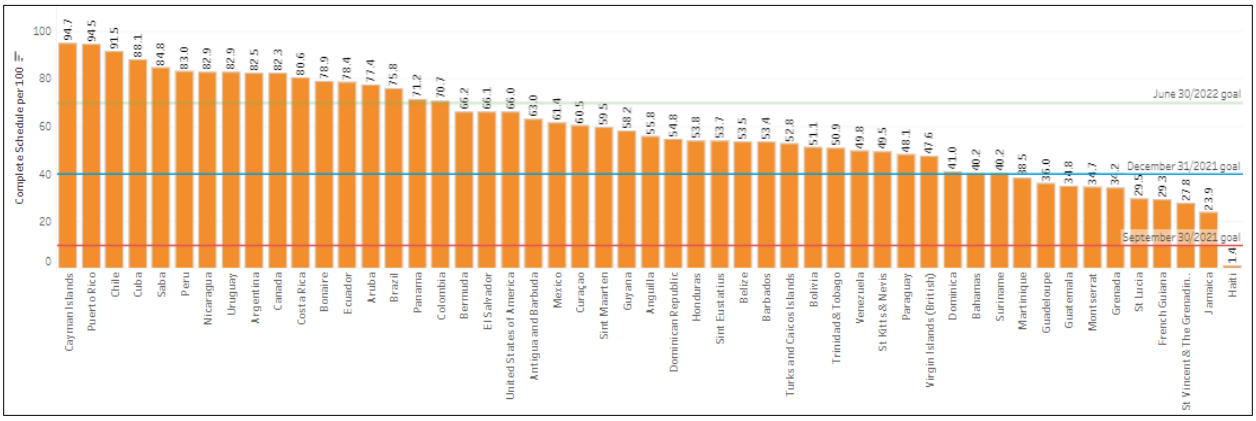
Updates on COVID-19 Vaccines and Vaccination Operations in the Americas

COVID-19 Vaccination Operations in the Americas

As of 15 July 2022, all 51 countries and territories have launched COVID-19 vaccination programs, using vaccines received through bilateral agreements with manufacturers, from the COVAX Facility, and from donations. More than 1.92 billion doses have been administered in the Americas and 68.8% of the population of Latin America and the Caribbean have received a complete schedule of the primary series of the COVID-19 vaccine. Of the 51 countries and territories, 41 had reached the 40% vaccination global target set by WHO for 31 December 2021, and 17 have achieved the 70% target set for 30 June 2022. Of the 10 countries and territories that remain below the 40% threshold, most are in the English-speaking Caribbean countries. Haiti remains the only country in the Region with a vaccination coverage rate below 10%.[3]

Vaccination coverage rates against COVID-19 vary considerably within countries and territories. While some have reached high coverage rates with at least two doses of the COVID-19 vaccine, other still have sizeable portions of the population who remain unvaccinated **(Figure 5)**. To date, there are 221 million persons in the Americas who have still not yet received a single COVID-19 vaccine dose.

Figure 5. Status of COVID-19 vaccination operations in the Americas, by country/territory (data as of 15 July 2022)



Until recently, WHO recommended that countries achieve the global target of 70% vaccination coverage rate against COVID-19 by 30 June 2022. *(28)* Now WHO recommends that all countries should continue vaccination operations until they have reached the 70% global target for the general population (document in print). Also, vaccination operations should strive to achieve 100% coverage for high-risk priority groups. *(29)* PAHO published its own recommendation along the same lines. *(30)*

PAHO also notes that the Region's vaccination coverage rate for the primary series has remained stagnant since October 2021 **(Figure 6)**. This status is reported across income groups **(Figure 7)**. This means that countries are now administering more booster doses than primary series doses.

[3] https://ais.paho.org/imm/IM_DosisAdmin-Vacunacion.asp

As a consequence, the number of zero-dose persons in the Region is not declining and countries may not achieve the 70% target before the end of 2022. This situation will generate two consequences. First, countries may remain at risk for high hospitalization and mortality rates due to new COVID-19 waves and variants. Second, the health, social, and economic impacts of the COVID-19 pandemic will continue to burden countries for a third consecutive year. At this time, the Region can ill afford continuous strain on its resources and recovery efforts – especially if another outbreak of a vaccine-preventable disease (VPD) were to occur.

Figure 6. Status of COVID-19 vaccination operations in the Americas by number of doses (data as of 13 July 2022)

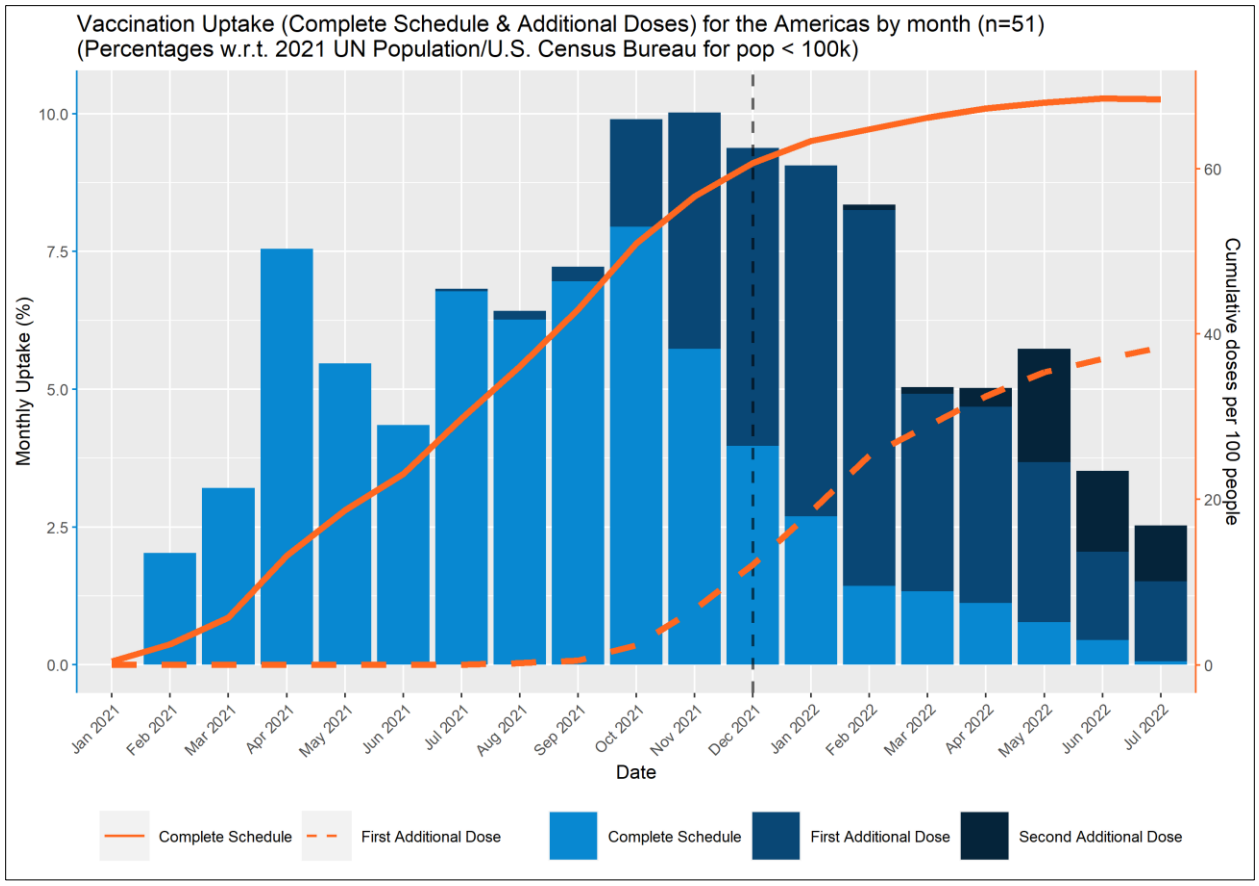
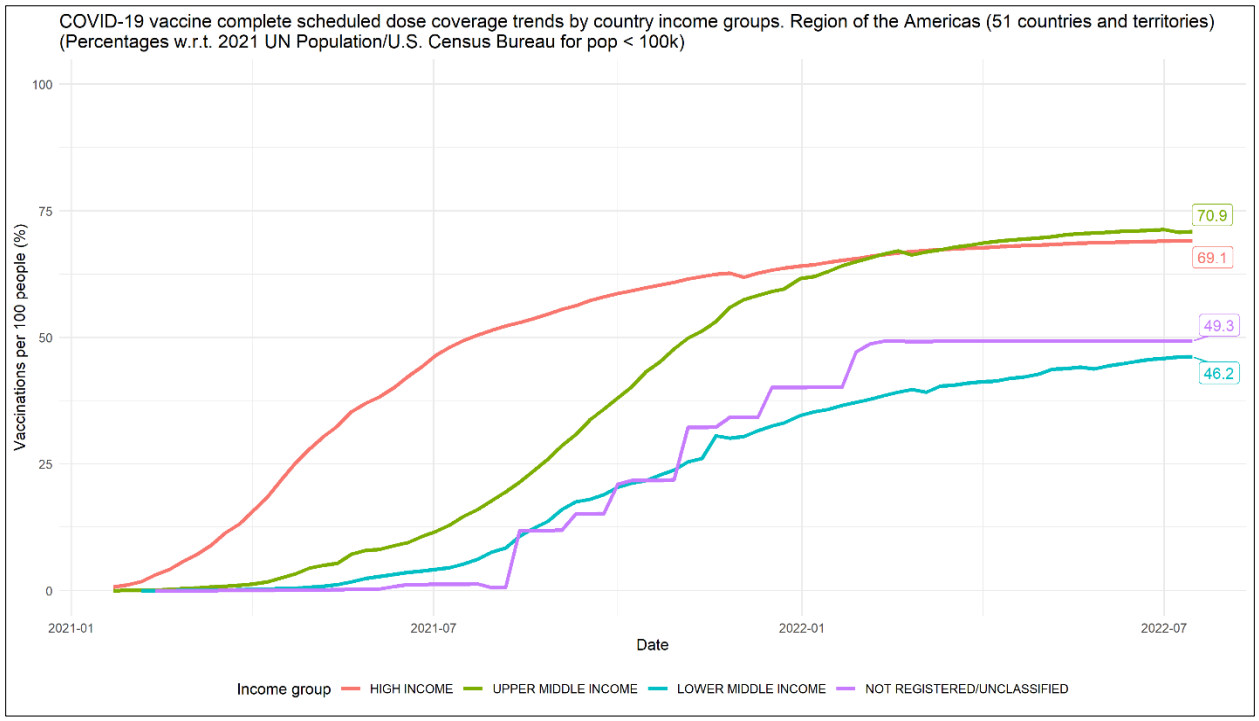


Figure 7. Status of COVID-19 vaccination operations in the Americas, by income level (data as of 13 July 2022)



COVID-19 Vaccination in Pediatric Populations

WHO and PAHO continue to recommend that people at highest risk of infection, hospitalization, and mortality from COVID-19 should receive all vaccine doses as soon as possible. This category includes children and adolescents younger than 18 years with comorbidities that increase their risk of severe disease. These recommendations were published in the SAGE Roadmap *(31)*, updated on 21 January 2022.

The COVID-19 COMIRNATY vaccine produced by Pfizer-BioNTech *(32)* has a pediatric version for children 5–12 years of age. The dosage and formulation of the pediatric version of the vaccine differ from those of the adult version. This version was reviewed by the FDA and the European Medicine Agency (EMA) and received approval from both regulatory agencies. *(33)* Based on this information, WHO recommended the Pfizer vaccine for the pediatric population in all countries of the world. The national regulatory authorities of each country used the same information to decide whether to approve the use of the Pfizer pediatric vaccine in their national territory.

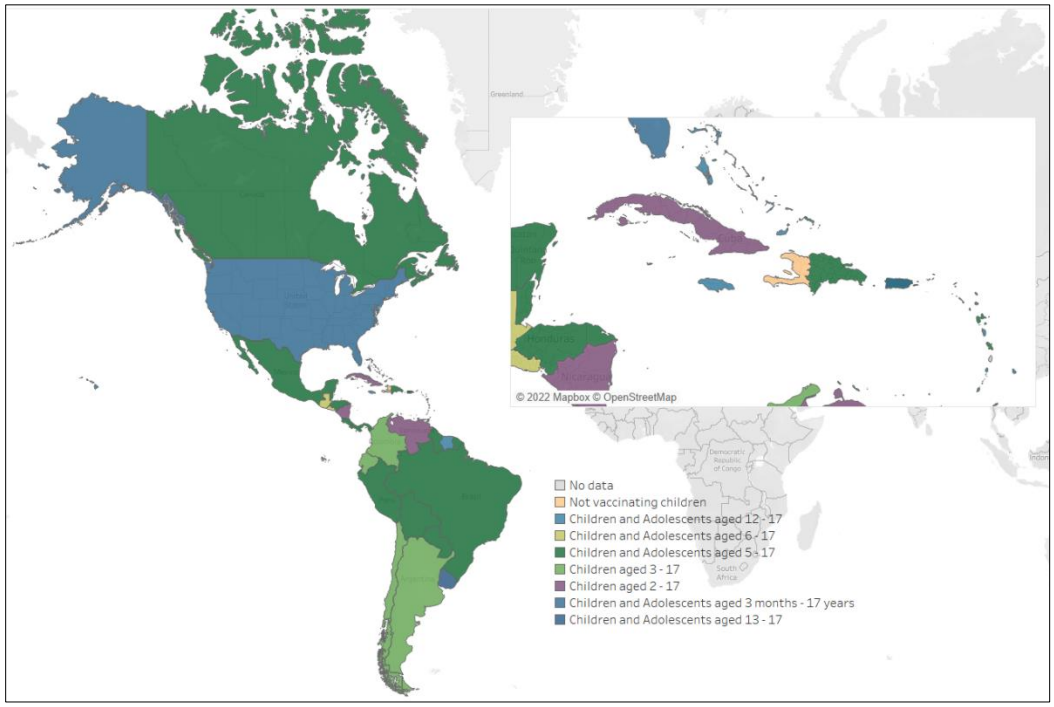
On 17 June 2022, the FDA amended its Emergency Use Authorization (EUA) to include the emergency use of the Moderna COVID-19 vaccine and the Pfizer-BioNTech COVID-19 vaccine for the prevention of COVID-19 to include use in children down to 6 months of age. The Agency determined that the known and potential benefits of the Moderna and Pfizer-BioNTech COVID-19 vaccines outweigh the known and potential risks in the pediatric populations authorized for use for each vaccine. *(34)* To date, WHO has not granted EUL to any COVID-19 vaccine for administration in children younger than 5 years. *(30)*

The Pfizer COVID-19 vaccine may be co-administered with the influenza vaccine, regardless of the age of the individual. *(29)* In the Southern Cone, many countries take advantage of the joint administration of the two vaccines against COVID-19 and influenza as a way to increase the vaccination coverage rate of both. To date, SAGE does not recommend the co-administration of the anti-COVID-19 vaccine with other antigens, regardless of the age of the individual.

Even if children report proportionally fewer symptomatic infections and cases with severe illness and deaths from COVID-19 compared to older age groups, pediatric vaccination is essential to reduce transmission of the SARS-CoV-2 virus in the population and protect people at higher risk (i.e., health personnel, older adults, pregnant women, and people with comorbidities). Also, a high vaccination rate in the pediatric population facilitates the economic recovery and schooling of a country. *(35)*

In the Americas, 50 of the 51 countries and territories administer the COVID-19 vaccine to children younger than 18 years **(Figure 8)**. Of these, 25 countries and territories offer vaccination to children between 5 and 17 years, while 13 others offer vaccination to children between 12 and 17 years. The remaining 11 countries and territories offer vaccination to the following target groups: 3 months to 17 years (1 country/territory), 2 to 17 years (3 country/territory), 3 to 17 years (4 country/territory), 6 to 17 years (2 country/territory), and 13 to 17 (1 country/territory). The Pfizer COVID-19 vaccine is the most used vaccine product for vaccination in children, with administration in in 45 countries and territories. The Moderna vaccine is used in 10 countries, while the Sinovac vaccine and the Finlay – Soberana-02 vaccine are used in 1 country each.

Figure 8. COVID-19 vaccination policies for pediatric populations in the 51 countries and territories of the Americas (data as of 15 July 2022)



COVID-19 Vaccine Produced by Janssen – Two-Dose Series

The COVID-19 vaccine produced by Janssen received a SAGE recommendation on 17 March 2021. The vaccine received EUL for a single dose at 0.5ml based on a phase 3 trial using a single dose. Given the simplicity of its schedule and cold chain requirements, this vaccine has been widely used to vaccinate persons living in situations of vulnerability, living in hard-to-reach areas, or living in transient conditions (ex., migrant populations).

However, on 6 June 2022, SAGE updated its recommendations to promote the use of a two-dose series, 2–6 months apart. *(36)* Immunogenicity data indicate that this additional dose 2 months substantially increases humoral immune responses (ELISA titers) by about 4-fold as compared to pre-boost levels. Overall, the Janssen vaccine has an acceptable reactogenicity profile after both the first dose and second dose, with the reactogenicity post-second dose being similar or milder than post-dose one. A comparison between the one-dose and the two-dose schedule on vaccine effectiveness is available on **Table 4**.

Table 4. Vaccine effectiveness of the Janssen vaccine at different points after the administration of the first and second doses

		Vaccine effectiveness *(36,37)*	
		One-dose schedule	**Two-dose schedule**
14 days from first dose	Moderate to severe/critical COVID-19	56% [95% CI, 51–61]	
	Severe/critical COVID-19	75% [95% CI, 65–82]	
6 months from first dose	SARS-CoV-2 infection	42% [95% CI, 36–47]	
	Severe/critical COVID-19	75% [95% CI, 65–82]	
2 months from last dose	Moderate to severe/critical COVID-19		75% [95% CI: 55–87]
	Severe/critical COVID-19		100% [95% CI: 33–100]

At this time, it is highly recommended that persons who received the first dose of the Janssen vaccine should receive the second dose of a COVID-19 vaccine. Like with any COVID-19 vaccine, the two-dose series may be homologous or heterologous. If administration of the second dose is delayed beyond 6 months, it should be given at the earliest opportunity. SAGE does not recommend that persons who received only one dose of the Janssen vaccine should be actively tracked to receive the second dose.

Countries may consider continuing the use of a single dose of Janssen vaccine only if there are vaccine supply constraints or vaccine delivery challenges. A single dose may be a preferred option for vaccinating hard-to-reach populations. Even in these populations, WHO recommends that all efforts should be taken to provide two doses, in particularly to the highest and high priority-use groups.

In the Americas, 23 countries and territories employ the Janssen vaccine.[4] To date, 52 million of vaccine doses have been administered, offering protection to 5% of the population of the Americas. To date, no country or territory has reported the introduction of the second dose of Janssen vaccine.

COVID-19 Vaccines against the Omicron Variant – New Formulation

The primary goals of COVID-19 vaccination using currently licensed vaccines continue to be to reduce hospitalization, severe disease, and death, and to protect health systems. The use of currently licensed vaccines based on the ancestral strain (i.e., the virus that was identified from the first cases of COVID-19 in December 2019) confers high levels of protection against severe disease outcomes for all variants, including omicron with a booster dose.

Given the uncertainties of further evolution, WHO considers it prudent to pursue an additional objective of COVID-19 vaccination of achieving broader immunity against circulating and emerging variants while retaining protection against severe disease and death. Available data indicate that the inclusion of omicron – as the most antigenically distinct SARS-CoV-2 Variant of Concern (VOC) – in an updated vaccine composition may be beneficial if administered as a booster dose. In contrast, WHO does not recommend an omicron-specific monovalent vaccine product as part of a primary series. *(38)*

The FDA also reviewed available information on omicron-specific vaccines and recommended that manufacturers should develop modified vaccines that add a spike omicron BA.4/5 protein component to the current vaccine composition – thus creating a two-component (bivalent) booster vaccine. The FDA concurred with WHO that an omicron-specific monovalent vaccine product for primary series is not recommended at this time. *(39)*

Potentially, this omicron-specific booster will be available for use in early to mid-autumn 2022 (at least in the USA).

[4] Antigua and Barbuda, Aruba, Barbados, Bolivia, Brazil, Bahamas, Belize, Canada, Colombia, Grenada, Guadeloupe, Guyana, Honduras, Haiti, Jamaica, St. Lucia, Mexico, Nicaragua, Puerto Rico, Trinidad and Tobago, United States, British Virgin Islands, and Sint Eustatius.

Update on Recent Progress and Challenges of the Regional Immunization Program

The world was experiencing a decline in routine immunization coverage even before the start of the COVID-19 pandemic. WHO reports that in 2019 only 85% of the world's children received the DTP3 vaccine, leaving 19.7 million children vulnerable to VPDs. Recently published estimates from the 2021 WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) *(40)* report that the DTP3 coverage rate has further declined to 80%. The disruptions of the COVID-19 pandemic and COVID-19 vaccination efforts strained health systems in 2020 and 2021. In 2021 alone, 25 million children missed out on vaccination – 6 million more than in 2019 and the highest number since 2008.

The Region of the Americas is facing an impending crisis around routine vaccination. *(41)* It has been reporting a steady decline in vaccination coverage since 2010 **(Figure 9)**. This fall is due to multiple reasons, including natural disasters, displacements, progressive urbanization, the political context, and growing inequities in healthcare access. The start of the COVID-19 pandemic in 2020 forced countries to implement strict lockdown practices, thus drastically reducing access to antigens of the national immunization program. Some recovery was seen in the second part of 2020, but the introduction of the COVID-19 vaccine in early 2021 brusquely diverted resources (financial, human, material, logistics) away from the national immunization routine program and towards COVID-19 vaccination activities.

While some countries are organizing vaccination campaigns, catch-up and mass vaccination events (ex., Vaccination Week in the Americas), these efforts are not sufficient to close the large immunity gaps that persist in all countries. A review of national immunization data provided to PAHO by the 51 countries and territories of the Americas through the PAHO/WHO-UNICEF joint reporting form (JRF) on immunization reveals that declines in coverage have been reported for all antigens of the Expanded Program on Immunization (EPI) **(Figure 10)**. Between countries and territories, those in the lower/middle income group (according to World Bank classification) reported steeper drops in DTP3 coverage compared to high or upper/middle income countries – possibly because their health systems were not as resilient to the impact of the pandemic **(Figure 11)**.

Figure 9. Trend of MMR1 and MMR2 vaccination coverage in the Americas, 2010-2021

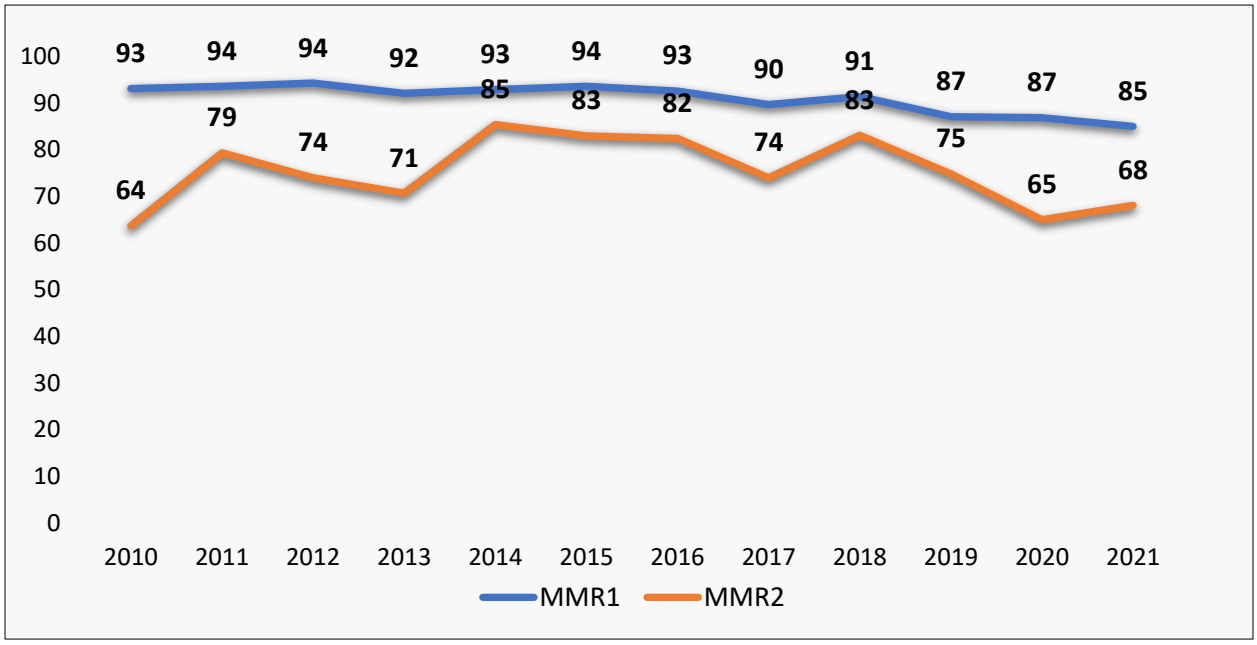
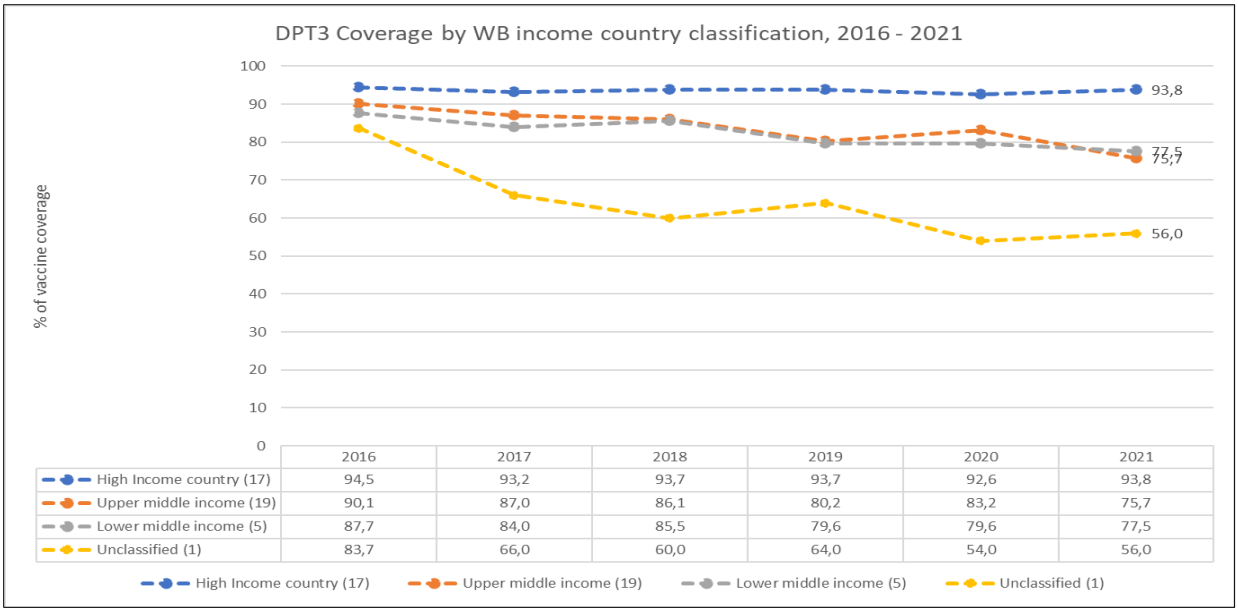


Figure 10. Vaccination coverage rate trends for all EPI antigens in the Americas, 2016-2021

	BCG	HepBB	DTP1	DTP3	Polio1/IPV1	Polio3	PCV3	Rotavirus	MMR1	MMR2
2016	94	76	95	91	92	87	84	80	93	82
2017	94	76	93	88	91	85	84	73	90	74
2018	93	74	92	89	90	87	87	79	91	83
2019	84	73	89	84	89	87	86	80	87	75
2020	69	68	89	84	89	82	80	76	87	65
2021	84	68	86	81	85	79	80	75	85	68

Figure 11. Vaccination coverage rate trend for DTP3 by income level, 2016–2021



The same pandemic has affected VPD surveillance systems **(Figures 12-13)**, with considerable drops in reported suspected cases for polio and measles/rubella. The performance of the laboratory surveillance system declined as well, because of the precedence given to the COVID-19 response and the diversion of financial resources towards COVID-19 vaccination operations. Consequently, the Region may not be able to detect the next VPD outbreak before it becomes a multi-country epidemic.

Figure 12. Acute flaccid paralysis (AFP) rate for the Americas, 2016–2021

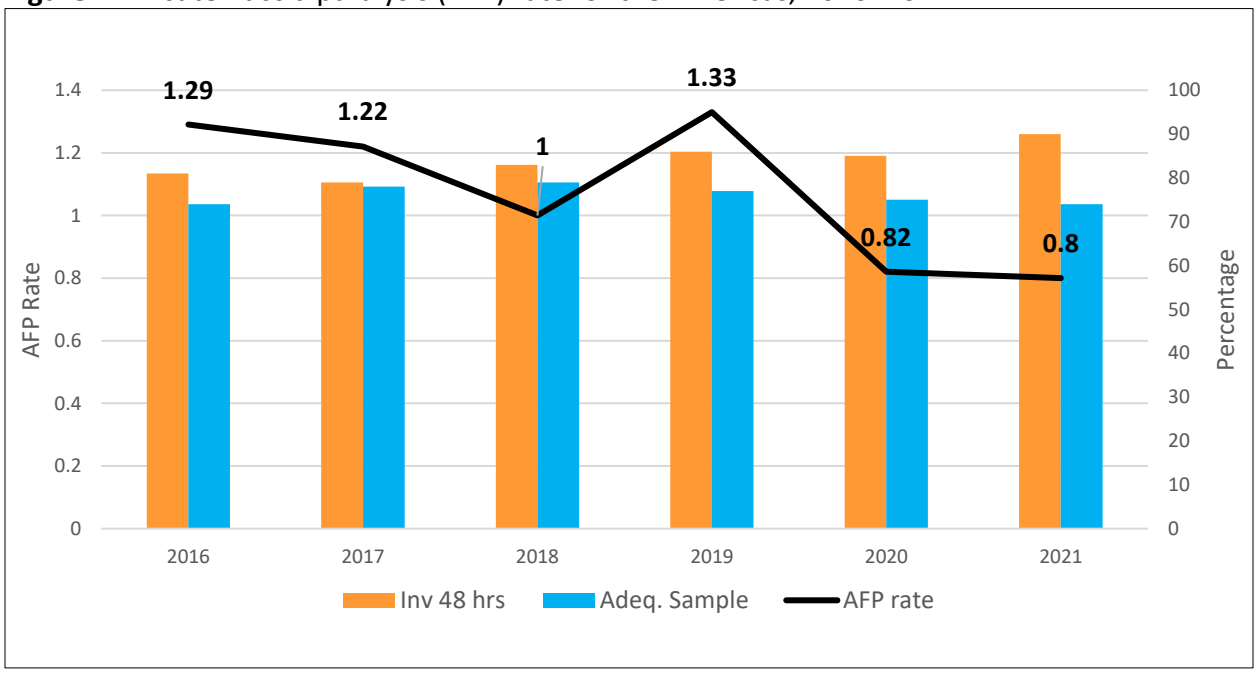
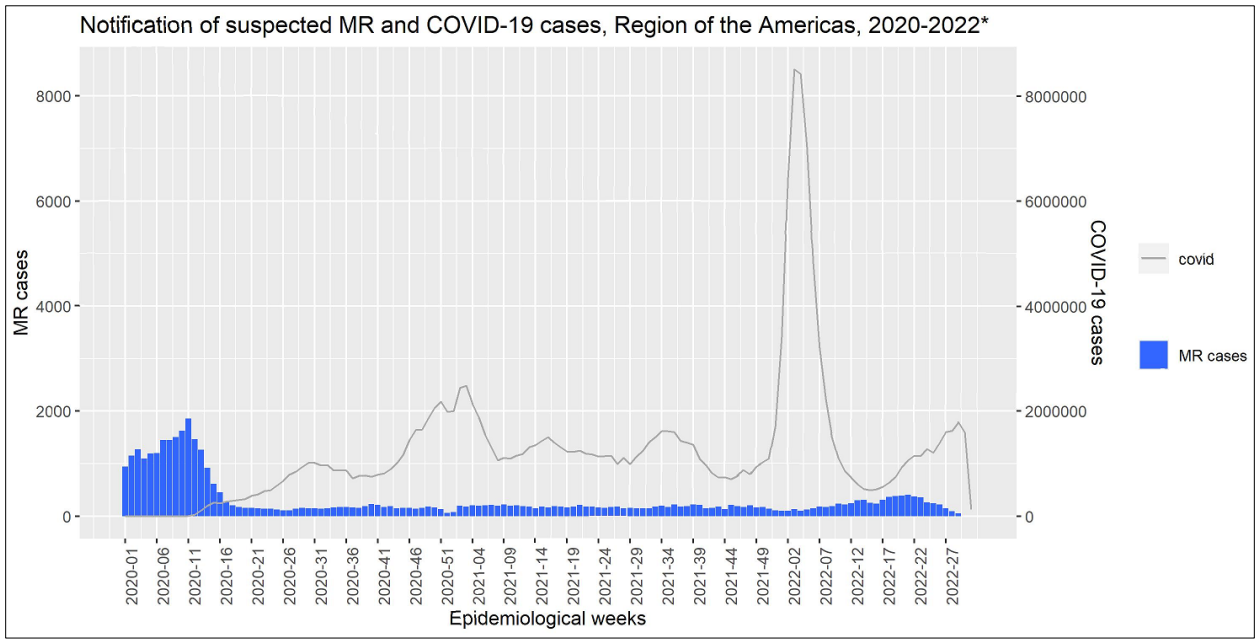


Figure 13. Impact of the COVID-19 pandemic on the notification of suspected cases of measles and rubella in the Americas, 2020 (epi week 1–52) to 2022 (epi week 1–29)



To address this challenging situation, PAHO's Comprehensive Family Immunization Unit proposed the resolution "Reinvigorating immunization as a public good for universal health," which was approved by the Regional Committee of WHO for the Americas in September 2021. *(42)* To bolster the implementation process, the Immunization Unit plans to hold a series of periodic conversations across levels to define our priorities, strategies, and operations. The result of these conversations will be a list of bottlenecks and response operations that can guide recovery in all countries and territories of the Americas. The goal is to halt the decline in DTP3 coverage by December 2023 and increase the vaccination coverage rates of the regional immunization program.

TAG ordered the following recommendations according to their degree of urgency:

1. TAG expresses grave concern regarding the serious decline in DTP3, polio3 and MMR2 vaccination coverage across the Americas and is disheartened to see that the achievements of 40 years are at risk of collapse. TAG strongly recommends that countries focus their political, technical, and financial commitments to halt the decline in vaccination coverage by December 2023. Countries must increase vaccination coverage for all antigens of the regional immunization program to achieve the 95% coverage threshold. These objectives must be prioritized given finite financial and human resources to address essential health needs and emerging health threats.
2. TAG strongly encourages PAHO to address this crisis at both the technical and political levels. Unless the political discourse leads to urgent action supported with the necessary resources, children are likely to die from several of the vaccine-preventable diseases. The first step is to stop the continued trend in declining vaccination coverage. The following objective will be to reach levels of coverage that the programs were so successful at attaining a decade ago.
3. In addition to ongoing consultations with ministries of health, PAHO must engage heads of government and ministries of finance as well as regional and global organizations such as the Organization of American States, the Inter-American Development Bank, and the World Bank, among other partners. PAHO should obtain unequivocal commitments to strengthen the regional immunization program, and work with these entities to establish clear goals and milestones to monitor progress. Further, PAHO should engage a broad range of donor organizations and partners to create a coalition for supporting national immunization programs at all levels. Such efforts should be a clear call to action to the governments and all stakeholders of the Americas to support action plans and multi-year budgets to implement the recommendations of Resolution CE168.R15 – Reinvigorating immunization as a public good for universal health. Resources should be provided to the PAHO regional secretariate to expand its field presence for prevention of VPDs in priority countries.
4. TAG is deeply concerned with the accumulation of large, multiple cohorts of under-vaccinated children across the Region. In 2021, 2.7 million children younger than 1 year across the Americas are unvaccinated or under-vaccinated, leaving them susceptible to many VPD (notably polio, measles, pertussis, diphtheria, rotavirus, and pneumococcal diseases). Countries must assess their vaccination coverage rates at the national and subnational levels to identify and vaccinate susceptible children. Where DTP3, polio3 or MMR2 coverage rates fall below 80%, countries should strengthen routine immunization service delivery and implement multi-antigen catch-up vaccination operations – periodic intensification of routine immunization (PIRI) activities, innovative local strategies (e.g., mobile vaccination teams, outreach activities, events where multiple health services are offered to the public in one location) – to close the immunity gap.
5. Because of the dangerous decline in population immunity for polio and measles, TAG strongly urges countries, where appropriate, to conduct multi-antigen vaccination follow-up campaigns in collaboration with PAHO technical assistance. For the priority groups at high risk for COVID-19 hospitalization and death, vaccination should be offered in these campaigns.

6. Given the risk of importations and cVDPV, TAG strongly recommends that countries that have not yet introduced the second dose of inactivated polio vaccine (IPV) in their national immunization schedule should do so immediately, in order to reduce the pool of children susceptible to poliovirus type 2 (PV2). Furthermore, countries should offer catch-up IPV1 and IPV2 doses to all eligible children immediately.
7. TAG reiterates its previous recommendation that countries do not discontinue the use of bOPV in favor of an IPV-only schedule at this time. Countries that have been classified as "very high risk", "high risk" or "medium risk" for polio by the RCC for at least one of the last three consecutive years should not stop the use of bOPV. It should be noted that many countries in the Region currently fall into this category.
8. Given the widening immunity gaps reported in all countries and territories of the Americas, TAG urges countries to expand the age range of their surveillance operations to include adolescents and adults who present with symptoms and signs of a VPD. For example, acute flaccid paralysis (AFP) cases should be investigated thoroughly for polio, even if the person is older than 15 years.
9. In accordance with WHO guidelines, countries must further reduce the number of persons in the Americas who have not received the primary series of COVID-19 vaccination. Countries should focus resources on high-risk priority groups such as the elderly, health workers and immunocompromised persons to reach 100% coverage with both primary series and booster doses to minimize hospitalization and death from COVID-19. Countries must achieve at least 70% vaccination coverage with primary series in the general population. At the same time, TAG recommends that government authorities reinstitute public health and social measures (i.e., mask wearing in crowded or closed locations, hand hygiene, social distancing) to minimize the spread of the SARS-CoV-2 virus in the population according to the epidemiological situation.
10. TAG recommends that countries continue to sensitize clinicians and other healthcare workers, and enhance surveillance and diagnostic capacity to identify and curtail spread of the multi-country monkeypox outbreak. TAG commends PAHO on its development of guidelines and training materials for clinicians to facilitate the detection of suspected monkeypox cases and recommends that the Organization expand these efforts to reach public and private health facilities and non-governmental organizations that cater to mainstream media networks and the general population.
11. Due to the extremely limited supply of vaccines against monkeypox, current allocation efforts must consider the geographic distribution of confirmed cases and the likelihood of viral spread. TAG recommends that the PAHO Revolving Fund for Vaccines (RFV) continue to work with vaccine manufacturers to map the expansion of vaccine capacity at the global level and promote the inclusion of equitable distribution of vaccine doses in the allocation algorithm.

References

1. World Health Organization. Polio Now. Geneva: WHO; 2022. Available from: https://polioeradication.org/polio-today/polio-now/ [Accessed 26 May 2022].
2. World Health Organization. OPV Cessation. Geneva: WHO; 2022. Available from: https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/opv-cessation/ [Accessed 15 April 2022].
3. Pan American Health Organization. Technical Advisory Group (TAG) on Vaccine-Preventable Diseases XXIII Meeting, Varadero, Cuba 1-3 July 2015. Washington, D.C.: PAHO; 2015. Available from: https://www.paho.org/hq/dmdocuments/2015/vaccine-preventable-diseases-tag23-2015-FinalReport-Eng.pdf [Accessed 15 April 2022].
4. World Health Organization. Country reports through the PAHO-WHO/UNICEF Joint Reporting Form (JRF). Geneva: WHO; 2022. Available from: https://immunizationdata.who.int/
5. World Health Organization. Polio endgame strategy 2019-2023: Eradication, integration, certification, and containment. Geneva: WHO; 2019.
6. World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, 22-24 March 2021: conclusions and recommendations. Geneva: WHO; 2021. Available from: https://www.who.int/publications/i/item/meeting-of-the-strategic-advisory-group-of-experts-on-immunization-22-24-march-2021-conclusions-and-recommendations [Accessed 15 April 2022].
7. Trueba G, Jeyaseelan V, Lopez L, Mainou BA, Zhang Y, Whittembury A, et al. Achieving high immunogenicity against poliovirus with fractional doses of inactivates poliovirus vaccine in Ecuador-results from a cross-sectional serological survey. Lancet Reg Health Am. 2022 Jul;11: Available from: https://www.sciencedirect.com/science/article/pii/S2667193X22000527
8. Pan American Health Organization. Technical Advisory Group (TAG) on Vaccine-Preventable Diseases XXI Meeting, Quito, Ecuador, 3-5 July 2013. Washington, DC: PAHO; 2013. Available from: https://www.paho.org/en/documents/21-tag-final-report-2013 [Accessed 15 April 2022].
9. World Health Organization. Inactivated polio vaccine. Geneva: WHO; 2022. Available from: https://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/ [Accessed 26 May 2022].
10. World Health Organization. Polio Eradication Strategy 2022–2026: Delivering on a promise. Geneva: WHO; 2021.
11. World Health Organization. nOPV2. Geneva: WHO; 2022. Available from: https://polioeradication.org/nopv2/ [Accessed 26 May 2022].
12. Kim–Farley RJ, Rutherford G, Lichfield P, Hsu ST, Orenstein WA, Schonberger LB, et al. Outbreak of paralytic poliomyelitis, Taiwan. Lancet. 1984 Dec 8;2(8415):1322-4.
13. Sutter RW, Patriarca PA, Brogan S, Malankar PG, Pallansch MA, Kew OM, Bass AG,et al. Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children. Lancet. 1991;338:715–720.
14. Asturias EJ, Dueger EL, Omer SB, Melville A, Nates SV, Laassri M, et al. Randomized trial of inactivated and live polio vaccine schedules in Guatemalan infants. J Infect Dis. 2007 Sep 1;196(5):692-8. doi: 10.1086/520546. Epub 2007 Jul 23. PMID: 17674310.

15. O'Ryan M, Bandyopadhyay AS, Villena RV, Espinoza M, Novoa J, Weldon WC, Oberste MS, et al. Inactivated poliovirus vaccine given alone or in a sequential schedule with bivalent oral poliovirus vaccine in Chilean infants: a randomized, controlled, open-label, phase 4, non-inferiority study. Lancet Infect Dis 2015; 15:1273–1282
16. Systematic review and meta-analysis of immunogenicity. SAGE WG Meeting, internal communication. 2020.
17. Pan American Health Organization. Weekly Situation Report on Monkeypox Multi-Country Outbreak Response - Region of the Americas. 15 July 2022. Washington, D.C.: PAHO; 2022. Available from: Weekly Situation Report on Monkeypox Multi-Country Outbreak Response - Region of the Americas. 15 July 2022 - PAHO/WHO | Pan American Health Organization [Accessed 17 July 2022].
18. Pan American Health Organization. Monkeypox cases - Region of the Americas. Washington, DC: PAHO; 2022. Available from: Monkeypox (pahobra.org). [Accessed 17 July 2022].
19. World Health Organization. Meeting of the International Health Regulations (2005) Emergency Committee regarding the multi-country monkeypox outbreak. Geneva: WHO; 2022. Available from: https://www.who.int/news/item/25-06-2022-meeting-of-the-international-health-regulations-(2005)-emergency-committee--regarding-the-multi-country-monkeypox-outbreak
20. World Health Organization. Vaccines and immunization for monkeypox: Interim guidance, 14 June 2022. Geneva: WHO; 2022. Available from: Vaccines and immunization for monkeypox: Interim guidance, 14 June 2022 (who.int)
21. The transmission potential of monkeypox virus in human populations. Fine PE, Jezek Z, Grab B, Dixon H.Int J Epidemiol. 1988 Sep;17(3):643-50. doi: 10.1093/ije/17.3.643.PMID: 2850277
22. McCollum AM, Damon IK. Human monkeypox. Clin Infect Dis. 2014;58(2):260 7. Available from: https://academic.oup.com/cid/article/58/2/260/335791
23. Conseil Supérieur del la Santé. Vaccination strategy against Monkeypox. Brussels: SHC; 2022. Available from: www.css-hgr.be
24. Centers for Disease Control and Prevention. Considerations for monkeypox vaccination. Atlanta: CDC; 2022.Available from: Considerations for Monkeypox Vaccination | Monkeypox | Poxvirus | CDC.
25. World Health Organization. Overview of available vaccines against smallpox & monkeypox Who R & D blueprint team meeting: "Monkeypox research: What are the knowledge gaps and priority research questions?" June 2 & 3, 2022. Geneva: WHO; 2022. Available from: https://www.who.int/news-room/events/detail/2022/06/02/default-calendar/who-monkeypox-research--what-are-the-knowledge-gaps-and-priority-research-questions
26. Robert Koch Institut. STIKO-Empfehlung zur Impfung gegen Affenpocken. Epidemiologisches Bulletin. 25/26 2022. 30 June 2022. Available from: https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2022/Ausgaben/25-26_22.pdf?__blob=publicationFile
27. Pan American Health Organization. Catalyzing ethical research in emergencies. Ethics Guidance, Lessons Learned from the COVID-19 Pandemic, and Pending Agenda.

Washington, DC: PAHO; 2022. Available from: https://iris.paho.org/handle/10665.2/56139
28. World Health Organization. Strategy to Achieve Global Covid-19 Vaccination by mid-2022. Geneva: WHO; 2021. Available from: https://www.who.int/publications/m/item/strategy-to-achieve-global-covid-19-vaccination-by-mid-2022
29. World Health Organization. Strategic preparedness, readiness and response plan to end the global COVID-19 emergency in 2022. Geneva: WHO; 2022. Available from: https://www.who.int/publications/i/item/WHO-WHE-SPP-2022.1
30. Pan American Health Organization. PAHO's recommendation regarding the WHO global target for COVID-19 vaccination coverage rate. Washington, D.C.: PAHO; 2022. Available from: https://www.paho.org/en/news/24-6-2022-pahos-recommendation-regarding-who-global-target-covid-19-vaccination-coverage-rate
31. World Health Organization. WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines. Geneva: WHO; 2022. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Prioritization-2022.1
32. World Health Organization. Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing. Geneva: WHO; 2022. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1
33. World Health Organization. COVID-19 Vaccines with WHO Emergency Use Listing. Geneva: WHO; 2022. Available from: https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued
34. United States Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Authorizes Moderna and Pfizer-BioNTech COVID-19 Vaccines for Children Down to 6 Months of Age. White Oak, Maryland: FDA; 2022. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-and-pfizer-biontech-covid-19-vaccines-children
35. World Health Organization. Interim statement on COVID-19 vaccination for children and adolescents. Geneva: WHO; 2021. Available from: https://www.who.int/news/item/24-11-2021-interim-statement-on-covid-19-vaccination-for-children-and-adolescents
36. World Health Organization. Interim recommendations for the use of the Janssen Ad26.COV2.S (COVID-19) vaccine. Geneva: WHO; 2022. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-Ad26.COV2.S-2021.1
37. New England Journal of Medicine. Final Analysis of Efficacy and Safety of Single-Dose Ad26.COV2.S. Massachusetts: NEJM; 2022. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2117608
38. World Health Organization. Interim statement on the composition of current COVID-19 vaccines. Geneva: WHO; 2022. Available from: https://www.who.int/news/item/17-06-2022-interim-statement-on--the-composition-of-current-COVID-19-vaccines
39. United States Federal Drug Administration. Coronavirus (COVID-19) Update: FDA Recommends Inclusion of Omicron BA.4/5 Component for COVID-19 Vaccine Booster

Doses. White Oak, MD: FDA; 2022. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-recommends-inclusion-omicron-ba45-component-covid-19-vaccine-booster

40. World Health Organization. Immunization dashboard. Geneva: WHO; 2022. Available from: https://immunizationdata.who.int/
41. Pan American Health Organization. XXVI Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases. Final Report, 2021. Washington, D.C.: PAHO; 2021. Available from: https://iris.paho.org/bitstream/handle/10665.2/54833/PAHOFPLIMCOVID-19210038_eng.pdf?sequence=1&isAllowed=y [Accessed on: 18 Jul 2022].
42. Pan American Health Organization. CE168.R15 - Reinvigorating Immunization as a Public Good for Universal Health. Washington, D.C.: PAHO; 2021. Available from: https://www.paho.org/en/documents/ce168r15-reinvigorating-immunization-public-good-universal-health