COVID-19

XXVI Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases

Vaccines bring us closer

14–16 July 2021
Virtual

COVID-19

XXVI Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases

Vaccines bring us closer

14–16 July 2021
Virtual

Washington, D.C., 2021

XXVI Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases. Vaccines bring us closer, 14–16 July 2021 (virtual)

PAHO/FPL/IM/COVID-19/21-0038

Table of Contents

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

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

*Not present at the meeting

Acronyms

AFP	Acute flaccid paralysis
AMC	Advance Market Commitment
bOPV	Bivalent oral polio vaccine, type 1 and 3
CDC	Centers for Disease Control and Prevention in the United States
COVAX	COVID-19 Vaccines Global Access
CRS	Congenital rubella syndrome
cVDPV	Circulating vaccine-derived poliovirus
cVDPV2	Type 2 circulating vaccine-derived poliovirus
DTP3	Diphtheria-tetanus-pertussis-containing vaccine, third dose
EPI	Expanded Program on Immunization
EUL	Emergency Use Listing
ESAVI	Event Supposedly Attributable to Vaccination or Immunization
GACVS	Global Advisory Committee on Vaccine Safety
GAPIII	WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use
GCC	Global Certification Commission
GDP	Gross domestic product
GPEI	Global Polio Eradication Initiative
HPV	Human papillomavirus
ICT	Information and communication technology
IEC	International Expert Committee for Documenting and Verifying Measles, Rubella and Congenital Rubella Syndrome Elimination in the Americas
IM	PAHO's Comprehensive Family Immunization Unit
IPV	Inactivated poliovirus vaccine
IPV2	Second dose of the inactivated poliovirus vaccine
JRF	PAHO-WHO/UNICEF joint reporting form
LAC	Latin American and the Caribbean
mL	Milliliter
MMR	Measles-mumps-rubella vaccine
MMR1	Measles-mumps-rubella vaccine, first dose
MMR2	Measles-mumps-rubella vaccine, second dose
MR	Measles and rubella vaccine
MR2	Measles and rubella vaccine, second dose
NCC	National Certification Committee
NIP	National Immunization Program
NITAG	National Immunization Technical Advisory Group
OPV	Oral polio vaccine
PAHO	Pan American Health Organization
PHSM	Public health and social measures
PCR	Polymerase chain reaction

PCV	Pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
RCC	Regional Certification Commission
RIAP	Regional Immunization Action Plan
RF	PAHO Revolving Fund for Access to Vaccines
SAGE	WHO Strategic Advisory Group of Experts on immunization
sIPV	Sabin inactivated polio virus vaccine
TAG	PAHO's Technical Advisory Group on Vaccine-Preventable Diseases
tOPV	Trivalent oral polio vaccine, type 1, 2 and 3
UNICEF	United Nations Children's Fund
VOC	Variants of concern
VPD	Vaccine-preventable disease
WHO	World Health Organization
WPV	Wild poliovirus
WPV1	Wild poliovirus, type 1

Introduction

Originally established in 1985 to discuss strategies for polio eradication, PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases convened its 26th meeting on 14-16 July 2021 to provide technical recommendations for the Region of the Americas and identify research needs to strengthen immunization programs.

PAHO's Assistant Director, Dr. Jarbas Barbosa da Silva, provided the opening remarks. In the two years since the last TAG meeting, the Region of the Americas has faced numerous public health emergencies. First, the Expanded Program on Immunization (EPI) in the Americas reported additional setbacks in routine vaccination and surveillance performance, reaching a 10% decline in DTP3 coverage over the last 10 years. The Region is at high risk of new and re-emerging outbreaks of vaccine-preventable diseases (VPDs). Second, the ongoing COVID-19 pandemic has put an additional strain on the national EPI and healthcare systems, while deflecting considerable resources to emergency response operations.

The combination of public health and social measures and the administration of COVID-19 vaccines are the main tools to mitigate the pandemic and can prevent serious illness and death. PAHO's priority is to ensure equitable access to COVID-19 vaccines for all people in the Region. PAHO remains committed to providing technical assistance to Member States while they implement national COVID-19 vaccination operations and intends to use the introduction process to further strengthen national routine immunization programs.

The TAG Chair, Dr. Peter Figueroa, opened the meeting by welcoming all participants: TAG members; representatives of national immunization programs; presidents of the National Immunization Technical Advisory Group (NITAG); Dr. Alejandro Cravioto, chair of WHO's Strategic Advisory Group of Experts (SAGE) on immunization; and all representatives from partner agencies. Dr. Figueroa took this opportunity to recognize the contributions of health workers and public health officials whose efforts during the pandemic saved lives while maintaining all operations of the national immunization programs. He concluded by issuing a strong call to Member States to act against the spread of VPDs in the time of COVID-19.

Update on Recent Progress and Challenges of the Regional Immunization Program

The world was experiencing a stall 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 third dose of the diphtheria, tetanus, and pertussis (DTP) vaccine, leaving 19.7 million children vulnerable to VPDs. Almost half of those children live in the African region.

The Region of the Americas has been reporting a steady decline in vaccination coverage since 2010. The Region's DTP3 coverage rate dropped from 94% to 84% between 2010 and 2020[i]. The decline in coverage occurred in most countries of the Region, leading to a larger population of individuals susceptible to VPDs. There are multiple reasons for the decline, including natural disasters, displacements, progressive urbanization, the political context, and growing inequities in access to healthcare. The COVID-19 pandemic exacerbated existing trends and forced governments to redirect scarce resources to emergency response operations. Access to healthcare services remains limited because of the demands of the pandemic response. As a result, between January 2019 and January 2020, DTP3 and MMR coverage declined 33% and 24%, respectively. The COVID-19 pandemic has also affected VPD surveillance systems. Reductions in the timeliness and quality of epidemiologic and laboratory surveillance contributed to outbreaks of measles and rubella, pertussis, diphtheria, yellow fever, and other VPDs. The report from the Economic Commission for the Latin America and Caribbean projects a 9.1% decline in the regional gross domestic product (GDP) for 2021, which greatly impacts funding for the healthcare sector.

Despite these challenges, many national immunization programs have been able to adapt and continue offering routine immunization and surveillance services. Many countries have implemented mass vaccination campaigns against measles/rubella, influenza, yellow fever, and polio to reduce the number of unvaccinated children and avoid VPD outbreaks. However, although immunization coverage levels had recovered to pre-COVID-19 pandemic levels by approximately August 2020, follow-ups of missed cohorts have so far been slow and incomplete.

The 2016-2020 Regional Immunization Action Plan (RIAP) lists 29 indicators; 15 have been attained; 9 are ongoing; and 5 are off track. PAHO's Comprehensive Family Immunization Unit (IM) has been working closely with PAHO country offices, the countries' National Immunization Technical Advisory Groups (NITAGs), ministries of health, and PAHO's Revolving Fund to implement the actions delineated in the RIAP. Below we report on the status of each indicator, by objective:

1. Sustain achievements: While the Region has remained polio-free and work continues to communicate the value of vaccines to individuals and communities, the Region has not regained its elimination status for measles and rubella. Also, the Region has not maintained its achievements in VPD control.

[i] Data up to 2 July 2021.

2. Address the unfinished agenda: The Region has eliminated neonatal tetanus and increased equitable access to immunization services. Nonetheless, vaccination coverage rates lag behind the established targets. Only 9 of the 34 countries in the Region achieved the 95% vaccination coverage target for DTP3, while 11 report coverage rates below 80%. Also, between 2019 and 2020, 8 countries reported 1%-5% decreases in the DTP3 coverage rate, and 16 reported decreases greater than 5%. In 7 countries, the DTP1-DTP3 dropout rate is higher than 10% and reaches 24% in Panama and 26% in Venezuela. The number of unvaccinated children in Latin American and Caribbean countries in 2020 stood at almost 2.2 million.

3. Tackle new challenges: During this five-year period, multiple vaccines (i.e., rotavirus, pneumococcus, HPV) were introduced in a sustainable manner. Efforts to base decision-making on high-quality data and impact assessments are ongoing. The working group responsible for the resolution "Defeating Meningitis by 2030" is working on a landscape analysis of the burden of disease in the Region; its goal is to prioritize countries for implementing the roadmap.

4. Strengthen health services: The Region is on track to achieve expected results proposed by the Sustainable Development Goals (SDGs) for reductions in infant and maternal mortality. Also, supplies are available through national resources on a sustainable basis. However, work continues to strengthen immunization services as part of comprehensive, well-run health services. Specifically, additional effort is needed to ensure that: a) all people have permanent access to vaccines, starting with the most disadvantaged; b) countries implement inter-programmatic coordination when submitting their demands to PAHO's Revolving Fund; c) cold-chain and supply logistics are well managed; and d) vaccine safety is paramount at all levels of the immunization program.

Moving forward, the Region of the Americas plans to implement its strategic priorities to support and maintain its national immunization programs. The goals are: a) reduce mortality and morbidity from VPDs for everyone throughout the life course; b) leave no one behind by increasing equitable access and the use of new and existing vaccines; and c) ensure good health and well-being for everyone by strengthening immunization in primary health care and by contributing to universal health coverage and sustainable development.

Also, given the ongoing weak performance of immunization programs and the COVID-19 pandemic, Member States endorsed the policy of "Re-invigorating Immunization as a Public Good for Universal Health" during the 168th session of PAHO's Executive Council (21-25 June 2021). This policy includes six strategic lines of action; they are embedded in the new Regional Immunization Action Plan 2021-2030 and aligned with the WHO's Immunization Agenda 2030:

1. Enhance monitoring of vaccine coverage and surveillance, incorporating digital intelligence strategies into routine analysis.
2. Strengthen the integration of immunization programs into the primary healthcare system towards universal health.
3. Develop innovative and strategic communication to build social awareness and trust in vaccines and increase access to services.
4. Strengthen human resource capacities for immunization programs.
5. Use scientific evidence to guide decision-making and program implementation.

Recommendations

- The TAG recognizes that, at this time, countries and governments must give priority to the COVID-19 pandemic response. However, the Region is facing an impending crisis around routine vaccination, and ongoing attention must be given to sustaining and strengthening the immunization and other essential health programs. Declining immunization coverage rates accompanied by loosening or cessation of public health and social measures (PHSM) will predictably result in increases in many VPDs, such as measles, influenza, diphtheria, pertussis, most likely involving several countries. Any failure to act now will generate additional outbreaks, which will further damage lives and economies.
- The TAG welcomes and fully endorses the policy of "Re-invigorating Immunization as a Public Good for Universal Health" that was approved by the 168th session of PAHO's Executive Council.
- TAG encourages countries to faithfully implement the lines of action laid out in this policy to reverse the dangerous decline in immunization coverage and surveillance indicators over the past decade, which were further impacted by the COVID-19 pandemic.
- Governments must commit themselves to taking full responsibility for their immunization programs as a priority of immense value, to invest the necessary resources in all components of the program, ensure an appropriate legal framework to sustain the program, and promote full vaccination across the life course. The TAG recommends that governments prioritize routine childhood immunizations and, whenever possible, conduct high quality, multi-antigen follow-up campaigns, which are adequately supported by human and financial resources.
- Governments must support their NITAGs, which play a critical role in providing independent expertise and guidance that enhances and provides credibility to immunization programs. In this context, the TAG calls for the re-establishment of the NITAG in Brazil.
- The TAG requests that PAHO include more detailed epidemiologic analysis of reported VPDs in its vaccination coverage and surveillance reports. The focus on gaps in coverage is warranted but should be complemented with more epidemiological information (e.g., incidence and mortality rates; stratification by age, sex, and geographical levels).

Digital Health in Immunization

The use of digital, mobile, and wireless technologies to support the achievement of health goals is known as digital health. It is a practical option to address multiple problems in immunization programs and digital health has become of primary interest to countries in the Region. To support its implementation, multiple resolutions and documents have been endorsed, including:

- United Nations General Assembly Resolutions 73/218 (2019) and 70/125 (2016)
- Sustainable Development Goals
- The World Health Assembly Resolution on Digital Health, approved unanimously by WHO Member States in May 2018
- Immunization Agenda 2030
- PAHO Resolutions:
    - Roadmap for the digital transformation of the health sector in the Region of the Americas
    - Policy on the application of data science in public health using artificial intelligence and other emerging technologies
    - Revitalization of immunization as a public good for universal health

Although digital health can be used in any area of health, countries of the Americas should take advantage of this opportunity to strengthen immunization programs.

Based on the theory of the change presented in the 2019 TAG meeting, we propose to include the eight guiding principles for digital health[ii] that frame and strengthen the use and quality of data on immunizations throughout the life course. These guiding principles should generate improvements in the management, demand, acceptability of, and confidence in vaccines in the Americas and the world. Governments must prioritize, as appropriate, developing, evaluating, implementing and expanding digital technologies in addition to implementing evidence-based digital health interventions.

A digital health intervention is defined as applying digital technology functionality to achieve health goals; it is implemented within digital health applications, and information and communication technology systems, including communication channels. WHO recently developed the classification of digital health interventions based on desired objectives. Some of the interventions can be adapted to the different components of the immunization program and during the life cycle. For example, databases for birth notifications can be interoperable with

[ii] 1. Ensure universal connectivity in the health sector by 2030. 2. Co-create digital public health goods for a more equitable world. 3. Accelerate toward inclusive digital health with an emphasis on the most vulnerable. 4. Implement interoperable, open, and sustainable digital health and information systems. 5. Mainstream human rights in all areas of digital transformation in health. 6. Participate in global cooperation on artificial intelligence and any emerging technology. 7. Establish mechanisms for trust and information security in the digital environment of public health. 8 Design public health architecture in the era of digital interdependence.

electronic immunization registries, so that these registries already incorporate the number children born and can more easily determine the proportion of unvaccinated children.

The COVID-19 pandemic has been an opportunity to introduce multiple digital solutions in healthcare systems of the Region, and these innovations can be used as the starting point for additional advances. Appointment scheduling, dashboards and electronic records are examples of how the Region has advanced in its digital transformation. However, there are many challenges, including subpar infrastructure, limited internet access, low digital literacy, implementation of interventions that were designed without considering the end-user, or interventions that were implemented without in-depth review or pilot testing/evaluation. These hasty or incomplete digital solutions put progress at risk.

Therefore, we propose that Governments compensate for the infrastructure and technology limitations of their country, and ensure both political and financial commitment. We also propose strengthening safety standards and interoperability, and to focus primarily on the training of healthcare workers to ensure their ability to adopt these innovations.

Recommendations

- The TAG welcomes and strongly supports the digital transformation of immunization programs and health services that PAHO has initiated in the Americas, and it endorses the eight principles that underpin the conceptual framework of the digital transformation of the health sector. The TAG acknowledges that this is a long-term endeavor that will require long-term commitment.
- The TAG commends countries for their rapid incorporation of a range of new digital tools and strategies to improve monitoring and response to the COVID-19 pandemic. These new tools should be retained and further developed to benefit national immunization programs and other essential health programs on a sustainable basis.
- The TAG recognizes the lack of adequate digital infrastructure in many areas of the Region and encourages the leadership of countries to take whole-of-government approaches and invest the necessary resources to ensure adequate infrastructure and provide internet connectivity to all healthcare organizations and staff.
- To promote digital literacy and competence among all health workers, the TAG encourages on-the-job training and developing and implementing educational courses and practical in health and training institutions.
- Countries should invest in identifying, hiring, and retaining health staff who are familiar with digital health technologies and who can incorporate them into everyday practices.

Regional Update in Measles/Rubella Elimination in the Region of the Americas

The COVID-19 pandemic hit the Region of the Americas harder than other regions of the world: 40% of cases and 48% of deaths were reported in our Region as of 29 June 2021. Additionally, the United States, Brazil, Argentina, and Colombia are among the top 10 countries with the highest number of COVID-19 cases reported globally. These countries, along with Mexico and Peru, are also on the list of countries with the highest number of deaths reported worldwide. Implementation of public health and social measures and lockdown by governments to mitigate the pandemic may have also impacted the circulation of other diseases transmitted by respiratory droplets and/or aerosols, including measles and rubella virus, and limited their importation and transmission at the country level.

Measles outbreaks in the Americas, 2020-2021

Between 1 January 2020 and 30 June 2021, the Americas reported 9,205 confirmed measles cases in nine countries[iii]. 97% of the cases were reported in Brazil, where endemic transmission has been sustained since February 2018.

In 2020, Argentina (n=61) and Mexico (n=194) successfully interrupted their outbreaks with a well-organized rapid response and innovative strategies to vaccinate susceptible individuals amidst the COVID-19 pandemic. Genotypes D8 and B3 were identified in 99% of cases in the Region where specimens for virus detection were available. The ongoing sequence analysis between the identified genotypes showed different lineages. Nevertheless, the lineage *Gir Somnath.IND/42.16* was identified in 69% of cases in 2020, with predominant circulation in Brazil.

As a result of the measles outbreaks, a total of 122 deaths were reported in the Americas for the period 2017-2021. Venezuela and Brazil reported the highest percentage of deaths (66% and 32%, respectively), which occurred primarily among children under five years.

Measles outbreak in Brazil and Venezuela

At the beginning of 2020, 21 of 27 states in Brazil had measles outbreaks; by the end of the year, only four states (São Paulo, Rio de Janeiro, Para, and Amapá) reported confirmed cases**.** These states conducted vaccination campaigns aimed at unvaccinated children younger than 15, and young adults; however, the coverage achieved was less than 40%. In 2021, measles virus continues circulating in the states of Para, São Paulo, and Amapá, where the highest proportion of cases (80%) has been reported.

In 2020, MMR1 and MMR2 vaccination coverage was reduced by 13% and 23%, respectively, in comparison to 2019. In addition, the low homogeneity of vaccination coverage (ranging between 42% and 56%) reported in the last three years (2018-2020) highlights the need for continuing to

[iii] For 2020: Argentina (n=63), Brazil (n=8,448), Bolivia (n=2), Canada (n=1), Colombia (n=2), Chile (n=2), Mexico (n=194), United States (n=13), and Uruguay (n=2). For 2021: Brazil (n=456) and United States (n=2).

implement tailored activities to close immunity gaps that fuel transmission of the measles virus. Some surveillance indicators were impacted by the pandemic as well. For example, reported annual notification rates and adequate investigation and sample indicators did not meet the regional target.

Venezuela successfully interrupted its measles outbreak in 2019 (rash onset of the last confirmed case: 19 August), with no confirmed cases reported; all suspected cases were discarded by laboratory. The country made significant efforts to sustain this achievement in 2020 amidst the COVID-19 pandemic. Two surveillance indicators (percentage of cases adequately investigated, and timely sample collection) were optimal; annual notification rates for suspected cases were also optimal, but the two laboratory indicators were negatively impacted by the pandemic. Like other countries, Venezuela reported that MMR1 vaccination coverage declined in 2020; it was down 18% compared to 2019. The country maintains its political commitment to sustain measles and rubella elimination and to this end, it has implemented actions such as lowering the age of MMR2 to 18 months, establishing sanitary checks in border areas, and intensifying surveillance actions in silent areas.

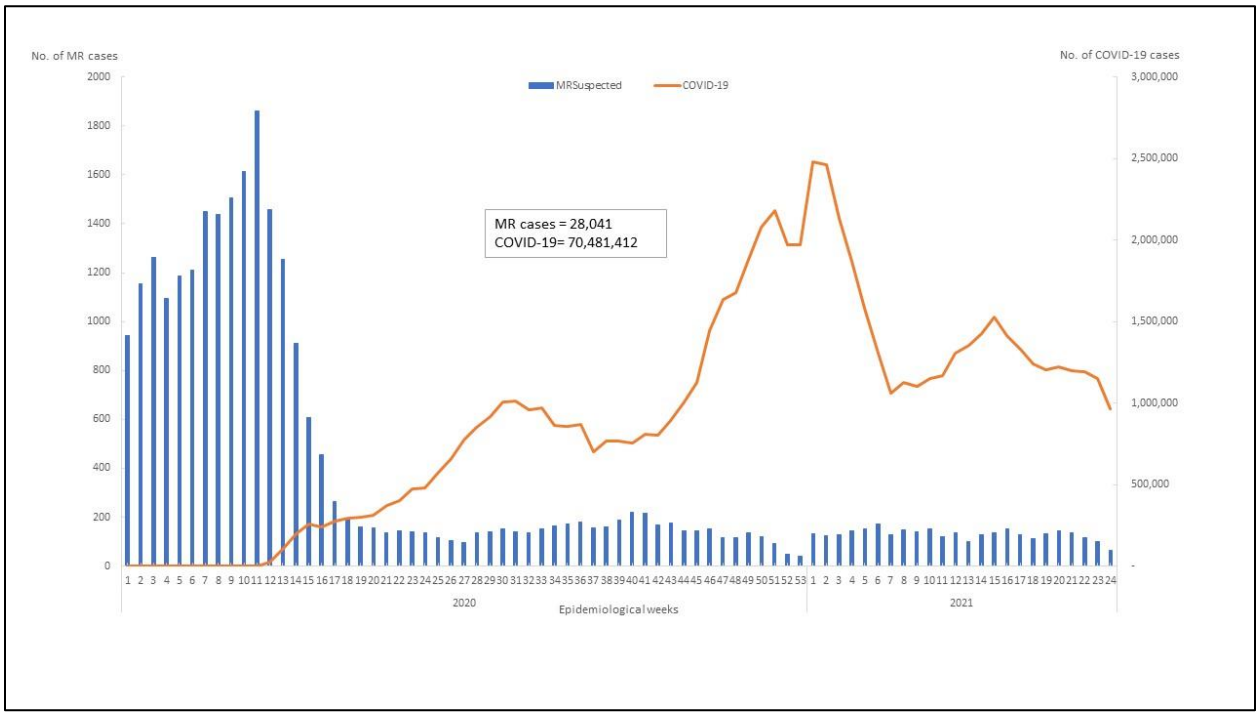
Rubella in the Americas, 2020-2021

Between 1 January 2020 and 30 June 2021, only two imported rubella cases were reported in the United States. No cases of congenital rubella syndrome were confirmed in any country of the Region. Integrated actions to eliminate measles, through vaccination and epidemiological surveillance, have made it possible to sustain rubella elimination over the last 10 years.

Performance of measles and rubella surveillance indicators

The COVID-19 pandemic has significantly affected the epidemiological surveillance of measles and rubella. **Figure 1** highlights the sudden downward trend in reporting suspected measles and rubella cases, which coincides with the peak of the COVID-19 pandemic in the Americas Region. The notification of suspected cases decreased by 73% in comparison to 2019. Fewer suspected cases reported allowed for optimal compliance ($\geq$80%) with the indicator of percentage of timely collected samples.

Figure 1. Notification of Measles, Rubella (MR), and COVID-19 Cases by Epidemiological Week, Region of the Americas, 2020-2021

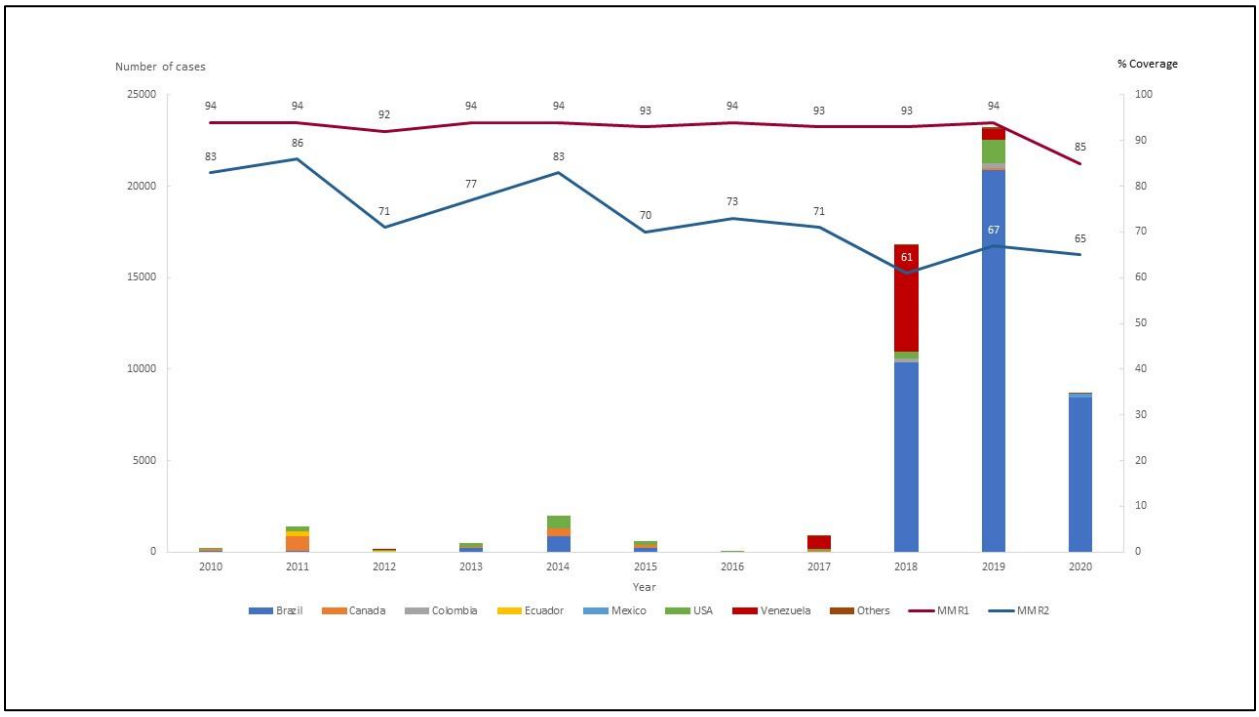


Source: Surveillance country reports sent to PAHO. Canada and the United States only report total number of confirmed measles cases. Data as of epidemiological week 24, 2021.

Vaccination coverage with MMR1 and MMR2

A steady regional coverage trend with MMR1 was observed for the period 2010-2019 (range between 92%-94%). Nevertheless, preliminary coverage data for 2020 indicate coverage fell to 85%, a 10% reduction. In contrast, regional vaccination coverage with the second dose has fluctuated sub-optimally during the 10-year period (range 65%-86%) without reaching optimal levels of 95%. The drop in coverage for the second dose between 2018 and 2020 was as much as 6% compared to 2017. Countries of the Americas introduced the second dose in their national schedules starting in 2000. The 2020 data are preliminary, as only 30 of 35 Member States and two territories submitted information to PAHO **(Figure 2)**.

Figure 2. Distribution of Confirmed Measles Cases and Regional Coverage for MMR1 and MMR2* in the Post-Elimination Era, The Americas, 2010-2020



Source: ISIS/MESS, Measles Epidemiological Alert and PAHO-WHO/UNICEF Joint Reporting Form (JRF). * Preliminary coverage data based on 30 countries and 2 territories. Data as of 22 June 2021.

Status of follow-up campaigns in 2020-21

A point in favor for the Region is the systematic implementation of follow-up campaigns in each country to maintain coverage with two doses among children under age five and among groups ages 5 to 10. Between 2020 and 2021, eight countries that had reported a decrease in MMR1 and MMR2 vaccination in 2020 compared to 2019 decided to implement follow-up campaigns to reduce the number of susceptible population and targeted to vaccinate 24.7 million children under age 10. The countries are Bolivia, Colombia, Chile, Dominican Republic, Honduras, Mexico, Paraguay, and Venezuela. As of 30 June 2021, Chile, Mexico, Colombia, and Bolivia have started or completed their campaigns; the levels of progress vary **(Table 1)**.

Table 1. Status of Measles/Rubella Follow-Up Campaigns, 2020-21

Country	Type of vaccine	Start Date	End Date	Target Age Group	Target Number to Vaccinate	Status	Other vaccines
Chile	MMR	10/2020	12/2020	1-6y	1,448,793	Completed (57%)	
Colombia	MR	04/2021	08/2021	1-10y	7,575,807	In progress	
Mexico	MR	04/2021	07/2021	1-9y	8,613,161	In progress	MMR, polio, hexavalent
Bolivia	MMR	06/2021	07/2021	1-5y	1,183,283	In progress	Polio
Honduras	MMR	08/2021	10/2021	1-5y	1,166,999	Planned	Polio
Paraguay	MR	10/2021	12/2021	1-8y	1,126,927	Planned	Polio
Dominican Republic	MR	10/2021	12/2021	1-5y	956,182	Planned	
Venezuela	MMR	10/2021	12/2021	1-5y	2,692,674	Planned	Polio

Molecular epidemiology

Molecular epidemiology has been useful in documenting the interruption of endemic virus transmission, and WHO has defined it as one of the criteria for evaluating progress in eliminating measles. A global reduction in the variability of measles genotypes was seen during the last three years and a similar situation was evident in the Americas; since 2018, only two measles genotypes (B3 and D8) were reported to the Measles Nucleotide Surveillance (MeaNS).

During 2018 to 2020[iv], 14 countries reported a total of 2,106 measles sequences to MeaNS[v]. Of this total, 94% corresponds to D8 genotype, for which nine different lineages were identified. Lineage MVi/Hulu Langat.MYS/26.11/ was mostly reported in 2018, while lineage MVs/Gir Somnath.IND/42.16/ was reported in 2019 and 2020, with a total of 306 and 1,152 sequences, respectively. Therefore, both lineages were frequently detected in outbreaks in countries such as Argentina, Brazil, Mexico, and Venezuela, among others. In addition, genotype B3 was only detected in confirmed measles cases reported by the United States, where seven different lineages were identified.

[iv] 2018 (508 sequences), 2019 (1301 sequences), and 2020 (298 sequences).

[v] Antigua and Barbuda, Argentina, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Ecuador, Guatemala, Mexico, Peru, United States, and Venezuela

Recommendations

- The TAG expresses concern that large declines in MMR coverage have led to a rapidly expanding pool of susceptible persons across the Region, which, coupled with the loosening of physical distancing measures, points to an impending measles epidemic that will likely involve several countries.
- The TAG calls on governments in the Americas to take urgent corrective actions to ensure 95% coverage with two doses of the MMR vaccine among children younger than two, to meet the standards of high-performing surveillance, and to conduct periodic follow-up and targeted campaigns for vulnerable populations and cohorts of older age groups.
- Countries are urged to ensure that the Region of the Americas once again achieves and sustains WHO's target of eliminating measles and rubella.
- Whenever possible, countries should conduct high-quality, multi-antigen follow-up campaigns that are adequately supported by human and financial resources.
- The TAG calls on WHO to establish a global target to support eliminating measles and rubella. Without such a target, it is becoming increasingly more difficult to sustain Measles and Rubella Elimination (MRE) in the Americas.
- The TAG recognizes the hard work and commitment of those countries that have already conducted campaigns to control outbreaks and follow-up campaigns.
- It is essential for Brazil to fully control the ongoing measles outbreak and prevent future resurgences.
- Both WHO and PAHO should mobilize political commitment to address the ongoing measles outbreak in Brazil. The first step should be to advocate for reactivating the Brazilian NITAG, which was disbanded in 2019. The NITAG can provide strong and independent technical recommendations to respond to the COVID-19 pandemic, end the measles outbreak, and prevent future outbreaks of VPDs.
- The TAG recommends that countries strengthen their national capacity for rapid response to virus importations outbreak by using e-learning courses in outbreak management. It also recommends that countries conduct training in risk assessment analysis for implementing tailored interventions at the local level.
- The TAG appreciates the critical role of the Regional Commission for Monitoring and Reverification of Measles, Rubella, and Congenital Rubella Syndrome Elimination and encourages it to continue its essential function. The commission will continue to work closely with the TAG to monitor progress and the status of MRE in the Americas.

COVID-19 Vaccination in the Americas

Progress and Lessons Learned from COVID-19 Vaccination in the Americas

Vaccination status at the global level

As of 12 July 2021, the world had recorded 185 million COVID-19 cases and over 4 million COVID-related deaths. Meanwhile, since December 2020, more than 3.6 billion doses of COVID-19 vaccines have been administered around the world.. Of these, 20% were administered in the Americas. All vaccines approved by WHO and national regulatory agencies are safe and efficacious against COVID-19. Despite this success, governments must be mindful of discontinuing public health and social measures. Lifting them too early could lose some of the gains that vaccines have made possible. Also, safe and effective vaccines alone cannot solve the pandemic.

Rapid diagnostics and life-saving therapeutics are vital to ending the pandemic and accelerating global recovery. However, these life-saving tools will only be effective if they are made available equitably and simultaneously to the most vulnerable people in all countries, and if strong health systems and services are in place to deliver them. Vaccines are effective against severe disease caused by the variants, but variants will continue to flourish if the globally inequitable rollout of vaccines is not addressed. As of July 2021, high-income countries had administered 69 times the number of vaccine doses as low/middle-income countries.

As of 9 July 2021, WHO was monitoring 291 candidate vaccines: 107 in a clinical phase and 184 in a pre-clinical phase. These vaccines represent different platforms, from viral vectors to inactivated/attenuated to messenger RNA. Six vaccines were reviewed and approved by WHO's Emergency Use Listing (EUL) process and the Strategic Advisory Group of Experts (SAGE) on immunization. The vaccines are produced by pharmacological manufacturers Pfizer, Moderna, Janssen, Sinopharm, Sinovac, and AstraZeneca. The latter produces its vaccine in multiple locations around the world: South Korea (SK Bio), India (Serum Institute of India), Italy (Catalent), China (Wuxi), and Spain (Chemo Spain). All the production sites have been reviewed and approved through EUL procedures.

Vaccination status of the Americas

As of 9 July 2021, the Region of the Americas reported that 647,435,811 doses of COVID-19 vaccine had been administered in 49 of its 51 countries and territories. As a result, 265,129,115 persons received a full series of the vaccine and can be considered to be fully immunized. Most of the vaccine doses have been administered in the United States (48.5%), while Latin America and Caribbean countries administered 42%. Among these, Brazil administered the greatest percentage: 13.6%. Of the 49 countries and territories, 35 are using the vaccine produced by AstraZeneca, making this the most widely used vaccine. However, if we consider the type of vaccine with the highest number of doses administered, the top vaccines are Pfizer (216 million)

and Moderna (140 million). Countries and Central and South America, in contrast, report vaccination rates below 20% after months of vaccination operations.

Vaccination status in sub-regions of the Americas

In North America, vaccination coverage rates for Canada and the United States are approximately 48.5%; Mexico reports that 15.9% of its population is fully immunized. In the United States, data reported by the US Centers for Disease Control and Prevention (CDC) show a clear decline in number of COVID-19 cases by age group as vaccination coverage rates increase. According to Yale University and the Commonwealth Fund, it is estimated that COVID-19 vaccines averted about 279,000 deaths in the USA by the end of June 2021. Around 1.25 million people would likely have been hospitalized were it not for the vaccines.

In Central America, vaccination rates range from nearly 20% in El Salvador to less than 1% in Honduras. In the latter country, deliveries of Pfizer and AstraZeneca from COVAX, a worldwide initiative aimed at equitable access to COVID-19 vaccines, have been very small, barely enough to cover 0.9% of the eligible population. Incoming donations of Moderna vaccine from the USA will alleviate some of the shortages

In the Andean region, vaccination rates also range widely, from nearly 16% in Colombia to less than 1% in Venezuela. In Brazil, nearly 13.6% of the adult population has been fully immunized. Many countries in this sub-region prioritized indigenous groups for vaccination. Indigenous groups were included among the high-risk priority populations in the national vaccination plans, civil societies were actively engaged in vaccination micro-planning, and additional resources were dedicated to reaching those populations. Brazil maintains the Region's only dashboard to monitor vaccination rates among indigenous groups, and the four Andean countries launched cross-border programs to reach all indigenous communities as soon as COVID-19 vaccines became available.

In the Southern Cone, vaccination rates are above 50% in Chile and Uruguay, but hover at about 10% in Argentina and 2% in Paraguay. The latter country depended heavily on COVAX for vaccine procurement and access, but delays in shipping have created a large gap in vaccine availability. Chile, on the other hand, significantly reduced the number of reported COVID-19 cases, hospitalizations, and deaths through a combination of COVID-19 vaccination and non-pharmaceutical mitigation measures. Also, Chile has been active in measuring "real world" vaccine effectiveness for Sinovac inactivated COVID-19 vaccine through a cohort of 10.5 million citizens.

In the Caribbean, vaccination rates vary considerably between countries and territories. A combination of bilateral agreements and COVAX shipments allowed small countries to receive enough vaccine doses to immunize all citizens. However, larger countries received the same small shipments as some countries in South America, and their vaccination coverage rates are below 10%. A clear example is the comparison between Bermuda (54% vaccination rate) and Jamaica

(9% vaccination rate). Also, some territories were included in the vaccination plans of European countries, and therefore received vaccine doses through that channel, too.

Vaccine dose forecasting

Up until now, vaccine allocation and administration have been marred by deep inequalities among countries in the Americas. As of 9 July, donated doses made up 70% of the COVAX Mechanism. Fortunately, starting in September 2021, WHO foresees a large increase in the availability of vaccine doses through the COVAX Mechanism. Indeed, starting in the third quarter of 2021, WHO predicts a pivot from supply constraints to demand constraints. In the second part of 2021, COVAX expects to receive 1.75 billion doses from vaccine manufacturers and donors. Of these, 1.36 billion will become available in the last quarter of 2021.

Ongoing challenges

Since COVID-19 vaccines were introduced in December 2020, their use has raised numerous questions about their safety, effectiveness, and quality. While some questions have been answered satisfactorily, many questions remain. Below are questions that were addressed during this TAG meeting:

- Access and distribution of COVID-19 vaccines to Member States
- Demand and confidence in COVID-19 vaccines
- Adverse events following immunization, including thrombosis with thrombocytopenia syndrome (TTS)
- Prioritization of high-risk groups (see updated SAGE roadmap)
- Interchangeability of COVID-19 vaccines
- Vaccination of pregnant and breastfeeding women
- Vaccination of children
- Vaccine effectiveness and variants of concern

COVID-19 Vaccine Allocation and Supply Mechanism: Challenges and Lessons Learned

Sustaining access to routine vaccines

The pandemic has drastically affected the Region's national immunization programs, especially the delivery of and demand for immunization services in communities and health centers. Globally, it has affected the timely availability and freight costs of many vaccines. Factors contributing to the shortages include a) problems in export licensing, scaling up production, and releases of batches; b) bilateral agreements locking in future doses (especially availability during 2021) with a risk portfolio approach that goes beyond national needs; and c) overly optimistic forecasts by suppliers regarding their projected production capacities, which are not materializing in 2021. The supply delays have impacted planned deliveries, putting participants' confidence and trust in the COVAX Facility at risk.

The PAHO Revolving Fund (RF) has played a critical role in ensuring the sustainability of immunization supply chains (for vaccines, safe injection devices, and cold chain equipment) during the pandemic. PAHO continues to work closely with national immunization programs in

preemptive planning for fluctuations in national vaccine demand, triaging supply allocations and monitoring national vaccine inventories. PAHO also works with vaccine manufacturers and international partners to carefully monitor disruptions in logistics and other risks that suppliers may be confronting.

Accurate demand-planning is more important than ever to minimize the risks of interrupted access to life-saving vaccines. The Revolving Fund Capital Fund continues to provide critical bridge-funding support for financial sustainability to requesting Member States. During 2019 and 2020, the average annual procurement value was approximately $765 million despite declining DTP3 and MMR1 coverage trends.

As of mid-July 2021, the Revolving Fund was in the process of consolidating 2022 routine vaccine demand through its improved PAHO-173 tool. The consolidated demand will be analyzed with programmatic projections for increased forecasting accuracy and multi-year contracting. The Revolving Fund is also in the process finalizing the design and implementation of an online demand collection platform for routine vaccines; the tentative release is October 2021, for Q1-Q2 2022 demand reconfirmations.

Update on the COVAX Facility progress and supply projections

The Revolving Fund provided briefings on access to COVID-19 vaccines to the Regional TAG on Vaccine-Preventable Diseases, which convened in August and October 2020. On 10 December 2020, there was a special session of the Directing Council to update Member States on "the COVID 19 Pandemic in the Region of the Americas, COVAX Preparedness, and Equitable Access to COVID-19 Vaccines[vi]." Two critical resolutions (CSSS1.R1)[vii] on COVID-19 vaccines access requested that the Director:

- Maintain coordination with international partners and advocate with them to leverage existing capacities and economies of scale through joint pooled procurement in order to obtain a low, flat price for PAHO Member States participating in the Revolving Fund so as to secure equitable access to COVID-19 vaccines for the population, including migrant populations.
- Negotiate to attain for those Member States participating in the Revolving Fund access to COVID-19 vaccines at the best possible price and, if necessary, make an exception and adjust the terms and conditions of the Revolving Fund to address the special circumstances needed to secure a supply of COVID-19 vaccines.

[vi] https://www.paho.org/en/governing-bodies/directing-council/special-session-directing-council
(Please see the working document CDSS1/2 and the final report CDSS1/FR in the link for details)
[vii] https://www.paho.org/en/documents/cdss1r1-update-covid-19-pandemic-region-americas-covax-preparedness-and-equitable-access

The most recent update to PAHO governing bodies was provided during the 168th Session of the Executive Committee on 21-25 June 2021. The document CE168/INF/1 provided updates on the access of COVID-19 vaccines and COVAX Facility progress [viii].

The Revolving Fund, as a key component of PAHO's overall COVID-19 pandemic response package, is an important platform by which Member States of the Americas can access vaccine through the COVAX Facility. A total of 26 self-financing Member States (including Canada) and territories participating in the COVAX Facility represent approximately 33% of the projected global procurement volume for the self-financing participants. Despite ongoing national budgetary and fiscal challenges during the pandemic, self-financing participants allocated more than $1.1 billion for down payments and financial guarantees in order to meet the COVAX Facility's financial requirements during Q4 2020.Another 10 Member States were eligible for the Advance Market Commitment (AMC) support through COVAX.

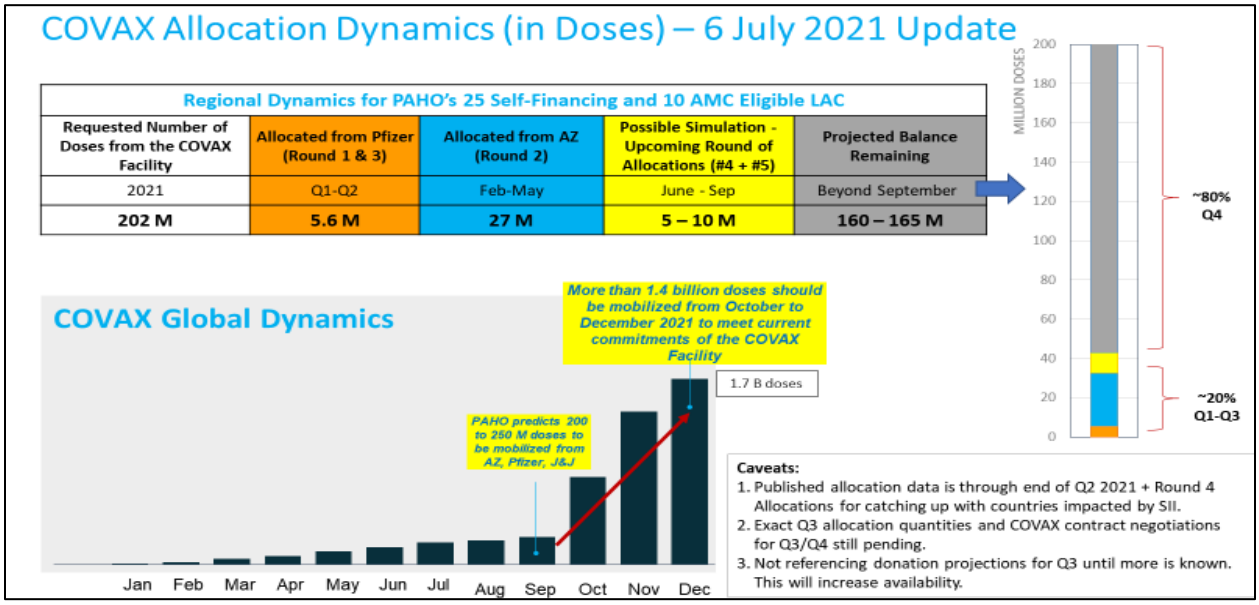
The commitments of the 36 countries participating in COVAX represent approximately 202 million vaccine doses from the COVAX Facility. However, compared to the contractual projections of Gavi advance purchase agreements, COVAX has been facing significant supply shortages since March 2021.

By the end of June 2021, only 24.7 million doses were delivered to participants through COVAX, representing just 12% of the commitment of 202 million doses, about 1.8% of the population coverage, on average. Based on the latest availability indications from COVAX, the Revolving Fund projects that a maximum of 35 million doses will be delivered (excluding donations) by the end of Q3 2021. This amount corresponds to coverage for approximately 2.5% of the population, on average.[ix]

[viii] https://www.paho.org/en/documents/ce168inf1-update-covid-19-region-americas

[ix] For some small island countries, deliveries in the first two quarters of the year may correspond up to 20% coverage due to minimum shipment sizes required by suppliers.

Graph 1. COVAX Allocation Dynamics (6 July 2021)



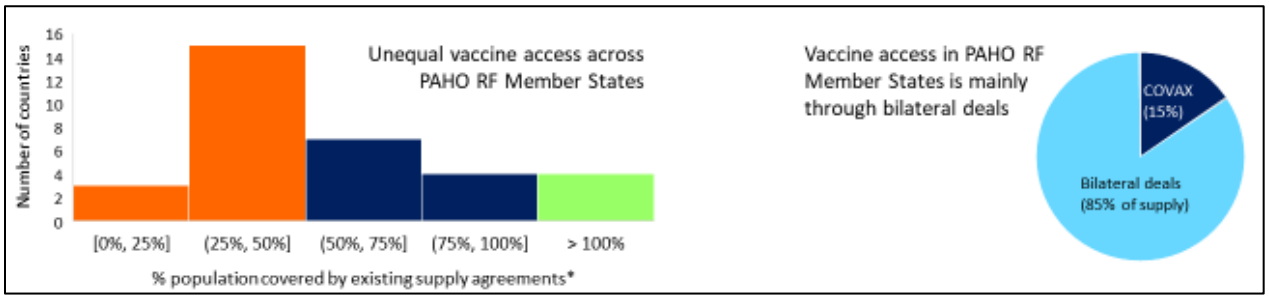
As shown in **Graph 1**, approximately 80% of doses committed by the COVAX Facility are projected to be mobilized in Q4 2021 and beyond. In theory, COVAX participants were projected to receive doses to vaccinate around 20% of their population—about 100 million people in LAC—by the end of 2021 to cover their high-risk populations. However, a higher rate of vaccination coverage is needed to control the pandemic.

While COVAX continues to experience supply bottlenecks during Q3 2021, donations from the U.S. government, EU, and other countries should help considerably to increase access. During Q3 2021, the U.S. government plans to donate 20 million doses through COVAX and possibly more than 10 million doses bilaterally. (Final details still pending.)

PAHO Revolving Fund regional plan of action for access

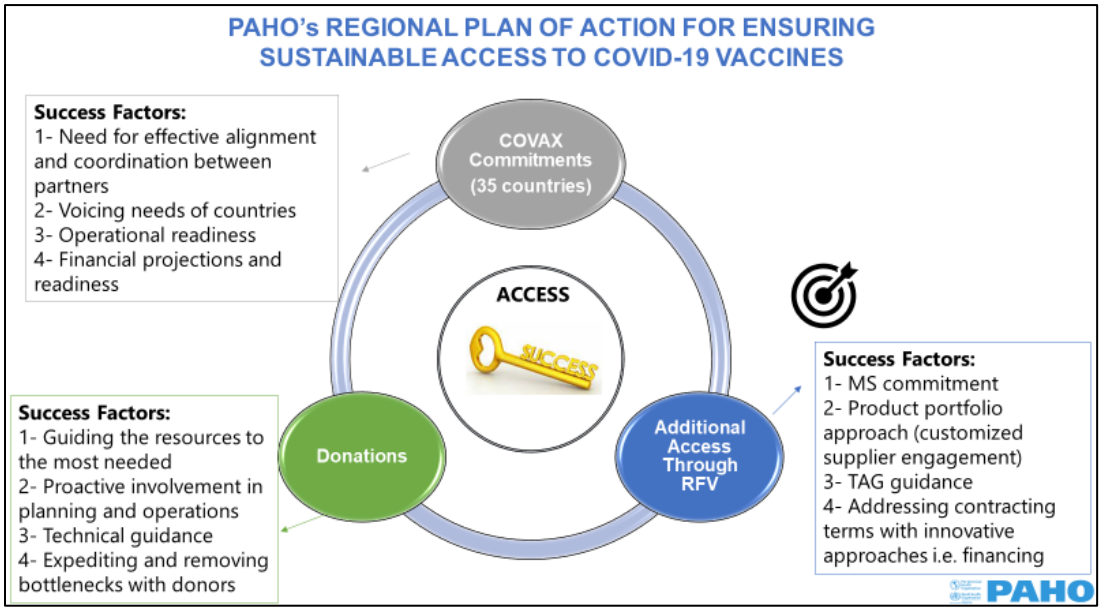
There has also been extraordinary interest across countries and country groupings in locking down early deals for COVID-19 vaccines. According to an unofficial PAHO analysis based on media reports and on information shared by Member States on an ad hoc basis, although some Member States have locked in bilateral deals to cover 100% or more of their populations, several other states (especially those with very limited financial resources and small countries in the Caribbean) are projected to cover only 20% to 50% of their populations, and will need to rely primarily on the COVAX Facility and possible donations **(Graph 2)**. This presents a significant inequity concern for the Region.

Graph 2. Unequal Vaccine Access Dynamics and Bilateral Deals across PAHO Member States (6 July 2021)



While improvements are expected in COVID-19 vaccine supply in Q4 2021 and during 2022, this still will not guarantee sufficient availability to meet the required demand. The Revolving Fund believes this situation will not correct itself without pooling demand and resources, and without leveraging the existing PAHO Revolving Fund mechanism. In response to Member State requests to intensify efforts to secure additional COVID-19 vaccines, PAHO is in the process of launching a regional plan of action for access based on three workstreams: (1) continued close collaboration with the COVAX Facility for completing current participation commitments of Member States, (2) facilitating donations to Member States through the COVAX Facility or bilaterally, and (3) creating means for additional access to COVID-19 vaccines through the Revolving Fund **(Graph 3)**.

Graph 3. PAHO's Regional Plan of Action for Ensuring Sustainable Access to COVID-19 Vaccines



RVF: Revolving Fund
MS: Member State

Currently, the Revolving Fund is projecting a deficit of COVID-19 vaccines in Member States by comparing number of people covered by existing supply agreements (including participation ratios in the COVAX, doses secured through bilateral deals, and donations) with the total adult population (older than 18) in each Member State. To address limitations in available data and to keep abreast of changing supply and demand dynamics, the Revolving Fund co-created an online COVID-19 vaccine demand-mapping platform that was released at the end of July 2021, under the leadership of Executive Management and with Comprehensive Family Immunization, Information Technology Services, and Procurement and Supply Management. The purpose of the platform is to validate information from Member States on target groups for vaccination and supply agreements, as well as requesting Member States to forecast future demand for COVID-19 vaccines provided through the RF along with their vaccine preferences. The online platform is also the first product of PAHO Revolving Fund's digitization strategy with the vision of transforming demand-planning to digital and automated platforms.

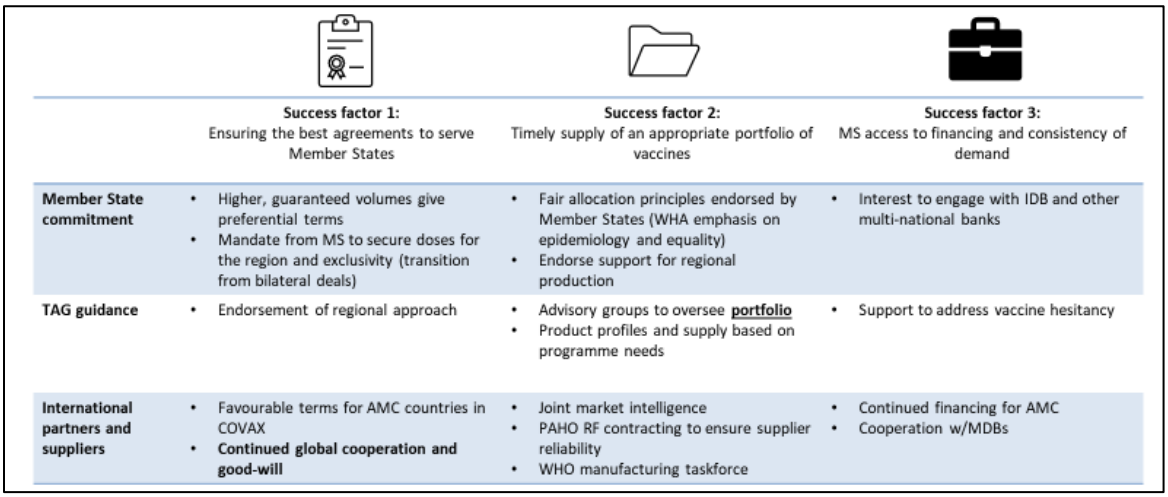
Orientations on the platform were provided to Member States and PAHO country offices on 29-30 June 2021. Member States were very receptive to the tool and used the opportunity to highlight epidemiological unknowns that might cause considerable fluctuations in demand (i.e., need for booster doses or not) and stressed the importance of guidance from the TAG.

Table 2. Important Epidemiological/Technical Considerations and Uncertainties That Impact Demand-Planning and Access to COVID-19 Vaccines

National COVID-19 Vaccination Strategy and Financing • Target populations • Coverage levels to control the disease	**National Immunization Program** • Capacity to reach target populations • Acceptability and uptake • Monitoring of safety (ESAVIs) and effectiveness
Variants of Concern (VOC) • Impact of VOC vaccine effectiveness • Potential need for additional doses/re-vaccination (i.e., on annual basis)	**Vaccine Profile** • Duration of protection • Prevention of transmission • Cold chain, storage, and handling conditions • Interchangeability with different vaccines • 2nd-generation vaccines

It will be critical to create an optimal product portfolio selection for future access focus based on evolving disease epidemiology, programmatic requirements, demand dynamics and supply market conditions. The Revolving Fund will follow customized supplier engagement strategies based on technical guidance on the above-mentioned dynamics. Given the supply market realities, it is important to have solid and executable commitments from Member States in their demand indications.

Table 3. Success Factors for Increasing Equitable Access to COVID-19 Vaccines under the Leadership of Executive Management



	Success factor 1: Ensuring the best agreements to serve Member States	Success factor 2: Timely supply of an appropriate portfolio of vaccines	Success factor 3: MS access to financing and consistency of demand
Member State commitment	• Higher, guaranteed volumes give preferential terms • Mandate from MS to secure doses for the region and exclusivity (transition from bilateral deals)	• Fair allocation principles endorsed by Member States (WHA emphasis on epidemiology and equality) • Endorse support for regional production	• Interest to engage with IDB and other multi-national banks
TAG guidance	• Endorsement of regional approach	• Advisory groups to oversee **portfolio** • Product profiles and supply based on programme needs	• Support to address vaccine hesitancy
International partners and suppliers	• Favourable terms for AMC countries in COVAX • **Continued global cooperation and good-will**	• Joint market intelligence • PAHO RF contracting to ensure supplier reliability • WHO manufacturing taskforce	• Continued financing for AMC • Cooperation w/MDBs

AMC: Advanced Market Commitment
WHA: World Health Assembly
IDB: Inter-American Development Bank
MDB: Multilateral Development Banks

Recommendations

- The TAG commends countries for their tremendous work in rolling out COVID-19 vaccines to help control the pandemic.
- The TAG is extremely concerned with the significant inequity in global access to vaccines and reaffirms the importance of the COVAX Facility and the PAHO Revolving Fund as key mechanisms to improve access to vaccines for low- and middle-income countries. Greater advocacy, coordination and action among immunization partners and political leaders are necessary to reduce this global inequity and promote justice for all.
- The TAG is also concerned with the significant disparities in the deployment and administration of vaccines between and within countries of the Region and recommends that greater attention be given to ensuring more equitable distribution of vaccines in keeping with our principles of Pan-Americanism and solidarity among countries.
- In view of the large COVID-19 vaccine deployments anticipated in Q4 2021 and 2022, governments should further strengthen planning and preparation, train their health workforce, expand their immunization staff where needed, install cold chain equipment (including ultra-cold chain where necessary), review and implement local micro plans, and update the National Deployment and Vaccination Plan.
- The TAG strongly advocates that governments should implement the SAGE roadmap for prioritization of COVID-19 vaccines and achieve high vaccination coverage among health and front-line workers, the elderly, and other high-risk groups before administering doses to adolescents (ages 12-15).
- Preliminary evidence suggests that natural immunity and vaccine immunity are effective in preventing severe disease, hospitalization, and death in those older than 1 year. At this

juncture, it is not known how long immunity will last, and there may be breakthrough infections that are mild or asymptomatic in fully immunized individuals. In the context of limited vaccine supplies and the roadmap's recommendations, introducing booster doses of vaccines is not recommended at this time. Currently, in countries with high vaccine coverage, most COVID-19 hospitalizations and deaths occur among people who are unimmunized or only partially immunized, and seldom in those who are fully immunized.

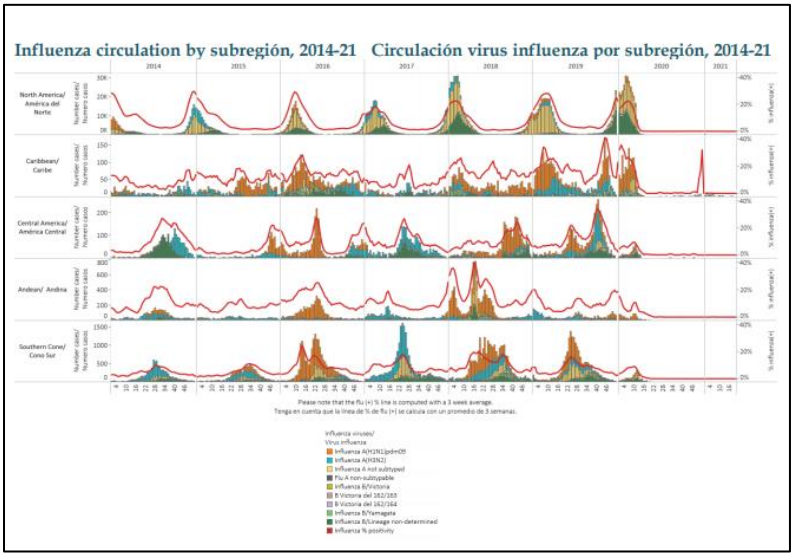
- Where possible, countries should implement COVID-19 vaccine effectiveness studies and/or contribute their data to the regional surveillance network REVELAC-i (managed by PAHO) to add to the Region's understanding of vaccine performance.

Vaccination of High-Risk Groups in the Context of the COVID-19 Pandemic

Influenza vaccination in the context of COVID-19

Although it is necessary to focus on the COVID-19 response, influenza viruses remain the likeliest pandemic pathogens and each year continue to cause seasonal epidemics that entail a significant health and economic burden. Before the COVID-19 pandemic, seasonal influenza had been associated with an estimated 36,500 deaths and 400,000 hospitalizations in the Region every year. However, surveillance data show that since March 2020, influenza transmission has been at historic lows and, in temperate areas, even absent **(Figure 3)**.

Figure 3. Influenza Circulation by Sub-Region in the Americas, 2014-21



Source: https://www.paho.org/en/documents/regional-update-influenza-epidemiological-week-22-june-16-2021

In 2004, PAHO's TAG first recommended that all countries establish an influenza vaccination policy that prioritizes high-risk groups: children ages 6-23 months, pregnant women, individuals with underlying conditions, older adults, and healthcare workers. In 2012, WHO's Strategic Advisory Group of Experts (SAGE) on immunization identified pregnant women as the highest priority group for vaccination, followed by, in no particular order, children, older adults, individuals with underlying health conditions, and healthcare workers. As of 2019[x], 39 of the 51 (76%) countries and territories in the Americas had an influenza vaccination policy targeting at least one of the five high-risk groups. Among them, 39 (76%) have a policy targeting vaccination of healthcare workers, 37 (73%) have a policy for vaccinating those with chronic disease, 33 (65%) have a policy for vaccinating the elderly, 33 (65%) have a policy for vaccinating pregnant women,

[x] Vicari AS, Olson D, Vilajeliu A, Andrus JK, Ropero AM, Morens DM, Santos JI, Azziz-Baumgartner E, Berman S. Seasonal Influenza Prevention and Control Progress in Latin America and the Caribbean in the Context of the Global Influenza Strategy and the COVID-19 Pandemic [Internet]. The American Journal of Tropical Medicine and Hygiene 2021; 2021 May 10. Epub ahead of print [cited 2021 May 10]. Available from: https://doi.org/10.4269/ajtmh.21-0339

and 30 (59%) have a policy for vaccinating children. Overall, 300 million seasonal influenza vaccine doses are administered each year (271 per 1,000 population, the highest rate globally).

In the context of the COVID-19 pandemic, maintaining influenza vaccination programs, particularly for high-risk groups, were deemed essential to decreasing influenza-related morbidity and mortality and preventing further strain on the healthcare system. An increased demand of influenza vaccine was expected in the context of limited supply. In March 2020, PAHO guidance stated that healthcare workers and older adults, followed by pregnant women, children, and individuals with underlying conditions should be prioritized to be vaccinated against influenza where it was feasible to do so, to ensure optimal control of influenza among groups at high risk of severe COVID-19 disease, as well as influenza illness. SAGE's September 2020 recommendations on vaccination of high-risk groups against seasonal influenza in the context of COVID-19 emphasized healthcare workers and older adults, to minimize the disruption of health services and reduce the burden on healthcare systems.

In 2020 and 2021, the Region has been able to capitalize on strong national immunization programs and on the regional initiative of Vaccination Week in the Americas to maintain influenza vaccination during the COVID-19 pandemic. Also, as with other vaccines, PAHO's Revolving Fund for Access to Vaccines (Revolving Fund, or RF) has played a critical role in Member States' procurement of seasonal influenza vaccines. This was evident in March-September 2020 when, amid the incipient COVID-19 pandemic, 13 countries in the Southern Hemisphere used the seasonal influenza vaccine to immunize over 100 million people, prioritizing older adults, people living with chronic illnesses, and healthcare workers. Latin America and Caribbean (LAC) countries implemented successful innovative vaccine delivery strategies to reach influenza high-risk groups. Some of these groups (e.g., healthcare workers) were also at high risk of SARS-CoV-2 exposure and/or severe COVID-19 (e.g., the elderly, people with chronic diseases, and pregnant women). Given the overlap with priority groups for COVID-19 vaccination, SAGE recommended 14 days between administering COVID-19 vaccines and any other vaccine, including the influenza vaccine. This recommendation may be amended as data on co-administration with other vaccines become available.

With influenza seasons occurring during the pandemic, some studies suggest that influenza vaccination could contribute to reduce susceptibility and improve clinical outcomes for COVID-19 patients:[xi,xii,xiii,xiv,xv,xvi]

- Decreased positive COVID-19 testing with a potential protection from COVID-19 conferred by the influenza vaccine;
- Greatest protection against COVID-19 in elderly patients who received the influenza vaccine in close proximity to COVID-19 exposure as compared to several months before;
- Lower rate of hospitalizations and length of stay in those who were vaccinated with the influenza vaccine;
- Decreased need for mechanical ventilation in COVID-19 patients who received the influenza vaccine;
- Decreased need for intensive care treatment and invasive respiratory support;
- Association between influenza vaccination and reduced mortality from COVID-19.

Countries and territories may experience severe influenza seasons once COVID-19-related public health and social measures are relaxed and international travel resumes. National immunization programs and seasonal influenza vaccination should be maintained and continuously strengthened, as they are investments that pay important dividends when emergencies occur. Moreover, and equally important, influenza vaccination reduces the seasonal influenza burden.

Recommendations on the Introduction of Pneumococcal Vaccines among Older Adults

Pneumococcal disease has a high burden among infants and children younger than 5 years and in adults aged 50 or older. In Latin America and the Caribbean, 37 of 52 (71%) countries and territories introduced PCV10 or PCV13 into national immunization programs for infants and young children. Two vaccines are currently available for the prevention of pneumococcal disease in adults: PPV23 and PCV13. Both vaccines were found to be immunogenic in adults age 50 and older.[xvii] The evidence from a systematic review supports the efficacy and effectiveness of both

[xi] Impact of the influenza vaccine on COVID-19 infection rates and severity. A. Conlon et al. / American Journal of Infection Control 00 (2021) 1–7.
[xii] Salem ML, El-Hennawy D. The possible beneficial adjuvant effect of influenza vaccine to minimize the severity of COVID-19. Med Hypotheses. 2020;140: 109752).
[xiii] Marín-Hernandez D, Schwartz RE, Nixon DF. Epidemiological evidence for association between higher influenza vaccine uptake in the elderly and lower COVID-19 deaths in Italy. J Med Virol. 2021;93:64–65.
[xiv] Fink G, Orlova-Fink N, Schindler T, et al. Inactivated trivalent influenza vaccine is associated with lower mortality among Covid-19 patients in Brazil [e-pub ahead of print]. BMJ Evid Based Med.
[xv] Zanettini C, Omar M, Dinalankara W, et al. Influenza vaccination and COVID19 mortality in the USA. medRxiv; 2020.
[xvi] Ragni P, Marino M, Formisano D, et al. Association between exposure to influenza vaccination and COVID-19 diagnosis and outcomes. Vaccines. 020;8:675.
[xvii] Winje BA, Berild JD, Vestrheim DF, Denison E, Lepp T, Roth A et al. Efficacy and effectiveness of pneumococcal vaccination in adults – an update of the literature. Oslo: Norwegian Institute of Public Health; 2019.

PPV23 and PCV13 against invasive pneumococcal disease in adults age 50 or older.[xviii] Few countries recommend pneumococcal vaccines for routine use in older adults because pediatric vaccination programs have reduced the overall circulation of pneumococcal strains included in the PCV vaccines, as well as the exposure of older adults to these strains. However, available data indicate that there is a substantial burden of disease attributable to *S. pneumoniae* among adults age 50 or older, and this burden is higher in low-income countries and in lower-middle-income countries.

The proportion of community-acquired pneumonia among adults age 50 or older due to *S. pneumoniae* and the proportions due to serotypes contained in currently licensed vaccines were estimated by conducting a meta-analysis of studies from the previous 10 years, which employed microbiological methods (serotype-specific urinary antigen detection [SSUAD] test and polymerase chain reaction [PCR] test of sputum). This analysis found prevalence ranging from 12% to 38% in pre-PCV13 studies and from 11% to 32% in the post-PCV13 period (more than one year after introduction). However, all these studies were set in high-income countries.[xix,xx]

The Institute of Health Metrics and Evaluation Global Burden of Disease study estimated the deaths due to pneumococcal low respiratory infection (LRI) and meningitis for 2017. The rates of pneumococcal LRI-related deaths were highest in low-income countries followed by lower-middle-income countries, and lowest in high-income countries. Overall, 203,104 (UR 79,949 to 349,924) deaths due to LRI in adults ages 50–69 years and 456,096 (UR 166,041 to 866,727) deaths due to LRI in adults ≥70 years were estimated to be attributable to *Streptococcus pneumoniae*. Also, 49% of *S. pneumoniae* LRI deaths in older adults were in LMICs. Regarding pneumococcal meningitis, in the same year, an estimated 5,395 (UR 4,551 to 7,399) deaths occurred in adults ages 50–69 years and 4,206 (UR 3568 to 5,768) in adults ≥70 years. Again, 78% of the pneumococcal meningitis deaths in older adults occurred in lower-middle-income countries.[20,xxi]

In the Region of the Americas, there are insufficient data on the burden of invasive pneumococcal disease in older adults, as well as data on the cost-effectiveness of PCV vaccination in this age

[xviii] Berild JD, Winje BA, Vestrheim DF et al. A systematic review of studies published between 2016 and 2019 on the effectiveness and efficacy of pneumococcal vaccination on pneumonia and invasive pneumococcal disease in an elderly population. Pathogens. 2020; 9(4).

[xix] Non-invasive pneumococcal pneumonia due to vaccine serotypes: a systematic review and meta-analysis. Lansbury L, Lim B, M McKeever T, Lawrence H, Shen Lim W. University of Nottingham, Nottingham, UK; National Institute for Health Research (NIHR), UK; University of Cambridge, Cambridge, UK; Nottingham University Hospitals NHS Trust, Nottingham, UK. In press to be published.

[xx] World Health Organization. Considerations for pneumococcal vaccination in older adults. Geneva: WHO; Weekly epidemiological record 2021 Jun 11; 96(23):217-228. Available from https://apps.who.int/iris/bitstream/handle/10665/341721/WER9623-eng-fre.pdf

[xxi] Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) results. Washington: Institute for Health Metrics and Evaluation; 2018 (http://ghdx.healthdata.org/gbd-results-tool, accessed 21 November 2020).

group. Furthermore, evidence suggests that high PCV coverage in children younger than 5 years helps to protect both children and older adults from invasive pneumococcal disease.

Evidence on COVID-19 co-morbidity and benefit of vaccination in relation to pneumococcus

Available evidence does not indicate that *S. pneumoniae* is a clinically significant co-pathogen or secondary pathogen in patients with COVID-19. Also, there is no evidence to suggest that pneumococcal vaccination will influence the severity or outcome of COVID-19.[xxii] Therefore, the current evidence is insufficient to support a recommendation to introduce an adult pneumococcal vaccination program in response to the COVID-19 pandemic. However, in countries with existing adult pneumococcal vaccination programs, improving vaccine coverage and thereby reducing pneumococcal disease may be expected to alleviate the related burden on health systems.[22]

Recommendations

- The TAG commends countries in the Region that offered other antigens during the COVID-19 vaccination campaigns, protecting millions from influenza and other VPDs.
- The TAG recommends that governments prioritize pneumococcal vaccination for children younger than 5 years rather than older adults. High coverage as per the recommended pneumococcal vaccine schedule for infants and children under 5 helps to protect both children and older adults from pneumococcal disease.
- In countries with a mature childhood pneumococcal immunization program reaching high coverages homogenously at local levels, decisions about initiating pneumococcal vaccination in older adults (using either PPV23 or PCV13) should consider the local disease burden and cost-effectiveness, as well as ensure that optimal coverage can be consistently achieved in the target population.
- The TAG acknowledges the limited availability of scientific data on the co-administration of COVID-19 and influenza vaccines and notes the SAGE recommendation to maintain an interval of 14 days between these vaccines.
- The TAG acknowledges the importance of not missing opportunities for immunization, but considering the potential for increased reactogenicity, particularly with influenza vaccines that might be more likely to cause local or systemic reaction, it recommends that NITAGs consider reviewing the available evidence, as well as their local epidemiology and capacity, and decide whether their country should co-administer COVID-19 and influenza vaccines. If countries decide to co-administer these vaccines, each vaccine should be given in a different arm, if possible, and the ESAVI surveillance network should monitor any adverse events.
- Available evidence does not indicate that *S. pneumoniae* is a clinically significant co-pathogen or secondary pathogen in patients with COVID-19, or that pneumococcal vaccination will influence the severity or outcome of COVID-19. However, in countries with existing adult pneumococcal vaccination programs, improving vaccine coverage and thereby reducing pneumococcal disease may alleviate the related burden on health systems.

[xxii] World Health Organization. Meeting of Strategic Advisory Group of Experts on Immunization, October 2020: conclusions and recommendations. Geneva: WHO; Weekly epidemiological record 2020 Nov 17; 95(48):594. Available from https://apps.who.int/iris/bitstream/handle/10665/337100/WER9548-eng-fre.pdf

Vaccine Hesitancy among Adults in the Caribbean

A look at vaccine acceptance among healthcare workers

An essential part of COVID-19 vaccine rollout are communication campaigns that target specific priority groups identified by each country, such as healthcare workers. COVID-19 vaccines have been significant targets of mis- and disinformation, leading to public mistrust and concerns about vaccine safety, including among healthcare workerss. Using data to understand the multiple factors and influences that shape vaccination acceptance in populations – including, but not limited to, misinformation – can help countries tailor responses and improve vaccine uptake.

PAHO carried out a cross-sectional online survey in 14 countries of the Caribbean[xxiii] in March-April 2021 to document healthcare workers' concerns and attitudes about COVID-19 vaccines and their intended practices. The survey gathered information on attitudes toward vaccines in general, COVID-19 vaccines, influenza vaccines, and vaccine intent. Almost 1,300 healthcare workers completed the survey, twice the calculated sub-regional sample size.

Principle findings:

- Respondents displayed widespread agreement that vaccines in general are a good way to protect oneself from disease (98%), that vaccines are safe (95%), efficient (97%), and that vaccine information is reliable and trustworthy (94%).
- However, 23% of respondents revealed COVID-19 vaccine hesitancy, and said that they "disagree" or "strongly disagree" with getting the vaccine as soon as possible. Nurses were twice as likely as doctors to be hesitant, and younger workers communicated more hesitancy than older ones. Only 4% of all participants stated an intention to refuse a COVID-19 vaccine altogether.
- Healthcare workers displayed some concern when it comes to new vaccines. When asked about general vaccine readiness, 56% of respondents agreed that new vaccines carry more risk than older vaccines. Also, 77% of respondents stated that they are concerned about serious adverse effects from vaccines.
- Overall, 92% of respondents agreed that a COVID-19 vaccine will protect against severe COVID-19, and 83% were confident in the scientific approval process for a COVID-19 vaccine.
- When asked about the reasons for their attitudes toward and perceptions of COVID-19 vaccines:
    - 30% of respondents indicated they do not yet know enough about the vaccine to decide.
    - 29% of respondents expressed a preference to gain natural immunity against SARS-CoV-2.

[xxiii] Antigua and Barbuda, Bahamas, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Jamaica, St. Kitts and Nevis; St. Lucia, St. Vincent and the Grenadines, Suriname, and Trinidad and Tobago.

- 47% of respondents said that the development of COVID-19 vaccines may have been rushed or the vaccine may not have been thoroughly tested.
- 48% of respondents indicated that the manufacturing country of a COVID-19 vaccine shaped their opinion of the vaccine.
- 30% of respondents reported that information they have seen on social media shaped their opinion of a COVID-19 vaccine.

When asked about delaying or refusing COVID-19 vaccines, respondents expressed concerns primarily related to the vaccines' benefits and safety, as well as overall trust in the new COVID-19 vaccines. Other respondents indicated that the brand of the vaccine available to them influenced their opinion. Among the answers falling under the social process domain, healthcare workers pointed to their confidence (or lack thereof) in government and health authorities.

Based on the survey results, PAHO is working with Caribbean countries to develop and implement communication campaigns to increase uptake of COVID-19 vaccines. These campaigns will include educational components, institutional and provider/influencer recommendations, and other activities to increase healthcare workers' perception of COVID-19 risk and improve their perception of COVID-19 vaccine safety and efficacy. PAHO plans to replicate this survey process in Latin America.

Recommendations

- The TAG commends PAHO and immunization programs for conducting a survey in the Caribbean sub-region to determine the acceptability of COVID-19 vaccines among healthcare workers, the reasons for any vaccine hesitancy, and for developing strategies to address them.
- The TAG encourages all countries to gather data on social and behavioral drivers for vaccination acceptance among different population segments, including healthcare workers, and to use these data to inform policies and strategies to increase vaccine uptake.

Communication and Demand for COVID-19 Vaccines

The decision by an individual to get vaccinated – or to bring a family member to get vaccinated – is complex and dependent on multiple factors, including trust in the immunization program, the healthcare system, the person offering the vaccines, and the vaccines themselves. Following TAG recommendations from 2019[xxiv] and November 2020[xxv], PAHO has supported Member States in their strategic communications and in generating demand for immunization, including COVID-19 vaccines. PAHO has published tools and guidance documents, held webinars and virtual training sessions, provided socializing instruments and offered guidance from WHO for healthcare workers, health authorities and the public. It has also maintained an active presence on social media to share messages about routine and COVID-19 vaccinations and to respond to misinformation spread as part of the infodemic.

Crisis communications plans

The proper management of an immunization-related crisis or event is of utmost importance, as public trust in the immunization program is at stake. Handling a crisis requires differentiated actions from those used to promote the benefits and importance of vaccines. The introduction of COVID-19 vaccines occurs in a complicated context that heightens the importance of trust in vaccines. The context includes concerns about vaccine safety and efficacy, the limited availability of vaccines, and multiple vaccines being introduced, as well as the politicization of vaccination and the pandemic at large, and constantly evolving information. PAHO developed guidance [xxvi] and held virtual sessions to support Member States with developing crisis communication plans to facilitate information that is timely, accurate, transparent, accessible, credible, empathetic, respectful, and coordinated. Additionally, sub-regional workshops on this topic will be held in the second semester of 2021 and a virtual course will be launched to continue supporting countries to plan, implement, and evaluate their plans.

Healthcare workers and communication about vaccines and vaccination

Multiple studies repeatedly showed that healthcare workers are highly trusted sources of information for their communities and users of health services when it comes to vaccination. They are critical both in advocating for immunization and in responding to any questions and

---

[xxiv] July 2019 Regional Immunization Technical Advisory Group (TAG) meeting recommendations:

- TAG urges PAHO to develop a regional strategy for vaccine access, acceptance and demand, and support countries in identifying social and behavioral determinants of vaccination and addressing barriers to vaccination.
- Countries should use theory-based approaches to identify local barriers and drivers to vaccination and use these insights to develop tailored, evidence-based interventions to reach vaccination coverage goals, evaluate their impact and share their findings with other countries. Countries should strengthen their preparedness and response to vaccine safety events that have the potential to erode trust in vaccine safety and in the health authorities delivering them.

[xxv] November 2020 Regional Immunization Technical Advisory Group (TAG) meeting recommendation:

- PAHO should develop a comprehensive strategy for communication and demand-generation for introducing COVID-19 vaccines.

[xxvi] Communication in Crises Related to Vaccine Safety: Technical Guidance

concerns that users of health services may have. Also, healthcare workers have generally been prioritized for COVID-19 vaccination, often making them among the first to be vaccinated.

At the same time, healthcare workers may themselves fall prey to misinformation, rumors, and doubts, potentially influencing their decision whether or not to get vaccinated; this, in turn, can impact the general public´s sentiments and decisions regarding vaccination.

PAHO published guidance[xxvii] and has held webinars to support healthcare workers in improving their interpersonal communication skills on issues related to vaccination, vaccine safety and promoting vaccination throughout the life course. In addition, a virtual course will be launched later in 2021. However, vaccine hesitancy among healthcare workers regarding COVID-19 vaccines is still reportedly high in several countries; this threatens to impact the acceptance of the vaccines not only in this sub-group but in the general population, too.

Additionally, PAHO and WHO published guidance[xxviii] and communication materials[xxix] on the topic of COVID-19 vaccination targeting healthcare workers and advised Member States to develop communication strategies specifically focused on healthcare workers, considering their dual roles as early vaccine recipients and advocates for immunization with peers and community members.

Recommendations

- The TAG strongly encourages governments to actively promote COVID-19 vaccines among their country's populations and to provide timely and accurate information on the vaccines' safety, effectiveness, and quality.
- The TAG strongly urges governments and international partners to work with healthcare workers to provide timely and accurate information, respond to their questions and concerns, and develop tools and materials to facilitate their work. The goal is to engage healthcare workers as advocates of COVID-19 immunization.
- The TAG recommends that governments organize coordinated communication campaigns and social engagement events to promote vaccination against COVID-19.
- The TAG recommends that with PAHO support, countries share lessons learned in rolling out vaccines to adult populations in real time and communicating effectively with sub-populations to address their concerns.
- The timing of promotional activities for COVID-19 must be carefully planned so community engagement activities coincide with the availability of vaccines in countries.

[xxvii] Communicating about Vaccine Safety: Guidelines to help health workers communicate with parents, caregivers, and patients; Mensajes y respuestas clave sobre la vacunación segura. Guía para el personal de salud.

[xxviii] Guide for the preparation of a risk communication strategy for COVID-19 vaccines: A Resource for the countries of the Americas.

[xxix] Ten Things Healthcare Workers Need to Know about COVID-19 Vaccines; Addressing COVID-19 Vaccine Myths. Material for general public and healthcare workers; Health worker communication for COVID-19 vaccination flow diagram.

Regional ESAVI Surveillance System for COVID-19 Vaccines

Regional ESAVI Surveillance System for COVID-19 Vaccines in The Americas

The ad-hoc meeting of PAHO's TAG on Vaccine-Preventable Diseases, held on 16 November 2020, presented PAHO's proposal to establish a regional ESAVI surveillance system for COVID-19 vaccines and issued the following recommendations:

- Strengthen national ESAVI surveillance capacities in relation to COVID-19 vaccines and other vaccines, and support creating a regional ESAVI surveillance system.
- Prepare special studies to monitor cohorts of vaccinated people to determine the safety of COVID-19 vaccines and the duration of the protection they confer and create a regional committee on COVID-19 vaccine safety.
- Emphasize the critical role of communication, including the use of social media; identify and enlist national influencers and personalities, as well as regional champions and ambassadors, to promote COVID-19 immunization once vaccines are available.

Following PAHO's TAG recommendations issued in November 2020, PAHO issued a Guidance for Implementing the Regional COVID-19 Vaccine ESAVI Surveillance System on 26 February 2021. The regional surveillance system is being planned to be sensitive, timely, standardized, and reliable, with participation from all vaccine safety actors, while maintaining public trust in vaccination and acceptance of immunization in the Americas.

The main guidance steps for countries to implement this system: 1) Use the Global and Regional Manuals for ESAVI and AESI Surveillance for the Introduction of COVID-19 Vaccines. 2) Improve coordination of actions among those responsible for ESAVI surveillance. 3) Promote activation of National Committees for Vaccine Safety. 4) Notify all serious ESAVIs to PAHO. 5) Use standardized notification and investigation forms in order to strengthen ESAVI causality assessments and final classifications. 6) Support establishment of sentinel surveillance. 7) Implement ESAVI strategies for risk and crisis communication.

Progress made toward the implementing this guidance is as follows:

- To strengthen national capacities in ESAVI surveillance in the Region, PAHO conducted 16 sub-regional workshops (four with each sub-region) between April and May 2021. All Latin American and English-speaking Caribbean countries were trained in standardizing the concepts and using tools for this surveillance.
- PAHO also conducted a regional survey to assess the maturity of surveillance and information systems. This survey provided valuable insights necessary to diagnose the ESAVI surveillance system at the country level and design a tailored system to close identified gaps.
- As of July 2021, 14 of 20 Latin American countries had officially confirmed their adherence to the regional surveillance system and their political willingness to share their databases for regional analyses of ESAVIs for all COVID-19 vaccines.

- A hospital-based regional sentinel network was also established, with participation from 40 hospitals in 11 Latin American countries and three English-speaking Caribbean countries; a protocol to standardize data collection was shared with those countries.
- PAHO's Director approved the formation of the Pan-American Advisory Committee on COVID-19 Vaccine Safety, with participation of 10 members from different areas and different countries in the Region. This Committee was convened in August to discuss the main findings in the Region.

The next step in the implementation of the regional ESAVI surveillance system is the receipt of ESAVI data from all the countries in the Region during the second semester of 2021. This data will allow for a regional database with case-by-case surveillance. The Regional Committee will receive first reports from this source to provide recommendations to PAHO and the Region.

Preliminary findings regarding ESAVI data consolidated from different sources in the Region

As part of the process of introducing and deploying COVID-19 vaccines, countries of the Americas are strengthening pharmacological surveillance systems as well as passive ESAVI surveillance. Evaluation and analysis of adverse events at the country and regional levels are essential to identify programmatic errors, as well as pick up unexpected events that may lead to additional research, help weigh potential risks, and support decision-making.

PAHO has consolidated information on adverse events following COVID-19 vaccination reported by 19 countries and coming from different sources **(Table 4)**: 1) data sets sent by some countries in the Region in response to specific requirements by PAHO; 2) data extracted from information tools and publications from country health authorities; and 3) information obtained from reports sent to the WHO Collaborating Center in Uppsala, Switzerland.

Until the regional system is consolidated, this information gives countries aggregated data that, even with certain limitations during the initial vaccination phase, allows them to generate better hypotheses, identify potential risks, facilitate their early management, and focus surveillance actions and safety measures on vaccine management.

Until 18 June 2021, there were 556,178,770 COVID-19 doses administered in 49 countries and territories in the Americas. The total number of ESAVIs reported in the Region through different sources of information are 540,899 (111.6 per 100,000 doses). The total number of serious ESAVIs is 41,154 (8.5 per 100,000 doses) and 9,233 deaths (1.9 per 100,000 doses). These events were not necessarily confirmed as associated or related to vaccination but, rather, were investigated to determine causality.

Table 4. Distribution of Numbers and Rates of Serious ESAVIs and Deaths Reported after COVID-19 Vaccination in the Americas

N	Contries	Total doses applied	Total events	Serious events	Deaths	Total event rate / 100,000 doses	Serious event rate / 100,000 doses	Death rate / 100,000 doses
1	*ARGENTINA[3]*	*5.493.153*	*27.704*	*11*		*504,3*	*0,2*	
2	BARBADOS[1,2]	153.350	263	38	5	171,5	24,8	3,3
3	BOLIVIA[1,2]	1.908.180	135	-		7,1		
4	*BRAZIL[3]*	*44.744.444*	*74.563*	*4.453*	*2.277*	*166,6*	*10,0*	*5,1*
5	CANADA[3]	30.084.080	6.186	1.646		20,6	5,5	
6	CHILE[1,4]	20.657.262	8.746	323		42,3	1,6	
7	COLOMBIA[4]	16.038.813	9.128	483	140	56,9	3,0	0,9
8	COSTA RICA[1,2]	2.150.520	4.037	39	6	187,7	1,8	0,3
9	ECUADOR[1,2]	3.133.387	2.036	61	1	65,0	1,9	0,0
10	EL SALVADOR[1,2]	2.294.464	1.591	7		69,3	0,3	
11	HONDURAS[1,2]	541.792	138	6		25,5	1,1	
12	JAMAICA[1,2]	194.315	203	31	11	104,5	16,0	5,7
13	*MEXICO[3]*	*24.860.006*	*5.820*	*360*	*1*	*23,4*	*1,4*	*0,0*
14	PANAMA[1,2,3]	1.370.894	542	41	2	39,5	3,0	0,1
15	PARAGUAY[2,3]	377.778	334	6	4	88,4	1,6	1,1
16	PERU[1,2,4]	6.061.707	8.942	77	2	147,5	1,3	0,03
17	ST VINCENT[1,2]	21.371	4	1		18,7	4,7	
18	URUGUAY[2,3]	3.472.817	868	20	1	25,0	0,6	0,0
19	USA[1,2,3]	320.956.125	389.659	33.551	6.783	121,4	10,5	2,1
Total		**484.514.459**	**540.899**	**41.154**	**9.233**	**111,6**	**8,5**	**1,9**

These results allow a first evaluation of the national ESAVI reporting systems that are emerging at the global level. Considerations may be general (e.g., reporting rates of serious/non-serious events in comparison to Europe) or specific (e.g., reporting frequencies of thrombosis with thrombocytopenia syndrome, anaphylaxis, myocarditis, pericarditis). Even so, the available Region-level data require further investigation.

The main limitations to collecting and consolidation data on ESAVIs are likely related to: a) incomplete data on the number of doses administered by type of vaccine (if data are available, they do not match the ESAVI reporting period); b) two or more institutions responsible for extracting data within the same country, which results in parallel reporting systems with different target populations; c) limited information on whether the reported events have been fully investigated or classified; d) lack of conformity in reporting (e.g, some countries report the number of events, while others report the number of cases); e) different case definitions for the same event. Some of these limitations might be overcome once the regional system is implemented. For a list of challenges and potential solutions regarding ESAVI reporting during the initial vaccination phase, please see **Table 5**.

Table 5. Challenges and Potential Solutions in Initial Vaccination Phase

CHALLENGES	POTENTIAL SOLUTIONS
Lack of completeness data of administered doses by type of COVID-19 vaccines	Improve electronic immunization registries at country level and reporting to the Regions
Lack of data harmonization to build adequate AEFI rates by type of COVID-19 vaccine, age, sex and number of dose	PAHO's Regional AEFI Surveillance System to improve interoperability between EPI and NRA at national, regional and global level
Need to improve coordination and data management among EPI and NRA	Set and promote this priority at national, regional and global agendas
Difficulty to train the subnational and local levels in ESAVI surveillance	Prioritize training of HCW in vaccine safety surveillance
Complex or lack of COVID-19 vaccines codification Standards	Development and harmonization of vaccines codification standards

Thrombosis with Thrombocytopenia Syndrome

Definition and background rates

Thrombosis with thrombocytopenia syndrome (TTS) is a condition where a patient presents with both acute venous or arterial thrombosis (confirmed through imaging, surgical, or pathology findings) and new onset thrombocytopenia (platelet count of less than 150,000/ µL). A study that collected data from six European countries (n=20,599,134) calculated background rates for cerebral venous sinus thrombosis (CVST) with thrombocytopenia at 0.1 per 100,000 person-years. The incidence of TTS increased with age, with those affected typically having more co-morbidities and greater medication use than the general population. TTS was also more often seen in men than women. A sizeable proportion of those affected were known to have taken antithrombotic and anticoagulant therapies prior to the TTS event.[xxx]

Events following vaccination with COVID-19 vaccines produced by AstraZeneca

Following the introduction of COVID-19 vaccines in December 2020, the first 22 cases of TTS were reported in Europe on 9 March 2021. As of 27 May, the UK Medicines & Healthcare products Regulatory Agency reported 236 TTS cases among 22,600,000 AstraZeneca vaccine doses administered. The case incidence rate was highest among people ages 18-29 (19.2 cases per 1 million doses administered) and ages 30-39 (17.4 per 1 million doses administered). Among women younger than age 50, the case incidence rate was 8.9 cases of CVST per 1 million doses administered.

Updated SAGE recommendations on the AstraZeneca vaccine (21 April) stated that: "A causal relationship between the vaccine and TTS is considered plausible […]." SAGE concluded that in countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against

[xxx] Burn E, Li X, Kostka K, Stewart HM, Reich C, Seager S, et al. Background rates of five thrombosis with thrombocytopenia syndromes of special interest for COVID-19 vaccine safety surveillance: incidence between 2017 and 2019 and patient profiles from 20.6 million people in six European countries. medRxiv [Internet]. 2021 May 13 [cited 2021 Jul 7]; 2021.05.12.21257083. Available from: https://www.medrxiv.org/content/10.1101/2021.05.12.21257083v1

COVID-19 far outweighs the risks. The benefit/risk ratio is greatest in older age groups, as the risk of severe COVID-19 disease outcomes (including TTS) increases with age. Nonetheless, people who have had blood clots associated with TTS after their first vaccine dose should not be given a second dose. Using available data, TTS is estimated to be present in 4-6 persons per 1 million vaccinated. Of the 51 countries and territories in the Region, 35 employ AstraZeneca vaccines.

Events following vaccination with COVID-19 vaccines produced by Janssen

On 13 April 2021, following 6 cases of thrombosis among 6 million vaccinated persons, the CDC suspected that the one-dose COVID-19 vaccine produced by Janssen was responsible. Ten days later, on 23 April, following a review of 15 TTS cases among 8 million vaccinated persons, the Advisory Committee on Immunization Practices (ACIP) recommended resuming vaccination operations with the Janssen vaccine. Finally, on 19 May, the GACVS stated that the current evidence suggests a plausible causal association between the Janssen COVID-19 vaccine and TTS; however, the benefits of the Janssen COVID-19 vaccine continue to outweigh the risks of TTS. Data from the United States reported that TTS is present in 28 persons among 8 million vaccinated. Of the 51 countries and territories in the Region, 4 including the United States, administer Janssen vaccines.

Additional data reviews

All case series published for the AstraZeneca vaccine included patients between the ages of 30 and 77, predominantly females. The most common event reported was CVST, followed by splanchnic venous thrombosis or pulmonary embolism. The platelet count was always under 150,000/µL and in some cases as low as 7,000/µL. With few exceptions, most patients were positive for antibodies against PF4. In most of the reported case series, the mortality rate was under 30% of reported cases.[xxxi, xxxii, xxxiii]

The case series from the Janssen vaccine displayed a similar pattern.[xxxiv] One historic cohort study developed in Denmark and Norway measured the risks of multiple thrombotic events and thrombocytopenia after AstraZeneca vaccination by comparing expected background rates with the observed rates in vaccinated individuals. For most events, there was no higher risk after introducing the vaccine. However, compared to expected rates, the risk of cerebral venous

[xxxi] Schultz NH, Sørvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, Ahlen MT, et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. N Engl J Med [Internet]. 2021 Jun 3 [cited 2021 Jul 7];384(22):2124–30. Available from: https://pubmed.ncbi.nlm.nih.gov/33835768/

[xxxii] Scully M, Singh D, Lown R, Poles A, Solomon T, Levi M, et al. Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination. N Engl J Med. 2021 Jun 10;384(23):2202–11.

[xxxiii] Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. N Engl J Med [Internet]. 2021 Jun 3 [cited 2021 Jul 7];384(22):2092–101. Available from: https://pubmed.ncbi.nlm.nih.gov/33835769/

[xxxiv] See I, Su JR, Lale A, Woo EJ, Guh AY, Shimabukuro TT, et al. US Case Reports of Cerebral Venous Sinus Thrombosis with Thrombocytopenia after Ad26.COV2.S Vaccination, March 2 to April 21, 2021. JAMA - J Am Med Assoc. 2021 Jun 22;325(24):2448–56.

thrombosis was 20.2 times higher, and the risk of intracerebral hemorrhage was 2.3 times higher. Therefore, among vaccinated persons, the number of cerebral venous thrombosis attributed to the vaccine was estimated to be 2.5 (0.9–5.2) cases per 100,000 vaccinations per year.[xxxv]

Possible biological mechanisms

The main hypothesis for TTS is the generation of anti-PF4 antibodies that produce immune complexes with the PF4 and an unknown polyanion derived from the vaccine. Those immune complexes activate the platelets and produce thrombosis with thrombocytopenia. Alternative explanations for this event are: 1) previous or current SARS-CoV-2 infection; b) reactivation of a previous immune response; or c) platelet activation by the viral vector directly; d) activation of other cell types. More evidence for testing these hypotheses is needed.[xxxvi]

Limitations

1. Background rates of thrombotic events are mostly calculated using data from European countries.
2. The case definition for TTS is not applied consistently across studies, which makes comparisons difficult and leads to different incidence rates within the same country.
3. The updated SAGE recommendations for the AstraZeneca vaccine (15 June 2021) note that, "There is considerable geographic variation with regards to the reported incidence, with very few cases reported from non-European countries, despite extensive use of the vaccine in these countries."
4. The biological mechanism linking COVID-19 vaccines and TTS events is not well understood.
5. The ESAVI surveillance network in most PAHO countries has limited ability to identify and record TTS events.

Recommendations

- TAG urges countries to establish or strengthen an electronic surveillance system for adverse events supposedly attributable to vaccines or immunization (ESAVIs); the system should be harmonized with the EPI and national regulatory agency data systems, and staff should be trained to use it. The goal is to collect ESAVI data specific to the Region (including for rare events) and calculate incidence rates of ESAVI associated with the COVID-19 vaccines used in the Americas.

[xxxv] Pottegård A, Lund LC, Karlstad Ø, Dahl J, Andersen M, Hallas J, et al. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: Population based cohort study. BMJ [Internet]. 2021 May 5 [cited 2021 Jul 7];373. Available from: https://pubmed.ncbi.nlm.nih.gov/33952445/

[xxxvi] Douxfils J, Favresse J, Dogné JM, Lecompte T, Susen S, Cordonnier C, et al. Hypotheses behind the very rare cases of thrombosis with thrombocytopenia syndrome after SARS-CoV-2 vaccination. Thromb Res [Internet]. 2021 Jul 1 [cited 2021 Jul 7];203:163–71. Available from: https://pubmed.ncbi.nlm.nih.gov/34029848/

- TAG also urges countries, in collaboration with PAHO, to estimate the background rates of events that may be associated with COVID-19 vaccines, in order to establish a Region-specific baseline and assess causality.
- All serious adverse events must be reported and investigated in a timely manner in order to identify associated risk factors and to estimate rates of their occurrence. National regulatory agencies must conduct timely causality assessments to determine whether an adverse event may have a causal link to a COVID-19 vaccine.
- Immunization and health staff must be trained to recognize the symptoms and signs of thrombosis with thrombocytopenia syndrome (TTS) and other serious adverse events potentially associated with COVID-19 vaccines, as well as the contraindications for the different vaccines being used.
- The TAG recommends that countries develop simple and effective messages to communicate with the public about adverse events, provide timely information on new types of events, and ensure transparency where a causal association is established with one or more COVID-19 vaccine(s).
- The TAG emphasizes the SAGE's recommendation that persons experiencing a TTS event should not receive the second dose of the AstraZeneca vaccine.
- In the event of a TTS event following the first dose of AstraZeneca vaccine, countries should strongly consider completing the vaccination series with an mRNA vaccine.

Statement of the TAG on COVID-19 Vaccines and Vaccination

The Secretariat asks TAG members to use this session to review the available evidence on the "hot topics" of COVID-19 vaccines and vaccination and provide recommendations to Member States on how to address each topic in Latin America and the Caribbean.

1. Roadmap for prioritizing target populations

The first iteration of the "WHO SAGE Roadmap for Prioritizing Uses of COVID-19 Vaccines in the Context of Limited Supply" (October 2020) worked under the assumption of initially very limited supply in stages from 0-10%, 11-20%, and 21-50% of the population, based on the expected supply of vaccines. Since then, more ambitious coverage targets have been called for and some countries have reached higher coverage levels.

As vaccine supplies increase, the strategy expands to reducing transmission so as to further reduce disruption of social and economic functions. The SAGE interim guidance on prioritizing uses of COVID-19 vaccines was updated again in June 2021. In its new iteration, the roadmap helps countries to prioritize high-risk populations based on their own vaccination coverage goals and available supply[xxxvii]. The rationale for including each prioritized vaccine use-case based on population sub-group is anchored in the principles and objectives of the values framework. Special attention is paid to functions that disproportionately impact children and to reducing morbidity and mortality in disadvantaged groups. The goal is to further reduce mortality/morbidity and contribute to reductions in transmission of SARs-CoV-2 in order to minimize disruption of social and economic function.

2. Vaccination of specific groups

a. Pregnant women

Pregnant women are at higher risk of severe COVID-19 compared to women of childbearing age who are not pregnant, and COVID-19 has been associated with an increased risk of pre-term birth. In addition, women are often employed in occupations (such as public-facing hospital workers, teachers, childcare providers, and caregivers) that may be associated with higher SARS-CoV-2 exposure. In a US study, COVID-19 mRNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to that observed in non-pregnant women. Therefore, the CDC stated that pregnant and lactating women could receive the COVID-19 vaccines, but it noted that more follow-up data are needed for people vaccinated just before or early in pregnancy.

In the updated SAGE roadmap, pregnant women (regardless of risk level) are positioned in Stage II of all epidemiological scenarios, to be included as part of the "Groups with comorbidities or health states determined to be at significantly higher risk of severe disease or death."

[xxxvii] WHO SAGE Roadmap for Prioritizing Uses of COVID-19 Vaccines in The Context of Limited Supply. Available at: https://www.who.int/publications/i/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply

When considering a specific vaccine for use during pregnancy, WHO recommends that countries consult the section on pregnant women in the interim guidance document.

b. Adolescents

Infected children, regardless of their symptom status, can transmit SARS-CoV-2. WHO is reviewing studies that assess the non-inferiority of immune response to the Pfizer COVID-19 vaccine in persons ages 12-15 compared to persons ages 16-25. Results suggest a favorable safety profile, with greater immune response in adolescents than in young adults. The TeenCOVE study of the Moderna COVID-19 vaccine in adolescents met its primary endpoint. The manufacturer is working to submit data to regulators in the coming months.

In the updated SAGE roadmap, children and adolescents with severe chronic comorbidities that put them at significantly higher risk of severe disease are included for vaccine prioritization in Stage II in the Community Transmission and Sporadic Cases/Clusters of Cases epidemiologic scenarios. Where there is evidence that adults in these groups are at higher risk than persons ages 12-18, adults should be prioritized.

c. Immunocompromised persons

Immunocompromised persons are at higher risk of developing severe symptoms of COVID-19. They were included in most clinical trials for COVID-19 vaccines (with the exclusion of Sinopharm and Sinovac). Nonetheless, available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons. Across studies where the AstraZeneca vaccine effectiveness was compared between HIV-positive and HIV-negative participants, the vaccine was found to be safe and immunogenic for those whose CD4 count was high. If the person has a condition or is taking medications that weaken the immune system, he/she may not be fully protected even when fully vaccinated. There is no known interaction between COVID-19 vaccines and medications. WHO SAGE recommendations state that immunocompromised persons should receive the COVID-19 vaccine since the vaccines are neither live virus nor replicating viral vector.

3. Heterologous/mixed schedules

WHO is reviewing multiple studies that assess the immunogenicity and efficacy of heterologous vaccination schedules, specifically when using a combination of the AstraZeneca and Pfizer or Moderna vaccines. The Com-COV multicenter, participant-masked, randomized heterologous prime-boost COVID-19 vaccination study in the United Kingdom identified an increased frequency of mild to moderate adverse reactions (but no other safety concerns) when administering a heterologous schedule of AstraZeneca and Pfizer vaccine doses. A phase 2, open-label, adaptive, randomized, controlled clinical trial implemented in Spain reported that the AstraZeneca-Pfizer heterologous vaccination schedule yielded antibody responses apparently stronger than those following a two-dose AstraZeneca-only regimen. Compared to a two-dose Pfizer regimen, the mixed sequence showed "a slightly increased, but acceptable reactogenicity with superior or similar immunogenicity results." A study from Germany supports the safety of

heterologous AstraZeneca/Pfizer prime-boost immunizations with a 12-week interval. On 1 June 2021, the Public Health Agency of Canada issued a discretionary recommendation, where either AstraZeneca/COVISHIELD COVID-19 vaccine or an mRNA COVID-19 vaccine product may be offered for the subsequent dose in a vaccine series started with an AstraZeneca/COVISHIELD COVID-19 vaccine. While these studies are encouraging, the SAGE recommends cautious interpretation given the limited sample size and lack of follow up, especially related to safety data. There are currently no vaccine effectiveness studies on the use of heterologous schedules. More observational data will be forthcoming and further recommendations will be issued. In the interim, the SAGE recommends that countries may consider using ChAdOx1-S [recombinant] products followed by a mRNA platform vaccine (i.e., BNT162b2, mRNA-1273), particularly in situations of interrupted supply; a heterologous schedule constitutes an off-label use of the respective vaccines. This mixed schedule reports increased, but acceptable reactogenicity, as well as higher neutralizing antibody levels and higher T-cell-mediated immune responses.

4. Intervals between vaccine doses

WHO is reviewing multiple studies to assess the immunogenicity and efficacy of extending the interval between priming and booster doses of different COVID-19 vaccines. For Pfizer, studies in the United Kingdom report that peak antibody responses after the second Pfizer dose are markedly enhanced in older people (age80+) when the interval between the two doses is 12 weeks. Nonetheless, WHO continues to recommend that the doses be administered 21-28 days apart.

For AstraZeneca, after vaccination with a single 0.5ml dose, an efficacy as high at 76.0% could be expected measured from 22 days after vaccination through 12 weeks. The SAGE recommends that the two doses should be administered 8-12 weeks apart. Additional studies report that vaccine efficacy is higher in those with a longer prime-boost interval (81.3% at ≥12 weeks) than in those with a short interval (55.1% at <6 weeks). These findings led WHO to recommend that, in the face of limited supply of the AstraZeneca vaccine, countries may elect a strategy of vaccinating a maximum number of persons within a higher number of priority groups with a first dose and preferentially planning for the second dose to be provided 12 weeks later.

5. Need for booster doses

The term “booster dose” refer to vaccine doses administered after primary (1 or 2-dose) series that are needed to increase immunity after the waning of initial immune response. Analyses[xxxviii] suggest that:

[xxxviii] A. https://www.nature.com/articles/s41591-021-01377-8
B. Dan, J. M. et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science 371, eabf4063 (2021) Choe et al. Antibody Responses 8 Months after Asymptomatic or Mild SARS-CoV-2 Infection. Emerg Infect Dis. 2021;27(3):928-931. Doria-Rose et al. Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19. N Engl J Med 2021; 384:2259-226 https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-confirm-high-efficacy-and-no-serious

- Vaccine starting with initial efficacy of 95% is expected to maintain high efficacy (77%) after 250 days.[A]
- Vaccine starting with initial efficacy of 70% may result in drop to lower efficacy (33%) after 250 days.[A]
- To date, antibody persistence is demonstrated for up to 8 months after COVID-19 infection and up to 6 months after the 2nd mRNA vaccine dose.[B]

The SAGE states that there is currently no evidence on the need for a booster dose or booster doses of any EUL-approved vaccine after the current two-dose vaccine series is complete. The need for, and timing of, additional doses is being assessed in clinical trials. The CDC concurs in this assessment.

6. Assessing vaccine effectiveness against new variants of concern

After seven months of vaccination campaigns in most countries, multiple studies are assessing the effectiveness of COVID-19 vaccines under real world conditions. Of particular interest is the vaccines' effectiveness against variants of concern (VOC). To date, all vaccines report >70% effectiveness rates against multiple VOC (except for the Janssen vaccine against the Beta VOC: in South Africa, vaccine effectiveness measured 52%.). Nonetheless, more data are needed to assess the effectiveness of each vaccine against each of the four VOC identified to date (Alpha, Beta, Gamma and Delta variants).

- Argentina report (data included persons age 60+, 740,153 vaccinated, >82 days follow-up):
  - Sputnik 2 doses: 93% reduction in mortality; 1 dose: 75% reduction in mortality
  - AstraZeneca 2 doses: 89% reduction in mortality; 1 dose: 80% reduction in mortality
  - Sinopharm 2 doses: 84% reduction in mortality; 1 dose: 62% reduction in mortality
- Chile
  - Study (preliminary data included 10.5 million, of which 4 million vaccinated, 14-days after second dose): Sinovac (CoronaVac) 67% reduction in any symptomatic SARS-CoV-2 infection, 85% reduction in hospitalization and 80% reduction in mortality
  - Study (data included 10.2 million, of which 46.3% vaccinated, 14-days after second dose): Sinovac (CoronaVac): 66% reduction in any symptomatic SARS-CoV-2 infection, 88% reduction in hospitalization and 86% reduction in mortality
- Uruguay report (n= 862,045 vaccinated people, 14-days after second dose):
  - Sinovac (CoronaVac): 57% reduction in any symptomatic SARS-CoV-2 infection and 97% reduction in mortality
  - Pfizer (Comirnaty): 75% reduction in any symptomatic SARS-CoV-2 infection and 80% reduction in mortality
  - AstraZeneca: no data at the time of publication.
- Brazil

- Sinovac (CoronaVac) 41.6% effectiveness (≥14 days after second dose) against any symptomatic SARS-CoV-2 infection in elderly population. Vaccine effectiveness ≥14 days after the 2nd dose declined with increasing age and was 61.8% (95% CI 34.8 to 77.7), 48.9% (95% CI 23.3 to 66.0) and 28.0% (95% CI 0.6 to 47.9) among individuals 70-74, 75-79 and ≥80 years of age. Among individuals ages 70-74 years, vaccine effectiveness was 80.1% (95% CI, 55.7 to 91.0) against hospitalizations and 86.0% (95% CI, 50.4 to 96.1) against deaths. No evidence of protection for one only dose.

PAHO is collaborating with research institutions and ministries of health to establish a multi-country collaborative research network to assess COVID-19 vaccine effectiveness in a diverse set of LAC countries using a standardized protocol. The study will be conducted in Brazil, (FIOCRUZ), Argentina (Hurlingham University), Colombia (National University and University of Cartagena), and Chile. Other countries may be included in the second phase of the study.

Also, PAHO's regional office maintains the REVELAC-i regional SARI sentinel surveillance network to assess the effectiveness of vaccines against influenza (and now COVID-19) in preventing hospitalizations in adults. This network offers the possibility of evaluating the effectiveness for different COVID-19 vaccines, including specific SARS-CoV-2 variants. Selected countries (Chile, Colombia, Costa Rica, Ecuador, Guatemala, and Paraguay) are adapting the regional protocol to start this evaluation during the second semester of 2021. (

Recommendations

- TAG recommends that countries update their National Deployment and Vaccination Plans to align with the updated SAGE roadmap. Health and front-line workers, the elderly and other high-risk population groups should be prioritized for COVID-19 vaccination. The primary goal is to further reduce severe morbidity and mortality from COVID-19. Countries need to ensure that they have adequate plans and preparation for the arrival of large quantities of vaccine doses in Q4 2021 and 2022.
- The TAG recommends that all pregnant and breastfeeding women receive the COVID-19 vaccine. COVID-19 morbidity and mortality rates among pregnant women are significantly higher in the Americas compared to other WHO regions, indicating that the benefits of vaccination far outweigh the risks. Where SARS-CoV-2 transmission is limited, pregnant women should be vaccinated after their first trimester. Pregnant adolescents should be encouraged to receive the vaccine.
- Adolescents who do not have a high-risk comorbidity should not be included in the national vaccination plan at this time. Vaccination with a COVID-19 vaccine is not a pre-requisite for children or adolescents returning to school.
- The TAG agrees with SAGE that immunocompromised persons should receive the COVID-19 vaccine. It is, however, advisable to delay vaccination in persons who are severely immunocompromised due to chemotherapy, radiation or active disease until they have recovered some immunity.

- The TAG considers the scientific evidence for the use of some mixed vaccine schedules to be limited, and maintains that it is best to use the same vaccine for the 1st and 2nd doses. Nonetheless, in situations of reduced vaccine availability and sustained community transmission of SARS-CoV-2, the TAG agrees with the SAGE recommendation that countries may consider using ChAdOx1-S [recombinant] products followed by a mRNA platform vaccine (i.e., BNT162b2, mRNA-1273).
- The TAG believes it is essential to deliver the first dose of vaccine to as many people as possible to reduce severe COVID-19 and mortality. To be fully protected, it also is important for persons to complete the 2-dose series with the same vaccine. There is preliminary data to suggest that delaying the second dose of AstraZeneca vaccine beyond 12 weeks elicits an effective immune response. With respect to Pfizer and Moderna vaccines, there are limited data about delaying the second dose of those vaccines beyond 4 weeks. Extended intervals between vaccine doses should be considered only in situations where vaccine supply is limited.
- The TAG strongly recommends that countries in the Region invest in designing and implementing vaccine effectiveness studies, especially for vaccines and circulating strains for which there are limited data, in order to collect information to guide COVID-19 vaccine use in the Region The data will help improve confidence in the vaccines.

Recommendations for the Final Phase of Polio Eradication in the Americas

Global update

Polio eradication experienced a major setback in 2020: in Afghanistan and Pakistan, there was circulation of type 1 wild poliovirus (WPV1) and type 2 vaccine-derived poliovirus (cVDPV2), expansion into areas that were previously polio-free[xxxix]; in the last half of 2020, (6 July 2020 to 5 January 2021), there was also an increase in the number of outbreaks due to cVDPV2 in another 16 countries and cVDPV1 in one country. According to the Global Polio Eradication Initiative (GPEI), the main problems faced by the polio program can be summarized by three major challenges[xl]:

1. The perceived lack of full country ownership for the polio situation in all of the endemic countries and some of the outbreak countries.
2. Very low population immunity against type 2 poliovirus, which poses a high risk for the international spread of type 2 vaccine-derived poliovirus.
3. The COVID-19 pandemic and its impact on the polio program, both on delivery of services and on costs and funding.

Because of the current situation, in May 2021, the International Health Regulation (IHR) Emergency Committee declared that the international spread of WPV and cVDPV continues to be a Public Health Emergency of International Concern (PHEIC) under the IHR. Despite the setback on progress towards polio eradication–and the COVID-19 pandemic– there were two very important achievements in 2020:

1. The African region was certified as free of wild poliovirus.
2. In November 2020, WHO's pre-qualification program approved a recommendation for type 2 novel oral polio vaccine (nOPV2) as an Emergency Use Listing (EUL).

Regional update

Since the last case of polio was detected in the Region of the Americas in 1991, maintaining high and homogenous immunization coverage and sensitive surveillance systems has been a challenge for all countries, especially considering the need to introduce new vaccines and the presence of other high-priority public health events. According to data submitted through the 2019 PAHO-WHO/UNICEF Joint Reporting Form, the regional IPV1 coverage rate was 89%, ranging from 77% to 100%. Polio3 immunization coverage in children younger than 1 year old in the Region of Americas was 87%, and preliminary data shows a further decrease in coverage for 2020. Only 13 countries/territories reported coverage ≥95% in 2019: Antigua and Barbuda, Aruba, Belize, Bermuda, Cuba, Curaçao, Dominica, Guyana, Jamaica, Montserrat, Nicaragua, Saint Kitts and Nevis, Saint Vincent, and the Grenadines. Only 2% of children younger than 1 year old of the

[xxxix] WHO. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2020 – conclusions and recommendations. Available at: https://apps.who.int/iris/handle/10665/337109

[xl] Independent Monitoring Board. 19th Report. The World is Waiting. December 2020. Available at: http://polioeradication.org/wp-content/uploads/2020/12/19th-IMB-Report-The-World-is-Waiting-20201223.pdf

Region live in these countries. In addition to low vaccination coverage, the TAG expresses concem about the poor quality of surveillance of acute flaccid paralysis (AFP) in 2020 and 2021.

In 2020, there was a significant reduction in the number of reported cases of AFP compared to pre-pandemic years. Furthermore, as of epidemiological week 28 of 2021, the situation had worsened: 3 countries in Latin America and the Caribbean (Cuba, Dominican Republic and Uruguay) had not reported a single case of AFP; and compared to reported cases in pre-pandemic years, the average number of reported cases was ≥50%: Argentina (96%), El Salvador (94%), Peru (83%), Panama (80%), the Caribbean sub-region (73%), Ecuador (63%), Brazil (73%), Nicaragua (73%), and Costa Rica (50%) (see **table 6**).

Table 6. Reported AFP Cases by Country, 2018-2021*

Sub Region	Country	Reported AFP cases epi. weeks 1-28			
		2018	2019	2020	2021
AND	Bolivia	26	13	7	9
	Colombia	85	82	57	39
	Ecuador	21	31	16	8
	Peru	53	79	36	9
	Venezuela	45	52	34	28
BRA	Brazil	274	257	144	103
CAP	Costa Rica	8	9	10	4
	Guatemala	29	33	19	22
	Honduras	26	26	28	19
	Nicaragua	11	15	7	5
	Panama	10	1	7	1
	El Salvador	26	22	8	1
CAR	CAR	4	5	3	1
LAC	Cuba	15	13	10	0
	Dominican Republic	10	12	5	0
	Haiti	6	8	4	3
NOA	Mexico	319	394	306	225
SOC	Argentina	97	106	53	3
	Chile	32	27	20	14
	Paraguay	14	14	5	7
	Uruguay	2	6	0	0
Total Region		1113	1205	779	501

*Data from epidemiological weeks 1-28 for 2018 through 2021, children <15 years. All data as of 17 July 2021. Source: Country reports.

In 2020 only three countries (Costa Rica, Nicaragua, and Mexico) met the three main surveillance indicators (AFP rate, percentage of cases investigated within 48 hours and percentage of cases with adequate sample); in the last 52 epidemiological weeks, no country in the Region has met these three indicators.

Considering the risk of having a polio outbreak due to an importation or emergence of cVDPV, the lack of capacity to rapidly detect its spread, and the potential of community transmission because of low coverages, the Ministries of Health of Haiti (2016) and Guatemala (2018), with

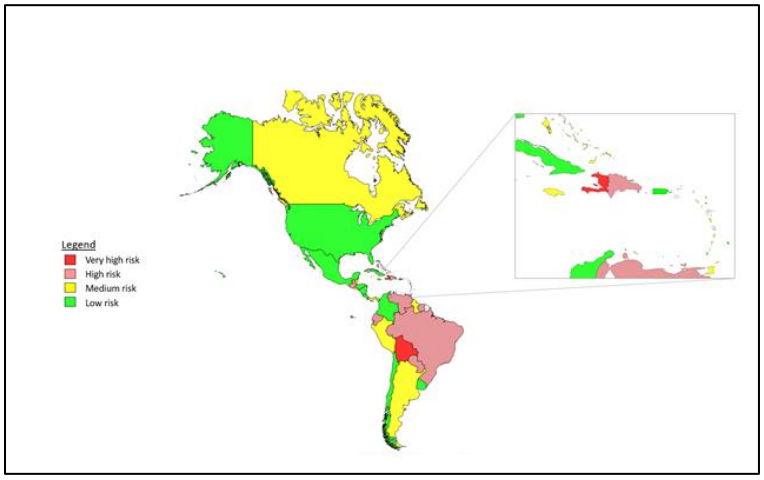
support from the CDC and PAHO, implemented environmental poliovirus surveillance to supplement AFP surveillance. In 2019, Guatemala detected three genetically unrelated VDPVs (2 VDPV1s and 1 VDPV3). National health authorities took immediate action to prevent poliovirus circulation. The action included a) a rapid response vaccination campaign; b) a national immunization campaign using bOPV and targeting children younger than 6 years; c) intensifying routine immunization activities with bOPV and IPV; d) introducing IPV2 into the national immunization schedule; and e) active case-finding of AFP cases. In addition, national health authorities took action to enhance AFP surveillance. As of July 2021, no cases of paralytic polio have been detected by the surveillance system and no additional VDPV have been isolated through environmental surveillance. However, surveillance performance is still below the established standards and vigorous efforts are required to improve the sensitivity and quality of AFP surveillance in the country. As of July 2021, an international group of experts is conducting an assessment of the response. The results and the conclusions of the evaluation will be shared with the next meeting of the TAG (date TBD).

Annual Polio Report 2019

The 12th Meeting of the Regional Certification Commission(RCC) for the Polio Endgame in the Region of the Americas was conducted virtually due to the COVID-19 pandemic. Following the Regional Framework for Review and Validation of Reports for Polio Eradication Certification, the commission reviewed and validated reports received from 21 countries + one sub-region. These represented a total of 34 countries and nine territories submitted by national authorities and National Poliovirus Containment Coordinators, endorsed by National Certification Committee and with information on the status of polio eradication activities from January to December 2019. The complete report is available at: https://www.paho.org/en/topics/poliomyelitis.

For the GAPIII containment report, the RCC validates the report in two parts: completion of the survey process and validation by type of material. Six countries are pending validation of containment reports: Brazil, Canada, Ecuador, El Salvador, Mexico, and the United States. As recommended by the Global Certification Commission, the RCC conducted a risk assessment for the Region of the Americas based on immunization coverage, surveillance, health determinants, containment status, and outbreak response preparedness. **Figure 4** shows the countries' overall classification.

Figure 4. Regional Polio Risk Assessment, 2020



Source: PAHO. Report of the 12th meeting of the Regional Certification Commission for the Polio Endgame in the Region of the Americas. Available at: www. https://www.paho.org/en/topics/poliomyelitis

Based on the evidence provided, the RCC concluded that all countries and territories in the Region remain polio-free. However, the RCC expressed concern over the sustainability of polio-free statuses in Bolivia, Brazil, Ecuador, Guatemala, Haiti, Paraguay, Suriname, and Venezuela. These countries, which represents 32.63% of the population of the Americas under 1 year of age have sustained low immunization coverage and weak surveillance systems, which poses a threat of cVDPV emergence or polio importation and subsequent circulation. The RCC formulated general and country-specific recommendations that were sent to the presidents of the NCCs and national authorities.

IPV global and regional supply status

In October 2012, WHO's Strategic Advisory Group of Experts (SAGE) on immunization recommended that all WHO Member States introduce at least one IPV dose into their routine vaccination schedules before withdrawing the type 2 component of the oral polio vaccine[xli].

In the Region of the Americas, the TAG recommended in 2015 that all the children under 1 year of age should receive at least one dose of IPV as part of routine polio vaccination. Member States began introducing IPV in preparation for the switch from tOVP to bOPV; tOPV was used for the last time in the Region on 1 May 2016.[xlii]

[xli] World Health Organization. Meeting of the Strategic Advisory Group of Experts on immunization, November 2012––conclusions and recommendations. *Weekly epidemiological record*, 4 January 2013. No. 1, 2013, 88, 1-16. Available on: http://www.who.int/wer/2013/wer8801.pdf.

[xlii] Pan American Health Organization. Final report of the XXIII Technical Advisory Group (TAG) Meeting on Vaccine-preventable Diseases, 1-3 July 2015, Varadero (Cuba). Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=31233&Itemid=270&lang=en.

Between 2016 and 2017, the supply of IPV was limited To mitigate the impact, PAHO shared periodical IPV supply briefings with ministers of health and EPI managers. Global IPV suppliers were monitored closely for changes in their supply plan while PAHO provided support to Member States in preparation for using fractional IPV doses (fIPV). IPV supply improved substantially after 2018[xliii].

In 2019, Gavi agreed to provide support for IPV2 procurement starting in 2021.[xliv] In October 2020, the SAGE noted that the supply of IPV had improved significantly, which made it possible to introduce a second IPV dose (IPV2) into the routine immunization schedules of the 94 countries that had been using one IPV dose and bOPV.

In the Americas, as of October 2020, there were 13 countries and territories that had not introduced IPV2 into their routine immunization schedules: Belize, Bolivia, Curaçao, Dominica, Dominican Republic, Haiti, Jamaica, Nicaragua, Saint Kitts and Nevis, Saint Lucia, Suriname, Trinidad and Tobago, and Venezuela. Gavi will support the introduction of IPV2 in Bolivia, Haiti, and Nicaragua but the date of introduction has not yet been determined. In March 2021, the SAGE recommended that remaining countries provide a second dose of IPV. The SAGE also recommended that countries should conduct IPV follow-up campaigns to provide type 2 immunity to those cohorts of children missed due to the earlier shortage of IPV supply.

Currently, 34 countries and territories use bOPV as part of primary immunization schedules or as booster doses, while 11 countries and territories use only IPV in their immunization schedules: Argentina, Aruba, Bermuda, Canada, Cayman Islands, Chile, Costa Rica, Mexico, Sint Maarten, Uruguay, and the United States.

In the context of the COVID-19 pandemic, the Revolving Fund for Access to Vaccines has played a crucial role in ensuring IPV supply for countries of the Americas. Monitoring IPV stocks in the countries, adjusting vaccine delivery schedules, and having an ongoing dialogue with suppliers have been key for this achievement.

Preferred IPV immunization schedule

In October 2020, the SAGE issued recommendations for the preferred IPV schedule for the countries planning on introducing IPV2. For these countries, the preferred IPV schedule is to administer the first dose at 14 weeks of age (with DTP3/Penta3) and to administer the second IPV dose after at least 4 months. This schedule provides the highest immunogenicity and may be carried out using full-dose IPV or fIPV without loss of immunogenicity. The SAGE added that

[xliii] Pan American Health Organization. Final report of the XXIII Technical Advisory Group (TAG) Meeting on Vaccine-preventable Diseases, 12-14 July 2017, Panama City (Panama). Available at: https://www.paho.org/hq/index.php?option=com_docman&view=download&category_slug=tag-final-reports-1626&alias=42498-24-tag-final-report-2017-498&Itemid=270&lang=en

[xliv] World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2020 – conclusions and recommendations. Available at: https://apps.who.int/iris/handle/10665/337109

countries may consider alternative schedules based on local epidemiology, programmatic implications, and feasibility of delivery.

As an alternative to the preferred schedule, countries may choose an early IPV schedule starting with the first dose at 6 weeks of age (with DTP1/Penta1) and the second dose at 14 weeks (with DTP3/Penta3). This alternative schedule offers the advantage of providing early-in-life protection, although lower total immunogenicity is achieved. If the second schedule is chosen, full dose IPV should be used rather than fIPV, due to the lower immunogenicity of fIPV at an early age. Regardless of the 2-dose IPV schedule used, the number of bOPV doses that are used in the routine immunization schedule should not be reduced after introducing the second IPV dose[14]. A summary is shown in **Table 7**.

Table 7. SAGE Recommendation for Polio Vaccination Schedule, October 2020

Polio Vaccination Schedule		Primary Series		Booster Doses
SAGE recommendations	**Preferred schedule**	14 weeks IPV fIPV	4 months after the first dose IPV fIPV	Number of bOPV doses that are used in the routine immunization schedule should not be reduced.
	Alternative schedule	6 weeks IPV	14 weeks IPV	

Sabin-IPV (sIPV)

The first Sabin-based inactivated poliovirus vaccine (sIPV) was prequalified by WHO in late 2020. The SAGE reviewed available data on the safety and immunogenicity of sIPV and concluded that sIPV and traditional Salk-based IPV (wIPV) were equivalent in terms of immunogenicity and safety. The SAGE recommended that sIPV could be used interchangeably with wIPV for routine immunization or campaign use. Since evidence on the use of fractional sIPV was lacking, SAGE did not recommend use of sIPV as a fractional dose. SAGE emphasized the long-term importance of sIPV as a strategic option to ensure an adequate global IPV supply.

Recommendations

- The TAG endorses the GPEI's "Global Polio Eradication Strategy 2022-2026 Delivering on a Promise," which should be adopted by countries of the Americas.
- The TAG is extremely concerned with the inadequate polio vaccination coverage and the weak surveillance systems, which are unable to sustain and verify polio eradication in the Americas; unless these are urgently improved, it fears that WPV1 and/or cVDPV outbreaks may occur in the Region.
- The TAG urges countries to achieve 95% coverage with Polio3, and strongly recommends governments to invest resources in achieving and maintaining this target. This immunization coverage target also applies to IPV1 and IPV2.
- The TAG noted the SAGE evaluation of the systematic review of IPV immunogenicity. The TAG then considered the previous TAG criteria regarding the use of IPV as the first dose to prevent

VAPP and the need to sustain gut immunity by administering bOPV. The TAG recommends the following vaccination schedule for the 13 countries that have not yet introduced the second dose of IPV:

Regional recommendation for polio vaccination schedule, the Americas, 2021

Vaccination schedule	Basic			Booster	
	1st	2nd	3rd	4th	5th
	2 months	4 months	6 months	12-18 months	4-5 years
	IPV	bOPV	IPV	bOPV	bOPV

- Countries that have already introduced two doses of IPV may consider adopting the above schedule or consider the interval of 4 months between IPV1 and IPV2. Their final decision should be based on a programmatic and epidemiological analysis.
- The TAG congratulates Ecuador for conducting a study on the effectiveness of the use of fractional dose of IPV. The results of this study should be used to determine if the current schedule is appropriate or if changes are needed.
- Given the constraints of the COVID-19 pandemic, the TAG does not recommend that countries discontinue the use of bOPV in favor of an IPV-only schedule at this time.
- The TAG endorses the recommendations given by the SAGE regarding the interchangeability of sIPV with wIPV. As of July 2021, sIPV is not recommended as a fractional dose.
- Given that the Region's AFP rate has reported only a slight increase between 2014 and 2019 (1.19 and 1.33, respectively), and stool adequacy has remained constant during the same period (76% and 77%, respectively), the TAG recommends that efforts must be made to improve the performance of both indicators to avoid missing cases of paralysis caused by polioviruses.
- Considering the sharp drop in vaccination coverage and surveillance rates, countries at very high risk of outbreaks (Haiti and Bolivia) or at risk due to ongoing population movement with a high-risk country (Dominican Republic) should consider the collection of a second stool sample. Given the workload and costs of collecting a second sample, these countries should implement this temporary recommendation while strengthening their immunization program and surveillance systems.
- If a stool sample cannot be collected from the AFP case within 14 days of the onset of paralysis, or if a stool sample arrives at a laboratory in poor condition, The TAG recommends that countries collect one stool sample from each of three contacts, preferably from close family members, household contacts, neighbors, or playmates (all younger than 5).
- The TAG strongly recommends consistent implementation of the 60-day follow-up visit to assess the presence of residual paralysis. (This assessment is currently completed in fewer than 20% of cases.)
- Environmental surveillance is an excellent addition to the national surveillance system. However, considering its very high cost, a country should consider implementing environmental surveillance only after improving the sensitivity of its AFP surveillance systems.

Managing Advantages and Risks in the Integration of Other Temperature Sensitive Health Products into the Vaccine Cold Chain

WHO and UNICEF published two joint statements permitting the integration of other health commodities into the vaccine cold chain system. The statements urge countries to consider integrating temperature-sensitive health products into national Expanded Program on Immunization (EPI) cold chain systems (including storage and transportation) whenever it is safe and feasible. The temperature-sensitive health products to be integrated include, but are not limited to, COVID-19 diagnostics and therapeutics, HIV diagnostic kits, oxytocin, insulin, and treatments requiring refrigeration. The decision to integrate pharmaceutical products should be guided by an assessment of cold chain capacity and an integration plan. This guidance on safe integration must be followed to ensure the quality and potency of all health products in the shared storage space. EPI refrigerators and vaccine carriers should never be used for storing COVID-19 laboratory specimens or samples.

Data collected by the WHO/UNICEF Joint Reporting Form for 2018, 2019, and 2020, specifically regarding EPI vaccine cold chain storage and transportation policies and practices, show that most countries have specific policies against storage and/or transportation of pharmaceuticals with vaccines. With regard to practices, most countries responded that they do not store and/or transport pharmaceuticals with vaccines.

PAHO's Comprehensive Family Immunization Unit has recommended exclusively storing vaccines in the cold chain of immunization programs because of the risk of serious programmatic errors arising from a healthcare worker mistakenly administering a dose of a drug instead of a dose of vaccine. Documented experiences confirm that healthcare workers have stored other biologicals or drugs in a vaccine refrigerator. As a result, "the staff mistakenly administered a muscle relaxant and, on another occasion, insulin, instead of a vaccine." This type of programmatic error will lead to decreased community confidence in the immunization program, especially with today's strong anti-vaccine movement. If another programmatic error occurs, it may cause further distrust in the value of vaccines.

There are risks and burdens to be considered when integrating pharmaceutical products into the EPI cold chain. Risks include: an increase in programmatic errors, such as the administration of a pharmaceutical instead of a vaccine, which could lead to a critical adverse event; breaching cold chain good practices (e.g., door openings, or preventing contaminations); an increase in mistakes caused by the high turnover rate among healthcare workers; and healthcare workers accidentally freezing temperature-sensitive pharmaceuticals and freeze-sensitive vaccines. Each country needs to review legal responsibilities for possible modifications in vaccine/pharmaceuticals regulations (assigned responsibilities).

Nonetheless, there are possible advantages when integrating storage and distribution of pharmaceutical products into the EPI cold chain. Integration may provide greater storage capacity and therefore greater availability of safely stored pharmaceuticals. This may facilitate the addition of other healthcare services in healthcare facilities and may achieve possible cost efficiencies.

Managers at all levels need to assess the impact of storing and transporting pharmaceuticals in the EPI cold chain. Special attention must be given to storage capacity, particularly at the local level. The following issues require a robust assessment of the time frame required for proper integration: the risk evaluation required at all levels for proper integration; possible restructuring of health programs in some countries; and defining metrics, such as how countries measure whether a cold chain is sufficiently flexible. Attention should be given to possible construction issues to increase refrigeration storage capacity. In addition, budgets may have to be increased for new refrigerator purchases and infrastructure space, as well as for changes to the management information system and support training and supervision.

For the last 40 years, the countries in the Americas have implemented norms and policies for building a safe and efficient cold chain for storing and transporting vaccines only. These practices have contributed to the extension of immunization services safely delivered at all levels.

Recommendations

- Due to the well-documented risk of patient safety breaches, the TAG agrees that countries should maintain the current recommendation on exclusive storage of vaccines in the EPI cold chain.
- If a country decides to integrate other pharmaceutical products into its EPI storage and distribution cold chain, it should make a complete assessment of the cold chain and take the necessary preparatory steps to address the additional complexity in inventory and management systems that this requires.