TECHNICAL DOCUMENT

Building better immunity

A life course approach to healthy longevity

PAHO Pan American Health Organization
World Health Organization Americas

TECHNICAL DOCUMENT

Building better immunity

A life course approach to healthy longevity

Washington, D.C., 2023

PAHO Pan American Health Organization World Health Organization Regional Office for the Americas

Building better immunity: A life course approach to healthy longevity

ISBN: 978-92-75-12744-5 (PDF)

ISBN: 978-92-75-12745-2 (Print version)

Suggested citation: Pan American Health Organization. Building better immunity: A life course approach to healthy longevity. Washington, D.C.: PAHO; 2023. Available from: https://doi.org/10.37774/9789275127445.

Cataloguing-in-Publication (CIP) data: Available at http://iris.paho.org.

HSS/HL/2023

Photographs: © PAHO

Contents

List of figures

List of tables

Acknowledgments

This publication represents the work and contributions of several experts within and outside the Pan American Health Organization (PAHO). The lead authors and editors of the publication are Evelyn Balsells, Margherita Ghiselli, Carolina Hommes, Ana Lucia Rosado Valenzuela, and Enrique Vega. PAHO is also grateful for the input of Shalini Desai (World Health Organization, Immunization, Vaccines and Biologicals Department) and Roy K. Philip (University of Limerick School of Medicine and Maternity Hospital).

Sincere thanks also for the technical support provided by the following PAHO personnel: Ernesto Bascolo, Andrés de Francisco Serpa, Natalia Houghton, Martha Velandia, and Beatriz Nascimento Lins de Oliveira. External collaborators included Aaron Wallace, Daniel Ehlman, and Ciara Sugarman (U.S. Centers for Disease Control and Prevention, Global Immunization Division).

As a result of the work and dedication of these and several other persons not mentioned here, this publication will help inform the discourse on immunity across the life course in the Region of the Americas.

Abbreviations and acronyms

BCG	bacillus Calmette–Guérin
HPV	human papillomavirus
IA2030	Immunization Agenda 2030
LCA	life course approach
PAHO	Pan American Health Organization
PHC	primary health care
VPD	vaccine-preventable diseases
WHO	World Health Organization

Introduction

The full benefits of vaccines extend across the life course. Vaccines can extend life expectancy, by preventing death, and improve the quality of life, by preventing disease and disabilities. By reducing the burden and transmission of infectious diseases, especially among children younger than 5 years, vaccines have saved millions of lives *(1)*. However, as life expectancy continues to increase, it is important to recognize that the wide range of vaccines available need to be administered at different points along the life course. In 2019, the global population of adults older than 65 years surpassed for the first time the population of children younger than 5 years *(2)*. In the Region of the Americas, 164 million persons were over 60 years of age in 2019, and this is estimated to surpass 310 million by 2050 *(3)*. There has never been a society with this age distribution before. Recognizing the opportunities and challenges associated with this trend in life expectancy, there is a need to maximize the impact of effective public health interventions, such as vaccination, which can contribute to living healthier lives and trajectories.

The countries and territories of the Americas have made tremendous progress in the implementation of vaccination programs for children, teenagers, adults, and older adults (*4–6*). Yet, there are multiple missed opportunities in the Americas for the population to fully benefit from vaccines at all stages of life. There is a need to recognize the full potential of promoting a life course approach (LCA) to immunizations, not only to prevent disease but also to promote health. This topic is especially timely following the acute phase of the COVID-19 pandemic, as all countries in the region have invested in vaccine platforms for all age groups (i.e., strategies to generate acceptance and uptake of vaccines across all age groups, as well as systems to track vaccine administration and evaluate performance). Also, vaccination coverage rates against multiple vaccine-preventable diseases (VPD) have fallen dramatically in the Americas over the last three years (for measles, polio, rubella, etc.) *(7)*. A renewed focus on the LCA in immunization can highlight the benefits of vaccines beyond childhood, as well as provide routine structured opportunities for catching up all persons who missed the recommended vaccine doses.

This technical document explains the key concepts of the LCA to health with a focus on immunization by vaccination, as well as the underlying biological mechanisms for the need for boosters and different vaccines in different life stages according to changes in epidemiology and changes to the immune system. Using examples of different vaccines, this document describes the impact of vaccines from the point of view of the LCA. Finally, this document provides several considerations for the implementation of this approach in national immunization programs. This publication is part of PAHO's efforts to introduce the concepts of the immunization across the life course to the countries and territories of the Americas and ensure that citizens reap all the benefits that vaccines can bestow.

Key messages

- The world, including the Americas, is undergoing a profound demographic shift where there are more persons over the age of 65 years than children younger than 5 years, and longevity continues to increase.
- This publication provides multiple examples of how different vaccines, when administered at the appropriate time, can generate health benefits beyond protection from a single pathogen.
- The effectiveness of vaccine doses administered early in life declines with time.
- The extension of vaccination services to all age groups, including the administration of booster and catch-up doses, can be implemented through a revision of the different elements of the national immunization program.
- National immunization systems must be redesigned to ensure full immunization of children as well as of adolescents, adults, and older adults.
- Ministries of health must consider vaccination services as a public health intervention that can be adjusted to close the immunity gaps of each age group.
- Closing immunity gaps helps to minimize the impact of disease, increase the body's capacity to stay healthy across the stages of life, and reduce all-cause mortality rates in the population.

Intended audience

- Technical staff of the national Expanded Program on Immunization (EPI) from ministries of health.
- Technical and financial partners involved in immunization programs and operations at the national and regional levels.
- Ministries of health who want to review key concepts and lessons learned from the implementation of the LCA in the Americas.

Objectives

Main objective

This technical document aims to present the biological framework of immunity across the life course and define its core principles and contributions to public health efforts in the Americas.

Specific objectives

- To introduce the concepts of the LCA and its application to immunizations.
- To describe the biological mechanisms that result in immune gaps, as well as the activation of the immunological system when vaccines are applied at specific moments in a person's life.
- To present examples for multiple vaccines and their benefits from a life course perspective.
- To describe the practical considerations required to integrate the LCA into existing national immunization programs.
- To present recommendations that ensure a continuum of immunization interventions and strategies across life stages, under the umbrella of a comprehensive primary health care approach.

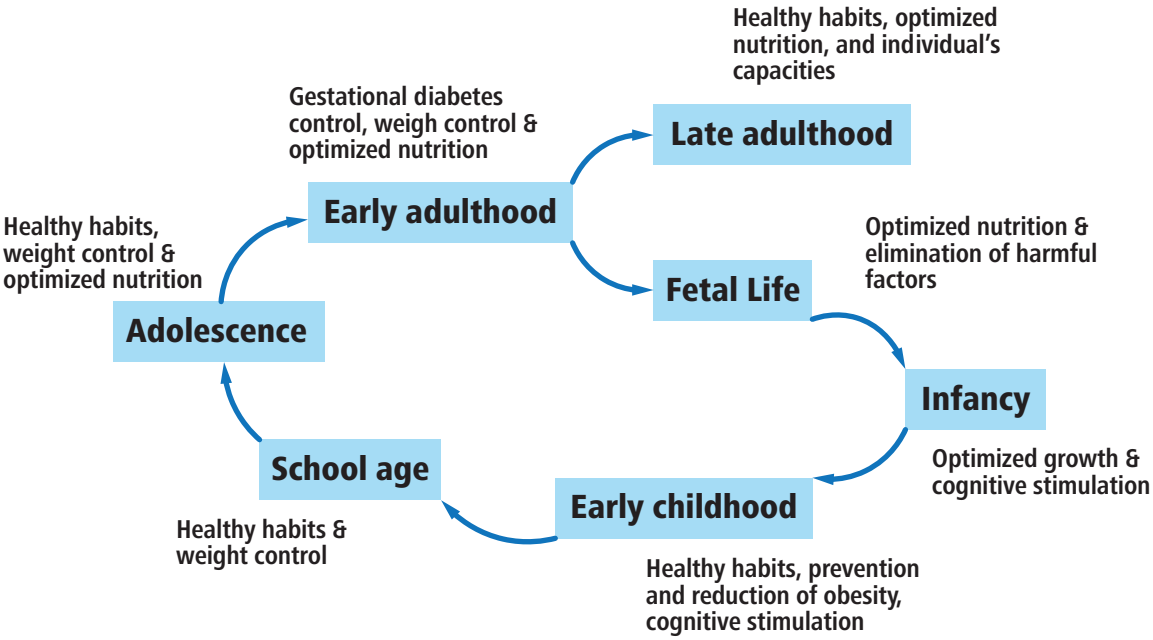
Key concepts

Life course approach

The LCA to health provides a framework to understand the health and well-being of individuals and populations as the sum of capacities that are built, sustained, and recovered across both life stages and generations *(8)*. The LCA explores the dynamic relationship between previous exposures (e.g., diseases, therapeutics, behaviors, environmental factors) and the subsequent results, as well as acknowledging the positive and negative factors that shape health and trajectories at the individual, family, community, and societal levels.

The LCA emphasizes that human health is a product of both genetics and the environment. The factors that shape a person's immune system include environmental influences, public health interventions, healthcare services, personal behaviors, and social constructs *(9)*. These factors interact continuously with a person's genetic predispositions. Combined, all these elements can impact the individual's health trajectory and contribute to the body's ability to fend off infections. Figure 1 presents examples of health interventions that affect individuals now, in the future, and in relation to other life stages.

Figure 1. Circular display of the life course approach and key priorities at various stages



Note: The list is not exhaustive.

Source: Adapted from Aagaard-Hansen J, Norris SA, Maindal HT, Hanson M, Fall C. What are the public health implications of the life course perspective? Global Health Action. 2019;12(1):1603491.

Principles

Eight key principles have been proposed in the LCA to health *(10)*. Each principle considers factors across space and time that may affect the health of individuals at different ages (see Table 1). The goal of this approach is to promote timely investments in health at different points in life to maximize the effectiveness of each intervention.

Table 1. Principles of the life course approach applied to examples on immunization

Principle	Definition	Example on immunization
Temporality	The historical period and the societal structure can have profound effects on the health status of a person. From a life course perspective, it is important to consider the moment when these impacts occur and that the results may vary as a person ages.	It has been estimated that, since 1988, the polio vaccine has allowed more than 18 million people to walk who would otherwise have been paralyzed.[1]
Cumulative impact	Previous experiences and exposures may have an impact on an individual's current state of health. Risk factors can accumulate throughout life and produce greater negative health outcomes. In the same way, the positive impact of health interventions can accumulate over time to produce maximum benefit.	There is a close synergy between measles and vitamin A deficiency that can result in xerophthalmia,[2] with corneal ulceration,[3] keratomalacia,[4] and subsequent corneal scarring or phthisis bulbi.[5] Measles blindness is the single leading cause of blindness among children in low-income countries, accounting for an estimated 15 000 to 60 000 cases per year.[6]
Critical and sensitive periods	Particular periods of life are sensitive because exposures provoke adaptive responses whose effects last into other life stages (e.g., prenatal stage). Many diseases are the result of risks accumulated throughout life, especially during its critical periods.	The Bacillus Calmette–Guérin (BCG) vaccine is administered within the first 24 hours of life to protect newborns from severe tuberculosis while their neutrophil functions (i.e., one of the first immune cells to respond) reach adult levels a few days after birth.[7]
Trajectories	In the life course approach, trajectories can reflect a decline or an improvement in health status. They are influenced by interdependent domains (e.g., work, school, reproductive life, migration) and factors (e.g., social, cultural, economic, political).	When administered before exposure to human papillomavirus (HPV) – that is, prior to sexual intercourse – the vaccine can prevent infection and minimize the likelihood of later development of precancerous and cancerous lesions.
Transitions	Between stages of life, there may be moments of change with biological, economic, psychological, social, political, or geographical origins. At these times, individuals may experience gain or loss of functions. At the population level, transition moments are evident in changing patterns of population distributions in relation to mortality, fertility, life expectancy, and leading causes of death.	The COVID-19 pandemic has caused over 750 million cases and over 7 million deaths worldwide. According to estimates, vaccination against COVID-19 prevented 14.4 million deaths (95% credible interval 13.7–15.9) in 185 countries and territories between December 2020 and December 2021.[8]
Linked lives	A person's health status is influenced by the generations that preceded them (e.g., parents, families, communities). The same factors can impact their offspring. Therefore, health interventions must consider genetic links, social roles, and networks as influencers of health.	Breast milk is the best source of nutrition for infants because it contains antibodies and other immunological factors that can help protect infants against respiratory diseases.
Transfer of traits and resources	Resources (e.g., socioeconomic status, behaviors, congenital traits) can be transferred between generations. Children learn habits and behaviors from their parents, which may be favorable or unfavorable to health. Also, they may acquire inherited traits and material goods (or debts) that impact their health status and well-being.	Parents of unvaccinated children were more likely to report that they do not trust COVID-19 vaccines, do not trust the government, and do not believe children need a COVID-19 vaccine compared to parents of vaccinated children.[9]
Human agency	Human agency is affected by social determinants (i.e., the conditions in which people are born, grow, work, live, and age). The life course perspective seeks to understand how health trajectories are shaped by the interaction between a person's agency (i.e., individual thoughts and actions) and social determinants.	Vaccine hesitancy – the reluctance or refusal to vaccinate despite the availability of vaccines – threatens to reverse progress made in tackling vaccine-preventable diseases. The reasons why people choose not to vaccinate are complex and include complacency, inconvenience in accessing vaccines, and lack of confidence.[10]

Notes:

1 U.S. Centers for Disease Control and Prevention. Polio. Atlanta: CDC; 2019. Available from: https://www.cdc.gov/globalhealth/newsroom/topics/polio/index.html#print

2 Medical condition in which the eye fails to produce tears.

3 Open sore in the outer layer of the cornea. The cornea is the clear front part of the eye.

4 Medical condition in which the cornea gets cloudy and softens.

5 Medical condition representing end-stage ocular response to severe eye injury or disease damage.

6 Semba RD, Bloem MW. Measles blindness. Surv Ophthalmol. 2004;49(2):243–255.

7 Pan American Health Organization. Maternal and Neonatal Immunization Field Guide for Latin America and the Caribbean. Washington, D.C.: PAHO; 2017 [cited 6 March 2023]. Available from: https://iris.paho.org/handle/10665.2/34150.

8 Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis. 2022;22(9):1293–1302.

9 Nguyen KH, Nguyen K, Mansfield K, Allen JD, Corlin L. Child and adolescent COVID-19 vaccination status and reasons for non-vaccination by parental vaccination status. Public Health. 2022 August;209:82–89.

10 Halfon N, Larson K, Lu M, Tullis E, Russ S. Lifecourse Health Development: Past, Present and Future. Matern Child Health J. 2014;18(2):344–365.

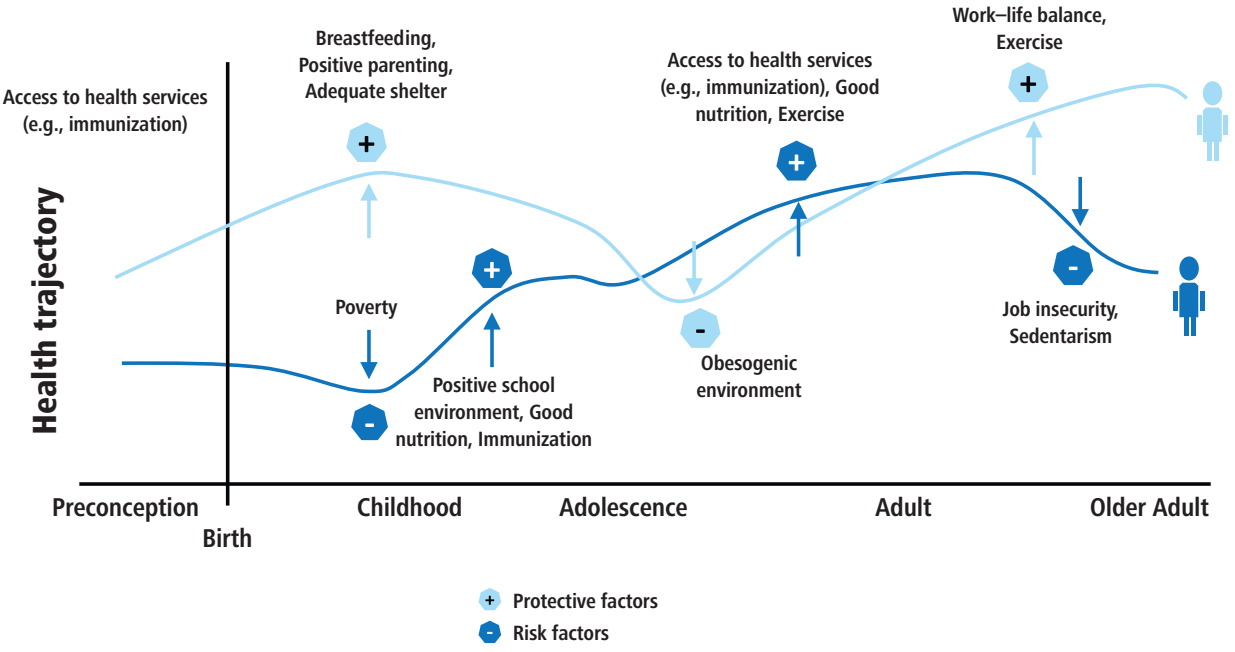
Source: PAHO.

Intergenerational impact

The LCA helps public health officials identify key moments where health interventions can be adjusted to obtain maximum benefits, thus improving the health trajectories of individuals and communities. This approach enables public health systems to respond to new health trends, fill long-standing gaps in health care and public health interventions, address health inequities, and help achieve greater outcomes with less resources *(11)*.

The development of health is influenced by multiple socioenvironmental factors (see Figure 2). Such factors may increase risks of disease (e.g., poverty, lack of access to health services, job insecurity, sedentarism, obesogenic environment) or protective influences (e.g., positive parenting, positive school environment, access to preventive health interventions, work–life balance, exercise). As these factors are dynamic, their impact on the health capacity of an individual and their offspring fluctuates across the life course. Early-life environmental exposures can impact the developing immune system, adversely affect the health of the exposed offspring later in life, and potentially extend to future generations through genetic changes *(12)*.

Figure 2. Variable health trajectories and protective and risk factors



Source: Adapted from Halfon N, Larson K, Lu M, Tullis E, Russ S. Lifecourse Health Development: Past, Present and Future. Matern Child Health J. 2014;18(2):344–365.

Biological factors associated with immune regulation

The immune system is a complex network of organs, cells, and proteins that defends the body against infection while protecting its own cells. There are different mechanisms involved in immune regulation, including feedback loops, negative regulation, and checkpoint molecules that help to prevent excessive immune activation. For example, regulatory T cells can suppress the activity of other immune cells to prevent the immune system from attacking the body's own tissues. Similarly, cytokines can have both stimulatory and inhibitory effects on immune cells, and the balance between these effects is critical for maintaining a healthy immune system.

According to the Pan American Health Organization (PAHO), immunization is defined as a process whereby a person's body generates resistance to an infectious disease, typically through the administration of a vaccine. Yet this definition can be expanded to include:

- **Acquired immunity:** Exposure to the disease organism through infection with the actual disease.
- **Maternal immunity:** The immune system starts to develop as early as two weeks post-conception *(13)* and is trained through contact and transfer of maternal antibodies in utero. This maternal protection lasts throughout the first year of life and is boosted through breastfeeding *(14)*.
- **Passive immunity:** Persons receive laboratory-made proteins (i.e., monoclonal antibodies *[15]*) that boost and mimic the immune system's ability to fight off harmful pathogens. This treatment can be used to protect very premature infants and young children with certain heart and lung conditions against severe respiratory syncytial virus (RSV) disease *(16)*.
- **Community immunity:** Persons who are not immunized through vaccination or infection are still protected from disease transmission because of the high vaccination rates achieved by the surrounding community.

Immunization reduces the incidence and prevalence of diseases, disabilities, and deaths associated with VPDs *(17)*. Building an immune system is critical for survival and healthy life expectancy. As people age, biological changes influence their immune capacity. Aging results in a shift toward adult blood cells (i.e., in the myeloid lineage, such as macrophages and granulocytes) at the expense of cells involved in the adaptive immunity and from the innate immune system (i.e., lymphoid progenitors such as T cells or B cells and natural killer cells). This shift results in an increase with age in the ratio of memory T cells to naïve T cells, which is advantageous as the host develops a memory cell repertoire against the pathogens encountered on a regular basis *(17)*. However, lymphocytes cannot proliferate indefinitely, which contributes to immunosenescence – the gradual decline in both acquired and innate immune functions *(18)*.

Immunosenescence can lead to the reemergence of infections even when the person was previously immune *(17)*. An example is shingles, which is a disease caused by varicella zoster virus, the same virus that causes chickenpox. After a person recovers from chickenpox, the virus stays dormant in the body and may reactivate years later, causing shingles. This explains the recommendation for shingles vaccination in those older than 50 years of age (*19–21*).

Also, as people age, they are increasingly susceptible to new infections, cancers, and other autoimmune diseases (*19, 20, 22*). For example, inflammaging is a chronic inflammatory process that is pathogen-independent (i.e., it is not caused by an infection) *(23)*. For some persons, chronic diseases are due to genetic traits; for others, these develop as one ages. For the latter, the older immune system has reduced ability to respond to a specific stimulus (e.g., inflammation, vaccination, pathogen) because of the interaction between the chronic disease and the increased presence of proinflammatory cells in the body *(24)*. An impaired ability to differentiate between stimuli can lead to increased vulnerability to diseases, decreased responses to some vaccines, and greater susceptibility to age-related inflammatory diseases (*19, 25)*.

1. A life course approach to immunization

Considering the LCA principles and the biological factors underpinning immunity, an LCA to immunization focuses on maximizing an individual's ability to protect against infections, as well as to boost the individual's immunity. Immunization is thus an intervention that builds health capacities of individuals, making them more resistant to other comorbidities and pathogens and able to maintain good health over their lifetime *(26)*. An LCA to immunization states that persons should receive all recommended vaccine doses along their life course to reap the maximum benefits at different ages, across generations, and within their communities. The timing of vaccine administration and the number of doses applied can bridge the immunological gaps of each age group, as well as enhance and extend the immunity that was developed in the first years of life.

Also, each infection, vaccination, and environmental exposure contributes to increasing the resilience of the innate and adaptive immune systems. Vaccination is the public health intervention that maintains this plasticity by continuously training the immune system to mount the appropriate immune responses needed to deal efficiently with the source of immune stimulation – a status called immune fitness *(27)*. Consequently, the immune system can be trained to recognize and continuously respond to internal and external immune challenges.

Both the concept and application of the LCA to immunization is essential to achieve the objectives of the Immunization Agenda 2030 (IA2030), which aims that "all people benefit from recommended immunizations throughout the life-course, effectively integrated with other essential health services" *(28)*. As such, health systems and public health departments are called to implement effective immunization programs and campaigns that reach individuals at every life stage. An LCA to immunization heightens our awareness of the different vaccination requirements to achieve optimal immunity.

Immunization beyond infectious diseases for a healthier life

The primary goal of vaccination is to prevent infection by specific pathogens. Yet, vaccines can have indirect effects on other illnesses *(29)*. Vaccines can reduce the burden associated with disabilities or chronic conditions. Table 2 shows examples of chronic or disabling medical conditions that arise as complications of VPDs. High vaccination coverage rates can reduce the prevalence of these conditions in the general population.

Table 2. Disabling health conditions that may be prevented by immunization

VPD	Associated chronic or disabling health condition prevented by immunization
Tuberculosis	Lung damage
Diphtheria	Myocarditis (damage to the heart muscle), polyneuropathy (nerve damage), kidney failure
Hepatitis B	Cirrhosis, chronic liver disease, liver cancer, liver failure
***Haemophilus influenzae* type b (Hib)**	Neurological sequelae, particularly in HIV-infected children, arthritis, osteomyelitis (inflammation of the bone), pericarditis (inflammation of membrane surrounding the heart)
Human papillomavirus	Cancers of the cervix, anus, vulva, vagina, penis, oropharynx, oral cavity, larynx
Measles	Hearing loss, vision loss[1,2]
Meningitis	Developmental delay, hearing loss, epilepsy, other neurological disorders[3]
Pertussis	Pulmonary, neurologic, and nutritional complications
Polio	Paralysis or severe muscle weakness
Rubella	Hearing loss, vision loss, liver or spleen damage, heart problems

Notes: VPD, vaccine-preventable disease.

1. Wright DO, Leigh B. The impact of the Expanded Programme on Immunisation on measles-induced sensorineural hearing loss in the western area of Sierra Leone. West Afr J Med. 1995;14(4):205–209.
2. Cohen BE, Durstenfeld A, Roehm PC. Viral Causes of Hearing Loss: A Review for Hearing Health Professionals. Trends Hear. 2014 October 17;18:233121651454136.
3. World Health Organization. Meningococcal vaccines: WHO position paper - November 2011. Geneva: WHO; 2011. Available from: https://www.who.int/publications/i/item/WER8647.

Source: PAHO.

The interaction between the chronic disease and the increased presence of proinflammatory cells in the body as one ages can further reduce the resilience of the immune system, leaving it more vulnerable to future infections. Therefore, in addition to reducing the risk of infection with a specific pathogen, vaccines administered earlier in life can minimize the likelihood of developing chronic diseases and disability, thus reducing the vulnerability of the immune system later in life. This is an example of how life trajectories can be adjusted through health interventions (in this case, vaccines) to minimize vulnerability at different points along the life course. Despite this evidence, quantifying these effects and consciously manipulating them to the advantage of the individual is not yet common practice and must be encouraged to understand the benefits of strong immunization trajectories.

Immunotherapy and therapeutic vaccines

Immunotherapy is a biological therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Some immunotherapies only target certain cells of the immune system; others affect the immune system in a general way. Types of immunotherapy include cytokines, vaccines, and some monoclonal antibodies *(30)*. For example, immunotherapy is a type of cancer treatment that helps the immune system fight cancer by helping the body recognize and eliminate cancer cells *(30)*. There are multiple immunotherapy drugs currently in use (e.g., anti-SARS-CoV-2 monoclonal antibodies) *(31)* in different countries.

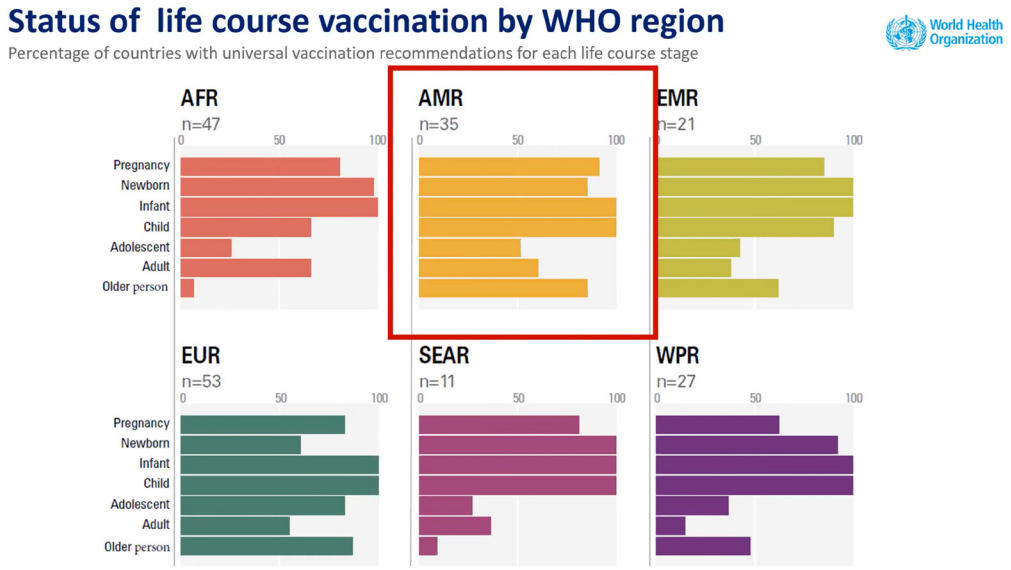
The experimental immunotherapies under development include vaccines for cancer treatment (*32–34*). These vaccines might mobilize T-cell responses against both tumor-specific antigens (TSA) and tumor-associated antigens (TAA). By activating tumor antigen-loaded dendritic cells, cancer vaccines may induce immune responses against a large array of intracellular antigens. Clinical trials are ongoing on therapies to combat hypertension, dyslipidemia, Alzheimer's disease, cancer, and multiple inflammatory diseases *(35)*. These potential vaccines are all in experimental stages, but progress has been reported for a vaccine against brain cancer (*36, 37)*.

Finally, recent work *(38)* to selectively target senescent cells (i.e., those deteriorated with age) associated with several pathologies has resulted in the creation of a peptide vaccine that primarily targets endothelial cells expressing high levels of glycoprotein nonmetastatic melanoma protein B (GPNMB) *(18)*, which is an endogenous glycoprotein recently identified as a biomarker of senescence. The vaccine reduces atherosclerotic plaque burden and metabolic dysfunction such as glucose intolerance in mouse models of obesity and atherosclerosis. For translation to humans, the activity of the vaccine will need to be tightly controlled, as the GPNMB target has multiple roles in normal physiology, including acting to inhibit and possibly resolve inflammation.

Current implementation in the Americas

The countries and territories of the Americas have made tremendous progress in the introduction of vaccines aimed to prevent diseases in different age groups (see Figure 3). Some countries in the Americas already incorporate the LCA in their health policies (*39, 40)*. Many countries already include different age groups in the national immunization schedule. Nonetheless, countries in the Americas still report missed opportunities to fully reap the benefits of their immunization programs, especially among adolescents and adults (*41, 42)*.

Figure 3. Percentage of countries with universal recommendations for seven life course stages, by World Health Organization region



Note: AFR, Africa Region; AMR, Region of the Americas; EMR, Eastern Mediterranean Region; EUR, Europe; SEAR South-East Asia Region; WPR, Western Pacific Region.

Source: Pan American Health Organization. Building a Better Immunity: A Pathway to Healthy Longevity. Washington, D.C.: PAHO; 2022 [cited January 2023]. Available from: https://youtu.be/xfqN0fTjHH4.

2. Considerations for implementation of a life course approach to immunization

An LCA to immunization must be considered as an essential part of every national immunization program (*43, 44*). This section provides considerations to support a country's decision to advance toward an LCA to vaccination. Each consideration is accompanied by the LCA principle (see Table 1) that best supports it.

Health of individuals

In addition to protecting a person from specific pathogens, vaccination can reduce the probability of severe disease and death from multiple conditions. Therefore, if a ministry of health wishes to improve the health of individuals, it should consider the following elements:

- The primary series of a vaccine should be delivered at the sensitive/critical periods of a person-specific immunity gap against that disease. Depending on the antigen, the vaccine provides long-term or lifelong protection against the disease. Catch-up doses should be included in the vaccination schedule to ensure that the whole length of the sensitive/critical period is used.
- The effects of immunosenescence have a cumulative impact on a person's ability to respond to infections. Booster doses replenish the antibody titers that may have waned over time. Therefore, after the recommended age of administration of the primary series, countries should consider including booster doses at the time when antibody titers against a specific antigen are known to have declined.
- Regardless of the antigen administered, vaccination throughout the life course helps maintain the plasticity of innate and adaptive immune systems to respond to external stimuli, whether infection or vaccination. Therefore, vaccine doses administered to adults and older adults can strengthen the overall immune system and optimize the body's response to infections or autoimmune disorders *(27)*.

Example: Tuberculosis

The innate immune system is muted at birth. This makes the newborn, and particularly the premature baby, susceptible to bacterial and viral infections. Neutrophil functions (i.e., one of the first immune cells to respond) reach adult levels after about four weeks *(45)*. The Bacillus Calmette–Guérin (BCG) vaccine – to be administered in the first 24 hours of life according to PAHO guidelines *(46)* – protects the newborn from infection with *Mycobacterium tuberculosis* bacteria. When administered within the first 24 hours of life, the effectiveness of the BCG vaccine against pulmonary tuberculosis has been recorded at 82%. This means that, of all the newborns vaccinated with BCG, 82% did not develop the disease. When vaccination is pushed back to school-age, the effectiveness has been estimated at 64% (*47–49*). These results suggest that immunization results can be optimized if administered within the recommended, sensitive period. Also, significant – although smaller – benefits can be achieved through vaccination at a later date.

Example: Human papillomavirus

Cervical cancer is the result of an unresolved infection with human papillomavirus (HPV) earlier in life. Infections with HPV may generate into precancerous lesions in the uterus, cervix, or other parts of the body, which then develop into cancerous cells. To prevent this outcome, the timely administration of the HPV vaccine is particularly important. When administered before exposure to HPV – that is, prior to sexual intercourse – the vaccine can prevent infection and minimize the likelihood of developing precancerous and cancerous lesions. Data show that, without vaccination, the cumulative incidence of cervical cancer among women is 94 cases per 100 000 for people aged 30 years. With vaccination between 17 and 30 years, the cumulative incidence among women is 54 cases per 100 000 people aged 30 years. When vaccination happens before the age of 17, the cumulative incidence among women is 4 cases per 100 000 people aged 28 years *(50)*.

Example: Varicella zoster

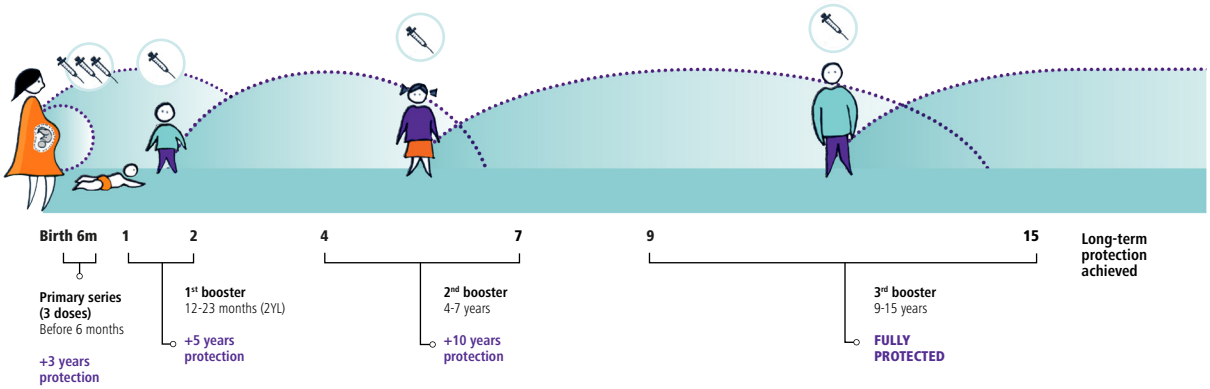
Varicella zoster virus is usually acquired in childhood and manifests as varicella disease (i.e., chickenpox). It can also appear as herpes zoster (i.e., shingles) later in life *(17)*, which is a dermatological condition that can cause more severe pain and complications than varicella, such as postherpetic neuralgia. The reappearance of the disease occurs because varicella zoster virus enters a latent stage in neuronal ganglia when the initial episode of disease resolves *(51)*. As immunosenescence happens, viral reactivation can occur. Varicella vaccination programs have shown remarkable decreases in the burden of varicella zoster disease across the general population, especially after the introduction of the two-dose series *(52)*. For instance, trends of varicella zoster disease among a cohort of unvaccinated people (>30 years old) in the United States of America show that incidence increased in the first decade after the introduction of the vaccine, but it has stabilized or declined once data from subsequent years are considered *(53)*. Among vaccinated cohorts in the United States, there is evidence of a reduction in varicella zoster disease in older children and adolescents who have benefited from a mature vaccination coverage and high coverage rates. While zoster vaccines are very efficacious, they are expensive and available only in high-income countries.

Example: Tetanus

Tetanus is an acute infectious disease caused by spores of the bacterium *Clostridium tetani (54)*. It is acquired when cuts or wounds become infected with the bacteria. People who recover from tetanus do not have natural immunity and can be reinfected. Therefore, all persons should be vaccinated periodically to maintain immunity. The World Health Organization (WHO) recommends that a person receive six doses (three primary plus three booster) of tetanus toxoid-containing vaccines (see Figure 4). The primary series should begin at 6 weeks of age, with subsequent doses administered with a minimum interval of four weeks between doses. The three booster doses should preferably be administered during the second year of life (12–23 months), at 4–7 years, and at 9–15 years. Ideally,

there should be at least four years between booster doses. As the length of the life span continues to increase, countries may consider adding new booster doses to the national immunization schedule to protect older adults.

Figure 4. World Health Organization recommended tetanus vaccination schedule for long-term protection



Source: World Health Organization. Protecting all against tetanus: guide to sustaining maternal and neonatal tetanus elimination (MNTE) and broadening tetanus protection for all populations. Geneva: WHO; 2019 [cited 9 March 2023]. Available from: https://apps.who.int/iris/handle/10665/329882.

Example: Measles

In the Americas, vaccination against measles is recommended at 1 year of age (first dose) and at 18 months (second dose) *(55)*. However, multiple studies suggest that vaccination may increase child survival rates by reducing mortality from conditions other than measles infection. Receipt of standard titer measles-containing vaccine is associated with a reduction in all-cause mortality (relative risk 0.74 [0.51 to 1.07] from four clinical trials and 0.51 [0.42 to 0.63] from 18 observational studies, at high risk of bias). This effect seemed stronger in girls than in boys *(56)*.

Immunization across generations

By taking advantage of the mechanisms of maternal immunity, one dose of vaccine benefits both the woman and her biological offspring. Therefore, if a ministry of health wishes to improve health across generations, it should consider the following elements:

- **Vaccination during pregnancy:** This ensures that maternal antibodies are transmitted to the fetus. It allows the newborn's immune system to respond immediately to the pathogens that cause the highest mortality rates in this age group. This example of linked lives ensures that the vaccination of one person directly affects the immune system of another person. Therefore, vaccination programs should (a) ensure that vaccines are scheduled and available for pregnant women, and (b) prioritize pregnant women for follow-up to ensure they receive all doses for which they are eligible. At this time, maternal vaccination is the only immunization strategy that directly benefits two generations through one intervention *(57)*.
- **Promote breastfeeding:** Breast milk includes maternal antibodies that can be shared with the baby and strengthen the child's passive immunity. Breastfeeding is associated with better health outcomes in infancy and throughout adulthood. The first milk from the mother (colostrum) is considered as nature's first vaccine *(14)*.

Example: Pertussis and tetanus

In 2020, more than 5 million children died worldwide from VPD before reaching their fifth birthday *(58)*. Almost half of these deaths occurred in the first month of life, when a newborn's immunity largely depends on the antibodies received in utero (see Figure 4). Therefore, infant mortality rates are strongly influenced by maternal vaccination rates. The Americas have made large strides in maternal immunization. In 2018, 34 countries included the adult vaccine against tetanus, diphtheria, and pertussis (Tdap) or influenza for pregnant women in their national vaccination schedule *(4)*. The Tdap vaccine during pregnancy was shown to be highly effective at preventing pertussis morbidity (69%–91%), hospitalizations (91%–94%), and death (95%) among infants *(57)*. Maternal immunization and infant health should be seen as a continuum, where one intervention positively impacts the well-being of two persons and builds intergenerational capacity to sustain immunity *(57)*. Thanks to this strategy, the Americas were able to eliminate maternal–neonatal tetanus in 2017.

Health of societies

When vaccination services are offered first to the most high-risk and vulnerable persons, the immunity generated by vaccines reduces the effect of risk cofactors (e.g., chronic medical conditions) on disease severity and death. As a result, the entire community has lower morbidity and mortality rates. Therefore, if a ministry of health wishes to improve the health of societies (i.e., persons subjected to the same socioeconomic determinants and healthcare access), it should consider the following elements:

- For vaccination programs, high-risk individuals are persons who experience the cumulative effect of risk factors through repeated exposures to the pathogen (e.g., health workers) or chronic health conditions (e.g., immunocompromised persons). Prioritizing the vaccination of these individuals is particularly cost-effective because it (a) reduces morbidity and mortality in these subgroups, (b) reduces the overall burden of disease and death in society, as the individuals most at risk are protected, and (c) reduces overall healthcare costs to treat cases of severe disease and its sequelae. Therefore, vaccination programs should ensure that high-risk individuals are identified and prioritized for vaccination. An example of this strategy was recommended by WHO during the COVID-19 pandemic *(59)*.
- Persons living in situations of vulnerability (e.g., migrants, Indigenous groups, refugees, internally displaced populations) are at higher risk of developing disease due to the unfavorable social determinants that affect their daily lives. These may be lack of access to essential services (e.g., potable water, health care), sanitation (e.g., latrines), foodstuffs, or security. For example, there is a well-documented association between vitamin A deficiency due to malnutrition and increased likelihood of incident measles, measles-related complications, and measles-related deaths *(60)*. High rates of vaccination coverage in these subgroups are especially important to reduce morbidity and mortality among those who already are predisposed to negative health outcomes because of their living situation. Additional health services may be offered jointly with vaccination to further reduce overall morbidity and mortality (e.g., preventive vitamin A administration, blood pressure testing, mosquito nets to prevent vector-borne diseases). Also, redirection of resources to these groups is at the foundation of the concept of equity in health care *(61)*.
- Vaccination of a large proportion of the eligible population as soon as possible (e.g., before the start of the influenza season) limits transmission of the pathogen in a community. This concept is known as "community immunity." Persons who did not receive the vaccine are protected from the disease because of the minimized circulation, rather than because their own immune systems mounted a response. This example of linked lives ensures that the vaccination of one person indirectly affects the immune system of another person. Consequently, vaccination

programs should ensure that (a) sufficient quantities of vaccine doses are available to the eligible population, and (b) community engagement and logistics resources are sufficient to promote high rates of vaccine uptake in a short period of time.

Example: Influenza

Vaccination against influenza is available for individuals of all ages, but it is highly recommended for persons whose immune system is weak because of age or concomitant health conditions (e.g., children between 6 months and 5 years, older adults, persons with chronic diseases, pregnant women), as well as persons at high risk of exposure to the virus (e.g., health workers) *(62)*. The impact of this vaccine is highest when it is administered before the start of the flu season; that is, before the virus starts circulating widely in the community. Considering the time required to mount an immune response to the antigens included in the vaccine, high-risk groups should be vaccinated during a specific window of time in order to receive the maximum protection offered by the influenza vaccine. If high coverage rates in the at-risk groups are achieved early, the individual is protected by both the vaccine-generated immunity and by community immunity. In four countries of the Americas, evidence showed earlier hospital discharge among vaccinated persons compared with their unvaccinated counterparts: adjusted hazard ratio (aHR) for fully vaccinated children 1.14 (95% confidence interval [CI] 1.01, 1.29); partially vaccinated children 1.24 (95% CI 1.04, 1.47), and vaccinated adults with preexisting medical conditions 1.78 (95% CI 1.18, 2.69). Compared with unvaccinated individuals, lower odds of intensive care unit (ICU) admission were found for children: partially vaccinated adjusted odds ratio (aOR) 0.64 (95% CI 0.44, 0.92) and fully vaccinated 0.52 (95% CI 0.28, 0.98). Lower odds of in-hospital death (0.62 [95% CI 0.50, 0.78]) were found in vaccinated versus unvaccinated older adults *(63)*.

Example: Vaccination to reduce antimicrobial resistance due to infections

Antimicrobial resistance is recognized as a major global emergency, causing around 1.27 million deaths each year *(64)*. It is accelerated by the overuse and misuse of antimicrobial drugs such as antibiotics, antivirals, and antifungals. Worldwide, more than half of all antibiotics are prescribed, distributed, or sold inappropriately. Antibiotics can be purchased without a prescription in 80% of the countries of the Americas. The COVID-19 pandemic catapulted antimicrobial resistance as a critical public health threat, fueled by an increase in the use of antibiotics to treat COVID-19 patients *(65)*. This may be explained by the increased antibiotic use due to concerns about bacterial coinfections, difficulty differentiating between COVID-19 and bacterial infections, and treatment for possible secondary infection. Moreover, antimicrobial-resistant bacteria are likely to have caused more COVID-19-related deaths, as secondary bacterial infections can worsen the outcome of severe and critical COVID-19 illness. In the fewer than 15% of cases where secondary bacterial infections were identified, outcomes were worse in individuals with severe or critical COVID-19 illness *(66)*. The use of vaccines to prevent viral and bacterial diseases (e.g., COVID-19, pneumococcal disease, typhoid) has a clear positive impact on global health, as mass vaccination helps reduce the prevalence of infectious diseases and subsequently the number of infections that are unnecessarily treated using antibiotics.

3. Integrating immunization programs with a life course approach into the primary health care system: key recommendations

WHO recognized the importance of incorporating the life course concept into strategic frameworks for immunization strategies and practices, starting with the Global Vaccine Action Plan (GVAP) of 2011–2020 *(67)* and continuing with the Immunization Agenda 2030 (IA2030) *(68)*. The main objective of IA2030 is to extend immunization to people of all ages while integrating vaccination services within other essential health services.

Re-orienting health systems toward a primary health care (PHC) approach is key in the integration of public health functions to meet people's health needs where they are, including immunizations *(69)*. The goal is to redesign the PHC system so that an individual receives a complete package of care according to his/her age and health needs, and barriers to essential health services are minimized. Therefore, immunization programs need to be integrated across the PHC system, rather than being vertical interventions that occur only at specific moments in an individual's life *(10)*. PAHO has set as one of its priorities the establishment of formal initiatives that integrate multiple essential services (including immunization) under the umbrella of PHC, in order respond to country needs and accelerate the elimination of diseases efficiently and effectively *(70)*.

The following recommendations are designed to promote this integration and bolster immunization operations across all age groups. These recommendations are rooted in the Operational Framework for Primary Health Care, which was approved in Astana *(69)*. They have been developed based on prior initiatives (*26, 41, 68, 71*), and should be carefully assessed, customized, and implemented by Member States to align with the specific national and local contexts.

Political commitment and leadership

To effectively implement an LCA for immunization systems within the PHC framework, strong support and advocacy from high-level officials and policymakers are crucial. This can be achieved by:

- **Increasing awareness of immunization beyond early childhood:** Messages emphasizing the social, economic, and health benefits of immunization in adolescents, adults, pregnant women, persons with comorbidities, and older individuals should be drafted to target decisionmakers, healthcare workers, and the general population.
- **Establishing expert groups:** These groups can develop plans to strengthen and extend vaccination programs at each stage of life, including the introduction of new vaccines *(72)* and/or the addition of booster or catch-up doses in the national immunization schedule. These same groups should identify other services within PHC that can be paired with age-specific vaccines, so to offer a complete package of care.

Governance and policy frameworks

To ensure the integration of an LCA to immunization within the larger PHC framework, governance structures and policy frameworks must align in support of this integrated model. This involves:

- **Strengthening policy development for integrated PHC services:** Health authorities should adapt or develop policies that facilitate and promote multisectoral collaborations and partnerships to effectively integrate essential health programs with immunization operations.
- **Incorporating the LCA into the PHC framework:** Immunization policy and strategy frameworks should explicitly integrate a PHC approach with a life course perspective. Each Member State should have a comprehensive package of essential health services (that includes immunizations) that is offered to all persons within each age group or high-risk population group. This ensures that immunization programs are aligned with the principles and strategies of PHC throughout the lifespan *(69)*.

Funding and allocation of resources

Implementing a PHC and life course approach to immunization requires adequate funding and allocation of resources to cover services for all age groups. This should be considered a long-term investment, given the benefits to individuals, families, and societies that vaccines can bestow. The following actions can help support this prioritization process:

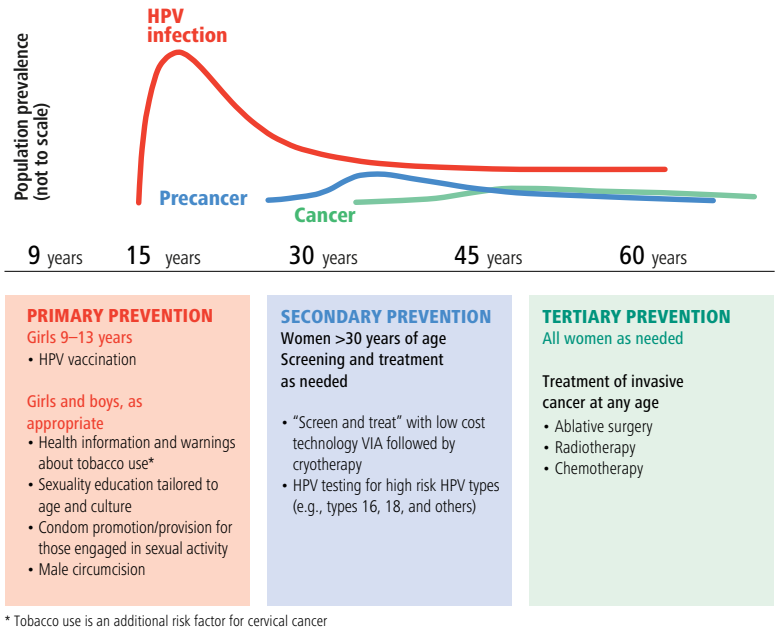
- **Demonstrating the economic and social benefits of life course immunization:** Highlight the potential cost savings associated with preventing VPDs such as hepatic cancer, cervical cancer, and chronic conditions. Emphasize the reduction in long-term healthcare costs resulting from the prevention of VPDs, their complications, and associated long-term disabilities. Also underscore the cost-effectiveness of pairing vaccination services with other essential care options for the same age group.
- **Generating new financing mechanisms:** Recognize that the need for human and financial resources within PHC will increase with the adoption of the LCA. Explore options for public–private partnerships as a strategy to increase funding availability and build capacity of health workers at each stage of the life course *(73)*.

Integrated and people-centered care

At the core of the LCA is the objective of addressing the health needs of individuals and communities over time. To achieve this, PHC programs and interventions must be redesigned to provide integrated and people-centered care, moving away from vertical approaches. The following actions can help facilitate this step:

- **Person-centered approach to immunization:** It is essential to meet people where they are by planning immunization services within easy reach of the general population. Encouraging school-based and work-based immunization programs and collaborating with other health programs and sectors (e.g., transportation) can enhance accessibility. Availability of other essential health services at the same time and place may encourage people to overcome remaining barriers to access. Ongoing collaboration between community and facility-based services is important, since feedback from community members will improve service delivery.
- **Increased availability and distribution of resources:** Adequate distribution of human resources and essential medicines (including vaccines) is crucial. This includes ensuring equitable distribution of health personnel, especially in primary care settings and underserved areas. Availability of vaccines, injectable materials, and other essential medicines should be ensured so individuals can receive essential care as close as possible to home.
- **Integration with other health programs:** Integrating immunization platforms and service delivery with other health and community services can lead to better health outcomes for the whole community *(74)*. By designing immunization services in conjunction with other preventive and therapeutic services, all encounters with the healthcare system can become an opportunity to administer missing vaccine doses. This comprehensive offering of health services can result in a cumulative impact of health interventions. An example of comprehensive services can be found in Figure 5, using HPV vaccine as a case study.

Figure 5. Overview of the programmatic interventions over the life course to prevent human papillomavirus infection and cervical cancer



* Tobacco use is an additional risk factor for cervical cancer

Note: HPV, human papillomavirus; VIA, visual inspection with acetic acid.

Source: World Health Organization. Working together: an integration resource guide for immunization services throughout the life course. Geneva: WHO; 2018 [cited January 2023]. Available from: https://apps.who.int/iris/handle/10665/276546.

- **Including sustainable immunization programs in national PHC strategies:** It is crucial to recognize immunization as an integral component of essential PHC strategies, as well as strategies for universal access to health and universal health coverage. By embedding immunization programs within the broader PHC framework, their long-term sustainability and effectiveness can be strengthened.

Engagement of community and other stakeholders

The positive impact of a PHC and life course approach on immunization must be communicated broadly to healthcare providers and population groups. Multiple tools and interventions can be found in the WHO position paper on Behavioral and Social Drivers for Vaccine Uptake *(75)*.

- **Training health workers on PHC and the LCA:** Health workers must be the first to understand the extended benefits of an LCA to immunization. By doing so, they will ask for, promote, and provide vaccines for patients at all life stages whenever they have contact with the health system. To ensure that health workers are the main promoters of vaccines at each stage of life, they must receive periodic training on this topic. Academic programs in health sciences should include this topic in their curriculum as well.
- **Building up acceptance and demand:** When individual actions shape health trajectories, demand generation toward preventive services such as vaccines should be fostered through targeted communication campaigns. These messages should be tailored to each age group and address the main concerns that are generating vaccine hesitancy.

Adjustment to population health needs

The benefits of implementing PHC and life course approaches to immunization need to be defined, monitored, and documented for continuous improvement.

- **Improve recording and tracking for longitudinal data:** If Member States want to be able to track the benefits of vaccination across the life course, they must have information systems that can monitor vaccination uptake and health outcomes across the life span of each individual. Tracking vaccination status can be leveraged through electronic immunization registries (EIRs) *(76)*. Additionally, it is important to apply LCA-specific indicators to the monitoring framework of national immunization programs. IA2030 currently recommends one indicator to track its Strategic Priority 4 – Life course and integration: 4.1 Breadth of protection (i.e., coverage for all WHO-recommended vaccine antigens, by country).
- **Promoting longitudinal research:** Implementation of the LCA requires long-term follow-up of interventions and an assessment of the long-term consequences of vaccination services on individual and community health. Health systems should invest in longitudinal research to track improvements in population health as well as the minimization of missed opportunities for vaccination.

Access and equity

Promoting access and equity in vaccination and, more broadly, PHC services is a crucial aspect that underlies all recommendations. Ensuring universal availability of vaccines to all age groups is essential to the success of this strategy. As mentioned previously, minority and vulnerable groups often face greater barriers in accessing immunization services than the general population. These access barriers are not uniform across a country's population. Effective immunization campaigns can help reduce these inequities throughout the life course and ensure that other essential services

are offered alongside these outreach vaccination interventions. To design effective operations, a nuanced understanding of the various factors that act as barriers to immunization services is essential. These strategies should ensure equitable access to vaccines and immunization programs, while actively working to mitigate the negative impacts of inequalities throughout the life course *(77)*. Ministries of health should establish targeted strategies at the subnational and local levels, tailored to the specific needs of these vulnerable populations *(78)*. This requires appropriate outreach strategies, cultural dialogues, and implementation approaches. With the renewed emphasis on strengthening PHC, there is an opportunity to prioritize policy initiatives that directly address the challenges of accessing immunization services. Understanding and addressing the full range of factors that serve as access barriers is a necessary and fundamental first step toward advancing comprehensive PHC.

4. Conclusions

The world (including the Americas) is undergoing a profound demographic shift, where there are more persons over the age of 65 years than children younger than 5 years. As we age, three processes negatively impact the body's ability to protect itself: (a) our immune system weakens over time in a process called immunosenescence, leaving the body exposed to diseases to which it had earlier gained immunity; (b) the effectiveness of vaccine doses administered early in life declines with time; and (c) older age is accompanied by the development of chronic diseases that exacerbate disease outcomes when coupled with infections later in life. The combination of these processes leaves individuals at increased risk of severe morbidity and mortality from vaccine-preventable diseases. Therefore, while national immunization programs were created to protect the youngest and reduce infant mortality rates, they now must be redesigned to ensure full protection for children as well as for adolescents, adults, and older adults. By reframing immunization programs through the lens of the life course approach, ministries of health can consider vaccination services as a public health intervention to be adjusted to close the immunity gaps of each age group – thus minimizing the impact of disease, increasing the body's capacity to stay healthy across stages of life, and reducing all-cause mortality rates in the population. This technical document provides multiple examples of how different vaccines, when administered at the appropriate time and to the most high-risk groups, can generate health benefits beyond protection from a single pathogen and which even protect unvaccinated persons. The extension of vaccination services to all age groups (including the administration of booster and catch-up doses) can be implemented through a careful revision of the different elements of the national immunization program (i.e., service delivery, demand generation, information systems, monitoring and evaluation). The pairing with other essential health services for each age group can create additional synergy to maximize the changes for a long and healthy life for individuals and populations.

References

1. World Health Organization, The Global Health Observatory. Under-five mortality rate (per 1000 live births) (SDG 3.2.1). Geneva: WHO; 2023 [cited 24 January 2023]. Available from: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/under-five-mortality-rate-(probability-of-dying-by-age-5-per-1000-live-births).
2. United Nations Department of Economic and Social Affairs, Population Division. World population prospects 2022: summary of results. New York: United Nations; 2022. Available from: https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/wpp2022_summary_of_results.pdf.
3. Pan American Health Organization. Data and Visualizations. Washington, D.C.: PAHO; 2019. Available from: https://www.paho.org/en/data-and-visualizations.
4. Velandia-González M, Vilajeliu A, Contreras M, Trumbo SP, Pacis C, Ropero AM, et al. Monitoring progress of maternal and neonatal immunization in Latin America and the Caribbean. Vaccine. 2021 July;39:B55–B63.
5. De Oliveira LH, Janusz CB, Da Costa MT, El Omeiri N, Bloem P, Lewis M, et al. HPV vaccine introduction in the Americas: a decade of progress and lessons learned. Expert Rev Vaccines. 2022;21(11):1569–1580.
6. Morales KF, Brown DW, Dumolard L, Steulet C, Vilajeliu A, Ropero Alvarez AM, et al. Seasonal influenza vaccination policies in the 194W WHO Member States: The evolution of global influenza pandemic preparedness and the challenge of sustaining equitable vaccine access. Vaccine X. 2021 August;8:100097.
7. Pan American Health Organization. Immunization Data and Statistics. Washington, D.C.: PAHO; [c2023]. Available from: https://www.paho.org/en/topics/immunization/immunization-data-and-statistics.
8. Pan American Health Organization. Healthy Life Course. Washington, D.C.: PAHO; 2023 [cited 24 January 2023]. Available from: https://www.paho.org/en/topics/healthy-life-course.
9. Kreitinger JM, Beamer CA, Shepherd DM. Environmental Immunology: Lessons Learned from Exposure to a Select Panel of Immunotoxicants. J Immunol. 2016;196(8):3217–3225.
10. Pan American Health Organization. Building Health Throughout the Life Course. Concepts, Implications, and Application in Public Health. Washington, D.C.: PAHO; 2021. Available from: https://iris.paho.org/handle/10665.2/53409.
11. Halfon N, Larson K, Lu M, Tullis E, Russ S. Lifecourse Health Development: Past, Present and Future. Matern Child Health J. 2014;18(2):344–365.
12. World Health Organization. Ten threats to global health in 2019. Geneva: WHO; 2019. Available from: https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019.
13. Park JE, Jardine L, Gottgens B, Teichmann SA, Haniffa M. Prenatal development of human immunity. Science. 2020;368(6491):600–603.
14. Pan American Health Organization. Breastfeeding and complementary feeding. Washington, D.C.: PAHO; 2023 [cited 24 January 2023]. Available from: https://www.paho.org/en/topics/breastfeeding-and-complementary-feeding.
15. World Health Organization. Monoclonal Antibodies (mAbs) for Infectious Diseases - Product & Delivery Research. Geneva: WHO; 2021 [cited 7 March 2023]. Available from: https://www.who.int/teams/immunization-vaccines-and-biologicals/product-and-delivery-research/monoclonal-antibodies-(mabs)-for-infectious-diseases.
16. U.S. Centers for Disease Control and Prevention. RSV in Infants and Young Children. Atlanta: CDC; 2022 [cited 6 March 2023]. Available from: https://www.cdc.gov/rsv/high-risk/infants-young-children.html.
17. Lord JM. The effect of aging of the immune system on vaccination responses. Hum Vaccin Immunother. 2013;9(6):1364–1367.
18. Saade M, Araujo de Souza G, Scavone C, Kinoshita PF. The Role of GPNMB in Inflammation. Front Immunol. 2021 May 12;12:674739.
19. Goronzy JJ, Weyand CM. Understanding immunosenescence to improve responses to vaccines. Nat Immunol. 2013;14(5):428–436.
20. Santoro A, Bientinesi E, Monti D. Immunosenescence and inflammaging in the aging process: age-related diseases or longevity? Ageing Res Rev. 2021 November;71:101422.

21. U.S. Centers for Disease Control and Prevention. Shingles. Atlanta: CDC; 2022. Available from: https://www.cdc.gov/shingles/index.html.

22. Pietrobon AJ, Teixeira FME, Sato MN. Immunosenescence and Inflammaging: Risk Factors of Severe COVID-19 in Older People. Front Immunol. 2020 October 27;11:579220.

23. Teissier T, Boulanger E, Cox LS. Interconnections between Inflammageing and Immunosenescence during Ageing. Cells. 2022;11(3):359.

24. Fulop T, Larbi A, Pawelec G, Cohen AA, Provost G, Khalil A, et al. Immunosenescence and Altered Vaccine Efficiency in Older Subjects: A Myth Difficult to Change. Vaccines. 2022;10(4):607.

25. Sadarangani SP, Young BE, Lian W, Phua HP, Chen MIC, Barr I, et al. DYNAMIC cohort study evaluating metabolic predictors of influenza vaccine immune response in older adults. NPJ Vaccines. 2022;7(1):135.

26. Aguado T, Goodwin J. A life-course approach to vaccination: adapting European policies. Available from: https://www.healthpolicypartnership.com/app/uploads/A-life-course-approach-to-vaccination-adapting-European-policies.pdf.

27. Laupèze B, Del Giudice G, Doherty MT, Van der Most R. Vaccination as a preventative measure contributing to immune fitness. NPJ Vaccines. 2021;6(1):93.

28. World Health Organization. Immunization Agenda 2030. SP4: Life-course & integration. Geneva: WHO; 2020. Available from: https://www.immunizationagenda2030.org/strategic-priorities/life-course-integration.

29. Benn CS, Netea MG, Selin LK, Aaby P. A small jab – a big effect: nonspecific immunomodulation by vaccines. Trends Immunol. 2013;34(9):431–439.

30. National Cancer Institute, National Institutes of Health. Immunotherapy to Treat Cancer. Bethesda, MD: NCI; 2019 [cited 24 January 2023]. Available from: https://www.cancer.gov/about-cancer/treatment/types/immunotherapy.

31. National Institutes of Health. Anti-SARS-CoV-2 Monoclonal Antibodies. Bethesda, MD: NIH; 2022 [cited 24 January 2023]. Available from: https://www.covid19treatmentguidelines.nih.gov/therapies/antivirals-including-antibody-products/anti-sars-cov-2-monoclonal-antibodies/.

32. Malekzadeh P, Yossef R, Cafri G, Paria BC, Lowery FJ, Jafferji M, et al. Antigen Experienced T Cells from Peripheral Blood Recognize p53 Neoantigens. Clin Cancer Res. 2020;26(6):1267–1276.

33. Melief CJM, van Hall T, Arens R, Ossendorp F, van der Burg SH. Therapeutic cancer vaccines. J Clin Invest. 2015;125(9):3401–3412.

34. Lin MJ, Svensson-Arvelund J, Lubitz GS, Marabelle A, Melero I, Brown BD, et al. Cancer vaccines: the next immunotherapy frontier. Nat Cancer. 2022;3(8):911–926.

35. Nakagami H, Hayashi H, Shimamura M, Rakugi H, Morishita R. Therapeutic vaccine for chronic diseases after the COVID-19 Era. Hypertens Res. 2021;44(9):1047–1053.

36. National Institutes of Health. Study of a Drug [DCVax®-L] to Treat Newly Diagnosed GBM Brain Cancer (GBM). Bethesda, MD: NIH; 2022 [cited 24 January 2023]. Available from: https://clinicaltrials.gov/ct2/show/NCT00045968.

37. Liau LM, Ashkan K, Brem S, Campian JL, Trusheim JE, Iwamoto FM, et al. Association of Autologous Tumor Lysate-Loaded Dendritic Cell Vaccination With Extension of Survival Among Patients With Newly Diagnosed and Recurrent Glioblastoma: A Phase 3 Prospective Externally Controlled Cohort Trial. JAMA Oncol. 2023;9(1):112.

38. Mendelsohn AR, Larrick JW. Antiaging Vaccines Targeting Senescent Cells. Rejuvenation Res. 2022;25(1):39–45.

39. Presidencia de la República de Colombia. Consejería Presidencial para la Niñez y la Adolescencia. Bogotá: Presidencia de la República de Colombia; 2023. Available from: http://www.deceroasiempre.gov.co/.

40. Ministerio de Desarrollo Social y Familia de Chile. Chile Crece Contigo. Santiago: Ministerio de Desarrollo Social y Familia; 2023 [cited 24 January 2023]. Available from: https://www.crececontigo.gob.cl.

41. Pan American Health Organization. Building a Better Immunity: A Pathway to Healthy Longevity. Washington, D.C.: PAHO; 2022 [cited January 2023]. Available from: https://youtu.be/xfqN0fTjHH4.

42. Tampi M, Carrasco-Labra A, O'Brien KK, Velandia-González M, Brignardello-Petersen R. Systematic review on reducing missed opportunities for vaccinations in Latin America. Rev Panam Salud Publica. 2022;46:e65. Available from: https://doi.org/10.26633/RPSP.2022.65.

43. Wallace AS, Ryman TK, Privor-Dumm L, Morgan C, Fields R, Garcia C, et al. Leaving no one behind: Defining and implementing an integrated life course approach to vaccination across the next decade as part of the immunization Agenda 2030. Vaccine. 2022 December;S0264410X22014529.

44. Philip RK, Attwell K, Breuer T, Di Pasquale A, Lopalco PL. Life-course immunization as a gateway to health. Expert Rev Vaccines. 2018;17(10):851–864.

45. Georgountzou A, Papadopoulos NG. Postnatal Innate Immune Development: From Birth to Adulthood. Front Immunol. 2017 August 11;8:957.

46. Pan American Health Organization. Maternal and Neonatal Immunization Field Guide for Latin America and the Caribbean. Washington, D.C.: PAHO; 2017 [cited 6 March 2023]. Available from: https://iris.paho.org/handle/10665.2/34150.

47. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. Proc R Soc B. 2015;282(1821):20143085.

48. Abubakar I, Pimpin L, Ariti C, Beynon R, Mangtani P, Sterne J, et al. Systematic review and meta-analysis of the current evidence on the duration of protection by bacillus Calmette–Guérin vaccination against tuberculosis. Health Technol Assess. 2013;17(37). Available from: https://www.journalslibrary.nihr.ac.uk/hta/hta17370/.

49. World Health Organization. BCG vaccines: WHO position paper – February 2018. Geneva: WHO; 2018. Available from: https://www.who.int/publications/i/item/who-wer9308-73-96.

50. Lei J, Ploner A, Elfström KM, Wang J, Roth A, Fang F, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med. 2020;383(14):1340–1348.

51. World Health Organization. Varicella and herpes zoster vaccines: WHO position paper, June 2014. Geneva: WHO; 2014. Available from: https://www.who.int/publications/i/item/who-wer-8925-265-288.

52. Marin M, Meissner HC, Seward JF. Varicella Prevention in the United States: A Review of Successes and Challenges. Pediatrics. 2008;122(3):e744–e751.

53. Leung J, Dooling K, Marin M, Anderson TC, Harpaz R. The Impact of Universal Varicella Vaccination on Herpes Zoster Incidence in the United States: Comparison of Birth Cohorts Preceding and Following Varicella Vaccination Program Launch. J Infect Dis. 2022;226(Suppl. 4):S470–S477.

54. World Health Organization. Tetanus: Prevention. Geneva: WHO; c2023. Available from: https://www.who.int/health-topics/tetanus#tab=tab_3

55. Pan American Health Organization. 160th Executive Committee. Resolution Ce160.R2- Plan of Action for the Sustainability of Measles, Rubella, and Congenital Rubella Syndrome Elimination in the Americas 2018-2023. Washington D.C.: PAHO; 2017. Available from: https://iris.paho.org/handle/10665.2/34254.

56. Higgins JPT, Soares-Weiser K, López-López JA, Kakourou A, Chaplin K, Christensen H, et al. Association of BCG, DTP, and measles containing vaccines with childhood mortality: systematic review. BMJ. 2016 October 13;355:i5170.

57. Kandeil W, van den Ende C, Bunge EM, Jenkins VA, Ceregido MA, Guignard A. A systematic review of the burden of pertussis disease in infants and the effectiveness of maternal immunization against pertussis. Expert Rev Vaccines. 2020;19(7):621–638.

58. World Health Organization. Child Mortality (under 5 years). Geneva: WHO; 2022 [cited 24 January 2023]. Available from: https://www.who.int/news-room/fact-sheets/detail/levels-and-trends-in-child-under-5-mortality-in-2020.

59. World Health Organization. WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines. Geneva: WHO; 2020. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Prioritization-2022.1.

60. Tran IC, Gregory C, O'Connor P, Imohe A, Do LAH, Suchdev PS. A scoping review on the associations and potential pathways between malnutrition and measles. medRxiv 2023.01.21.23284872 [cited 6 March 2023]. Available from: https://doi.org/10.1101/2023.01.21.23284872.

61. World Health Organization. WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination. Geneva: WHO; 2020. Available from: https://apps.who.int/iris/handle/10665/334299.

62. World Health Organization. Vaccines against influenza: WHO position paper – May 2022. Geneva: WHO; 2022. Available from: https://www.who.int/publications/i/item/who-wer9719.

63. Regan AK, Arriola CS, Couto P, Duca L, Loayza S, Nogareda F, et al. Severity of influenza illness by seasonal influenza vaccination status among hospitalised patients in four South American countries, 2013–19: a surveillance-based cohort study. Lancet Infect Dis. 2023;23(2):222–232.

64. The Lancet. Antimicrobial resistance: time to repurpose the Global Fund. Lancet. 2022;399(10322):335.

65. Ansari S, Hays JP, Kemp A, Okechukwu R, Murugaiyan J, Ekwanzala MD, et al. The potential impact of the COVID-19 pandemic on global antimicrobial and biocide resistance: an AMR Insights global perspective. JAC Antimicrob Resist. 2021;3(2):dlab038.

66. Pan American Health Organization. Antimicrobial Resistance, Fueled by the COVID-19 Pandemic. Policy Brief November 2021. Washington, D.C.: PAHO; 2021 [cited 7 March 2023]. Available from: https://iris.paho.org/handle/10665.2/55864.

67. World Health Organization. Global Vaccine Action Plan 2011–2020. Geneva: WHO; 2013. Available from: https://apps.who.int/iris/handle/10665/78141.

68. World Health Organization. Immunization Agenda 2030: A Global Strategy to leave no one behind. Geneva: WHO; 2020. Available from: https://cdn.who.int/media/docs/default-source/immunization/strategy/ia2030/ia2030-draft-4-wha_b8850379-1fce-4847-bfd1-5d2c9d9e32f8.pdf.

69. World Health Organization, United Nations Children's Fund. Operational framework for primary health care: transforming vision into action. Geneva: WHO and UNICEF; 2020. Available from: https://apps.who.int/iris/handle/10665/337641.

70. Silva JB. Inaugural address of Dr. Jarbas Barbosa as PAHO Director, 31 January 2023. Washington, D.C.: PAHO; 2023. Available from: https://iris.paho.org/handle/10665.2/57272.

71. International Federation of Pharmaceutical Manufacturers & Associations. Implementing a Life-Course Approach to Immunization. Geneva: IFPMA; 2019. Available from: https://ifpma.org/publications/implementing-a-life-course-approach-to-immunization/.

72. World Health Organization. Principles and considerations for adding a vaccine to a national immunization programme. Geneva: WHO; 2014. Available from: https://apps.who.int/iris/handle/10665/111548.

73. World Health Organization. Roadmap for Access to Medicines, Vaccines and Health Products 2019–2023: Comprehensive support for access to medicines, vaccines and other health products. Geneva: WHO; 2019. Available from: https://apps.who.int/iris/handle/10665/330145.

74. World Health Organization. Working together: an integration resource guide for immunization services throughout the life course. Geneva: WHO; 2018 [cited 20 January 2023]. Available from: https://apps.who.int/iris/handle/10665/276546.

75. World Health Organization. Understanding the behavioural and social drivers of vaccine uptake. WHO position paper – May 2022. Available from: https://apps.who.int/iris/handle/10665/354458.

76. Pan American Health Organization. Electronic Immunization Registry: Practical Considerations for Planning, Development, Implementation and Evaluation. Washington, D.C.: PAHO; 2018. Available from: https://iris.paho.org/handle/10665.2/34865.

77. Pan American Health Organization. Analizar y superar las barreras de acceso para fortalecer la atención primaria de salud. Washington, D.C.: PAHO; 2023. Available from: https://iris.paho.org/handle/10665.2/57800.

78. The Value of Immunization Compendium of Evidence (VoICE). Equity and Immunization: Shrinking the Gaps. Baltimore: International Vaccine Access Center; c2023. Available from: https://immunizationevidence.org/featured_issues/equity-and-immunization-shrinking-the-gaps/.

As the Americas undergo profound demographic change and there are more persons aged 65 years or older than children younger than 5 years, it is crucial to recognize that national immunization programs must be redesigned to ensure comprehensive protection for individuals across the lifespan. By adopting a life course approach to immunization, vaccination programs can be tailored to close immunity gaps at different stages of life. The life course approach foresees the establishment of multiple strategies to reduce missed opportunities for vaccination according to age group. This technical document explains the key concepts of the life course approach with a focus on immunization by vaccination, as well as the underlying biological mechanisms that require the application of different vaccines at different life stages according to changes in the immune system and in the epidemiological situation of a community. Multiple examples from different vaccines are provided. Finally, this document delivers several considerations for the implementation of the life course approach in national immunization programs. This document is part of Pan American Health Organization efforts to introduce the concepts of immunization across the life course to the countries and territories of the Americas and ensure that all persons reap all the benefits that vaccines can bestow. By recognizing the lifelong impact of vaccinations and embracing the life course approach, countries can minimize the impact of diseases, enhance the body's resilience during the whole lifetime, and reduce overall mortality rates. Immunization programs, once primarily focused on early childhood, can evolve into adaptable public health interventions, safeguarding the health and well-being of individuals of all ages.

PAHO Pan American Health Organization World Health Organization Regional Office for the Americas

9 789275 127445