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Review

Strengthening vaccination policies in Latin America: An evidence-based approach

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ABSTRACT

Despite many successes in the region, Latin American vaccination policies have significant shortcomings, and further work is needed to maintain progress and prepare for the introduction of newly available vaccines. In order to address the challenges facing Latin America, the Commission for the Future of Vaccines in Latin America (COFVAL) has made recommendations for strengthening evidence-based policy-making and reducing regional inequalities in immunisation. We have conducted a comprehensive literature review to assess the feasibility of these recommendations. Standardisation of performance indicators for disease burden, vaccine coverage, epidemiological surveillance and national health resourcing can ensure comparability of the data used to assess vaccination programmes, allowing deeper analysis of how best to provide services. Regional vaccination reference schemes, as used in Europe, can be used to develop best practice models for vaccine introduction and scheduling. Successful models exist for the continuous training of vaccination providers and decision-makers, with a new Latin American diploma aiming to contribute to the successful implementation of vaccination programmes. Permanent, independent vaccine advisory committees, based on the US Advisory Committee on Immunization Practices (ACIP), could facilitate the uptake of new vaccines and support evidence-based decision-making in the administration of national immunisation programmes. Innovative financing mechanisms for the purchase of new vaccines, such as advance market commitments and cost front-loading, have shown potential for improving vaccine coverage. A common regulatory framework for vaccine approval is needed to accelerate delivery and pool human, technological and scientific resources in the region. Finally, public–private partnerships between industry, government, academia and non-profit sectors could provide new investment to stimulate vaccine development in the region, reducing prices in the long term. These reforms are now crucial, particularly as vaccines for previously neglected, developing-world diseases become available. In summary, a regionally-coordinated health policy will reduce vaccination inequality in Latin America.

Contents

Abbreviations: ACIP, [U.S.] Advisory Committee on Immunization Practices; AMC, advance market commitment; CDC, Centers for Disease Control; COFVAL, Commission for the Future of Vaccines in Latin America; DILAVAC, [Latin American Diploma on Vaccinology]; EMA, European Medicines Agency; EPI, Expanded Program on Immunization; IFFIm, International Finance Facility for Immunisation; NHA, national health accounts; NIP, national immunisation programme; NITAG, National Immunization Technical Advisory Groups; NRA, national regulatory agency; OECD, Organisation for Economic Co-operation and Development; PAHO, Pan American Health Organization; PANDRH, Pan American Network on Drug Regulatory Harmonization; R&D, research and development; VAC, Vaccine Advisory Committee; VENICE, Vaccine European New Integrated Collaboration Effort; VPD, vaccine-preventable disease; WHO, World Health Organization.

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1. Introduction

The adoption of the Expanded Programme on Immunization (EPI) has played a pivotal role in reducing mortality and morbidity due to vaccine-preventable diseases (VPDs) in Latin America, with successes including the elimination of polio, measles and congenital rubella syndrome (CRS), and dramatic decreases in neonatal tetanus and Hib infections [1–3]. However, there remain significant shortcomings of vaccination programmes throughout Latin America and further work is needed to maintain current progress and prepare for future advances including the introduction of newly available vaccines [4].

In order to address the challenges of implementing vaccination polices in Latin America, the Carlos Slim Health Institute convened the Commission for the Future of Vaccines in Latin America (COFVAL) to make recommendations for reducing regional inequalities in coverage and outcomes [4]. Using a consensus-building approach, COFVAL aims to produce and implement regionally applicable recommendations to renew Latin America's leading role in immunisation.

Following a series of recommendations made by COFVAL in 2008 [4], we have conducted a comprehensive literature review (supplementary method 1) to assess their evidence-basis and feasibility, and here we present the key findings and discuss each recommendation in the context of existing VPD control strategies.

2. Current challenges in Latin America

The Commission outlined a number of challenges currently facing Latin America and these are summarised in Fig. 1. COFVAL have suggested that by addressing these concerns, Latin America can sustain achievements in immunisation, address widening inequalities in the region and continue to be a leader in immunisation policy as a new generation of vaccines, specifically targeted to developing countries, is introduced [4].

Regional data on effective coverage or epidemiological risk are poorly detailed, often using inconsistent criteria or collection methods. Standardisation of criteria would allow comparison between countries and evidence-based decision-making to drive policy.

Regional inequalities in vaccine coverage exist, both between countries and within countries (Table 1). A regional reference scheme for vaccine introduction and vaccination scheduling would go some way to reduce the gaps between countries with different incomes.

As vaccines succeed in eliminating diseases, social awareness of their benefits recedes and, in turn, political motivation for extending coverage also decreases. Training and education for vaccine providers and other healthcare personnel are deficient and out of date, contributing to variation in quality and coverage.

Immunisation inequality between countries is compounded by a weak international coordination between countries in the region. Since infectious diseases do not respect borders, better planning between neighbouring countries would increase the efficiency of vaccination programmes.

Thirteen out of thirty-four Latin American countries surveyed by WHO/UNICEF lack an independent advisory committee to provide ongoing guidance on vaccine introduction and scheduling [5]. Such bodies could facilitate the uptake of new vaccines and support evidence-based decision-making in the implementation of national immunisation programmes (NIPs).

A lack of appropriate financing mechanisms is delaying the introduction of new vaccines, and the primary mechanism for acquisition, the Pan American Health Organization (PAHO) Revolving Fund (described in more detail below), has become a rigid structure with limited financial capacity to meet the future demands of the region. For example, despite recommendation by WHO to include pneumococcal vaccination in NIPs, and the existence of the Revolving Fund, it has taken over a decade longer for Latin American countries to introduce the vaccine compared to North America and Western Europe [6]. Innovative finance mechanisms are needed to meet the costs of new vaccines and ensure investment in immunisation programmes in the region.

The introduction of new vaccines to Latin America is often delayed by lengthy and inefficient regulatory procedures, which need to be streamlined. A coordinated effort between countries in the region to strengthen regulatory authorities, and limit their dependence on outside organisations, is needed.

Local capacity for research, development and production of vaccines is limited, and investment in these areas would expedite the introduction of new vaccines and reduce costs in the medium and long term. Partnerships between private and public sectors may prove a mutually beneficial way to deliver such investment.

Based on the issues outlined above, COFVAL made seven key recommendations, for which we discuss the evidence base and feasibility in the following sections.

3. Standardised performance indicators for assessing vaccine impact

COFVAL recommended the standardisation of performance indicators in six areas: (1) burden of disease and vaccine coverage, (2) epidemiological surveillance, (3) national health accounts, (4) evaluation of functional health, (5) human resources performance, and (6) financial protection [4]. We found supporting evidence that standardisation of the first three would help to ensure reliability and comparability of data used to assess the effectiveness of vaccination programmes.

3.1. Burden of disease and vaccine coverage

Harmonisation of indicators for VPD burden and vaccine coverage is needed to aid comparison between countries, allowing implementation and evaluation of evidence-based policies across

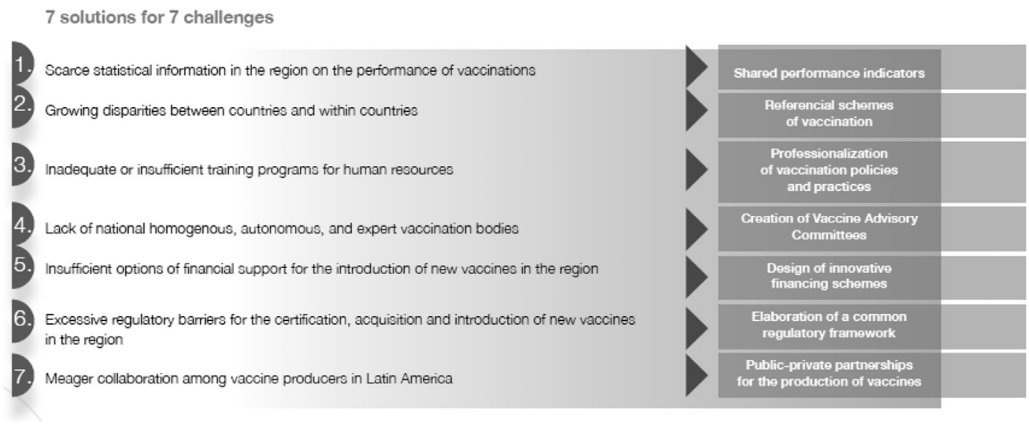

Fig. 1. 7 solutions for 7 challenges. This diagram summarises the challenges to vaccine policy and coverage equality currently facing Latin America. For each challenge, a solution is identified. This paper further details these solutions and examines the evidence-basis for them.

Latin America. Studies have considered various methods of data collection [7,8] and suggest that the ideal method for measuring vaccine impact is a benchmarking approach based on the World Health Organization (WHO)'s concept of 'effective coverage' – defined as the proportion of potential health gain from a NIP that is actually delivered compared to the maximum health gain that could be obtained with the NIP [9]. For example, if the health system could, through complete immunisation coverage, prevent all cases of a given disease, but prevents only 50% of cases, then effective coverage for this intervention is 50%. While this approach requires costly analysis and supporting infrastructure, an alternative is to assess the number of vaccines purchased versus the number administered, then compare this rate to data on raw coverage and correlate with morbidity and mortality rates [10]. Data can then be disaggregated by national, state and municipal levels as necessary, reflecting the fact that coverage may vary between centralised and decentralised countries [11].

Where coverage is not uniform, high-risk communities should be identified to ensure equality in vaccine provision. PAHO recommends estimating the number and proportion of communities with a coverage level of ≥95% and thereby the proportion of the population living in communities with suboptimal coverage [12]. This method is dependent on good local record-keeping practices and accurate population estimates, therefore, it is recommended that rapid coverage surveys, using the extensively described methodology recommended by WHO [13–17], are carried out to obtain the necessary information.

3.2. Epidemiological surveillance

Robust and coordinated national and regional epidemiological surveillance is crucial for responsiveness and preparedness for VPD outbreaks. Surveillance is also important for estimating VPD burden, setting of objectives for disease control and evaluating intervention programmes [18]. Harmonisation of definitions and best practice guidelines will aid timely information exchange between and within countries. For example, to ensure effective immunity between countries, North America has regional networks to coordinate the sharing of information between national surveillance centres [19].

3.3. National health accounts

National health accounts (NHAs) are an economic tool to assist policy-makers in understanding and improving health systems, showing resource flows through the system [20]. Latin American and other developing countries are currently transitioning to reporting immunisation expenditure according to Organisation for Economic Co-operation and Development (OECD) methodology [21,22]. Using standardised methodology for NHAs, including subaccounts for child health and immunisation, will provide detailed, internationally comparable data on expenditure, allowing deeper analysis of how best to finance and provide services [21].

Table 1
Inequalities in vaccine coverage both between and within countries.

	Belize	Costa Rica	El Salvador	Guatemala	Honduras	Mexico	Nicaragua	Panama
BCG (national)	100	91	72.7	97.6	98	85.4	99.2	97
BCG (poorest 20%[a])	100	–	76.1	97.9	96	87.4	99.5	97
DPT (national)	98.3	73	64.7	62.6	97	82	88.7	75
DPT (poorest 20%[a])	100	69	65.3	72.0	98	83.5	85.3	79
Polio (national)	96.6	78	67.4	67.3	96	85.2	88.5	78
Polio (poorest 20%[a])	100	82	69.3	74.7	97	87.6	84.4	83
Measles (national)	91.5	83	54.4	74	85	70.7	80.7	90
Measles (poorest 20%[a])	84.6	94	54.5	76.7	85	74	79.6	89
Pneumo (national)	97	85	54	75	94	80.8	82	85
Pneumo (poorest 20%[a])	–	–	–	–	–	–	–	–
Rotavirus (national)	0	0	0	0	0	0	98	0
Rotavirus (poorest 20%[a])	–	–	–	–	–	–	–	–

Data from [76].

[a] Poorest 20% refers to the population living in municipalities with the lowest 20% of household income. BCG, Bacillus Calmette–Guérin (vaccine against tuberculosis); DPT, diphtheria, pertussis and tetanus combined vaccine; Pneumo, pneumococcal vaccine.

4. Regional vaccination reference schemes

Although PAHO, through its Technical Advisory Group has outlined the mechanisms necessary to ensure coordinated implementation of the EPI [23], organisational, socio-economic, epidemiological and cultural factors have led to widening inequalities between countries in the introduction of new vaccines. This impedes reduction of VPD burden, and is compounded by factors such as migration, poverty, lack of education and under-resourcing, which disproportionately affect the more deprived sectors of the population [24,25].

To effectively reduce the inequality gap in vaccine availability between countries in the region, a comprehensive regional reference scheme, which harmonises national immunisation schedules, is possible with international cooperation and effective health information systems to evaluate the impact of interventions, estimate effective coverage rates and support evidence-based decision-making [26].

COFVAL has recommended a Latin American referential vaccination scheme to be used by each country as a guideline for goal setting and designing their immunisation schedules [4]. The scheme should be implemented in several stages:

1. Vaccines to achieve the WHO's Millennium Development Goal to reduce child mortality by two-thirds by 2015; including acellular pertussis vaccines, rotavirus, conjugated pneumococcal vaccine and hepatitis A, as well as safer combined vaccines
2. Vaccines to secure achievements in immunisation such as injectable polio vaccine (IPV)[1] and practical and economic vaccine combinations such as the measles, mumps, rubella and varicella vaccine
3. Vaccines to curb chronic and emerging morbidity, mortality and economic harm, such as human papillomavirus (HPV) and influenza

The national bodies responsible for vaccination policies in each country should make a significant contribution to developing these reference schemes, setting concrete and feasible goals for the introduction of new vaccines, according to their particular conditions and needs.

Information exchange networks such as the Vaccine European New Integrated Collaboration Effort (VENICE) have been used with some success in Europe to monitor vaccine introductions and develop best practice models for decision-making [27]. Similar efforts to establish best practice in Latin America have been led by PAHO [28]; however, the region suffers from income inequality and the high prices of new vaccines have made them unaffordable to some countries.

5. Professionalising immunisation policies and practices

Evidence suggests that an under-skilled health workforce is a key barrier to successful vaccine introduction and effective vaccination coverage [29–31]. Therefore, COFVAL has recommended that governments consider a strategy of continuous pre- and in-service training, to increase the quality and effectiveness of programmes [4].

COFVAL suggests that the ideal training programme should reach all levels of the health system, including nurses, doctors, managers, researchers and policy-makers, and be well-structured to allow periodical updates. A distance learning approach should be considered since this widens access and helps to develop a sense of community among vaccinology professionals. Topics covered should include: vaccine biology and effectiveness, epidemiology, vaccine distribution, storage and administration, economic analysis and decision-making processes for vaccine introduction, legal and regulatory issues and national health accounts [4,32,33]. Finally, in order to maximise the coverage of vaccines, healthcare providers must be trained in advocacy skills and community mobilisation strategies, with an emphasis on provider-patient communication to explain the risks and benefits of vaccination. This is particularly important since the healthcare provider may be a patient's only point of contact with the wider system [34,35].

Examples of successful immunisation training schemes include a PATH programme modelled in Andhra Pradesh, India, which combined on-site training and supervision with an ongoing mechanism to identify areas for improvement in all areas of vaccination practice. Under this scheme, coverage rates for hepatitis B increased from 58% to 72% and measles vaccination drop-out rates decreased from 22% to 8% [36].

Between 2000 and 2004, a regional training effort in Africa was jointly implemented by the WHO, USAID, UNICEF and the Network for Education & Support in Immunization. The objective was to provide information to middle management personnel involved in the operation of vaccination programmes. Results were positive but the project showed that, to be sustainable, education needs to be continuously provided to all relevant stakeholders [37].

The Carlos Slim Health Institute in Mexico recently introduced a Latin American Diploma on Vaccinology (DILAVAC), based on COFVAL recommendations [38]. DILAVAC is a Spanish language distance-learning programme that aims to: standardise knowledge on vaccines and the biological, social, cultural, economic and political issues that have an impact on coverage; allow participants to contribute to successful implementation of immunisation programmes and reduce the burden of VPDs; and promote evidence-based decision-making in health services at the subnational and local levels. In its first year, DILAVAC has provided access to (otherwise unavailable) training in vaccinology for more than 500 healthcare workers directly involved in NIPs in 12 Latin American countries.

6. Vaccine Advisory Committees

Although 20 out of 34 Latin American countries surveyed have Vaccine Advisory Committees, also known as National Immunization Technical Advisory Groups (NITAGs), not all have a formal legislative basis and some lack experience and independence [5,39]. COFVAL has proposed the institution of permanent Vaccine Advisory Committees (VACs) in every country, in order to facilitate uptake of new technology and information and support evidence-based decision-making in NIP administration [4].

A successful model is the US Advisory Committee on Immunization Practices (ACIP), consisting of 15 voting members who are experts in vaccinology, immunology, paediatrics, internal medicine, infectious diseases and public health. Also included are eight representatives of other federal agencies and 30 non-voting representatives of liaison organisations who contribute related immunisation expertise [40,41]. Members meet throughout the year, often as part of dedicated workgroups, and perform in-depth evaluations of available data using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for developing evidence-based recommendations [42]. ACIP provides expert external advice and guidance to the Director of the Centers for Disease Control (CDC) and the Secretary of the US Department of Health and Human Services. Recommendations for the routine use of vaccines are issued by the CDC and are harmonised with recommendations made by the American College of

[1] Unlike the oral polio vaccine, IPV uses an inactivated form of the virus, eliminating the risk of vaccine-associated paralysis.

Obstetricians and Gynecologists, the American Academy of Family Physicians, the American Academy of Pediatrics and the American College of Physicians. Each recommendation is widely distributed and incorporates their rationale [43,44].

Recommendations made by a VAC may include guidance on including a vaccine in the NIP according to target population, age, dose required and methodology for assessing impact and safety [45]. This process may be supported by PAHO's ProVac initiative, which provides standardised tools to assist with economic and cost–benefit analyses [46,47].

VACs should also evaluate compliance with their recommendations, such as the CDC's Comprehensive Clinic Assessment Software Application (CoCASA), which can be used to assess immunisation practices within clinics and other settings [48]. Finally, analyses conducted in one country should be made available to other countries in the region, and opportunities for expertise sharing and mentorship by more established VACs should be exploited as a regional strategy.

7. Innovative financing mechanisms for purchasing vaccines

New vaccines typically enter the market at a high introductory price set by the producer to offset the cost of research and development (R&D), and the uncertainty of future sales. This situation drives inequality within Latin America, since low- and middle-income countries must often wait until prices are lowered to introduce vaccines. Furthermore, countries may certify a vaccine but lack the funds to add it to the NIP, leading to further inequality within the country, since the vaccine is then only accessible to individuals with higher incomes. It is, therefore, crucial to implement financial and economic mechanisms to drive down the price of vaccines, allowing developing countries to rapidly acquire them and introduce them into their NIPs.

Currently, PAHO's Revolving Fund, established in 1979, is the primary mechanism for facilitating vaccine purchase in Latin America. The Fund operates by charging member countries a 3% surcharge on vaccines it purchases, and by pooling demand for vaccines in the region, achieves economies of scale for individual countries [49]. The Fund also enjoys considerable bargaining power, and has successfully negotiated an arrangement whereby producers cannot offer lower prices to other customers without also offering the Revolving Fund the same prices [50].

However, COFVAL has suggested that the Revolving Fund is no longer the leading facilitator in Latin America since vaccines purchased by the Fund must be certified by WHO, often causing delays[2] [51]. Furthermore, the rising costs of new vaccines for an increasing population have led to several higher-income countries reaching out directly to producers [4]. COFVAL therefore recommends an overhaul of the Revolving Fund mechanism, to radically strengthen its negotiating power and re-capitalise where necessary, using support from banks and the international capital markets. A more dynamic fund could expand its services to include technical and financial advice to member countries, as well as providing new, innovative purchasing strategies to gain greater access to new vaccines. In recent years, there has been great improvement in this respect, as the Revolving Fund's operating procedures have been updated and countries can now purchase vaccines that have been approved by National Regulatory Agencies such as the FDA, EMA, or others recognised by PAHO [52].

One potential financial strategy is price regulation; however, evidence suggests that this strategy has mixed success, since limiting drug prices reduces producer expenditure on R&D [53]. Differential pricing arrangements will only work if higher-income countries are willing to forego importing lower-priced vaccines from developing countries or demanding lower prices with reference to the arrangements for low-income countries. Otherwise, producers may prefer to delay introduction of a vaccine to a low-income country.

Financial alternatives include advance market commitments (AMCs), whereby donor nations and non-profit organisations finance the purchase of new vaccines at a pre-arranged price in order to drive investment into late-stage development and manufacturing capacity. Producers agree to supply the vaccine for a prolonged period at a reduced price and benefit from guaranteed demand, reduced marketing costs and not sharing the market with subsequent competitors [54]. AMCs may be useful for addressing diseases such as HIV/AIDS, malaria, tuberculosis, dengue and leishmaniasis [54,55]. A pilot scheme that introduced second-generation pneumococcal vaccines into the world's poorest countries, demonstrated a more rapid rollout than for the first-generation vaccines [56,57]. However, critics of the scheme raise the concern that developing countries may find themselves tied to a specific producer even when more effective alternatives become available [58], suggesting that further refinement may be needed [57].

New sources of funding are also emerging, with varying success. One of the more successful is the International Finance Facility for Immunisation (IFFIm) [59], which has benefitted from US$6.3 billion in donor contributions over 23 years from developed countries' governments.

A financing mechanism proposed by IFFIm is to front-load financial resources (i.e. concentrate costs in an early period of development) and to guarantee predictable funding. Front-loading ensures that resources are in place to immunise large populations as soon as a vaccine becomes available. Evidence suggests that combining these two strategies can increase the impact of vaccine coverage by 22% [60]. Latin American countries can finance front-loading via development loans from the World Bank and the Inter-American Development Bank [61].

8. A common regulatory framework for vaccine approval

Introduction of new vaccines in Latin America is often delayed by excessive regulatory procedures, relating to evaluation and certification. Historically, vaccines used in Latin America had first been approved and used in US and European markets. However, new vaccines targeted against tropical diseases may be used exclusively in developing markets [62]. The WHO has recognised the need to strengthen national regulatory agencies (NRAs) in the developing world but many countries still rely on PAHO's certification process, which requires a lengthy pre-qualification by the WHO [4,62,63]. To streamline this, PAHO has been working with NRAs in the region to recognise them as National Regulatory Authorities of Regional Reference so that they can participate in quality assurance, safety and efficacy processes for products purchased by the PAHO on behalf of countries [64]. To support this aim, COFVAL has proposed a model vaccination law for Latin America, a legal template that can be used by legislators in the region [4].

The Pan American Network on Drug Regulatory Harmonization (PANDRH) has already made significant progress in defining the prerequisites for a harmonised regulatory process in Latin America

[2] Certification is granted if a vaccine is included in the United Nations prequalification system, or, the vaccine has been registered and released by the United States Food and Drug Administration (FDA), the European Medicines Agency (EMA), the Canadian Biologics and Genetic Therapies Directorate (BGTD), Therapeutics Good Administration (Australia), or the Korea Food and Drugs Administration (KFDA). However, for vaccines produced in Latin America countries, local vaccine producers must be approved by WHO, often delaying the purchase of the vaccine.

[65]. COFVAL has suggested that, with regional cooperation, such a framework could eventually replace the requirement for WHO pre-qualification, while better meeting the specific needs of Latin American countries [4]. Furthermore, a regional body, similar to the European Medicines Agency (EMA) could pool human, technological and scientific resources in the region, producing an agency with far more capacity and scientific rigour than any country agency working individually. Indeed, the PANDRH proposals for harmonisation also included a future vision of a common registration system for vaccines [65].

9. Public–private partnerships for the production of vaccines

Advances in technology used to discover and produce vaccines have led to increased costs. Currently, Latin American producers lack the facilities required to comply with standards, limiting the region's manufacturing capacity and access to new vaccines [66]. Furthermore, investment in R&D in developing countries is scarce, and the public sector is often unwilling to use resources in this way. Overall, this provides little incentive for pharmaceutical companies to invest in vaccines for use mainly in developing countries. Tropical diseases affect the productivity and economic growth of developing countries, leading to an increasing prevalence of "poverty-promoting diseases" [67].

The WHO Commission on Macroeconomics and Health has identified partnerships with high-income countries as essential to advance new health products, processes and policies in the developing world [68]. COFVAL strongly recommends that such efforts are delivered through the greater use of public–private partnerships, in particular, between pharmaceutical companies, non-profit organisations, research institutes and governments to stimulate the design and development of new vaccines [4]. Public–private partnerships will boost competition in the region, stimulate investment and growth in the research sector and cut prices for vaccines in the medium and long term. Incentives for pharmaceutical companies include an increased market, particularly for vaccines against tropical diseases, and increased feasibility. Evidence suggests that products developed in a partnership tend to have a higher probability of success, at least in more complex Phase II and III trials, and particularly if the licensee is a large firm [69].

Examples of worldwide private–public partnerships are increasing in number, with the Sabin Vaccine Institute's Product Development Partnership a particular success [70]. The partnership was established to develop vaccines against neglected tropical diseases such as hookworm, schistosomiasis, Chagas disease and others [71,72]. Donors include several multinational pharmaceutical companies, as well as not-for-profit organisations such as PATH and the Bill & Melinda Gates Foundation. Partners include universities and research institutes from Australia, Brazil, China, Mexico, the UK and the US. In the last decade, the Sabin Institute has built a sustainable infrastructure and capacity for research, development, scale-up and mid-scale manufacturing, whilst operating primarily from academic institutions [71–73].

Private–public partnerships are also underway in Latin America, with Brazil and Mexico positioned as the main leaders in research and development [73–75]. The Carlos Slim Health Institute, has begun a collaboration with Baylor College of Medicine, the Sabin Vaccine Institute, the Autonomous University of Yucatan and the Center for Research and Advanced Studies of Mexico, to launch an initiative to develop vaccines for leishmaniasis and Chagas disease [73]. This programme aims to develop vaccines from the discovery to scale-up stages, then transfer the technology at the large-scale production stage.

10. A call for action

Through the recommendations outlined above, COFVAL aims to restore Latin America's global leading role in immunisation and reduce vaccination inequality in the region. A comprehensive review of the literature has shown an evidence basis for these recommendations, and therefore supports their implementation.

Despite the evidence for these recommendations, countries in the region have not moved towards their implementation. COFVAL states that a paradigm shift is now needed, to put in place systems and processes suitable for the development and introduction of a new generation of vaccines, including those designed specifically for the developing world. This shift will require coordinated efforts between governments and stakeholders in the public and private sectors, as well as non-profit organisations and non-governmental organisations.

COFVAL has called upon stakeholders to move away from traditional aid mechanisms and engage in social investment, updating the processes for evaluation and regulation of vaccines, and forming a regionally coordinated heath policy that will reduce inequality and benefit the whole population.

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Supplementary methods

Literature search.

Relevant literature was obtained by searching major electronic databases: Cochrane Library, CAB Abstracts, EMBASE, vLex, LegalTrac, LILACS, MedlinePlus, PubMed, SIGLE and TRoPHI, using primary search terms or the key topics of COFVAL's seven major recommendations. Other sources were also used to identify relevant publications, including WHO and PAHO reports, other international public health agencies' websites, government documents, and search engine searches such as Google Scholar. The relevant references were selected using manual analysis of the abstracts.

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