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Review

COVID-19 in Latin America: Clinical and immunological insights, vaccine development, and lessons for pandemic preparedness

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ABSTRACT

The COVID-19 pandemic had a profound impact on Latin America, exposing structural inequalities, fragmented healthcare systems, and longstanding technological dependence. The region experienced a high burden of infection and excess mortality, influenced by socioeconomic vulnerability and a high prevalence of metabolic comorbidities. In response, countries expanded diagnostic capacity, strengthened genomic surveillance, and increased participation in clinical research and therapeutic evaluation. Coordinated regional collaboration facilitated the detection and tracking of emerging SARS-CoV-2 variants. Local innovation also advanced diagnostic platforms and vaccine development, leading to regionally produced vaccines such as Soberana, Abdala, ARVAC, and Patria. These initiatives generated valuable clinical and immunological data, including characterization of inflammatory biomarkers associated with severe disease and evidence of hybrid immunity in highly exposed populations. However, persistent inequities in healthcare access, research investment, and manufacturing capacity continue to constrain regional self-sufficiency. Although collaboration among academia, industry, and government reduced certain external dependencies, structural limitations in funding stability, regulatory harmonization, and large-scale production remain. The Latin American experience highlights both adaptive scientific capacity during crisis conditions and the challenges of consolidating emergency-driven advances into durable preparedness. Sustained investment and coordinated governance will likely determine whether short-term responsiveness translates into long-term regional strengthening.

1. Introduction

The COVID-19 pandemic, declared in early 2020, represented an unprecedented challenge for Latin America, a region characterized by heterogeneous healthcare systems, high population density, and marked disparities in hospital infrastructure as well as diagnostics and therapeutic manufacture [1,2]. The first confirmed case of SARS-CoV-2 infection in the region was reported on February 26, 2020, in Brazil, and the first death attributed to the disease occurred on March 7 in Argentina [3].

The high prevalence of metabolic comorbidities, combined with socioeconomic inequalities and limited access to specialized medical care, substantially increased the risk of severe disease and mortality across the region [3]. These structural vulnerabilities also facilitated the early and accelerated spread of the virus in low- and middle-income countries, which accounted for a disproportionate share of global cases during the first months of the pandemic [3]. In response, coordinated efforts among the public, academic, private, and pharmaceutical sectors enabled the

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development of a more comprehensive strategy to confront the health crisis. Public health policies, risk communication initiatives, and epidemiological surveillance systems were strengthened, while clinical trials, therapeutic approaches, and vaccines were developed alongside local production of medical supplies. However, most of these pharmacological advances initially emerged in high-income countries, and their timely availability in Latin America was limited by supply inequities and regulatory delays [4–6].

Altogether, Latin America transitioned from an initial stage of vulnerability to one of institutional and scientific resilience, enhancing its diagnostic, surveillance, clinical, and bioproduction capacities. However, these advances unfolded in the context of deep structural deficiencies in health systems including chronic underfunding, fragmentation, and unequal access to healthcare that represented major challenges during the pandemic and continue to persist across much of the region. The lessons learned during this period constitute a crucial precedent for confronting future health emergencies with greater autonomy, preparedness, and a renewed commitment to health system strengthening.

To develop this review, we drew upon evidence from regional and international public health agencies—including the Pan American Health Organization (PAHO), the World Health Organization (WHO), and national ministries of health such as Mexico's Secretaría de Salud—alongside peer-reviewed scientific literature. Priority was given to multicenter studies, regional surveillance reports, and country-level publications that provided robust epidemiological, clinical, and immunological data. National reports from Mexico, Cuba and the Caribbean, Colombia, Peru, Brazil, Chile, and Argentina were incorporated when they contributed population-level estimates, detailed genomic surveillance findings, or insights into vaccine rollout strategies. While the review does not aim to be exhaustive, it highlights representative and high-quality examples. Together, these sources allowed us to synthesize both regional patterns and country-specific dynamics essential for understanding the trajectory of COVID-19 across Latin America.

2. Social and health determinants of the impact of COVID-19 in Latin America

The COVID-19 pandemic intersected with pre-existing structural inequalities in the region, contributing to a concurrent health, economic, and social crisis. Conditions of vulnerability reflected in high levels of poverty, informal employment, and limited access to essential services hindered compliance with preventive measures, particularly physical distancing and home isolation [7].

During 2020, global economic activity contracted by approximately 3.4%, while Latin America and the Caribbean experienced a regional decline between 6.4% and 7%, representing one of the most significant contractions in recent decades [7–9]. Unemployment increased from pre-pandemic levels of 7–8% to approximately 11.5%, disproportionately affecting informal sectors that account for more than half of total employment in the region [8]. These socioeconomic conditions were associated with challenges in implementing prolonged mobility restrictions and may have contributed to increased exposure in economically vulnerable populations [8]. In this context, structural economic fragility appears to have influenced transmission dynamics and health outcomes across multiple countries in the region.

Excess mortality in several Latin American countries ranked among the highest globally during peak waves [10,11] reflecting both direct effects of SARS-CoV-2 infection and indirect consequences associated with disruptions in essential health services, including maternal care, routine immunization, and chronic disease management. Temporal patterns were heterogeneous across the region: a severe first wave occurred between April and July 2020 in countries such as Bolivia and Ecuador, followed by subsequent peaks in late 2020 and early 2021 in Mexico, Peru, Brazil, Colombia, and Paraguay. Model-based excess-mortality estimates suggest that, in contrast to Western Europe—where mortality declined after early vaccination rollout—several Latin American countries experienced sustained or recurrent mortality surges over extended periods [11]

Within this broader regional pattern, the burden was not evenly distributed. Indigenous communities in remote rural areas, residents of densely populated urban settlements, and populations with limited access to healthcare services faced heightened vulnerability. Structural conditions—including geographic isolation, overcrowding, limited sanitation infrastructure, and constrained healthcare capacity—were associated with delayed diagnosis and reduced access to timely care [1,2]. In many settings, these factors likely contributed to persistently elevated excess mortality, illustrating how social and health-system inequities intersected with pandemic dynamics.

In response to these challenges, governments across Latin America implemented public health and social protection measures (Table 1). Across the region, the policy packages adopted in 2020 amounted on average to 4.6% of GDP—substantially lower than the 12.7% of GDP

Table 1
Examples of Non-Pharmaceutical Interventions and Social Protection Policies Implemented in Latin America During the COVID-19 Pandemic.

Country	Public Health Measures	Social Protection and Economic Support	References
Brazil	Implementation of national guidelines for hospital management and intensive care expansion, coordination through the Unified Health System (SUS).	Auxílio Emergencial (Emergency Aid) providing cash transfers to informal workers, and fiscal support to small businesses.	[143,144]
Peru	Early border closure and nationwide quarantine; rapid hospital reconversion and deployment of oxygen supply systems.	Bono Familiar Universal (Universal Family Grant) for low-income households, temporary employment programs, and support for small enterprises.	[145]
Mexico	Gradual implementation of the "Epidemiological Stoplight" system for mobility control; strengthening of hospital networks and RT-PCR testing capacity.	Social welfare transfers through Programa Bienestar and temporary economic relief for small enterprises (Créditos a la Palabra).	[146]
Argentina	Early nationwide lockdowns, expansion of genomic surveillance through the PAIS Network, and strengthening of intensive care capacity.	Ingreso Familiar de Emergencia (IFE) (Emergency Household Income Support) program, salary subsidies for affected workers, and expansion of unemployment benefits.	[13,147,148]
Chile	Mass testing and contact tracing strategy; decentralization of diagnostic laboratories and early large-scale vaccination campaigns.	Ingreso Familiar de Emergencia (Emergency Household Income Support) and direct fiscal transfers to families and independent workers; support for SMEs.	[147,149]
Colombia	Widespread testing and digital contact tracing through CoronApp; strengthening of regional hospital networks and ICU capacity.	Ingreso Solidario (Solidarity Income Program) program providing monthly transfers to vulnerable families and subsidies for utilities.	[150,151]
Uruguay	Mobility reduction measures and strong recommendations for physical distancing; Partial border closures	Unemployment subsidies and monetary subsidies were reinforced to fight the negative economic effects	[152]

mobilized by advanced economies to confront the health emergency [7,12]. Despite this gap, these resources enabled the expansion of hospital capacity, the strengthening of diagnostic networks, and the rollout of the largest vaccination campaign ever conducted in Latin America. National ministries of health, in coordination with regional bodies such as the Pan American Health Organization (PAHO), sought to align emergency public-health measures with economic constraints and social protection priorities. Countries including Chile, Brazil, and Mexico implemented large-scale testing and national immunization strategies as vaccines became available, although the timing, scale, and impact of these efforts varied across settings.

At the national level, the strategies reflected each country's institutional diversity and response capacity, some examples are: Brazil invested heavily in intensive care expansion and vaccine production; Peru implemented early lockdowns and border closures; Mexico applied phased distancing measures through its "epidemiological stoplight" system and public communication campaigns; and Argentina reinforced genomic surveillance through the Proyecto Argentino Interinstitucional de Genómica de SARS-CoV-2 (PAIS Network) [13]. These policies, along with direct transfer and social support programs, partially contained the health emergency and mitigated its most severe socioeconomic effects. Collectively, the pandemic exposed Latin America's structural fragilities but also catalyzed reforms and interinstitutional alliances that enhanced its response capacity. The articulation between public health, social protection, and scientific cooperation laid the foundation for regional resilience, enabling a gradual transition toward pandemic control and a more national equitable recovery.

3. Epidemiological and genomic surveillance of SARS-CoV-2 in Latin America

During the early months of the pandemic, SARS-CoV-2 genomic surveillance in Latin America was severely limited by restricted sequencing infrastructure, shortages of reagents, and insufficient bioinformatics capacity. Despite these constraints, several countries were able to report viral sequences in 2020, including Brazil, Peru, Colombia, Chile, Mexico, Costa Rica, Ecuador, Uruguay, Suriname, Argentina, Guatemala, Venezuela, Curaçao, the Dominican Republic, Jamaica, Aruba, and Cuba [14].

A major turning point came with the establishment of PAHO's Regional Genomic Surveillance Network (RESVIGEN) at the end of 2020. Through this initiative, more than 30 national laboratories began routine SARS-CoV-2 sequencing, substantially strengthening early variant detection and cross-country data sharing [15]. The network incorporated eight regional reference laboratories—located in Brazil, Chile, Colombia, Costa Rica, Mexico, Panama, Trinidad and Tobago, and the United States Centers for Disease Control and Prevention—to support member states in generating and analyzing viral genomes [15,16].

This coordinated regional effort increased both the volume and geographic representation of SARS-CoV-2 sequences submitted to the Global Initiative on Sharing All Influenza Data (GISAID). As of September 2025, countries in Latin America had deposited over 650,000 SARS-CoV-2 sequences into GISAID (Table 2) [17]. The development of RESVIGEN and national genomic surveillance platforms was associated with expanded molecular diagnostic and epidemiological capacities and facilitated the regional detection and monitoring of SARS-CoV-2 Variants of Concern (VoC) and Variants of Interest (VoI).

3.1. Regional Genomic Surveillance and Variant Emergence

Latin America contributed to the identification and characterization of several SARS-CoV-2 variants recognized by the WHO as VoC) or VoI. Notably, the Gamma (P.1) variant was first described in Manaus, Brazil, in November 2020; Lambda (C.37) emerged in Peru and became predominant in parts of the Andean region; and Mu (B.1.621) was identified in Colombia in early 2021, reaching substantial local prevalence before being displaced by Delta [18–22]. In addition to these internationally recognized variants, locally circulating lineages such as B.1.1.389 in Costa Rica accounted for a significant proportion of cases before being replaced by more transmissible strains [21].

Subsequently, the Delta (B.1.617.2) variant entered Latin America in mid-2021, with Mexico among the earliest countries to document its rapid expansion and displacement of the Gamma and Lambda lineages within a few months [23]. Later, the Omicron variant (BA.1–BA.5), detected in the region at the end of 2021, triggered the largest surge of infections recorded during the pandemic [24]. Despite the marked increase in case numbers, hospitalizations and mortality rates declined relative to earlier waves, a trend temporally associated with expanded vaccine coverage and increasing levels of hybrid immunity in several countries [25,26]. These observations were enabled by expanded genomic surveillance efforts across the region. Countries such as Brazil, Mexico, Peru, Chile, and Colombia accounted for the largest number of SARS-CoV-2 sequences submitted to GISAID (Table 2) [27]. However, absolute numbers only partially capture the region's sequencing capacity. When normalized by population size, smaller countries such as Costa Rica, Chile, Panama, Puerto Rico, and French Guiana exhibit the highest number of sequences per million inhabitants, revealing robust genomic surveillance systems despite their limited size (Table 2).

The scale of sequencing activities varied across countries and was influenced by differences in infrastructure, funding, and laboratory networks. Nevertheless, the expansion of national and regional genomic platforms during the pandemic contributed to improved regional capacity for variant detection, phylogenetic analysis, and molecular surveillance. These developments illustrate how existing scientific networks were leveraged and, in some cases, expanded in response to the demands of SARS-CoV-2 monitoring.

The pandemic's impact extended beyond SARS-CoV-2 genomic surveillance and was also reflected in shifts in the circulation of other seasonal and endemic infections. The widespread implementation of

Table 2
SARS-CoV-2 sequences uploaded to GISAID by Latin American countries [27].

Country	Registered genomes	Genomes per millon	GDP 2020 per capita	GDP per capita 2025
Brazil	269,300	1270	7074	10,816
Mexico	100,200	766	8841	13,630
Peru	58,200	1701	6133	8570
Chile	51,100	2585	13,115	17,927
Colombia	31,700	599	5340	7895
Argentina	28,100	615	8536	12,054
Costa Rica	14,400	2807	12,394	18,722
Ecuador	12,800	706	5464	6941
Puerto Rico (USA)	32,700	10,086	31,427	38,515
Guatemala	7000	380	4478	6682
Panama	7000	1550	13,291	20,092
Dominican Republic	3800	333	7135	12,452
Paraguay	4000	577	5365	6033
Uruguay	2400	709	15,758	24,080
Cuba	1900	173	9605	-
Venezuela	1800	63	-	4122
Nicaragua	1100	159	1938	3074
El salvador	1100	174	3997	5893
Haití	1600	136	1290	2435
Bolivia	796	64	3100	4121
French Guiana	6400	20,744	6776	30,650

Note: Data obtained from the GISAID global report "hCoV-19 Data Sharing by Country: 215 Countries and Territories" (cumulative sequences reported up to September 2025). "Genomes per million" refers to the number of registered SARS-CoV-2 genomes per million inhabitants. Population estimates correspond to mid-2024 values (UN World Population Prospects 2024, medium-fertility variant, as reported by Worldometer) [153]. GDP per capita values for Latin America correspond to estimates from 2020 and 2025, based on data from Explore the World Population Through Data [154].

non-pharmaceutical interventions—including social distancing, mask use, mobility restrictions, and enhanced hygiene practices—coincided with substantial disruptions in the seasonal dynamics of multiple respiratory viruses worldwide [28–31]. Data from global influenza surveillance systems reported a marked reduction in influenza circulation during 2020–2021, with positivity rates declining by more than 50% in many countries, including those in Latin America, compared with prepandemic seasons [32].

In addition to public health measures, biological interactions between viruses may have influenced these patterns. Experimental evidence suggests that SARS-CoV-2 infection can induce interferon-mediated antiviral states that transiently inhibit subsequent influenza infection [33]. Conversely, clinical reports have documented SARS-CoV-2 and influenza coinfections associated with increased disease severity [34]. Although viral interference has been proposed as a contributing factor to reduced influenza circulation during periods of intense SARS-CoV-2 transmission, disentangling biological effects from the impact of mitigation policies remains challenging. Respiratory syncytial virus (RSV) displayed similar disruptions. RSV cases declined substantially across Latin America in 2020, and subsequent circulation gradually returned to prepandemic seasonal trends, with modest shifts (1–4 weeks) in peak timing—except in Mexico and Colombia—and variable season duration (4–32 weeks). In several countries, RSV and SARS-CoV-2 activity showed predominantly negative correlations, further supporting the possibility of viral interference. Notably, RSV subtype A predominated after 2022 [35].

Dengue, a long-standing endemic arboviral infection in tropical regions of Latin America, provides an illustrative example of how pandemic measures influenced non-respiratory pathogens. Multinational analyses across Southeast Asia and Latin America reported an approximate 40% decline in dengue incidence during 2020 compared to pre-pandemic levels, temporally associated with mobility restrictions and other COVID-19 control measures [36]. However, these effects varied across countries and were followed, in several settings, by notable resurgence in 2023. Such patterns raise questions regarding shifts in population susceptibility, vector ecology, and continuity of surveillance systems.

Together, these observations suggest that COVID-19 mitigation policies extended beyond SARS-CoV-2 transmission, influencing the epidemiology of co-circulating pathogens. This broader impact highlights the importance of integrated, multi-pathogen surveillance frameworks in regions characterized by diverse endemic infectious diseases.

4. Diagnostic strategies and technological autonomy in the response to COVID-19

Diagnostic capacity was one of the central pillars for containing the spread of SARS-CoV-2. However, in Latin America, the initial response was constrained by dependence on imported diagnostic kits, limited numbers of certified laboratories, and an unequal distribution of technical and human resources. These structural gaps delayed early case detection and hindered the traceability of community transmission during the first months of 2020 [37].

To address these challenges, the PAHO coordinated the creation of a regional network of national reference laboratories in January 2020, standardizing molecular detection using RT-qPCR. This effort relied primarily on two internationally validated assays: the protocol developed by the Centers for Disease Control and Prevention (CDC, USA) and the assay designed by the Charité–Universitätsmedizin Berlin in collaboration with Erasmus MC, Public Health England, and the German company TibMolBiol [38]. The rapid public release of both protocols provided an accessible and robust technical framework for molecular diagnosis across the region.

The implementation of these assays led to the establishment of the first molecular surveillance nodes in Latin America and facilitated the progressive decentralization of diagnostic capacity from national reference centers to state-level and hospital laboratories. This expansion was crucial for sustaining epidemiological surveillance and mitigating diagnostic bottlenecks as case numbers increased.

4.1. Local innovation and development of regional diagnostic tests

As the pandemic progressed, Latin American institutions rapidly mobilized scientific and technological resources to develop in-house diagnostic solutions that reduced dependence on international suppliers and strengthened local diagnostic sovereignty. These efforts included the adaptation of international molecular protocols, the development of entirely local assays, and the establishment of domestic production platforms for recombinant viral antigens (Table 3).

Beyond the initial adoption of imported diagnostic platforms, the pandemic period was associated with expanded local biotechnological capacity in several Latin American countries. A central component of this process was the development of in-country systems for the production of recombinant SARS-CoV-2 proteins, supporting molecular diagnostics, serology, serosurveillance, and vaccine evaluation.

In Mexico, research groups at the Instituto de Biotecnología (UNAM) and at the Tecnológico de Monterrey developed scalable platforms for generating pseudotyped lentiviral particles, enabling neutralization assays in BSL-2 laboratories [39]. These platforms facilitated the characterization of vaccine-induced immune responses and population-level antibody dynamics. Complementary approaches, including phage-display antibody libraries such as the ALTHEA system, demonstrated the feasibility of rapidly identifying neutralizing antibodies and antigen-specific binders against SARS-CoV-2 [40]. Their adaptability illustrates the potential of modular antibody platforms for diagnostic and research applications in response to emerging variants. In Argentina, the COVIDAR initiative exemplified nationally produced recombinant antigen platforms supporting large-scale serological testing and informing public health decisions [41]. Additional efforts expanded recombinant protein production pipelines—including insect cell expression systems—to generate locally produced antigens for immunoassays [42]. Similarly, in Chile, academic and public health institutions developed in-house ELISAs based on nucleocapsid and RBD antigens to enable combined IgA/IgM/IgG detection, adapted to local epidemiological conditions and laboratory capacities [43].

Collectively, these initiatives reflect regional efforts to reduce reliance on imported diagnostic technologies and to expand locally developed platforms. Nevertheless, structural constraints within national innovation ecosystems continue to limit large-scale integration, long-term sustainability, and industrial scalability of these tools. Continued investment in research infrastructure and regulatory pathways may enhance regional preparedness for future emerging infectious diseases.

4.2. Expansion of serological testing and sero-epidemiological surveillance

As the pandemic evolved, countries across Latin America diversified their diagnostic strategies by incorporating rapid antigen tests and IgG/IgM serological assays, enabling the detection of prior infections and estimation of population-level immunity. In Mexico, national serosurveillance studies relied on quantitative IgG assays and neutralizing antibody measurements to assess community exposure and track the evolution of humoral responses over time [44]. In parallel, epidemiological surveillance systems incorporated digital reporting platforms such as SINAVE in Mexico and EPIVIGILA in Chile integrated molecular testing, hospitalization, and mortality data, allowing near real-time monitoring of epidemic dynamics and supporting timely public health interventions [45,46]. While many of these advances were implemented under emergency conditions, the pandemic period was associated with improvements in institutional coordination, laboratory capacity, and technological development. The extent to which these gains can be consolidated and sustained will depend on continued policy support,

Table 3
Selected Locally Developed Diagnostic Technologies in Latin America.

Country	Institution(s)	Technology developed	Type of use	Origin/adaptation	Regulatory status	References
Mexico	UDIBI–IPN	UDITEST-V2G® ELISA for anti-SARS-CoV-2 IgG using locally produced Spike/RBD	Antibodies, Serosurveillance	Antibody quantification based on an indirect ELISA format	Authorized by COFEPRIS for manufacture & commercialization	[155]
	CINVESTAV/IMSS	ATR-FTIR spectroscopy + chemometric analysis for rapid COVID-19 detection	Research / screening; potential application as rapid screening tool in resource-limited settings.	Adaptation of FTIR-based diagnostic frameworks used in Europe/Asia	Candidate	[156]
	CINVESTAV/IMSS	RT-LAMP assays adapted for low-resource settings	Rapid molecular diagnosis	Adaptation and validation using CDC and Charité RT-qPCR protocols as reference	Candidate	[157]
Argentina	CONICET; ICT Milstein; Pablo Cassará	NEOKIT-COVID-19 RT-LAMP kit approved by ANMAT	Point-of-care molecular diagnosis	Local adaptation of LAMP technology with in-country manufacturing	Validated/authorized by ANMAT	[158]
	Fundación Instituto Leloir; CONICET	COVIDAR IgG ELISA	Serosurveillance; vaccine evaluation	Fully local development using recombinant antigens produced in Argentina	Candidate	[41]
Colombia	Instituto Nacional de Salud; Univ. del Norte; Univ. Simón Bolívar	Colorimetric RT-LAMP assays for SARS-CoV-2 detection in nasopharyngeal swabs	Molecular diagnosis	Local optimization of international RT-LAMP methodologies; validation vs Charité RT-qPCR	Candidate	[159]
Peru	Instituto Nacional de Salud (INS)	In-house RT-LAMP assay, standardized and validated	Molecular diagnosis at national and peripheral labs	Local design of primers and workflow using Charité qPCR as comparator	Candidate	[160]
Brazil	Fiocruz; IBMP; Tecpar	Nationally produced RT-PCR kits	Routine clinical diagnostics; surveillance	Adaptation of WHO/Charité RT-PCR designs with local reagent production	Candidate	[161]
Chile	Pontificia Universidad Católica de Chile; Clínica Alemana–UDD	Antigen-based rapid detection test for the diagnosis of SARS-CoV-2 in respiratory samples (fluorescence immunochromatographic)	Emergency diagnostics	This assay could serve as a valuable option for early SARS-CoV-2 detection, especially in settings where access to molecular diagnostics is limited.	Candidate	[162]

funding stability, and regional collaboration.

International technical cooperation—primarily coordinated by PAHO and WHO—supported these efforts through technology transfer, personnel training, and the harmonization of diagnostic protocols. As a result of these coordinated initiatives, testing capacity expanded substantially across South America, increasing from fewer than 2 daily tests per million inhabitants in early 2020 to more than 140,552 daily tests by 2022 [47]. Beyond the immediate emergency, the pandemic catalyzed lasting improvements in institutional coordination, analytical capacity, and local technological development. Today, the region has gained diagnostic infrastructure that could serve as an essential foundation for preparedness against future epidemic threats.

5. Clinical and immunological findings in response to COVID-19 in Latin America

The clinical presentation of COVID-19 in Latin America reflected the region's epidemiological diversity and the high burden of obesity, metabolic and cardiovascular comorbidities. From the earliest phases of the pandemic, tertiary-care centers in several countries reported a predominance of moderate-to-severe disease among older adults and individuals with chronic conditions, placing pressure on intensive care units and contributing to periods of hospital saturation [48–50].

Across multicenter studies, hypertension, diabetes, and obesity consistently emerged as the most common comorbidities among hospitalized patients. Each was associated with an increased likelihood of requiring mechanical ventilation and with mortality rates that frequently exceeded global averages [49,51]. In Brazil, for example, an analysis of more than 600,000 hospitalized patients captured through the SIVEP-Gripe surveillance system showed a high prevalence of cardiovascular disease and diabetes among fatal cases, along with a clear increase in mortality between the first and second waves [50]. Additional insights were provided by the AstraZeneca LIVE observational–prospective study (NCT05282017) [52], conducted across five Latin American countries (Brazil, Colombia, Costa Rica, Mexico, and Panama) using a test-negative case-control design. Among the 786 participants recruited during the Omicron wave, nearly three-quarters (73%) had at least one comorbidity—most commonly cardiovascular disorders. Most COVID-19 cases were classified as moderate disease (51.1%), and more than half of the participants were unvaccinated (56.3% among cases vs. 38.2% among controls) [48].

Similarly, in Peru, hospital-based cohorts reported high fatality rates during the early pandemic waves, driven by limited intensive care capacity and the substantial burden of metabolic comorbidities—including obesity, hypertension, and diabetes—among hospitalized patients [53]. These patterns were consistent across the region. Mexico, for example, has one of the highest global prevalences of overweight and obesity (>75% of adults), a factor that contributes to the early onset of metabolic disease. As a result, nearly 30% of adults aged $\geq$ 40 years are hypertensive and approximately 20% are diabetic—conditions strongly associated with an increased risk of severe COVID-19 and mortality [53,54].

In contrast, pediatric COVID-19 cases across Latin America generally presented with milder acute respiratory disease than adults. However, a subset of children developed severe outcomes, including multisystem inflammatory syndrome in children (MIS-C) and post-acute sequelae. A large regional multicenter study [55] identified independent risk factors for hospitalization, including age < 1 year, Indigenous or Native ethnic background, and the presence of at least one comorbidity. Importantly, coinfections remain clinically relevant in pediatric populations during the Omicron era. In a study of children in China, the predominant circulating lineages were BF7.14 and BA.5.2, and infections with other respiratory pathogens decreased over the same period. Despite this decline, SARS-CoV-2 coinfection with other respiratory viruses in outpatients was associated with more severe respiratory symptoms, highlighting coinfection as a phenomenon warranting attention and

reinforcing the need for integrated surveillance and prevention strategies, including vaccination [56].

Among comorbid conditions, metabolic or endocrine disorders, immune deficiency, chronic cardiopulmonary diseases, chronic gastrointestinal or neurologic disorders, and preterm birth markedly increased the likelihood of requiring hospitalization. Furthermore, children presenting with anemia, radiological peribronchial wall thickening, hypoxia, altered mental status, seizures, or shock were significantly more likely to require admission to the Pediatric Intensive Care Unit (PICU) [55]. Conversely, symptoms such as pharyngitis, myalgia, or diarrhea were inversely associated with hospitalization. Beyond individual risk factors, the study also highlighted the role of socioeconomic disparities and unequal access to specialized pediatric care, which contributed to differences in outcomes across countries in the region.

Finally, obesity and type 2 diabetes emerged as key determinants of COVID-19 severity in Latin America [49,54,57]. Current estimates indicate that more than 67% of adults in the Americas are overweight or obese and 37.6% of children and adolescents aged 5–19 years are affected [58]. This long-standing burden of metabolic disease creates a chronic pro-inflammatory environment that amplifies the immune dysregulation triggered by SARS-CoV-2. Consequently, individuals with metabolic comorbidities are predisposed to multisystem complications, which may have contributed to higher rates of severe disease and mortality observed in several countries.

5.1. Immunopathogenesis and systemic inflammation

Regional studies have documented systemic hyperinflammatory profiles among patients with severe COVID-19 across Latin America that are comparable to those described in other regions. These profiles are characterized by profound lymphopenia, elevated IL-6, TNF-α, IL-8, and IL-10 levels, and biomarkers consistent with widespread endothelial dysfunction [59–62]. Similar patterns have been reported in North America, Europe, and Asia, where dysregulated innate immune activation and cytokine elevation are recognized as central features of severe disease [63–65]. Collectively, these findings do not support the existence of a distinct inflammatory signature unique to Latin American populations.

In several Latin American cohorts, elevated serum IL-6 and D-dimer levels, together with marked lymphopenia and increased neutrophil-to-lymphocyte ratios, were identified as important prognostic biomarkers of fatal outcomes in hospitalized patients, particularly those with chronic comorbidities [59,62]. Complementing these observations, critically ill patients exhibited overexpression of HIF-1α and myelopoiesis-related genes in circulating myeloid cells, indicating persistent hypoxia and sustained inflammatory activation. This transcriptional profile was accompanied by a shift toward an "immature myeloid" phenotype consistent with emergency hematopoiesis [60,61]. Such dysregulated hematopoietic responses are consistent with a maladaptive stress program described in acute systemic inflammation and aging, where cytokine-mediated and hypoxia-driven signaling favors the expansion of immature myeloid progenitors at the expense of lymphoid regeneration [60,66–68].

Immunophenotyping further revealed features of T-cell dysfunction in severe COVID-19, including increased frequencies of plasmablasts and activated $CD8^+$ and $CD4^+$ T cells, alongside higher proportions of $PD\text{-}1^+$ subsets indicative of exhaustion and impaired antiviral capacity [69]. Additional evidence from studies conducted at the Hospital General de México and the IMSS showed that pregnant women with COVID-19 displayed significantly elevated frequencies of $CD39^+$ monocytes, together with increased serum TNF-α, IL-6, IL-4, and MIP-1β compared with non-pregnant women [70]. These findings suggest a dynamic interplay between pro- and anti-inflammatory responses that may influence disease severity during pregnancy. Comparable inflammatory patterns have been reported in international cohorts [71–73] supporting the notion that SARS-CoV-2–associated immune alterations during pregnancy are broadly consistent across diverse populations.

Finally, profound lymphopenia, features of T-cell exhaustion [69], and cytokine hyperactivation—particularly involving IL-6 and IL-1β—have been consistently associated with severe COVID-19 and proposed as prognostic biomarkers in both Latin American and international studies [66,69,74–76]. These inflammatory observations, together with findings from major international clinical trials, contributed to the incorporation of immunomodulatory therapies such as corticosteroids and tocilizumab into hospital treatment protocols in several countries across the region.

5.2. Adaptive immunity and seroprevalence

Although studies on adaptive immunity in the region remain limited, available evidence indicates that natural infection, vaccination, and especially their combination are associated with the development of hybrid immunity.

In Mexico, multiple nationwide serosurveys conducted during 2020 revealed a substantial rise in SARS-CoV-2 exposure across the population. A national study analyzing more than 24,000 serum samples collected throughout the year reported an increase in seroprevalence from 3.5% to 33.5%, with neutralizing activity detected in 86% of seropositive individuals—suggesting that infection incidence may have been substantially higher than estimates based solely on PCR-confirmed cases [44]. Complementing these findings, a second nationally representative survey conducted between August and November 2020, which included 9640 serum samples, estimated a seroprevalence of 24.9%. Seropositivity was lower among adults aged ≥ 60 years and significantly higher in urban and metropolitan areas, among individuals with low socioeconomic status, lower educational attainment, and those engaged in the workforce. Notably, 67.3% of seropositive individuals reported no symptoms, underscoring the high proportion of asymptomatic infections and the magnitude of undocumented community transmission in Mexico [77]. In Chile, a population-based study across three cities (Santiago, Talca, and Coquimbo–La Serena) estimated an average seroprevalence of 10.4% just 267 days after the first imported case, with wide geographic variability [78]. Similar surveys conducted in other Latin American countries (Brazil, Chile and Dominican Republic), documented rapidly increasing seroprevalence during 2020, which expanded further following the rollout of the first vaccination campaigns [79–81].

Beyond humoral responses, bioinformatic analyses of SARS-CoV-2 structural proteins identified conserved B- and T-cell epitopes within Spike and N proteins, maintaining functional persistence against emerging variants [82]. The widespread rollout of vaccination also contributed to a significant reduction in severe outcomes during the Delta and Omicron waves, as reported in Mexican cohorts [83], consistent with findings from other regional studies. In addition, obesity has consistently been associated with higher SARS-CoV-2 seropositivity rates, aligning with evidence from regional studies showing increased proportions of seropositive individuals with class I and class II obesity, as well as meta-analytic data indicating that people with obesity face a significantly elevated infection risk [84].

Emerging cohort and seroprevalence data from Latin America indicate that the combination of prior SARS-CoV-2 infection and full vaccination commonly referred to as "hybrid immunity" has become an increasingly common component of the region's immunological landscape. Evidence from a national multistage household survey in the Dominican Republic showed that nearly one-third of adults had both infection- and vaccine-derived immunity, illustrating the rapid accumulation of hybrid immunity in at least part of the region [81]. Additional regional cohorts confirmed that individuals with documented infection followed by vaccination (or vice versa) developed higher and more durable neutralizing antibody titers, along with significantly lower risks of hospitalization and death during reinfections between delta and omicron waves [83,85].

Collectively, these findings highlight that widespread hybrid

immunity—shaped by successive waves of natural infection and expanding vaccination coverage—likely contributed to increased population-level protection in several countries across Latin America. This cumulative immunity may partly explain the decline in severe cases and mortality observed since 2022, even as new variants with partial immune escape continued to emerge. Notably, these epidemiological improvements occurred despite the limited availability of updated, variant-adapted vaccines in the region at that time, suggesting that hybrid immunity may have played a role in mitigating severe outcomes despite limited access to updated vaccine formulations against SARS-CoV-2.

6. Evolution of clinical treatment and therapeutic guidelines in Latin America

The clinical management of COVID-19 in Latin America was initially marked by uncertainty and the scarcity of therapeutic options. In the absence of specific antivirals, several countries adopted empirical treatments such as hydroxychloroquine, azithromycin, and lopinavir/ritonavir based on early observational reports and preliminary international guidance. However, controlled trials conducted between 2020 and 2021, including the WHO Solidarity Trial, demonstrated that these drugs offered no clinical benefit and were associated with potential adverse effects, leading to their progressive removal from national treatment guidelines [86,87].

6.1. The role of corticosteroids, anticoagulation, and emerging regional therapies

Beginning in 2021, Latin American countries progressively integrated robust evidence derived from international and regional clinical trials. The use of dexamethasone was consolidated as first-line therapy for hospitalized patients requiring supplemental oxygen following the RECOVERY Trial, which demonstrated a significant reduction in mortality and number of ventilator-free days among these patients [88,89]. Additional evidence from regional cohorts and randomized studies in critically ill individuals such as the CoDEX Trial performed in Brazil reinforced the benefit of dexamethasone in severe forms of the disease [89]. At the same time, anticoagulant prophylaxis with low-molecular-weight heparin became standard practice for all hospitalized patients, supported by recommendations specifically adapted for low- and middle-income settings [90].

For example, in Mexico translational and clinical research efforts explored novel anti-inflammatory strategies targeting both systemic and neuroinflammatory components of COVID-19. Early studies demonstrated that nasal and systemic glucocorticoid treatment modulated proinflammatory cytokines and reduced disease severity in hospitalized patients [91]. A multicenter randomized clinical trial compared intranasal versus intravenous administration of dexamethasone, reporting that the intranasal route was more effective at reducing systemic inflammation and improving clinical outcomes in hospitalized patients [92,93]. These findings highlighted the potential of targeted corticosteroid delivery for mitigating inflammation at both pulmonary and central nervous system levels.

Follow-up studies further revealed that a subset of post-COVID-19 patients developed persistent neuropsychiatric sequelae, including cognitive impairment, anxiety, and depression. A recent prospective pilot study in an open Mexican population identified long-term neuropsychiatric alterations associated with prior infection and systemic inflammation, underscoring the need for integrated management strategies beyond acute care [94]. Altogether, these national and regional advances illustrate how Latin American clinical research contributed not only to the refinement of global treatment protocols but also to the development of innovative therapeutic approaches tailored to the region's epidemiological and socioeconomic context.

6.2. Incorporation of immunomodulators and antivirals

The recognition of systemic hyperinflammation as a central driver of COVID-19 progression prompted the adoption of targeted immunomodulatory therapies. Tocilizumab, an IL-6 receptor blocking monoclonal antibody, was evaluated in multicenter randomized trials such as EMPACTA, which included sites in the United States, Mexico, Brazil, and Peru, and demonstrated a reduced risk of progression to mechanical ventilation in hospitalized patients with hyperinflammatory syndromes [95–97].

Between 2020 and 2023, the introduction of antivirals such as remdesivir, molnupiravir, and nirmatrelvir/ritonavir (Paxlovid) further expanded the therapeutic arsenal available across the region. Their deployment was guided by continental efforts to prioritize evidence-based treatments; in this regard, PAHO clinical guidelines recommended agents such as nirmatrelvir/ritonavir for outpatient management while clearly discouraging therapies with no demonstrated clinical benefit, including hydroxychloroquine and ivermectin [98,99]. In addition, countries such as Argentina, Brazil, Mexico and USA participated in international trials evaluating baricitinib (JAK1/2 inhibitor), which showed benefits in reducing recovery time and improving oxygenation in hospitalized patients [100,101]. However, its use was largely restricted to tertiary hospitals due to its high cost and limited availability.

At the beginning of the pandemic in 2020, convalescent plasma was widely administered under compassionate-use protocols. However, controlled clinical studies later demonstrated limited or no clinical benefit, leading to its restriction to research settings or to selected cases of severe immunosuppression [102]. In Cuba, the HSP60-derived altered peptide ligand CIGB-258 emerged as a promising immunomodulatory candidate. The peptide showed anti-inflammatory and Treg-inducing activity in preclinical studies and demonstrated safety in early rheumatoid arthritis trials. In severe and critically ill COVID-19 patients, intravenous CIGB-258 reduced IL-6, IL-10, TNF-α, granzyme B, and perforin while increasing regulatory T cells, with all treated individuals showing clinical improvement [103]. These findings support its potential as an adjunct therapy for severe COVID-19 and other cytokine-driven conditions.

6.3. Consolidation of clinical guidelines and post-acute management

Between 2021 and 2023, most Latin American countries updated their clinical guidelines to include the rational use of corticosteroids, anticoagulants, and immunomodulators, with clinical risk stratification based on biomarkers such as D-dimer, ferritin, and lymphocyte counts (Table 4).

By 2023, regional updates emphasized post-acute COVID-19 management ("long COVID"), focusing on pulmonary rehabilitation, cardiometabolic follow-up, and comprehensive care for neurological and psychological sequelae [104]. These developments reflect a decisive shift from empirically driven interventions to evidence-based therapeutic strategies, informed by emerging clinical and immunological insights across Latin America and the world. The generation of locally grounded data, ranging from inflammatory biomarkers to treatment response profiles, enabled more precise and adaptive protocols, tailored to the region's epidemiological realities. This transformation was improved by unprecedented collaboration among public health institutions, research centers, and clinical networks, which collectively strengthened the region's capacity to evaluate, validate, and implement effective COVID-19 treatments. As a result, Latin America not only expanded its therapeutic arsenal but also laid the foundation for a more resilient system better equipped to confront future public health emergencies with agility and rigor.

Table 4
Evolution of COVID-19 clinical treatment guidelines in Latin America (2020–2023).

Year	Clinical management guidelines	Reference
2020 (Mar–Jun)	Publication of the first provisional clinical management guidelines recommending early oxygen therapy and discouraging the routine use of antibiotics or antivirals without supporting evidence.	[163]
2020 (Apr–Sep)	Initial inclusion of hydroxychloroquine, azithromycin, and lopinavir/ritonavir; later withdrawn due to lack of efficacy and adverse event reports.	[164,165]
2021 (Jan–Jun)	Incorporation of evidence from the RECOVERY trial: dexamethasone recommended for patients requiring supplemental oxygen.	[88,89, 166]
2021 (Jul–Dec)	Introduction of low-molecular-weight heparins guided by the IMPROVE bleeding risk model and severity biomarkers (D-dimer, ferritin, lymphocyte count).	[167]
2021 (Aug–Dec)	Standardized use of corticosteroids and anticoagulants; convalescent plasma not recommended outside clinical trials.	[90,168]
2022 (Jan–Jun)	Update including antivirals (remdesivir and molnupiravir), prioritized according to availability.	[99,167]
2022 (Jul–Dec)	Unified guidelines emphasizing early treatment, stepwise oxygen therapy, and risk-adjusted anticoagulation.	[169]

6.4. Long-COVID

Long COVID refers to the wide range of persistent and long-term health complications that follow SARS-CoV-2 infection. It is a multifaceted, multisystem condition capable of affecting virtually every organ and causing substantial functional impairment. Globally, it is estimated that nearly 400 million people have experienced this syndrome. Multiple biological mechanisms are thought to contribute to its development, including viral persistence, immune and complement dysregulation, mitochondrial impairment, endothelial inflammation, and alterations in the microbiome. Given its complexity, chronicity, and high prevalence, Long COVID has profound effects not only on affected individuals but also on healthcare systems and national economies [105].

Although extensive research on post-acute sequelae of SARS-CoV-2 infection (PASC or Long COVID) has been conducted in the United States and Europe, evidence from Latin America remains comparatively limited, heterogeneous, and shaped by gaps in surveillance and unequal access to health services [106]. Across the region, reported prevalence tends to be lower than global estimates—a pattern that likely reflects under-diagnosis, reduced clinical follow-up, and barriers to specialized care rather than true population-level resilience [106].

Nevertheless, emerging regional analyses are beginning to clarify the magnitude of the condition. A multicountry cross-sectional study conducted in 16 Latin American nations surveyed over 2400 individuals and found that 48% experienced symptoms lasting $\geq$ 3 months after infection, most frequently fatigue, cognitive impairment (“brain fog”), and musculoskeletal pain [107]. Participants also reported substantial disruptions in daily functioning and increased demand for post-COVID healthcare services.

In Mexico, a nationally representative cohort identified persistent symptoms in 12.44% of adults aged $\geq$ 20 years, with over one-quarter reporting symptom duration $\geq$ 6 months and 14.05% describing incapacitating manifestations—underscoring the clinical and public health relevance of PASC in the country [108]. Additional clinical–epidemiological studies documented frequent neuropsychiatric presentations and persistent fatigue, particularly among individuals with metabolic comorbidities [109], while complementary neuropsychiatric research reported long-term impairments in attention, memory, and mood [94]. Similarly, a longitudinal study from Brazil in 2023 demonstrated measurable cognitive decline among individuals with post-COVID conditions. The occurrence of Long COVID symptoms followed a clear dose–response pattern, with higher prevalence and more severe cognitive impairment observed in those who had experienced severe acute disease [110].

Despite growing recognition of long-COVID as a major post-pandemic challenge, Latin America continues to face structural barriers to its diagnosis, management, and surveillance. Limited access to multidisciplinary rehabilitation programs, insufficient integration of primary care networks, and the absence of standardized diagnostic criteria across health systems hinder timely identification and follow-up. Furthermore, the scarcity of prospective studies and biomarker-based approaches, constrains understanding of the biological mechanisms driving persistent inflammation and neuroimmune dysregulation. Addressing these gaps will require coordinated regional strategies that combine epidemiological monitoring with translational research, emphasizing equitable access to post-COVID care and the development of evidence-based rehabilitation models adapted to the socio-economic realities of the region.

7. COVID-19 clinical research landscape across Latin America

The COVID-19 pandemic was associated with a substantial increase in Latin American participation in clinical research (Table 5 and Supplementary Table 1), contributing to the strengthening of regulatory and clinical trial capacities across the region. Although most pivotal studies originated in North America and Europe, Latin America emerged as a key partner in the evaluation of therapeutics serological/epidemiological, pathogenesis and vaccines.

Latin America registered 597 COVID-19–related clinical trials on ClinicalTrials.gov up to the end of 2025. Participation was markedly heterogeneous across the region. Brazil, Mexico, and Argentina accounted for more than 65% of all registered studies, with Brazil contributing 32.2% of the regional total (192 trials), followed by Mexico (19.3%) and Argentina (13.7%). Intermediate contributors included Colombia (10.4%), Chile (5.5%), Peru (4.9%), and Puerto Rico (4.7%), while most remaining countries registered fewer than ten protocols. This distribution reflects structural differences in research infrastructure, funding availability, and clinical trial capacity across the region.

Vaccine and therapeutic trials accounted for the majority of clinical research activity in the region, whereas countries with more limited resources contributed mainly through observational studies, serological surveys, and small-scale immunopathogenesis protocols. Overall, the distribution of trials reflects both the rapid research mobilization observed during the pandemic and the persistent disparities in research capacity across Latin American countries.

7.1. Regional vaccine innovation and the expansion of scientific autonomy

In parallel, the pandemic was associated with the expansion of multiple vaccine development initiatives across Latin America, reflecting efforts to enhance local production capacity and reduce reliance on external supply chains.

In Cuba, the vaccine candidates Soberana-02 (an RBD conjugated to tetanus toxoid), Soberana-Plus (a dimeric RBD formulation with alumina) [111], and Abdala (a recombinant RBD produced in *Pichia pastoris*) all received emergency use authorization. Notably, the Abdala vaccine reported an efficacy above 92% against symptomatic COVID-19, making Cuba one of the first countries in the region to develop, manufacture, and deploy domestically produced COVID-19 vaccines [112]. In Argentina, a public–private consortium led by the National University of San Martín developed the ARVAC Cecilia Grierson vaccine, a recombinant RBD-based protein booster formulated with Gamma and Omicron BA.4/BA.5 antigens in a hydrogel platform. ARVAC successfully completed phase II/III clinical trials, demonstrating a favorable safety profile and strong immunogenicity against multiple SARS-CoV-2 variants—and even cross-reactive responses to SARS-CoV-1 [113,114]. In

Table 5
Overview of Latin America's Participation in SARS-CoV-2 Clinical Trials.

Country	Total trials*	Vaccines	Therapeutics (antivirals / immunomodulators)	Serological / epidemiological	Immunology / pathogenesis	Others
Argentina	82	14	37	6	1	24
Bolivia	2	-	-	1	-	1
Brazil	192	20	103	6	1	62
Chile	33	5	10	2	0	16
Colombia	62	8	27	4	1	22
Costa Rica	5	-	-	1	1	3
Dominican Republic	9	3	3	-	-	3
Ecuador	4	1	-	1	1	1
French Guiana	5	-	-	2	-	3
Guatemala	4	1	2	-	-	1
Honduras	6	4	-	-	-	2
Jamaica	1	-	1	-	-	-
Mexico	115	14	64	7	2	28
Panama	7	3	2	-	-	2
Paraguay	1	-	-	-	1	-
Peru	29	3	15	1	1	9
Puerto Rico	28	2	14	2	-	10
Venezuela	2	-	1	-	-	1

Note: The "Others" category includes studies whose primary focus could not be clearly assigned to vaccines, therapeutics, serological/diagnostic tools, or immune-characterization based on the available metadata. Supplementary Table 1 lists the specific interventions classified under this category. All data were obtained from clinical trials registered in ClinicalTrials.gov up to the end of 2025.

Brazil, the Instituto Butantan advanced the development of Butanvac, an inactivated NDV-LaSota–based viral vector vaccine that successfully completed phase I/II clinical trials, demonstrating an acceptable safety profile and robust immunogenicity [115]. In Mexico, the national vaccine initiative centered on AVX/COVID-12 "Patria", developed by the biopharmaceutical company Laboratorios Avimex in collaboration with the Icahn School of Medicine at Mount Sinai (USA) and a broad consortium of academic and public health institutions, including CONAHCyT, IMSS, INER, UNAM, and IPN. The Patria vaccine is based on a replication-competent NDV-LaSota vector engineered to express the prefusion-stabilized SARS-CoV-2 Spike protein containing six proline substitutions (S-6P). Preclinical studies in mice, hamsters, and pigs demonstrated that the platform is safe, well tolerated, and strongly immunogenic, eliciting high titers of neutralizing antibodies [116,117]. These findings were subsequently supported in phase I and II clinical trials in adult volunteers, which evaluated both intramuscular and intranasal administration routes. The intramuscular regimen was primarily assessed for systemic immunogenicity and prevention of symptomatic disease, demonstrating induction of humoral and cellular immune responses consistent with protection against severe and critical COVID-19.

As with most first-generation COVID-19 vaccines globally, these trials were not designed to measure secondary transmission, and direct comparative data between vaccine platforms—including mRNA-based vaccines—remain limited. The intranasal approach was explored to assess mucosal immunity in addition to systemic responses. Early-phase data demonstrated induction of local antibodies alongside circulating neutralizing responses, suggesting potential relevance for limiting viral replication at the site of entry [118–120]. The NDV platform reflects a shared translational framework between institutions in the United States and Mexico. Although definitive population-level evidence of transmission reduction is still limited, the observed induction of systemic and mucosal responses supports continued evaluation of intranasal NDV-based vaccination strategies [119–121].

In the phase II/III trial, AVX/COVID-12 met its non-inferiority endpoint compared with the AstraZeneca AZD1222 vaccine and induced neutralizing antibodies against Omicron-lineage variants, supporting its use as a heterologous booster in adults [119,120,122]. Subsequent immunological analyses of the updated Patria vaccine targeting the Omicron BA.2.75.2 subvariant revealed robust and high titers of neutralizing antibodies. In the same study, the first-generation vaccine demonstrated broader immunological coverage, effectively recognizing the ancestral Wuhan strain as well as several emerging variants, including JN.1 [123]. Moreover, sera and T cells from individuals infected with or vaccinated against Omicron variants were able to recognize the Wuhan S protein expressed in the AVX/COVID-12 "Patria" vaccine [124]. Together, these findings indicate that Latin American vaccine platforms can elicit immune responses with broad variant recognition and potential relevance for hybrid immunity.

By 2024, more than fifteen regionally developed vaccine candidates had advanced to preclinical or clinical stages. Among these, Argentina's ARVAC, Cuba's Soberana-02, Soberana-Plus, and Abdala, and Mexico's AVX/COVID-12 "Patria" obtained regulatory authorization for use in the population. Together, these initiatives reflect an expansion of regional scientific and manufacturing capabilities during the pandemic, highlighting both the progress achieved and the ongoing challenges related to scalability, regulatory harmonization, and sustained investment.

7.2. Milestones and barriers in Latin America's mass vaccination campaigns

The introduction of COVID-19 vaccines marked an important shift in the course of the pandemic. However, achieving equitable access to doses posed one of the region's greatest challenges. During the first half of 2021, high-income countries secured the majority of the global vaccine supply, forcing Latin American nations to rely on multilateral mechanisms such as COVAX, bilateral agreements, and local production programs to ensure vaccine availability [125]. Thanks to the pre-existing infrastructure of National Immunization Programs, Latin America successfully implemented large-scale vaccination campaigns with high public acceptance. By the end of 2022, full vaccination coverage surpassed 71.1% of the regional population [126].

Despite progress in vaccination rollout, low and middle countries income continued to face substantial logistical and structural challenges. Limitations in cold-chain infrastructure and digital connectivity hindered the equitable distribution of mRNA vaccines particularly those requiring ultra-low-temperature storage (–70 °C) in rural and remote areas [127]. Persistent intra- and inter-country disparities were evident: while nations such as Chile and Uruguay achieved full vaccination rates exceeding 60% by mid-2021, supported by robust public health infrastructure and centralized distribution systems, others, including Ecuador, Guatemala, Argentina, Brazil and Mexico remained below 25% coverage during the same period. These contrasts reflected enduring inequalities in access, procurement capacity, and healthcare logistics across the region [128].

To address these challenges, countries adopted diverse vaccine

acquisition strategies, combining multilateral mechanisms such as COVAX, bilateral agreements, donations, and, in a few cases, local production initiatives. Table 6 summarizes the main vaccines deployed in Latin America, the mechanisms of acquisition, and the extent of regional participation in production and fill–finish processes, illustrating the heterogeneity and innovation that characterized the continent's vaccination landscape [129].

At the societal level, although vaccine acceptance in Latin America exceeded the global average, pockets of hesitancy persisted, particularly in rural and Indigenous communities [130]. Targeted science-communication initiatives were implemented to address misinformation and contributed to expanding coverage across these areas. Regional cooperation also played a critical role: through its Revolving Fund, PAHO distributed more than 20 million doses among member states by early 2022, facilitating joint procurement and equitable allocation mechanisms [131]. In parallel, several countries updated their national immunization guidelines to strengthen coverage. For example, Mexico expanded its recommendations to include pediatric populations, prioritizing mRNA and recombinant vaccine platforms for children and adolescents, while emphasizing the need for sustained monitoring of safety signals and long-term immune protection [132].

8. Lessons learned and future perspectives for health system strengthening

The COVID-19 pandemic exposed long-standing structural weaknesses within Latin American health systems, including fragmented governance, uneven resource allocation, and limited technological self-sufficiency. Although the region demonstrated capacity for rapid institutional adaptation during the emergency, many of these vulnerabilities remain insufficiently resolved. Strengthening basic health infrastructure, expanding equitable access to care, and reinforcing social protection systems represent central components of future preparedness. The rapid spread of SARS-CoV-2 in densely populated urban settings underscored the close link between epidemiological risk and socioeconomic inequality. Effective public health strategies therefore depend on sustained integration of prevention, community-based education, and equitable healthcare access within long-term policy frameworks rather than emergency-only interventions. The post-pandemic resurgence of other respiratory pathogens, including influenza and respiratory syncytial virus, further highlighted the need for continuous surveillance and integrated respiratory disease control beyond a single outbreak response.

8.1. Scientific resilience and regional cooperation

The pandemic stimulated unprecedented regional collaboration in molecular surveillance, clinical research, and technological development. Expanded diagnostic capacity, genomic networks, and locally developed vaccine platforms represented measurable advances in regional scientific capability. However, much of this progress relied on emergency mobilization and temporary funding rather than consolidated structural reform.

Coordination among academia, public health institutions, and industry proved feasible under shared emergency objectives; however, manufacturing capacity remained dependent on imported active ingredients, specialized reagents, and advanced equipment, underscoring persistent structural constraints. At the same time, the crisis revealed latent scientific capacity that extended beyond laboratory expansion and clinical trial participation. Early scientific communication by

Table 6
COVID-19 vaccines, acquisition mechanisms, and regional production participation in Latin America [129].

Subregion	Countries	Main Vaccines Used	Platforms	Acquisition Mechanisms	Local Production (API)	Fill-Finish Activities	Coverage (by end of 2022)	Notes / Highlights
Southern Cone	Argentina, Brazil, Chile, Uruguay, Paraguay	AstraZeneca, Pfizer-BioNTech, CoronaVac (Sinovac), Sputnik V	mRNA, viral vector, inactivated	COVAX + bilateral (UK, China, Russia, US)	Argentina: AstraZeneca (mAbxience) Brazil: AstraZeneca (Fiocruz, via technology transfer)	Brazil: AstraZeneca (Fiocruz) Brazil: CoronaVac (Butantan)	80–90%	Early access and robust local manufacturing; Chile and Uruguay among first to reach > 60% by mid-2021
Andean Region	Peru, Colombia, Ecuador, Bolivia, Venezuela	Sinopharm, Pfizer, AstraZeneca, Sputnik V, Janssen	Inactivated, mRNA, viral vector	COVAX + bilateral (China, Russia, US)	None	None (small-scale university research initiatives only)	70–85%	Strong national programs but limited cold-chain capacity; high heterogeneity across altitudinal and rural areas
Central America and Mexico	Mexico, Guatemala, Honduras, El Salvador, Costa Rica, Panama	AstraZeneca, Pfizer, CanSino, Moderna, Sputnik V, Abdala	Viral vector, mRNA, protein subunit	COVAX + bilateral (China, Russia, US, Cuba)	None	Mexico: Liomont (AstraZeneca)	65–80%	Mexico led regional innovation; Central America faced supply delays and inequities in rural distribution
Caribbean	Dominican Republic, Haiti, Trinidad & Tobago, Jamaica, Barbados, Antigua & Barbuda, Bahamas, Granada, Cuba	AstraZeneca, Sinopharm, Pfizer-BioNTech, Janssen, Soberana-02, Abdala, Soberana Plus	Viral vector, inactivated, mRNA, Protein subunit	COVAX + bilateral agreements + donations (mainly via PAHO Revolving Fund); Cuba: fully integrated domestic development and manufacturing (BioCubaFarma)	Cuba: Abdala; Soberana 02; Soberana Plus (BioCubaFarma)	Cuba: Abdala; Soberana 02; Soberana Plus (BioCubaFarma)	55–80%; Cuba (>90%)	Reliance on PAHO distribution; heterogeneity linked to tourism recovery and island logistics; Cuba was the only country in the Caribbean region to design, manufacture, and deploy domestically developed COVID-19 vaccines.

Note: API: Active Pharmaceutical Ingredient.
Adapted from UNESCO–CEPAL [129], "Repercusiones en América Latina y el Caribe de la pandemia de COVID-19 en la educación, la ciencia y la cultura" [129].

professional societies played a critical role during the initial phase of the pandemic. Across Latin America, national and regional organizations rapidly translated emerging evidence into practical guidance for clinicians and the public.

In Mexico, societies such as the Mexican Society of Immunology, the Mexican Society of Virology, the Mexican Society of Respiratory Medicine, and the National Academy of Medicine organized academic forums and issued expert recommendations that contextualized evolving immunological and clinical data [133–135]. Similar efforts were observed in Colombia, Chile, Brazil, and Peru, where infectious disease societies developed consensus documents and clinical management guidelines at a time when international recommendations were still evolving [136–139]. These initiatives complemented governmental public-health messaging, addressed misinformation in traditional and digital media, and facilitated dialogue between researchers, healthcare professionals, and policymakers. Collectively, these experiences suggest that institutional scientific networks functioned as stabilizing actors during uncertainty, reinforcing evidence-informed responses while also revealing the need for sustained structural support beyond emergency mobilization.

Real-time evidence generation was sustained largely by the extraordinary commitment of healthcare and research professionals, many of whom combined clinical duties with scientific activities. While this human capital was central to the response, reliance on individual effort rather than institutionalized research support exposed systemic fragility. Regulatory strengthening, technical training, and laboratory infrastructure investments provide an important foundation for improved responsiveness. Their durability, however, depends on consistent governance, regulatory harmonization, and stable financing across the region.

8.2. *Challenges and opportunities for future preparedness*

Latin America continues to face technological dependence, unequal research capacity, institutional fragmentation, and chronic underinvestment in science and public health—typically far below 1% of regional GDP [140,141]. These factors constrain the consolidation of pandemic-era advances and maintain vulnerability to external supply-chain disruptions.

The transition from emergency mass vaccination to sustained booster strategies has posed challenges worldwide. In the EU/EEA between September 2023 and July 2024, median COVID-19 vaccination coverage reached 14.0% among adults aged $\geq$ 60 years and 21.5% among those aged $\geq$ 80 years, despite the administration of approximately 31 million booster doses, predominantly with the Omicron XBB.1.5–adapted vaccine [142]. These data illustrate the global difficulty of maintaining booster uptake once acute pandemic waves subsided. For Latin America, this context underscores the need to integrate COVID-19 vaccination into long-term immunization strategies targeting high-risk populations rather than relying exclusively on emergency campaign models.

Future preparedness will likely depend on sustained regional coordination, integrated genomic surveillance, strengthened vaccine manufacturing, specialized workforce training, and robust real-time data systems. Without long-term institutional support, collaborative networks built during COVID-19 risk becoming episodic rather than structural. Pandemic-driven research also enabled the creation of large longitudinal cohorts that have produced valuable data on Long COVID and related metabolic, cardiovascular, and immunological outcomes. Preserving these research platforms may be critical for maintaining regional scientific continuity.

Ultimately, translating emergency-driven innovation into durable preparedness will depend on embedding scientific collaboration within stable policy frameworks rather than relying on crisis momentum alone.

9. Conclusions

Latin America confronted COVID-19 under conditions of profound social inequality and institutional heterogeneity. Coordinated efforts mitigated part of the immediate impact, yet the crisis simultaneously exposed persistent structural constraints. Scientific mobilization during the pandemic expanded surveillance networks, clinical research, and vaccine development platforms. These developments represent important progress but remain uneven and incomplete, reflecting ongoing technological dependence and variable investment patterns. A central lesson emerging from the pandemic experience is that effective preparedness appears to depend on sustained public investment, equitable healthcare systems, continuous surveillance, and institutionalized regional cooperation. The region's experience illustrates both adaptive capacity and structural limitation. Whether the gains achieved during the pandemic will translate into durable structural transformation remains an open question in the post-pandemic period.

CRediT authorship contribution statement

Constantino López-Macías: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Funding acquisition, Conceptualization. **Rosana Pelayo:** Writing – review & editing. **Laura Bonifaz:** Writing – review & editing. **Dalia Ramírez-Ramírez:** Writing – review & editing. **Arturo Cérbulo-Vázquez:** Writing – review & editing. **Lourdes Arriaga-Pizano:** Writing – review & editing. **Eduardo Ferat-Osorio:** Writing – review & editing. **Tania Rivera-Hernández:** Writing – review & editing. **Eduardo Bautista-Sebastián:** Writing – review & editing. **Alejandro Torres-Flores:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Data curation, Conceptualization.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.smim.2026.102025.

Data availability

No data was used for the research described in the article.

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