Infect Dis Ther
https://doi.org/10.1007/s40121-022-00748-z

REVIEW

# COVID-19 in Latin America: A Snapshot in Time and the Road Ahead

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Received: September 2, 2022 / Accepted: December 14, 2022


## ABSTRACT

Since its initial detection in Brazil in February 2020, SARS-CoV-2 and the associated COVID-19 pandemic have continued to devastate Latin America. Specific comorbidities, as well as sociodemographic and lifestyle factors that may be more prevalent in underserved areas, have been identified as risk factors for COVID-19 infection or associated adverse outcomes. Dynamics of infections and deaths in Latin America have varied by country and temporally, as has SARS-CoV-2 variant prevalence; however, more recently, the Delta and subsequent Omicron variants have become ubiquitous. Successful pandemic responses have involved robust infection mitigation measures, testing, and smart deployment of healthcare resourcing. While in some Latin American countries up to 90% of the population is fully vaccinated (i.e., 2 doses) against COVID-19, other countries have failed to reach the World Health Organization's 70% target. Continued focus on comprehensive surveillance, strategies to maximize vaccine availability and uptake, and mitigation of collateral damage on other aspects of public health and social services are critical for managing the COVID-19 pandemic. This review summarizes the COVID-19 experience in Latin America, including epidemiology and vaccination. Key learnings and future considerations for the ongoing pandemic response are also discussed.

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Published online: 12 January 2023

**Keywords:** BBIBP-CorV; BNT162b2; ChAdOx1 nCoV-19; COVID-19; Epidemiology; Gam-COVID-Vac; Inactivated vaccine; Latin America; mRNA-1273; SARS-CoV-2; Vaccination

**Key Summary Points**

COVID-19 continues to impact countries in Latin America.

Disease burden and causative variants have varied by country and over time.

Vaccine rollout has been heterogeneous, with low vaccination rates in some regions.

Surveillance and vaccination remain critical.

## INTRODUCTION

For more than 2 years since being declared a global pandemic by the World Health Organization (WHO), COVID-19 has resulted in more than 612 million confirmed cases and > 6.5 million associated deaths worldwide as of September 26, 2020 [1]. Although, initially, COVID-19 predominantly affected adult populations, particularly the elderly, children and adolescents are now accounting for a greater proportion of cases, and this population has also sustained many indirect effects of the pandemic, including school closures and adverse effects on social-emotional development [2–5]. Other indirect effects of the pandemic include disruptions to health services, economic instability, and exacerbating inequalities [6].

The impact of COVID-19 has been particularly pronounced in Latin America and the Caribbean, accounting for 25% of SARS-CoV-2 infections globally [6], although great variability in the effect of the pandemic throughout the region has been observed. This can be attributed, at least in part, to differences in healthcare infrastructure, political leadership, poverty, and inequality, as well as variability in individual responses to the pandemic and access to vaccines.

To understand the successes and challenges in Latin America's response to the evolving COVID-19 pandemic, this review outlines the epidemiology of COVID-19 in the region, as well as initial public health measures and vaccination strategies. A critical appraisal of Latin America's response and transferable lessons and future considerations are provided. The review is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

## EMERGENCE OF COVID-19 IN LATIN AMERICA

The first case of COVID-19 in Latin America was confirmed in São Paulo, Brazil, on February 26, 2020, in an individual who had returned from a trip to northern Italy [7]. The next several cases reported in Brazil were also in travelers from Italy but were characterized by different viral genomic sequences compared with the first case [8]. The first case in Chile was confirmed on March 3, 2020, in an individual who had traveled in Southeast Asia [9]. Many of the first cases of COVID-19 in other Latin American countries were linked to individuals who had recently traveled to or were tourists from Italy or Spain [10]. On March 7, 2020, Argentina became the first country in Latin America to report a COVID-19-related death [11].

## REGIONAL EPIDEMIOLOGY OF COVID-19

### Infection and Case-Fatality Rates

By September 26, 2022, > 149.9 million COVID-19 cases and > 3.2 million associated deaths had been reported in Latin America, with the greatest numbers of cases reported in Brazil (> 34.6 million), Argentina (> 9.7 million), Colombia (> 6.3 million), and Cuba (> 1.1 million) [12]. The overall case fatality rate in Latin

America has ranged from 0.8% in Cuba to 6.2% in Peru among Latin American countries with ≥ 300,000 cumulative cases [13]. Additionally, although children and adolescents comprise a low percentage of COVID-19 cases in Latin America [14] (e.g., 12.5% in Chile through October 2021 [15]), COVID-19-associated hospitalizations and deaths in this population have been reported [14, 16]. Deaths among children and adolescents (aged 0–19 years) ranged from 0% of the total number of COVID-19–associated deaths in Argentina, Chile, Costa Rica, Cuba, and Honduras to 9.1% in Haití [14].

The dynamics of COVID-19–related infections and deaths are continually changing throughout Latin America, and differ by country (Fig. 1) [17, 18]. Variations between countries may be attributed, at least in part, to differences in the extent of COVID-19 testing, political leadership, wealth, and equality, as well as the existence of informal economies and having regions and populations with limited access to health services [19, 20]. In Ecuador, for example, all-cause mortality rose by 64% in 2020, and was markedly higher in indigenous groups, which have been historically underserved by healthcare services [21]. Notably, confirmed COVID-19 deaths in Ecuador accounted for only 21% of excess deaths, highlighting limitations in diagnostic testing [21].

In South America, during 2021, monthly cases increased between January and June and then overall began to decline in July; similarly, deaths peaked in April 2021 and generally declined thereafter [17]; a similar pattern was also observed in other Latin American regions [18]. As in many other regions worldwide, this second wave of COVID-19 infections occurring in 2021 was more severe than the first, causing immense strain on affected public health systems [22–25]. For instance, in Brazil, especially in Manaus, the second wave caused one of the worst public health crises in history [22, 25], and 1 year after the emergence of COVID-19, > 2610 per million excess deaths were recorded in Peru, which was nearly 2 times that of the United States and more than other large countries [26].

COVID-19 cases decreased in Latin America toward the end of 2021 [27]. However, like other global regions [28], Latin America experienced a dramatic increase in weekly COVID-19 cases by the end of 2021 and into 2022, far surpassing previous highs, in connection with the Omicron variant (B.1.1.529) [17, 27, 29]. The doubling time for new cases during December 1, 2021, and January 14, 2022, was as little as 1.7–5.6 days among Latin American countries [17]. In the context of simultaneous influenza outbreaks, increasing hospitalization for chronic disease, trauma, other infectious diseases, or elective procedures, and absenteeism of healthcare workers, the Omicron or potential subsequent waves of COVID-19 have the potential to pose grave challenges to healthcare systems [17].

Multisystem inflammatory syndrome in children (MIS-C) has emerged as an important complication of SARS-CoV-2 infection among low- and middle-income countries, and in particular in Latin America, with associated challenges in clinical diagnosis and treatment [30, 31]. Data from Latin America suggest that patients with MIS-C may experience worse outcomes than in other regions (i.e., higher rates of pediatric ICU admission and mortality including among infants), and high rates of antibiotic use and co-presentation with acute abdomen with or without appendicitis have been described among Latin American children [31–33].

## Circulating Variants

A number of SARS-CoV-2 variants are in circulation, and new variants have been first identified in Latin America, becoming global WHO variants of concern (VoC) or interest (VoI) [29, 34, 35]. As in other regions [36], tracking variants in some Latin American countries was initially challenging because of limited capabilities and resources for genomic surveillance [37]. Two reference laboratories in Chile and Brazil provided the majority of genomic sequencing, with limited capacity in other countries. By way of illustration, Colombia's genomic sequencing capacity in 2020 was the same as that for an average day in London [37]. However, since the creation of the Genomic

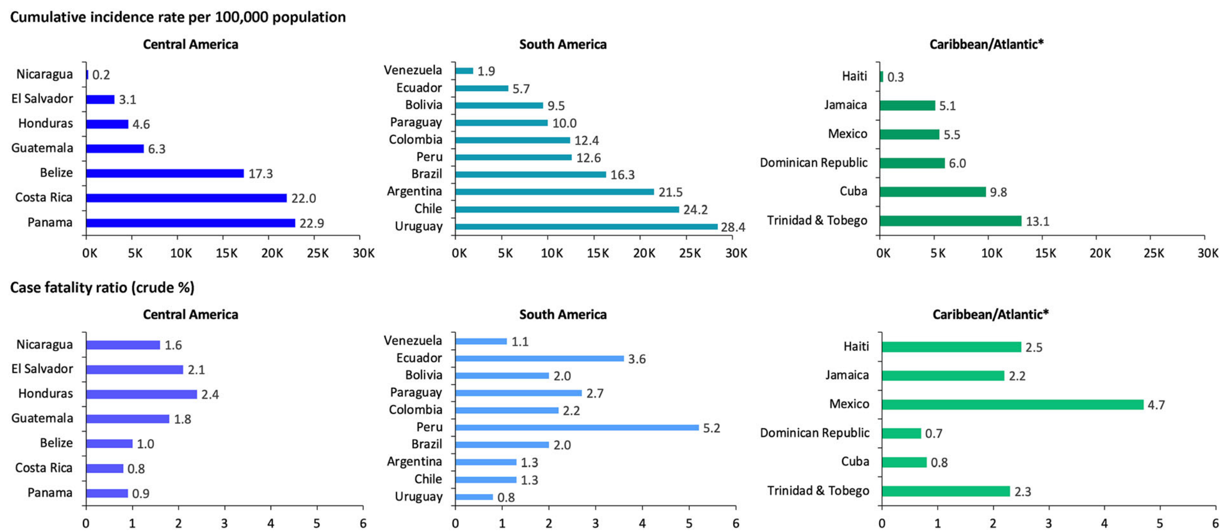


**Fig. 1** Incidence and case fatality ratio in Central America, South America, and the Caribbean/Atlantic [18]. Data are current as of October 5, 2022. [a]Includes Mexico and countries with a population of > 1 million

Surveillance Regional Network by the Pan American Health Organization (PAHO) in 2020, the situation has improved, with a total of 33 laboratories across the region now performing routine in-country or regional genomic sequencing of SARS-CoV-2 [38].

Based on current knowledge, major variants first identified in Latin America include Gamma (P.1; WHO VoC), Lambda (C.37; WHO VoI), and Mu (B.1.621; WHO VoI) [29, 35], all of which harbor mutations in the SARS-CoV-2 spike protein [39]. The Gamma variant was first identified in Brazil in November 2020, then spread to neighboring countries, becoming particularly pronounced in Uruguay and Paraguay (Fig. 2) [29, 35, 40]. In Chile in particular, the Gamma wave occurring during the greater part of 2021 was associated with the highest peak in daily cases through the end of 2021 [28, 29]. The same month that the Gamma variant was identified, the Lambda variant was first detected in Peru and rapidly became the dominant circulating strain; after Gamma, this variant was the second predominant variant during much of 2021 in Chile and Argentina [29, 41]. The Mu variant was first identified in Colombia in January 2021, and quickly became the predominant variant there, but spread to other countries was not particularly pronounced [29, 35, 42, 43]. In Costa Rica, a local PANGOLIN lineage B.1.1.389 comprised nearly one-third of cases by the end of 2020, decreasing to 22% of cases by April 2021, but was only observed in other countries at a frequency of < 1% [44]. By contrast, after its initial identification in India in December 2020, the Delta variant (B.1.617.2; WHO VoC) became globally widespread. In Latin America, the Delta variant was initially largely limited to Mexico, but ultimately accounted for the majority of circulating variants in many other Latin American countries during the second half of 2021 [29, 35, 45]. Similarly, the Omicron variant was identified in multiple countries in November 2021 and, as mentioned, exhibited rapid global spread, including in Latin America [29].

## Risk Factors

Risk factors relevant to Latin America have been identified that independently correlate with a higher likelihood of COVID-19 infection, hospitalization, and/or death. Broadly, a population-based study conducted in Spain found that being born in Latin America was significantly associated with SARS-CoV-2 infection, as well as hospitalization, intensive care unit (ICU) admission, or death associated with COVID-19 [46].

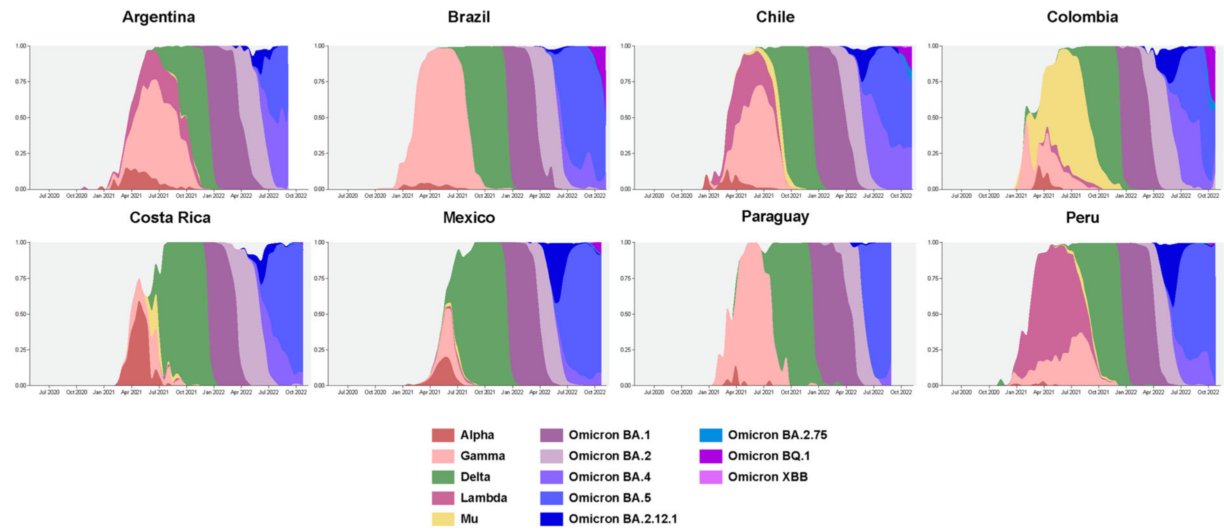


**Fig. 2** Epidemiology of COVID-19 variants in select Latin American countries [29]. Data are current as of October 31, 2022

Studies have identified particular comorbidities that are risk factors for COVID-19 and associated adverse outcomes specifically within the Latin American population. A systematic review and meta-analysis found that individuals in Latin America with specific comorbidities (e.g., diabetes mellitus, cardiovascular disease, obesity, lung disease, chronic kidney disease, liver disease) had higher fatality rates from COVID-19 compared with those from other regions [47]. In a meta-analysis of global data that examined risk factors on a regional level, statistically significant pre-existing conditions that were associated with adverse COVID-19 outcomes in Latin America included diabetes (ICU admission, death), chronic kidney disease (hospitalization), chronic obstructive pulmonary disease (hospitalization, death), respiratory disease (hospitalization), hypertension (ICU admission), obesity (ICU admission, death), immunosuppression (hospitalization, death), and neurologic disease (death) [48]. Additionally, a single-center study in Peru found that the most frequent comorbidities identified among SARS-CoV-2–positive patients during March–August 2020 were hypertension, obesity, and diabetes [49]; these comorbidities were also identified as statistically significant predictors of mortality among the populations of 8 Latin American countries during January–July 2020 [50].

Sociodemographic and lifestyle attributes may also affect dynamics and outcomes of SARS-CoV-2 infection. A study in Santiago, Chile, found that lower socioeconomic status was related to mortality associated with COVID-19, particularly among younger people, with this effect likely related to inadequate testing and incompatibility of poor economic status with adherence to lockdowns; the authors also suggested that increased prevalence of comorbidities and crowding in poorer communities may have influenced their findings [51]. A separate narrative review suggested that, in addition to comorbidities, factors that may contribute to rapid spread and severe outcomes of COVID-19 in Latin America include lack of physical activity, unhealthy diet, air pollution, and frailty [52]. Relatedly, large urban populations, low testing rates, and poor adherence to COVID-19 prevention measures have been identified as drivers of the second wave in Latin America [22, 24].

According to data reported by the United States Census Bureau, the greatest impact of COVID-19 on life expectancy in Latin America was observed in 2020, with the largest declines reported in Peru (loss of almost 8 years), followed by Bolivia and Ecuador (both a loss of > 6 years) [53]. Although the rate of change in life expectancy was slower in most countries after the pandemic's first year, marked decreases due to COVID-19 persisted beyond 2020 in Colombia (loss of ~ 2.5 years) and Honduras (loss of ~ 2 years) [53].

### Seroprevalence

Estimates of population immunity after SARS-CoV-2 infection, derived from sero-surveys, vary widely across Latin America. Surveys of seroprevalence across Latin America during April–November 2020 reported rates ranging from a low of 0.2% to a high of 70.0%, with a pooled seroprevalence of approximately 25–35% [54–57]. Of those infected by SARS-CoV-2, approximately 30% were asymptomatic [55, 58], and these individuals showed lower immunoglobulin (Ig)M/IgG levels and neutralizing antibody activity compared with symptomatic patients [54, 59].

Despite the relatively high seroprevalence rates in the absence of vaccination in Latin America versus other regions, infection of unexposed individuals is still a concern, as is reinfection due to waning immunity and the emergence of new SARS-CoV-2 variants [56]. For example, in Manaus, Brazil, despite an estimated 76% attack rate in October 2020, a sharp increase in infections and hospitalizations was observed in January 2021; while likely attributed, in part, to waning immunity, these increases were also probably potentiated by poor infection control measures [40, 60]. Case reports confirm the possibility of reinfection among individuals in Manaus [61, 62].

## INITIAL PUBLIC HEALTH MEASURES AGAINST COVID-19 IN LATIN AMERICA

With the emergence of COVID-19 cases in Latin America, many governments in the region swiftly responded to control the outbreak and to limit detrimental economic and social effects [63]. For instance, several countries mandated use of masks in public spaces, including public transport, schools, churches, and stores. Several countries also ordered lockdowns, recommended telework, and closed educational institutions [64].

The countries in Latin America had variable initial success regarding the lockdown measures. For instance, Argentina had high adherence to instituted lockdown measures, which was attributed, at least in part, to close coordination between the different levels of government and providing public outreach regarding these measures [64]. In contrast, apart from initial responses early in the pandemic (e.g., creation of a Public Health Emergency Operations Center), control measures in Brazil were generally implemented at the municipal and state level, which is suggested to have contributed to the increased number of cases recorded in Brazil in the first year of the pandemic.

Several approaches to manage strains on the healthcare sector in Latin America were also implemented in the initial response to the pandemic. These included increasing hospital and ICU capacity, construction of temporary field hospitals, implementation of telemedicine services, deployment of medical brigades to provide basic treatment, and sourcing of medical supplies, such as personal protective equipment and ventilators [63, 64]. Innovative strategies to bolster healthcare capacity were also used, including rollout of the "Brazil Counts on Me" initiative, which enlisted nearly 1 million healthcare providers to help in the pandemic through an advanced timeline of graduation [63, 65].

Many Latin American countries also focused on case identification and testing [63]. For instance, Argentina approved a polymerase chain reaction (PCR) COVID-19 test kit in October 2020, and, in June 2021, a rapid testing kit was approved by the national drug regulatory agency with 100,000 kits to be produced monthly [63]. In response to identified challenges within the existing Chilean testing system, government funding was provided to universities to combat limitations in COVID-19 diagnostic capacity [66], and the country expanded laboratory screening capacity to include all national institutions with PCR equipment, and supplied reagents throughout the laboratory network, which led to Chile having one of the highest testing rates in the region [64]. In Costa Rica, which has a well-established primary healthcare system and provides universal healthcare to all citizens, all COVID-19 diagnostic tests were made free for all residents [63, 64]. Another critical component identified early in the pandemic as part of the public health response was having a strong epidemiologic and health surveillance system [64]. PAHO has worked with governments in the region to provide technical expertise and to expand surveillance capabilities [67].

## VACCINATION AGAINST COVID-19 IN LATIN AMERICA

Beginning late in 2020, clinical data on the efficacy and safety of COVID-19 vaccines emerged, with publication of data from the phase 2/3 study of the mRNA BNT162b2 vaccine (Pfizer; New York, NY, USA, and BioNTech, Mainz, Germany) in individuals from 16 years of age [68]. Emergency use authorizations in several countries soon followed, with Mexico being one of the first countries in the world and the first in Latin America to grant authorization to BNT162b2 (occurring before December 14, 2020) [69]. This successful early authorization is attributed, at least in part, to focused regulatory efforts by the Mexican government.

Although authorizations for COVID-19 vaccines began in the first year of the pandemic, procurement and delivery of limited vaccine supplies became a global challenge, particularly for low- and middle-income countries. Latin American countries have been able to obtain vaccines through participation in the COVAX Facility, bilateral negotiations with pharmaceutical companies, donations from other countries, and additional support from the PAHO Revolving Fund [70, 71], with varied success as described in the following sections.

### Available Vaccines and Vaccination Rates

A variety of COVID-19 vaccine types have been procured and administered throughout Latin America [72]. Types include mRNA vaccines such as BNT162b2 and mRNA-1273 (Moderna, Cambridge, MA, USA), inactivated virus vaccines such as the ones manufactured by Sinovac Biotech (Beijing, China) and BBIBP-CorV (Sinopharm, Beijing, China), viral vector vaccines such as ChAdOx1 nCoV-19 (AZD1222; AstraZeneca, Cambridge, UK), Ad26.COV2.S (Janssen; Beerse, Belgium), and Gam-COVID-Vac (Gamaleya Research Institute of Epidemiology and Microbiology, Moscow, Russia), and protein subunit vaccines such as FINLAY-FR-2 (Instituto Finlay, Havana, Cuba) and CIGB-66 (Center for Genetic Engineering and Biotechnology, Havana, Cuba) [72, 73].

Vaccination priority tiers in the early stages of the pandemic varied by country, with most prioritizing healthcare workers, but prioritization of the elderly was more heterogeneous [70]. In Brazil, intermediate priority was given to vaccination of pregnant women [70], despite the exclusion of this population from initial phase 3 pivotal studies of contracted vaccines [68, 74–79].

Despite a slow initial rollout in most Latin American countries, vaccination rates notably increased in mid-2021 [70, 72]. As of September 2022, vaccination rates, as well as the specific vaccines administered, vary by country within Latin America (Fig. 3; Table 1) [72]. The majority of countries have vaccination rates (rates of receiving $\geq 1$ dose of a COVID-19 vaccine) below the global average of 68%. Among the larger Latin American countries, those with vaccination rates below the global average include the Dominican Republic (66.5%), Honduras (62.9%), Paraguay (54.9%), Bolivia (54.0%), and Guatemala (48.1%) (Fig. 3) [28, 72]. Additionally, a number of countries have not yet met the WHO goal of 70% vaccination in each country [72, 80].

A number of Latin American countries are now vaccinating children < 12 years of age, with some vaccinating children as young as 2 (e.g., Cuba, Nicaragua, Venezuela) or 3 (e.g., Argentina, Chile, Colombia) years of age [81]. In Brazil and Peru, the BNT162b2 vaccine was also approved for children 5–11 years of age beginning in December 2021 [81, 82]. Several other Latin American countries are also vaccinating

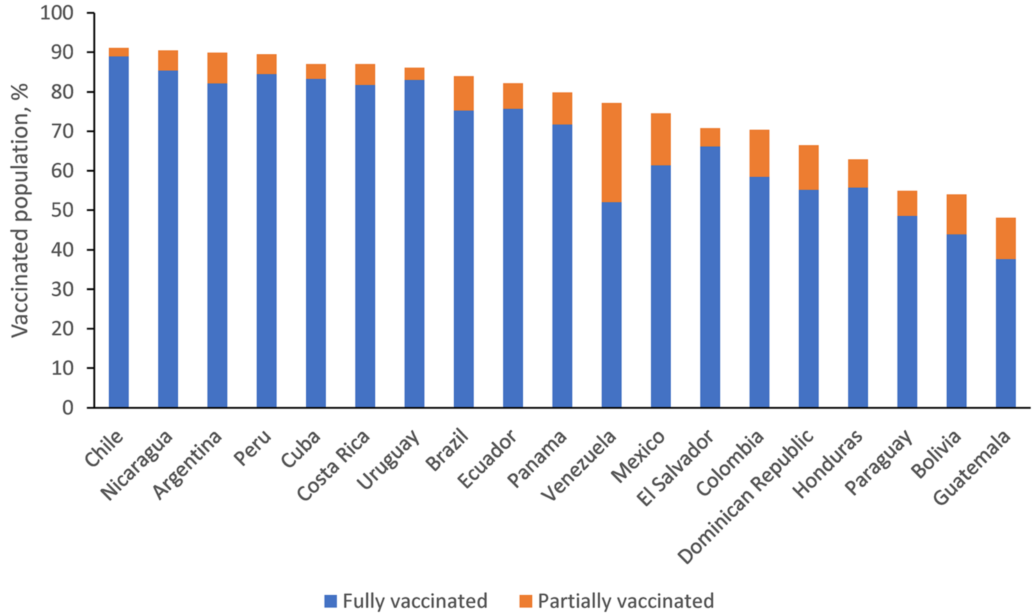


**Fig. 3** COVID-19 vaccination rates in select Latin American countries [72]. Data are current as of September 23, 2022, and are the percentages of the total population in each individual country who are either fully or partially vaccinated

**Table 1** Administered COVID-19 vaccines by country in Latin America [72]

| Country | Doses administered by vaccine (manufacturer), %[a,b] | | | | | | |
|---|---|---|---|---|---|---|---|
| | BNT162b2 (Pfizer-BioNTech) | mRNA-1273 (Moderna) | ChAdOx1 nCoV-19 (AstraZeneca) | Gam-COVID-Vac (Gamaleya) | BBIBP-CorV (Sinopharm) | Inactivated vaccine (Sinovac Biotech) | Other[c] |
| Argentina | 17 | 12 | 24 | 19 | 26 | | 2 |
| Brazil | 41 | | 31[d] | | | 23 | 6 |
| Chile | 44 | 9 | 5 | | | 42 | < 1 |
| Ecuador | 29 | | 19 | | | 50 | 2 |
| Guatemala | 21 | 41 | 23[d] | 15 | | | |
| Honduras | 59 | 23 | 17 | | | | < 1 |
| Paraguay | 52 | 6 | 23 | 10 | 3[e] | 4 | 2 |
| Uruguay | 62 | | 1 | | | 37 | |
| Venezuela | | | | 23 | 62 | 6 | 8 |

Data are current as of September 30, 2022
[a]Countries for which all data are available are included
[b]Rounding may lead total percentages to be less or more than 100
[c]Includes Ad5-nCOV (CanSino Biologics), ChAdOx1 nCoV-19 (SII), Ad26.COV 2.5 (Janssen), BBV152 (Bharat Biotech International), Gam-COVID-Vac ("Sputnik Light"; Gamaleya), Abdala (BioCubaFarma), and Soberana-02 (Finlay)
[d]Listed as "Nonspecified AZ"
[e]Listed as "Nonspecified Sinopharm"

children from 5 years of age with the BNT162b2, BBIBP-CorV, or Sinovac vaccines (e.g., Bolivia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Uruguay) [83–85].

In addition to primary vaccination courses, booster doses have been administered in most Latin American countries, with booster vaccination rates ranging from 0% in Nicaragua to 81.4% in Chile, as of September 2022 [72, 74]. Booster doses are sometimes being administered using a mixed schedule (e.g., Brazil, Chile, Colombia, Cuba, Uruguay), wherein the specific booster vaccine differs from that used for primary vaccination [86–90]; this strategy is also being used in Argentina for the 2 primary vaccine doses [91].

## Vaccine Clinical Trials and Observational Vaccine Effectiveness Studies

Numerous studies of COVID-19 vaccines have been conducted in Latin American countries (Table 2) [92], contributing to the body of knowledge regarding vaccine immunogenicity, safety, efficacy, and effectiveness.

The pivotal BNT162b2 phase 2/3 study of BNT162b2 in ≥ 16-year-olds included sites in Argentina ($n = 1$; 5764 participants) and Brazil ($n = 2$; 2284 participants) [68]. Vaccine efficacy, as measured 7 days after the second dose, was similar between the overall population (95.0%) and participants from Argentina (97.2%) and Brazil (87.7%). An updated analysis at approximately 6 months of follow-up, which included participants who were 12 years and older, reported vaccine efficacy of 91.3% in the overall population, and of 86.5% and 86.2% in participants from Argentina and Brazil, respectively [93]. Recently, efficacy results from a phase 3 trial assessing a third dose of BNT162b2 in participants who had received the 2-dose primary series in the pivotal trial, including 1164 participants from Brazil, have been reported [94]. At a median follow-up of 2.5 months, relative vaccine efficacy of the third dose in participants without evidence of previous SARS-CoV-2 infection was 95.3% in the overall population and 100% in participants from Brazil.

Efficacy/effectiveness studies focused on Latin American countries also include a pooled interim analysis of 4 randomized studies of the ChAdOx1 nCoV-19 viral vector vaccine, 1 of which was conducted in Brazil [95]. Findings indicated that the vaccine had an overall efficacy rate for prevention of SARS-CoV-2 infection of 70.4%, with 64.2% efficacy in Brazil (with 2 standard doses) [95]. In a large randomized phase 3 study in Cuba, 2 doses of the protein subunit vaccine FINLAY-FR-2 were associated with efficacy estimates of 71.0% against symptomatic SARS-CoV-2 infection, 63.0% against severe COVID-19, and 59.0% against COVID-19–associated death [88]. Administration of a booster dose of FINLAY-FR-1A, which is a different formulation from FINLAY-FR-2, was associated with respective efficacy estimates of 92.4%, 100%, and 100% [88].

In addition to randomized studies, a prospective observational study evaluating the effectiveness of the Sinovac inactivated virus vaccine in a national cohort of ≥ 16-year-olds in Chile found that the estimated adjusted vaccine effectiveness in individuals who received 2 doses was 65.9% for prevention of symptomatic COVID-19, 87.5% for prevention of hospitalization, 90.3% for prevention of ICU admission, and 86.3% for prevention of COVID-19–related death [96]. In a matched test-negative case–control study evaluating the effectiveness of the same vaccine in ≥ 70-year-olds during an epidemic of the SARS-CoV-2 Gamma variant in São Paulo, Brazil, the effectiveness in individuals who received 2 doses was 47% for prevention of symptomatic COVID-19, 56% for prevention of COVID-19–associated hospital admissions, and 61% for prevention of COVID-19–associated deaths [97]. In Colombia, observational data during March–August 2021 from a cohort of ≥ 60-year-olds who received the Ad26.COV2.S, BNT162b2, ChAdOx1 nCoV-19, or Sinovac vaccines, estimated vaccine effectiveness of 69.9% against hospitalization without death, 79.4% against death following hospitalization, and 74.5% against death without hospitalization [98]. Analyses by individual vaccine found that BNT162b2 was the most effective against all 3 outcomes, with respective effectiveness estimates of 90.3%, 98.5%, and

Table 2 COVID-19 vaccine clinical trials conducted in Latin American Countries [92]

| Country | Type of vaccine | Trials, n | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Phase 1 | Phase 1/2 | Phase 2 | Phase 2/3 | Phase 3 | Phase 4 | N/A |
| Argentina | Inactivated virus | | | | | 1 | | |
| | Nonreplicating viral vector | | | 7 | | 3 | | |
| | mRNA | | | | 2 | | | |
| | Virus-like particle | | | | 1 | | | |
| Brazil | Inactivated virus | 1 | | | | 2 | 6 | |
| | Nonreplicating viral vector | | 1 | 2 | 2 | 5 | 3 | 1 |
| | Protein subunit | | | 1 | 3 | | 1 | |
| | mRNA | 1 | 1 | 2 | 4 | 4 | | |
| | mRNA + nonreplicating viral vector | | | | | | 1 | |
| | Virus-like particle | | | | 1 | | | |
| | DNA | | | | | 1 | | |
| Chile | Inactivated virus | | | 1 | | 2 | | |
| | Nonreplicating viral vector | | | | | 5 | | |
| Colombia | Inactivated virus | | | | | 2 | | |
| | Nonreplicating viral vector | | | | | 3 | 1 | |
| | Replicating viral vector | | | | | 1 | | |
| | Protein subunit | | | | 4 | 1 | | |
| | mRNA | | | | 1 | | | |
| | mRNA + nonreplicating viral vector | | | | | | 1 | |
| | DNA | | | | 1 | 1 | | |
| Cuba | Protein subunit | 3 | 7 | 5 | | 2 | | 2 |
| Dominican Republic | Protein subunit | | | | 2 | | | |
| | mRNA | | | | 1 | | | |
| Ecuador | Protein subunit | | | | | 1 | | |
| Guatemala | Protein subunit | | | | 2 | | | |
| Honduras | Protein subunit | | | | 1 | 1 | | |
| | mRNA | | 1 | | | | | |

**Table 2** continued

| Country | Type of vaccine | Trials, *n* | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **Phase 1** | **Phase 1/2** | **Phase 2** | **Phase 2/3** | **Phase 3** | **Phase 4** | **N/A** |
| Mexico | Nonreplicating viral vector | | | 1 | | 2 | | |
| | Protein subunit | | | 1 | 1 | 3 | | |
| | Replicating viral vector | 1 | | 1 | | | | |
| | mRNA | | | 1 | 2 | 1 | | |
| | Virus-like particle | | | | 1 | | | |
| | DNA | | | | 1 | 1 | | |
| Panama | Protein subunit | | | | 3 | | | |
| | mRNA | | | 2 | 1 | 1 | | |
| Paraguay | Nonreplicating viral vector | | | | | 2 | | |
| Peru | Inactivated virus | | | | | 2 | | |
| | Nonreplicating viral vector | | | | | 3 | | |
| | mRNA | | | 2 | 1 | | 1 | |
| Latin America total[a] | Inactivated virus | 1 | | 1 | | 9 | 6 | |
| | Nonreplicating viral vector | | 1 | 10 | 2 | 23 | 4 | 1 |
| | Protein subunit | 3 | 7 | 7 | 16 | 8 | 1 | 2 |
| | Replicating viral vector | 1 | | 1 | | 1 | | |
| | mRNA | 1 | 2 | 7 | 12 | 6 | 1 | |
| | mRNA + nonreplicating viral vector | | | | | | 2 | |
| | Virus-like particle | | | | 3 | | | |
| | DNA | | | | 2 | 3 | | |
| | **All types** | **6** | **10** | **26** | **35** | **50** | **14** | **3** |

Data are current as of September 29, 2022

[a]Many trials were conducted in multiple Latin American countries

89.2% [98]. Additional data from the entire Colombian population ≥ 30 years of age during November 2021–January 2022 identified hospitalization rate ratios comparing unvaccinated with vaccinated (vaccine not specified) individuals of 2.3–5.0 depending on age group; rate ratios for mortality were 4.2–9.9 [99].

Two studies have evaluated the effectiveness of the Sinovac vaccine specifically among healthcare workers in Brazil. In a cross-sectional study of healthcare workers at a university hospital in southern Brazil who were vaccinated with either the Sinovac vaccine or ChAdOx1 nCoV-19, a 62% reduction in new COVID-19 cases was observed 7 weeks after vaccine rollout [100]. Additionally, a matched test-negative case–control study conducted in Manaus, Brazil, during a period of high SARS-CoV-2 Gamma-variant transmission, estimated vaccine effectiveness at 49.4% starting 14 days after the first dose and 37.1% after 2 doses [101].

Preliminary data regarding effectiveness of a COVID-19 vaccine booster dose was released by the Chilean Ministry of Health in October 2021 [86]. Among nearly 5 million ≥ 16-year-olds who received the Sinovac vaccine for primary vaccination and boosting with the Sinovac vaccine, the BNT162b2, and ChAdOx1 nCoV-19 vaccines increased effectiveness against COVID-19 infection or COVID-19–related hospitalization from 56–80%, 90%, and 93%, respectively [86].

Additional studies performed outside the Latin America region have evaluated the in vitro neutralizing activity of vaccine-elicited serum antibodies against multiple SARS-CoV-2 variants. A synopsis of in vitro efficacy data reported that many approved vaccines were associated with up to a 3- to 5-fold reduction in neutralizing activity against the SARS-CoV-2 Gamma variant [102]. Additionally, 1 study showed that serum samples taken from individuals who had received 2-dose vaccination with BNT162b2 efficiently neutralized 5 different SARS-CoV-2 strains with variant spike proteins, including the Gamma variant, at titers > 1:40 [103]. More recently, preliminary data from Pfizer/BioNTech indicated that sera from individuals who received 2 doses of BNT162b2 had substantially reduced neutralizing activity against the Omicron variant compared with the wild-type strain; however, a third dose restored neutralizing activity to levels similar to those following 2 doses for the wild-type strain [104].

## LESSONS LEARNED AND FUTURE CONSIDERATIONS

### Evaluation of Overall Public Health Response

Latin American countries have varied from one another and over time with respect to public health responses to the COVID-19 pandemic. A composite "stringency index" reflecting 9 response indicators, including school closures, workplace closures, and travel bans, provides 1 measure of this heterogeneity. For example, Argentina was characterized by an initially stringency index (100 on a scale of 1–100) that only decreased below 70 in October 2021; by contrast, the stringency index in Mexico at the pandemic's outset was < 85 and fell to < 50 by March 2021 [28].

COVID-19 testing has also varied per country. Daily COVID-19 testing in Chile reached 1 per 1000 individuals by June 2020, and generally rose thereafter to between 2 and 4 per 1000 through late 2021, with a corresponding positivity rate that largely remained below 10% during July 2020–December 2021 [28]. By contrast, the daily testing rate in Ecuador largely remained below 0.25 per 1000 through early 2022, with positivity rates generally remaining between 20 and 40% from late 2020 through late 2021 [28].

Strong leadership with regard to infection mitigation measures, robust testing and healthcare resourcing, and financial assistance have been lauded as critical attributes of a successful pandemic response [19, 20]. Providing adequate healthcare resourcing may require bolstering existing infrastructure, as was done in several Latin American countries [20, 63, 64, 105].

### Surveillance

Some Latin American countries continue to work to develop robust surveillance infrastructures for monitoring SARS-CoV-2 VoCs as a tool to bolster the pandemic response. Uruguay has developed a PCR-based genomic surveillance program for real-time monitoring of SARS-CoV-2 VoCs [106]. In Argentina, a small percentage of SARS-CoV-2 samples derived during October 2020–October 2021 from diverse regions was subjected to molecular surveillance as a cost-effective method of characterizing variant evolution in the country overall during this period [107]. The Chilean Ministry of Health periodically publishes reports concerning circulating variants [108].

Other surveillance systems are focused on SARS-CoV-2 infection and outcomes. Chile is performing surveillance through SARS-CoV-2 IgG detection among vaccinated and unvaccinated individuals within its most populated cities to trace IgG seropositivity over time, and is making the data publicly available [109]. Chile's Ministry of Health is also making a COVID-19 database publicly available that reports COVID-19 tests performed, cases, hospitalizations, deaths, vaccinations, and other factors [110]. Daily reports published by the Brazilian Ministry of Health reporting similar measures are also publicly available [111]. In Bogóta, Colombia, the CoVIDA project combined PCR tests in mostly asymptomatic individuals during June 2020–March 2021 with the number of detected cases to estimate the true number of cases in the region [112].

Contact tracing may also play an important role in mitigating adverse outcomes of COVID-19. A retrospective cohort study utilizing nationwide data from Colombia found that tracing $\geq$ 5 contacts per COVID-19 case could reduce the risk of death within the chain by 48%; unfortunately, each case had a median of only 1 contact at the time of analysis, underscoring the gaps in tracing [113]. A similar study in Colombia using modeling predicted that an increase of 10% in the proportion of cases identified through contact tracing could lead to mortality reductions of 0.8–3.4% [114].

Overall, a need remains for consolidating regional COVID-19 data in Latin America in a way that is both comprehensive and easily understood.

## Vaccination

Effective vaccination strategies against COVID-19 require coordinated efforts focused on development and production, affordability, deployment, and allocation of vaccines [115]. However, vaccine rollout and uptake in Latin America vary considerably by country (Fig. 3) [72]. Logistical challenges have also slowed vaccine delivery (e.g., due to supply problems) or the ability to use certain vaccines (e.g., ultra-cold chain requirements for certain mRNA vaccines) [70, 116]. In cases of limited supplies, health authorities suggest prioritizing populations for vaccination based on epidemiologic risk and equity criteria [e.g., age, race, underlying conditions, occupation, socioeconomics, LGBTQ (lesbian, gay, bisexual, transgender, and queer) status] [70].

An important strategy to alleviate COVID-19 vaccine shortages in Latin America is local vaccine manufacturing. Latin America has a rich tradition of vaccine development and manufacturing, beginning with the smallpox vaccine in the twentieth century and continuing to a wide array of modern vaccines, with current manufacturing particularly concentrated in Brazil and Cuba [117, 118]. In addition to 2 protein subunit COVID-19 vaccines developed to date in Cuba [73], several Latin American countries have announced partnerships with foreign pharmaceutical companies to locally manufacture COVID-19 vaccines [119–121]. These include production of the Russian Gam-COVID-Vac viral vector vaccine by the Mexican pharmaceutical company Laboratorios de Biológicos y Reactivos de México, production of the AstraZeneca ChAdOx1 nCoV-19 viral vector vaccine by the Bio-Manguinhos Institute at Fiocruz in Brazil, and production of the Pfizer/BioNTech BNT162b2 mRNA vaccine by Eurofarma Laboratórios SA in Brazil [119–121]. Additionally, in September 2021, PAHO selected Bio-Manguinhos/Fiocruz and Sinergium Biotech as centers in Brazil and Argentina, respectively, for local development and production of mRNA vaccines [122]. In January 2022, the Colombian Minister of Health announced a commitment to consolidate capacity for vaccine production among the PROSUR (Argentina, Brazil, Chile, Columbia, Costa Rica, Ecuador, Paraguay, Peru, and Uruguay) countries [123]. Investments in additional capacity for vaccine production could save numerous lives, while minimizing short- and long-term economic harm, with a recent analysis estimating that capacity for production of 3 billion annual vaccine courses would result in a global benefit of US$17.4 trillion [124].

In addition to maintaining focus on reducing logistical challenges (e.g., refrigeration or room-temperature storage vs. ultra-cold storage), as well as affordability and accessibility, production of new COVID-19 vaccines should be subject to approval by stringent regulatory authorities or the WHO to promote increased vaccine confidence [115]. Indeed, vaccine hesitancy, particularly among individuals with low health literacy, remains a challenge in Latin America [125]. As such, national and regional health authorities must increase their efforts to bolster trust in health information sources and to educate the public regarding COVID-19 vaccination [125]. These efforts may have far-reaching effects beyond the pandemic, as demonstration of the real-world impact of vaccines may help further educate and motivate the population regarding the broader importance of vaccines.

The design of clinical trials should continue to support access to safe and effective vaccines. To minimize barriers to vaccination caused by delays in regulatory approvals, regulatory bodies could consider immunobridging studies in lieu of traditional placebo-controlled disease endpoint trials for authorizing new COVID-19 vaccines [126]. In addition, ongoing evaluation of currently approved vaccines, such as real-world effectiveness studies [127], should continue.

Moving forward, effective vaccination strategies should include use of COVID-19 vaccine boosters and potential coadministration with other vaccines, such as influenza, when possible; in addition to convenience, vaccine coadministration is an established strategy for increasing uptake [128, 129].

## Effects on Public Health and Social Services

The COVID-19 pandemic has also inflicted considerable collateral damage on aspects of public health and social services not directly related to SARS-CoV-2. For example, although the onset of the COVID-19 pandemic was associated with reduced incidence of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* infections in many countries worldwide [130], this was accompanied by a substantial increase in the number of children, particularly in poor and developing countries, who did not receive routine childhood vaccines [131]. A series of surveys conducted by PAHO in Latin American countries echoed these findings [132]. Another study conducted in Colombia using health records identified differences in vaccine coverage between 2019 and 2020 of $\geq 13.1\%$ for each individual vaccine, with rural residence significantly associated with increased differences in children $< 12$ months and 5 years of age [133]. As such, strategies to maximize vaccination rates should focus on all recommended vaccines, not just those targeting SARS-CoV-2. The importance of prioritizing routine vaccinations against vaccine-preventable diseases was emphasized in a Latin American forum of experts on infectious diseases held in September 2020 [134].

Similar to observed decreases in routine vaccination, consultations and treatments for cancer plummeted in Latin America with the onset of the pandemic, likely leading to increases in cancer-related mortality and overwhelming demand for these services in the post-pandemic period [135]. In addition to health-related effects, the United Nations Children's Fund (UNICEF) has noted that Latin America and the Caribbean have had long uninterrupted school closures in connection with the COVID-19 pandemic, and has stressed the critical importance of children's return to in-person learning [3].

## Support from Global Organizations

Supranational organizations such as PAHO have played a critical role in supporting Latin American countries in controlling SARS-CoV-2 transmission. PAHO has built a regional genomic surveillance network to aid sequencing efforts aimed at monitoring the emergence and spread of SARS-CoV-2 variants [136]. As mentioned, PAHO also launched a collaborative platform for manufacturing of COVID-19 mRNA vaccines in Latin America [122], and, through use of its Revolving Fund, is helping to procure vaccines for the region above the 20% offered through COVAX [71]. Beyond PAHO, the World Bank has pledged to contribute US$160 billion globally, much of which will benefit Latin American governments, to address COVID-19–related impacts [137]. UNICEF is also requesting US$29.1 million to address COVID-19–related humanitarian needs and to support overall emergency preparedness and response across Latin America [138].

## CONCLUSIONS

The COVID-19 pandemic has posed a great challenge to public health within Latin America. Recovery from the pandemic in this respect will likely take time, and long-term effects and collateral damage secondary to COVID-19 may not yet be well defined.

Vaccination against SARS-CoV-2 has faced great challenges in terms of research and development, in turn leading to initiatives within the Latin America region to promote local vaccine production aided by partnerships with foreign pharmaceutical companies. The approach to COVID-19 vaccination programs has required continued adaptation, necessitating implementation of exceptional regulatory, budgetary, logistic, and social measures. The Latin America region has been recognized for its leadership in COVID-19 vaccination, with many countries also implementing pediatric vaccination programs. Vaccination against COVID-19 is a consistent pillar among varying pandemic responses across Latin American countries that, together with surveillance and other public health interventions, is critical to overcome the pandemic and to optimize preparedness for future public health challenges.

## ACKNOWLEDGEMENTS

***Funding.*** This work was supported by Pfizer Inc. Pfizer was involved in all aspects of the work, including the conception of the report, analysis and interpretation of relevant data, writing the report, and deciding to submit the report for publication. Publication of the work, including the journal's Rapid Service fee, were funded by Pfizer Inc.

***Medical Writing and Editorial Assistance.*** Editorial and medical writing support was provided by Allison Gillies, PhD, Judith Kandel, PhD, and Kara Nyberg, PhD (ICON; Blue Bell, PA) and was funded by Pfizer Inc.

***Author Contributions.*** Jorge LaRotta, Omar Escobar, María L. Ávila-Aguero, Juan Pablo Torres, Rodrigo Sini de Almeida, Graciela del Carmen Morales, and Amit Srivastava all drafted and/or critically revised the manuscript.

***Disclosures.*** Jorge LaRotta, Omar Escobar, Rodrigo Sini de Almeida, and Graciela del Carmen Morales are employees of Pfizer Inc and may hold stock or stock options. Amit Srivastava was an employee of Pfizer Inc at the time of the study and is now employed by Orbital Therapeutics. Juan Pablo Torres and María L. Ávila-Aguero have no conflicts of interests to declare.

***Compliance with Ethics Guidelines.*** This review article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

***Data Availability.*** Data are available from the cited references.

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