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Review

Differential Diagnosis in the Management of Acute Respiratory Infections through Point-of-Care Rapid Testing in a Post-Pandemic Scenario in Latin America: Special Focus on COVID-19, Influenza, and Respiratory Syncytial Virus

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Abstract: This review provides a comprehensive summary of evidence to explore the role and value of differential diagnosis in the management of Acute Respiratory Infections (ARIs) through point-of-care (POC) rapid testing in a post-pandemic scenario, paying particular attention to coronavirus disease 2019 (COVID-19), influenza, and respiratory syncytial virus (RSV). The document builds on a review of literature and policies and a process of validation and feedback by a group of seven experts from Latin America (LATAM). Evidence was collected to understand scientific and policy perspectives on the differential diagnosis of ARIs and POC rapid testing, with a focus on seven countries: Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico, and Peru. The evidence indicates that POC rapid testing can serve to improve ARI case management, epidemiological surveillance, research and innovation, and evidence-based decision-making. With multiple types of rapid tests available for POC, decisions regarding which tests to use require the consideration of the testing purpose, available resources, and test characteristics regarding accuracy, accessibility, affordability, and results turnaround time. Based on the understanding of the current situation, this document provides a set of recommendations for the implementation of POC rapid testing in LATAM, supporting decision-making and guiding efforts by a broad range of stakeholders.

Keywords: acute respiratory infections; point-of-care testing; rapid testing; diagnostic testing; COVID-19; influenza; respiratory syncytial virus; health policies; Latin America

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1. Scope and Methodology

This document seeks to explore and position the role and value of differential diagnosis in the management of Acute Respiratory Infections (ARIs) through point-of-care (POC) rapid testing in a coronavirus disease 2019 (COVID-19) post-pandemic scenario, paying particular attention to COVID-19, influenza, and respiratory syncytial virus (RSV). The document provides an overview of the types of tests available for POC testing, the value of differential diagnosis for the management of ARIs, the policies and current recommendations by international organizations for ARI testing, and the challenges and barriers to implementing POC rapid testing. Based on the available evidence, the document provides a set of actionable solutions (recommendations) to the challenges and barriers identified. By illustrating a path forward, the recommendations can support decision-making and guide efforts by a broad range of stakeholders, including governments, the academic community, and international organizations.

The methodology employed to build this document derives from a review of literature and policies, followed by a process of validation and feedback with a group of seven experts on relevant fields. Experts were selected based on their academic merit and experience. Their disciplinary backgrounds include infectious diseases, public health, diagnostics, and microbiology. An in-depth understanding of diagnostics, the ARI policy landscape, and the COVID-19 pandemic were deemed essential.

Global, regional, and country-level evidence from seven focus countries—Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico, and Peru—was collated and analyzed between 13 March and 5 July 2023. Data and evidence came from diverse sources, prioritizing peer-reviewed pieces, and official governmental and international organizations' sources. Sources were selected and prioritized to capture the following dimensions:

- Multidimensional impact of ARIs in the region and focus countries.
- Opportunities and challenges for the management of ARIs in a COVID-19 post-pandemic scenario.
- Scientific perspectives and positions on the role and value of testing, POC rapid testing, and differential diagnosis for the management of ARIs.
- The current international guidelines and recommendations regarding testing for ARIs, including POC rapid testing regionally and in focus countries.
- Key policies, frameworks, and recommendations for the management of ARIs regionally and in focus countries.

The information was synthesized in a working document which was then discussed, reviewed, and validated by all experts during three online panel sessions (2, 6, and 21 June 2023) and rounds of offline review. All participating experts approved the final document.

2. Background and Introduction

On 31 December 2019, Chinese authorities reported a novel coronavirus causing a cluster of pneumonia-like cases. The virus was later identified as the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and the disease caused by this new virus is COVID-19. By March 2020, only three months later, the World Health Organization (WHO) characterized the COVID-19 outbreak as a pandemic [1]. In July and October 2020, the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) approved the first COVID-19 treatment (remdesivir) [2,3]. With the objective of putting a halt to the pandemic, LATAM countries began vaccination during December 2020 and January 2021 [1]. Finally, in May 2023, the WHO declared an end to COVID-19 as a global health emergency [4].

The timeline of the measures taken and the key events that characterized the influenza pandemic ten years earlier are similar, especially regarding the accelerated development and introduction of treatment and immunization technologies (Figure 1). The first human infection of the latest registered pandemic of influenza A (H1N1) virus was recorded in California on 15 April 2009. Only a few days later, on 27 April, the FDA issued the emergency authorization of two neuraminidase inhibitors (zanamivir and oseltamivir

phosphate) for the treatment and prophylaxis of influenza [5]. By June 2009, the WHO characterized the influenza outbreak as a pandemic [6,7]. In July of the same year, clinical trials to develop a vaccine began, and by September, both the FDA and EMA announced the approval of four vaccines [6–8]. Since then, and as of today, annual vaccination is recommended for high-risk groups [6,7]. As the number of cases decreased, the WHO declared an end to the pandemic on 10 July 2010 [6,7].

Likewise, the development and introduction of tests for COVID-19 and influenza happened within the first month of the first recorded case [6,9]. As cases increased and demand rose, health systems had to quickly adapt to ensure the availability of tests and laboratory capacity to process samples [10,11]. The influenza and COVID-19 pandemics led to changes in the diagnostic algorithms, prioritizing the novel virus. After the influenza pandemic, the diagnostic algorithm remained without significant changes from 2009 to 2020, when testing priorities rapidly shifted due to the arrival of COVID-19 [12–14]. While SARS-CoV-2 continues to be predominant, testing for this pathogen will continue to be prioritized [15].

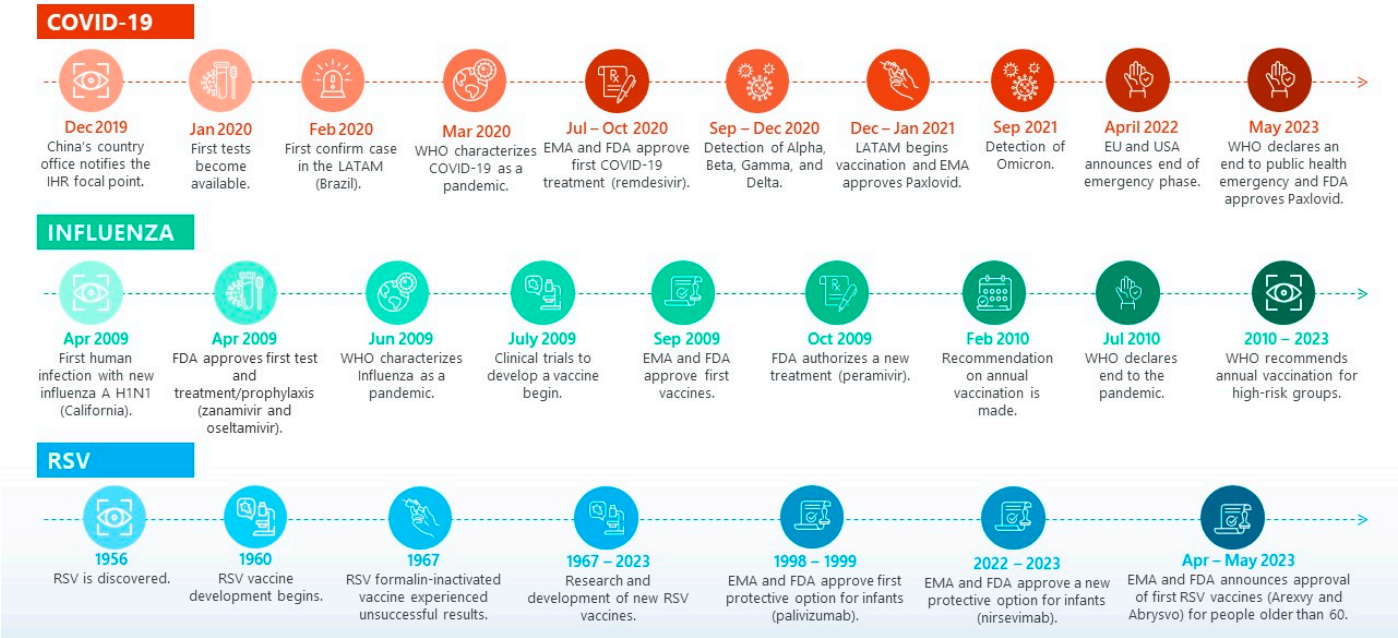

Figure 1. ARI key events timeline. Source: elaborated based on reviewed reports and literature [1–8,16–33].

In contrast, the timeline of key events for RSV shows a pattern of slower progress, mainly attributed to knowledge gaps regarding immunological protection and the unsuccessful results of RSV formalin-inactivated vaccine development experienced in 1967 [20]. In a turn of events, over the past decade there has been significant progress in the knowledge of RSV molecular and structural biology and the human immune response, leading to several promising monoclonal antibodies (mAbs) [34] and RSV vaccines undergoing clinical trials [35]. These efforts have culminated in the approval by the EMA and FDA of two protective options for infants: palivizumab (approved by the FDA in 1998 and by EMA in 1999) [32] and nirsevimab (approved by the EMA in September 2022 and by the FDA in July 2023) [22,33], as well as the first RSV vaccines (Arexvy and Abrysvo) for people older than 60, between April and May 2023 [23,24,27].

While the WHO declared the end of COVID-19 as a public health emergency, this does not mean that COVID-19 is no longer a global threat; only the acute phase of the pandemic is over [4]. COVID-19 will not disappear, but countries will be able to transition towards integrating COVID-19-related measures into routine health services and programs, eventually reaching an endemic stage [36]. Endemicity does not necessarily mean a disease

is rare or mild, posing no public health risks. Rather, it means that infection rates remain static, even if high SARS-CoV-2 variants will likely continue to emerge, some of which might be more transmissible and immune-evasive [37]. While it is true that population immunity against SARS-CoV-2 continues to accumulate and may help compensate for the impact of such a scenario, SARS-CoV-2 evolution is inherently unpredictable. It is possible that a recombinant could emerge with high transmissibility linked to intrinsic biology and novel antigenic properties [38]. Thus, while countries transition to a post-pandemic scenario, COVID-19 efforts, including testing and surveillance, should continue as a priority.

Endemicity is an epidemiological term used to describe a state of constant presence and/or usual prevalence of a disease or infectious agent in a population within a geographic area [39]. When an infection becomes endemic, there are different ways in which immunity provides protection without eliminating the virus. In the case of SARS-CoV-2, where neither vaccination nor infection warrants life-long immunity, understanding how different aspects of protection (reduction in susceptibility to infection and reduction in pathology) wane with time and how they are boosted by natural infection and vaccination is critical [40,41]. As the world moves into an endemic stage, countries will also face the challenge of increasing lagging vaccination rates [42,43], while at the same time having the opportunity to improve the technology and reach of testing [44]. In this context, the value of innovative testing technologies, such as rapid tests (including multiplex tests), might become evident [44].

2.1. Vaccines and Treatments Available and in the Pipeline for ARIs

An overview of the vaccines and treatments available and in the pipeline for ARIs demonstrates a considerable investment in innovation. The development of new technologies might open an opportunity to question the role and value of the differential diagnosis of ARIs, as diagnosis might be a gatekeeper to access adequate treatment.

There are currently three types of vaccines available against COVID-19: mRNA vaccines, protein subunits vaccines, and viral vector vaccines [45]. As of May 2023, there are currently four vaccines undergoing the review/market authorization process in the EMA [46]. The same number have received emergency use authorization by the FDA [47]. Regarding treatments, there are currently three main types available: antiviral medication, immune modulators, and mAbs. Antiviral medicines are used in mild to moderate COVID-19 cases for people who are more likely to get very sick and can be administrated through oral and IV infusion forms [48]. Immune modulators are prescribed to help suppress hyperinflammation when COVID-19 triggers a hyperactive reaction of the immune system. These drugs are used to treat adults and children who are hospitalized and require supplemental oxygen or mechanical ventilation [49]. mAbs are proteins made in laboratories that act like antibodies. Laboratory-made mAbs help stimulate the immune system and are a prime example of personalized therapeutics. While both the FDA and EMA have authorized antiviral medications and immune modulators [3,49–51], the FDA has not yet authorized mAbs for COVID-19 [49]. As of October 2022, there are 111 COVID-19 treatments in the research and development phase according to the EMA, of which 62 are antiviral medicines [51]. Similarly, according to data from the FDA (as of January 2023), there are 720 drug-development programs in the planning stages, and 440 trials have been reviewed [47].

For influenza, there are multiple types of vaccines available in the market, including standard-dose flu shots, cell-based flu shots, recombinant flu shots, high-dose flu shots, adjuvanted flu shots, and live attenuated flu nasal spray vaccines. Influenza vaccine composition is updated regularly according to the incidence of circulating variants from the previous year (these may or may not be new) [52]. Regarding treatment, antiviral medicines for influenza can be used to prevent or treat infection. There are two classes of antiviral agents that are globally approved and available: neuraminidase inhibitors (NAIs) and M2 inhibitors (adamantanes) [53,54]. Since adamantanes are not active against influenza B strains and there is widespread resistance among H1N1 and H3N2 influenza

A strains [53,55], NAIs are the only influenza antivirals currently recommended by the WHO [54]. There is only a small number of alternative agents with potential effectiveness against NAI-resistant strains [56]; thus, the development of novel drugs with a broad spectrum, better bioavailability, easier administrative pathways, and fewer adverse effects is crucial [54,57]. So far, the FDA has authorized three NAIs and one adamantane [57,58], while the EMA has authorized two NAIs and no adamantanes [53]. At the time of this study, there are six influenza antiviral medicines that are in the pipeline and have received EMA advice [59].

Regarding RSV, there are currently two vaccines (Arexvy and Abrysvo) recommended for older adults recently approved by the EMA and FDA [23,24,27,60], one for pregnant women and newborns from birth through 6 months through passive protection (Abrysvo) [60,61] and one preventive option for infants up to 24 months (nirsevimab) [22,33]. In light of the global RSV vaccine development pipeline, the WHO developed a guideline in 2020 to facilitate the international development and assessment of candidate RSV vaccines [21,62]. As of January 2023, there are 12 vaccines and mAbs in phases 2 and 3 of clinical trials [63].

2.2. Misdiagnosis of ARIs and Its Impact on Drug Resistance

While resistance to antiviral drugs is often a consequence of virus evolution, a natural phenomenon, evidence indicates a growing drug resistance due to drug-induced selective pressure [55,56,64]. Antimicrobial resistance seems to be accelerated due to the inappropriate use of antimicrobials, as well as their excessive prescription [65]. In fact, antibiotics are frequently unnecessarily administered for ARIs [66,67], often due to incorrect diagnoses, apprehension regarding bacterial co-infections, or dismissal of the detrimental effects of unnecessary antibiotic use [67]. Evidence indicates that up to half of patients' use of antibiotics is unnecessary or inappropriate [65]. Thus, there is a need to improve patient treatment stewardship, prescription guidelines, and monitoring resistance [64,66,68]. Better and adequate use of treatments requires timely and accurate diagnosis, for which access to sensitive and timely diagnostic tests is particularly important [66,69]. This benefit has been documented in influenza cases, where rapid diagnostic testing has helped reduce the unnecessary use of antibiotics in positive cases and led to adequate treatment of bacterial infections in negative cases [70].

3. Impact of ARIs and COVID-19 in LATAM

As of 22 November 2023, the WHO reported 772,166,517 confirmed cases of COVID-19, leading to 6,981,263 deaths worldwide [71]. According to the reported number of cumulated deaths, the Americas profile as the worst-hit region of the world, even though it only accounts for 8.4% of the world's population [72]. Deaths reported in the region sum to 2,983,561, which equates to approximately 42.7% of confirmed associated deaths worldwide [71]. Within the Americas, LATAM countries have been hit the hardest by the COVID-19 pandemic. Whereas reported deaths per million people are 875.38 globally, in the Americas this figure increases to 2689.55 for North America and Central America, and 3105.43 for South America (as of 18 November 2023) [73]. Excess mortality estimates also confirm the disproportionate effect of COVID-19 in the region. Excess deaths in LATAM (combining 2020 and 2021) are estimated at 2,273,620, which represents 15% of the total excess deaths in the world [74].

Based on cumulative deaths per million inhabitants, as of 18 November 2023, Peru (6511.89) and Brazil (3272.71) are disproportionately affected compared to countries like Costa Rica (1819.78) and Mexico (2625.69) [73]. According to excess mortality, Peru and Mexico suffer more than other countries in the region, recording estimates of 45.50% and 34.35%, respectively [74]. Current data on the burden of diseases of COVID-19 must be considered carefully, as some LATAM countries stopped reporting and/or updating COVID-19 cases and deaths on 31 May 2023. This can lead to an artificial perception of a drop in both measures [75].

Regarding testing, according to COVID-19 tests applied per 1000 inhabitants, it is possible to see that Chile had a stronger testing strategy, making tests available to more of the population when compared to other countries in the region (see column 6 of Table 1) [76,77]. Similarly, regarding vaccination, Chile has the highest vaccination rate among the focus countries, with a rate of 92.68%, 20 percentage points above the LATAM estimate. Mexico, on the other hand, is the only focus country that performed below LATAM estimates, recording a vaccination rate of 63.09% (see column 8 of Table 1) [71].

Table 1. Impact of COVID-19 in focus countries: Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico, and Peru.

Country/ Region	Cumulative Cases per Million Inhabitants (As of 18 November 2023) [73]	Cumulative Deaths per Million Inhabitants (As of 18 November 2023) [73]	Excess Mortality (As of 31 December 2021) [a] [78]	Tests per Confirmed Case [b] [77]	Tests Applied per 1000 Inhabitants [76]	Type of Tests Reported [c] [79]	Vaccination Rate (As of 24 November 2023) [d] [71]
LATAM [e]	NA: 207,377.11 SA: 157,588.76	NA: 2689.55 SA: 3105.43	Not available by region	Not available by region	Not available by region	PCR tests Antigen test Selection of serology tests	71.21 [f]
Argentina	220,929.56	2866.87	19.24%	3.50 (4 June 2022)	809.77 (4 June 2022)	-	83.73
Brazil	175,194.53	3272.71	22.34%	Not available	330.91 (11 March 2022)	PCR tests Antigen test Selection of serology tests	80.66
Chile	269,794.54	3143.13	18.54%	6.70 (22 June 2022)	2040.37 (22 June 2022)	PCR tests Antigen test	92.68
Colombia	123,068.00	2755.56	28.70%	11.80 (16 June 2022)	684.08 (16 June 2022)	PCR tests Antigen test	72.76
Costa Rica	239,128.20	1819.78	11.49%	5.70 (29 May 2022)	713.53 (29 May 2022)	PCR tests	85.57
Mexico	60,336.25	2625.69	34.35%	2.00 (18 June 2022)	122.88 (18 June 2022)	PCR tests Antigen test	63.09
Peru	132,820.23	6511.89	45.50%	111.10 (5 April 2022)	859.28 (5 April 2022)	PCR tests Antigen test Serology test	86.91

[a] Excess mortality: The percentage difference between the cumulative number of deaths since 1 January 2020, and the cumulative projected deaths for the same period based on previous years. [b] How many tests did a country take to find one COVID-19 case (based on 7-day rolling average), determined by the number of tests divided by the number of confirmed cases. [c] According to the type of test used to report cases as indicated in this table (PCR tests, antigen tests, or serology tests). [d] Persons vaccinated with a complete primary series per 100 population. [e] Due to data availability, evidence is presented according to two regions: North America (NA), including Costa Rica and Mexico, among others, and South America (SA), including Argentina, Brazil, Chile, Colombia, and Peru, among others. [f] The information is presented for the WHO Americas region average. Source: Elaborated based on available data from Our World in Data and the World Health Organization.

Nevertheless, a cautious and critical perspective is essential when looking at official COVID-19 statistics, as circumstances might be much worse. Countries in the region faced challenges regarding the detection and reporting of cases and deaths, which may have led to an under-registry of COVID-19 cases. This reality might considerably limit efforts to compare impact across countries. LATAM countries use two systems of collection and reporting of COVID-19-associated deaths, one from civil registries (e.g., Brazil) and the other from health system reports derived from surveillance systems and the synthesis of hospital reports and clinical histories (e.g., Mexico) [80,81]. Even though countries followed Pan American Health Organization (PAHO) recommendations to certify and code deaths [82], figures are not fully comparable between countries given the influence of data collection and publication systems [80]. Furthermore, data are also subject to changes and updates. For example, most countries consider within their protocols the recodification of deaths due to new test results and change accordingly in the registry or update the death certificates [83–87].

In terms of the burden of the disease of other ARIs, during the COVID-19 pandemic, influenza and RSV activity declined globally and most notably at the onset [12,88]. Nonetheless, this decline was also heterogeneous across countries and trimesters between March 2020 and September 2021, according to demographic, socio-economic, weather, and COVID-19 characteristics [88]. The observed reduction in the community prevalence of non-SARS-CoV-2 ARIs during the COVID-19 pandemic is undeniably multifactorial. Many authors attribute this reduction to changes in the circumstances derived from the implementation of SARS-CoV-2 control measures, such as the use of non-pharmaceutical interventions, changes in health behaviors, reductions in people's mobility (travel), virus-specific transmission factors, changes in testing priorities and surveillance systems, and repurposing of hospitals and test centers [12–14,89–92]. However, changes in the prevalence of non-SARS-CoV-2 ARIs could also be associated with the displacement of other ARI viruses as a novel agent is incorporated (in this case SARS-CoV-2). This is better known as the theory of the ecological niche of viruses, referring to the place each virus occupies in the ecosystem as it dynamically varies according to weather conditions and the presence of other pathogens. According to this theory, the incorporation of a new seasonal virus usually causes a displacement of other viruses (positive interactions between viruses might also be observed) [93,94].

Looking beyond the pandemic, the literature demonstrates a gap in the reporting of respiratory infections in the region. The quality of the data and the possible under-reporting of influenza morbidity and mortality limits the possibility of accurately calculating the burden of disease [95]. Similarly, for RSV, there is a considerable scarcity of data in LATAM [96,97]. National and subnational surveillance is weak in most parts of the world due to the limited capacities of the National Influenza Centers (NICs), insufficient funds, lack of intersectoral coordination, and varying commitment to surveillance by local governments [98].

To investigate the viruses in circulation, the WHO established the Worldwide Influenza Centre in 1948 and the Global Influenza Surveillance and Response System (GISRS) in 1952 [99]. The GISRS is a global mechanism of surveillance, preparedness, and response, undertaking epidemiology and disease monitoring and global alerts for novel influenza viruses and other respiratory pathogens, and collects evidence from the NICs [100]. Surveillance systems enabled the WHO to issue recommendations regarding influenza vaccine composition, which has been performed annually since 1973 and biannually since 1999. Today, the WHO issues two different sets of recommendations every year: one for the northern hemisphere in February and one for the southern hemisphere in September [101].

The WHO piloted a surveillance strategy for RSV based on the GISRS [102]. The pilot took place in two phases (the first covering 2016–2018, and the second between 2018 and 2021) [103]. Today, most LATAM countries use their Severe Acute Respiratory Infection (SARI) and influenza-like illness (ILI) systems to identify possible RSV cases [104]. RSV surveillance data efforts aim to collect evidence on the more severe cases, virus types, seasonality, risk groups, and disease burden, using this evidence to support public health measures and inform RSV vaccination policy [102,104]. Nonetheless, evidence suggests the under-reporting of RSV as algorithms for respiratory diseases only consider RSV testing in limited scenarios [105,106].

According to FluNet's (a global web-based tool for influenza virological surveillance that records data from the NICs) latest report (2023) [107], influenza and SARS-CoV-2 are the two highest respiratory virologic pathogens in the Americas based on the percentage of recorded cases, accounting for approximately 7% and 13%, respectively. Within the Americas, Central America is the subregion with the highest percent of positivity for SARS-CoV-2 (17.1%) and influenza (14.9%). Notably, approximately 12% of respiratory cases in the Americas correspond to other unidentified respiratory viruses, accounting for 32% of recorded cases in Central America. Even though ARIs are surveilled through the GISRS and are included in epidemiological surveillance weekly reports, the data reported by NICs are heterogeneous. This often creates an inability to recognize many different

respiratory viruses, challenging the possibility of capturing the real burden of ARIs and the accurate comparison between countries.

Regarding focus countries, Brazil records the highest burden in terms of prevalence and incidence of both upper and lower respiratory infections, followed by Colombia in the case of upper respiratory infections and Peru for lower respiratory infections (Table 2) [108]. According to evidence on the cumulative percent positivity rate of influenza and RSV (2022), Mexico profiles as the country most affected by influenza (34%), and Argentina and Chile for RSV (7%) [109]. It is important to note that a high positivity rate can be observed when there is a high number of positive tests, but the same holds if the number of total tests is too low [110]. When comparing the number of samples for influenza, Mexico has 10,314, while Argentina has more than 20,000 samples [110].

Table 2. Impact of respiratory infections, influenza, and RSV in focus countries: Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico, and Peru.

Country/ Region	Prevalence Lower Respiratory Infections (Rate; 2019) [108]	Prevalence Upper Respiratory Infections (Rate; 2019) [108]	Incidence Lower Respiratory Infections (Rate; 2019) [108]	Incidence Upper Respiratory Infections (Rate; 2019) [108]	Cumulative Percent Positivity Influenza (2022) [109]	Cumulative Percent Positivity RSV (2022) [109]
LATAM	149.99	3751.78	6862.71	272,487.36	6%	3%
Argentina	123.31	3782.42	5612.97	274,577.70	11%	7%
Brazil [a]	190.22	4204.29	8738.58	305,180.61	Fiocruz: 2% Adolfo Lutz: 6% Evandro Chagas: 18%	Fiocruz: 0% Adolfo Lutz: 4% Evandro Chagas: 1%
Chile	87.05	3715.18	4066.10	269,742.74	11%	7%
Colombia	120.14	4115.23	5597.67	299,095.86	1%	4%
Costa Rica	143.72	3194.20	6629.07	232,100.73	6%	5%
Mexico	102.01	3442.71	4616.49	250,202.90	34%	4%
Peru	210.70	3754.46	9628.63	272,846.31	11%	1%

[a] Brazil does not report national-level information on cumulative cases of influenza. Fiocruz, Adolfo Lutz, and Evandro Chagas are the institutions reporting on these indicators [109]. Source: Elaborated based on available data from the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease (GBD) database and Our World in Data.

It is also important to consider the implications directly associated with long COVID and other COVID-19 sequels (e.g., multisystem inflammatory syndrome [111]). Long-COVID's prevalence in LATAM might reach 29 million cases [112]. Characterized by multiple symptoms such as chronic fatigue, lung damage, anxiety, and depression [113,114], long COVID is a multidimensional disability that negatively impacts physical, mental, and cognitive health, affecting daily activities and social, family, and employment relationships [113]. Often, patients suffering from long COVID lack an understanding of their condition, leading them to not seek help or prioritize recovery [115]. In LATAM, where health systems often fail to adequately prevent and control chronic diseases, the impact is expected to be higher [116]. Thus, there is a pressing need to design and implement measures to address this new pandemic [112]. The unveiling of long COVID has come alongside an increased understanding of long-term sequels of other respiratory diseases as well. For example, sequels associated with RSV on children's developmental trajectory of reduced lung function have also been evidenced in the literature [117,118].

The COVID-19 pandemic's long-lasting impacts go beyond health, transcending social and economic dimensions. In LATAM, the pandemic led to an economic contraction and a regression in social indicators. In 2020, LATAM experienced a 6.8% drop in Gross Domestic Product (GDP) and a 7.7% drop in GDP per capita, the largest annual decline observed in the 120-year statistical history of the region [119–121]. Due to an increase in the unemployment rate (3% between 2019 and 2020) [119,122] and declining income, people's capacity to access basic services worsened, leading to a rise in poverty and extreme poverty in the region. According to estimates from 2021, approximately 86 million people are living in extreme poverty, and 201 million people are living in poverty, which represents 13.8% and 32.1% of the total LATAM population, respectively [119–121]. The pandemic also increased social

inequalities [122]. COVID-19 did not affect all population groups equally; women, children, and essential workers were most impacted [122]. As countries struggled to cope with the pandemic, the region also witnessed an eruption of social protests and a shift in political trends characterized by an increase in authoritarian practices and corruption, weakened democratic institutions, politicized judicial systems, and overall high levels of crime and violence [120].

Other ARIs also have negative socio-economic implications in LATAM. A literature review on influenza, for example, concluded that there is a significant economic burden related to hospitalization, treatment, and other resource expenses [95]. In South America, ARIs have been found to negatively impact health and productivity, representing a cost of USD 834 million, 0.024% of the combined GDP of countries [123]. Similar to the socio-economic spillover of the COVID-19 pandemic, a study on the impact of the influenza pandemic of 2009 in Mexico found that the costs associated with medical care during the pandemic were a smaller fraction than the costs associated with the impact on other sectors due to the measures taken to prevent the transmission [124].

Many valuable lessons can be learned from the COVID-19 pandemic regarding the management of public health emergencies and the pivotal role health plays in sustainable development and well-being. The pandemic exacerbated long-standing challenges faced by health systems across the LATAM region, including the fragmentation of services, inequalities in access, and limited funding and capacity for responding to public health emergencies [122]. The pandemic highlighted that comprehensive health policies are necessary to keep health at the center of sustainable development [125,126], and reinforced the urgent need to restructure health systems, prioritizing a people-centered model based on Universal Health Coverage, guaranteed through more public health expenditure and financial sustainability [126–128].

The disruption of ongoing health services, such as screenings and immunization programs, caused by the pandemic [122], as well as behavioral changes (e.g., vaccine hesitancy), calls for measures directed at restoring and reinforcing health programs [127–130]. Such measures must pay particular attention to mental health and populations that have been disproportionally affected [126,131,132]. Pandemic recovery efforts must be accompanied by global and regional cooperation and coordination mechanisms and frameworks to respond to and prevent public health emergencies. Based on lessons learned from the COVID-19 pandemic, governments across the globe should develop a new pandemic agreement, update the current International Health Regulations (IHR), create a Global Health Fund, and implement national strategies for the prevention and preparedness of respiratory virus-based epidemics and pandemics using an integrated approach [125].

4. Overview of Testing Options Available for ARIs

There are currently four primary types of tests available for respiratory infections: (1) nucleic acid amplification tests (NAATs), which detect the genetic material (nucleic acids) of the virus using upper respiratory specimens; (2) antigen tests, which detect the nucleocapsid protein antigen; (3) serology tests, which detect the presence of antibodies; and (4) viral culture tests, which use culture-based systems for virus isolation.

Testing options can also be organized according to their design to measure or detect a single pathogen or multiple pathogens. While most ARI tests are designed to detect only a single pathogen, such as COVID-19 or influenza, multiplex tests can simultaneously detect or identify multiple pathogens in a single sample [133]. There are two types of rapid multiplex tests currently available that are relevant for POC: antigen and molecular. Multiplex diagnostic tests, sometimes called combo tests, are a particularly valuable tool to reduce misdiagnosis or incomplete diagnosis of infectious diseases that have shared symptoms and clinical features, such as SARS-CoV-2, influenza A or B, and RSV [133–135]. Ideally, the diagnosis of infections should be approached by testing for all the potential pathogens rather than testing for just the most likely pathogen and then conducting other tests if the results are negative [133].

4.1. Types of Tests Available for Detecting COVID-19

There are currently three types of tests available for the detection of SARS-CoV-2: NAATs, antigen tests, and serology tests. NAATs detect the genetic material of the virus, in this case the ribonucleic acid sequences, using upper respiratory specimens [136,137]. The reverse transcription-quantitative chain reaction (RT-qPCR) is the reference method for the detection (diagnosis) of current SARS-CoV-2 infection [136]. RT-qPCR tests are commonly applied in laboratory facilities by trained professionals, as sensitivity is higher under these conditions [137]. Moreover, RT-qPCR requires ideal storage conditions for the samples to guarantee sensitivity [138]. Given these conditions, while RT-qPCR testing takes 30 min to 4 h (depending on the test), transportation of specimens might be required. Thus, RT-qPCR test results are usually available within 24 h [136].

Although the RT-qPCR is the most common type of amplification technique used to diagnose COVID-19, its use for POC remains limited due to the potential of error amplification and sequence mismatch [139–141] and mandatory requirements for thermal cycling conditions [142]. An effective rapid alternative for POC is the nucleic acid amplification method called isothermal amplification [143]. The loop-mediated isothermal amplification (LAMP) and the nicking enzyme-assisted reaction (NEAR) are two rapid nucleic acid amplification techniques that have gained recent traction.

LAMP is a DNA amplification method that, in combination with reverse transcription (RT-LAMP), has been successfully used for the detection of SARS-CoV-2 [144]. RT-LAMP is a viable alternative to RT-qPCR given its high specificity and sensitivity, cost-effectiveness, minimal instrumentation requirements, and fast turnaround time (typically within 30 min) [145,146]. Nonetheless, this technology has its limitations, namely the difficulty of designing new assays and the risk of false positives (which will require more strict control measures than RT-qPCR) [146]. The risk of false positives has been associated with unintentional primer cross-reactivity at concentrations that result in a quantification cycle (Cq) of 38 and above by RT-qPCR (with matching samples) [147,148] and the premature color change of pH-based dyes for colorimetry [146,149,150]. Recent studies, however, suggest that RT-LAMP can reliably detect viruses in samples that amplify by RT-qPCR at Cq < 30, reaching similar or better sensitivity than RT-qPCR [145,147]. Evidence also indicates promising efforts to reduce the risk of false positives associated with pH-based dyes by using custom saliva stabilization solutions or an alternative extraction method (nucleic acid extraction) [149,151–154].

NEAR is a novel technique that uses nicking enzymes to improve ordinary isothermal amplification, creating a very promising automated rapid option for POC [146,155]. NEAR has at least three main advantages: the potential for high sensitivity, easy application, and clinically relevant turnaround time. NEAR uses two enzymes, nicking endonuclease and DNA polymerase, for DNA amplification [156,157], with the second having shown improved sensitivity in the past [158]. Since NEAR tests can take place inside the manufacturer's instrument, they are easy for non-laboratory staff to use, requiring only the instrument and a cartridge to be applied [146]. Given the small size of the amplicon compared to other molecular tests, NEAR has also reduced the results turnaround time significantly (to approximately 5 min for positive results and 15 min for negative results) [159]. Finally, NEAR also seems to adapt better to different temperatures, likely due to the use of different primers, polymerases, and nicking enzymes [146]. Among the disadvantages of NEAR is the risk of false negatives at higher Cq values (usually above 35) and under some conditions, such as the dilution associated with the use of viral transport media prior to amplification [146,160–162].

Antigen tests detect viral proteins using upper respiratory specimens. Most often presented in a lateral flow immunoassay (LFIA) format, antigen-detection rapid diagnostic tests (Ag-RDTs) are used to diagnose current SARS-CoV-2 infection. Test sensitivity is higher when performed within five to seven days after symptoms onset [163,164]. Given the brief window of opportunity to provide life-saving treatments, such as Paxlovid, antigen tests might profile as a suitable alternative for timely diagnosis. Paxlovid, which is currently

approved for use on mild-to-moderate COVID-19 cases in adults who are at high risk of severe disease (including hospitalization or death), should be initiated within five days after symptoms start [26,28]. Antigen tests are available for professional use, and self-testing is applicable both in hospital and POC settings (home facility, primary care, physician office, pharmacy, etc.), with results available within 15–30 min [136]. Thus, although not as sensitive as RT-qPCR, rapid antigen tests provide a fast, inexpensive, portable, and effective method of testing in laboratory and non-laboratory settings [165]. Due to their conditions and costs, they have been the preferred tests used for diagnosis of SARS-CoV-2 acute infection in LATAM (for more details please see Section 7).

Nevertheless, antigen tests also have certain limitations. Evidence indicates a variable sensitivity among LFIA rapid antigen tests and a generally lower sensitivity when compared to NAAT [166–171], resulting in an ongoing debate over the utility of these tests (especially considering that the WHO recommends an 80% sensitivity and $\geq$97% specificity for these tests) [172]. One of the main factors leading to decreased sensitivity of these tests is the emergence of new virus variants [170,171], inspiring the development of innovative methods to enhance sensitivity. A study comparing the performance of rapid antigen tests for the detection of different SARS-CoV-2 variants and sub-variants found that a test using a flow immunoassay meter was able to detect more virus variants than other tests, which might be due to the meter facilitating a lower limit of detection compared to other options [173,174].

Sensitivity in relation to viral concentration values shows that sensitivity of rapid antigen tests decreases dramatically with increasing Cq value (decreasing viral load), leading to more false-negative results [173,175]. Although there is no definitive Cq value threshold beyond which antigen tests consistently result in false negatives, evidence indicates that rapid antigen tests are frequently negative in RT-qPCR-positive samples with Cq values above 24–28 [176] and have a 100% correlation to RT-qPCR at Cq values $\leq$ 22 [177]. This is particularly relevant since the Centers for Disease Control and Prevention (CDC) indicates that a Cq value > 33 might reflect a non-contagious stage [178]. Thus, early detection using rapid antigen tests is recommended. Nevertheless, efforts have also been made to create an LFIA test that could detect SARS-CoV-2 in low concentrations through the implementation of sensitivity-boosting strategies such as an increase in antibody concentration in the test line, and the insertion of an intermembrane between the conjugate pad and the nitrocellulose membrane to increase antibody–antigen interaction time, showing promising results [179].

Serology tests detect antibodies generated against the virus from prior infection or vaccination using serum/plasma or whole blood specimens. SARS-CoV-2 antibodies are usually detectable one or two weeks after infection or vaccination. Serology testing is not recommended as a standalone test to identify an active SARS-CoV-2 infection but can be used for retrospective diagnosis, surveillance, and research purposes. Results are usually available within 24 h when performed in hospital settings and within 10–30 min in POC settings [180–182].

4.2. Types of Tests Available for Detecting Influenza

There are currently four main types of tests available for the detection of influenza: NAATs, antigen tests, serology tests, and viral cultures. The most common NAATs for the detection of influenza are the rapid molecular assays, since they present sensitivity and specificity values close to those of RT-qPCR, with certain advantages for application at POC [70,183]. These rapid tests, eligible for POC, are usually able to detect influenza type A and type B (wide range of targets) in approximately 30–60 min (instead of the 24 h turnaround time of RT-qPCR). Rapid molecular assays are applied using a nasal swab by medical staff, not necessarily a lab technician, to run a molecular test [70]. Other molecular assays can detect and discriminate between infections with influenza A and B viruses and identify specific seasonal influenza A virus subtypes. The results may take from 45 min to several hours depending on the assay. Among the influenza molecular tests

are multiplex assays, particularly useful for the management of critical patients, such as severely immunosuppressed individuals [184,185].

Influenza antigen tests can be divided into two categories: rapid antigen influenza diagnostic tests (RIDTs) and immunofluorescence antigen detection assays. While some RIDTs are approved for use in outpatient settings, others must be used only in a moderately complex clinical setting. RIDTs can differentiate between influenza types (A and B) but do not provide information on influenza type A subtypes. RIDT results are often available in 10 to 15 min, and negative results are recommended to be confirmed with molecular assays. The immunofluorescence antigen detection test delivers results in approximately two to four hours. Like RIDTs, these tests can distinguish between influenza A and B, but not subtypes [184,185].

Serology tests for influenza are not recommended for clinical decision-making but can be used for research, monitoring, and surveillance purposes. A single serum specimen is not reliable for differentiating antibodies for influenza A or B. These tests are not recommended for clinical diagnosis as this would require paring acute and convalescent sera collected two to three weeks apart [184,185].

Viral culture tests for influenza are not recommended to inform clinical management due to their lengthy turnaround time. Shell-vial tissue culture results may take one to three days and traditional tissue-cell viral culture three to ten days. Viral culture methods, however, have an important public health role. Viral culture tests allow for extensive antigenic and genetic characterization of influenza viruses. They are essential for the surveillance and characterization of new seasonal influenza A and B virus strains, facilitating critical information for the biannual review of influenza vaccine composition [184,186].

4.3. Types of Tests Available for Detecting RSV

The main types of tests used for the detection of RSV are the same as for influenza, including NAATs, antigen tests, serology tests, and viral cultures. NAATs for RSV detection are more sensitive than viral culture and antigen testing. NAATs are the recommended method for diagnosing RSV in infants, young children, and the elderly. They are mostly used for critical patients in hospital settings, according to the diagnostics algorithm in their respective countries [19]. Antigen tests are considered an effective method for diagnosing RSV infection in infants and young children. The sensitivity of antigen detection tests generally ranges from 80% to 90% in this age group. Antigen tests are not sensitive for older children and adults as they may have lower viral loads in their respiratory specimens [19]. Serology tests and viral culture for RSV are not used routinely to diagnose infection but may be used by public health officials to track RSV infections [187]. Viral culture for RSV is particularly costly, difficult to perform, and has a lengthy turnaround time, limiting its clinical role. However, viral culture methods may be useful for public health surveillance purposes [19].

While RSV is one of the most common causes of significant respiratory illness in young children and older adults [188], RSV testing is not routinely recommended and often not performed [189,190]. Evidence indicates that this is, at least in part, due to the limited availability of treatment and prophylaxis options [69] and the common underappreciation of the severity of RSV for some populations [189–191]. Since antibiotics are often unnecessarily administered for ARIs due to incorrect diagnoses [66,67], RSV diagnostic testing could help improve antibiotic prescription. Furthermore, diagnosing will also help reduce the current limited availability of real-world RSV epidemiology data [192,193]. In the absence of this information, decision-makers often rely on estimates gathered through prospective studies which are often limited to a small sample size and short study periods [193,194].

4.4. Types of Tests Eligible for POC Rapid Testing

Table 3 summarizes the types of tests eligible for POC rapid testing according to ARI. The table also provides a high-level overview of the advantages and disadvantages associated with the use of antigen rapid tests, the alternative considered one of the most suitable for POC in LATAM. It is important to highlight that while some of these disadvantages are associated with the intrinsic characteristics of such tests, measures can be undertaken to improve performance. These have been presented in Section 4.1.

Table 3. Types and characteristics of ARI POC rapid tests.

ARI	Types of POC Rapid Tests	Advantages of Rapid Antigen Test	Disadvantages of Rapid Antigen Tests
COVID-19	• Rapid antigen tests, serology tests, and rapid molecular tests (especially LAMP and NEAR) [145,146,155,195] • Rapid antigen tests are considered the most suitable alternative for LATAM [196]	• Results within 15–20 min [166,196,197] • Portable and easy to perform [166] • Less costly than laboratory tests [166,196,197] • Implementation requires minimal training [166,196,197] • Cheaper and faster to manufacture than molecular tests [197]	• LFIA formats not as sensitive as NAATs at lower viral loads [196,197] • LFIA formats vary in sensitivity across virus variants [196] • Difficult to assure quality [196] • Positive results require confirmation in low-prevalence settings [197] • Risk of false negative results, especially at lower viral loads [196]
Influenza	• Rapid antigen tests and molecular tests [198]	• Results within 15 min [70,198] • Portable and easy to perform [70,198] • Implementation requires minimal training [70,198]	• Not as sensitive as NAATs or viral culture [70,198] • The sensitivity to detect influenza B is lower than for influenza A [198] • Narrow range of targets (some tests do not distinguish between influenza A or B, nor provide information on the virus subtype) [70,198] • Risk of false positive results, especially when influenza activity is low [198] • Risk of false negative results, especially when influenza activity is high [198]
RSV	• Rapid antigen and molecular tests [19,199] • Rapid tests are especially considered to diagnose infection in infants and young children [19]	• Results within an hour in most cases [187] • 80–90% sensitivity for infants and young children [19] • Easy to perform on-site, in health care practitioner's office or emergency room [187]	• Limited sensitivity for patients in other age groups [19] • Results are recommended to be interpreted by experienced laboratorians [19]

Source: elaborated based on overviewed sources [19,70,145,146,155,166,187,196–199].

Rapid antigen testing might be one of the most suitable alternatives for POC testing in many LATAM countries. While molecular testing continues to be the recommended method for the diagnosis of COVID-19, the broad use of this method is constrained in low-resource settings due to limited testing capacity, shortages of reagents/supplies, lack of skilled personnel, long turnaround times, and high costs [200,201]. A study on the optimal use of rapid testing in low-resource countries found that the inclusion of Ag-RDTs in testing strategies was cost-effective and critical in increasing timely testing access. The study found that, regardless of the epidemic phase, all countries sampled had insufficient molecular testing capacity to meet the calculated required testing demand within a relevant clinical time (48 h turnaround time) [201]. Furthermore, two studies in Brazil evaluating the replacement of RT-qPCR with Ag-RDTs found that they profile as a cost-effective alternative for the expansion of testing, combating COVID-19, and reducing the impact on the local economy [202,203]. One of these studies found a reduction in the total cost per patient of between USD 130.43 to USD 166.97 and unwanted clinical outcomes (avoiding 2406 to 3208 new cases of COVID-19, 457 to 609 hospitalizations, and 172 to 230 deaths per 38,000 antigen tests performed) [203]. Moreover, maintaining the use of RT-qPCR as the first choice for diagnosing COVID-19 in working-age patients was found to potentially lead to an additional USD 207,515.14 in management costs in the municipality of Itaberá [202].

Evidence from high-resource countries, such as Germany and Italy, have also found economic benefits in using rapid antigen tests in both emergency rooms [204] and COVID-19 testing services [205].

However, additional cost-effectiveness studies are needed to validate the accuracy of the tests as part of such economic evaluations [202] and the role treatment pathways have on potential benefits based on actual practice [206]. Ultimately cost-effectiveness information on POC rapid testing should be used alongside other considerations, such as budget impact and feasibility, as part of a transparent decision-making process [207]. Decisions on the use of rapid molecular and antigen options, and/or the combination of both (e.g., antigen testing for initial screening and molecular testing in case of negative results) should consider cost-effectiveness, saturating testing demand, molecular testing capacity, test accuracy, and testing turnaround times. This is particularly important as new rapid molecular testing technologies become available. While rapid molecular testing is in general more expensive than RT-qPCR, studies from high-resource countries have shown promising results on the cost-effectiveness of such methods in emergency rooms and hospital settings [208,209].

Aside from rapid antigen and rapid molecular tests, POC testing can be supported by the use of rapid multiplex tests [210,211]. Multiplex testing allows for simultaneous on-site detection of different analytes using a single specimen, one of the main reasons why multiplex platforms have recently gained attention, especially for resource-limited settings [212]. There are two main types of rapid multiplex tests currently available for ARIs. The first is the NAAT, a rapid multiplex PCR [213,214]. These tests include various combinations such as influenza A, influenza B, and SARS-CoV-2; influenza A, influenza B, RSV, and SARS-CoV-2; and 20 of the most common respiratory viruses and bacteria causing upper respiratory illness. Information provided through these tests may be used for diagnosis, clinical management, and epidemiological surveillance (including the burden of disease virus surveillance) [215]. The second type is the rapid multiplex antigen test. The most common combinations of these tests include SARS-CoV-2, influenza A, and influenza B [213,216]. These tests can easily be implemented at POC with minimal training [172–174]. Rapid multiplex antigen tests can be used for diagnosis, in clinical correlation with patient history and other diagnostic information. As for epidemiological surveillance, these tests can support monitoring of the burden of disease.

5. What Is POC Rapid Testing?

In this section, we present a brief description of POC rapid testing, where (in what settings) this strategy can be implemented, and the benefits this strategy might bring. Using James H. Nichols' (2020) definition, POC testing involves performing a test outside of laboratory conditions, closer to the site of patient care [217], seeking to better identify or manage chronic diseases and acute infections [218]. POC testing can be performed and interpreted by health personnel or by the individual, a family member, or a caregiver of the individual being tested [195]. In the context of ARIs, POC testing can be used to diagnose current or detect past SARS-CoV-2, influenza, and RSV infections [19,184,195]. Based on the experience of COVID-19, POC testing can be implemented in various settings, including but not limited to physician offices, urgent care facilities, pharmacies, school health clinics, long-term care facilities and nursing homes, temporary locations including drive-through sites managed by local organizations, home self-testing, and other locations such as cruise ships and national and subnational borders [195].

The use of POC testing has several advantages, enabling decentralized, rapid, sensitive, and low-cost diagnosis [219]. Studies demonstrate that effective treatments for confirmed COVID-19 have the potential to offer value for money to healthcare systems, especially if they confer a survival benefit and reduce the need for hospitalization. In this context, diagnostic tests are more likely to be cost-effective if they can provide accurate results quickly [220]. While clinical evidence on the cost-effectiveness of POC testing for COVID-19 is limited and immature [220], even studies using high-cost methods, such as

rapid molecular tests, show considerable cost-saving benefits down the line [208,209]. For example, a study found that the use of rapid COVID-19 molecular testing in an emergency department and shock room led to a reduction of USD 285.23 in direct costs in admissions with subsequent surgery, and USD 79.02 without surgery [208]. As evidence grows, a common model for assessing the value for money of COVID-19 diagnostics and treatments, able to capture decision points applicable to different settings and use all available evidence (including real-world evidence), would be beneficial [220].

According to the literature, POC testing can help achieve four main goals [198,217,221]:

1. Disease identification: facilitates identifying the disease in a quick manner, allowing decisions to be made regarding adequate treatment and care, which in turn can reduce hospital follow-up visits.
2. Disease monitoring: allows monitoring of the disease, including aspects such as the response to medicines.
3. Behavior modification: contributes to patients' capacity to modify behaviors to avoid further transmission swiftly and to improve the patient's outcome.
4. Reduced barriers to care: can also help reduce disparities in access to diagnosis in remote settings.

6. The Role and Value of POC Rapid Testing in the Diagnosis and Management of ARIs in a Post-Pandemic Scenario

This section provides an overview of the role and value of POC rapid testing for the diagnosis and management of ARIs, particularly in a COVID-19 post-pandemic scenario. As the world moves into a post-pandemic scenario, all types of tests will continue to have a critical function from a public health perspective. This is in part determined by certain COVID-19 characteristics. The fact that asymptomatic and presymptomatic populations drive transmission, the duration of infectiousness, the persistent emergence of variants of concern, and the potential for reinfection, makes diagnostic testing a key tool to prevent further infection. In a post-pandemic scenario, COVID-19 testing can be used to (1) improve case management, (2) inform public health policy decision-making, (3) control outbreaks and prevent infections, and (4) support surveillance efforts [197]. With such great value, there is an undeniable pressing need to continue investing in the development of diagnostic technologies and advocacy for broader access to differential diagnosis and testing.

Differential diagnosis of ARIs through POC testing can improve the clinical management of cases, as it supplies health practitioners with critical information to provide adequate and timely treatment and care. In particular, evidence indicates that timely and decentralized diagnosis can reduce the unnecessary or prolonged use of antibiotics (antimicrobial stewardship); improve antiviral prescribing; reduce recurrent infections and persistent secondary infections, hospital admissions, and burden on secondary and tertiary health facilities; and shorten hospital or emergency department lengths of stay [70,133,222–228]. A systematic review that examines the effects of influenza POC testing found that diagnosis resulted in significantly higher rates of antiviral prescription [70]. Since antivirals are most clinically beneficial if taken within 48 h of symptom onset [229–231], faster result turnaround times (facilitated through POC testing) [232–234] are especially critical for their effective use [70].

By removing diagnostic uncertainty, POC testing was also found to reduce unnecessary antibiotic prescriptions (in positive influenza cases) and allow bacterial infection to be treated promptly (in negative influenza cases) [70]. This is particularly important as patient-treatment stewardship can help reduce the risks of antibiotic resistance, both at patient and large-scale levels [64,66,68–70]. The value of differential diagnosis for case management of influenza might be more easily acknowledged by decision-makers given the availability of treatments and antiviral prophylactics for the general population, unlike RSV [22,69,189–191,222,223].

POC testing can also help reduce emergency room length of stay, which can in turn lead to improving clinical outcomes by preventing nosocomial spread (intrahospital room

assignment) and easing the burden on the healthcare system. The latter is particularly important as emergency room length of stay can be influenced by hospital capacity conditions, including the availability of beds, overcrowding, and efficiency of healthcare providers, among others. To enhance this positive impact, decision-makers will need to update management protocol and emergency room collaboration to improve clinical decision-making and patient workflow [70].

Furthermore, rapid testing at POC can be an effective way of addressing inequalities in access to diagnosis (a common challenge in LATAM) by reducing the barriers that negatively impact vulnerable communities and rural areas [219,226,235]. By improving access and turnaround times, decentralized testing can help curb the spread of the infection through early diagnosis and optimize infection-control practices [223,226,235,236]. Thus, POC rapid testing can play a role in policy-making, tailoring the response to pandemics, epidemics, and outbreaks according to the needs of each context and epidemiological moment. Diagnostic tests will serve as the eyes and ears of the health care system, sounding alarms about unusual disease patterns or outbreaks that enable an early response [197].

From a policy perspective, information gathered through POC rapid testing can allow for the evaluation of measures used and guide the planning and implementation of programs (including resource allocation) to help prevent and control disease [237]. In this way, POC testing can empower states to adopt newer, faster, and tailored technologies and tracing methods by building rapidly reactive health systems [226,235,236], and the scientific community can continue learning about the viruses (including routes of transmission and immunity) by supplying and analyzing much-needed data [219].

As countries move from pandemic response to living with the virus, one of the main roles of testing will shift toward surveillance efforts. The pandemic unveiled the need for countries to invest in diagnostic and surveillance systems, as well as data connectivity, so that clinicians and policymakers have tools at their disposal to practice precision medicine and rapidly investigate early alerts of possible outbreaks [197]. In LATAM, the PAHO recognized the need to adjust the current ARI surveillance systems to, among other goals, guarantee correct monitoring of the transmission, severity, and impact of COVID-19, as well as the immune response to sequels or episodes after infection [238]. The PAHO also recognized the role of both sentinel and non-sentinel surveillance systems, and the WHO called for continuing the triangulation of sentinel-generated data with other sources (e.g., event-based surveillance, non-sentinel surveillance, and mortality surveillance) [238,239]. Data generated through POC testing, if recorded and reported correctly, can support surveillance efforts. ARI surveillance through POC testing would improve the understanding of the real burden of these diseases, motivating further investment in research and development of new technologies, including vaccines and treatments [240,241].

LATAM has made outstanding progress in strengthening the information and surveillance systems of ARIs during the COVID-19 pandemic. It is essential to continue investing in diagnostic testing and the integration of information systems. This is relevant for all technologies, including ultra-sophisticated detection methods and sequencing technologies at higher levels, but also POC diagnostics at the community level [197]. Evidence points to rapid antigen and serological tests as the most cost-effective alternative to scale COVID-19 POC testing [242,243]. Rapid molecular tests that do not require sophisticated instruments could be an alternative if the higher risk of cross-contamination can be mitigated [242].

Finally, there are many elements that need to be considered for the adequate implementation of POC rapid testing strategies. A study identified 18 key enablers for the successful and rapid implementation of decentralized POC testing [226]:

1. National policy, guidelines, and implementation plans.
2. Strong governance and consultation.
3. Champions from government, community, and health services.
4. Shared responsibilities between the POC program and jurisdictional stakeholders.
5. Staggered roll-out to learn lessons from the first tier of sites.
6. Transparent but strict inclusion criteria due to limited test supply.

7. Funding for diagnostics and personal protective equipment.
8. Local supply of quality control and external quality assurance materials.
9. Robust quality-control development, overcoming cold-chain barriers.
10. Use of platforms already in place by a subset of health services.
11. Reactive supply chain systems.
12. Program website for rapid dissemination of program resources.
13. Flexible connectivity systems.
14. Referral pathways with accredited pathology providers.
15. Capacity-building for health-care workers through a comprehensive set of procedures, posters, and other resources.
16. Training and competency assessments delivered virtually, meaning no face-to-face contact is required.
17. Monitoring and evaluation systems, including a real-time dashboard to enable management of stock and monitoring of the implementation progress.
18. Flexibility in the implementation model to meet different jurisdictional and health service needs.

7. Current Recommendations on the Use of POC Rapid Testing for the Diagnosis and Management of ARIs

Having explored the role and value of POC testing, in this section we provide an overview of the current global, regional, and national policies and recommendations relevant to POC rapid testing. Regarding COVID-19, as of 5 July 2023, the WHO continues to recommend the use of both NAATs and Ag-RDTs for the diagnosis of COVID-19, with the first being defined as the gold standard. However, Ag-RDTs are recommended in settings where NAAT testing capacity is limited [164], a common reality among LATAM countries. In fact, evidence indicates that Ag-RDTs are currently the tests of choice for diagnostic purposes in the focus countries (Table 4) [85,244–250]. Furthermore, the WHO recognizes the value of Ag-RDTs for POC testing. According to the organization, Ag-RDTs are recommended for community settings, as they do not require sophisticated clinical and laboratory conditions. The organization recommends that in such cases, Ag-RDTs should be performed and interpreted by trained operators, ensuring the accuracy of the results [164]. During the pandemic, antigen tests were largely distributed in many countries, sometimes without proper quality verification or even formal market approval (public health authorities enforced exceptions by fast-tracking approvals through Emergency Use Authorizations) [251]. This may have caused the circulation of low-sensitivity tests in certain countries [252,253].

Following WHO recommendations, the CDC put forward a guide for POC SARS-CoV-2 rapid testing [195]. The guide provides information on the regulatory requirements for POC settings, the collection of samples, and the conditions required to perform rapid tests safely and adequately. In terms of regulatory requirements, the CDC regulates POC testing through four different types of Clinical Laboratory Improvement Amendments (CLIA) certificates. A CLIA-certified laboratory or testing site is obliged to report all positive diagnostic and screening results to the person who was tested or its healthcare provider but is not required to report negative test results. The testing site or laboratory also must report the positive test results to their state, tribal, local, and territorial health department systems [195].

To support the country's transition from pandemic response to living with the virus, the WHO issued a Strategic Preparedness and Response Plan in May 2023 (2023–2025). According to this plan, testing is transitioning to priority risk groups and individuals with moderate or severe symptoms [254]. In this context, widespread screening of asymptomatic individuals is not currently recommended [255], unless for specific groups at a higher risk due to exposure, such as contacts of confirmed cases [255].

Regarding influenza, the WHO recommends applying laboratory diagnostic testing to differentiate an infection with influenza from other ARIs, outside of epidemic situa-

tions and in periods of low activity [18]. Similarly, the CDC conveys the importance of diagnostic testing to differentiate between influenza and COVID-19, particularly as both cannot be differentiated based solely on symptoms [256]. However, during periods of increased influenza activity, the CDC does not recommend diagnostic testing in outpatients. Under such circumstances, testing is only recommended when it can help inform clinical management and decision-making, such as when patients are being admitted to hospital and arrangement of rooms to avoid further intrahospital spreading [184]. WHO and CDC recommendations are similar for RSV. Laboratory testing is only advised to differentiate from other viral respiratory and bacterial infections when the disease is severe or when a patient is admitted to the hospital. Mild and asymptomatic presentations of the disease, or during seasonal outbreaks, are not tested [19,21].

As for surveillance, the WHO calls for countries to maintain core surveillance activities by applying multiple approaches, including sentinel, environmental, participatory, seroepidemiology, and event-based surveillance, among others [254]. The WHO recommends that SARS-CoV-2 testing be integrated into existing respiratory disease surveillance activities, including the GISRS and the Global Coronavirus Laboratory Network (CoViNet) [254]. Furthermore, countries are encouraged to continue strengthening their capacities for genomic surveillance and real-time data collection [254]. Aligned with the WHO, the PAHO has already integrated COVID-19 into the surveillance report of influenza and other ARIs [104].

In this context, the use of multiplex assays is considered a potential asset by the WHO, PAHO, and CDC to support surveillance efforts [15,100,257]. In 2021, the PAHO published a guiding document for the implementation of influenza + SARS-CoV-2 multiplex RT-PCR assay into influenza and COVID-19 integrated surveillance activities [15]. While multiplex assays are currently not recommended for universal COVID-19 surveillance as SARS-CoV-2 is still predominant, it is considered that under a scenario of high or very high influenza community transmission, SARS-CoV-2 confirmation should be prioritized [15]. The CDC recognized the value of multiplex assays for differential diagnosis and surveillance efforts (particularly the influenza + SARS-CoV-2 multiplex) as it helps differentiate SARS-CoV-2, influenza A, and/or influenza B viruses in one test [258]. Undeniably, multiplex assays may assist the process of integrating COVID-19 testing services with testing for other respiratory illnesses such as influenza and RSV [100,257].

Table 4 summarizes the current landscape of relevant policies for the management of ARIs in focus countries. Notably, all countries currently include respiratory illnesses in their National Health Plans and have specific national policies for both respiratory illnesses and influenza. On the contrary, none of the countries have a national policy for RSV. Given the call by international organizations [238] to integrate COVID-19 into ongoing services, we found that by July 2023, most of the countries of interest had incorporated COVID-19 into the National Policy for Respiratory Illnesses (at least by the protocols for surveillance), with Costa Rica and Peru lagging behind [85,103,244,257,259–262]. While policy progress for respiratory infections is evident, the challenges of implementing said policies remain a concern, particularly regarding the allocation of sufficient resources.

Table 4. National guidelines and recommendations for the management and testing of ARIs in focus countries: Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico, and Peru.

Country	National Health Plan Includes Respiratory Illnesses	National Policy Program for RSV	National Policy Program for Influenza	National Policy for Respiratory Illnesses (NPRI)	NPRI Integrates COVID-19, Influenza, and RSV [a]	Current Preferred Diagnostic Method for COVID-19	Purpose of COVID-19 Rapid Testing	Current Recommendations Relevant to ARI Multiplex Testing	Are Multiplex Tests Available in the Market? [b]
Argentina	Yes [244]	No	Yes [244]	Yes [244]	Yes [244]	Antigen test [244]	Diagnosis, clinical management, surveillance, and control [244]	Recommended for pediatrics (less than 5 years old) and hospitalized patients [244]	Yes [263,264]
Brazil	Yes [265]	No	Yes [266,267]	Yes [268]	Partial [c] [259]	Antigen test [245,246]	Diagnosis, surveillance, and control [245,246]	No mention of multiplex tests in the national guidelines [245,246]	Yes [269]
Chile	Yes [270]	No	Yes [271]	Yes [272]	Yes [260]	Antigen test [247]	Diagnosis, surveillance, and control [247,273]	No mention of multiplex tests in the national guidelines	Yes [274]
Colombia	Yes [275]	No	Yes [276,277]	Yes [278,279]	Yes [d] [261]	Antigen and PCR tests [248]	Diagnosis and surveillance [248]	Recommended for hospitalized patients with a negative PCR for COVID-19 [261]	Yes [280]
Costa Rica	Yes [e] [281]	No	Yes [282]	Yes [282]	No	Antigen test [249]	Diagnosis and surveillance [249]	No mention of multiplex tests in the national guidelines [249]	Yes [f] [283]
Mexico	Yes [284]	No	Yes [285]	Yes [85]	Yes [85,262]	Antigen and PCR test [85,286]	Diagnosis and surveillance [85,262]	Recommended in serious cases and deaths covering only 10% of cases [85]	Yes [287]
Peru	Yes [288]	No	Yes [289]	Yes [290]	No [250,290]	Antigen test [250]	Diagnosis Surveillance [250]	No mention of multiplex tests in the national guidelines [250]	Yes [291]

[a] Assess integration of COVID-19, influenza, and RSV in NPRI. Yes, if all three integrate; partial, if only two integrated; no, if none integrated. [b] Assess approval of multiplex tests (for at least two pathogens) by the regulatory agencies. [c] Focused on COVID-19 but includes information for surveillance of influenza and other respiratory viruses. [d] Plan 2016–2020 outdated, no new plan available. [e] Specific protocol for surveillance. [f] Costa Rica has bioequivalence for the approval of products from the agencies of other focus countries included in this research that have approved multiplex tests [292]. Source: Elaborated based on available data from official governmental sources (Ministry of Health, National Health Institutes, Departments of Surveillance, National Regulatory Agencies).

According to current recommendations, the purpose of testing in focus countries centers around diagnosis and epidemiological surveillance [85,244–250,262,273]. Regarding the use of multiplex tests, only Argentina, Colombia, and Mexico currently have clear recommendations for the use of these assays. Even within these countries, the role of multiplex tests is circumscribed to specific high-risk population groups [85,244,261]. While conditions on when to use multiplex tests for respiratory diseases are not explicit in relevant guidelines, evidence indicates that multiplex tests (SARS-CoV-2, influenza A and B, and other respiratory pathogens), including rapid methods, are currently approved by the regulatory agencies in all focus countries [263,264,269,274,280,283,287,291].

8. Challenges and Barriers to POC Rapid Testing of ARIs in a Post-Pandemic Scenario

A reflection on the value and role of POC rapid testing for ARIs would not be complete without acknowledging the challenges and barriers to the implementation of this strategy identified by international organizations, the scientific and academic community, and governments. Based on the evidence, concerns can be categorized into four groups: challenges and barriers related to (1) intrinsic test limitations and characteristics, (2) the availability of tests and capacity to implement POC rapid testing strategies, (3) the capacity to make adequate use of POC rapid testing results for surveillance purposes, and (4) policies and regulations for POC rapid testing.

8.1. Challenges and Barriers Related to Intrinsic Tests Limitations and Characteristics

Each testing methodology has both benefits and limitations; therefore, decisions on which type of tests to use for POC are based on a tradeoff between test sensitivity, costs, turnaround times, and application requirements. While molecular tests are the gold standard for ARI diagnosis due to their high sensitivity, test results may not be available in a relevant time frame to inform clinical management at POC [293]. Some of the conditions for application, such as the type of equipment needed and sample storage requirements, may limit their application for outpatient or emergency care [293]. Furthermore, while there are some rapid options available, such as for influenza able to detect the virus type A and type B in a reasonable timeframe for POC (15–30 min) [184], molecular tests are in general more expensive.

Although antigen tests are more affordable and easier to implement and use, they are less sensitive than molecular tests [196]. The sensitivity of antigen tests varies according to different factors, including the assay applied [294], the timeframe of sampling after exposure, age groups due to the viral load (as is the case with RSV antigen tests for example), and community prevalence of the virus (populations with low expected prevalence) [198,295]. Less sensitivity may lead to a higher risk of false negative results in people with low viral loads [294]. Thus, in some cases, diagnostic confirmation by a molecular test is required [198]. Use of these tests is not recommended in settings or populations with low expected prevalence of disease and where confirmatory testing by molecular is not readily available [296].

While serology tests have also been considered as an alternative for POC [195], they are not recommended for the diagnosis of an active infection and have limited value for case management [297,298]. The presence of antibodies should not be equated to the individual's immunity or an active infection [219]. Furthermore, serology tests have not been evaluated to assess the level of protection, which means that if interpreted incorrectly, there is a potential risk of increased transmission due to the false sense of security [219]. Evidence also indicates the possibility of cross-reactivity with other coronaviruses (in the case of COVID-19), posing a challenge to the use of these tests for surveillance purposes [299].

Finally, all test types need constant performance checks. This is particularly challenging for the use of multiplex at POC. Performance assessment of multiplex assays is needed across all known variants at the time of validation, considering simultaneously the potential impact of future variants [219]. The use of rapid multiplex tests at POC is further limited by the conditions needed for their use and current availability and access in the

region. Although multiplex tests allow for the detection of different analytes simultaneously on-site [212], not all types of multiplex tests are eligible for POC, as many require laboratories that are certified to perform high-complexity tests (especially for molecular multiplex assays) [210,211]. Eligible rapid multiplex PCR tests for POC can detect a broader range of analyte combinates than multiplex rapid antigen tests; however, only a few options are currently available [213,214]. On the other hand, multiplex rapid antigen tests are more affordable and easier to use at POC [213,216]. Multiplex rapid antigen testing can be conducted outside of a laboratory setting with minimal training [166,196,197]. Finally, the design of better and context-appropriate multiplex techniques is also bounded by the limited availability of epidemiological information on the community circulation of ARIs.

8.2. Challenges and Barriers Regarding the Availability of Tests and Capacity to Implement POC Rapid Testing Strategies

Evidence indicates that POC testing devices have in general limited availability relative to their need in developing countries [300]. Furthermore, major gaps in access to diagnostics have been observed, especially when looking at primary care settings [301]. Access is affected by the high costs of tests, uncertainty regarding who covers their cost, heterogeneous pre-existing infrastructure, and limited availability of financial resources [300,301]. This is particularly concerning as the current health expenditure (% of GDP) for LATAM and the Caribbean is considerably lower than the global value (8.6 and 10.9, respectively, according to data from 2020), and is polarized, ranging from 3.2 in Haiti to 12.4 in Cuba [302]. This means that many countries in the region might struggle to cover the costs associated with POC testing, including adequate capacity building. Furthermore, these circumstances might also position LATAM rural populations at a higher risk. Although transmission may be lower in small cities, access to diagnostics remains essential given the limited capacity these contexts have to manage severe cases and control transmission [122,303].

Other challenges regarding the implementation of POC testing include ensuring adequate use of the tests, from the collection of the sample to the interpretation of the results [219]. Storage conditions of devices may also impact the quality of the results [304]. Furthermore, depending on the type of test used, the limited availability of qualified personnel might be a concern, as the healthcare expert ratio to the general population is relatively low in LATAM [300]. Efforts to build healthcare professional capacity are impeded by significant time constraints and high turnover rates among health service staff [300]. Regarding the interpretation of the test results, the accuracy of RIDTs depends largely on the conditions under which they are used. Minimizing false positive or false negative results must be a consideration [198].

8.3. Challenges and Barriers Regarding the Capacity to Make Adequate Use of POC Rapid Testing Results for Surveillance Purposes

Existing surveillance systems of respiratory viruses face the challenge of integrating COVID-19 into their schemes. According to current recommendations, sentinel surveillance should be one of many sources of information used to triangulate data, including event-based surveillance, non-sentinel surveillance, and mortality surveillance [237–239]. Genomic surveillance continues to be essential in a post-pandemic scenario, providing critical information for monitoring the evolution and distribution of circulating variants, and unveiling their association with severity, comorbidities, and age groups, among other risk factors [238]. Genomic surveillance must actively look for emerging agents and new variations in viruses already reported in circulation, and collect samples from different sources, such as humans, animals, and the environment [197,254].

A good surveillance system will need to be able to couple all these conditions in an environment of constrained resources. Failure to address these challenges may lead to under-ascertainment, under-reporting, lack of timeliness of the reports, and incompleteness of the surveillance data [237,305]. There is a need to establish homogeneous regional guidelines and ensure technical support to guarantee that lessons learned, and capacities acquired during the COVID-19 pandemic, translate into better surveillance practices [238].

Reporting and completeness of surveillance data are also restricted by challenges in the registry and reporting of results, especially due to limited capacity and connectivity in remote areas [226]. Reported results sometimes cannot be confirmed due to the inadequate execution of testing and voluntary anonymous reporting. This in turn limits the type and quality of information available to take action during periods of high disease prevalence, such as for case investigation or contact tracing [294].

8.4. Challenges and Barriers Related to Policies and Regulations for POC Rapid Testing

There is a general absence of clear regulatory standards for introducing POC tests. Currently, POC testing is only addressed by laboratory guidelines [300]. There is a need for a regulatory framework that supports access and reimbursement of these technologies. The lack of inclusion of tests in Essential Diagnostic Lists generates uncertainty as to who should cover the tests, negatively impacting access [301]. Moreover, policies for POC testing will need to cover aspects from procurement and approval of tests to the registry of results for surveillance purposes [226]. Moving into a post-pandemic scenario, funding for POC testing might be limited. In this context, testing strategies will need to be strategically deployed to guarantee access to those who need them the most [219]. As to the question of whether differential diagnosis should be a public health priority, there is an imperative need to demonstrate the value and cost-effectiveness of testing strategies, understanding the opportunity for saving costs and reducing suffering down the line, as further burden of the disease on the health system and society is prevented [219].

9. Policy Recommendations

Based on the reviewed evidence, this document puts forward a set of 24 recommendations for the adequate inclusion and implementation of POC testing strategies in LATAM countries in the context of a post-pandemic scenario. The first group of recommendations identifies actions needed to develop evidence and address knowledge gaps. The second and third groups seek to strengthen the capacity to implement POC rapid testing and guarantee adequate means of implementation. Finally, the fourth group addresses the inclusion of POC rapid testing in the local and regional respiratory policies. The recommendations seek to support decision-making in a variety of contexts and guide efforts by a broad range of stakeholders. Considering LATAM's diverse realities, the following recommendations serve as an 'umbrella' that countries can choose from and use according to their needs, priorities, and resources.

9.1. Actions to Develop Evidence and Resolve Knowledge Gaps

(a) There is a need to continue developing evidence on the cost-effectiveness of ARI POC rapid testing. Research institutes and the academic community, coordinated and motivated by governments, should undertake further studies that can provide insights into the value of differential diagnostics for respiratory infections. These studies could focus on generating evidence on the different POC rapid testing methods and their value for clinical management, prognosis, and surveillance.

(b) Governments should commit to and implement measures and policies to actively identify the causing agents of ARI cases in the region, providing a more complete picture of the challenges and priorities that need to be addressed through POC testing, including the use of rapid tests and multiplex tests.

(c) Governments should promote and conduct longitudinal and multicenter studies to overcome the knowledge gaps for the cost-effective use of multiplex tests at POC. Regional collaboration, under the leadership of flagship research centers, might help overcome logistical, resource, and capacity challenges to run such studies individually. As a result, recommendations should be made to enhance the adequate use of these tests for case management, surveillance activities, and public health policy decision-making. Studies should explore the potential benefits of using multiplex tests at POC in terms of costs saved by the health system, including costs associated with

the course of the diseases (e.g., hospitalization, multiple interactions with healthcare providers, etc.).

(d) Efforts to resolve knowledge gaps to understand the value of differential diagnostics at POC should pay particular attention to the multidimensional socio-economic impact of ARIs. Studies should also ensure that measures are taken to enhance the comparability of data across countries, allowing evidence to be shared across the region. Countries that have the capacity, ability, and resources to implement studies to develop knowledge and resolve gaps should collaborate with countries that require support, to share knowledge and evidence that can be extrapolated to inform policy decision-making.

(e) Funding the research and development of new tests should be prioritized as new ARI virus variants will continue to emerge that might impact the accuracy of existing tests. Research and development strategies should consider performance verification and validation against potential future variants.

(f) Test innovation efforts should consider the multiple uses of these technologies, including those beyond diagnostic (e.g., tests that are able to provide a prognosis). Tests should be accompanied by detailed guidelines to ensure their adequate use and interpretation.

9.2. Actions to Strengthen Capacity to Implement POC Rapid Testing

(a) The use of antigen or molecular rapid tests for POC differential diagnosis should be considered according to the health systems' capacity (including laboratory and technical capacity), resources, and costs. Given persistent financial constraints in the health sector in many LATAM countries and the advantages outlined by antigen rapid tests, they profile as the more suitable alternative for POC testing in the region.

(b) Decisions regarding the use of antigen or molecular rapid tests for differential diagnosis need to balance and consider the use of the information provided by such tests, their cost-effectiveness, and other considerations, such as budget impact, feasibility of its implementation in actual practice, testing demand, laboratory capacity, tests accuracy, and testing turnaround times. Using a combination of both for different purposes and contexts might be considered (e.g., using molecular tests for sentinel surveillance purposes and antigen tests for POC diagnostics and case management, or using antigen tests for initial screening and molecular tests in case of negative results).

(c) Governments should allocate dedicated resources to implement an ARI POC diagnostic strategy, addressing aspects of health workforce capacity-building, regulation and procurement of quality diagnostic tests, accessibility, and research and development. In context with limited financial resources, governments might benefit from building public-private partnerships to support addressing capacity-building concerns.

(d) Governments should install and promote a training strategy on POC testing to guarantee that healthcare providers have the necessary skills and knowledge to guarantee the proper use, implementation, and interpretation of POC rapid tests. Training opportunities should be provided at different levels of care and with a particular focus on primary health care.

(e) Governments should prioritize strengthening local capacities and mechanisms for genomic and metagenomic surveillance to be able to timely identify new pathogens associated with respiratory disease outbreaks. This may require investment in infrastructure, laboratory capacity, and technology.

(f) Governments and international organizations should ensure the integration of ARI surveillance systems, both at national and international levels, promoting the interconnectivity between the different surveillance agencies in the LATAM region. Surveillance systems should capture and associate variants with severity, comorbidities, and age groups, among other risk factors.

(g) Governments should ensure that the information collected through POC rapid testing is integrated with a broader health information platform, enhancing the opportunity to continue learning about the risk factors and health impact of COVID-19 and other ARIs.

9.3. Actions to Ensure Adequate Means of Implementation

(a) International organizations (e.g., the PAHO and Southern Common Market) and professional societies should provide guidance and support to national decision-makers on the use of POC rapid tests across different settings and conditions.
(b) International organizations and Ministries of Foreign Relations should align and provide guidelines to regulatory agencies in the region to ensure that approval procedures guarantee high-quality tests are available in the territories. Approval processes should be standardized across the region and ensure tests include information about the conditions and limitations of each methodology.
(c) Policymakers, payers, medical societies, and healthcare providers should form a cross-functional partnership to collaborate on the ongoing development of knowledge related to the diagnosis of respiratory infections.
(d) There should be a multistakeholder strategy for healthcare system strengthening, improved market sustainability, and integration of differential diagnostics into existing epidemic and pandemic response and preparedness plans. This strategy should be informed and supported by governments, medical societies, academic communities, and universities, among others.

9.4. Actions for the Inclusion of POC Rapid Testing in Respiratory Policies

(a) Governments should consider using POC rapid testing to support case management. The differential diagnosis of ARIs at POC might positively impact the clinical management of high-risk patients and the management of disease in the general population when treatments are available, as well as reducing unnecessary or prolonged antibiotic courses (improved antimicrobial stewardship) and hospital admissions.
(b) Given the risks of long COVID and COVID-19-related sequels, as well as sequels from other ARIs, the use of POC rapid testing should be prioritized to promote the early diagnosis of cases and prevent the further spread of infections.
(c) Governments should consider using POC rapid testing to support the monitoring of infections and diseases as well as surveillance efforts. Evidence generated through POC rapid testing can be used for policy decision-making purposes. Evidence collected through POC testing can help monitor the burden of disease over time, control transmission, and prevent and control future outbreaks.
(d) Governments should provide regulatory standards for POC rapid testing considering the conditions for approval, implementation, and the information registry. Regulatory standards will contribute to guaranteeing the quality of the tests (including sensitivity) and proper implementation, contributing to the accuracy of the results. Regulatory standards should be the norm in both the public and private sectors.
(e) Creating a consistent regulatory framework for the standardized approval of COVID-19 rapid tests across LATAM countries might be beneficial. This could include collaborating to establish a regional body similar to EMA for harmonizing the approval process; developing standardized technical requirements for the validation and registration of tests (including sensitivity, specificity, sample type, and testing conditions); creating a common technical dossier format for test manufacturers to submit; establishing and strengthening mutual recognition agreements between countries; and developing comprehensive regulatory guidelines that detail the approval process, including pre-market evaluation, quality control, post-market surveillance, and transparent decision-making, among others.

(f) Governments should consider including POC rapid tests in their national Essential Diagnostic Lists, based on the recognition of the value of diagnosis and disease monitoring and surveillance. Civil societies and patient advocacy groups could advocate for this inclusion.
(g) Governments should include clear guidelines regarding POC rapid testing in relevant respiratory infections policies. Guidelines should specify which test to use, and in what setting, considering test characteristics of sensitivity, accuracy, accessibility, affordability, and the test result turnaround time. The guidelines should also address strategies to reduce access inequalities in the territories.

10. Conclusions

In this document, we provide a comprehensive overview of POC testing, including its benefits, available options, limitations, and challenges. POC testing is an essential tool for the adequate management of ARIs in a COVID-19 post-pandemic scenario, guaranteeing better ARI clinical management and health outcomes. However, evidence also highlights several challenges to the implementation of this strategy, mainly associated with the uncertainty on how to operationalize testing policies in a post-pandemic scenario. Based on the challenges identified, this document puts forward a set of actionable solutions for the implementation of POC rapid testing in LATAM countries. Recommendations illustrate a path forward and can support critical decision-making, guiding efforts by a broad range of stakeholders, including governments, researchers, and academic institutions, among other relevant stakeholders.

There is indisputable evidence of the role and value of POC testing strategies, especially for LATAM countries. Information gathered through POC rapid testing can serve to improve case management, epidemiological surveillance, research and innovation, and evidence-based decision-making. With multiple types of rapid tests available for POC, decisions regarding which tests to use will require careful consideration of the testing purpose and resources available, while also balancing test characteristics regarding accuracy, accessibility, affordability, and results turnaround time. The transition from a COVID-19 pandemic to a post-pandemic scenario risks the prioritization and funding for ARI testing. International organizations have voiced clear concerns and recognized the pivotal role testing will continue to play in the management of COVID-19 and other ARIs moving forward. The benefits of continuing to invest in testing policies may outweigh the costs associated with the economic burden imposed on health systems down the line.

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