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The impact of SARS-CoV-2 in dementia across Latin America: A call for an urgent regional plan and coordinated response

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Abstract

The SARS-CoV-2 global pandemic will disproportionately impact countries with weak economies and vulnerable populations including people with dementia. Latin American and Caribbean countries (LACs) are burdened with unstable economic development, fragile health systems, massive economic disparities, and a high prevalence of dementia. Here, we underscore the selective impact of SARS-CoV-2 on dementia among LACs, the specific strain on health systems devoted to dementia, and the subsequent effect of increasing inequalities among those with dementia in the region. Implementation of best practices for mitigation and containment faces particularly steep

Butler, Julian Bustin, Claudia Duran-Aniotz, Daisy Acosta, Diana L Matallana, Diego Acosta-Alvear, Dominic Trépel, Elisa De Paula França Resende, Fabrício Ferreira de Oliveira; Francisco Ibanez, Fernanda G. De Felice, Gorka Navarrete, Ioannis Tarnanas, Irene B. Meier, Jerusa Smid, Jorge Llibre-Guerra, Juan J Llibre-Rodriguez, Laís Fajersztajn, Leonel Tadao Takada, Lissette Duque, Maira Okada de Oliveira, Maria Aparecida Camargos Bicalho, María Isabel Behrens, Maritza Pintado-Caipa, Mario Parra, Maxwell Z. Wilson, Myriam De La Cruz Puebla, Nilton Custodio, Rodrigo Santibanez, Rodrigo Bernardo Serafim, Ronnielly Melo Tavares, Stefanie Danielle Piña Escudero, Tomas Leon Rodriguez, Walter Dawson are listed alphabetically.

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challenges in LACs. Based upon our consideration of these issues, we urgently call for a coordinated action plan, including the development of inexpensive mass testing and multilevel regional coordination for dementia care and related actions. Brain health diplomacy should lead to a shared and escalated response across the region, coordinating leadership, and triangulation between governments and international multilateral networks.

KEYWORDS

coronavirus, dementia, health system, Latin American and Caribbean countries, SARS-CoV-2

1 | WHY LATIN AMERICA REQUIRES A REGIONAL STRATEGY

The brunt of the SARS-CoV-2 pandemic is hitting the aged and particularly those who are disadvantaged.¹ Often neglected is the devastating impact of COVID-19 for individuals with dementia and for their caregivers.^{2,3} Across the world, while every age group is susceptible to SARS-CoV-2 infection, older adults suffer a much higher mortality with the disease. As health systems become overwhelmed, access to dementia programs is becoming even more restricted. Implementing physical distancing in people with dementia is difficult.³ The combination of reduced work and quarantine can greatly disrupt family dynamics. Dementia-associated comorbidities such as hypertension, diabetes, cardiovascular disease, and cerebrovascular disease all impact SARS-CoV-2 severity.⁴ Central nervous system deficits such as smell and taste impairments and even hallucinations have been observed in association with COVID-19^{5,6} and rates of delirium are high in elders in intensive care units (ICU), particularly for those on a ventilator. Inflammatory responses elicited by infection may trigger long-term mechanisms of neurodegeneration.⁷ For example, a still poorly understood condition linked with the 1918 flu pandemic is post-encephalitic Parkinsonism, with degeneration of the substantia nigra and the presence of neurofibrillary tangles but without senile plaques. The long-term consequences of COVID-19 remain completely unknown, although our centers are beginning to see post-COVID patients with cognitive complaints.

Clearly, the coronavirus compromises dementia patients;³ however, the impact is not equally distributed across the population. Here we describe that patients, families, and health professionals in Latin

America and Caribbean countries (LACs) now face an extremely challenging situation. LACs remains a hot spot of the disease, and available data show similar upward slopes of deaths in LACs similar to those in North America, Europe, or Asia (Figure 1). LACs have a reproduction number (R) greater than one⁸ meaning that the number of cases is growing exponentially. In addition, there is a fundamental lack of preparedness to deal with the pandemic.⁹ We have recently raised awareness of the critical influence in LACs' dementia patients.² Beyond awareness, the situation requires an adequate response across the region that can coordinate our approaches for the dementia population. Here, collaborators from LACs and beyond first explore these specific regional impacts and then urgently call for a collaborative response to anticipate the upcoming challenges.

2 | THE PANDEMIC THREATENS THE COLLAPSE OF HEALTH SYSTEMS ACROSS LACs

Health care in the region was already precarious before the pandemic with a per capita expenditure of \$949 a year,¹⁰ (only one quarter of the average rate for countries of the Organization for Economic Cooperation and Development [OECD]). Further, in LACs expenditures are highly dependent on self-payment (LACs' average = 34% of total health spending, OECD average = 21%). Universal health needs are uncovered by insurance services, with unequal distribution between rural/urban areas and public/private services. About 30% of the LACs' population lacks regular access to health services and the number of hospital beds is small (2.7 per 1000 inhabitants, with a very small portion of intensive care beds,¹⁰ compared to the OECD average of 4.7).

Heterogeneity and fragmentation characterize the health systems specialized for dementia across LACs, with few available mechanisms for coordination among governmental and private providers. Countries with stronger public health systems can develop specific responses. Mexico implemented an epidemiological surveillance system that receives feedback from medical centers, and Chile has recently developed pilot care centers in primary and specialized care centers in the public sector enabling remote care during the outbreak, even when coverage is limited.¹¹ Cuba has also bet on its primary care system to proactively detect coronavirus cases in the population through general screening questionnaires and contact tracing.¹² In Uruguay, to date, the coronavirus has been well controlled. By contrast, most of the other countries do not have specific resources for the pandemic, and have important barriers to care, particularly in rural areas and among poorer urban populations. According to the Pan-American Health Organization (PAHO),¹³ the LACs will fail to provide basic responses to the pandemic including (1) widespread and massive testing with active isolation, (2) intensive and intermediate care units, (3) ventilators and supplementary oxygen by nasal cannula, (4) access to pharmacological treatments, and (5) guaranteed protection for health workers. On the horizon, we are also concerned about future access to a vaccine once one becomes available.

By 2050, the prevalence of dementia across LACs will increase four-fold, and patients from LACs suffer reduced social and health-care access.¹⁴ The pandemic is already impacting these people (see Box 1 for testimonies from across the region) and most countries are not ready to provide the necessary support to deliver social and residential care. The large drop in consultation rate in hospitals¹⁵ involves a significant deficit of care for non-coronavirus-related diseases, such as dementia. A regional lack of sufficient numbers of ventilators will raise painful moral dilemmas for decision making regarding patients with dementia. Most public clinics have cancelled patients' appointments to make room to attend the pandemic, so there are few physicians to receive those dementia patients needing medical attention.

The LACs' high prevalence of noncommunicable diseases¹⁶ across vulnerable dementia patients will worsen COVID-19 health complications. Conditions such as hypertension, cardiovascular disease, and chronic obstructive pulmonary disease all increase mortality attributed to COVID-19.¹⁷ Cardiovascular diseases (CVD) are a recognized risk factor for dementia in LACs.¹⁸ Almost half of COVID-19 patients who have been hospitalized show scan abnormalities that resemble the early stages of heart failure.¹⁹ The impact that such interactive effects will have on LACs' vulnerable older populations is unknown. Assisted living facilities and nursing homes have often been sites with very high rates of infection.²⁰ Specific co-morbidities in LACs such as the dengue epidemic that has affected >3 million individuals and caused more than 1500 deaths, mainly in the socioeconomically deprived population, has an unknown interaction with COVID-19. About 500 million people in LACs are at risk of contracting dengue. Overlapping infections and co-occurrence of both diseases increase the severity of patients,²¹ especially in those suffering from dementia and related comorbidities.

RESEARCH IN CONTEXT

1. Systematic review: The authors reviewed the literature using traditional sources (eg, PubMed). The unique critical situation for dementia patients in Latin America and the Caribbean countries (LACs) in the coronavirus era is reviewed. Other imperative calls for awareness of COVID-19's impact on dementia have been raised at a global level, as well as the unique influence of pandemic on LACs' health. However, no previous work has proposed a coordinated response to the LACs' selective impact on dementia patients yet.
2. Interpretation: We review the current situation of dementia patients across LACs under the pandemic. Then we present recommendations for a coordinated action plan. Collaborators from LACs and beyond first explore these specific regional impacts and then urgently call for a collaborative response to anticipate the upcoming challenges.
3. Future directions: We propose specific actions and a regional brain health diplomacy framework to coordinate urgent responses for the dementia population.

Limited telemedicine capabilities, as well as restricted access to the Internet in the region create additional complications for dementia care. Although telemedicine cannot replace face-to-face care, it is an extremely important tool in pandemic times,²² in particular to support the care of dementia patients.²³ However, many LAC hospitals do not provide virtual consultation or medical prescription with a digital signature.²⁴ As reported by some of the co-authors of this report working in hospitals, in specific areas of Argentina, Brazil, Colombia, Ecuador, Dominican Republic, and Peru, many patients cannot be reached by telephone or e-mail. In Brazil, most dementia consultations in the public health system are in person, with neither telemedicine nor remote consultation. Approximately 40% of hospitals are unable to provide remote consultations.²⁵ Web pages, videos, and free dementia helplines are underused by relatives of dementia patients. Barriers include geographic and economic conditions at remote and rural sites and impoverished urban areas.

The imbalance in access to health systems²⁴ is more severe when considering family dynamics. Formal long-term care (LTC) facilities are insufficient in the region,²⁶ and deficient for vulnerable populations.

Dementia patients often remain with their families even at the final stages of the disease, providing indirect care. The extended families in LACs with frequent social gatherings that ordinarily create a protective emotional environment for patients, will become dangerous, resulting in further strain due to physical isolation.²⁷ Family caregivers are facing paradoxical challenges regarding care and the contagious risk of patient contact. Amidst the pandemic

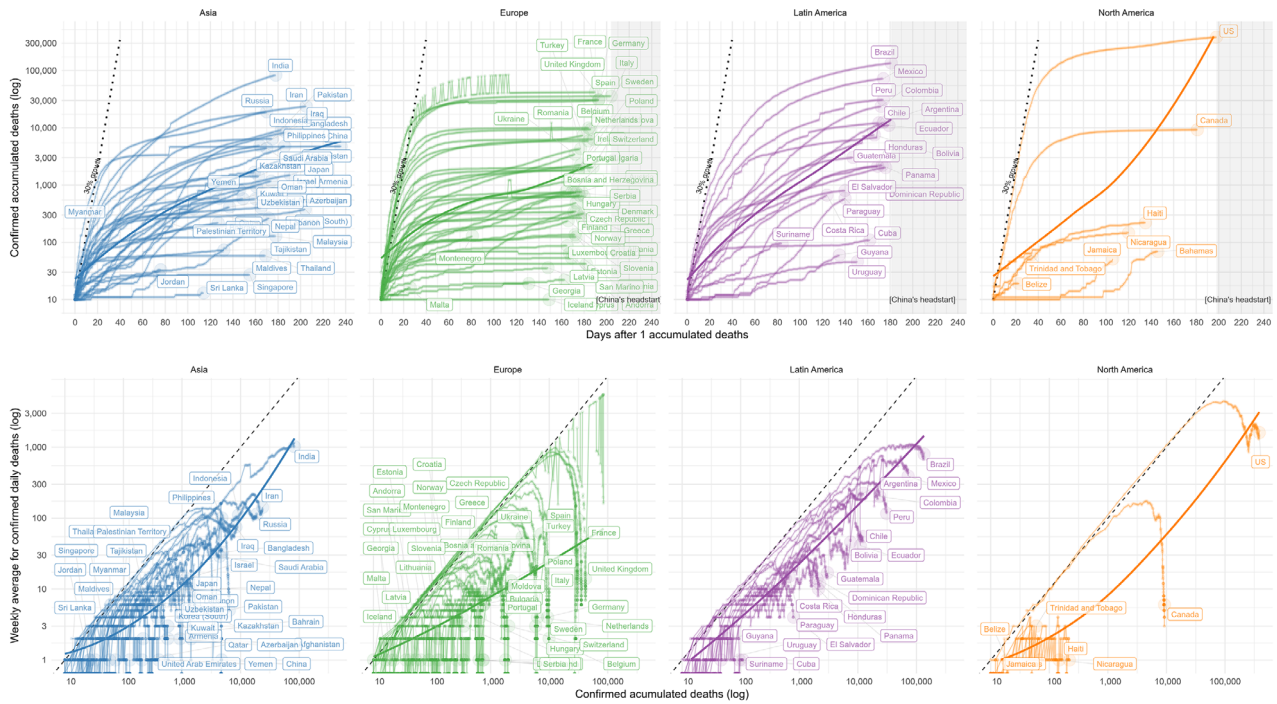


FIGURE 1 Patterns of COVID-19 death toll by regions and countries. A, Temporal dynamics of accumulated deaths. The accumulated deaths for all the countries and regions are shown per day. The slope represents growth rate. A dashed line of 30% growth in each region helps to visualize the similar growth rate across countries and regions. A gray headset in the top panels of Europe, Latin America, and North America also helps to identify the time gap in comparison to the start of the COVID-19 outbreak in China. Latin American and Caribbean countries (LACs) are in the early days compared to other regions, although their growth is in line with Europe or North America. B, Exponential growth of confirmed daily deaths by countries and regions. Rate of change shown as new deaths (per week average) divided by total deaths. In this panel, the new deaths in the past week are plotted against the total confirmed deaths to date. When plotted in this way, exponential growth is represented as a straight line that slopes upward. Diagonal slopes indicate exponential growth rate. The rate of change in LACs is exponential. Plots provide a line for each country, plus a bold line for the regional smooth conditional mean (Loess method). Both panels show how the epidemic started relatively late in LACs. Despite this, global trajectories of the region suggest similar exponential growth. Data retrieved from Johns Hopkins CSSE (<https://github.com/CSSEGISandData/COVID-19>) through <https://covid19api.com/> on July 20, 2020. The code for the creation of these plots can be found in <https://github.com/gorkang/2020-coronavirus-LATAM>. A daily updated interactive website to explore the data can be found in <https://gorkang.shinyapps.io/2020-coronavirus-LATAM/>

and the incumbent social distancing, caregivers will experience increased burnout syndrome, and dementia patients may face additional mental health risks and mistreatment.²⁸ Social isolation will contribute to already prevalent neuropsychiatric symptoms in elders, such as depression, distress, loneliness, anxiety, and sedentary behavior.

Finally, health professionals themselves, including neurologists and mental health workers, are among the vulnerable and their incapacity reduces the health delivery workforce. Adequate protective equipment and medical support for health-care workers is scant across LAC.²⁵ Health-care workers suffered an enormous toll in mortality, and simultaneously weaken the health-care systems in LAC. In Brazil, LTC facilities have shown one of the highest rates of nurses' deaths,⁹ and in Mexico, one fifth of health workers have died.²⁹ Assisted living facilities and LTC facilities have often been sites with very high rates of infection²⁰ and are facing critical supply and staff shortages in LAC.⁹ These factors not only increase the burden upon health professionals, but also the shortage of health-care responses to dementia patients.

3 | SARS-CoV-2 AMPLIFIES THE INHERENT INEQUALITIES IN DEMENTIA CARE IN LACS

According to the World Bank, Latin America is the most unequal region in the world. LACs host 8 of the 20 most unequal countries in the world, and three quarters of the LAC countries are low or lower-middle income. The LAC economic projection for 2020 was initially pessimistic, and the COVID-19 outbreak has now escalated these problems. Weak institutional structures for intervention, fractured multinational cooperation, teetering health systems, low economic growth, poverty, inequality, and unemployment are all precipitating an unprecedented moment in the region's history. LACs' poverty is pervasive (~185 million needy individuals, 68 million in extreme poverty), creating unstable and informal jobs (>50% of the regional population of workers) and restricting access to sanitation systems and essential services (water and sewerage). These overcrowded populations are forced by SARS-CoV-2 to a double tragedy: should they break the quarantine to search for resources and increase the risk of contagion for dementia patients or observe the quarantine and fall more deeply

BOX 1—Voices About Coronavirus from Latin American Countries

We selected particular testimonies across Latin American and Caribbean countries highlighting different dimensions of the coronavirus outbreak and the impact on dementia patients and families.



Pictures showing four histories and testimonies from Peru: Enrique (top left), Juana (top right), Enedina (bottom left) and Rosita (bottom right). See below.

Argentina

This country has developed an early, preventive, and compulsory social isolation quarantine, but contagion in overcrowded vulnerable neighborhoods may still challenge the health system. María Berude, a member of the Argentinean network of physicians said in an open letter: “We are people who have courage, but we are also afraid of dying. ... We have uncertainty and anxiety, because we are human beings. ... Neither gods, nor heroes, nor murderers, nor mercenaries. Simply medical doctors.”

Brazil

The coronavirus in the largest country in the region has increased exponentially. Jerusa Smid (co-author) summarized the private/public gap: “I work in a privileged private hospital, they are prepared to amplify the ICU beds from 43 to 280. I also work in a public hospital which is now out of rooms.” Leonel Takada (co-author) said he was “told to reschedule [dementia patients’] appointments to after June ... we couldn’t reach some of them by telephone and we don’t have their email addresses. This puts them into risk of not obtaining prescriptions.”

Chile

In 2019, the Chilean health system incorporated dementia care; however, the pandemic has suspended its implementation. For Andrea Slachevsky (co-author) “most of dementia patients are taken care by family members at home. Therefore, COVID-19 is imposing a hard burden on these families”. Claudia Duran (co-author) and basic scientist said: “I had to sacrifice most of my transgenic mice to decrease the load of work of veterinarians and technicians. ... Concerning laboratory experiments, all of them are stopped.”

Colombia

In Colombia the response to pandemic encompasses a reduction of care for dementia patients. Alejandra Guerrero (co-author) said that “in public hospitals the government has implemented actions that impact in patients with dementia, including preventing people above 70 years old from going out, stopping their outpatient consults and leaving them without their prescriptions. Vulnerable populations do not have internet access for telemedicine or even phone consultation.”

Cuba

Rather than opting for mitigation, Cuba is a regional exception and has also bet on its primary care system and added a containment plan (prevention and control). For Juan J. Llibre (co-author), “Medical students, and health workers were mobilized nationwide for door-to-door surveys to identify vulnerable people including people living with dementia and check for symptoms, and roll out a testing program according to WHO standards. Furthermore, contact tracing and early contact isolation procedures have been imposed on all confirmed cases.”

Dominican Republic

For Daisy Acosta (co-author) “The Dominican Alzheimer’s Association is cooperating with the department of mental health. Initially, we knew about the virus but nobody took seriously the protective measures announced. The curfew has been violated by thousands of citizens. As a consequence they have been taken to jail to force them to observe the rules.”

Ecuador

For Myriam de la Cruz (co-author), the pandemic “increases social isolation and diminishes public attention to dementia patients, even reducing food availability for elders.” A resident of Guayaquil (Carol Neira) commented “Many deceased people and their bodies were not removed, people do not respect the curfew, and hospitals have not enough capacity for so many infected.” For Lissette Duque (co-author) “COVID-19 will place our country’s economy in a critical situation. This will probably hit not only the unemployment, but also the capacity of the public health system to support vulnerable people.” For Gabriel Trueba (University San Francisco Quito) “there are reports in some indigenous communities, specifically Shushufindi-Cuyabeno, presenting with pneumonia; however, nobody has tested them due to difficulties reaching them.”

Mexico

The country also struggles with great disparities of a fragmented health care system. For Stefanie Piña (co-author) ,“If a person with dementia requires treatment for COVID-19, the hospital lacks capacity to prevent hospital-related adverse outcomes. At nursing homes and in the community, primary and secondary prevention measures are demanding extra effort from caregivers. This is leading to compromised safety for the dyad and to severe caregiver burnout that may end in patient mistreatment.”

Peru

The pictures above illustrates the people’s vulnerabilities and the unpreparedness of the health system. Top left: Enrique (64 years old, Trujillo) suffers from diabetes mellitus but cannot get medication since two months ago. He is a shoemaker working with a small mobile stall, and after months of quarantine, he has to go out to work. Top right: Juana (64 years old, Trujillo) is a merchant diagnosed with coronavirus 3 months ago, which led to her needing supplemental oxygen and intravenous medications. Given the collapse of the hospitals, she was treated at home by her daughter. She said the thought might lose her life, unable to perform simple activities (such as walking and eating) without great efforts. Now she is recovering. Bottom left: Enedina (65 years old, Lima) lives with her youngest son who lost his job due to the pandemic restrictions. They live in a precarious room, without electricity, water, or drainage. Bottom right: On the other side of Lima, 83-year-old Mrs. Rosita lives with her family in a wealthy district. Her daughter has noted typical dementia symptoms, which exacerbated since the quarantine. She doesn’t understand the isolation, needs constant monitoring, and urgently requires a neurological evaluation, but there are no services available due to the pandemic.

Photos and testimonies from Peru documented by Alexander Kornhuber and Maritza Pintado Caipa. Individuals and relatives portrayed in the photos have provided written consent for reproduction.

into poverty. Inequalities amplify the hardships of a pandemic.⁹ For vulnerable populations, quarantine is often an unreachable luxury as they have to work to survive.

Social containment measures can have a devastating impact on LACs’ households. Informal workers represent a significant share of the LACs’ workforce. Most have no access to social protection, and almost no savings to carry them through the pandemic.² Informal employees are the first to lose their jobs, while self-employed workers such as street sellers and small service providers are left with no source of income as streets became empty. Working from home may be a solu-

tion for educated middle-class workers, but it is out of reach for the most vulnerable.

Dementia is compromised by intersectional inequalities, including socioeconomic factors³⁰ and modifiable risk-related social determinants of health (SDH).³¹ These factors are stronger determinants of dementia prevalence than race or cultural identifiers,³⁰ are more accentuated in LACs,^{31,32} and will be violently worsened by COVID-19. Vulnerable and ethnic minorities suffering with dementia often receive inadequate care (access to diagnostic testing and medications, and near absence of 24-hour care)³³ and now will be exposed

BOX 2—Recommendations for Latin American and Caribbean Countries (LACs)**A. General recommendations**

- Coordination and integration of isolated actions to support dementia patients (prevention actions, test development, epidemiologic measures, awareness of dementia risk, recommendations for dissemination).

B. Specific recommendations**Testing dementia populations**

- Dementia patient inclusion in priority lists allowing widespread point-of-service testing will permit contact tracing and containment for those who test positive.
- Massive testing in LACs for priority populations including people living with dementia with allow innovative solutions (scalable technologies with low-cost instrumentation, non-specialized training, and available reagent supply chain).

Boosting regional coordination to actively engage in global response

- Coordination between available standards (i.e., Organization for Economic Co-operation and Development Policy Response to COVID-19, G20's large-scale coordination) and regional non-governmental organizations (NGOs).
- Networking between interregional agencies and multicentric research and interventions.
- Action-to-knowledge framework to prioritize most vulnerable dementia patients.
- Developing essential care required for dementia patients in different contexts considering the vast heterogeneity across LACs.

C. Brain health diplomacy actions

- Brain health diplomacy must build international partnerships to improve dementia care at micro- (individual), meso- (community), and macro- (national and transnational) levels.
- Multiregional NGOs focused on dementia (Alzheimer's Association, Alzheimer's Disease International, the Global Brain Health Institute), in partnership with local institutions must coordinate a leadership action plan.

to new constraints. With the anticipated poverty increase, most SDH will worsen. Coronavirus-related burnout syndrome, mental health risks, and patient mistreatment²⁸ will be accentuated by new economic inequalities. Among the more vulnerable, for example, Venezuelan refugees (with 8000% increase) have no guaranteed access to health and social services.³⁴ Similarly, the pandemic is already spreading across the LACs' rural indigenous communities,³⁵ which includes 42 million people in the region who are typically exposed to large inequalities.³⁶ Indigenous peoples suffer from early onset dementia and elevated mortality rate, with greater vulnerability to cognitive disorders.³⁷ In Brazil, the coronavirus-related indigenous death toll rate is double that of the general population.³⁶ These people are themselves invisible in most the health statistics. But dementia patients from these vulnerable populations are even less visible³⁶ during the pandemic.

4 | AN URGENT CALL FOR A COLLABORATIVE ACTION PLAN

The rise of SARS-CoV-2 pandemic creates an uncharted scenario that will undoubtedly impact LACs' long-term responses to dementia, even in the post-pandemic era. A LACs taskforce on dementia may help to articulate prevention actions, implement inexpensive SARS-CoV-2 test development, improve epidemiologic measures, increase awareness of atypical SARS-Cov-2 in people with dementia, identify best practices in underserved populations, offer information about dissemination

mechanisms, as well as transition to tailored levels of telemedicine and serve as a model for cooperation throughout LACs (see Box 2 for the actionable recommendations proposed in this paper). We assess two main actions requiring urgent response: testing and regional coordination. These actions are critical to avoid a long delay in the required actions toward public policy changes for dementia in LACs.¹⁴

4.1 | Toward massive testing to assess dementia populations

Strategies adopted elsewhere in the world as "flatten the curve" certainly apply to LACs and dementia populations, but the challenges of implementation of quarantine and social isolation are far greater. Along with these measures we need widespread point-of-service testing, contact tracing, and containment for those who test positive. How to implement a program of mitigation followed by containment is an enormous challenge and even greater challenge for elders especially those with dementia across LACs. In particular, the combination of socioeconomic constraints and patient conditions will make general quarantine unsustainable for the region in the long term. Therefore, we need reliable, massive, and efficient testing. Moreover, testing programs need to consider LTC facilities as a priority sector.

Any global action plan requires massive testing.^{38,39} Given the current limited testing capacity, the current diagnosis strategies are mainly restricted to priority lists (hospitalized patients and health care, aging, and underlying conditions, among others),⁴⁰ thereby reducing

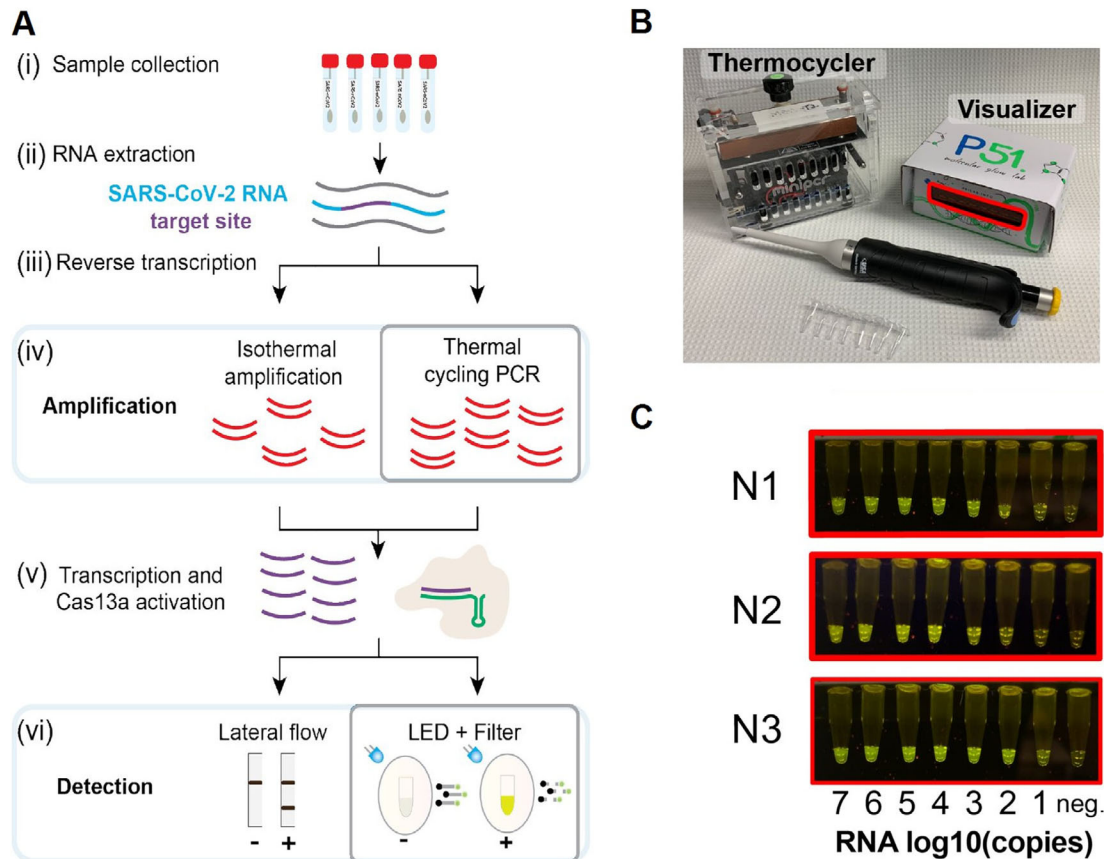


FIGURE 2 Cas13-based methods and detection of SARS-CoV-2 RNA using Cas13-based, Rugged, Equitable, Scalable Testing (CREST). A, Overview of Cas13-based detection methods and CREST modifications: (i–iii) Standard sample collection, RNA extraction, and reverse transcription. (iv) Amplification using cost-effective Taq polymerase and portable thermocyclers instead of isothermal reactions. (v) Transcription and Cas13 activation are followed by visualization with blue LED (~495 nm) and orange filter. B, Detection of SARS-CoV-2 RNA using CREST. The miniPCR mini16 thermocycler and P51 molecular fluorescence visualizer used in this study. Both are portable, can be operated with batteries, and have minimal footprint. C, Fluorescence visualization of N1, N2, and N3 synthetic targets using P51 visualizer. Reproduced with authorization from Rauch et al.⁴¹

the availability of massive testing among dementia patients. Testing for dementia patients will help the entire population because they represent a significant number of patients with severe complications requiring intensive health support. The percentage of dementia patients being infected appears to be high. According to the World Health Organization (WHO), COVID-19 mortality data in people with dementia is elevated, with most of COVID-19 deaths coming from LTC (two thirds of people in LTC have dementia); and is estimated that 75% of all COVID-19 care home deaths are people with dementia.

Massive testing in LACs for priority populations including dementia needs innovative actions. A variety of testing approaches exist. These include direct testing for the viral genome which in the cases of SARS-Cov2 is an RNA, testing for the viral protein called the antigen and testing for immune response to the virus, which involves detection of the antibodies. These tests provide different types of information. For example, detection of the viral genome indicates active infection even if the person is asymptomatic and detection of antibodies indicates a history of infection. Most of the current emphasis is on testing for the presence of the viral genome sequences using Reverse Transcription-

Polymerase Chain Reaction (RTqPCR) with a throat or nasal swab. Unfortunately, RTqPCR is limited, especially in underserved regions due to expensive reagents, a constricted supply chain, specialized instrumentation, and trained personnel. In comparison, CRISPR-based detection allows scalable, non-specialized performance and a more available reagent supply chain. Several of the authors (MZW, KSK, DA-A, CA) have developed such a test called CREST (Cas13-based, Rugged, Equitable, Scalable Testing⁴¹). CREST pairs commonplace and reliable biochemical methods (PCR) with low-cost instrumentation, without sacrificing detection sensitivity (Figure 2). CREST uses fluorescence visualizers for a quick binary interpretation of results, and provides a scalable sample collection (laboratory-made viral transport media, 3D-printed swabs) that is highly sensitive and requires minimal infrastructure. Results can be provided with Bluetooth-enabled thermocyclers that run using mobile device applications, combined with simple light-emitting diode (LED) visualizers, and uploaded with a smartphone camera. CREST can provide a point-of-care solution to increase COVID-19 surveillance and diagnostic testing. The same group has also reported a field-deployable RNA-extraction procedure called

PEARL.⁴² Use of the test in Ecuador is currently under way. Similarly, a laboratory in Brazil has developed a SARS-CoV-2 detection method in saliva, using RT-LAMP (loop mediated isothermal amplification),⁴³ which is also scalable and relatively inexpensive. Researchers from Havana's Immunoassay Center (CIE) designed a diagnostic test that uses the enzyme linked immunosorbent assay (ELISA) technique, which identifies small particles and germs that cause disease, and is based on ultramicroanalytic (SUMA) technology. Argentina is also developing potential massive testing kits, including CRISPR-based detection approaches.⁴⁴ In the future, these affordable and non-technically demanding tests may be combined via machine learning with clinical symptoms, exposure history, and clinical imaging (chest tomography) to improve diagnosis.⁴⁵ However, alternative testing strategies are not without limitations, in particular test sensitivity involving both false positive and false negative rates. Similar limitations of local technology availability call for additional cooperation, pondering the procedures with less time to obtain test results. Human recourses (delivered by health-care systems and dementia-related non-governmental organizations [NGOs]) are critical for providing local logistics for test administration.

The current testing capacity for coronavirus across LACs is limited, and an established infrastructure for diagnostic and laboratory testing is not available in several hospitals and related institutions in the region.⁹ Affordable and simple massive testing approaches like CREST would allow the tracking of people with cognitive impairment and dementia patients who are exposed to higher risks. Early identification of dementia patients with SARS-CoV-2 will reduce costs and mortality considerably.

Once testing of dementia patients is widely available, the next step is following up with the positive cases. To achieve this, international cooperation is critically need. For instance, the WHO-Alzheimer's Association International Cohort Study of Chronic Sequelae of SARS-CoV-2 (CNS-SARS-CoV-2) has established a global consortium to longitudinally assess individuals and characterize neurological and neuropsychiatric sequelae. As this consortium includes dementia patients, and several LACs are part of the initiative, the outcomes of this project will be relevant for the region. In particular, the CNS-SARS-CoV-2 initiative will provide a clearer picture of the role of viral infections on cognitive decline and dementia risk, and their impact in symptom development (eg, loss of smell/taste, seizures, stroke, delirium, etc.). The study of genetic and social determinants of health risks and their interaction with SARS-CoV-2 may also provide relevant pathways to understand the impact on the most vulnerable dementia patients in the region, as well as other long-term unexplored consequences of coronavirus-induced cognitive decline and dementia.

4.2 | Boosting regional coordination to actively engage in global responses

The COVID-19 pandemic has become a brain health catastrophe, and global actions coordinating economic, health, scientific, and technological actions are required to rebuild living standards and to anticipate

future pandemic scenarios.⁴⁶ The OECD Policy Response to COVID pointed to the complex, nested, interconnected systems needed to deliver solutions.⁴⁷ The G20 countries have called for large-scale coordination and science-based global response to overcome the pandemic. Solidarity is a key component for action. Clinical trials and subsidies must be coordinated and based on knowledge and solution sharing.⁴⁸ The European Parliament has requested that EU-funded medical technologies should be made available, accessible, and affordable. The SOLIDARITY trial (ISRCTN83971151) is a large global study (45 countries to date) to provide estimations of safety and efficacy of treatments that will allow stressed hospitals to participate. Small and non-coordinated trials are considered unethical under the current circumstances.⁴⁸ Networking has become crucial for developing global advances. Different interregional agencies (Horizon 2020, the National Institutes of Health, US Department of Defense) have facilitated multicentric research and interventions. Overburdened global health systems can be supported by free and open source scientific and medical hardware (FOSH).⁴⁹ FOSH works through a united global community and constitutes a key strategy highlighted in the 2019 Novel Coronavirus Global Research and Innovation Forum. Similarly, collaborative responses such as the High Performance Computing Consortium, or the Coronavirus Census Collective (an open-access platform that helps to predict the location of future outbreaks by combining surveys, diagnostic results, and geospatial data) are just some examples⁵⁰ of global networking. Consistent scientific evidence needs to be verified, composed, and evaluated with large-scale efforts.⁵¹ Any delay in joining global actions will worsen the consequences of the pandemic.

More tailored solutions are requested for Latin America. The combination of health, political, and economic emergency triggered by the coronavirus make the regional networks best placed to assess needs and lead planning, especially in low and middle income countries (LMIC)⁵² and LACs.⁵³ Regional coordination should also establish the priorities for the most vulnerable and orchestrate compensatory actions for patient suffering. LAC scientists, advocates, and health policymakers need to be included as equal partners in the global plans. This will allow the efficient distribution of global resources, as is the case of support from the Asia-PAHO collaboration for the general population of Latin America.⁹ Strategies for developing essential care required for dementia patients in different contexts should be identified at regional bases. As Latin America became a hot spot of the pandemic, the role of its regional initiatives connected with global responses becomes critical.⁵⁴ These actions, preliminary and imperfect, will require coordinated efforts to evolve toward more equitable solutions.⁵²

4.3 | Acknowledging the challenges of non-homogeneous scenarios across LACs

One important step to deliver an efficient regional action plan consists in identifying and incorporating the large heterogeneity across the region. Latin America is a very heterogeneous region, with socioeconomic and cultural contrasts, as well as different political,

health, and diplomacy structures. Homogenizing a vast region with widespread diversity will not work. LACs are not uniform, and some cities with stronger health organization and resources to face dementia needs (such as Havana, Medellin, Montevideo, Buenos Aires) can respond better than others (such as Guayaquil, Manaus, Lima, Iquitos). Even within the same country, this scenario has been highlighted in Guayaquil, Ecuador where health services were so overwhelmed that they were unable to clear the numerous bodies from the street. This situation contrasts with SARS-CoV-2 cases and mortality in Quito, where case numbers have been more comparable to other regions. These local differences may be explained by the acceptance of physical distancing and the use of masks in the community; however, it would be useful to survey for local viral strains that may be associated with phenotypic differences. Importantly, regional assessments must be conducted down to the level of municipalities and even more locally to guide remediation toward the areas of greatest need. In Peru, Lima is suffering one of the most severe impacts of COVID-19, but Cuzco, a very crowded tourist destination at high altitude, has had few deaths.⁹ Similar differences are also observed between countries in available resources, with Guatemala and Haiti having less than 200 ventilators between them,²⁴ but Argentina having more than 10,000.

Given this heterogeneity, not all initiatives will work well in different settings. The response to the pandemic is influenced by local, regional, national, and global policies and political decisions. Early containment measures in Germany lowered COVID-19 incidence and mortality, but these strategies might not be feasible or could have unintended consequences in Latin America. Similar positive results in some countries within LACs should be extrapolated to others with caution. Cuba, Argentina, and Costa Rica had better management of this unique situation by developing strict enforcement of social distancing and lockdown. In the Caribbean, specific actions for dementia include special focus on LTC, developing 24/7 help-lines, assessing mental health disorders in elders, and providing caregiving training and strategies to cope with loneliness.⁵⁵ Although many of these strategies can be potentially extrapolated to other countries in the region, they seem to work better for containment when the numbers are small, but less well for mitigation. Moreover, specific links among scientists, health workers, non-governmental organizations, and government should be carefully considered in each case when implementing regional strategies to deal with the full manifestation of the coronavirus.

Beyond these acknowledged differences, common problems triggered by the pandemic impacting dementia patients require a coordinated response supporting aggressive governmental investment. Importantly, the planet is globally connected and a highly infectious disease in one place will not remain there despite the radical solution of sealing off an entire country. Responses can be sustainable only if control measures are implemented nationally, regionally, and globally. PAHO has estimated that an additional \approx \$100,000,000 is required to support a basic response in the region to face the short-term effects of the crises. Beyond monetary efforts, urgent calls for organizational coalitions are required for LMIC¹ and dementia patients in LACs.⁵³

The Latin American and Caribbean consortium on dementia (LAC-CD), has developed a regional action plan for a coordinated and multilevel response to fight dementia.⁵⁶ This plan includes a knowledge-to action-framework (KtAF) to deliver coordinative programs involving hundreds of local institutions and carry out additional triangulation with regional NGOs. The LAC-CD coordinative plan must urgently consider additional challenges imposed by the pandemic,² connecting both local initiatives and global dementia strategies (as has been recently done in dementia care and prevention).

5 | THE ROLE OF NGOs AND BRAIN HEALTH DIPLOMACY FOR DEMENTIA IN LACs

Regional cooperation and shared experience for dementia cannot be ignored in this time of crisis. In other regions, coordinated plans improved the adequate responses to SARS-CoV-2 in aging populations.⁵⁷ Brain health diplomacy^{58,59} can help build international partnerships to improve dementia outcomes for LACs at micro- (individual), meso- (community), and macro- (national and transnational) levels. Large-scale diplomatic action may include efforts to coordinate lessons learned across other countries; share protocols; and establish multi-national agreements for research, advocacy, clinical care, and public health. By increasing coordination across countries, disciplines, and sectors already working on coronavirus and dementia in the region can bring novel solutions to current challenges. Brain health diplomacy should be led by multiregional NGOs focused on dementia such as the Alzheimer's Association (AA), Alzheimer's Disease International (ADI), or the Global Brain Health Institute (GBHI), in strong partnership with local institutions on the ground that can coordinate a leadership action plan supported by multilateral networking.

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AUTHOR CONTRIBUTIONS

Agustin Ibanez and Kenneth S. Kosik designed the proposal. Agustin Ibanez, Hernando Santamaria-Garcia, and Kenneth S. Kosik provided the first complete draft and searched the literature. All authors contributed to the draft. Gorka Navarrete prepared Figure 1. Kenneth S. Kosik and Bruce L. Miller provided revisions. All authors participated in discussing the content of the paper, contributed to editing, and approved the final version of the article.

CONFLICTS OF INTEREST

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