OPEN LETTER

Lessons from coronavirus disease 2019 (COVID-19) testing strategies in three lusophone countries [version 1; peer review: 1 approved with reservations]

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Abstract

During the coronavirus disease 2019 (COVID-19) pandemic, uncoordinated national responses have been observed around the world which have contributed to the difficulties in controlling the spread of the virus. This lack of dialogue between nations reflects several key determinants including the lack of platforms for non-English speaking researchers and healthcare professionals to engage with critical matters in their native languages. Here, we demonstrate how setting up a dedicated forum for Portuguese-speaking professionals from Brazil, Mozambique and Portugal facilitated the comparison of testing strategies undertaken by those countries during 2020. This working group was established in response to an open workshop conducted in Portuguese in March 2020, in which renowned scientists from lusophone countries were invited to share the COVID-19 responses in their respective countries. To date, the group has convened to address actions, in turn identifying the opportunity to publish the different established approaches to testing strategies undertaken by their countries. This effort highlighted that the governments of those three countries took very different

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Any reports and responses or comments on the article can be found at the end of the article.

approaches, from case definition to type of test most commonly deployed. This piece emphasizes the need for international bodies to acknowledge the importance of creating forums which are more inclusive to non-speaking English professionals who are at the frontline of healthcare response in challenging settings such as low- and middle-income countries. Finally, fostering approaches like this could represent an efficient strategy to facilitate dialogue, building the necessary steps for a more coordinated response to future global threats.

Keywords

covid-19, testing, public health, international collaboration

This article is included in the [Coronavirus \(COVID-19\)](#) collection.

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Introduction

The current coronavirus disease 2019 (COVID-19) pandemic has shed light on the need for coordinated international strategies to prepare and respond effectively to pandemics. Since the beginning of 2020, while active transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) crossed borders and affected all continents, countries pursued different approaches attempting to bring it under control¹. The adherence - or lack thereof - to scientific, evidence-based response strategies has impacted the performance of each country during this pandemic period, despite the fast-growing body of scientific evidence.

Examples of this uncoordinated international response include the unbalanced vaccine roll-out² and other public policies which were paramount before the approval of effective vaccines (and which are still important especially for countries that do not have access to sufficient vaccine doses). For instance, testing strategies and campaigns for public understanding of prevention methods varied widely in different countries. Whilst considering the effectiveness of communication strategies relies heavily on understanding cultural context, testing strategies should be guided by international standards, acknowledging that the variation in economic abilities will be an important driver in implementation and that political aspects should not be ignored.

In that context, The Global Health Network hosted an open virtual workshop on 31 March 2020 with researchers from Portuguese-speaking countries to engage in multilateral dialogue about ongoing local responses (recording available here: <https://youtu.be/ZUQwa4Mfex4>). In response, a working group (WG) was established as a forum for collaborative consultations in Portuguese, which enabled the core participation of several healthcare professionals and academics who might otherwise be excluded from international forums hosted in English. An email invitation was sent to all the participants who attended the open virtual workshop and the first WG meeting was held on 7 August 2020. Until March 2021, another 6 online meetings were held, where the group members discussed about the differences in testing strategies adopted by their countries and other gaps in the overall national COVID-19 responses. Importantly, the three countries represented in the WG shared a common cultural heritage but display acutely different economic status - each one representing a different tier of per capita gross national income according to the World Bank and United Nations classification: Portugal (high income), Brazil (middle income), and Mozambique (low income)³. This piece is a result of the sustained activity of the WG, in which different national testing strategies were observed and characterised, including the definitions of confirmed cases, the importance given to different types of tests and the reported testing capacity in the three countries during 2020.

Portugal

The Portuguese Directorate-General of Health indicated reverse transcriptase real-time polymerase chain reaction (RT-PCR) testing for people presenting acute respiratory symptoms with cough (new or aggravated), fever above 38.0°C or difficulty breathing/dyspnoea with no other known cause or contacts of confirmed cases⁴. The contact-tracing strategy adopted was to perform RT-PCR in all individuals (high and low risk) who were exposed to a confirmed case while they were in the transmission period. When the confirmed case was symptomatic, transmission period was considered from 48h before the symptoms started until the end of their isolation period (10–20 days according to symptomatology). For asymptomatic confirmed cases, transmission period was considered from 48h before the positive sample was collected for testing until the end of their isolation period (10 days after case confirmation)⁵. If RT-PCR tests are not available, sensitive ($\leq 90\%$) and specific ($\leq 97\%$) antigen rapid tests can be used to confirm infection⁶.

SARS-CoV-2 RT-PCR tests were performed by the Portuguese Public Health Service, including Instituto Nacional de Saúde Doutor Ricardo Jorge (INSA) and other laboratory hospitals trained for this purpose. In addition to these tests assured by the Portuguese Public Health Service, tests were available through private laboratories.

On 28th November 2020, testing rate was above 25 tests/1000 inhabitants/week, which is higher than the testing rate recommended by the World Health Organisation (WHO) to reliably evaluate transmission control^{7,8}. Importantly, in that period, the positive case rate in Portugal was 12.7% - WHO recommendations indicate that a pandemic is under control when the positive rate is $\leq 5\%$ ^{8,9}.

Brazil

The Brazilian Ministry of Health (MoH-Brazil) defined that a COVID-19 case can be confirmed based on diagnostic tools performed in clinical laboratories (RT-PCR or serological tests) or in drugstores by pharmacists (Lamp-PCR, antigen or antibody rapid tests), but also based solely on other findings, such as clinical manifestations of SARS-CoV-2 infection combined with anosmia or ageusia without known causes, or SARS combined with close contact with a confirmed case (14 days before symptom manifestations), or SARS combined with ground-glass opacity findings on lung imaging¹⁰. Importantly, each of the 27 subnational states had a specific protocol for managing suspected cases, which meant different cohorts of the population were tested based on their location.

Response to COVID-19 relied mostly on the free and universal public health system (Unified Health System - SUS). Since January 2020, RT-PCR tests for SARS-CoV-2 were performed at National Influenza Centers, with the support of PAHO/WHO. Additionally, the Oswaldo Cruz Foundation (Fiocruz) trained all 27 Central Public Health Laboratories for SARS-CoV-2 diagnostics, contributing to decentralizing testing capacity which allowed for testing in remote areas. Furthermore, public

universities and health institutions such as Fiocruz provided additional laboratory support.

In an effort to increase national testing capacity, the Brazilian National Agency of Sanitary Surveillance implemented an expedited process for testing options, and by 23rd November 2020, had approved a total of 722 diagnostic kits (RT-PCR and serologic rapid tests) for COVID-19¹¹. Importantly, of those, 493 were serologic rapid tests and 107 RT-PCR kits. This finding may indicate a governmental preference to invest in serological rapid tests as opposed to RT-PCR to diagnose COVID-19, which is against WHO recommendations¹². Of note, serological rapid tests are cheaper than RT-PCR tests. To date, there are no national guidelines from the MoH-Brazil on the use of antigen rapid tests to strengthen the Brazilian testing strategy.

According to MoH-Brazil reporting, since the end of July 2020, Brazil has sustained the screening rate higher than 1 test/1000 inhabitants/week, as recommended by WHO. Alarming, the national positive case rate in November 2020 was 30.81%¹³ which far exceeds the 5% positive rate endorsed by WHO as an indicator that the pandemic is under control.

Mozambique

The Ministry of Health Mozambique recommends RT-PCR testing for the diagnosis of COVID-19 in suspected cases, as indicated clinically and/or by epidemiological link¹⁴. Suspected cases include those detected passively in one of the surveillance health facilities or actively through contact tracing of confirmed cases. In October 2020, antigen rapid tests were also authorised to be used when and where RT-PCR tests were not available, and patients were in critical need of a diagnosis¹⁵.

Samples collected from public health centres were sent to the reference laboratory at the National Institute of Health (INS). Initially, RT-PCR testing capacity was limited, constrained

to 600 samples per day. In November 2020, testing was established at 1500 tests per day, as a result of the expansion of laboratory facilities. Furthermore, testing was also initiated in private hospitals, which were initially sending their samples to South African and Portuguese laboratories. The main challenges ranged from the lack of decentralized testing facilities to the unavailability of testing kits and personal protective equipment. In addition, delays in notifying patients have been observed due to a weak communications system in the public facilities. Nonetheless, the country's response upgraded gradually, with a comprehensive approach and multisector involvement, such as increased lab capacities and donation of kits, and PPE provided by governments and agencies, such as the WHO, the Korean Government and philanthropic organizations.

Despite the efforts to increase local capacity, in November 2020 the testing rate was still below 1 test/1000 inhabitants/week. Therefore, considering WHO guidelines⁸, the 6.6%⁹ positive rate registered at that time could not be used to evaluate the pandemic control in this country. In addition, the INS have started serological surveys in June 2020 to assess the evolution of the epidemic at the community level. Antibody prevalence was reported to be below 10% and, importantly, these surveys portrayed a heterogeneous pattern of community transmission between regions as well as among different working groups¹⁶.

Final considerations

Several important factors affect the responses deployed by each country. Therefore, countries need support to develop and maintain stronger health systems to undertake internationally standardised strategies, as they must be able to: (i) rapidly process samples and obtain results, (ii) communicate with patients; and (iii) implement effective contact tracing. Interestingly, even though two types of tests were predominantly used worldwide to track disease transmission and inform governmental mitigation interventions during 2020, national strategies varied widely, and no international guideline was followed in practice (Table 1).

Table 1. Commonly available diagnostic testing options for coronavirus disease 2019 (COVID-19).

REVERSE TRANSCRIPTASE REAL-TIME POLYMERASE CHAIN REACTION (RT-PCR)		
Target	Advantages	Critical considerations
Viral nucleic acid molecules	According to the latest World Health Organisation (WHO) guidance on SARS-CoV-2 diagnosis, RT-PCR is the only recommended test for case confirmation ¹⁷ . RT-PCR results can indicate patients who are currently infected and most likely able to transmit the virus to others.	RT-PCR tests require appropriate laboratory space, reagents, and trained staff to be performed and results take hours to days to be obtained. Appropriate timing of sample collection is also critical, as the viral load present in symptomatic and asymptomatic patients are reported to vary from several days before and after symptoms onset.
ANTIGEN RAPID TESTS		
Target	Advantages	Critical considerations
Viral antigens	Tests that detect SARS-CoV-2 antigens (such as proteins). They can be performed rapidly and at the point of care and thus may be more accessible with faster results compared to RT-PCR and commonly have high specificity ($\geq 97\%$).	These tests commonly lack sensitivity when compared to RT-PCR, which can lead to false-negative results. WHO recommends that only tests that meet the minimum performance requirements of $\geq 80\%$ sensitivity and $\geq 97\%$ specificity compared to a nucleic acid amplification reference assay should be used, and specifically in settings where RT-PCR is unavailable or where extensive turnaround times undermine clinical utility ¹⁸ .

SEROLOGICAL RAPID TESTS		
Target	Advantages	Critical considerations
Host antibodies against the virus	Tests that detect SARS-CoV-2 antibodies can be performed rapidly and at the point of care and thus may be more accessible with faster results compared to RT-PCR. Large-scale serologic screening with validated tests may be able to provide a measure of disease activity (by identifying people who were not diagnosed by RT-PCR or who may have had asymptomatic or subclinical infection) and also identify individuals who may have immunity to infection.	Cross-reaction with other coronaviruses can be a challenge to serological tests and the unknown duration of the immune response can also present a drawback. In addition, test performance, accuracy, sensitivity and specificity are variable and present a real challenge to the use of such tests. Also, the extent and duration of immune responses are still unclear, as current data show that the presence of antibodies alone may not confer immunity. In addition, the recent surge of novel variants may in itself undermine this strategy.

Note: The number of tested samples that come back as positive for SARS-CoV-2 (positive rate), is an important measure to evaluate if transmission is under control. According to WHO recommendations, a positive rate of less than 5% is one indicator that the pandemic is under control. Nevertheless, this indicator is only useful for countries where the testing rate is 1 test/1000 inhabitants/week⁸. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2, RT-PCR=reverse transcriptase real-time polymerase chain reaction.

Conclusion

Here, we provide evidence to support the need for active mechanisms for international discussion in different languages to enable fair access to relevant knowledge in local communities. This experience must be replicated for other languages such as Spanish, French, Arabic, among others. Speaking our native language, we were able to discuss and identify testing discrepancies in our home countries that might have played an important role in pandemic control. Importantly, different testing strategies, likely influenced by factors such

as gross per capita income, government ideology and weak national surveillance systems, will undermine the efficacy of global pandemic control. Therefore, only with efforts to engage local players in discussions to strengthen and coordinate international responses will it be possible to build an effective global strategy to mitigate the impact of future pandemics.

Data availability

No data are associated with this article.

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The aim of the article is unclear.

It is concluded that "we provide evidence to support the need for active mechanisms for international discussion in different languages to enable fair access to relevant knowledge in local communities", but the article does not show any type of comparative result, such as tables, figures, etc., on the main results and conclusions of the meetings with the working group. Perhaps it would be convenient to take several of the main points of the participation of the different members of each country in the forum (YouTube video) and place them in a comparative table for this open letter.

Although it is true that these three countries represent countries with different per capita rates, there are examples of non-English-speaking countries with different per capita indexes that handled the diagnosis and epidemiological data very well.

The government entities dedicated to managing the epidemiological data of each country have accredited personnel and laboratories to give a diagnosis and to record official data.

Accreditation is generally given by an international entity, which implies that accredited personnel understand and correctly handle the diagnosis. Once the staff and the laboratory are accredited, the language barrier is not a problem.

Is the rationale for the Open Letter provided in sufficient detail?

Partly

Does the article adequately reference differing views and opinions?

Partly

Are all factual statements correct, and are statements and arguments made adequately

supported by citations?

Yes

Is the Open Letter written in accessible language?

Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?

Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Virology, Microbiology, Emerging and Re-emerging viruses, Infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.