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Early response to COVID-19 in Brazil: The impact of a targeted approach to suspected cases and on epidemiological surveillance efforts ☆

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entered Brazil before travel restrictions and border closures were imposed. This study reports the characteristics of suspected and confirmed coronavirus disease 2019 (COVID-19) cases among symptomatic international travelers in Brazil and their contacts.

Methods: The REDCap platform developed by the Brazilian Ministry of Health was analyzed to identify and investigate suspected cases of COVID-19 recorded during the period January 1 to March 20, 2020. The impact of Brazil's targeted approach to suspected cases from specific countries on epidemiological surveillance efforts during the early stages of the COVID-19 pandemic were analyzed.

Results: Based on molecular RT-PCR tests, there were 217 (4.2%) confirmed, 1030 (20.1%) unconfirmed, 722 (14.1%) suspected, and 3157 (61.6%) non-investigated cases among travelers returning from countries included on the alert list for surveillance, as defined by the Ministry of Health. Among the 3372 travelers who went to countries not included on the alert list, there were 66 (2.0%) confirmed, 845 (25.3%) unconfirmed, 521 (15.6%) suspected, and 1914 (57.2%) non-investigated cases. A comparison of the characteristics of confirmed cases returning from alert and non-alert countries did not reveal a statistically significant difference in symptoms. Almost half of the hospitalized travelers with known travel dates and hospitalization status (53.6%) were inbound from countries not included on the alert list, and RT-PCR tests were reported for only 30.5%.

Conclusions: Policies adopted at entry points to contain the introduction of SARS-CoV-2 in Brazil were not ideal. An analysis of the early response shows that surveillance of travelers, including testing strategies, data standards, and reporting systems, was insufficient.

1. Introduction

On December 31, 2019, China confirmed an outbreak of atypical pneumonia with unknown etiology in Wuhan, Hubei Province [1]. With evidence of the growing dissemination of the novel coronavirus, formally named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the World Health Organization (WHO) declared a Public Health Emergency of International Concern on January 30, 2020, and a pandemic on March 11, 2020. Global travel was crucial to the rapid growth of cases in Wuhan and internationally. Indeed, air travel intensity to a country was identified as a robust predictor of the announced virus arrival time of SARS-CoV-2 in 2020 [2]. The main objective of this study was to analyze the impact on epidemiological surveillance efforts of Brazil's targeted approach of restricting suspected cases to travelers from specific countries during the early stages of the COVID-19 pandemic.

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There were many changes in guidelines for case definitions issued by countries in the early stages of the COVID-19 pandemic. Definitions of a suspected case generally account for sensitivity, while definitions of a confirmed case increase specificity. There were significant differences in case definition for 'suspected cases' of COVID-19 across countries in the early response to COVID-19 [3]. Greater sensitivity is important if cases are to be detected preemptively to ensure the containment of outbreaks. A more expansive criterion will result in greater sensitivity for case detection and more cases being confirmed, but will decrease specificity. The restricting of suspected case definitions may result in increased specificity. However, this negatively affects the sensitivity of case detection and the number of cases detected. During the COVID-19 pandemic, the sensitivity and specificity of case definitions were further complicated by the limited testing capacities in most countries [4].

Brazil did not close its borders preemptively and adopted a more restricted approach to the definition of suspected cases. The country concentrated its strategy on monitoring symptomatic international travelers from a restricted list of countries where community spread had been confirmed [5]. Surveillance efforts focused on travelers from this limited list, even though WHO guidelines updated on January 10, 2020 recommended investigating and testing gravely ill hospitalized individuals without a travel history. By examining whether there were consequences for epidemiological surveillance due to Brazil's decision to target its suspected case definition to travel from specific countries, it is hoped to contribute to a greater understanding of how travel restrictions can affect early outbreak responses.

There are several reasons why it is crucial to study how Brazil responded in the early stages of the pandemic. A country of continental dimensions, Brazil is home to 13 of the 20 largest air travel hubs in South America and more than half of all passengers that travel on the continent [6]. In Brazil, the right to health is constitutionally guaranteed, and public authorities must enact policies to reduce the population's risk of disease, including coordinating surveillance programs. The early response to SARS-CoV-2 in Brazil was distinct from previous health emergencies, such as the case of influenza A(H1N1)pdm09.

2. Methods

A retrospective analysis of COVID-19 cases reported in Brazil between January and March 2020 was conducted, with a focus on the impact of case definitions for travelers returning from specific countries on Brazil's early pandemic response. The study area was Brazil, and the study population was individuals who were suspected of having COVID-19 and reported to the Ministry of Health's REDCap platform between January 1 and March 20, 2020. The case definitions adopted in the study were based on the criteria used by the WHO and Brazilian government for identifying suspected and confirmed cases of SARS-CoV-2 infection, as well as the criteria for confirming community spread. The inclusion criteria for the study were suspected COVID-19 cases reported to the REDCap platform with a declared travel history or a history of contact with a traveler. The exclusion criteria were cases with missing information on travel history and duplicates.

The analysis strategy applied in the study was a quantitative analysis of cases registered on the REDCap platform, using variables such as travel dates, countries visited, final case classification, symptoms, laboratory test results, and hospitalization outcomes. The cases were analyzed by declared country of travel and declared dates of travel, and were quantified by country of origin and travel dates across five different periods. The policies recommended by the WHO and Brazilian government concerning international travel and epidemiological surveillance were also analyzed through an examination of official government laws, decrees, and ordinances.

WHO and Brazilian government bulletins and guidelines were reviewed to identify case definitions, the criteria used to identify suspected and confirmed cases of SARS-CoV-2 infection, and when community spread was confirmed in specific countries (see Table 1). Any instructions outlined in these documents regarding epidemiological surveillance policies for inbound travelers, including investigating and testing criteria for laboratory reverse transcription PCR (RT-PCR) tests, were also reviewed. Furthermore, additional information and clarifications were solicited through a transparency portal of the Brazilian government.

To analyze whether restrictions on the case definition for travelers returning from specific countries impacted Brazil's early COVID-19 pandemic response, the cases registered in the Ministry of Health's REDCap platform [7], which was created to report suspected COVID-19 cases, were analyzed. The platform includes information on travel dates, countries visited, final case classification (confirmed, probable, or discarded), symptoms, laboratory test sample collection, RT-PCR test results, and hospitalization outcomes for each case. All cases registered from January 1 to March 20, 2020 were analyzed, by declared country of travel and declared dates of travel. The end date for the study was defined as the period when community transmission was declared in Brazil.

Cases were quantified by country of origin and travel dates considering five periods: January 22–27, 2020 (during epidemiological weeks 4 and 5), January 28 to February 20, 2020 (during epidemiological weeks 5–8), February 21–23, 2020 (during epidemiological week 8), February 24 to March 3, 2020 (during epidemiological week 9), and March 3–20, 2020 (during epidemiological weeks 10–12). The list of countries included by the Ministry of Health increased from one city (Wuhan) in Period 1 to one country (China) in Period 2 and then to several countries in Periods 3, 4, and 5. Policies recommended by the WHO and the Brazilian government concerning international travel and epidemiological surveillance were also mapped based on an analysis of official government laws, decrees, and ordinances.

3. Results

3.1. Definitions of a suspected case

In the early stage of the pandemic, COVID-19 case definitions issued by both the WHO and the Brazilian government evolved as knowledge about the routes of transmission and disease manifestations improved [8]. On January 11, 2020, surveillance guidelines issued by the WHO emphasized a travel history to Wuhan, China, where the initial outbreak occurred, and a narrowly defined set of symptoms [9]. Concomitantly, the WHO recommended the investigation of severe acute respiratory infection (SARI) cases in healthcare workers and those with an unexpected evolution in outcomes. WHO guidelines on January 24, 2020, emphasized entry and exit screening of travelers [10]. The WHO advised investigating acute respiratory infections in healthcare workers and contacts of COVID-19 confirmed cases. By February 27, 2020, the WHO recommended that all cases involving SARI requiring hospitalization and acute respiratory infections without another diagnosis be considered suspected cases regardless of travel history [11].

The Ministry of Health adopted five definitions for suspected cases from January 22 to March 20, 2020 (see Table 1). The first definition was introduced on January 22, 2020. Before this period, there was no guidance on the investigation criteria. Therefore, cases in the REDCap platform with a travel date before January 22 were entered retrospectively and denominated as belonging to Period 0 [12]. Among travelers, suspected cases were those with fever, cough and/or respiratory symptoms and a history of travel to Wuhan Province in the last 14 days. A second period commenced on January 28, 2020 [13]. The criteria for identifying suspected cases were expanded based on whether an individual had returned from a country with community spread of SARS-CoV-2 with respiratory symptoms. On this date, the Ministry of Health announced that China was the only country meeting this condition [14]. (According to the Ministry of Health, "We define local transmission as laboratory confirmation of transmission of COVID-19 between people with a proven epidemiological link. Cases that occur among close family members or health professionals on a limited basis will not be

Table 1
Definitions of a suspected case adopted by the Ministry of Health (Brazil) and the World Health Organization, January 10 to March 20, 2020.

WHO		Ministry of Health, Brazil	
January 10, 2020[a]	February 27, 2020[b]	January 22, 2020[c]	January 28, 2020[d]
Suspected case 1 SARI (fever + cough) + hospital admission AND ONE OF FOLLOWING (1) Travel to Wuhan, Hubei Province, China, in the 14 days prior to symptom onset; OR (2) Health care worker working with SARIs; OR (3) Unusual or unexpected clinical course, without regard to the place of residence or history of travel. Suspected case 2 Acute respiratory illness of any degree of severity who, within 14 days before the onset of illness, had any of the following exposures: (1) Close physical contact with a symptomatic confirmed COVID-19 case; OR (2) A healthcare facility in a country where hospital-associated SARS-CoV-2 infections have been reported; OR (3) Direct contact with animals (if the animal source is identified) in countries where SARS-CoV-2 is circulating in animal populations.	Suspected case 1 Acute respiratory infection (fever + at least one sign or symptom of respiratory disease) AND no other etiology AND a history of travel to or residence in a country, area, or territory that has reported local transmission of COVID-19 disease during the 14 days prior to symptom onset. Suspected case 2 Acute respiratory illness AND contact with a confirmed or probable case of COVID-19 disease 14 days prior to the onset of symptoms. Suspected case 3 SARI (fever + at least one sign or symptom of respiratory disease) AND hospitalization AND no other etiology that fully explains the clinical presentation.	Suspected case 1 Fever AND/OR respiratory symptoms (e.g., cough or difficulty breathing) AND History of international travel to Wuhan 14 days before the onset of symptoms Suspected case 2 Fever AND/OR respiratory symptoms (e.g., cough or difficulty breathing) AND Close contact with SARS-CoV-2 suspect case 14 days before the onset of symptoms. Suspected case 3 Fever OR respiratory symptoms (e.g., cough or difficulty breathing) AND Close contact with a SARS-CoV-2 confirmed case 14 days before the onset of symptoms.	Suspected case 1 Fever AND at least one respiratory symptom (e.g., cough or difficulty breathing) AND History of international travel to country* with community spread 14 days before the onset of symptoms Suspected case 2 Fever OR respiratory symptoms (e.g., cough or difficulty breathing) AND Close contact with SARS-CoV-2 suspect case 14 days before the onset of symptoms. Suspected case 3 Fever OR respiratory symptoms (e.g., cough, or difficulty breathing) AND Close contact with a SARS-CoV-2 laboratory-confirmed case 14 days before the onset of symptoms.

COVID-19, coronavirus disease 2019; SARI, severe acute respiratory infection; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.
Sources:
[a] World Health Organization: Laboratory testing of human suspected cases of novel coronavirus (nCoV) infection; interim guidance, 10 January 2020.
[b] World Health Organization: Global surveillance for COVID-19 disease caused by human infection with the novel coronavirus (COVID-19); interim guidance, 27 February 2020.
[c] Ministério da Saúde: Boletim Epidemiológico, Vol. 51, No. dia 04/2020.
[d] Centro de Operações de Emergência em Saúde Pública para Doença pelo Coronavírus 2019 (COE-COVID-19), Ministério da Saúde: Boletim Epidemiológico 1 - Infecção pelo novo Coronavírus (2019-nCoV) 2020.
* The list of countries with community spread was modified and updated in the MOH epidemiological bulletins. See Table A1 in the Suplementary Materials.

considered local transmission. So far, the only area with local transmission is China. Areas with local transmission will be updated and made available on the Ministry of Health website." Authors' translation.) The respiratory infection symptoms that qualify as a suspected case were further detailed. The Ministry of Health expanded the definition of suspected cases to include those returning from an additional seven (on February 21) [15] and eight (on February 24) countries. These are the third and fourth periods, respectively. On March 3, the fifth period, the Ministry of Health expanded its case definition to include travelers from 12 additional countries [16]. In addition to São Paulo state, where the first case was confirmed, several states, including Bahia, Rio de Janeiro, and Espírito Santo, also registered SARS-CoV-2 infections before community transmission was declared. Community transmission was declared on March 20, 2020.

On January 10, 2020, the WHO guidelines recommended investigating and testing suspected cases using molecular RT-PCR tests [17]. From the onset of the COVID-19 pandemic, Brazil's reporting and testing eligibility criteria did not follow all of the WHO's recommendations. The suspected case definitions adopted by Brazil recommended the notification and laboratory investigation with RT-PCR testing for patients with acute respiratory illness or SARI with a history of travel to designated countries and their contacts. Hospitalized patients with unexplained clinical evolution were not included as cases that should be tested until community transmission was confirmed on March 20, 2020 [18].

3.2. REDCap results

After excluding duplicates and cases with missing information (n = 24 766), a total of 29 221 cases registered in the REDCap system were analyzed. Fig. 1 reports the volume of inbound travel from designated and non-designated countries. Of these cases, 9438 had travel history information, and the remainder were registered as contacts of persons who had traveled abroad (n = 19 783) (see **Supplementary Material** for contact analyses). Of those with a known travel history (n = 8498), 39.4% (n = 3346) had trip dates to countries that were not on the designated country list (see Table 2). There were 940 cases where the countries and/or travel dates were not informed, including travel to countries on the designated list.

The number of cases used by the Ministry of Health as a criterion to include a country on the alert list was heterogeneous [19] (see Supplementary Material Table A1). The Ministry of Health expanded its listing of China as a designated country of travel on January 28, 2020. On this date, the WHO reported 17 238 acute cases, and the organization no longer recommended targeting China as a limiting criterion for case definition. The Ministry of Health listed countries with no transmission (North Korea) and Cambodia with only one case recorded in the Epidemiological Bulletins of the WHO on the designated list of countries qualifying a case as a suspected case. In other countries with an expressive number of cases, the listing was delayed or not adopted. For example, although the United States reported its first case on January 23, 2020, the Ministry of Health did not consider inbound travelers from this country as suspected cases until March 3, 2020, even though nearly 50% of inbound travel to Brazil originated from this country and community transmission had been declared on February 26, 2020 [20].

Among travelers, 311 individuals from the REDCap system were confirmed by molecular diagnostic criteria by March 20, 2020 (see Table 2). However, only 217 (69.8%) of these cases were of travelers who had returned from the Ministry of Health's designated list of

Table 2
Inbound travelers with suspected cases from designated and non-designated countries by date of travel.

Designated countries (suspect cases) Non-designated countries (cases not considered suspect)							
Period	Countries	Confirmed[b]	Unconfirmed[c]	Suspected[d]	Not investigated[e]	Percentage RT-PCR test reported	Total
Period 0[a] 2020/01/01 to 2020/01/21	Asia: China, Hong Kong, Macao, and Thailand Europe: France, Italy, and Portugal Middle East: Israel South America: Argentina and Paraguay Southeast Asia: Philippines	0	17	1	8	65.4%	26
Period 1 2020/01/22 to 2020/01/27	Asia: Wuhan (China)	0	2	0	1	66.6%	3
	Africa: Angola, Ethiopia, Kenya, Nigeria, and South Africa Asia: China, Hong Kong, Japan, Macao, Malaysia, Singapore, Thailand, and Taiwan Europe: Austria, Denmark, England, Finland, France, Germany, Italy, Portugal, Spain, and Turkey Middle East: Egypt, Israel, Jordan, and Qatar North America: Canada and the United States of America Oceania: Australia South America: Argentina and Paraguay Southeast Asia: India and the Philippines	0	13	0	14	48.1%	27
Period 2 2020/01/28 to 2020/02/20	Asia: China	0	23	1	9	69.7%	33
	Africa: Angola, Cabo Verde, Morocco, and South Africa Asia: Cambodia, Indonesia, Japan, Malaysia, Maldives, Singapore, South Korea, Thailand, Taiwan, and Vietnam Europe: Andorra, Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Netherlands, Poland, Portugal, Russia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom, and the Vatican Middle East: Bahrain, Egypt, Iran, Israel, Qatar, and the United Arab Emirates North America: Bahamas, Canada, Costa Rica, Dominican Republic, Jamaica, Mexico, Panama, and the United States of America Oceania: Australia and New Zealand South America: Argentina, Bolivia, Chile, Colombia, Paraguay, Peru, Uruguay, and Venezuela	7	294	63	224	51.2%	588
Period 3 2020/02/21 to 2020/02/23	Asia: Cambodia, China, Japan, North Korea, Singapore, South Korea, Thailand, and Vietnam	0	9	0	6	60%	15
	Africa: Cabo Verde and Morocco Asia: Malaysia Europe: Austria, Belgium, Croatia, Czech Republic, Denmark, Germany, France, Hungary, Ireland, Italy, Malta, Netherlands, Poland, Portugal, Russia, San Marino, Slovenia, Spain, Switzerland, Turkey, United Kingdom, Ukraine, and the Vatican Middle East: Bahrain, Egypt, Israel, Qatar, and the United Arab Emirates North America: Canada, Grenada, Panama, and the United States of America Oceania: Australia South America: Argentina, Chile, Uruguay, and Venezuela Southeast Asia: India	8	152	40	97	53.9%	297

(*continued on next page*)

Table 2 (*continued*)

Designated countries (suspect cases)
Non-designated countries (cases not considered suspect)

Period	Countries	Confirmed[b]	Unconfirmed[c]	Suspected[d]	Not investigated[e]	Percentage RT-PCR test reported	Total
Period 4 2020/02/24 to 2020/03/02	Asia: Cambodia, China, Japan, Malaysia, North Korea, Singapore, South Korea, Thailand, and Vietnam Europe: Germany, France, and Italy Middle East: Iran and the United Arab Emirates, Oceania: Australia Southeast Asia: Philippines	22	448	137	406	46.4%	1013
	Africa: Angola, Cabo Verde, Morocco, Saint Helena, and South Africa Asia: Indonesia, Sri Lanka, Taiwan, Timor-Leste Europe: Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, Greece, Hungary, Iceland, Ireland, Latvia, Netherlands, Norway, Poland, Portugal, Russia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine, and the United Kingdom North America: Aruba, Bahamas, Canada, Cuba, Dominican Republic, Jamaica, Mexico, Panama, Puerto Rico, and the United States of America, Middle East: Egypt, Israel, Jordan, Kuwait, and Qatar Oceania: New Zealand South America: Argentina, Bolivia, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Uruguay, and Venezuela Southeast Asia: India	31	250	176	485	29.8%	942
Period 5 2020/03/03 to 2020/03/20	Asia: Cambodia, China, Indonesia, Japan, Malaysia, North Korea, Singapore, South Korea, Thailand, and Vietnam Europe: Croatia, Denmark, Finland, France, Germany, Greece, Italy, Netherlands, Norway, San Marino, Spain, Switzerland, and the United Kingdom Middle East: Iran, United Arab Emirates North America: Canada and the United States of America Oceania: Australia Southeast Asia: Philippines	195	548	584	2735	18.3%	4062
	Africa: Algeria, Angola, Cabo Verde, Ethiopia, Morocco, Mozambique, Nigeria, Rwanda, Saint Helena, Sao Tome and Principe, South Africa, and Tunisia Asia: Afghanistan, Maldives, Nepal, and Pakistan Europe: Albania, Austria, Belgium, Bulgaria, Czech Republic, Hungary, Ireland, Luxembourg, Malta, North Macedonia, Poland, Portugal, Russia, Slovakia, Sweden, Turkey, and Ukraine Middle East: Bahrain, Egypt, Israel, Qatar, and Saudi Arabia North America: Bahamas, Belize, Caribe, Costa Rica, Cuba, Curaçao, Dominican Republic, El Salvador, Grenada, Guadeloupe, Guatemala, Haiti, Honduras, Jamaica, Martinique, Mexico, Nicaragua, Panama, Puerto Rico and Saint Lucia Oceania: New Zealand South America: Argentina, Bolivia, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Uruguay, and Venezuela Southeast Asia: India	20	136	242	1094	10.4%	1492

(*continued on next page*)

Table 2 (*continued*)

Designated countries (suspect cases)
Non-designated countries (cases not considered suspect)

Period	Countries	Confirmed[b]	Unconfirmed[c]	Suspected[d]	Not investigated[e]	Percentage RT-PCR test reported	Total
No country or period information[f]	Africa: South Africa Asia: Cambodia, China, Hong Kong, Japan, South Korea, Thailand, and Vietnam Europe: Austria, Belgium, Denmark, France, Germany, Greece, Hungary, Italy, Malta, Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Spain, Sweden, Switzerland, Turkey, United Kingdom, and Vatican Middle East: Egypt, Israel, United Arab Emirates, and Saudi Arabia North America: Bahamas, Barbados, Canada, Cuba, Dominican Republic, Grenada, Guatemala, Mexico, Panama, Puerto Rico, the United States of America, and the United States Virgin Islands Oceania: Australia and New Zealand South America: Argentina, Bolivia, Chile, Colombia, Guyana, Paraguay, Peru, Uruguay, and Venezuela Southeast Asia: India	28	83	81	748	11.8%	940
Designated countries subtotal	217	1030	722	3157	24.3%	5126	
Non-designated countries subtotal	66	862	522	1922	27.5%	3372	
Total	311	1975	1325	5827	24.2%	9438	

Sources: REDCap and Epidemiological Bulletins of the Ministry of Health, Brazil (2020).

[a] In Period 0, the Brazilian government had not yet defined a list of restricted countries, and the REDCap notification system had not been created. During this period, the Ministry of Health reports investigated cases that were rumored to be likely related to travel.

[b] A confirmed case is a case with a positive test result based on an RT-PCR test.

[c] An unconfirmed case is a case with a negative test result based on an RT-PCR test.

[d] A suspected case not investigated was either not tested, or a test result was not registered.

[e] A case that was not investigated was either discarded (for unknown reasons) or had an invalid value (NA) in the final classification variable.

[f] The case contains no information about the country of inbound travel or the travel dates.

countries. The remaining confirmed cases, including the first seven positive RT-PCR tests among travelers recorded in Period 2, originated from international travelers from countries outside the Ministry of Health's designated list ($n = 66$), or had missing country or travel dates ($n = 28$). The remaining positive cases were identified among close contacts ($n = 323$). (There were also 3518 cases in which individuals were tested; of these, 23.7% were confirmed. However, no travel or contact information was available for these individuals. These cases were not analyzed in this study.)

A substantial proportion of travelers were not tested regardless of the inbound country of travel (75.8%). These cases are classified as not investigated and were either discarded or their outcomes were not registered. Among travelers on the Ministry of Health's designated country list (24.3% who were tested), the proportion of individuals tested with RT-PCR tests decreased as additional countries were included on the alert list. The proportion of travelers on the designated list who were tested was highest in Period 2 (69.7%) and decreased in Period 3 (60%), Period 4 (46.4%), and Period 5 (18.3%).

The share of uninvestigated cases was highest for travelers on the non-designated list of countries compared to those who had returned from countries on the designated list. Testing was undertaken for travelers outside the designated country list in 27.5% of cases. The proportion of travelers on the non-designated lists for which a sample was collected and an RT-PCR test was recorded was highest in Period 3 (53.9%). The share of cases that were not investigated was highest in Period 4 (70.2%) and Period 5 (89.5%). In the earlier periods, roughly 50% of suspected cases were tested even though their travel was to countries outside the designated list.

The percentage of travelers reporting symptoms was higher in those suspected cases who had entered Brazil after traveling to a non-designated country. The *P*-values in column 3 of Table 3 ($P < 0.001$) confirm a higher share of travelers on the official designated list with fever, shortness of breath, difficulty breathing, and cough. For all other symptoms, the percentage of travelers with self-identified manifestations was higher for those on the non-designated country list, and the difference in the proportion was statistically different with at least 95% confidence.

Information on hospitalization and travel dates was available for 8104 travelers (53.6% who had traveled to non-designated countries). Of these, the share of travelers requiring hospitalization was 6.3% ($n = 511$) (see Table 4). Of travelers who had traveled to a non-designated country, 7.3% ($n = 274$) were hospitalized. In contrast, of those who had traveled to designated countries, 4.8% ($n = 237$) were hospitalized. However, there are an additional 458 travelers without hospitalization information and 876 cases where hospitalization outcomes were reported, but the travel country or period was unavailable.

The highest proportion of travelers who required hospitalization due to their symptoms occurred in the earlier periods. The hospitalized travelers returned to Brazil from China, France, Hong Kong, Israel, Italy, Paraguay, and Portugal. Among these hospitalized travelers, RT-PCR samples were collected from 90.9% of these cases, but tests were conducted in only 63.6% of samples, and all of these were negative. When suspected cases were confined to inbound travelers from Wuhan in Period 1, a higher number of hospitalized travelers returned from another city and/or country ($n = 7$) versus Wuhan ($n = 2$). Although samples were collected to diagnose specimens for SARS-CoV-2 infection in the majority of these cases regardless of the country of travel, tests were

only performed for 50% of travelers from Wuhan and 42.8% from other countries.

These patterns were repeated in Period 2, when the Ministry of Health restricted suspected cases to those who had traveled to China (n = 7). Most hospitalized cases in this period were travelers who had not traveled to China (n = 77). One of these cases was a traveler from France who returned to Brasilia and was confirmed as having COVID-19 while hospitalized. A reduced proportion of these travelers (89.6%) had laboratory specimens collected, and of these, an even lower percentage (66.2%) had tests performed.

Period 3 was short but represented the first effort by the Ministry of Health to consider suspected cases from countries other than China.

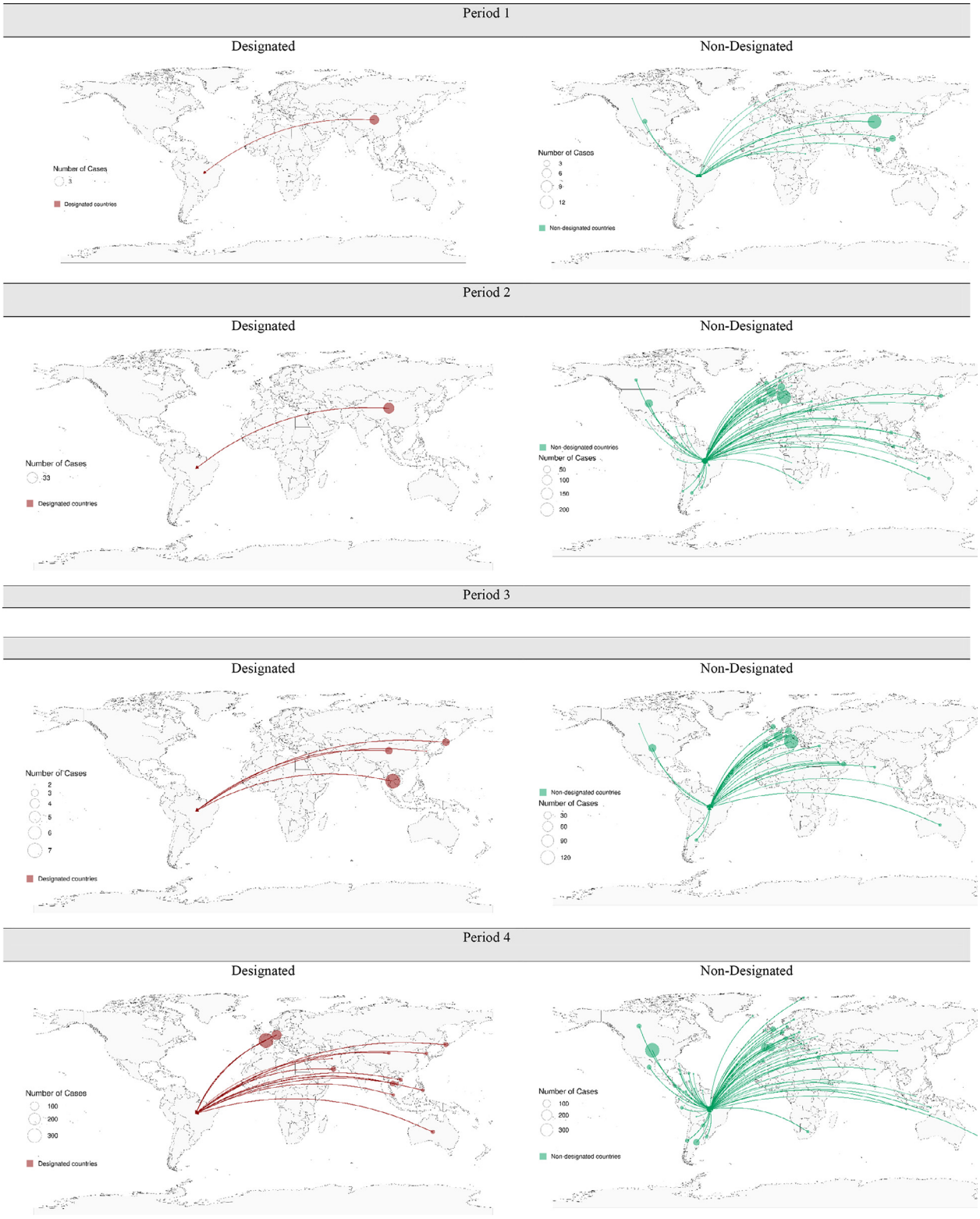
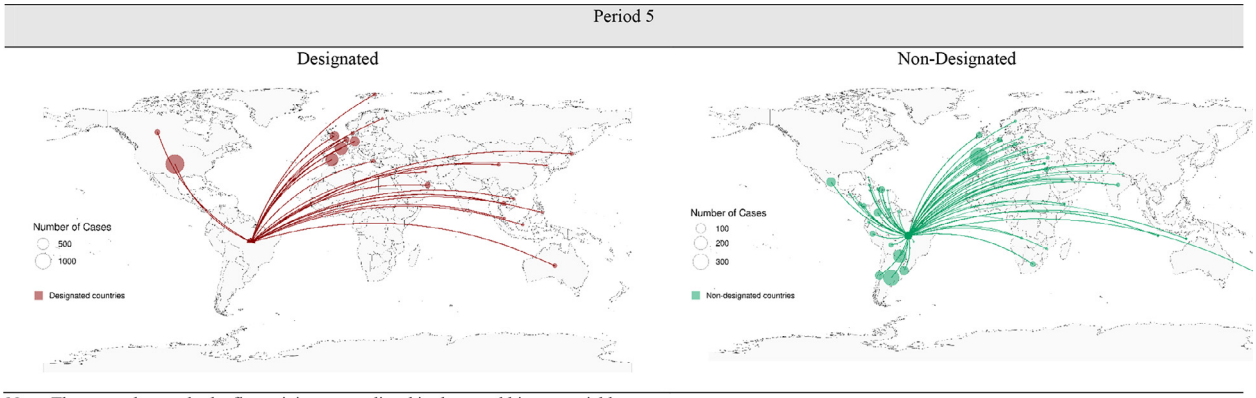


Fig. 1. Inflow of travelers from designated and non-designated countries to Brazil during the five periods.



Note: The maps show only the first origin country listed in the travel history variable.

Fig. 1. Continued

Table 3
Number of cases (%) registering different symptoms for travelers from designated and non-designated countries.

Symptom		Travelers from designated countries (TFDC) $n = 5126$	Travelers from non-designated countries (TFNDC) $n = 3372$	*P*-value for the difference in proportions of TFDC and TFNDC
Fever and respiratory symptoms	Fever	3216 (62.7%)	2380 (70.6%)	<0.001*
	Shortness of breath or difficulty breathing	1110 (21.6%)	922 (27.3%)	<0.001*
	Cough	3904 (76.2%)	2768 (82.1%)	<0.001*
Other symptoms	Headache	1571 (30.6%)	1152 (34.2%)	<0.001*
	Sore throat	2462 (48.0%)	1769 (52.5%)	<0.001*
	Myalgia or arthralgia	1091 (21.3%)	837 (24.8%)	<0.001*
	Congestion or runny nose	2924 (57.0%)	1966 (58.3%)	0.259
	Weakness	646 (12.6%)	510 (15.1%)	0.001**
	Sputum production	315 (6.1%)	263 (7.8%)	0.003**
	Other symptoms[a]	1643 (32.1%)	1247 (37.0%)	<0.001*

Source: REDCap and Epidemiological Bulletins of the Ministry of Health, Brazil (2020).
*Significant at 0.1%. **Significant at 1.5%. ***Significant at 10%.
[a] This category includes the following symptoms: diarrhea, nausea or vomiting, irritability or confusion, chills, conjunctivitis, difficulty swallowing, red spots on the skin, swollen lymph nodes, nasal flaring, O_2 saturation <95%, cyanosis signs, and intercostal retraction.

The Ministry of Health restricted suspected cases to travelers from other Asian countries (e.g., Cambodia, China, Japan, North Korea, Singapore, South Korea, Thailand, and Vietnam). Few hospitalized travelers from these countries returned to Brazil ($n = 2$). Individuals requiring hospitalization who had returned from traveling to other countries ($n = 28$) were less likely to have laboratory specimens collected (92.8%) or processed (50%). One of these hospitalized travelers who returned to Sao Paulo from Italy tested positive for SARS-CoV-2. He had his sample collected on March 5, 2020.

There was a significant rise in the number of hospitalized cases in Period 4 among travelers ($n = 125$). Hospitalized cases were highest in individuals who had returned from designated countries ($n = 72$) and the majority of these cases were of individuals who had returned to Brazil from Italy and the Middle East. Among hospitalized cases from designated countries with known travel and hospitalization dates, RT-PCR test results were only reported for 70.8%. For travelers who had returned from countries that were not on the Ministry of Health's designated list and for whom hospitalization information was available ($n = 53$), only 37.7% of RT-PCR test results were reported.

In Period 5 (March 3–20, 2020; during epidemiological weeks 10–12), there were 5554 travelers reported, and 73.1% of these referred to travel originating in the now-expanded list of designated countries. The percentage of hospitalized suspected travelers was 4.0% ($n = 154$) for the designated list of countries and 6.9% ($n = 98$) for the non-designated countries. In both groups, the percentage of laboratory specimens collected was relatively high (85.1% for designated country travelers and 89.8% for non-designated country travelers), but only a small proportion of RT-PCR test results were reported, 25.3% and 17.3%, respectively. Seventeen travelers who had returned from designated countries and two travelers to non-designated countries tested positive for SARS-CoV-2.

4. Discussion

The early response to SARS-CoV-2 in Brazil was distinct from that for influenza A(H1N1)pdm09. Brazil adopted a coordinated national emergency response program that included coordination at the federal, state, and municipal levels to ensure the monitoring of incoming travelers at airports, procurement, and widespread distribution of testing and treatment [21]. In 2005, the Ministry of Health prepared a plan to deal with a possible influenza pandemic, following the WHO guidelines, dividing it into an inter-pandemic period, pandemic alert, and post-pandemic [22].

Table 4
Number of hospitalization cases for travelers by travel arrival date, percentage RT-PCR samples collected, and percentage RT-PCR tests reported.

Period	Hospitalized		Not hospitalized		Unknown/invalid hospitalization data		Total
	Travelers from alert countries	Travelers from non-alert countries	Travelers from alert countries	Travelers from non-alert countries	Travelers from alert countries	Travelers from non-alert countries	
Period 0[a]	0	11	0	14	0	01	26
2020/01/01 –	(0%)	(90.9%)	(0%)	(100%)	(0%)	(0%)	(92.3%)
2020/01/21	(0%)	(63.6%)	(0%)	(71.4%)	(0%)	(0%)	(65.4%)
Period 1	02	07	01	19	0	01	30
2020/01/22 –	(100%)	(85.7%)	(100%)	(94.7%)	(0%)	(100%)	(93.3%)
2020/01/27	(50%)	(42.8%)	(100%)	(47.4%)	(0%)	(100%)	(50%)
Period 2	07	77	23	486	03	25	621
2020/01/28	(100%)	(89.6%)	(91.3%)	(84.4%)	(100%)	(76%)	(85.2%)
–2020/02/20	(85.7%)	(66.2%)	(60.9%)	(49.4%)	(100%)	(40%)	(52.2%)
Period 3	02	28	12	257	01	12	312
2020/02/21 –	(100%)	(92.8%)	(75%)	(89.1%)	(100%)	(83.3%)	(88.8%)
2020/02/23	(100%)	(50%)	(50%)	(54.9%)	(100%)	(41.7%)	(54.2%)
Period 4	72	53	902	842	39	47	1955
2020/02/24 –	(93%)	(90.6%)	(87.5%)	(85.3%)	(84.6%)	(65.9%)	(86.2%)
2020/03/02	(70.8%)	(37.7%)	(44%)	(29.7%)	(56.4%)	(23.4%)	(38.4%)
Period 5	154	98	3718	1319	190	75	5554
2020/03/03 –	(85.1%)	(89.8%)	(82.9%)	(79.5%)	(63.1%)	(48%)	(81.2%)
2020/03/20	(25.3%)	(17.3%)	(18%)	(10%)	(18.4%)	(9.3%)	(16.2%)
No country or period	22	50	316	488	31	33	940
information[b]	(90.9%)	(86%)	(80.4%)	(81.3%)	(64.5%)	(42.4%)	(79.6%)
	(36.4%)	(6%)	(13.3%)	(10.9%)	(3.2%)	(12.1%)	(11.8%)
Total with travel	237	274	4656	2937	233	161	8232
dates and	(88.1%)	(90.1%)	(83.8%)	(83%)	(67.4%)	(60.2%)	(85.7%)
hospitalization status	(41.7%)	(40.9%)	(23.3%)	(26.6%)	(26.2%)	(21.1%)	(26.4%)
Total	259	324	4972	3425	264	194	9438
	(88.4%)	(89.5%)	(83.6%)	(82.8%)	(67%)	(57.2%)	(82.6%)
	(41.3%)	(35.5%)	(22.7%)	(24.4%)	(23.5%)	(19.6%)	(24.2%)

Sources: REDCap and Epidemiological Bulletins of the Ministry of Health, Brazil (2020).
[a] In Period 0, the Brazilian government had not yet defined a list of restricted countries, and the REDCap notification system had not been created.
[b] The case contains no information about the country of inbound travel or the travel dates.

In the early stage, from the first reported cases in California in April to the declaration of community transmission in Brazil in July 2009, the Ministry's protocol encouraged the widespread testing and investigation of symptomatic international travelers and suspected cases among contacts without limiting suspected cases to a restricted list of countries.

In the case of SARS-CoV-2, health authorities established criteria to limit which cases should be tested [23]. The evidence revealed by the analysis of the early response data for Brazil underscores the importance of adopting case definition criteria that have increased sensitivity for identifying suspected cases in the early stages of a global pandemic, such as the COVID-19 pandemic. The first RT-PCR tests that tested positive for SARS-CoV-2 were among travelers from outside the Ministry of Health's designated list of countries. The first positive cases occurred in Period 2 when seven of these travelers tested positive for SARS-CoV-2 (28/01/2020 to 20/02/2020) and when the Ministry of Health limited suspected cases to those travelers who were inbound from China. The travelers who tested positive in this period were inbound from France, the Netherlands, Spain, and the United States of America. These travelers arrived in Brazil between February 10 and 19, reported symptoms from February 26, and were notified to the Ministry of Health between February 28 and March 18. In contrast, no positive cases were identified among travelers from the targeted list of countries for this period. A similar pattern occurred in Period 3. Eight travelers returning from Germany, Italy, Netherlands, Switzerland, and the United States of America tested positive for SARS-CoV-2, and no individuals tested from the designated inbound country travel list were identified as positive.

Since early January 2020, WHO guidelines advised monitoring hospitalization outcomes where the evolution was unexpected, regardless of travel history. The Ministry of Health could have used hospitalization data among travelers to expand the list of suspected cases, thus increasing the possibility of case detection. As early as epidemiological week 4, the REDCap system received notifications of the first cases of travelers requiring hospitalization for the treatment of respiratory infection. The rate of hospitalized travelers was higher in the first weeks of 2020 for travelers from countries not on the Ministry of Health's country alert list. These trends could have been used as an early warning.

In conclusion, in this study, it was observed that several factors affected the effectiveness of containment of the spread of SARS-CoV-2 in Brazil. The study results stress that pandemic preparedness can be significantly enhanced by improving policy decisions for travelers, their contacts, hospital workers, and hospitalized cases, including decisions directed at securing and ensuring an effective testing program and health data system infrastructure. There are some features of the Brazilian response that could have potentially helped the early response to be more effective. Both the unified public health system and the system mandating the notification of severe respiratory infection cases were assets that could have enhanced Brazil's capabilities in the early COVID-19 pandemic to undertake epidemiological surveillance. However, it is important to note that SIVEP-Gripe was not developed to monitor asymptomatic and/or acute respiratory infection cases, or the travel history of patients and their close contacts.

There is growing consensus that each country's actions have affected other nations in the COVID-19 pandemic. The findings of the present study corroborate those of studies that have shown that Brazil contributed to the worsening of the pandemic spread within its borders and, as a result, in other countries. Over the short and medium term, some studies have shown how the impact of insufficient surveillance of travelers and border monitoring resulted in Brazil contributing to infections in other countries. Furthermore, as cases surged, the rising infections also contributed to the rise of new variants.

Declarations

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Ethical approval: This study used anonymized data collected by the Ministry of Health. Ethical approval was not required.

Conflict of interest: The authors declare no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2023.04.011.

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