Pandemic H1N1 influenza in Brazil: Analysis of the first 34,506 notified cases of influenza-like illness with severe acute respiratory infection (SARI)

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Recently, the brunt of the current influenza pandemic has been felt in the southern hemisphere. We report an analysis of the first 34,506 cases of influenza-like illness with severe acute respiratory infection (SARI) notified in Brazil during the epidemiological weeks 16 to 33. The 5,747 confirmed cases of pandemic H1N1 influenza showed two incidence peaks across the age span: one in children up to the age of five years (3.8/100,000) and one in individuals aged 20 to 29 years (4.6/100,000). People over the age of 60 had the lowest incidence (1.1/100,000 inhabitants). The epidemic peaked rapidly. Ninety-four percent of cases were concentrated in two of Brazil's five geographic regions – the south and southeast, regions that have a more temperate climate and thus colder winters. Case-fatality of pandemic H1N1 influenza presenting with SARI was 11.2% (95% confidence interval (CI): 10.4%-12.1%). People with a reported comorbidity had approximately twice the risk of those without (relative risk=1.89; 95%CI: 1.64-2.18).

Introduction

Brazil is second in the Americas and fifth in the world in population, and, as of 14 September, one of the countries most affected by the H1N1 influenza pandemic . The first laboratory-confirmed case of pandemic H1N1 influenza was detected in Brazil on 7 May 2009, during the epidemiological week 17 (EW17, ending 2 May). Until early July, most cases detected in Brazil through a surveillance system specifically set up for pandemic H1N1 influenza, were associated with recent travel to North America (Canada, Mexico and the United States) or Argentina, or had been in contact with suspected and confirmed cases with recent travel to affected areas. On 16 July (EW28), Brazil acknowledged its first case due to sustained transmission. Thereafter, notification of cases without link with international travel increased steadily, and cases spread across the country. As of 21 August 2009 (EW 33), 110,113 confirmed cases had been notified in all 35 countries in the Americas, with 1,876 deaths, 82% (1,876/2,185) of the total deaths worldwide [1,2].

The present paper describes the epidemiological profile of influenza-like illness (ILI) with severe acute respiratory infection (SARI), occurred during EW16 to 33 in Brazil. Case-fatality by sex and presence of comorbidity is also presented.

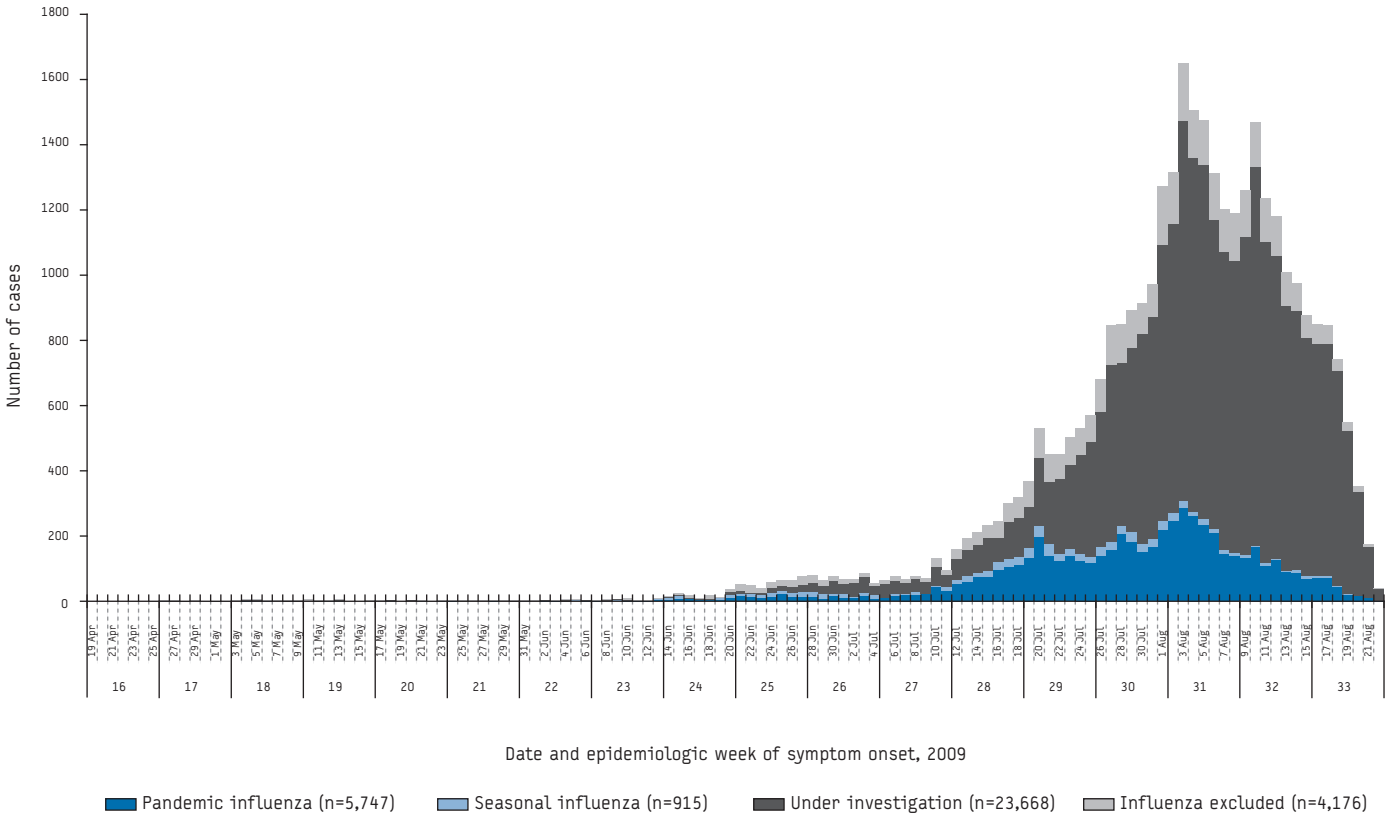
Methods

We obtained data from Brazil's case notification system for influenza-like illness by the pandemic influenza A(H1N1)v virus. Seasonal influenza case notification is not mandatory in Brazil, unless a novel strain is detected or there is a severe seasonal outbreak [3]. In Brazil, such notification is implemented through our national surveillance information system of notifiable diseases (SINAN). For pandemic influenza, an online form is utilised which gathers, among other things, information on demographics, presence of pregnancy, clinical findings, risk factors (including comorbidity) and outcome [4]. Comorbidities that historically represent an increased risk of poor outcome, such as chronic cardiovascular, respiratory, metabolic or renal conditions, haemoglobinopathies and immunodepression, are entered through check-boxes. An open field allows entering of additional information about specific clinic-related conditions.

Brazil initially adopted a case definition of influenza A(H1N1) v that included the following: fever >38ºC, cough, and close contact with an infected person or a travel history to countries with documented cases in the last 10 days. Additional symptoms could include headache and muscle or joint pain. That case definition, which served during the containment phase of the epidemic in Brazil, lasted until epidemic week 28. After EW28, given evidence of sustained influenza transmission within the country, the Brazilian Ministry of Health changed the definition for mandatory notification of suspected influenza cases to fever >38ºC, cough, and dyspnoea or death, i.e. the case definition was limited to cases of SARI. Laboratory investigation was also restricted to SARI cases. The presence of SARI, during both phases, was captured through the above-mentioned surveillance information system; these online records are updated whenever necessary, including outcome.

Figure 1

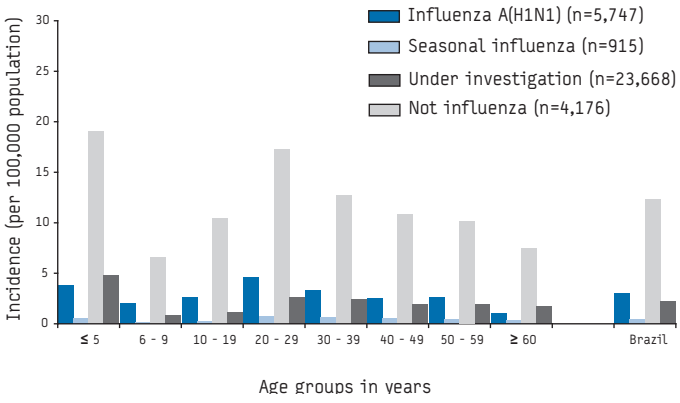
Number of notified cases of influenza-like illness with severe acute respiratory infection by date and week of symptom onset, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506)



Source: SINAN/MoH Brazil

Figure 2

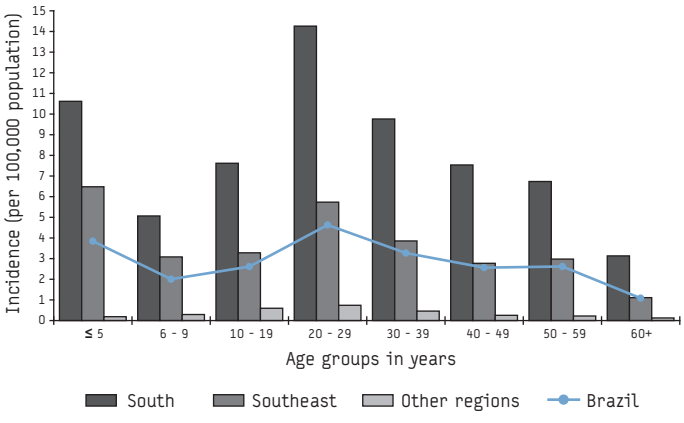
Incidence of notified cases of influenza-like illness with severe acute respiratory infection by age group, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506)



Source: SINAN/MoH Brazil

Figure 3

Incidence of laboratory-confirmed cases of pandemic H1N1 influenza 2009 with severe acute respiratory infection by age and geographical region, Brazil, epidemiological weeks 16 to 33, 2009 (n=5,745)



Source: SINAN/MoH Brazil

Laboratory diagnosis of influenza and the causative influenza virus strain was confirmed in respiratory samples (nasopharyngeal and pharyngeal swabs) with real-time RT-PCR with specific primers for pandemic H1N1 influenza, performed at reference laboratories of the Brazilian National Health System throughout the country. This report analyses data obtained until the end of EW34.

We describe the incidence of cases of ILI with SARI by age and geographic distribution of the cases as well as by calendar and epidemiologic weeks, the latter as defined by the Pan American Health Organization (PAHO) and the World Health Organization (WHO) [5], We also describe the frequency of and case-fatality by sex, pregnancy and the presence of reported comorbidities, presenting relative risks with 95% confidence intervals.

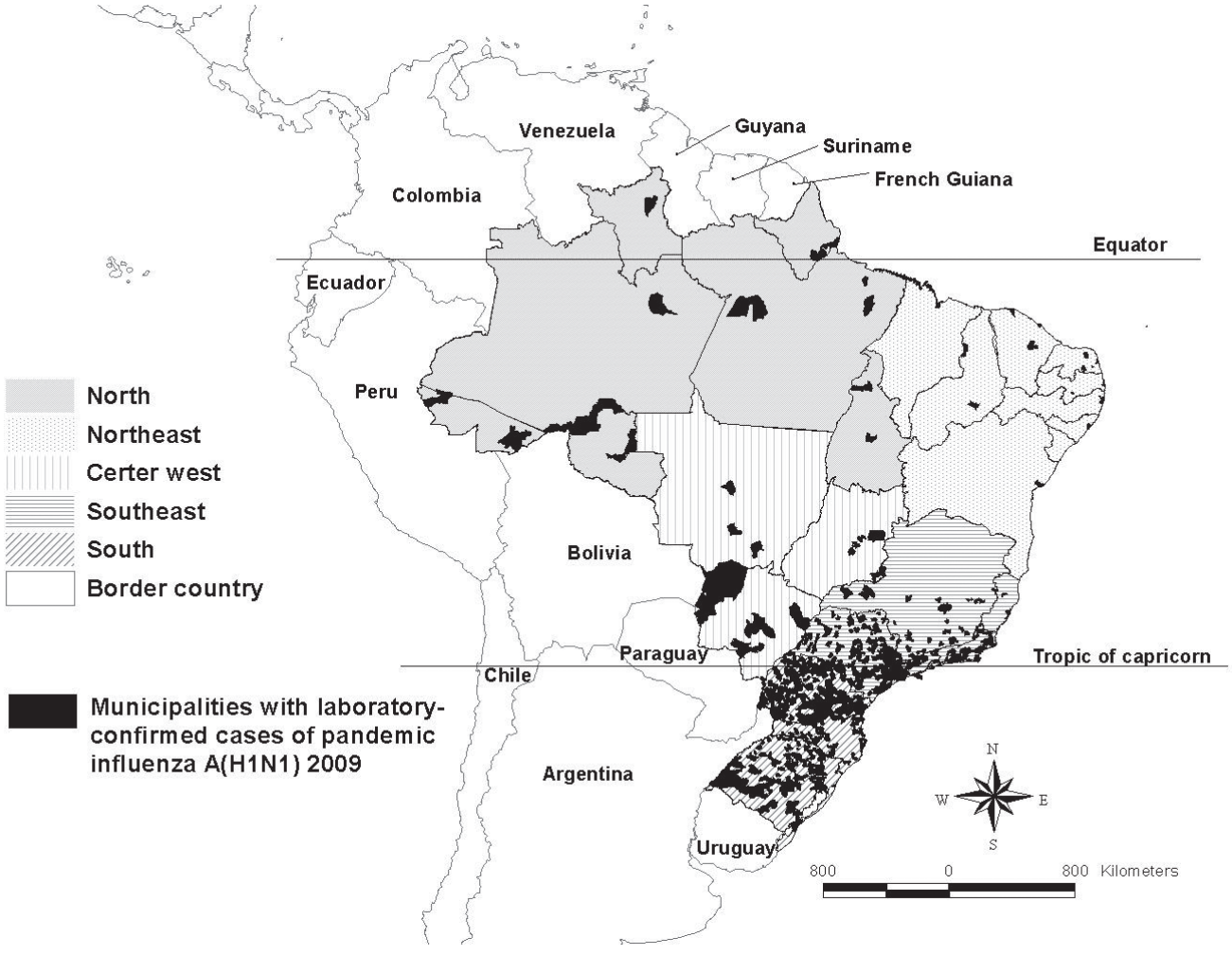
Results

During EW16-33, a total of 34,506 cases of influenza-like illness with SARI were reported in Brazil (Figure 1). From mid-July, the number of cases increased considerably. A total of 5,747 (16.7%) cases were laboratory-confirmed as pandemic H1N1 influenza. Of the remaining SARI cases, 915 (2.7%) were confirmed to be seasonal influenza, for 4,176 (12.1%) influenza was excluded as a cause, and the remaining 23,668 (68.6%) were either still under investigation at the end of EW34, when we closed our database for analysis (approximately 50% of those remaining), or were without specimen for investigation.

Of the 5,747 confirmed cases of pandemic influenza, 3,249 (56.5%) were women. The median age of all confirmed cases was 26 years (range: 0-90 years). The majority of cases (56%) were between 20 and 49 years-old. In addition to SARI-defining symptoms, the most frequent symptoms reported among the confirmed cases were myalgia (62.2%), rhinorrhoea (54%) and chills (53.4%).

Figure 4

Laboratory-confirmed cases of pandemic H1N1 influenza 2009 with severe acute respiratory infection by municipality. Brazil, epidemiological weeks 16 to 33, 2009 (n=5,747)



Data Source: SINAN (Brazilian Information System of Compulsory Notification); Shape File: IBGE (Brazilian Institute of Geography and Statistics).

Figure 2 shows the incidence of influenza-like illness with SARI during the study period according to the aforementioned diagnostic categories and age groups. The incidence was 3.0/100,000 inhabitants with two peaks – one in the group of up to five year-olds (3.8/100,000) and one in the group of 20-29 year-olds (4.6 per 100,000).

The spatial distribution of overall influenza-like cases amongst the five Brazilian regions is shown in Figures 3 and 4. Brazil's southeastern and southern regions were most affected, with incidences of 3.7/100,000 inhabitants and 8.6/100,000 inhabitants, respectively. Incidence was highest in municipalities bordering Argentina, Uruguay and Paraguay, and in temperate zone states with a more rigorous winter season. The other regions (North, Northeast and Center West) jointly contributed only with 6% of total cases.

Among the 2,256 women of childbearing age (15-49 years), 525 (23.3%) were pregnant (Table 1). Table 1 also presents the frequency of comorbidity in cases of SARI, and among those with confirmed pandemic influenza. For 33.3% of all SARI cases, at least one comorbidity was noted, chronic lower respiratory disease being the most frequently reported (27.2%), followed by chronic metabolic diseases (16.2%).

A total of 1,567 deaths occurred among cases of ILI with SARI, 645 of which were confirmed for pandemic influenza (Table 2). The case fatality rate was 4.5% among all ILI with SARI cases and 11.2% among those with confirmed pandemic influenza. Case fatality varied little between men and women (11.4% versus 11.1% for SARI due to pandemic influenza and 4.9% versus 4.3% for SARI overall). Confirmed cases for whom a comorbidity was reported had

Table 1

Frequency of characteristics among cases of influenza-like illness with severe acute respiratory infection, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506 including 5,747 confirmed pandemic H1N1 influenza cases)

Characteristics	Pandemic influenza A (H1N1) (n=5,747)		All SARI cases (n=34,506)	
	N	%	N	%
Sex				
Female	3,249	56.5	19,850	57.5
Male	2,498	43.5	14,656	42.4
Pregnancy (among women aged 15-49 years)				
No	1,323	58.6	8,276	61.7
Yes	525	23.3	2,789	20.8
1st trimester	86	3.8	544	4.1
2nd trimester	192	8.5	1,093	8.1
3rd trimester	225	10.0	1,046	7.8
Unknown gestational age	22	1.0	106	0.8
Unknown	408	18.1	2,353	17.5
Comorbidity*				
No comorbidity	3,763	65.5	23,012	66.7
One or more comorbidities	1,984	34.5	11,494	33.3
Chronic lower respiratory disease	564	28.4	3,125	27.2
Metabolic disorders	341	17.2	1,857	16.2
Diabetes mellitus	87	4.4	544	4.7
Obesity	105	5.3	514	4.5
Morbid obesity	17	0.9	69	0.6
Cardiovascular disease	271	13.7	1,886	16.4
Immunosuppression	254	12.8	1,446	12.6
HIV/AIDS	25	1.3	155	1.3
Kidney diseases	86	4.3	486	4.2
Haemoglobinopathies	43	2.2	278	2.4
Others	865	15.1	4,809	13.9

*Multiple answers for comorbidities were possible.
AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus; SARI: severe acute respiratory infection.

greater case fatality, both for SARI (relative risk (RR)=2.16; 95% confidence interval (CI): 1.96-2.38) and for pandemic influenza (RR=1.89; 95% CI: 1.64-2.18).

Case fatality among pregnant women and non-pregnant women of childbearing age with pandemic influenza were similar, respectively 12.6% (66/525) and 11.7% (155/1,323) (RR=1.07; 95% CI: 0.82-1.41). When pregnancy was associated with at least one comorbidity, case fatality differed slightly between pregnant women with and without reported comorbidity, respectively 16.1% versus. 10.5%; (RR=1.54; 95% CI: 0.98-2.41).

Discussion

The H1N1 influenza pandemic was expected to extend to the countries in the southern hemisphere during the recent winter season (June to September). In addition to low temperatures and rainfall which encourage gathering in closed public areas, the vacation season in July increased international travel and thus virus transmissibility [6].

Brazil was seriously affected by the pandemic H1N1 influenza: 34,506 influenza-like SARI cases had occurred by EW33, of which 5,747 were confirmed as pandemic influenza, as reported by EW34. Men and women were similarly affected, although a large fraction of SARI cases among women of childbearing age were pregnant. The incidence showed two peaks across the age span, one in children until the age of five years (3.8/100,000) and one, slightly higher, in the age group of the 20-29 year-olds (4.6/100,000). Interestingly, those aged 60 years and older had the lowest incidence. Of note, most of the cases (94%) concentrated in two of Brazil's five geographic regions, the south and southeast, which have a more temperate climate and thus colder winters. Although in absolute numbers Brazil has, as of EW34, had the largest number of deaths (645) worldwide due to pandemic influenza, the mortality rate in the population was 0.39/100,000, compared with 1.26/100,000 in Argentina, 0.80/100,000 in Chile and 0.22/100,000 in Canada [1]. The epidemic peaked rapidly and then, by EW 32, the number of cases started to decline, assuming no important delays in reporting. In Brazil, the epidemic peak was seen in EW31, about four weeks after the peak in Argentina, Chile and Uruguay [7-9].

Within Brazil, the pandemic showed characteristics similar to those reported in other countries. The age distribution of incidence was quite different from that of seasonal influenza, with young adults bearing the heaviest burden and older people not very strongly affected. The distribution of comorbidities between the cases of SARI also showed a similar pattern to that found in other countries [7-9]. Though deaths were frequent in individuals with no known underlying disease, the presence of a comorbidity posed a greater risk of death [11].

Although a spatial and temporal analysis within the countries in the region has not been performed, most of the cases detected in the beginning of the epidemic in Brazil were associated with recent travel to Argentina, Chile and Uruguay, especially in municipalities bordering these countries. The most affected regions have long stretches of border with Argentina, Uruguay and Paraguay, with several points of heavy traffic and many additional, minimally monitored points of crossing.

The epidemiological characteristics of the pandemic – with the first cases identified near the border between Mexico and the United States [10], and the path of the epidemic within the Southern Cone of South America sweeping across land frontiers – indicate the need to develop a surveillance plan for land frontiers and to establish actions across countries to ensure travellers' and migrants' health. In addition to national surveillance systems, better sharing of information between bordering countries may help timely decision making in such highly contagious epidemics.

Our study has some limitations. We analysed influenza secondary data from the Brazilian national surveillance notification system, which has been used on a large scale for the first time during this epidemic. The simplicity and wide availability of direct online notification certainly stimulated a greater use of the surveillance

Table 2

Case fatality reported among cases of influenza-like illness with severe acute respiratory infection, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506)

		Number of deaths	Total	Case fatality (%)	RR (95% CI)	*P* value
SARI						
Comorbidity	Yes	813	11,494	7.1	2.16 (1.96-2.38)	<.001
	No	754	23,012	3.3		
Total		**1,567**	**34,506**	**4.5**		
Pandemic influenza A(H1N1)						
Comorbidity	Yes	322	1,984	16.2	1.89 (1.64-2.18)	<.001
	No	323	3,763	8.6		
Total		**645**	**5,747**	**11.2**		
Pandemic influenza during pregnancy						
Comorbidity	Yes	31	192	16.1	1.54 (0.98-2.41)	.06
	No	35	333	10.5		
Total		**66**	**525**	**12.6**		

CI: confidence interval; RR: relative risk.

system. That this report encompasses only influenza-like illness with SARI, generally treated in reference hospitals within the public system, in the context of heightened general concern about the pandemic, strengthens our belief that such reporting, at least for these seriously ill cases, was relatively complete. The comprehensiveness of reporting and of the information undoubtedly varied across healthcare settings. The option of marking check-boxes as well as spontaneously providing additional information regarding comorbidity in an open field added to this variability. In addition, as the number of confirmatory tests needed exceeded the capacity of the Brazilian laboratories network, which consists mainly of the National Influenza Centers, only a fraction of the reported SARI cases had laboratory classification at the time of this report. Considering that laboratory confirmation of severe cases was given priority and that most cases for which no specimen was received were probably milder ones, the case fatality rate for confirmed cases of influenza is likely to be overestimated. With the increase in the number of public health diagnostic laboratories now performing these tests, the interval between the date of collection and the result will be considerably reduced in the future. It is also possible that deaths that were not due to laboratory-confirmed pandemic influenza were notified and updated less frequently than those due to pandemic influenza. This could explain part of the lower case-fatality seen for total SARI cases. Finally, although there may be regional variation in the completeness of reporting, it is unlikely that the observed differences in incidence across the regions are due to differences in reporting. The health system is well organised in all regions of the country and historically, influenza peaks in the more temperate regions during the winter season. In fact, large areas of Brazil had very limited sustained pandemic influenza transmission during the period analysed here, similar to the experience of other countries of similar latitude.

In conclusion, although predominantly a tropical country, Brazil was seriously affected by pandemic influenza. Most of the cases occurred during the winter season in southern and southeastern Brazil, regions with temperate climate situated next to other heavily affected Latin American countries. Additional observational studies are currently underway to further characterise the epidemic in these regions. The intensification of regional collaborative initiatives within Latin America, especially in the Southern Cone, may enhance each country's capacity to respond to future influenza epidemics.

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References

1. Pan American Health Organization (PAHO). Cases of Human Infection with Pandemic (H1N1) 2009 Virus in the Americas by Epidemiological Week (EW). Washington: Human cases of Pandemic (H1N1) 2009: confirmed cases, Cumulative to: EW 35. PAHO. 14 September 2009. Available from: http://new.paho.org/hq/images/atlas/en/atlas.html
2. World Health Organization (WHO). Pandemic (H1N1) 2009 - update 63. WHO. 23 August 2009. Available from: http://www.who.int/csr/don/2009_08_28/en/index.html
3. Brazil Ministry of Health. Mandatory Diseases Notification Act of 2006 Official Journal. 21 February 2006. Portuguese. Available from: http://portal.saude.gov.br/portal/arquivos/pdf/portaria_5_2006.pdf
4. Brazil Ministry of Health. Influenza form to National Surveillance Information System of Notifiable Diseases (SINAN). Portuguese. Available from: http://dtr2004.saude.gov.br/sinanweb/novo/Documentos/SinanNet/fichas/Influenza.pdf
5. Pan American Health Organization (PAHO). Norms and Standards in Epidemiology: Epidemiological Calendar 2000. PAHO. Available from: http://amro.who.int/english/sha/be993calend.htm
6. Daufenbach LZ, Carmo EH, Duarte EC, Campagna AS, Teles CAS. Influenza-Related causes of hospitalization in elderly in Brazil, 1992 to 2006. Epidemiol Serv Saúde. 2009:18(1):29-44. Portuguese.
7. Argentina Ministry of Health. Pandemic (H1N1) 2009: Weekly Epidemiological Report no 34. 4 September 2009. Spanish. Available from: http://www.msal.gov.ar/archivos/Informe_SE_34-_ARG_COM.pdf
8. Chile Ministry of Health. Pandemic (H1N1) 2009: Weekly Report. 26 August 2009. Spanish. Available from: http://www.redsalud.gov.cl/minsalaudios/reporte26agosto.pdf
9. Uruguay Ministry of Health.Influenza A(H1N1) Weekly report: Uruguay. Epidemiological Week 34. 7 September 2009. Spanish. Available from: http://www.msp.gub.uy/ucepidemiologia_3429_1.html
10. Novel Swine-Origin Influenza A(H1N1) Virus Investigation Team, Dawood FS, Jain S, Finelli L, Shaw MW, Lindstrom S, et al. Emergence of a novel swine-origin influenza A(H1N1) virus in humans. N Engl J Med. 2009;360(25):2605-15.
11. Vaillant L, La Ruche G, Tarantola A, Barboza P, for the epidemic intelligence team at InVS. Epidemiology of fatal cases associated with pandemic H1N1 influenza 2009. Euro Surveill. 2009;14(33):pii=19309. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19309