

The epidemic wave of influenza A (H1N1) in Brazil, 2009

A onda epidêmica de Influenza A (H1N1) no Brasil, 2009

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Abstract

This study describes the main features of pandemic influenza A (H1N1) in Brazil during 2009. Brazil is a large country that extends roughly from latitudes 5°N to 34°S. Brazil has tropical and sub-tropical climates, a heterogeneous population distribution, and intense urbanization in the southern portions of the country and along its Atlantic coast. Our analysis points to a wide variation in infection rates throughout the country, and includes both latitudinal effects and strong variations in detection rates. Two states (out of a total of 23) were responsible for 73% of all cases reported. Real time reproduction numbers demonstrate that influenza transmission was sustained in the country, beginning in May of 2009. Finally, this study discusses the challenges in understanding the infection dynamics of influenza and the adequacy of Brazil's influenza monitoring system.

Influenzavirus A; Epidemics; Surveillance

Introduction

This study describes the main features of the 2009 epidemic wave of influenza A (H1N1) in Brazil, a large country extending roughly from latitudes 5°N to 34°S. Brazil has tropical and sub-tropical climates, a heterogeneous population distribution, and intense urbanization in the southern portion of the country and along its Atlantic coast. Our current knowledge of influenza dynamics comes mostly from studies in temperate regions. This is the first time an influenza epidemic has been closely monitored in Brazil, which is a large tropical to subtropical country.

On April 25, 2009, in response to alerts issued by the World Health Organization (WHO), Brazil implemented active surveillance of suspected cases of influenza, targeting symptomatic persons with a recent history of international travel and their contacts ¹. As predicted by influenza infection models, this virus disseminated rapidly throughout global airline networks ². In Brazil, influenza cases arrived mainly from the United States, Argentina and Chile ³ into São Paulo and the major tourist cities in the south. On July 16, 2009, public health officials declared sustained influenza transmission on a national level. Following the WHO's guidelines, mandatory reporting of influenza infections were restricted to those with severe acute respiratory illness (SARI). SARI is defined as a case presenting fever, cough and dyspnea. Mandatory reporting was also

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required for influenza outbreaks in closed populations and influenza cases in high risk groups¹. The epidemic curve reached its peak in the first week of August and then steadily declined thereafter.

The goal of this study is to characterize this influenza epidemic by estimating the reproductive number and providing descriptions of observed temporal and spatial heterogeneities in attack rates.

Methods

Data

The database of reported cases was provided by the Brazilian Ministry of Health. Up until September 24, 2009, 124,013 suspected cases of H1N1 influenza A had been reported. From this total, 17.4% were discarded, because flu symptoms were found to be from other causes. From the remaining 102,435 suspected cases, 26,396 were confirmed as H1N1 influenza A, by either laboratory or epidemiological criteria. 61% of the cases remained either untested or their status was not updated in the database. Infection onset day was missing in approximately 10% of the cases. This missing information was filled by imputation. This value corresponded to the day of onset of flu symptoms minus 2.76 days (the average time between the onset of symptoms and actual reporting).

We classified each case based on the symptoms, described in the notification dataset, as SARI (for those presenting with fever, cough and dyspnea), and mild acute respiratory illness (ARI), otherwise. To obtain the epidemic curves and calculate attack rates, data was aggregated at the national level, the state level and the metropolitan level. For the latter, only the following metropolitan regions were considered: São Paulo, Campinas (State of São Paulo), Rio de Janeiro, Belo Horizonte (State of Minas Gerais), Brasília, Curitiba (State of Paraná), Londrina-Maringá (State of Paraná), Foz do Iguaçu-Cascavel (State of Paraná), the eastern part of the State of Santa Catarina and Porto Alegre (State of Rio Grande do Sul) (Figure 1). These metropolitan regions were responsible for 58% of all reported cases during the epidemic period.

Attack rates

Three measures of attack rates were considered: the naïve *attack rate* (simply the sum of all reported cases divided by the population) the *SARI attack rate* (calculated as the sum of severe cases

divided by the population size). We expected the report of severe cases to be more uniform and more adequate for comparison between states. At last, we calculated a *corrected attack rate* which sought to estimate the attack rate of (mild + severe) cases in a scenario that assumed that all states reported severe cases with the same effort and that the true mild to severe case ratio was the same in all states. This procedure described below, sought to unify the collected data from different efforts, in different places.

During the first phase of the epidemic in Brazil, when both ARI and SARI cases were being reported, the epidemic was concentrated in São Paulo. The proportion of SARI cases reported during this period and in this place was $s = 0.137$ (95%CI: 0.123-0.151). We used this as a best estimate of the true proportion of SARI cases. In each state or metropolitan region, we calculated the number of mild cases as “reported SARI multiplied by $1/s$ ”. This calculation assumed that the reporting of SARI cases was homogeneous throughout the time, and that ARI to SARI ratios would be the same, independently of the city. This approach is similar to the procedure used⁴ to correct the US data.

Severity

To evaluate the differences in mild to severe case reports, throughout time and space, we fitted an additive logistic model, with the type of case as the response variable (ARI or SARI). Place and time were considered as explanatory variables. This regression model is an extension of the generalized linear model that allows the inclusion of nonparametric smoothing terms, in the place of constant parameters⁵. The “place” variable, corresponded to the 10 metropolitan regions, included as fixed effects. The “time” variable, was the day of the onset of flu symptoms, and was introduced into the model as a smooth term.

To identify risk factors for SARI, we used (standard) logistic regression, with the explanatory variables: age and belonging to high risk groups for influenza (< 2 years-old, > 60 years-old and “presenting with co-morbidities”). For this specific analysis the dataset was restricted to cases with infection onset before July 1, 2009 in order to minimize the impact of changing the detection rate of mild cases.

Reproduction number

To estimate the basic reproduction number of the epidemic, the exponential method was used⁶. Taking into consideration the uncertainties regarding the epidemic generation time and

Figure 1

Map of Brazil showing the number of cases of A H1N1 reported per municipality during the autumn and winter of 2009.



the exponential growth time window, we considered several scenarios ^{7,8}.

Furthermore, in order to obtain a more dynamic portrait of the epidemic, we calculated the real time reproduction number (R_t), which is a measure of the average number of secondary cases generated per each case, during the epidemic ⁹. Values above 1 indicated sustained infection transmission and values below 1 indicated a tendency towards un-sustained infection transmission. All analyses were performed using R 2.9.2 software (The R Foundation for Statistical Computing, Vienna, Austria; <http://www.r-project.org>).

Contact patterns

Information on the potential source of infection was available for a small subset of cases. This information, collected during the initial phase of the epidemic, was recorded during the active search for suspected infection cases. Despite the effort to define the source of infection, this information was missing from most of cases. Only 169 case pairs were collected and analyzed. For this subset of cases, we compared the age of infectors and infectees as well as the most likely location of the infection transmission. Current theory on directly transmitted infectious disease highlights the importance of population mixing patterns in disease dynamics. Age is also one of the major factors that influence the structure of human contact patterns ¹⁰.

Results

The epidemic curve

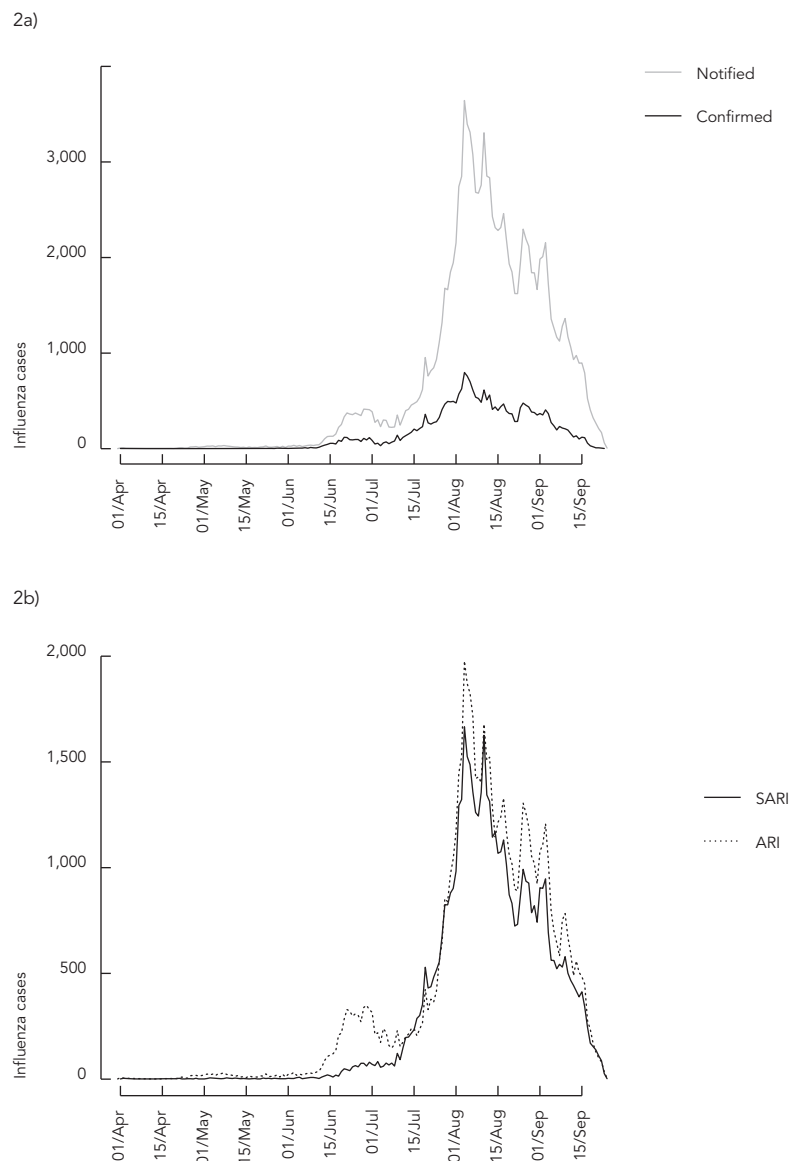
Figure 2a shows the epidemic curve of influenza AH1N1 in Brazil. The valley between the two peaks reflects the change in the detection rate, characterized by a drop in the report of milder

cases after July (Figure 2b). Geographically, cases were concentrated in the large metropolitan regions, with more diffuse spatial spread observed only in the southern and southeastern states.

The reporting rate was very heterogeneous throughout the country. The states of Paraná and São Paulo were responsible for 73% of all reported cases (52% and 21%, respectively)

Figure 2

Time series of reported and confirmed cases in Brazil (2a) and time series of reported cases of mild acute respiratory illness (ARI) and severe acute respiratory illness (SARI) (confirmed or not) (2b).



Note: the y-axis scale varies between graphs.

(Table 1). São Paulo is the most densely populated state, with 40 million inhabitants, half of which are living in the capital and its metropolitan region; São Paulo is also the nation's most important international point of entry for those travelling by air.

The state of Paraná, the southern state bordering São Paulo, is an important point of entry by land for persons coming from Argentina and Paraguay. Paraná's population of 10 million is four times smaller than that of São Paulo, with 3 million living in the state capital of Curitiba. The next top three states reporting influenza cases were Rio de Janeiro – the second most populated state in Brazil with 6.8% of all cases, followed by the southernmost states of Rio Grande do Sul (5.2% of all cases) and Santa Catarina (4.4% of all cases). These five states together (out of Brazil's 27 states), represented 88% of all influenza cases reported on a national level. The naïve attack rate was very similar in the states of São Paulo, Rio de Janeiro and Rio Grande do Sul (52 to 67 per 100,000); the state of Santa Catarina was approximately 30% higher (91 per 100,000). The attack rate was unexpectedly 10 times higher in the state of Paraná, with 643 cases per 100,000. The same pattern is observed when we calculate the attack rates of SARI (Table 1).

Figure 3 shows the epidemic curve per state. São Paulo, Rio de Janeiro and Rio Grande do Sul showed strong influenza activity during the initial phase, with high notification of mild cases. After the change in case reporting, in July, the number of mild cases dropped sharply in all states, except Paraná. While in São Paulo and Rio de Janeiro, both SARI and ARI curves almost coincide, in Santa Catarina and Rio Grande do

Sul, the SARI curve greatly exceeds that of the ARI curve. The only exception to this pattern is Paraná, which had a significantly higher report rate of mild cases.

The coverage of diagnostic testing also varied between states. In São Paulo, 73% of influenza cases were tested, while in the other four states, 36% or less (in the case of Rio Grande do Sul) of influenza cases were tested (Table 1). The greater availability of diagnostic testing reagents in the reference laboratory located in São Paulo, explains in part, these findings. The results of a majority of tested cases were negative, for influenza virus A (H1N1) (more than 90% in each state) in 2009. These results introduce uncertainties in the interpretation of the curve of suspected cases. The percentage of positive test results was significantly higher in São Paulo (8.7%) when compared to Paraná (0.2%).

Reproduction number

From late May 2009 to June 23, the number of confirmed cases of influenza A H1N1 grew exponentially at a rate of 0.17 ± 0.007 new cases per day ($r^2 = 0.95$). Suspected cases grew at a similar rate (0.16 ± 0.0067 ; $r^2 = 0.93$). Transforming these rates into reproduction numbers requires several assumptions regarding population mixing patterns, susceptibility to infection and the distribution of epidemic generation time. Assuming complete susceptibility, homogeneous mixing and a gamma generation time distribution, R_0 was estimated between 1.31 and 1.78. If cross immunity with previously circulating influenza A H1N1 is considered, as has been suggested¹¹, then this estimate is better interpreted

Table 1

Number of suspected cases of A H1N1 reported per state during the autumn and winter 2009 in Brazil, % tested and % confirmed (among the tested population).

State	Population (million)	Notified cases (% country)	Attack rate (per 100,000)	SARI attack rate	% tested (% confirmed tested)
Paraná	10	64,383 (51.9)	643	227	27 (0.2)
São Paulo	41	26,801 (21.6)	67	35	73 (8.7)
Rio de Janeiro	16	8,444 (6.8)	52	26	27 (1.4)
Santa Catarina	6	5,478 (4.4)	91	58	21 (2.9)
Rio Grande do Sul	11	6,462 (5.2)	58	31	36 (2.7)
Brazil (total)		124,013 (100.0)			

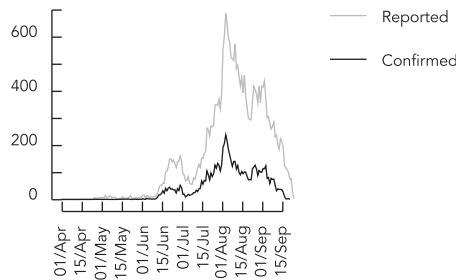
SARI: severe acute respiratory illness.

Note: only the 5 most affected states are shown.

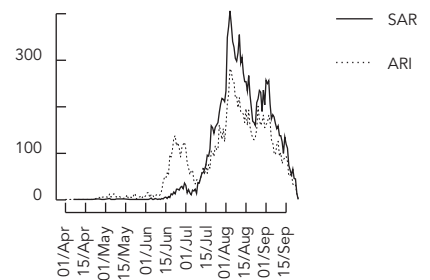
Figure 3

Time series of reported and confirmed H1N1 cases (3a, 3c, 3e, 3g, and 3i) and time series of reported cases of mild acute respiratory illness (ARI) and severe acute respiratory illness (SARI) (3b, 3d, 3f, 3h, and 3j) in the 5 most affected Brazilian states: São Paulo, Rio de Janeiro, Paraná, Santa Catarina e Rio Grande do Sul, located in Southeast and Southern Brazil.

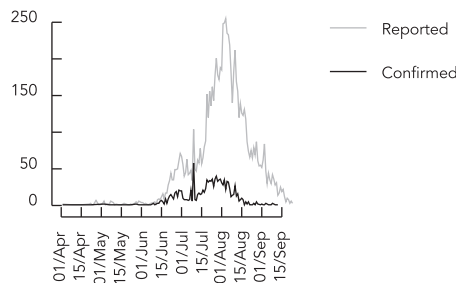
3a) Cases in São Paulo (H1N1)



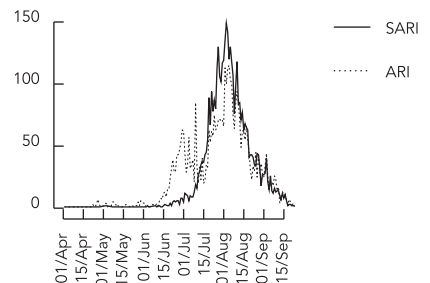
3b) Cases in São Paulo (ARI and SARI)



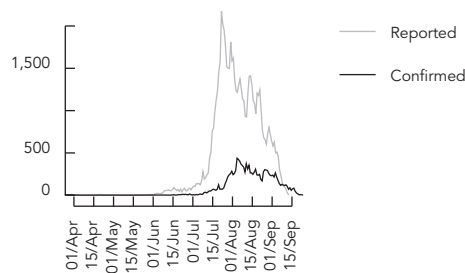
3c) Cases in Rio de Janeiro (H1N1)



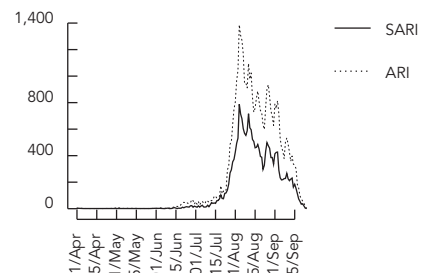
3d) Cases in Rio de Janeiro (ARI and SARI)



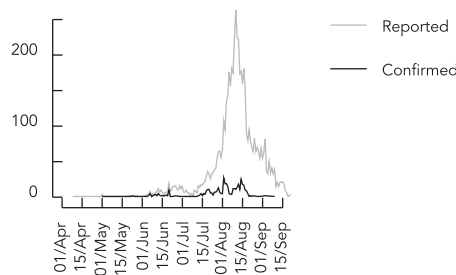
3e) Cases in Paraná (H1N1)



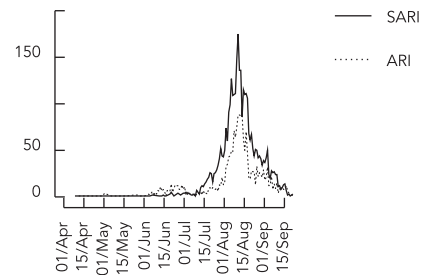
3f) Cases in Paraná (ARI and SARI)



3g) Cases in Santa Catarina (H1N1)



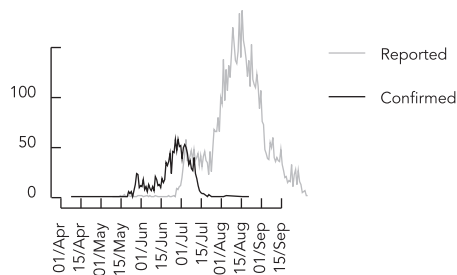
3h) Cases in Santa Catarina (ARI and SARI)



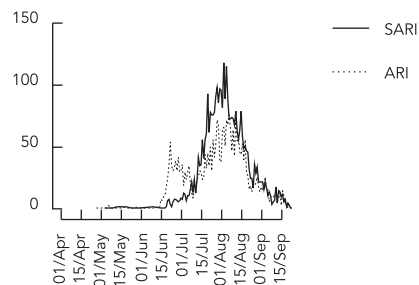
(continues)

Figure 3 (continued)

3i) Cases in Rio Grande do Sul (H1N1)



3j) Cases in Rio Grande do Sul (ARI and SARI)



Note: the y-axis scale varies between graphs.

as the maximum effective reproductive number (R_e)¹².

Severity

During the initial phase of the epidemic, the mean age of the cases was 29 years, with 10% of the cases between 10 and 18 years. This age profile is older than that reported in the United States, where 40% of the cases were in the 10-18 years age group¹³. In Australia, the age profile of cases was more similar to Brazil's¹⁴. SARI during this phase was significantly more prevalent in individuals belonging to the high risk group ($\chi^2 = 31.7$; $df = 1$; $p < 0.0001$), with pneumopathy as the strongest predictor (OR = 3.6; 95%CI: 1.5-8.9), followed by the diffuse category of "other comorbidities" (OR = 2.93; 95%CI: 1.8-4.7).

As the epidemic progressed and reporting shifted to severe cases, the demographic profile of cases changed, with the mean age decreasing to 25 years. The proportion of cases in the teenager group increased to 15%, and the proportion of children less than 2 years increased from 5 to 10%. Among those with SARI, the proportion of children below 2 years increased from 0.6 to 10%. This change in the age profile may be due to the increased emphasis on monitoring and reporting cases in infants, or may be attributed to the greater exposure of this population to infection as the epidemic progressed. In the beginning of the epidemic, most cases were associated with international travel, where adults predominate.

Contact patterns

Approximately 50% of the contact pairs of infectors and infectees were of the same age group,

while the other half of contact pairs had approximately 25 years of age difference between them. Infection transmission between same age groups were observed in schools and work settings, while infection transmission between generations were mostly reported in households.

Differences in mild-to-severe reporting rates between metropolitan regions

We further investigated the reporting data aggregated at metropolitan level, considering the ten urban areas reporting the majority of the cases (Table 2). These metropolitan regions together, were responsible for 58% of all identified cases. We used a logistic regression model to estimate the odds of reporting mild cases in each metropolitan region. In Figure 4a, it is clear that the impact of changes in the number of cases identified as mild cases, dropped sharply after July 1, 2009. In Figure 4b, we see that the odds of reporting a mild case in Paraná was significantly higher than that of any of the other state.

In an effort to standardize the reporting rates, we calculated a "corrected attack rate" which disregards all mild cases reported and uses severe cases instead. Accordingly, this inflated the mild to severe ratio estimated for São Paulo. Figure 5a shows the comparison of the naïve attack rate and the corrected attack rate per metropolitan region. It is clear that the correction does not affect the ranking of the cities, although it seems to somewhat reduce the differences between them. Despite the differences in attack rates, the estimated real time reproduction number for each metropolitan region shows a similar temporal profile (Figure 5b). Transmission remained sustained from May until the first week of

Table 2

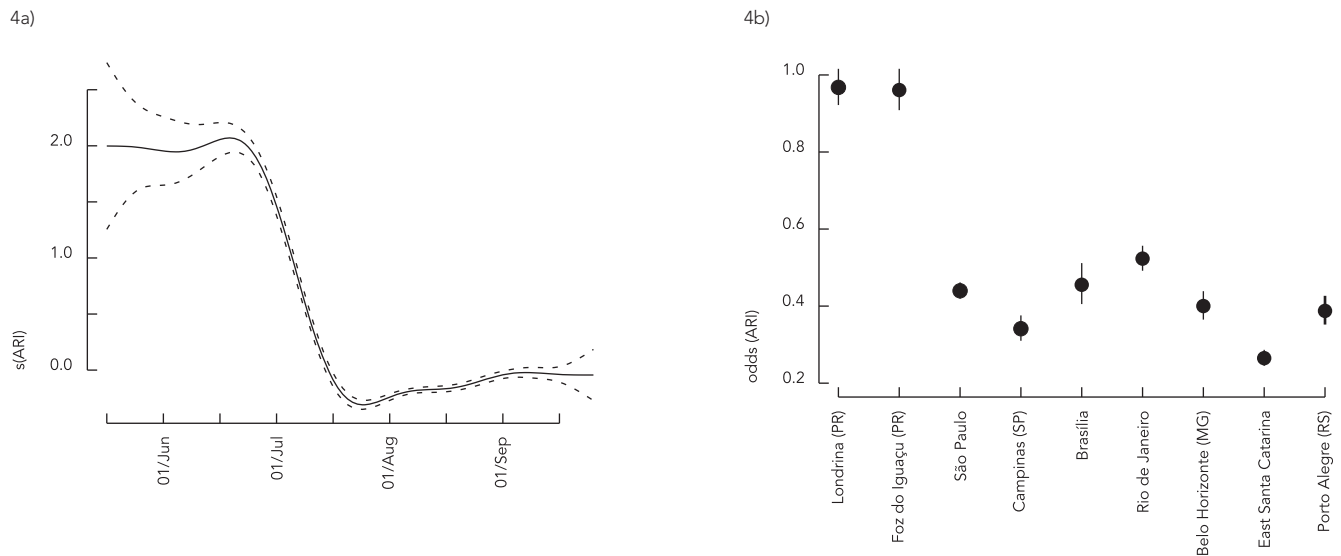
Number of suspected cases of A H1N1 and proportion of severe acute respiratory illness (%SARI) notified in the 10 most affected metropolitan regions in Brazil during the 2009 epidemic wave (autumn-winter 2009). Labels correspond to positions in the map (Figure 1).

Label	City	Latitude (S)	Population (millions)	Climate	Cases	% SARI
A	Brasília	15°4'	2.4	Tropical, dry winter	1,349	51
B	Metropolitan Region of Belo Horizonte (MG)	19°5'	5.4	Tropical, dry winter	2,422	51
C	Metropolitan Region of Rio de Janeiro	22°5'	11.0	Tropical	6,655	47
D	Metropolitan Region of Campinas (SP)	22°9'	2.6	Subtropical	2,153	58
E	Metropolitan Region of São Paulo	23°3'	19.0	Subtropical	15,546	51
F	Londrina-Maringá (PR)	23°1'	1.3	Subtropical	14,992	36
G	Metropolitan Region of Curitiba (PR)	25°2'	3.2	Temperate	14,102	36
H	Foz do Iguaçu-Cascavel (PR)	25°3'	1.1	Subtropical	8,800	37
I	Metropolitan Region of Porto Alegre (RS)	30°0'	3.9	Temperate	2,220	53
K	East Santa Catarina	27°3'	3.7	Temperate	3,699	66

MG: Minas Gerais State; PR: Paraná State; RS: Rio Grande do Sul State; SP: São Paulo State.

Figure 4

Temporal and spatial variation in mild-to-severe case reporting, estimated from additive logistic regression: temporal variation in mild-to-severe case reporting due to change in notification procedure (4a); spatial heterogeneity in the mild-to-severe case reporting between metropolitan regions (4b).



ARI: mild acute respiratory illness; MG: State of Minas Gerais; PR: State of Paraná; RS: State of Rio Grande do Sul; SP: State of São Paulo.

Note: reference = Curitiba (State of Paraná).

August when the reproduction number dropped below one, in all metropolitan regions.

Discussion

The 2009 influenza A H1N1 pandemic offered a rare opportunity to study influenza dynamics in tropical countries and compare simultaneously occurring epidemics across several latitudes¹². In the Americas, national level comparisons, show wide variations in attack rates, ranging from > 30 confirmed cases per 100,000 inhabitants, in Chile and Canada, to < 1 confirmed cases per 100,000 inhabitants in Brazil, Colombia, Guyana and few Caribbean islands (data from Pan-American Health Organization until July 18). This variation has been attributed to latitudinal effects, seasonality and differences in reporting and laboratory confirmation rates¹².

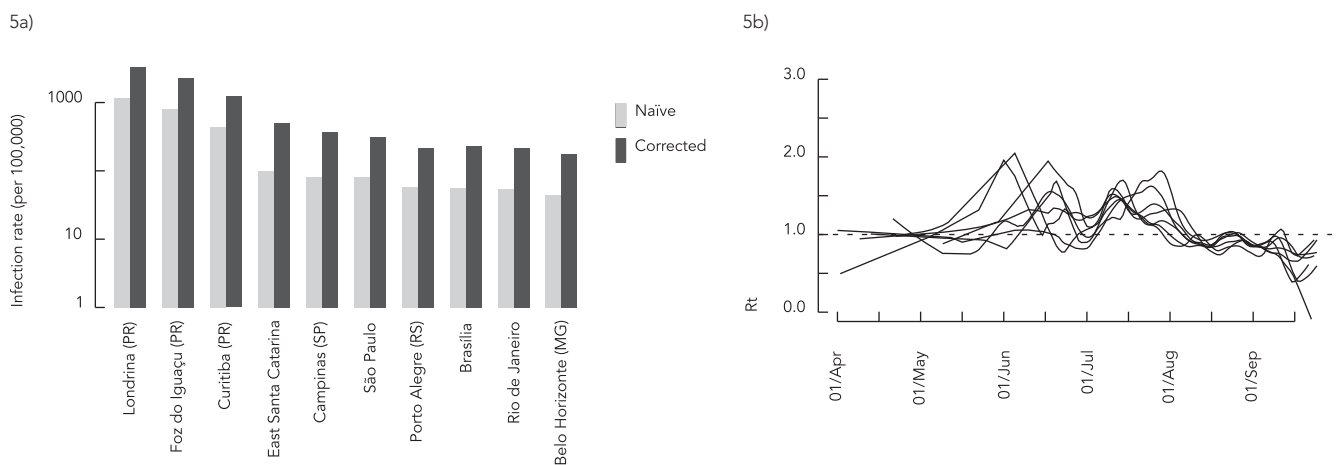
In this study, we analyzed the 2009 influenza A H1N1 pandemic in Brazil, the largest country of South America. Our results point to a wide variation in attack rates within the country, with both latitudinal effects and variations in detection rates. Latitudinal effects are inferred from the accumulation of cases in the sub-tropical portion

of the country, compared to the tropical region. Four out of the top 5 states with the largest attack rates are located in the sub-tropical region. This pattern changed in 2010, with the Northern states taking the lead in incidence rates: 16.67 per million in the North region, 11.08 in the South region and 1.12 in the Southern region (until September 2010). Note, however, notification data from 2010 cannot be directly compared to 2009 because in 2010, reported data only included hospitalized cases.

Sharp differences in detection rates between state-level influenza surveillance systems were also observed. The State of Paraná (with a 10 times greater infection rate compared to other states) presented a influenza surveillance system with greater sensitivity and lesser specificity than any other, while the State of São Paulo presented the influenza surveillance system with the highest specificity. These two states contributed three fourths of the total number of cases reported. These results suggest that care should be taken when comparing influenza statistics at the national level or geographically. It is desirable to implement a sensitive influenza surveillance system during the initial phase of a threatening new epidemic, but to sustain such effort over the long

Figure 5

Comparison of the infection rates of influenza A H1N1 between the most affected metropolitan regions (5a). The naive infection rate presented is the crude estimate, whereas the corrected attack rate is a modified measure that seeks to homogenize the observed differences in mild-to-severe case reporting. Real time reproductive number (R_t) of the A H1N1 influenza epidemic during the autumn and winter of 2009 (5b), in the 10 most affected metropolitan areas in Brazil (listed in Table 2 and mapped in Figure 1).



MG: State of Minas Gerais; PR: State of Paraná; RS: State of Rio Grande do Sul.

Note: values above 1 indicate sustained transmission.

term may be prohibitive. Furthermore, the best specificity/sensitivity trade-off is probably context based, as it depends on local facilities, personnel, resources, etc. Two criteria (among others) have been used to qualify disease surveillance programs¹⁵, flexibility (the ability to adapt during epidemics and applicability when used in other settings), and representativeness (the ability to describe spatial and temporal patterns). A flexible disease surveillance program may be necessary to deal with an epidemic in a continental country like Brazil, whose systems are capable of adapting both spatially and temporally. However, flexible systems will not provide representative data, unless the variations in detection effort is monitored in a controlled way.

The 2009 influenza A (H1N1) epidemic grew exponentially from late May to the first week of August when it reached its peak. Initial growth was concomitant with the epidemic expansion in Chile and Argentina but was earlier than in Peru¹². On July 15, 2009, when sustained transmission was officially declared (triggering the implementation of new intervention and surveillance protocols); at least one month of sustained infection transmission had already passed. This delay, possibly inevitable within the context of the surveillance routine, did not cause harm to the population, but may have overtaxed the teams involved in the response to the epidemic, as they were still investing in active search and localization efforts, in a situation where large scale infection transmission was already happening. Innovative methods for real time measurement of infection transmissions which were developed and improved during the course of the 2009 influenza A (H1N1) epidemic^{7,16}, may help to achieve optimal response in future epidemics.

Despite the differences at the onset, the epidemic wave eventually dropped in a synchronized way. This synchronization in the ending phase may suggest the presence of external forces. In influenza, synchronization has been attributed to climate variations (due to the effect of temperature and humidity on host susceptibility or virus persistence in the environment) or changes in social mixing. The end phase of influenza transmission in Brazil coincided with the end of the school break. No significant variation in temperature was observed during this month (data not shown). Thus, the reasons for the drop in the number of cases remain unclear. Other possible explanations are the implementation of intervention strategies (although it is important to note that vaccination was only available in 2010) or changes in case reporting.

The basic reproductive number of influenza A H1N1 was estimated as 1.31-1.78. These val-

ues are compatible with those reported in other South American countries, which range from 1.3 to 2.1. Lessler et al.¹², in their study on influenza A H1N1 in the Americas, show a linear relationship between R_0 and the latitude of the country's capitals, with more intense infection transmission in the southern countries. Comparing our estimates with theirs, and using the latitude of Brasília (the capital) as the reference for Brazil, our estimates of R_0 fall below those expected by their trend line. The reason for this finding might be the large size of Brazil and consequently the large variation in latitudes, making it unreasonable to apply such a simple correlation to a country of this magnitude. On the other hand, this result may indicate an underestimation of the true reproductive number of influenza A H1N1 in Brazil.

Care should always be taken when interpreting reproductive numbers as they are based on strong assumptions regarding population mixing¹⁷, generation time^{7,8} and the length of the exponential period^{7,18}. In face of such uncertainty, we suggest reporting the exponential growth rate together with the reproduction number, in any study. This measurement can be converted to R_0 in different ways depending on the underlying model and any researcher willing to compare values between countries or regions should be able to calculate them, using the same underlying model. Wearing et al.¹⁹ show how assumptions regarding the appropriate distributions for the latent period and infectious period affect the expected effectiveness of intervention strategies for the same epidemic curve.

Differently from this new influenza virus was shown to be very mild, only leading to severe syndromes in a small fraction of cases (mainly pregnant women, and those with underlying respiratory diseases). The monitoring of diseases with a large proportion of asymptomatic and oligosymptomatic cases is a major challenge, and the strategies adopted have had consequences on the type of data gathered, their comparability, model parameterization and the appropriate choices of intervention strategies. Specific methods are required, in order to monitor silent infections, as in the case of new influenza strains, dengue fever²⁰ and other diseases. Our analysis was only feasible because it was possible to discern between severe cases and mild cases. From this information, it was possible to infer differences in sensitivity and specificity between different influenza surveillance systems and develop correction factors. We recommend that in future epidemic situations, efforts are taken to monitor more than one case definition – mild and severe syndromes, for example. Other sources of

information, such as serological surveys, are also fundamental in estimating correction factors and evaluating the risk of new epidemics. Initiatives in systematic surveillance, such as the one based on pregnant women, are very interesting and should be encouraged²¹.

As in all secondary data analysis, the main limitation of this study refers to the quality of data obtained during a public health emergency. Although it was possible to make some corrections to the database, as outlined in the methodology, one must take into account that more complete data may lead to a more robust analysis.

Due to the low testing rate, we cannot estimate with precision the extension of virus co-circulation during this epidemic, but there was

evidence of co-circulation of influenza A pandemic and seasonal strains in the autumn and early winter of 2009. During the 2009 Australian winter season, there was co-circulation of the new influenza A H1N1 and influenza A H3N2 viruses, while seasonal influenza A H1N1 and influenza B viruses were uncommon²². In Spain, the new influenza A H1N1 co-circulated with influenza C²³.

We expect that the results presented in this study will contribute to the development of a more global perspective on influenza epidemic dynamics and enable the development of improved surveillance strategies, adapted to more silent infections.

Resumo

Este estudo descreve a primeira onda de influenza A (H1N1) no Brasil, um país que se estende entre as latitudes 5°N e 34°S, caracterizado por climas tropicais e subtropicais, com distribuição populacional heterogênea e intensa urbanização ao longo da costa e na região sul-sudeste. Nossa análise indica grande variação geográfica nas taxas de ataque no país, com efeitos longitudinais e variação na taxa de detecção. Dois estados foram responsáveis por 73% de todos os casos registrados: São Paulo e Paraná. O número reprodutivo em tempo real demonstra que a transmissibilidade se sustentou no país desde maio de 2009 até pelo menos agosto de 2009. Este trabalho por fim discute os desafios de estudar e monitorar doenças emergentes de sintomatologia inespecífica, como a influenza, e a adequação do sistema de vigilância.

Influenzavirus A; Epidemia; Vigilância

Contributors

C. T. Codeço contributed with the conception of this paper, writing and data analysis. J. S. Cordeiro contributed with the conception of this study, calculation of the reproductive numbers and critical revision of the manuscript. A. W. S. Lima contributed with the calculation of the reproductive numbers, the conception of this paper and critical revision. R. A. Colpo contributed with data analysis and organization and with the conception of this paper. O. G. Cruz contributed with data analysis and organization, with the conception and critical revision of this paper. F. C. Coelho contributed with data analysis and organization, and critical revision. P. M. Luz, C. J. Struchiner and F. R. Barros contributed with the conception and critical revision of this paper.

Acknowledgments

C. T. Codeço and F. C. Coelho performed part of this work as visiting researcher and post-doc at the Instituto Gulbenkian de Ciência, Portugal, respectively. This work was commissioned by the Brazilian Ministry of Health (process number 530001/10). C. T. Codeço received a post-doc fellow ship from CNPq.

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Submitted on 14/Apr/2011

Final version resubmitted on 31/Oct/2011

Approved on 08/Feb/2012