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## Regional differences in mortality associated with pandemic Influenza A H1N1 in Brazil

Diferenças regionais na mortalidade associada à influenza A H1N1 pandêmica no Brasil

Diferencias regionales en la mortalidad asociada a la gripe A H1N1 pandémica en Brasil

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### Abstract

*The aim of this article is to examine regional differences in mortality associated with influenza from 2006 to 2010 in Brazil. Syndromic surveillance, which includes deaths from pneumonia and influenza recorded in the Mortality Information System, only showed an increase in mortality during the pandemic in the South, Southeast, and Central, regions. In these regions, especially in the South, this increase occurred from July to September 2009. A review of deaths from confirmed influenza cases reported to the Information System for Notifiable Diseases showed different temporal patterns in the South/Southeast and the North/Northeast, with an increase from July to November 2009 for all regions and another peak, only for the latter, in March 2010, before the vaccination campaign. The results show regional differences in the intensity and temporal distribution of pandemic influenza and highlight the need for specific surveillance tools and control strategies for regions of the country.*

*Human Influenza; Epidemics; Mortalidade*

### Resumo

*O objetivo deste artigo é examinar as diferenças regionais na mortalidade associada à influenza entre 2006 e 2010 no Brasil. A vigilância sindrômica, que inclui óbitos por pneumonia e influenza registrados no Sistema de Informações sobre Mortalidade, mostrou aumento na mortalidade durante a pandemia apenas nas regiões Sul, Sudeste e Centro-Oeste. Nessas regiões, principalmente na Região Sul, esse aumento ocorreu entre julho e setembro de 2009. Avaliando-se os óbitos de casos confirmados de influenza notificados ao Sistema de Informações de Agravos de Notificação, verificou-se um padrão temporal diferente entre as regiões Sul/Sudeste e as regiões Norte/Nordeste, com aumento entre julho e novembro de 2009 para todas as regiões e outro pico em março de 2010, antes da campanha de vacinação, apenas para as últimas. Os resultados mostram diferenças regionais na intensidade e na distribuição temporal da pandemia de influenza e apontam para a necessidade de instrumentos de vigilância e de controle específicos para as regiões do país.*

*Influenza Humana; Epidemias; Mortalidade*

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## Introduction

Influenza is a viral disease with a worldwide distribution, transmitted by the respiratory route and by contact with secretions<sup>1</sup>. Frequent antigenic changes in the virus are associated with complex epidemiological patterns in its spread, making control of the disease a challenge<sup>2</sup>. In 2009, the emergence of a new influenza subtype classified as A/California/7/2009 H1N1 gave rise to the first pandemic of the 21<sup>st</sup> century<sup>3</sup>. This new influenza virus led to an increase in mortality from respiratory diseases in various parts of the world, including Brazil, where it was identified for the first time in May 2009, soon becoming the predominant strain circulating in the country<sup>4</sup>.

Beyond the subtype's properties and population immunity, environmental, demographic, and behavioral factors also influence the epidemiology of the influenza virus<sup>5</sup>. Temperate regions show a typical seasonal pattern, with peak incidence in the winter, while tropical regions do not show this same pattern<sup>6</sup>. Since Brazil is a continental-size country, its territory displays a climatic, environmental, and socio-demographic diversity whose impact on the circulation of influenza is still not fully understood<sup>7</sup>. Understanding the epidemiology of influenza in Brazil is crucially important for health surveillance and particularly for planning annual influenza vaccination, which currently has a single recommendation for the entire country. Influenza-associated mortality has already proven to be related to circulation of the virus in Brazil<sup>7</sup>, and the current study thus aimed to examine regional differences in mortality associated with influenza from 2006 to 2010 in the country.

## Materials and methods

The 26 States of Brazil and the Federal District are grouped in 5 geographic regions: North, South, Southeast, Northeast, and Central. A retrospective descriptive ecological study was used to analyze monthly mortality related to influenza in the five geographic regions from 2006 to 2010.

The Mortality Information System (SIM) of the Brazilian Ministry of Health was used to identify deaths from pneumonia and influenza from 2006 to 2010. The study extracted deaths identified by ICD-10 codes J10 to J18 and J22<sup>7</sup> and grouped by month, year, and region. Calculation of mortality rates per 100,000 inhabitants used data from the 2010 Population Census and the inter-census estimates provided by the Brazilian Institute of Geography and Statistics from 2006

to 2009 (<http://www.ibge.gov.br>, accessed on 01/Mar/2012). The average mortality rate was calculated for the three years prior to the pandemic (2006-2008) for purposes of comparison. Data were used from the Information System for Notifiable Diseases (SINAN) to analyze the number of confirmed influenza cases, grouped by month and region, for the years 2009 and 2010.

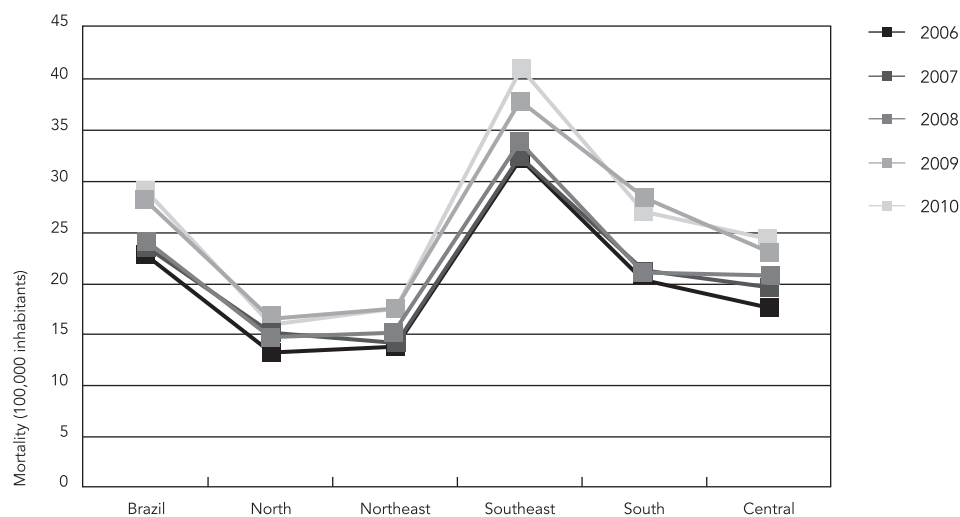
## Results

Mortality associated with influenza in Brazil showed an upward trend from 2006 to 2010, with the largest increase from 2008 to 2009, the year of the pandemic (Figure 1). The breakdown by region highlighted some similarities between the areas, e.g., the increase in mortality in 2009 and the maintenance of high rates in 2010. However the differences are more striking than the similarities. The first is variation in the intensity of influenza's regional impact. While the mean annual rates in 2009 reached 37.99 deaths/100,000 inhabitants in the Southeast and 28.05 in the South, in the North and Northeast these rates were 16.53 and 17.48, respectively, suggesting a much lower circulation of influenza virus in the States farther to the North. Another difference is the increase in rates from 2009 to 2010 only in the South and Central, with stabilization or decline in the other regions. Second, there were different patterns in the temporal distribution of mortality (Figure 2). In the South and Southeast, which had recorded the most deaths in July during the previous years, presented peak mortality in August during the pandemic year, reflecting seasonal distribution of cases, especially in the South. The Central also showed seasonal distribution, although not pronounced. Meanwhile the North and Northeast showed a uniform distribution, without the classical seasonal pattern. In these regions the month of May recorded the highest number of deaths.

Notification of influenza to the SINAN database began in epidemiological week 16 in 2009. An analysis of the absolute number of deaths recorded in SINAN in confirmed influenza cases (Figure 3) showed that the monthly distribution in the South and Southeast was similar to that observed in the Mortality Information System, peaking in August 2009, when it varied from 600 to 900 deaths. Meanwhile the North and Northeast showed a monthly variation not perceptible in the SIM data. After an initial increase from July to August 2009, the number of deaths decreased slowly until rising again in January 2010, forming a new peak in March that year.

Figure 1

Mortality associated with influenza (ICD 10: J10 to J18 and J22) in Brazil and regions, 2006 to 2010.



## Discussion

The regional aggregate data suggest heterogeneity in the spatial and temporal distribution of mortality from pneumonia and influenza during the pandemic in Brazil. The mortality rates increased from North to South, and the concentration of deaths in the winter months also increased towards the South. Deaths with etiological confirmation of influenza show a pattern in the North and Northeast which due to the small number is not reflected in the syndromic data in the SIM.

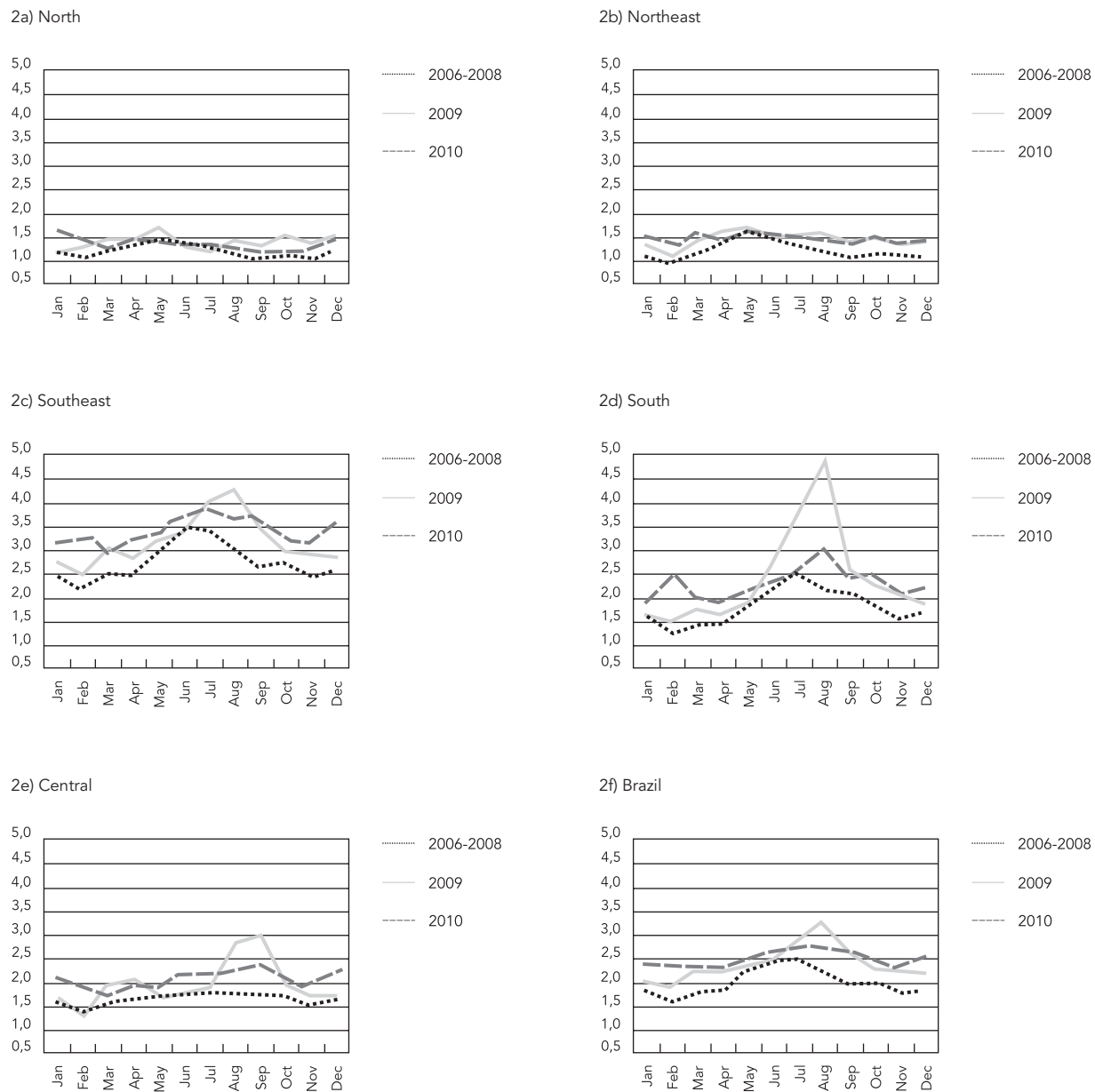
The pattern of occurrence of the influenza virus in tropical regions has still not been completely elucidated<sup>7,8,9</sup>. Two different patterns have been described in Brazil for circulation of the virus over the course of the year. In the North and Northeast, peak incidence of the disease is associated with the rainy season, from March to May, with an increase in cases during the winter months as observed in the other regions<sup>7,8,9</sup>. In a previous study that evaluated mean monthly mortality from pneumonia and influenza from 1996 to 2005 in State capitals in the North and Southeast, the peak occurred in March in the North, but in June in the Southeast<sup>8</sup>. This pattern of circulation indicates that the influenza season begins in the North and Northeast in Brazil<sup>7</sup>. According to the SIM the emergence of the pandemic strain did not have a notice-

able impact on mortality from pneumonia and influenza in these regions, but deaths in the SINAN database suggest a peak in the winter immediately after introduction of the virus, which would already differ from the usual pattern in the region, in addition to a peak in March 2010, thus before the beginning of specific vaccination. In the States closest to the temperate zone the “second wave” of pandemic influenza would be expected some three months after the peak in the tropical zone, usually in the month of June<sup>7,8</sup>, when the population had already experienced the vaccination campaign, which could explain the absence of a new increase in deaths in the SINAN databases in these regions. The South and Southeast were also affected more intensely by influenza in 2009, and the local population's higher immunity could mean lower risk of illness as compared to the inhabitants of the States to the North<sup>8</sup>.

Studies have demonstrated that deaths from pneumonia and influenza are an adequate outcome for studying mortality associated with influenza<sup>2,7</sup>. The correlation has also been demonstrated between data from the Mortality Information System and virological and clinical surveillance information to identify circulation of the influenza virus<sup>4,7</sup>. SIM data would thus be adequate for evaluating pandemic influenza in 2009. However, low influenza activity in the North and Northeast could limit the sensitivity of

Figure 2

Monthly mortality associated with influenza (ICD 10: J10 to J18 and J22) in Brazil and regions (deaths/100,000 inhabitants), 2006 to 2010.



syndromic surveillance for detecting changes in its epidemiology.

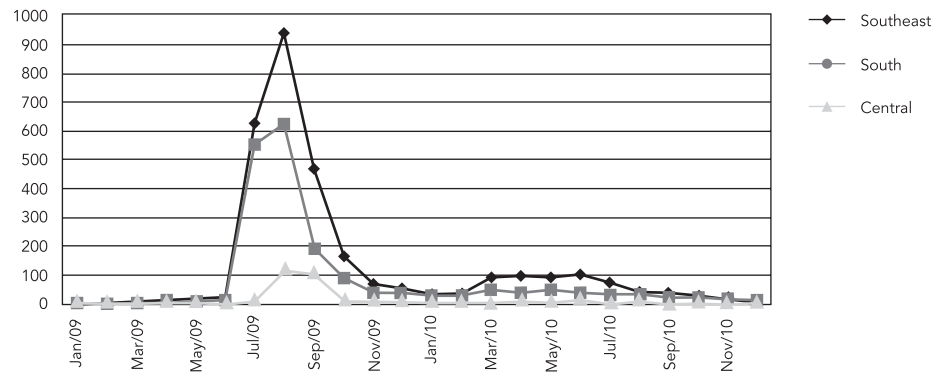
Influenza dynamics is determined not only by the characteristics of the circulating strain, population immunity, and climatic factors, but also by other factors that vary in the degree and scale to which they influence transmission and

development of the illness<sup>5</sup>. Thus, age structure, prevalence of comorbidities, environmental pollution, living habits, population crowding, and co-seasonality with other infectious agents are examples of factors not considered in this study and that could in some way influence regional differences in the epidemiology of influenza.

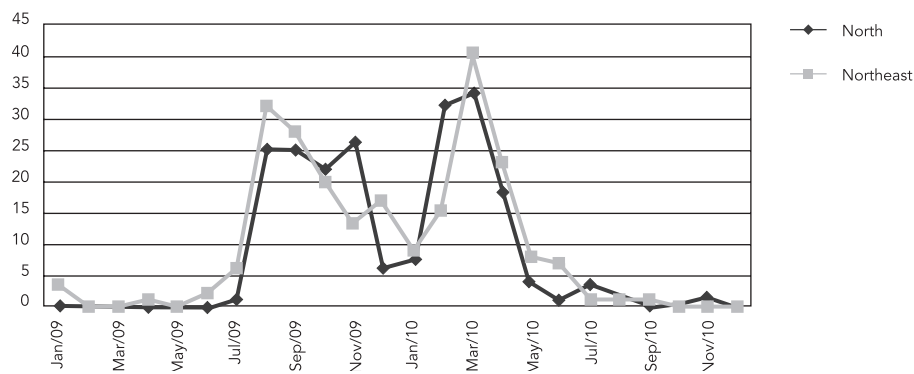
Figure 3

Monthly deaths in confirmed influenza cases reported in the Information System for Notifiable Diseases (SINAN) database by geographic regions of Brazil, 2009 to 2010.

## 3a) Southeast, Central, and South



## 3b) North and Northeast



The role of these variables in regional differences should be explored in studies for this purpose. It is also essential to improve local laboratory surveillance to elucidate the etiological profile of respiratory diseases, producing evidence that allow understanding the relevant socio-environmental determinants and supporting syndromic surveillance.

The data in this study call attention to the need to seek more specific strategies for the prevention and control of influenza according to local and regional epidemiological characteristics. The ideal moment for influenza vaccination is an example of a national recommendation that could be more effective if designed regionally, further considering the narrow period between determination of the strains circulating in the world and production of the annual vaccine.

## Resumen

*El objetivo de este artículo es examinar las diferencias regionales en la mortalidad asociada a la gripe, entre 2006 y 2010, en Brasil. La vigilancia de sindrómica, que incluye óbitos por neumonía y gripe, registrados en el Sistema de Información sobre Mortalidad, mostró un aumento en la mortalidad durante la pandemia sólo en las regiones Sur, Sudeste y Centro-Oeste. En esas regiones, principalmente en la Región Sur, ese aumento ocurrió entre julio y setiembre de 2009. Evaluándose los óbitos de casos confirmados de gripe, comunicados al Sistema de Información de Agravamientos por Notificación, se verificó un patrón temporal diferente entre las regiones Sur/Sudeste y las regiones Norte/Nordeste, con un aumento entre julio y noviembre de 2009 en todas las regiones y otro pico en marzo de 2010, antes de la campaña de vacunación, solamente en las últimas. Los resultados muestran diferencias regionales en la intensidad y en la distribución temporal de la pandemia de gripe, y apuntan a la necesidad de instrumentos de vigilancia y de control específicos para las regiones del país.*

*Gripe Humana; Epidemias; Mortalidad*

## Contributors

J. Cerbino Neto participated in the project's conceptualization and data analysis and interpretation, writing of the article, and approval of the final version for publication. G. O. Penna participated in the data analysis and interpretation, relevant critical review of the intellectual content, and approval of the final version for publication. G. L. Werneck participated in the project's conceptualization and data analysis and interpretation, relevant critical review of the intellectual content, and approval of the final version for publication.

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