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Impact of seasonality and annual immunization of elderly people upon influenza-related hospitalization rates

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SUMMARY

Objective: The objective of this study was to estimate the impact of seasonality and immunization on hospitalization rates of elderly people in a southern Brazilian state.
Methods: An epidemiological study of ecological design, combining time-series in the period 1995–2009, was carried out. The medical records of individuals residing in Santa Catarina aged ≥60 years were obtained from the Hospital Information System of the Brazilian National Health System. Multiple linear regression analysis was used to calculate the impact exerted by seasonality and by influenza immunization coverage on hospitalization rates.
Results: A decrease of 5.73% in the rate of hospitalization was observed in the first quarters of the years, and an increase of 8.75% in the third quarters of the years, showing the impact of seasonality. The results also showed that as the vaccination coverage rate increased 1%, a decrease of 0.1% was observed in the hospitalization rate.
Conclusion: Seasonality and immunization had an impact on the hospitalization rates of individuals aged ≥60 years in the state of Santa Catarina during the period studied.

1. Introduction

Despite the changing profile of morbidity as a result of demographic and epidemiological transitions experienced in recent decades,[1] infectious diseases are the leading causes of death in many countries, across all age groups.

The most common morbidities affecting the elderly population are respiratory system diseases, which have become the second leading cause of hospitalization in the southern Brazilian state of Santa Catarina, accounting for 57 425 hospital admissions between 2007 and 2009.[2]

Acute respiratory infections are disorders of the upper or lower respiratory tract that may produce mild to severe illness, and at times can even lead to death. Respiratory tract infections are the most common infections affecting humans and represent an important factor of morbidity and mortality worldwide. Among them, viral causes are predominant.[3]

Influenza morbidity rates can vary depending on the circulating virus and the degree of immunity and degree of susceptibility in the general population. In 2008, the Brazilian Epidemiological Surveillance System for Influenza recorded the cases of more than four million people; among them, 9.5% had seasonal influenza. Of 6317 nasopharyngeal specimens analyzed, 19.1% shed respiratory viruses, and of these, 25% were positive for influenza.[4]

In recent decades, the main strategy used by the Brazilian Government to reduce mortality rates and lower spending on hospital admissions related to influenza, has been vaccination with inactivated virus, consisting of three different strains. Starting in 1999 the Brazilian Ministry of Health carried out vaccination campaigns against influenza for people aged ≥65 years. Since 2000, the target population has been elderly people aged ≥60 years.[5]

The annual vaccination campaign takes place in the months just before winter, usually between April and May, and lasts 2 to 4 weeks. Protective antibodies act in the first or second week, and the peak of action occurs between the fourth and sixth weeks. In 2008 the coverage rate in Brazil reached 80%, and 37.6% of the municipalities had vaccinated more than 80% of the elderly population.[5] In the 1999/2009 period, the mean vaccination coverage rate in the state of Santa Catarina was 76.2% (standard deviation 9.9%), with a minimum rate of 56.8% in 2000 and a maximum rate of 89.7% in 1999.[2]

The impact of influenza is known worldwide, especially among vulnerable groups such as the elderly. The influenza surveillance process has been intensified each year in Brazil, in order to minimize health and economic consequences. The main objective of this study was to estimate the impact of seasonality and annual

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immunization against the influenza virus over the hospitalization rates of people aged ≥60 years in the southern Brazilian state of Santa Catarina.

2. Methods

A study of ecological design, combining an analysis of time-series between 1995 and 2009, was carried out. Hospital-based data for Santa Catarina were collected and arranged by month and year of occurrence of admissions, from the Public Brazilian National Health System, for people aged ≥60 years. This system covers approximately 70% of all hospitalizations in Brazil.

The diagnoses of influenza-related diseases were analyzed according to the International Classification of Diseases (ICD) 9th revision codes for data up to 1997, and using ICD-10 codes for the period 1998–2009. Data relating to population estimates were based on demographic censuses, population counts, and population estimates, obtained from the Brazilian Institute of Geography and Statistics (IBGE) for each year of the study. Hospitalization rates were calculated using the number of hospitalizations as the numerator and the resident population in the same age-group, sex, and period considered as the denominator. The standardization of rates was performed by the direct method considering the population in Santa Catarina in the year 2000 as standard.

Multiple linear regression analysis was performed, where the hospitalization rates (dependent variable y) were estimated by the ordinary least-squares method. The independent variables were the quarter-by-quarter seasonality (dummies) and the vaccination coverage rates. It was necessary to include a further two dummies after the analysis of data: the periods from January to February 1998 and from June to July 1998. This was necessary because in the year 1998, admission rates decreased greatly followed by a large increase, representing quite different behavior from that occurring in the other study years.

Post estimation was performed to assess the adjustment of the multiple linear regression model. The graph of residues allowed the detection of atypical observations in the data, such as failure in the assumption of homoscedasticity. The Durbin–Watson test was used for autocorrelation observation between residues.[6] The White test was used to testing homoscedasticity of residues.

The coefficient of determination (R^2) was used to estimate the proportion of variance in hospitalization rates. The statistical significance level adopted for all estimates was set at a p-value of <0.05.

3. Results

In the 1995–2009 period, 277 938 records of influenza-related hospital admissions of people aged ≥60 years were analyzed, representing 21% of total admissions in Santa Catarina, excluding hospitalizations for parturition.

The monthly rates of hospital admissions per year during the period analyzed are shown in Figure 1. The analysis of the series indicated a decreasing trend in hospitalization rates over time. A seasonal pattern could be observed, with high rates followed by periods of low rates.

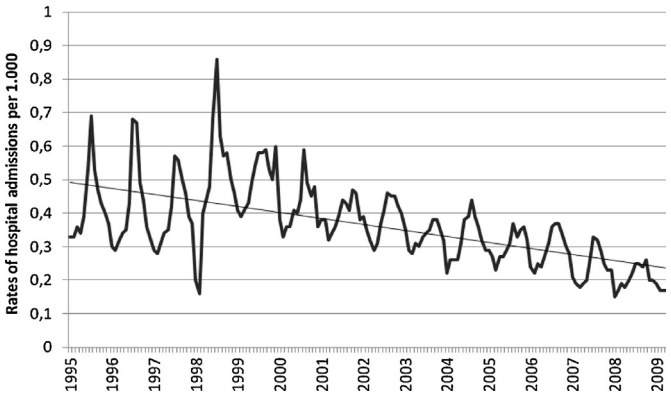

Figure 1. Rates of influenza-related hospitalization of people aged ≥60 years in Santa Catarina during the period 1995–2009.

In the correlation analysis it was possible to observe significant correlations between the first and third quarter variables, vaccination coverage rates, and the months January–February and June–July of 1998 and the trend in hospitalization rates.

The Durbin–Watson statistic (D = 1.758) pointed to there being no autocorrelation in the first order in the analysis of residues, which showed a normal distribution ($p = 0.164$; Shapiro–Wilk test). Based on the White test, it was possible to conclude that there was no heteroscedasticity of residues.

Pearson's multiple correlation coefficient was 0.850, indicating that there was a high correlation between the variables. The model's explanatory power (adjusted R^2) was 0.440, indicating that 44.0% of the variability of influenza-related hospitalization rates was explained by the variability in the independent variables used in the modeling process (Table 1). Thus, it could be inferred, with statistical significance, that the effect of the first quarter of each year variable decreased the rates of influenza-related hospitalization by 5.73% on average, holding constant the effect of the other studied variables. The effect of the third quarter of each year increased the rates by 8.75% on average, holding constant the effect of the other studied variables. The results also showed that as the vaccination coverage rate increased 1%, a decrease of 0.1% was observed in the hospitalization rate, holding constant the effect of the other variables.

4. Discussion

From the results of the present study, it can be stated that influenza-related hospitalization rates in Santa Catarina varied due to seasonality. These variations could hypothetically be related to the winter months in the south of Brazil. Some studies have suggested that seasonality influences the increase in influenza cases, for example the study performed in Portugal from 1990 to 2004.[7] Another study carried out in the southern Brazilian state of

Table 1
Multiple linear regression for rates of influenza-related hospitalization of people aged ≥60 years in Santa Catarina during the period 1995–2009 and independent variables

Independent variables	Coefficient (95% CI)	SE	t Statistic	p-Value
First quarter of each year	−0.0573 (−0.0909 to −0.0237)	0.0170	−3.370	0.001
Third quarter of each year	0.0875 (0.0544 to 0.1206)	0.0167	5.220	<0.001
Vaccination coverage rates	−0.0013 (−0.0017 to −0.0009)	0.0002	−6.380	<0.001
Months of January and February 1998	−0.1844 (−0.3174 to −0.515)	0.0673	−2.740	0.007
Months of June and July 1998	0.3045 (0.1735 to 0.4355)	0.0664	4.590	<0.001

CI, confidence interval; SE, standard error.

Rio Grande do Sul concluded that the winter months favor an increase in hospitalizations for respiratory problems.[8] In a study conducted in the USA,[9] it was reported that the winter affected the observed increase in medical demand and influenza-related hospitalizations and deaths. Brazil's south, midwest, and southeast regions have also shown seasonality, with peaks of greater magnitude between May and August of each year.[10]

In this study, a positive effect of vaccination coverage was observed. The assumption of the positive effect of influenza vaccination has been demonstrated in studies conducted in other countries, such as the USA.[9,11,12] These studies have concluded that vaccination has a positive effect in reducing hospital admissions.

Jefferson et al.[13], in a systematic review aimed at observing the evidence of efficacy and effectiveness of influenza vaccines in individuals aged ≥65 years, concluded, after adjustment for confounders, that vaccine performance was improved for admissions to hospital for influenza or pneumonia, respiratory diseases, and for all-cause mortality. However, Osterholm et al.[14], in another systematic review on the efficacy and effectiveness of influenza vaccine, concluded that the influenza vaccine provides moderate protection in some seasons, and may be reduced or absent in others. They also mentioned the lack of studies providing this evidence of a positive effect among elderly people aged ≥60 years. Another meta-analysis on the effects of vaccine against influenza in people aged ≥65 years living in close communities, pointed to a reduction in the influenza incidence of 35%, a reduction in hospitalization for pneumonia and influenza of 47%, and a reduction in mortality from all these causes in 50%.[15]

In Brazil, Daufenbach et al.[10] concluded that the decrease in influenza morbidity rates may be related to the onset of vaccination campaigns in 1999. In the state of Rio Grande do Sul, a reduction in the hospitalizations for pneumonia was observed as the effect of vaccination. Also in southern Brazil a study analyzed the decrease in influenza-related hospitalizations and deaths and pointed to a decrease in hospitalizations and deaths in the surveyed population after the year 1999.[16] Other studies conducted in southeastern Brazil[17,18] and in the Federal District[19] have indicated a positive effect of vaccination, especially in places where seasonality is more relevant, as is the case in the southern states. A reduction in hospital admissions by 25.2%, mainly after 1999, was reported in Porto Alegre, another Brazilian city.[20]

Considering the vaccination strategy adopted by the Brazilian Ministry of Health is relatively recent, since only 10 years of immunization have passed, the results presented in this study are relevant. However, it is important to highlight issues related to vaccine coverage, since a large number of elderly people are not vaccinated. This fact may be considered as a limitation of the present study and could have influenced the results. The research design did not allow investigators to determine whether the subjects were or were not immunized.

Access of the elderly population to vaccination may affect vaccine coverage, negatively influencing the increase in hospitalization rates. An example is the year 2000 when vaccination coverage in Santa Catarina was only 56.8%.[2] Another important issue is related to the strains used for the manufacture of the influenza vaccine. Vaccination is effective when there is a match between the strains that make up the vaccine and the circulating viruses.[21]

The effects of influenza immunization shown in this study should be viewed with caution because in most cases of hospital admission, no laboratory confirmation was performed. In addition, complications of influenza can also be derived from other viral or bacterial agents, which may lead to an overestimation of hospitalization rates. Comorbidities can also favor the onset of complications.

Studies of longitudinal design are suggested, since the elderly who have undergone immunization could be monitored and have their basic pathologies assessed. Population-based studies should be conducted to enhance the evidence of the effects of vaccination campaigns in the different age subgroups.

This study used the database of the Brazilian National Hospital Information System with details from the Hospital Admission Authorization formulary; these are used to support the transfer of funds to hospitals. Private health care services were excluded, which may have led to an underestimation of the hospitalization rates. In addition, the change from ICD-9 (used until 1997) to ICD-10 may have resulted in doubts in filling in the hospital admission codes.

In conclusion, significant impacts of seasonality and immunization campaign coverage upon influenza-related hospitalization rates were observed among the elderly population in Santa Catarina during the study period. Based on the results of this study, it is strongly recommended that influenza immunization campaigns are reinforced among the elderly. The benefits of the vaccine, such as the prevention of complications and deaths from influenza, should be publicized. Also, a greater engagement of health professionals, including physicians, nurses, and community health agents, is necessary to counter the myths surrounding the vaccine. They should clearly inform the elderly and other population groups that the vaccine does not cause influenza, as well as educating the public about the circulation of other viruses that can cause similar clinical pictures.

Conflict of interest: No competing interest declared.

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