Population Dynamics in the Elderly: The Need for Age-Adjustment in National BioSurveillance Systems

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Abstract. With the growing threat of pandemic influenza, efforts to improve national surveillance to better predict and prevent this disease from affecting the most vulnerable populations are being undertaken. This paper examines the utility of Medicare data to obtain age-specific influenza hospitalization rates for historical analyses. We present a novel approach to describing and analyzing age-specific patterns of hospitalizations using Medicare data and show the implications of a dynamic population age distribution on hospitalization rates. We use these techniques to highlight the utility of implementing a real-time nationwide surveillance system for influenza cases and vaccination, and discuss opportunities to improve the existing system to inform policy and reduce the burden of influenza nationwide.

Keywords: real-time surveillance, influenza, age-adjustment, elderly, Medicare

1 Introduction

Influenza is a significant public health problem in the United States. From 1968 to 1998, annually, there were, on average, over 6,000 deaths that were directly attributable to influenza [11], and over 36,000 annual deaths considered to be pneumonia, induced by influenza, or influenza-related (P&I) [13]. Nationwide, there are over one million hospitalizations in the population age 65 and over for P&I-related conditions annually [14]. An influenza pandemic could result in serious economic consequences, as well. In the US alone, a pandemic causing infection in 15-35% of the population could result in nearly $170 billion in direct and indirect costs [5].

The elderly are particularly vulnerable to the morbidity and mortality associated with influenza. The age-specific mortality rate from P&I deaths is nearly 100 times higher in people aged 65 and over (22.1/100,000 person-years) than for children under 1 year of age, the group with the second-highest influenza mortality rate (0.3/100,000 person-years). From 1990 through 1998, 90% of influenza-associated deaths occurred among the population age 65 and older [13].

Accurate and timely surveillance of influenza at the nationwide level is challenging. In the US, influenza surveillance is accomplished primarily through reporting of laboratory-confirmed cases to the Centers for Disease Control and Prevention (CDC). As part of the influenza surveillance effort, CDC also maintains a specialized mortality and morbidity reporting system, the 121 Cities Mortality Reporting System, where influenza deaths are reported from 122 cities and metropolitan areas throughout the US within two to three weeks of the death. These surveillance issues become even more important when considering that this disease is largely preventable [4].

This report examines the Center for Medicare and Medicaid Services (CMS) surveillance data on influenza-associated hospitalizations. We describe the utility and accuracy of using smoothed data-based, age-specific P&I hospitalization rate model parameters as an outcome measurement of P&I morbidity. We also examine the effect of population dynamics, namely, the rapidly changing age distributions in the elderly population, on estimating rates of age-specific P&I hospitalizations. This case study will underscore the shortcomings in the current national surveillance systems for influenza and highlight some potential opportunities for improvement.

2 Methods

2.1 Data

The data for this analysis come from two sources: CMS and the US Census Bureau. The CMS dataset contains all hospitalization records from 1998 through 2002. The populations served by Medicare include the general population age 65 and over, along with those with end-stage renal disease. The Medicare database covers 98% of the US population age 65 and above [7]. The US Census data used in this analysis consisted of the state-level age-specific population by state from Census 2000, abstracted from Summary File 1.

2.2 Data Abstraction

We abstracted approximately 6.2 million records containing all P&I hospitalizations (ICD codes 480-487) for the Medicare population age 65 to 99. We excluded cases from the population age 100 and over. The cases extracted occurred between July 1998 and June 2002 by single year of age, state of primary residence, and influenza year. An influenza year was defined to start on July 1 and end on June 30 of the following year. We examined four consecutive influenza years in this analysis (1998-99 through 2001-02).

To obtain the denominator of the age-specific P&I hospitalization rate, we gathered data from the 2000 US Census containing the population distribution of each state by single year of age for April 1, 2000. The total count of P&I cases by age, state, and season was then divided by the Census 2000 population for that state and age to obtain P&I hospitalization rates for each influenza season.

2.3 Estimation of P&I Hospitalization Parameters

Because the morbidity rates for P&I morbidity tend to increase exponentially with age in the elderly population [2], the age-specific rates were modeled against age according to the model

$$\log(\text{rate}_{ij}) = \beta_{0i} + \beta_{1i}(\text{age}_j\text{-}65) + \varepsilon_i, \quad \text{where } i = \text{state},\ j = \text{age} \qquad \mathbf{(1)}$$

Thus, β_{0i} represents the estimated intercept for the state, which represents the log of the estimated P&I hospitalization rate in each state at age 65. β_{1i} is the rate of change in the log-transformed P&I hospitalization rates by age for each state. The larger the value of β_{1i} was, the sharper the increase in P&I hospitalization rates by age in the state was. These model parameters comprised the two main variables of analysis.

2.4 Statistical Analysis

Validity of Outcome Measures. To ensure that the outcome measures, the state-specific model parameters for the P&I hospitalization rates regressed against age, provide reliable estimates of the true rates, we obtained R-squared statistics for each of the regression models for each state and for each influenza season.

Sensitivity and Adjustment for Population Change. Because the age-specific population used in the denominator of the P&I hospitalization rates changes over time, we explored the relationship between using a dynamic denominator, based on US Census Bureau estimates for the population in each year (1998-2002) and using the static measures from Census 2000. The results of changing this denominator are illustrated using a series of Lexis diagrams with contour plots of population change. Lexis contour maps are derived from Lexis diagrams, which are graphical tools commonly used in demographic research. Lexis contour maps have calendar time, often expressed in years, on the horizontal axis and age on the vertical axis. The contours can represent any variable in which one seeks to analyze age and time effects simultaneously.

Software. SAS version 9.0 was used for all statistical analyses. For graphs, Microsoft Excel 2003 was used, along with S-PLUS version 7.0 for Lexis contour maps.

3 Results

3.1 Validity of Outcome Measures

The state-level age-specific P&I rates were regressed against age to obtain the outcome measures, the slope and intercept of the models by state. To assess the model fit, we obtained R-squared values for each state and season (Table 1).

Table 1. R-squared values of state-level regression models by season.

State	**Season**				**State**	**Season**			
	1998-1999	*1999-2000*	*2000-2001*	*2001-2002*		*1998-1999*	*1999-2000*	*2000-2001*	*2001-2002*
Alabama	0.976	0.968	0.966	0.984	Montana	0.782	0.942	0.801	0.723
Alaska	0.740	0.555	0.785	0.765	Nebraska	0.920	0.918	0.930	0.971
Arizona	0.862	0.938	0.936	0.916	Nevada	0.895	0.968	0.854	0.705
Arkansas	0.965	0.955	0.910	0.952	New Hampshire	0.876	0.921	0.819	0.741
California	0.983	0.991	0.990	0.957	New Jersey	0.982	0.979	0.965	0.933
Colorado	0.963	0.897	0.955	0.936	New Mexico	0.961	0.886	0.956	0.898
Connecticut	0.943	0.974	0.945	0.918	New York	0.987	0.975	0.974	0.975
Delaware	0.791	0.826	0.756	0.811	North Carolina	0.955	0.945	0.965	0.973
DC	0.852	0.873	0.828	0.875	North Dakota	0.946	0.889	0.961	0.951
Florida	0.966	0.990	0.970	0.983	Ohio	0.963	0.973	0.966	0.948
Georgia	0.972	0.961	0.977	0.963	Oklahoma	0.934	0.907	0.991	0.984
Hawaii	0.814	0.503	0.786	0.797	Oregon	0.880	0.897	0.923	0.908
Idaho	0.727	0.900	0.828	0.873	Pennsylvania	0.959	0.961	0.933	0.954
Illinois	0.977	0.969	0.988	0.972	Rhode Island	0.879	0.899	0.865	0.912
Indiana	0.992	0.959	0.966	0.949	South Carolina	0.949	0.942	0.937	0.966
Iowa	0.933	0.973	0.974	0.952	South Dakota	0.926	0.939	0.935	0.967
Kansas	0.943	0.959	0.967	0.940	Tennessee	0.983	0.973	0.985	0.969
Kentucky	0.975	0.963	0.974	0.978	Texas	0.977	0.960	0.976	0.979
Louisiana	0.986	0.975	0.896	0.960	Utah	0.887	0.754	0.881	0.903
Maine	0.843	0.895	0.924	0.954	Vermont	0.895	0.835	0.887	0.900
Maryland	0.968	0.950	0.879	0.948	Virginia	0.968	0.957	0.938	0.937
Massachusetts	0.974	0.927	0.960	0.957	Washington	0.978	0.979	0.887	0.940
Michigan	0.978	0.920	0.955	0.937	West Virginia	0.929	0.949	0.931	0.949
Minnesota	0.959	0.945	0.968	0.957	Wisconsin	0.927	0.966	0.927	0.830
Mississippi	0.923	0.988	0.971	0.955	Wyoming	0.769	0.901	0.821	0.775
Missouri	0.966	0.975	0.945	0.979					

In general, this approach to parameterizing the state-level age-specific P&I mortality rates in the older population was fairly precise. In 145 of the 204 cases (71.1%), the R-squared value was above 0.90, verifying that P&I hospitalization rates increase nearly exponentially with age from age 65 to age 99. These exponential models tended to perform less accurately in some states, such as Hawaii, where in the 1999-2000 season, the model R-squared was only 0.503. Moderate R-square values were seen in states such as Wyoming (0.769-0.901), Montana (0.723-0.942), Alaska (0.555-0.785), and others.

Figure 1 shows a comparison of two states where the model performed markedly differently: Hawaii in the 1999-2000 season (R^2 = 0.503) and Indiana in 1998-1999 (R^2 = 0.992). This example suggests that much of the deviation from the predicted P&I rates for Hawaii comes from the population in the oldest age groups. The predicted rates are similar to the actual rates for ages 65 through the late 80's. From the late 80's through age 99, the actual rates show more random variation from year to year. This is most likely due to extremely small age-specific populations in this age group in Hawaii.

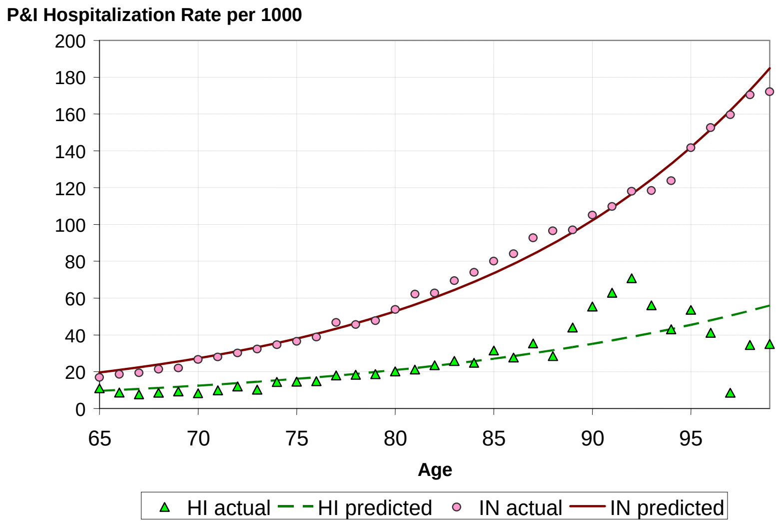


Fig. 1. Actual and model-based predicted P&I rates by age for Hawaii (1999-2000) and Indiana (1998-1999).

The same holds true for other states, as well. In contrast, the actual and predicted P&I rates are much more similar in Indiana throughout all age groups. Thus, one advantage of this technique is to smooth P&I hospitalization rates in cases such as Hawaii where the actual rates may have extra variation due to small population size leading to more noise in the estimates.

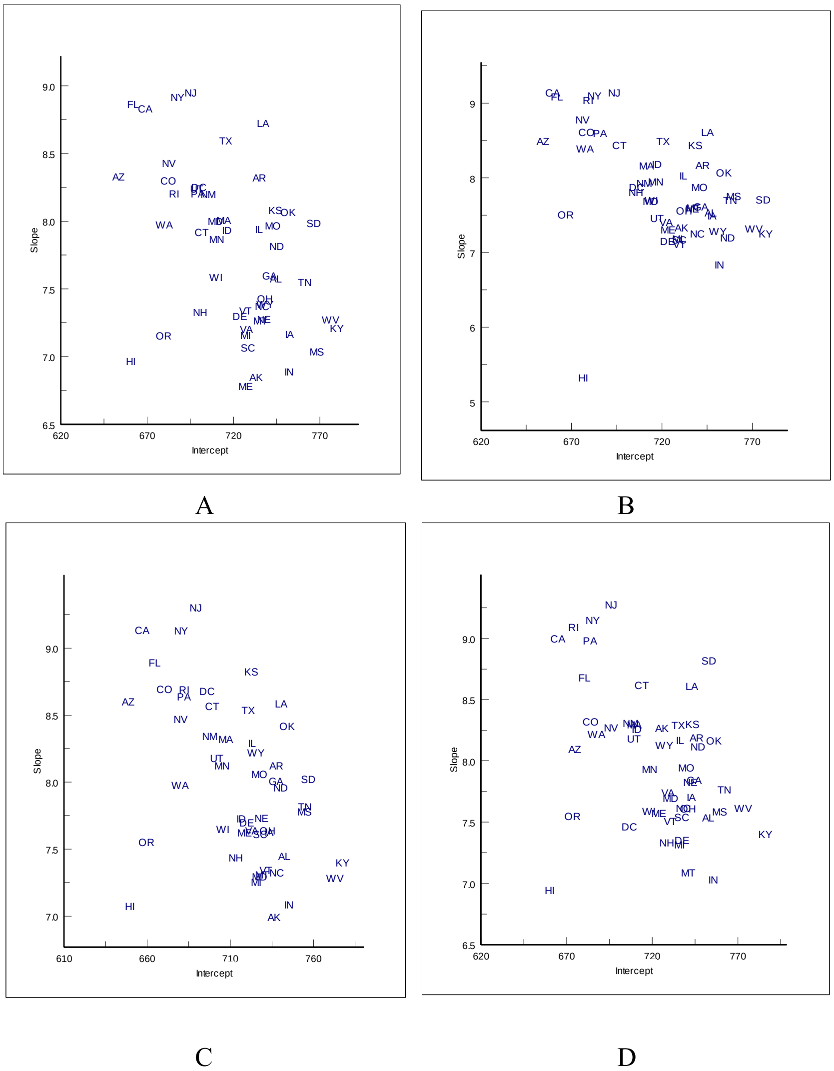
To simplify the estimation procedure, we log-transformed the P&I rates as described above and multiplied those parameters by 100. The results of the models are shown as descriptive statistics in Table 2.

Table 2. Descriptive statistics for derived intercept and slope outcome variables.

	Minimum	Maximum	Mean	Std. Dev.
Intercept 98-99	653.2	779.7	720.1	30.7
Slope 98-99	6.79	8.96	7.79	0.59
Intercept 99-00	654.0	777.2	720.5	31.6
Slope 99-00	5.34	9.16	7.87	0.71
Intercept 00-01	648.4	777.2	715.2	30.9
Slope 00-01	7.00	9.31	8.01	0.59
Intercept 01-02	659.9	785.8	723.4	29.5
Slope 01-02	6.96	9.29	8.01	0.56

This table shows that the intercept and slope parameters remained fairly steady over the time period of analysis.

Figure 2 illustrates the relationship between slope and intercept by state for each of the four seasons examined.



A

B

C

D

Fig. 2. Scatterplots of the relationship between state-specific slopes and intercepts for 1998-1999 (Panel A), 1999-2000 (Panel B), 2000-2001 (Panel C), and 2001-2002 (Panel D).

The slopes and intercepts in each state were inversely related to each other. States with higher intercepts tended to have lower slopes. This means that, typically, a state that had higher rates of P&I hospitalization at the younger ages had a lower subsequent rate of increase in P&I hospitalizations with age.

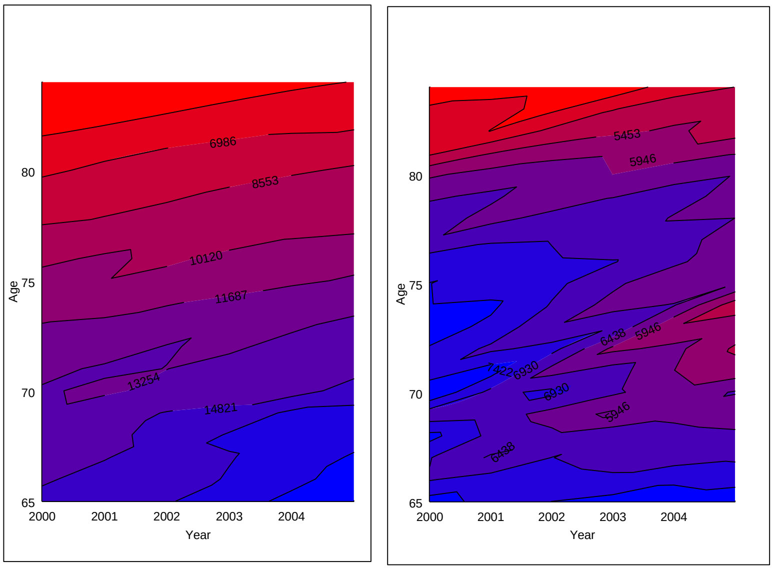
3.2 Adjustment for Population Change

The age-specific population estimates extracted from the US Census Population Estimates Branch for 2000-2005 are shown in Figure 3 for two states for ages 65-84. These panels show two examples of distinct patterns of population change on the state level. In Nevada, there was rapid population growth in the entire population age 65-84 over time. For example, there was a 25% increase in the population age 65 in Nevada between 2000 and 2005, and a 31% increase in the same time period in the population age 80. Rhode Island (Panel B), however, experienced population decline in the younger age brackets (67-79), but had a growing population in the oldest age groups (80-84). The Rhode Island population declined by 17% between 2000 and 2005, while the population age 84 increased by 15% over that same five-year span.

These have important implications for the calculation of P&I hospitalization rates. For example, in Nevada, where population growth is among the highest in the country, using Census 2000 populations in the denominator of rates would have a noticeable impact on the rates of disease. Figure 4 shows the percent difference between the age-specific P&I hospitalization rate using Census 2000 and Census estimates for individual years for the years 2000-2003. This graph shows that if Census 2000 is used instead of Census estimates for years other than 2000, the discrepancies between P&I rates generally grow with time.

The color gradient depicts the change in population as the following: yellow to red colors represent increases in age-specific populations, while green regions represent decreases in age-specific populations compared to Census 2000. Most of the graph shows yellow and red regions, which represent ages and years in which the P&I rate would be overestimated if using Census 2000 because the population has grown since the 2000 Census. There is a small section of the graph that appears green. There was a small population decline from 2000 to 2003 at age 72. If Census 2000 figures were used to calculate P&I hospitalization rates for 72-year-olds in 2003, this figure would actually represent a minor overestimate, since the population has decreased.

Some recent events illustrate that large-scale events can cause rapid changes to the structure and size of city- and state-level populations. In the case of Hurricane Katrina, for instance, the widespread mortality and out-migration that occurred because of the storm caused the population of New Orleans and Louisiana to change dramatically in a relatively small time interval. Migration and death due to the storm did not affect the population equally at all ages [15]. These changes can have serious consequences in the estimation of disease incidence that would not be captured if using population data only from the Decennial Census.



A- Nevada

B- Rhode Island

Fig. 3. Lexis contour plots of age-specific population for two states over time.

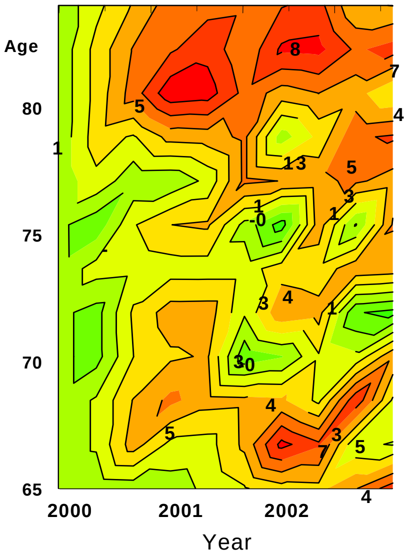


Fig. 4. Percent difference in P&I hospitalization rates by age and year for Nevada comparing Census 2000 and individual year Census estimates as the denominator.

4 Discussion

4.1 Implications of Analysis

The results of this analysis have important implications for national surveillance of influenza. In terms of analytical techniques, a useful means of assessing the cumulative, season-based P&I hospitalization rates when single-year age-specific P&I rates are available is the method we employed, based on the regression of log P&I rate on age for each state. For most states, the model parameters obtained through this technique accurately reflected the actual P&I rates abstracted through the CMS data.

This approach also simplifies a vast amount of data into two straightforward, relevant characteristics about the P&I influenza rates in each state. The intercept provides the general level of P&I hospitalizations in each state, while the slope provides information on the most vulnerable section of the population, the oldest old. The slope, arguably, is the more important measure for several reasons. The actual age-specific P&I hospitalization rates are orders of magnitude higher in the oldest ages compared to the younger elderly. This means that small differences in slopes between states could potentially translate to large differences in the rates of P&I hospitalization in the oldest elderly population. One may challenge this notion by stating that although the P&I hospitalization rates are highest in the oldest age groups, the actual numbers of elderly in those age groups affected by P&I morbidity is low, simply because of smaller age-specific population sizes in the oldest elderly population. However, given that the majority of influenza-related hospitalizations and deaths occur in the older age categories, monitoring and modeling P&I hospitalization rates on this vulnerable population is particularly critical to prevent morbidity and delay mortality.

This method also adjusts for differences in the population composition between states. This is because the method is based on rates, as opposed to counts of cases, and those rates are specific to the state population age distribution. This method could also be applied to smaller areas of observation, such as counties, although the models would be expected to be less accurate due to smaller, less stable populations.

An important consideration when using this method, as with any other methods involving rates of disease, is the selection of the population as the denominator. As observed in the above results, small changes in population size have a noticeable effect on infection rates, especially considering the small population size in the older age groups.

4.2 Example: Establishing a Vaccination Surveillance System

A key function of the surveillance system is its utility in the monitoring and prevention of disease in the population. In regard to influenza prevention, the current national disease surveillance system does not contain information on the most widespread prevention mechanism: vaccination.

According to the Centers for Disease Control and Prevention (CDC), the primary means of controlling the detrimental effects of influenza is through annual vaccination [12]. The CDC currently recommends that certain population groups be vaccinated on an annual basis. Given an insufficient vaccine supply necessary for universal vaccination, the CDC recommends immunizing the elderly against influenza, and then people age 2 to 64 with comorbid conditions and who would be more susceptible than others in this age group, then the elderly who have comorbid conditions. Fourth on the list of priority groups are children age 6 to 23 months.

Although vaccinating the elderly against influenza has been shown to reduce P&I morbidity and mortality [8], recent research has questioned the policy of vaccinating the elderly for several reasons. First, vaccine efficacy in the elderly is low compared to other population subgroups [3]. Second, there is mounting evidence that herd immunity may form in the elderly as a result of vaccinating other population subgroups in which vaccine efficacy is high [9], [10]. Future research could help elucidate if an effective strategy to control influenza-related outcomes would be to vaccinate children, and if certain population-level factors modify morbidity and mortality in the elderly population [6], [16].

This research can be accomplished by improving the current national surveillance system for influenza. One way of improving national surveillance efforts is to implement a national surveillance system for influenza vaccination. Currently, influenza vaccination coverage in children, adults, and the elderly is conducted only through surveys, such as the National Immunization Survey and the Behavioral Risk Factor Surveillance System. As with any survey, the results are susceptible to biases, such as selection bias, and are associated with a level of uncertainty because the survey represents just a sample of the population. Another issue pertains specifically to the National Immunization Survey, which provides data on child immunizations. This survey provides data only on children age 19 to 35 months for influenza vaccinations. This excludes children age 3 years and older, which represents a large segment of the child population. This segment of the population could potentially be as or more important than the population age 19 to 35 months in transmitting influenza virus for several reasons. First, the population size of 3-17-year-olds is substantially larger than the population age 19 to 35 months in each state. Second, and perhaps more importantly, this population subgroup may potentially have a greater role in transmitting influenza virus both within their own population subgroup, as well as to other population subgroups, compared with the population 19 to 35 months of age. The influenza virus acquired in these settings could then be transmitted to other population subgroups through family contacts and in other public settings [7]. Thus, having a nationwide surveillance system that includes age-specific influenza vaccination coverage for all ages could further this research and help elucidate which population subgroups to vaccinate against influenza in order to achieve the maximum benefit in terms of morbidity and mortality reduction.

Timing is another key feature of a proposed national surveillance system for influenza vaccination. Theoretically, people are vaccinated before the influenza season begins, which typically occurs in the fall. However, the current vaccination surveys typically ask whether a person has been vaccinated against influenza in the past calendar year. If the period of interest is, for example, January through December of a given year, the vaccinations that are recorded in this survey may be from late in the prior season or in the fall of the current season, which would tend to push any potential associations between vaccination and indirect benefits toward the null. A nationwide surveillance system in which the timing of vaccination is recorded would reduce this contamination, and afford the opportunity to determine if the timing of vaccination is related to the timing and amplitude of the seasonal peak in P&I hospitalizations by population subgroups.

4.3 Opportunities to Improve National Influenza Surveillance

Medicare data on P&I hospitalizations can be used to perform a historical analysis, such as the one presented in this paper. However useful from an analytical perspective, Medicare data does not provide information in real-time. From an analytical perspective, this CMS data contains information on the entire Medicare-eligible population, as opposed to a sample of the elderly population. One can extract and model the timing, amplitude, and other features of the P&I hospitalization rates by state over time, and, in conjunction with improved immunization data quality, could estimate the relationships between immunization timing and intensity with P&I hospitalization timing and intensity.

Since Medicare data is not provided in real-time, it has little utility for measuring the burden of influenza in the current influenza season. This data also covers only one segment of the population. The best source of data on real-time influenza cases from the entire population is from the CDC’s 121 Cities Mortality Reporting System. This provides up-to-date information on the latest reported influenza cases in the 122 cities and metropolitan areas associated with this reporting system. This system, however, does not include all of the rural areas of the country. According to a recent report by RAND [1], hospitalizations for acute infectious diseases actually occur more frequently in rural areas than in urban areas, suggesting that a simple extrapolation of the 121 Cities Mortality Reporting System to the national level would underestimate the true burden of influenza morbidity in the general population, especially in rural states.

5 Conclusion

This is just some of the rationale to underscore the importance of establishing and maintaining a real-time nationwide surveillance system for influenza. Combining the precision and coverage of the CMS data along with the timeliness of the 121 Cities Mortality Reporting System, a real-time surveillance system would be beneficial, not only for researchers, but for policymakers and other stakeholders involved with influenza prevention and control. This becomes especially critical, given the present threat of a worldwide influenza pandemic in the near future.

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