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Spatio-temporal analysis of pneumonia and influenza hospitalizations in Ontario, Canada

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Abstract. Pneumonia and influenza represent a significant public health and health care system burden that is expected to increase with the aging of developed nations' populations. The burden of these illnesses is far from uniform however, with recent studies showing that they are both highly spatially and temporally variable. We have combined spatial and time-series analysis techniques to examine pneumonia and influenza hospitalizations in the province of Ontario, Canada, to determine how temporal patterns vary over space, and how spatial patterns of hospitalizations vary over time. Knowledge of these patterns can provide clues to disease aetiology and inform the effective management of health care system resources. Spatial analysis revealed significant clusters of high hospitalization rates in northern and rural counties (Moran's I = 0.186; P <0.05), while county level time series analysis demonstrated significant upward trends in rates in almost a quarter of the counties (P <0.05), and significant seasonality in all but one county (Fisher-Kappa and Barlett Kolmogorov Smirnov tests significant at the level P <0.01). Areas of weak seasonality were typically seen in rural areas with high rates of hospitalizations. The highest levels of spatial clustering of pneumonia and influenza hospitalizations were found to occur in months when rates were lowest. The findings provide evidence of spatio-temporal interaction over the study period, with marked spatial variability in temporal patterns, and temporal variability in spatial patterns. Results point to the need for the effective allocation of services and resources based on regional and seasonal demands, and more regionally focused prevention strategies. This research represents an important step towards understanding the dynamic nature of these illnesses, and sets the stage for the application of spatio-temporal modelling techniques to explain them.

Keywords: pneumonia, influenza, hospitalization, spatio-temporal analysis, Ontario, Canada.

Introduction

The utility of spatial and time-series analysis techniques are increasingly recognized in health research as a means to better understanding disease processes and health care system demands (Morris and Munasinghe, 1994; Carey et al., 2003; Dowell et al., 2003; Crighton et al., 2005). Individually, however, these techniques are limited in that there is always a danger that important temporal changes may be missed by aggregating over time, and important spatial changes may be missed by aggregating over space. Stemming from our past work which identified both significant spatial and temporal variability in pneumonia and influenza hospitalizations in Ontario, Canada (Crighton et al., 2007a,b), this

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study combines these dimensions to seek evidence of spatio-temporal interaction. The application of spatio-temporal analysis techniques to health services data such as pneumonia and influenza hospitalizations has been largely unexplored to date. A better understanding of the patterns of health service use will serve to better inform more effective allocation of resources and services, and provide clues to the determinants of diseases such as pneumonia and influenza.

Pneumonia and influenza represent a significant public health and health care system burden across the developed world. In Canada, these illnesses are the most frequent cause of death from infectious disease, and with between 60,000 and 70,000 hospitalizations per year, pneumonia and influenza are the most common respiratory disease diagnoses contributing to hospitalization (Health Canada, 2001). The weight of this burden, however, is by no means felt uniformly across space or time. Past time-series studies have identified various pneumonia and influenza outcomes to be significantly seasonal in nature, demonstrating highly consistent peaks in winter months and troughs in summer months (Keistinen et al., 2001; Dowell et al., 2003). Variations in the seasonal timing of peaks and troughs by age groups, have also been reported (Crighton et al., 2004). Associations between air pollution, low air temperature, and most significantly, circulating viruses, are among the factors that have been linked to these patterns (Glezen et al., 1996; Donaldson and Keatinge, 2002).

Spatial variability in pneumonia and influenza hospitalizations have also been reported. A study in the United Stated (US) (Morris and Munasinghe, 1994) revealed marked regional patterns in pneumonia hospitalizations, which were explained in part by socio-economic and health care system factors including education, income and physicians per capita. Our work similarly found significant geographic clustering in hospitalization rates at the Ontario county level, by age and gender (Crighton et al., 2007a). Factors associated with these patterns include education, proportion of Aboriginal populations, behavioural factors such as smoking and drinking, influenza vaccination and temperature (Crighton et al., 2007b). While each of these studies has contributed to our understanding of either the spatial or temporal patterns of pneumonia and influenza, the underlying processes driving these patterns are inherently spatial and temporal in nature. This represents an important limitation that is increasingly becoming recognized by epidemiologists and health geographers alike (Earickson and Meade, 2000; AvRuskin et al., 2004; Assuncao et al., 2005; Greiling et al., 2005).

While research on spatial and temporal dimensions of disease is not new, the availability of datasets and improved computing capacity have led to an increased interest in the development and application of spatio-temporal analytical methods (Earickson and Meade, 2000; AvRuskin et al., 2004; Assuncao et al., 2005; Greene et al., 2005). This has perhaps been most notable in the study of chronic diseases such as cancer (Carlin and Xia, 1998; Earickson and Meade, 2000; AvRuskin et al., 2004; Assuncao et al., 2005; Greene et al., 2005; Greiling et al., 2005), although factors such as the 9-11 attacks in New York have stimulated research on rare disease outbreak detection (Kleinman et al., 2004). Studies on spatio-temporal patterns of influenza have also been conducted. These include work by Boussard et al. (1996) who, using weekly sentinel data from France, produced time-series maps of influenza to characterize the spatio-temporal spread of the disease. Although strictly descriptive, this work allowed for the visualization of disease evolution over time and space, and has significant potential for helping to establish disease control measures and understand disease aetiology. More recently, Assuncao et al. (2005), tested a space-time permutation scan statistic on daily New York City hospital influenza surveillance data. Primarily methodological in focus, the results of this work revealed the statistic was effective in detecting clusters prior to a city wide flu outbreak. Finally, a study from Greene et al. (2006) examined spatio-temporal patterns of pneumonia and influenza mortality in

people over 65 years of age in the 48 contiguous US states. Here correlograms and regression models were used to estimate the relation between synchrony and dominant virus subtype during influenza seasons. Among the results was the finding that the degree of regional correlation in mortality patterns varied according to the dominant circulating virus subtype. Although important, these studies only represent a starting point for our understanding of spatio-temporal patterns of pneumonia and influenza.

In an effort to better understand the spatio-temporal patterns of these illnesses, we have incorporated descriptive spatial and time-series analysis techniques to the study of monthly, county level pneumonia and influenza hospitalizations data for the province of Ontario (see Fig. 1). Specifically, this study attempts to determine how temporal patterns of pneumonia and influenza hospitalizations vary over space and how spatial patterns of hospitalizations vary over time.

Materials and methods

Study site

We conducted a retrospective, population-based study to assess spatio-temporal patterns in hospitalizations for pneumonia and influenza in the province of Ontario (Fig. 1). There were approximately 12 million Ontario residents as of 2001 included in this analysis. For residents of Ontario, access to health care services is universal through the Ontario Health Insurance Program. Ontario is a geographically diverse region covering an area larger than France and Spain combined. Northern areas of the province are sparsely populated with resource-based economies. Northern summers are mild and winters prolonged and cold. Southern Ontario is made up of both sparsely populated rural agricultural areas, and the province's major urban centres (i.e. Toronto, the provincial capital;

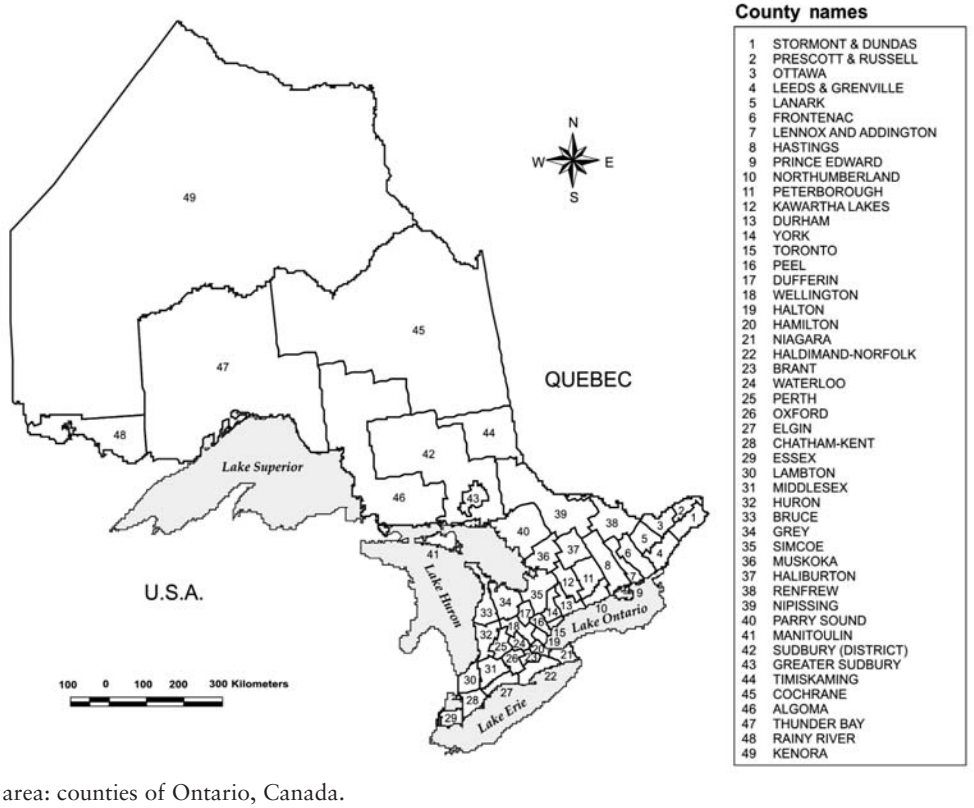

Fig. 1. Study area: counties of Ontario, Canada.

Hamilton; Windsor; and London). Ottawa, the Nation's capital, is located in the far east of the province. In these areas, summers are hot, and winters, while still well below freezing, are somewhat more moderate.

Data

The Canadian Institute for Health Information (CIHI) Discharge Abstract Database was used to obtain information on hospitalizations for pneumonia and influenza as the principal diagnosis, by county of patients' usual residence. This database records discharges from all inpatient hospital stays in Ontario acute care hospitals, documenting diagnoses as coded by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Nine years of CIHI hospitalization data were examined, covering the period between April 1st, 1992 and March 31st, 2001. The temporal unit of analysis used are months, and the geographic unit of analysis are census divisions or "counties" (N = 49).

Researchers using this database have found that CIHI diagnoses are coded with a high degree of accuracy (Williams and Young, 1996). There is very little missing information in the Ontario database; other province-level studies have similarly found that less than 1% of the basic information on patients is missing (Bedard et al., 1994; Malcolm and Rawson, 1995). The reliability of the coding of data collected by the CIHI is 74% to 96% for the ICD-9 diagnosis. For pneumonia, however, the reliability of specific aetiologic information is low (approximately 52%) (Durant et al., 1987), in aggregate form, pneumonia and influenza have been found to be reliably coded (81%) (Upshur, 1997). Influenza and pneumonia are commonly examined in aggregate (ICD-9 codes: 480-487) as the influenza virus often precedes secondary bacterial pneumonia and influenza is one of the main causes of viral pneumonias (Upshur, 1997; Upshur et al., 1999; Crighton et al., 2004, 2007a,b).

All records with a principal discharge diagnosis of influenza or pneumonia (ICD-9 code: 480-487) were selected (N = 241,803). The total number of discharges for each county were assessed over the study period. All transfers from within one acute care hospital to another within this study group were excluded from the analysis. Annual county level population data for residents of Ontario were provided by Statistics Canada (Statistics Canada, 2004). Monthly population estimates were derived through linear interpolation, and from these data, directly age and gender standardized rates were calculated (Breslow and Day, 1987). Rates were further standardized for length of month.

Analysis

Analysis of the data involved combining time series and spatial analysis techniques to explore spatio-temporal patterns of pneumonia and influenza hospitalizations.

Spectral analysis was conducted to test for county level seasonality. Spectral analysis detects periodicity in time series (Fuller, 1976). Two tests for the null hypothesis that the series is strictly white noise were conducted. The Fisher-Kappa (FK) test is designed to detect one major sinusoidal component buried in white noise, whereas the Bartlett Kolmogorov Smirnov (BKS) test accumulates departures from the white noise hypothesis over all frequencies (Priestly, 1981). The autocorrelation function (ACF) was then used to measure the correlation between observations at different time lags (Box and Jenkins, 1976). Stationarity of the time series were assessed by visually inspecting their autocorrelation and partial ACFs. R-squared autoregression coefficients ($R^2_{Autoreg}$) were then calculated. Autoregression can be used for quantifying the strength of the seasonality within a set of serially correlated observations as occurs with time-series data (Crighton et al., 2003). Finally, a linear regression model was used to estimate the trend in hospitalization rates over the study period.

Spatial analysis was done to assess the degree of spatial autocorrelation in the county level time-series results, and on the monthly aggregated data,

using the global Moran's I statistic. Significant spatial autocorrelation indicates a regular pattern in the data over space such that a value at a given location depends on, and is similar to, a value of defined spatial neighbours. Neighbour relationships are typically expressed in a row standardized spatial weights matrix *W* whose elements *wij* represent the binary spatial weights assigned to pairs of units *i* and *j* (Cliff and Ord, 1981; Bailey and Gatrell, 1995). For this analysis, neighbours are defined using rook's case adjacency, which considers all counties with common borders as neighbours.

Moran's I is a global test and does not detect localized patterns. Further analysis was therefore conducted using the local indicator of spatial association (LISA; Anselin, 1995). The LISA allows for the decomposition of the Moran's global indicator into the contribution of each individual observation. The LISA statistic indicates the degree of local spatial clustering of similar or dissimilar observations of an attribute. To test for significant departures from zero autocorrelation, a Monte Carlo permutation approach was used, and a Bonferroni correction applied to adjust for multiple testing.

All analyses were performed using SAS 8.2 (SAS Institute Inc., Cary, NC, USA), ArcView GIS, version 3.3, software (ESRI Inc, Redlands, CA, USA) and Space Time Intelligence System (STIS), version 1.11, software (TerraSeer, Inc. Crystal Lake, IL USA).

Results

There were a total of 241,803 pneumonia and influenza hospitalizations in Ontario over the study period, representing a mean yearly provincial rate of approximately 242 per 100,000 population, with mean monthly county rates ranging from 14 to 56 per 100,000 (Table 1). The spatial pattern of mean pneumonia and influenza hospitalization rates can be seen in Figure 2. The highest rates are in northern and rural counties, including Manitoulin, Kenora and Timiskaming, and the lowest rates in southern and predominately urban counties including York, Ottawa-Carleton, Toronto and Peel. The Moran's I statistic shows a moderate, statistically significant degree of spatial autocorrelation in the data (Moran's I = 0.186; P = 0.023), indicating that counties with similar hospitalization rates are clustered together. A sequence of monthly time-series maps covering the 9-year study period were produced (data not shown). These revealed that the general north-south, urban-rural spatial patterns seen in the aggregate data, appear to persist when the data is disaggregated over the study period, although significant spatial autocorrelation is typically only seen between the late spring and autumn.

Table 1 shows the mean minimum and maximum rates by county along with their corresponding months. Seasonal minimum rates consistently occurred between July and September with rates ranging from less than 10 per 100,000 in the predominately urban southern counties including York, Ottawa-Carleton and Middlesex, to over 30 per 100,000 in the rural northern counties of Manitoulin and Kenora. Seasonal maximum rates occurred between January and March, with the lowest rates again in the urban southern counties, and the highest rates in the northern and rural counties. These seasonal patterns for select counties are illustrated in Figure 3. The coefficient of variation (CV), defined as the standard deviation expressed as a percentage of the mean, was used to assess the variation in rates (Table 1). The lowest CVs (e.g. <35%) are seen primarily in the urban and southern counties where the lowest hospitalization rates were identified. CVs in the northern and rural counties are frequently above 45%, and in two counties exceed 60%.

Consistent and significant seasonality in pneumonia and influenza hospitalizations was observed in 48 of 49 counties (FK and BKS tests were significant at the level of P <0.01; Table 1). In one county, Haliburton, the FK test was not significant (P >0.05) although the BKS test was. The $R^2_{Autoreg}$ ranged from 0.18 in Haliburton, which is interpreted as very weak seasonality, to 0.75 in Ottawa-Carleton, which is interpreted as strong seasonality.

Table 1. County level summary statistics and time-series analysis results for pneumonia and influenza hospitalizations in Ontario, Canada, between 1992 and 2001.

County	Mean rate /100,000[a]	Mean minimum rate (month)	Mean maximum rate (month)	CV[b]	FK[c†]	BKS[d†]	$R^2_{autoreg}$	Trend
Stormont & Dundas	33.9	17.5 (8)	56.1 (3)	45.0	34.99	0.570	0.74	1.60 *
Prescott & Russell	23.1	11.1 (8)	35.8 (2)	42.6	24.93	0.413	0.53	0.72 *
Ottawa-Carleton	14.1	9.0 (8)	19.9 (2)	31.2	34.37	0.543	0.75	0.33
Leeds & Grenville	27.3	15.8 (7)	40.3 (3)	38.9	27.40	0.534	0.69	-0.01
Lanark	27.3	18.3 (7)	41.4 (3)	35.3	20.43	0.419	0.59	0.72 *
Frontenac	21.8	13.1 (8)	34.3 (3)	40.6	28.46	0.489	0.66	0.62
Lennox & Addington	23.2	13.8 (8)	34.9 (1)	46.1	12.76	0.338	0.33	1.73 *
Hastings	23.8	14.7 (8)	35.2 (2)	37.4	24.66	0.428	0.55	0.29
Prince Edward	29.6	17.3 (8)	48.4 (3)	50.7	19.12	0.359	0.47	1.24
Northumberland	27.1	13.7 (8)	38.6 (1)	42.7	18.37	0.297	0.44	-0.59 *
Peterborough	23.4	11.2 (8)	36.9 (3)	43.9	28.82	0.520	0.65	0.76 **
Kawartha Lakes	35.6	18.0 (8)	64.8 (2)	45.0	32.20	0.525	0.70	0.82
Durham	23.7	14.3 (8)	34.0 (1)	31.1	32.76	0.553	0.72	0.21
York	14.1	8.5 (8)	20.9 (1)	32.6	30.57	0.526	0.67	-0.02
Toronto	16.2	11.0 (8)	23.4 (1)	28.8	33.50	0.545	0.75	0.24
Peel	15.8	10.2 (9)	25.8 (1)	36.2	32.18	0.512	0.73	0.40
Dufferin	32.5	18.6 (8)	45.4 (2)	42.4	18.73	0.336	0.46	0.39
Wellington	21.3	12.1 (7)	31.8 (1)	40.8	30.15	0.478	0.64	-0.03
Halton	16.5	10.3 (8)	24.3 (2)	35.5	32.11	0.531	0.66	0.57 *
Hamilton	17.3	11.5 (8)	26.0 (1)	35.7	24.74	0.525	0.63	0.76 **
Niagara	19.2	11.2 (8)	27.9 (3)	36.8	32.79	0.547	0.69	0.59
Haldimand-Norfolk	24.8	15.0 (8)	34.9 (1)	37.3	24.31	0.463	0.57	0.23
Brant	24.9	14.8 (9)	41.0 (2)	44.3	29.89	0.512	0.64	0.31
Waterloo	19.4	11.1 (8)	30.5 (1)	40.2	29.66	0.493	0.69	0.66 *
Perth	24.2	12.7 (8)	36.3 (3)	48.7	23.02	0.383	0.49	0.22
Oxford	20.6	11.9 (7)	32.6 (3)	45.5	25.22	0.498	0.63	0.75
Elgin	23.6	15.6 (8)	36.0 (1)	46.8	20.17	0.456	0.51	-0.23
Chatham-Kent	26.0	16.4 (9)	38.6 (1)	41.8	23.55	0.408	0.54	0.42
Essex	18.2	11.7 (9)	27.6 (1)	36.7	26.44	0.455	0.67	0.00
Lambton	23.6	13.5 (7)	37.6 (2)	47.2	27.45	0.550	0.67	-0.27
Middlesex	14.2	8.1 (8)	21.8 (1)	37.6	27.21	0.457	0.62	0.15
Huron	31.4	18.2 (7)	47.1 (3)	42.7	23.57	0.415	0.50	0.16
Bruce	32.1	19.6 (8)	53.7 (3)	43.7	28.05	0.428	0.61	0.57
Grey	28.9	15.2 (8)	46.5 (1)	49.0	26.44	0.456	0.59	0.40
Simcoe	25.3	13.8 (8)	37.9 (1)	36.5	31.56	0.513	0.70	0.81 *
Muskoka	25.8	14.5 (8)	40.3 (1)	48.0	18.10	0.372	0.44	0.41
Haliburton	25.3	13.9 (6)	30.5 (1)	60.7	6.47	0.167	0.18	-0.89
Renfrew	25.5	15.3 (7)	38.6 (2)	40.1	26.93	0.471	0.59	0.21
Nipissing	29.2	13.0 (8)	40.2 (1)	39.9	25.34	0.457	0.56	0.36
Parry Sound	25.9	14.5 (8)	38.1(3)	49.4	17.52	0.389	0.41	0.78
Manitoulin	56.1	30.9 (9)	93.1 (3)	60.6	17.36	0.328	0.36	1.42
Sudbury (district)	25.4	14.6 (8)	35.3 (1)	52.5	12.10	0.244	0.28	-0.31
Greater Sudbury	20.5	13.5 (8)	33.1 (1)	42.7	20.69	0.370	0.53	0.93 **
Timiskaming	38.8	26.1 (8)	52.6 (3)	37.3	13.49	0.366	0.41	1.01
Cochrane	33.2	19.2 (9)	49.7 (3)	38.9	20.45	0.422	0.55	0.25
Algoma	24.4	14.1 (8)	37.7 (3)	40.5	26.68	0.494	0.65	0.95 *
Thunder bay	26.2	15.2 (8)	38.3 (1)	36.5	22.19	0.432	0.56	0.34
Rainy river	31.9	16.7 (9)	48.5 (1)	58.5	15.37	0.294	0.39	0.72
Kenora	48.8	30.7 (8)	64.8 (1)	36.2	17.96	0.427	0.53	1.81

*P <0.05; **P <0.01; [a]Rates have been standardized for age, gender and length of month; [b]CV = coefficient of variation; [c]FK (Fisher Kappa test) tests the null hypothesis that the series is Gaussian white noise against the alternative. Hypothesis that the series contains an added deterministic periodic component of unspecified frequency. The 5% and 1% critical values for this test are 7.16 and 8.65, respectively; [d]BKS (Bartlett's Kolmogorov-Smirnov test) tests the null hypothesis that the series is white noise. The 5% and 1% critical values for this test are 0.149 and 0.179, respectively; †BKS and FK tests were significant for all counties at the level of P <0.01 with the exception of Haliburton where FK was not significant (P >0.05) and BKS was significant at the level of P <0.05.

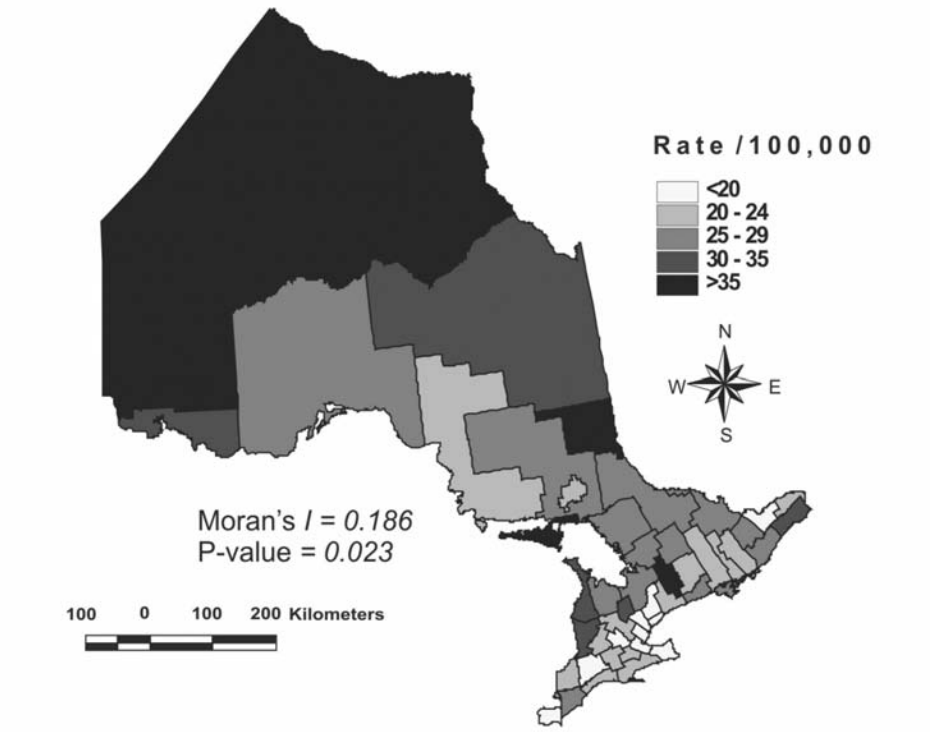

Fig. 2. Age and gender standardized mean pneumonia and influenza hospitalization rates per 100,000 population in Ontario from 1992 to 2001.

The linear regression model estimating trends in county level hospitalizations (Table 1), revealed significant increases in rates in 11 of 49 counties. Significant trends ranged from increases of 0.57 to 1.73 per 100,000 per year, or approximately 2.5% to 5.6% over the study period (Table 1). A small but significant downward trend was identified in one county with rates decreasing by 0.59 per 100,000 per year, or 1.6% over the study period.

The results of the county level seasonality analyses were mapped and tests of global and local autocorrelation were conducted to explore spatial patterns of the time series results (Table 2; Fig. 4). Figure 4 illustrates the spatial pattern of the $R^2_{Autoreg}$. Areas with the strongest seasonality ($R^2_{Autoreg}$) are seen in both urban and rural counties in the south and east, and include counties with both relatively high and low rates of hospitalization. Areas of weak seasonality are found most commonly in rural counties in north central Ontario near Sudbury, and include counties with typically high rates of hospitalizations. The Moran's I statistic indicates that there is a high degree of spatial autocorrelation in $R^2_{Autoreg}$ values (Moran's I = 0.305, P = 0.003). LISA analysis revealed local clusters of significantly high $R^2_{Autoreg}$ values around the urban area of Toronto and York, and significantly low values around Hastings in the east. Similar spatial patterns were seen for the FK and BKS values (Table 2).

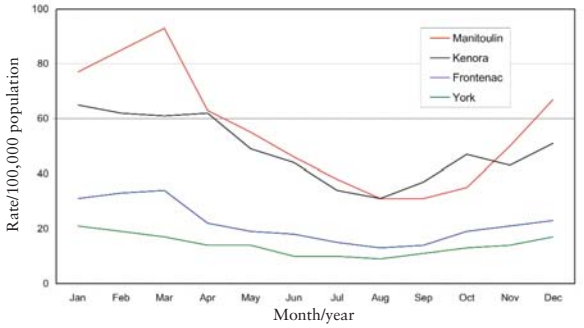

Fig. 3. Monthly aggregated pneumonia and influenza hospitalization rates for select Ontario counties from 1992 to 2001.

Table 2. Spatial autocorrelation of county level time-series results for pneumonia and influenza hospitalizations in Ontario from 1992 to 2001.

	Moran's I	P-value
FK	0.321	0.002
BKS	0.264	0.002
$R^2_{Autoreg}$	0.305	0.003
Trend	-0.097	0.212

No significant global or local spatial autocorrelation in the county level temporal trend data was found (Table 2).

Results from the Moran's I statistics for the mean monthly pneumonia and influenza hospitalization rates (Table 3) indicates that there is a moderate, statistically significant degree of positive autocorrelation in the data for the months of April through to October, when rates are typically at their lowest (Fig. 3). The strongest autocorrelation is seen in May and June (Moran's I = 0.308 and 0.295, respectively). Significant clusters of high hospitalization rates are seen during these months in northern counties, including Kenora, Rainy River, Cochrane and Thunder Bay. Between the months of November and March, when hospitalization rates are at their highest, no significant global spatial autocorrelation was detected (Table 3), although a significant local cluster of low rates centered around Toronto was seen in February and March (data not shown).

Discussion

To our knowledge, this paper represents the first study to examine spatio-temporal patterns of hospitalizations for pneumonia and influenza. The findings provide evidence of spatio-temporal interaction over the 9-year study period, with marked spatial variability in temporal patterns, and temporal variability in spatial patterns.

The heterogeneity in pneumonia and influenza hospitalization rates and significant spatial clustering identified (Moran's I = 0.186, P = 0.023; Fig. 2) confirms findings from previous work (Crighton et al., 2007a). The highest rates are seen in rural and northern areas, and the lowest rates in urban and more southern areas. An examination of time-series maps suggests that although county rates and spatial autocorrelation fluctuated on a monthly basis, the overall spatial pattern seen in the data remained generally consistent on a year to year basis over the study period. This suggests that the underlying processes that determine these monthly patterns also remained consistent over the study period.

A significant upward trend in hospitalization rates in almost a quarter of Ontario counties was identified here. A similar trend over the same time period (1992 to 2001) was not found in our previous work which used provincially aggregated data (Crighton et al., 2004). While rates of pneumonia hospitalizations might be expected to increase due to Ontario's aging population structure (Statistics Canada, 2004), this cannot explain the findings here, as our data was directly age standardized. More likely explanations for these findings include county level changes in factors including socioeconomic conditions, environmental conditions and health care services (Morris and Munasinghe, 1994; Crighton et al., 2007b). The theoretical nature of these relationships has been illustrated in a conceptual framework linking broad health determinants to pneumonia over space and time (Crighton et al., 2007b). Further research is required to assess these relationships. While the increase in rates identified here are not large, they are significant and should be monitored.

The consistent significant seasonality of hospitalization rates identified in all but one of Ontario's counties (Table 1) suggests that the factors determining seasonal patterns of pneumonia and influenza at the province level are similarly important at the county level. Factors reported in the literature to be associated with these patterns include the presence of circulating influenza virus (Black et al., 1999; Goel et al., 1999; Cox et al., 2000), respiratory syncytial virus (RSV) (Crowcroft et al., 2002), temperature (Glezen et al., 1996; Friger and Lieberman, 1999) and air pollution (Glezen et al.,

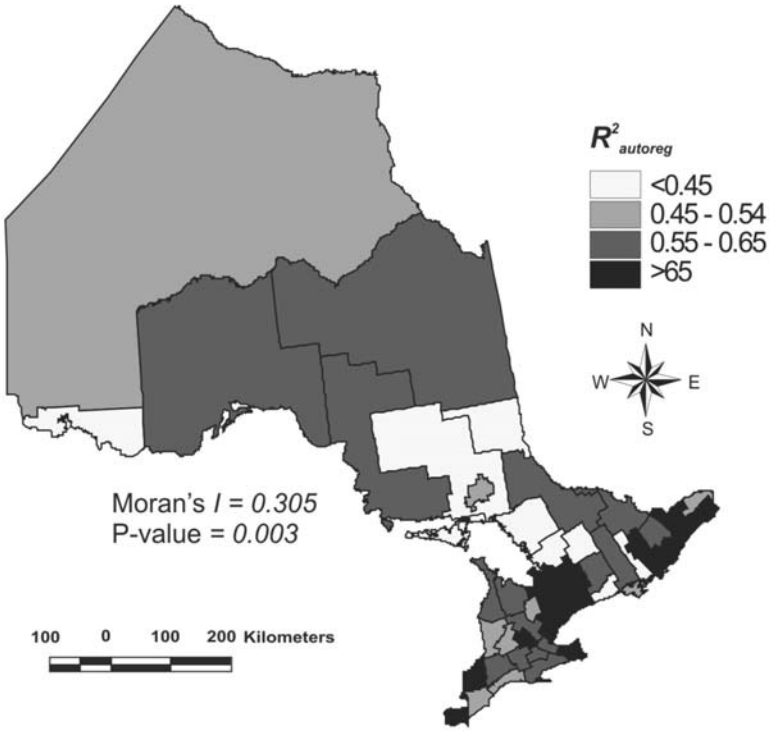

Fig. 4. County level results of the R^2 autoregression ($R^2_{autoreg}$) measuring the strength of seasonality, for pneumonia and influenza hospitalizations from 1992 to 2001.

1996). Considerable county level variability in the seasonality measures are seen, however, with the $R^2_{Autoreg}$ values ranging from 0.18, indicating very weak seasonality, to 0.75, indicating strong seasonality, with like values clustering over space (Table 2, Fig. 4). This spatial variability suggests that regional differences in seasonal determinants such as those mentioned above, are leading to these differences, or, perhaps more likely, that significant interactions are occurring with other spatially-explicit factors, including socio-economic status and health care service. Multivariate spatio-temporal modelling controlling for the effect of spatial and temporal variable factors is required to help unravel these relationships. The particularly weak and inconsistent seasonality identified in Haliburton could be further related to unreliable rates due to a small county population, or even to chance alone.

The maximum spatial autocorrelation of pneumonia and influenza hospitalizations occurs in months

Table 3. Spatial autocorrelation of county level, monthly aggregated pneumonia and influenza hospitalizations in Ontario from 1992 to 2001.

Month	Moran's I	P-value
January	0.155	0.053
February	0.071	0.160
March	0.144	0.058
April	0.263	0.016
May	0.308	0.006
June	0.295	0.011
July	0.173	0.043
August	0.177	0.044
September	0.237	0.007
October	0.155	0.032
November	0.060	0.202
December	0.097	0.102
Overall	0.186	0.023

when rates are lowest (i.e. April to October) and the minimum when rates are highest (November to March). While there is no simple explanation for this finding, it could be expected that seasonal and spatial differences associated with different pneumonia aetiologies plays a role. The aggregated ICD-9 codes used in this analysis consist of a variety of bacterial and viral pneumonias, some of which have been shown to differ in their seasonal distribution (Dowell et al., 2003), and could also be expected to vary in their geographic distribution. Currently the reliability of specific aetiologic information for pneumonia in ICD-9 data is low (Durant et al., 1987), and in the majority of cases, the causative organism is unspecified. Specific, reliable etiologic data would greatly improve our understanding of these illness patterns, however, enhanced diagnostic codes and diagnostic capacity is required. Given the importance of pneumonia on the health care system, and our renewed interest in respiratory diseases post-SARS, such improvements would be timely.

This is a largely descriptive study. While we have employed a previously developed conceptual framework to inform our findings (Crighton et al., 2007b), we have not analytically examined the determinants of the spatio-temporal patterns. The modifiable areal unit problem (MAUP) represents another potential limitation, in that patterns identified here may depend on the areal aggregations used (Openshaw, 1983). A similar issue exists with the temporal aggregations used. Furthermore, the use of hospitalizations is not necessarily reflective of morbidity in the population and does not account for differential access to services (Eyles et al., 1991). However, given that health insurance is universal in Ontario, hospitalizations are believed to represent a good estimate of severe morbidity.

Conclusions

The findings from this study demonstrate the presence of marked spatio-temporal variability in pneumonia and influenza hospitalizations in Ontario. In doing so, they point to the need for the effective allocation of services and resources based on regional and seasonal demands, more regionally focused prevention strategies such as influenza vaccination programmes, and better infectious disease surveillance programmes. An important methodological contribution comes from the application of spatio-temporal analysis techniques to population level, health services data. However doing so, has revealed a number of practical data limitations. These include the inevitable problem of small case counts as data is disaggregated over time and space, and data quality issues resulting from limited diagnostic capacity and crude diagnostic codes. While options for addressing the former are limited, improvements in diagnostic capacity for diseases such as pneumonia and influenza is obtainable and should be encouraged. This study lays the foundation for future work including the examination of alternative pneumonia and influenza outcome measures such as physician visits and mortality, formal testing of spatio-temporal clusters, and multivariate spatio-temporal modelling.

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References

Anselin L, 1995. Local indicators of spatial association - LISA. Geogr Anal 27, 93-115.

Assuncao R, Hartman J, Hefferman R, Kulldorff M, Mostashari F, 2005. A space-time permutation scan statistic for disease for disease outbreak detection. PLoS Med 2, e59.

AvRuskin GA, Jacquez GM, Kaufmann AM, Meliker JR, Slotnick MJ, 2004. Visualization and exploratory analysis of epidemiological data using a novel space time information system. Int J Health Geogr 3, 26.

Bailey T, Gatrell A, 1995. Interactive spatial data analysis. Prentice Hall, pp. 413.

Bedard M, Davidson W, Molloy DW, Somers G, 1994. Relation between physician characteristics and prescribing

for elderly people in New Brunswick. CMAJ 150, 917-921.

Black C, Finlayson G, Macwilliam L, Menec V, Nowicki D, Roos N, 1999. Seasonal patterns of Winnipeg hospital use, Manitoba Centre for Health Policy and Evaluation.

Boussard E, Flahault A, Valleron AJ, Vibert JF, 1996. Sentiweb: French communicable disease surveillance on the World Wide Web. BMJ 313, 1381-1382; discussion 1382-1384.

Box G, Jenkins G, 1976. Time series analysis: forecasting and control. Holden-Day, pp. 575.

Breslow N, Day N, 1987. Statistical methods in cancer research. IARC Scientific Publications, Lyon, France, pp. 406.

Carey TS, Gesler W, Hertz-Picciotto I, Joines JD, Suchindran C, 2003. A spatial analysis of county-level variation in hospitalization rates for low back problems in North Carolina. Soc Sci Med 56, 2541-2553.

Carlin G, Xia H, 1998. Spatio-temporal models with errors in covariates: mapping Ohio lung cancer mortality. Stat Med 17, 2025-2043.

Cliff AD, Ord JK, 1981. Spatial processes: models and applications. Pion, London, UK, pp. 266.

Cox NJ, Fukuda K, Schonberger LB, Simonsen L, 2000. The impact of influenza epidemics on hospitalizations. J Infect Dis 181, 831-837.

Crighton EJ, Elliott SJ, Kanaroglou P, Moinnedin R, Upshur R, 2007a. An exploratory spatial analysis of pneumonia and influenza hospitalizations in Ontario by age and gender. Epidemiol Infect 135, 253-261.

Crighton EJ, Elliott SJ, Kanaroglou P, Moinnedin R, Upshur R, 2007b. A spatial analysis of the determinants of pneumonia and influenza hosptializations in Ontario. Soc Sci Med 64, 1636-1650.

Crighton EJ, Mamdani M, Moinnedin R, Segal AO, Upshur R, 2005. Group hospitalizations in Ontario. Pediatrics 116, 51-55.

Crighton EJ, Mamdani M, Moinnedin R, Upshur R, 2003. Autoregression as a means of assessing the strenght of seasonality in a time series. Popul Health Metr 1, 10.

Crighton EJ, Moinnedin R, Mamdani M, Upshur R, 2004. Influenza and pneumonia hospitalizations: a population level time series analysis. Epidemiol Infect 132, 1167-1174.

Crowcroft NS, Edmunds WJ, Gay NJ, Muller-Pebody B, Zambon MC, 2002. Contribution of RSV to bronchiolitis and pneumonia-associated hospitalization in English children, April 1995 - March 1998. Epidemiol Infect 129, 99-106.

Donaldson GC, Keatinge WR, 2002. Excess winter mortality; influenza or cold stress? Observational study. BMJ 12, 89-90.

Dowell SF, Rose CEJ, Schuchat A, Whitney CG, Wright C, 2003. Seasonal patterns of invasive pneumococcal disease. Emerg Infect Dis 9, 573-579.

Durant H, Marrie TJ, Sealy E, 1987. Pneumonia-the quality of medical records data. Med Care 25, 20-24.

Earickson R, Meade M, 2000. Chapter 8: Disease diffusion in space. In: Medical Geography, Guilford Press, pp. 501.

Eyles J, Birch S, Chambers S, Hurley J, Hutchison B, 1991. A needs-based methodology for allocating health care resources in Ontario, Canada: development and an application. Soc Sci Med 33, 489-500.

Friger MD, Lieberman D, 1999. Seasonal variation in hospital admissions for community-acquired pneumonia: a 5-year study. J Infect 129, 134-140.

Fuller W, 1976. Introduction to statistical time series, John Wiley & Sons, New York, USA, pp. 478.

Glezen WP, Kim PE, Musher DM, Nahm WK, Rodriguez-Barradas MC, 1996. Association of invasive pneumococcal disease with season, atmospheric conditions, air pollution, and the isolation of respiratory viruses. Clin Infect Dis 22, 100-106.

Goel V, Knight K, Upshur R, 1999. Time-series analysis of the relation between influenza virus and hospital admissions of the elderly in Ontario, Canada, for pneumonia, chronic lung disease, and congestive heart failure. Am J Epidemiol 149, 85-92.

Greene DA, Jacquez GM, Kaufmann AM, Rommel RG, 2005. Spatio-temporal pattern of viral meningitis in Michigan, 1993-2001. J Geograph Systems 7, 85-99.

Greene SK, Ionides EL, Wilson ML, 2006. Patterns of influenza-associated mortality among US elderly by geographic region and virus subtype, 1968-1998. Am J Epidemiol 163, 316-326.

Greiling DA, Jacquez GM, Kaufmann AM, Rommel RG, 2005. Space-time visualization and analysis in the Cancer Atlas Viewer. J Geograph Systems 7, 67-68.

Health Canada, 2001. Respiratiory disease in Canada. Ottawa, Canada.

Keistinen T, Saynajakangas P, Tuuponen T, 2001. Seasonal fluctuations in hospitalization for pneumonia in Finland.

Int J Circumpolar Health 60, 34-40.

Kleinman K, Lazarus R, Platt R, 2004. A generalizaed linear mixed models approach for detecting incident clusters of disease in small areas, with application to biological terrorism. Am J Epidemiol 159, 217-224.

Malcolm E, Rawson N, 1995. Validity of the recording of cholecystectomy and hysterectomy in the Saskatchewan health care datafiles. Pharmaco-epidemiology Research Consortium.

Morris RD, Munasinghe RL, 1994. Geographical variability in hospital admission rates for respiratory disease among the elderly in the United States. Chest 106, 1172-1181.

Openshaw S, 1983. The modifiable areal unit problem. In: Concepts and techniques in modern geography. Geo Books, Norwich, pp. 40.

Priestly M, 1981. Spectral analysis and time series. Academic Press, pp. 890.

Statistics Canada, 2004. Annual demographic statistics 2003. Catalogue No. 91-213-XPB., Ottawa, Canada.

Upshur REG, 1997. Measuring the impact of influenza on hospitalization of the elderly in Ontario. In: Department of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Canada.

Upshur REG, Knight K, Goel V, 1999. Time-series analysis of the relation between influenza virus and hospital admissions of the elderly in Ontario, Canada, for pneumonia, chronic lung disease, and congestive heart failure. Am J Epidemiol 149, 85-92.

Williams J, Young W, 1996. Appendix 1: a summary of studies on the quality of health care administrative databases in Canada. In: Patterns of Healthcare in Ontario. The ICES practice atlas, Canadian Medical Association, pp. 353.