

Influenza and pneumonia hospitalizations in Ontario: a time-series analysis

ERIC J. CRIGHTON^{1*}, RAHIM MOINEDDIN^{2,3}, MUHAMMAD MAMDANI^{4,5,6}
AND ROSS E. G. UPSHUR^{1,2,3}

¹ Primary Care Research Unit, Sunnybrook and Women's College Health Sciences Centre, Toronto, ON, Canada

² Department of Family and Community Medicine, University of Toronto, Toronto, ON, Canada

³ Department of Public Health Sciences, University of Toronto, Toronto, ON, Canada

⁴ Institute for Clinical Evaluative Sciences, Toronto, ON, Canada

⁵ Health Policy Management and Evaluation, University of Toronto, Toronto, ON, Canada

⁶ Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

(Accepted 30 June 2004)

SUMMARY

A comprehensive examination of gender and age-specific influenza and pneumonia hospitalization seasonality is currently lacking. Using population-based data for Ontario, Canada between April 1988 and March 2002 ($n = 339\,803$ hospitalizations), findings from this study revealed clear seasonality [Fisher's Kappa (FK) test = 68·64, $P < 0\cdot001$; Bartlett's Kolmogorov–Smirnov (BKS) test = 0·68, $P < 0\cdot001$] with consistent summer troughs and winter peaks for both sexes and all ages combined. The very young (both sexes 0–4 years) demonstrated the strongest seasonality ($R^2_{\text{autoreg}} = 0\cdot97$) and females aged 10–19 years, the weakest ($R^2_{\text{autoreg}} = 0\cdot59$). Gender differences were most pronounced in the oldest age groups (80+ years) where females had an average annualized peak rate of 250/100 000 compared to 400/100 000 for males. These findings can contribute to more population-specific prevention strategies and effective resource and service allocation based on seasonal and specific population demands.

INTRODUCTION

Influenza and pneumonia represent the leading causes of death from infectious disease and are among the leading causes of hospitalizations in Canada and other Western nations [1–4]. In the United States, influenza and pneumonia are the sixth leading cause of death overall and account for over 600 000 hospitalizations annually [4]. Characterized by a high degree of seasonality and particularly high morbidity and

mortality among the very young and the elderly, influenza and pneumonia place a significant burden on the health-care system. A better understanding of the seasonal patterns that influence influenza and pneumonia hospitalizations represents an important step towards the development of more informed and targeted policies and preventative strategies.

Pneumonia can be directly linked to numerous aetiological agents which have been shown to vary according to the age of the individual, presence of comorbidities, severity of pneumonia and the locus of acquisition (i.e. community vs. hospital). Among adults, the most common causal agents include *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, as well as influenza virus which often precedes secondary

* Author for correspondence: E. Crighton, Primary Care Research Unit, Sunnybrook and Women's College Health Sciences Centre, 2075 Bayview Ave, no. E-349, Toronto, ON, Canada M4N 3M5.
(Email: eric.crighton@sw.ca)

bacterial pneumonia. In young children, respiratory syncytial virus (RSV) and other respiratory viruses are the main causes of pneumonias [1, 4–6].

The seasonality of influenza and pneumonia has been well documented, with the focus of much of the research being on mortality [7], specific sub-populations such as the very young [8] and the elderly [9] or particular aetiological agents [10, 11]. Studies have consistently reported distinct seasonal patterns, with peak mortality and morbidity occurring in the winter and troughs in the summer [11–13]. Variations in the seasonal timing of peaks and troughs by age group have also been reported. Saynajakangas et al. [12] found age-specific admission patterns, with the youngest age group (0–16 years) demonstrating December hospitalization peaks, compared to March for those of working age (17–64 years). Numerous studies have attempted to explain these seasonal patterns [8, 9, 11, 14–16]. Simonsen et al. [14] for example, found strong positive associations between the presence of circulating viruses and hospitalizations. Kim et al. [10] looking at environmental factors, found hospitalizations to be correlated negatively with air temperature and positively with air pollution (sulphur dioxide).

Influenza and pneumonia seasonality studies have frequently been characterized by a number of methodological limitations including the use of annualized monthly aggregations [12], short time-periods [11], as well as inappropriate age aggregations [12, 14]. We believe that annualizing monthly rates obscures year-to-year variations and, along with use of short study periods, does not allow for the examination of trends over time. Also, the use of highly aggregated age groups (e.g. <16 years or >65 years of age) can be expected to obscure major age variations, an important limitation given the increased morbidity and mortality risk associated with extreme age (i.e. very young or very old) [17]. Furthermore, much of the time-series analyses of influenza and pneumonia hospitalizations have focused on the explanation of seasonal effects [9, 11, 18, 19] while the nature of the effects themselves is largely taken for granted.

In order to address the above limitations and to better understand the seasonality of influenza and pneumonia, this study examines influenza and pneumonia hospitalizations using population-based data for the province of Ontario, over a 14-year period. Specifically, the objectives are: (1) to examine the seasonal patterns for hospitalizations for influenza and pneumonia by age and gender; (2) to assess the

strength of the seasonal patterns; and, (3) to measure the overall trends in hospitalizations during this 14-year period.

METHODS

We conducted a retrospective, population-based study to assess temporal patterns in hospitalizations for influenza and pneumonia from 1 April 1988 to 31 March 2002. Approximately 14 million residents of Ontario eligible for universal health-care coverage during this time were included for analysis. The Canadian Institute for Health Information Discharge Abstract Database was used to obtain information on hospitalizations for influenza and pneumonia as the principal diagnosis. This database records discharges from all in-patient hospital stays in Ontario acute care hospitals, documenting a scrambled patient identifier, date of admission and discharge, up to 16 diagnoses as coded by the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), and up to 10 procedures.

Researchers using this database have found that diagnoses are coded with a high degree of accuracy [20]. 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 [21–23]. The reliability of the coding of data collected by the Canadian Institute for Health Information is 74–96% for the ICD-9 diagnosis. Although for pneumonia, the reliability for specific aetiological information is low (approximately 52%) [24]; in aggregate form, influenza and pneumonia have been found to be reliably coded (81%) [25].

All records with a principal discharge diagnosis of influenza or pneumonia (ICD-9 code: 480–487) were selected ($n = 339\,803$). The total number of discharges by age and gender were assessed for each month. Annual census data for each age group for residents of Ontario were provided by Statistics Canada (Ottawa, ON, Canada). Monthly population estimates were derived through linear interpolation. Using this data, monthly hospitalization rates per 100 000 population, normalized for length of month, were calculated. All transfers from within one acute care hospital to another within this study group were excluded from the analysis.

Analysis of the data involved the use of several statistical techniques in order to assess the statistical

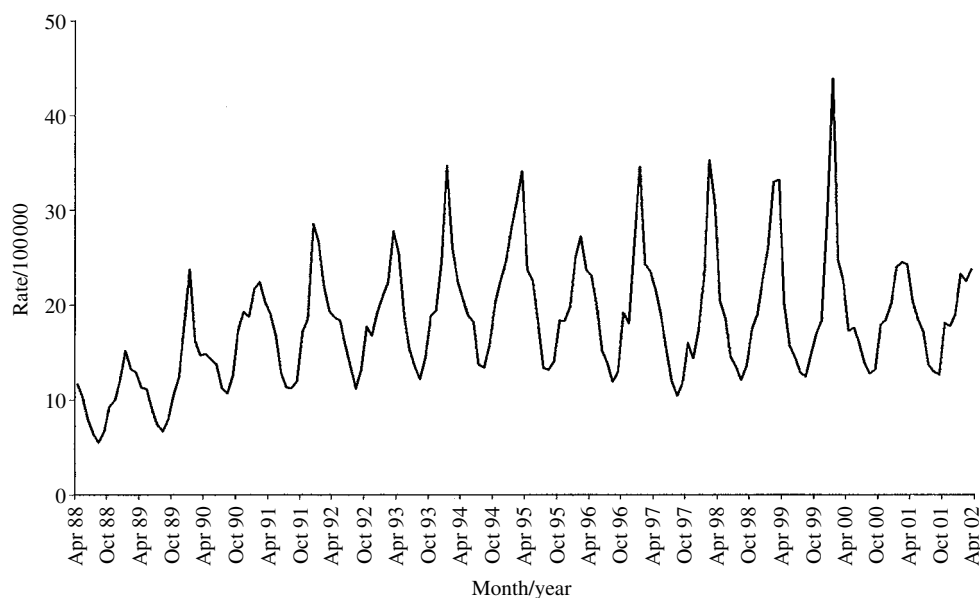


Fig. 1. Influenza and pneumonia hospitalization rates per 100 000 population in Ontario (1988–2002).

significance of seasonal patterns and the consistency and magnitude of seasonal effects. Spectral analysis was conducted to test for seasonality. Spectral analysis detects periodicity in time series [26]. The data was de-trended using moving averages prior to conducting spectral analysis. Two tests for the null hypothesis that the series is strictly white noise were conducted. Fisher's Kappa (FK) test is designed to detect one major sinusoidal component buried in white noise, whereas Bartlett's Kolmogorov–Smirnov (BKS) test accumulates departures from the white-noise hypothesis over all frequencies [27]. The autocorrelation function (ACF) was then used to measure the correlation between observations at different time-lags [28]. A strong correlation between the observations at 12 time-lags indicates a strong seasonality of the period 12. Finally, R^2 autoregression coefficients (R^2_{autoreg}) were calculated. Autoregression uses the coefficient of determination of the autoregressive regression model fitted to the data, and can be used for quantifying the strength of the seasonality within a set of serially correlated observations as occurs with time-series data [29]. The R^2_{autoreg} is interpreted the same way as the coefficient of determination in classic regression: values from 0 to less than 0.4 represent non-existent to weak seasonality, 0.4 to less than 0.7 represent moderate to strong seasonality, and 0.7 to 1 represent strong to perfect seasonality. All statistical analyses were performed using SAS 8.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

There were a total of 339 803 influenza and pneumonia hospitalizations over the 14-year period. A clear and statistically significant seasonal pattern for the overall population was observed (Fig. 1, Table 1). Peak hospitalizations occurred in winter (January) at an average rate of approximately 27/100 000 and the trough occurred in August at a rate of just over 11/100 000. Spectral analysis indicates a consistent 12-month period seasonality (data not shown).

Consistent and significant seasonality was observed in each age group and both sexes (FK and BKS test statistics were significant for all age groups and both sexes at a level of significance of <0.01 , Table 1). The ACF found the seasonality to be most consistent in the youngest (0–4 years, $\text{ACF}=0.90$) and oldest age groups (80+ years, $\text{ACF}=0.74$, data not shown). Seasonal peaks occurred in January for all adult age groups (20+ years) and both sexes (Figs 2 and 3) and February for the 0–4 years age group. The peak rates occurred earlier (November or December) for the 5–9 and 10–19 years age groups and also begin to increase earlier – September compared to October or November for all other groups. There are also marked differences in monthly hospitalization rates by age group. The highest seasonal monthly rates for both genders combined were seen among the youngest (0–4 years: 80/100 000) and oldest groups (70–79 years: 109/100 000; 80+ years: 297/10 000) and the lowest

Table 1. Results of the spectral analysis testing the seasonality of influenza and pneumonia hospitalizations by age and gender between the years 1988 and 2002

Age group (years)	Male		Female		Both genders	
	FK*	BKS†	FK	BKS	FK	BKS
0–4	76.53	0.766	77.29	0.775	77.58	0.778
5–9	47.58	0.426	50.29	0.460	52.83	0.487
10–19	44.54	0.396	32.99	0.282	45.33	0.408
20–59	58.78	0.566	60.00	0.580	62.32	0.607
60–69	52.30	0.493	53.58	0.501	56.33	0.533
70–79	52.45	0.495	58.91	0.558	57.35	0.546
80+	56.77	0.537	61.77	0.599	61.42	0.595
All ages	68.52	0.673	67.92	0.668	68.64	0.675

All test statistics were significant at the level of $P < 0.01$.

* FK (Fisher's 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 7.1628 and 8.6457 respectively.

† 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 0.1493 and 0.1789 respectively.

were seen among the adolescent (10–19 years: 4.9/100 000) and middle age groups (20–59 years: 7.7/100 000).

A similar winter peak and summer trough seasonal pattern was seen for both males and females when aggregated by age (data not shown). Overall, males were hospitalized at rates approximately 10% higher than females. This gender difference was most pronounced in the oldest age groups where there was a two-fold difference in peak rates: females aged 80+ years were hospitalized at an annualized peak rate of 250/100 000 compared to males at 400/100 000. A similar, though less marked difference was observed in the 0–4 years age group. Here males were hospitalized at an annualized peak rate of approximately 90/100 000 compared to 70/100 000 for females.

The R^2_{autoreg} for the overall series (all ages and both genders) is 0.90 and only slightly lower for each gender, indicating a very strong seasonal effect (Table 2). The strongest seasonality was found among males and females aged between 0 and 4 years and with females aged between 70 and 79 years, where the R^2_{autoreg} values were 0.97, 0.97 and 0.91 respectively (Table 2), representing near perfect seasonality. The weakest seasonality was found for females in the

10–19 years age group who had an R^2_{autoreg} of 0.59, indicating moderate to strong seasonality.

From the overall time-plot graph (Fig. 1), an upward trend in hospitalizations between April 1988 and April 1991 was evident, representing an increase of over 100% over the 3-year period ($\beta = 0.321$, $P < 0.001$). From this date forward there was a levelling off and average annual rates remained approximately constant. The biggest increase was observed among elderly males (80+ years) where average annual rates jumped from approximately 80/100 000 to over 250/100 000 between 1988 and 1991 ($\beta = 5.727$, $P < 0.001$). No similar increase was found among other age groups or over other years within this study period (Figs 2 and 3).

DISCUSSION

This research shows first, that there is a clear and consistent seasonality with troughs occurring in the summer months and peaks in the winter for both sexes and all ages. Second, the strength and variability of the seasonality vary by age with the old and young demonstrating the strongest seasonality and the greatest variability. Third, there are clear gender differences in hospitalization rates, particularly among the most elderly where males in the peak period were hospitalized at rates approximately twice that of females. Finally, a significant upward trend in total influenza and pneumonia hospitalizations occurred between 1988 and 1991 followed by a levelling off, a trend driven largely by the elderly (i.e. 80+ years, Fig. 3).

The occurrence of winter peaks and summer troughs in influenza and pneumonia morbidity or mortality are commonly attributed to factors including the presence of circulating influenza virus [14, 15, 18], RSV [8], temperature [9, 10, 30], and air pollution [10, 11]. Ontario is characterized by extreme seasonal fluctuations in temperature, the average winter outdoor temperature being well below 0 °C. This fact combined with the increased presence of circulating viruses in winter months may also explain the seasonal patterns found here. The pattern varies somewhat by age, with school-age children (5–9 and 10–19 years) demonstrating increased hospitalizations starting in September and peaking in December compared to November and January for most other age groups. Children in a school environment are in increased contact with respiratory infections

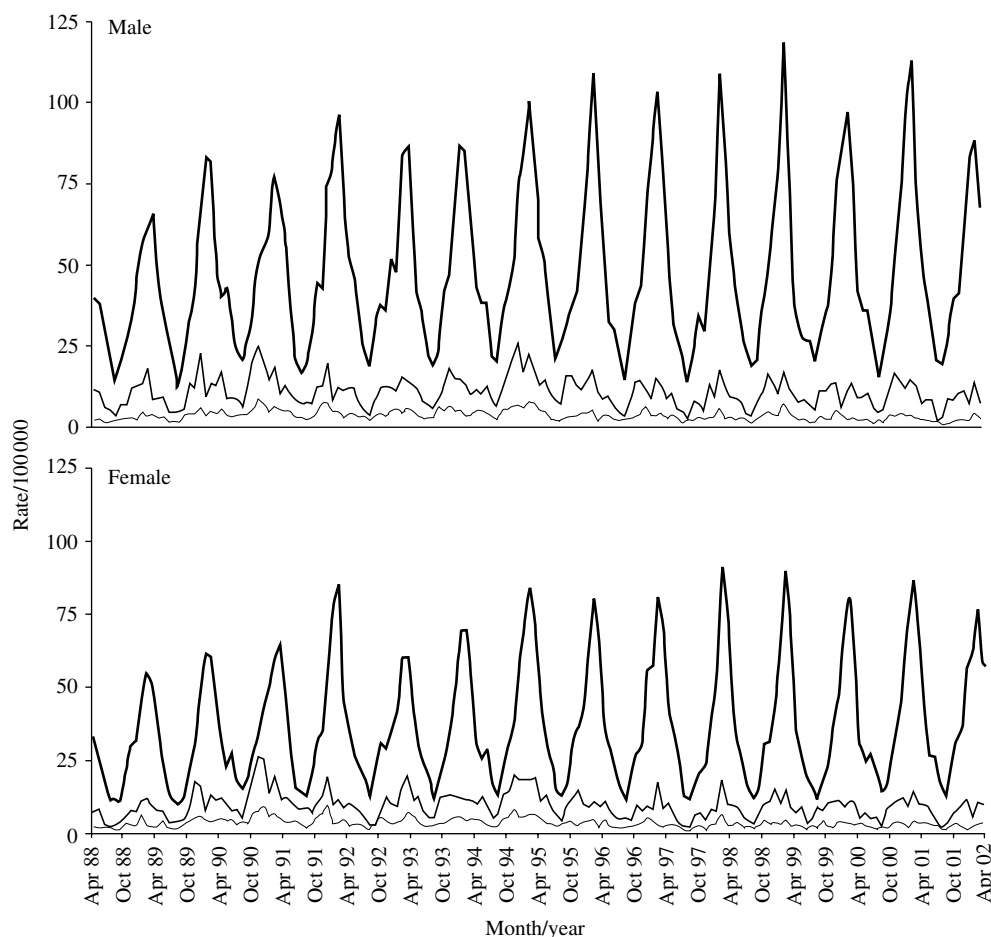


Fig. 2. Male and female influenza and pneumonia hospitalization rates per 100 000 population in Ontario (1988–2002) for age groups 0–4 (—), 5–9 (—) and 10–19 (—) years.

following the summer holidays. This contact may hasten the spread of infections.

The seasonal variability in total hospitalizations seen in the overall rates (Fig. 1), although present in all age groups, is predominately driven by the high rates among the very young (0–4 years) and the elderly (70–79 and 80+ years). The higher rates of admissions among the oldest age groups may be explained by an increased likelihood of comorbidities, and a compromised immune system associated with age. An underdeveloped immune system can explain the high rates in the 0–4 years age group. The difference in hospitalization rates by gender is somewhat less clear although higher rates of recognized influenza and pneumonia morbidity risk factors such as chronic obstructive pulmonary disease (COPD) and congestive heart failure among elderly males [31] may explain at least part of the difference. The existence of gender and age differences have not gone unnoticed in the literature, however, the extent of these differences

has been hidden as a result of over-aggregation by age (e.g. [12, 14, 18]) or the analysis techniques employed.

The dramatic increase in influenza and pneumonia hospitalizations between 1988 and 1991 is difficult to explain. One possibility is that incidence rates of influenza and pneumonia increased significantly during this period, however, there is little corroborating evidence to support this theory. A second possibility is that the increase represents a coding artefact, although there are again problems with this explanation. A similar upward trend was found in a recent study of total hospitalizations (all diagnostic codes combined) covering the same population and time-period [32]. Unlike with influenza and pneumonia, a change in any one coding practice would not have an effect on total rates, only the proportion of a given outcome to the total. A change in admission practices for influenza and pneumonia represents a third possible explanation. Similar upward trends have been identified for other health conditions including

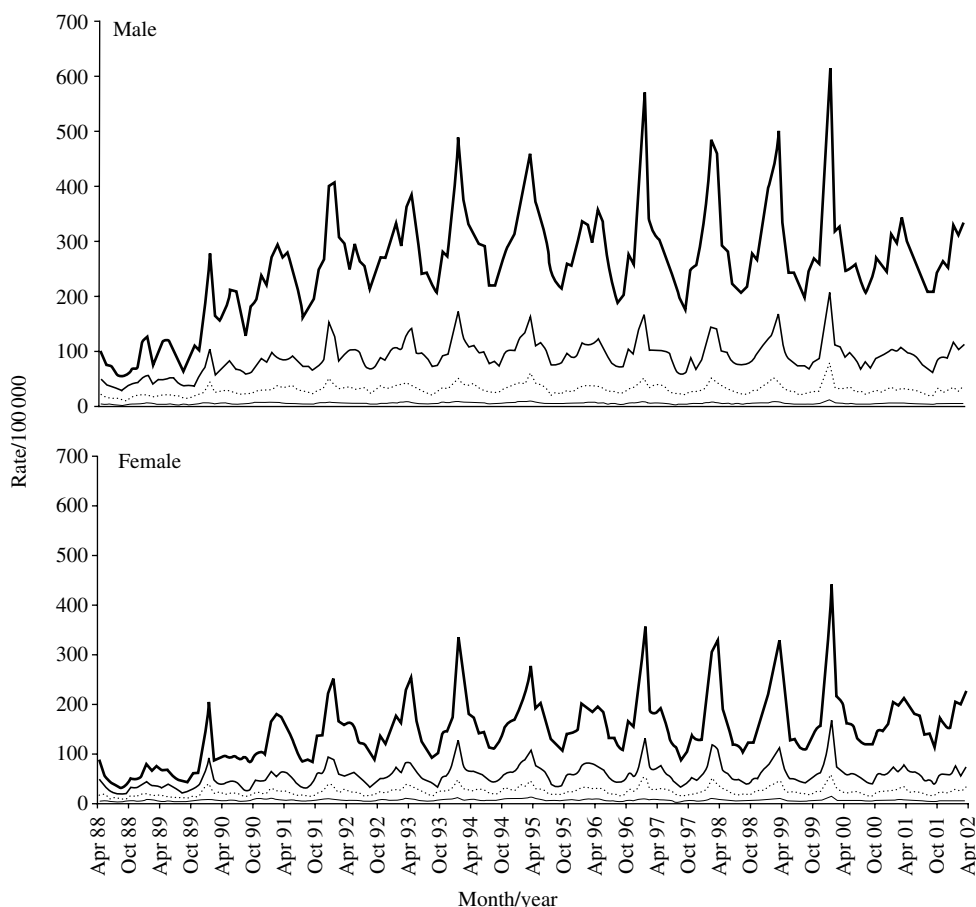


Fig. 3. Male and female influenza and pneumonia hospitalization rates per 100 000 population in Ontario (1988–2002) for age groups 20–59 (—), 60–69 (.....), 70–79 (---) and 80+ (-.-) years.

Table 2. Results of the R^2 autoregression (R^2_{autoreg}) for influenza and pneumonia hospitalizations by age and gender (1988–2002)

Age group (years)	Male	Female	Both genders
0–4	0.97	0.97	0.97
5–9	0.82	0.81	0.87
10–19	0.77	0.59	0.81
20–59	0.84	0.86	0.83
60–69	0.77	0.81	0.84
70–79	0.81	0.91	0.84
80+	0.81	0.84	0.84
All	0.90	0.87	0.88

myocardial infarction, COPD and coronary heart failure (data not shown). This suggests that increases in influenza and pneumonia may in fact be reflective of changes in admission practices across the hospital

system as a whole. To our knowledge, similar trends in influenza and pneumonia hospitalizations have not been identified in other populations.

This is a largely descriptive study and as such does not address potential factors which may explain the seasonal patterns identified here. Furthermore, we could not assess seasonal variations in less severe forms of health services used such as emergency department or physician visits. The strengths of the study lie in its longitudinal base and large population size combined with the use of a comprehensive time-series analysis approach applied to age and gender. These results add significantly to our understanding of gender and age differences as well as overall trends in influenza and pneumonia hospitalizations in Ontario, and confirm previous findings regarding hospitalization seasonality [11, 14, 18, 30]. The findings can further contribute to more population-specific prevention strategies such as influenza vaccination campaigns targeted at high-risk groups, as well

as to the effective allocation of resources and services based on seasonal and specific population demands.

ACKNOWLEDGEMENTS

This research was supported by an operating grant from the Canadian Institutes of Health Research (Grant MOP57928). The authors thank Shari Gruman for her expert assistance in formatting the manuscript.

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