Université de Montréal

The potential utility of age, triage score, and disposition data contained in emergency department electronic records for influenza-like illness surveillance in Montreal

par

Noémie Savard

Département de médecine sociale et préventive

Faculté de médecine

Mémoire présenté à la Faculté de médecine
en vue de l'obtention du grade de Maître ès sciences (M.Sc.)
en santé communautaire

Mars 2013

Université de Montréal
Faculté des études supérieures et postdoctorales

Ce mémoire intitulé :

The potential utility of age, triage score, and disposition data contained in emergency department electronic records for influenza-like illness surveillance in Montreal

Présenté par :

Noémie Savard

a été évalué par un jury composé des personnes suivantes :

Julio C. Soto, président-rapporteur
David Buckeridge, directeur de recherche
Robert Allard, co-directeur
Lucie Bédard, co-directrice
Clément Dassa, membre du jury

Résumé

La surveillance de l'influenza s'appuie sur un large spectre de données, dont les données de surveillance syndromique provenant des salles d'urgences. De plus en plus de variables sont enregistrées dans les dossiers électroniques des urgences et mises à la disposition des équipes de surveillance. L'objectif principal de ce mémoire est d'évaluer l'utilité potentielle de l'âge, de la catégorie de triage et de l'orientation au départ de l'urgence pour améliorer la surveillance de la morbidité liée aux cas sévères d'influenza. Les données d'un sous-ensemble des hôpitaux de Montréal ont été utilisées, d'avril 2006 à janvier 2011. Les hospitalisations avec diagnostic de pneumonie ou influenza ont été utilisées comme mesure de la morbidité liée aux cas sévères d'influenza, et ont été modélisées par régression binomiale négative, en tenant compte des tendances séculaires et saisonnières. En comparaison avec les visites avec syndrome d'allure grippale (SAG) totales, les visites avec SAG stratifiées par âge, par catégorie de triage et par orientation de départ ont amélioré le modèle prédictif des hospitalisations avec pneumonie ou influenza. Avant d'intégrer ces variables dans le système de surveillance de Montréal, des étapes additionnelles sont suggérées, incluant l'optimisation de la définition du syndrome d'allure grippale à utiliser, la confirmation de la valeur de ces prédicteurs avec de nouvelles données et l'évaluation de leur utilité pratique.

Mots-clés : Dossiers électroniques; Influenza; Santé publique; Surveillance; Surveillance syndromique; Syndrome d'allure grippale; Urgence; Vigie sanitaire

Abstract

Surveillance of influenza relies on a wide array of data, including emergency department based syndromic surveillance data. An increasing number of variables are recorded in emergency department electronic records and are available for surveillance. The main objective of this research is to evaluate the potential utility of age, triage scores, and disposition data for enhanced monitoring of the burden of severe influenza cases. Data from a subset of Montreal hospitals was used, from April 2006 to January 2011. Pneumonia and influenza hospitalizations were taken as a measure of the burden of severe influenza cases, and were modeled using a negative binomial regression approach, taking into account seasonal and secular trends. Age-, triage score-, and disposition-stratified influenza-like illness visits improved the fit of predictive models for pneumonia and influenza hospitalization, as compared to overall influenza-like illness visits. Before integration of these variables into the Montreal surveillance system, additional steps are suggested, including the optimization of an influenza-like illness syndrome definition, the confirmation of the value of these predictors using new data, and the evaluation of their practical utility.

Keywords : Emergency department; Electronic records; Influenza; Influenza-like illness; Public health; Surveillance; Surveillance, syndromic

Table of contents

List of tables v

List of figures vii

List of abbreviations ix

Acknowledgements / Remerciements xiii

Chapter 1: Introduction 1

1.1. Context 1

1.2. General objective 4

Chapter 2: Review of literature 7

2.1. ILI syndrome definition 7

2.2. Influenza-related hospitalizations and mortality – An overview 17

2.3. Relationship between ILI emergency department visits and influenza-related hospitalizations and mortality 19

2.4. Methodological considerations 28

2.5. Gaps in knowledge and specific objective 31

Chapter 3: Methodology 33

3.1. Study setting 33

3.2. ED ILI-visits: choice of syndrome definitions 36

3.3. Value of age, triage score, and disposition data for predicting influenza-related hospitalizations 40

Chapter 4: The potential utility of age, triage score, and disposition data to improve emergency department-based surveillance of influenza-like illness in Montréal, Canada: a time series analysis from 2006 to 2011 45

4.1. Abstract 47

4.2. Background 48

4.3. Methods 49

4.4. Results 52

4.5. Discussion 60

4.6. Conclusion 63

4.7. References 65

4.8. Supplementary material 69
Chapter 5: Additional results 77
5.1. Descriptive statistics: number of ED visits and use of the electronic system… 77
5.2. Descriptive statistics: ILI visits 79
5.3. Correlations 83
Chapter 6: Discussion 85
6.1. Results, implications, and limits 85
6.2. System limitations 86
6.3. Recommendations 88
Chapter 7: Conclusion 91
References 93
Appendix 1: Descriptive statistics and time series i

List of tables

Table 2-I. Studies evaluating ILI syndrome definitions based on ED diagnoses 10

Table 2-II. Studies evaluating ILI syndrome definitions based on ED chief complaints 11

Table 2-III. Studies evaluating ILI syndrome definitions based on ED diagnoses and chief complaints 12

Table 2-IV. Studies evaluating the association between overall ILI ED visits and influenza-related hospitalizations and mortality 20

Table 2-V. Studies evaluating the association between age-stratified ILI ED visits and influenza-related hospitalizations and mortality 21

Table 2-VI. Studies evaluating the use of ED disposition data for ILI/respiratory syndrome surveillance 22

Table 3-I. Comparison of data sources 34

Table 3-II. Date of entry into *ERU* and *RQSUCH* systems, per ED 35

Table 3-III. Keywords for ILI syndrome definitions 38

Table 4-I. Mean number of weekly influenza-like illness emergency department visits according to visit characteristics, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 53

Table 4-II. IRR of overall P&I hospitalizations, for each SD increase in ILI visits, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 57

Table 4-III. Mean number of weekly influenza-like illness – sensitive definition - emergency department visits, according to visit characteristics, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 71

Table 4-IV. IRR of overall P&I hospitalizations, for each unit increase in ILI visits (specific definition), hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 72

Table 4-V. IRR of overall P&I hospitalizations, for each unit increase in ILI visits (sensitive definition), hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 73

Table 4-VI. IRR of overall P&I hospitalizations, for each SD increase in ILI-Se visits, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 74

Table 4-VII. Akaike's information criterion (AIC) of predictive models for pneumonia and influenza hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 75

Table 5-I. Number of emergency department (ED) visits, proportion with chief complaint, and number of chief complaint per visit in *ERU*, from date of entry to November 14, 2011 78

Table A1-I. Number of emergency department (ED) visits: daily mean per period of analysis, *ERU* i

Table A1-II. Proportion of emergency department (ED) visits with chief complaints recorded: daily mean per period of analysis, *ERU* ii

Table A1-III. Mean number of chief complaint codes per emergency department (ED) visits, per period of analysis iii

Table A1-IV. Number of emergency department (ED) visits obtained from *ERU* and *RQSUCH*: daily mean, percent agreement, and outliers iv

Table A1-V. Proportion of emergency department (ED) visits with ILI-Sp: daily mean per period of analysis, *ERU* v

Table A1-VI. Proportion of emergency department (ED) visits with ILI-Se: daily mean per period of analysis, *ERU* v

Table A1-VII. Proportion of emergency department (ED) visits with ILI-R: daily mean per period of analysis, *RQSUCH* vi

Table A1-VIII. Proportion of emergency department (ED) visits with influenza-like illness (ILI), according to data source and syndrome definition vi

List of figures

Figure 4-1: Weekly emergency department (ED) visits with influenza-like illness (ILI) and pneumonia and influenza (P&I) hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 54

Figure 4-2. Baseline model of weekly pneumonia and influenza (P&I) hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 56

Figure 4-3. Akaike's information criterion (AIC) of predictive models for pneumonia and influenza hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 59

Figure 4-4. Weekly emergency department (ED) visits with influenza-like illness (ILI), hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 69

Figure 4-5. Akaike's information criterion (AIC) of predictive models for pneumonia and influenza hospitalizations, using ILI-Se visits, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011 70

Figure 5-1. Proportion of emergency department (ED) visits with influenza-like illness (ILI), according to emergency department, data source, and syndrome definition 80

Figure 5-2. Lowess-smoothed time series of daily proportion of emergency department (ED) visits with influenza-like illness (ILI), total and selected EDs, 2006 to 2011 82

Figure 5-3. Correlation between *ERU*-derived syndrome components and *RQSUCH*-obtained influenza-like illness (ILI) counts 84

Figure A1-1. Average daily number of emergency department (ED) visits, stratified per year and ED, 2006 to 2011 i

Figure A1-2. Proportion of emergency department (ED) visits with chief complaint recorded: daily mean stratified per year and ED, 2006 to 2011 ii

Figure A1-3. Mean number of chief complaint codes per emergency department (ED) visits, stratified per year and ED iii

Figure A1-4. Smoothed time series of daily proportion of emergency department (ED) visits with influenza-like illness (ILI), 2006 to 2011 vii

List of abbreviations

ARIMA	Autoregressive integrated moving average
CDC	Center for Disease Control and Prevention
CI	Confidence interval
CTAS	Canadian Triage Acuity Score
Distribute	Distributed Surveillance Taskforce for Real-time Influenza Burden Tracking and Evaluation
DSP	*Direction de santé publique* (Public Health Department)
ED	Emergency department
ERU	*Entrepôt régional des urgence* (Regional Emergency Department Warehouse)
ESSENCE	Electronic Surveillance System for the Early Notification of Community-based Epidemics
GLM	Generalized linear model
ICD	International Classification of Diseases
ILI	Influenza-like illness
ILI-R	Influenza-like illness as reported in *RQSUCH*
ILI-Se	Sensitive definition of influenza-like illness
ILI-Sp	Specific definition of influenza-like illness
NPV	Negative predictive value
NYC	New York City
P&I	Pneumonia and influenza
PPV	Positive predictive value
RQSUCH	*Relevé quotidien de la situation à l'urgence au centre hospitalier* (Daily Report on Emergency Department and Hospital Situation)
SD	Standard deviation
URT	Upper respiratory tract
U.S.	United-States
WHO	World Health Organization

À mon grand-père et confrère, le Dr Marc Savard

Acknowledgements / Remerciements

J'aimerais remercier mes directeurs David Buckeridge, Robert Allard et Lucie Bédard, pour leur aide constante et leurs judicieux conseils.

I would also like to thank the whole McGill Surveillance Lab team, for their regular comments and suggestions. Special thanks to Aman Verma for his much appreciated help with SQL.

J'aimerais finalement remercier André Bilodeau, de l'équipe Surveillance épidémiologique et vigie de la Direction de santé publique de Montréal, pour son aide précieuse avec les banques de données.

Chapter 1: Introduction

1.1. Context

1.1.1. Influenza syndromic surveillance

Influenza remains a disease of public health importance, because of its annual morbidity and mortality and its pandemic potential (Nicholson *et al.* 2003). The World Health Organization (WHO) considers influenza surveillance important for ensuring rapid detection of epidemics, characterizing circulating virus, guiding vaccine development, planning appropriate public health control measures, and evaluating the burden of disease and associated costs (World Health Organization 2006).

Influenza surveillance systems exist at multiple levels, from international to local, to address a range of objectives, from informing vaccine production to guiding local outbreak response (Brammer *et al.* 2009). The sources of data for surveillance vary from system to system, but often multiple sources are used within a system. These sources are sometimes understood as being either traditional or syndromic.

Syndromic surveillance generally differs from traditional surveillance in terms of specificity, frequency of data collection and analysis, timeliness, and objectives (Shmueli and Burkom 2010; Tsui *et al.* 2008). Whereas traditional surveillance uses data such as laboratory confirmed influenza diagnoses, cases of influenza-like illness (ILI) reported by sentinel physicians, and cause-specific mortality, syndromic surveillance data are prediagnostic and nonspecific, describing symptoms or care-seeking behaviors. Syndromic surveillance data sources include emergency department chief complaints, outpatient clinic visits, medication sales, and school/work absenteeism (Fricker 2011; Shmueli and Burkom 2010). These data are usually collected daily, as opposed to weekly or more infrequently for traditional surveillance. Finally, syndromic data tend to be timelier than traditional data, with respect to disease event occurrence, consistent with the objective of providing early event detection (Tsui *et al.* 2008).

In recent years, the surveillance community has recognized another objective for syndromic surveillance, namely, situation (or "situational") awareness; however, this concept is poorly and not consistently defined (Buckeridge 2011). One definition is the activity of "monitoring disease trends or other markers of community health in situations where there is a need for prompt information" (Buehler *et al.* 2008). Specific objectives may include assessing the absence or limited size of unusual disease events, assessing and monitoring disease burden, detecting virulence shifts, tracking known events, and anticipating demands and planning for health care services (Buehler *et al.* 2009; Burkom 2011; Hanni 2011; van den Wijngaard *et al.* 2011). In any case, whether for early event detection or situational awareness, the focus of syndromic surveillance is typically on achieving near "real-time" surveillance (Buehler *et al.* 2008).

Syndromic surveillance of influenza – in particular using emergency department (ED)-based data – can provide information that is timelier than laboratory data (Buehler *et al.* 2009; Dailey *et al.* 2007; Schindeler *et al.* 2009; Zheng *et al.* 2007). It can potentially represent a greater number of encounters than traditional surveillance data, and provide additional details relative to time, age, and geographical trends (Buehler *et al.* 2009). Monitoring influenza is considered by some public health practitioners to be one of the greatest utilities of syndromic surveillance (Buehler *et al.* 2008).

1.1.2. Surveillance of severe cases

Monitoring severe events due to influenza, such as influenza-related hospitalizations or influenza-related mortality, is an important aspect of situation awareness during an influenza epidemic. However, hospitalization and mortality data may not be available to public health departments in a timely manner for prospective surveillance purposes; hence the motivation to find other data sources reflective of the burden of severe influenza cases.

In contrast to hospitalization and mortality data, records of emergency department (ED) visits are available in many public health settings through existing syndromic surveillance systems. Many public health agencies monitor these ED visits for influenza-like-illness (ILI), but due to variations in care seeking behavior and other factors, ED visits do not necessarily represent severe disease. Existing syndromic surveillance systems that use ED visit data are therefore limited in their ability to monitor severe cases of influenza.

However, the severity of illness for patients presenting to EDs is increasingly captured in electronic information systems. For example, indicators such as standardized triage scores and disposition information could be used to enhance surveillance of the burden of severe influenza disease. In addition, a wide array of patient or encounter characteristics may be captured in electronic records. Among these, age has been used to identify subgroups whose ILI visits correlate with later counts of hospitalizations or mortality. (Brownstein *et al.* 2005; Chan *et al.* 2011; Olson *et al.* 2007; Sebastian *et al.* 2008). Thus, in addition to markers of severity such as triage score and disposition, demographic information such as age may contribute to monitoring and potentially predicting the burden of severe influenza cases.

1.1.3. Montreal Context

The Montreal Public Health Department (*Direction de santé publique de Montréal, DSP*) is responsible for a population of 1.85 million . It conducts routine influenza surveillance using multiple sources of data, both traditional and syndromic.

The syndromic component includes ED-based data. The DSP currently receives daily counts of ILI visits from all EDs in its jurisdiction, through the Daily Report on Emergency Department and Hospital Situation (*Relevé quotidien de la situation à l'urgence et au centre hospitalier – RQSUCH*). These data are created by daily manual entry, in each hospital, of the number of patients registering to the ED with influenza-like illness symptoms, and are transmitted to the DSP, where they are analyzed daily.

The DSP also has access to detailed ED data for a subset of the Montreal hospitals, via the Regional Emergency Departments Warehouse (*Entrepôt Régional des Urgences* - *ERU*). These data are extracted routinely from triage information systems in each ED and loaded into a data warehouse at each institution before being transferred at least daily to the regional data warehouse. Records from this source contain data on each ED visit in participating hospitals, including chief complaint, ED diagnosis, age, sex, triage category, and disposition information. This data source is not currently used for surveillance in Montreal. Counts of ILI visits may be derived from either the chief complaint or the diagnosis. The DSP is considering adopting this source in place of the *RQSUCH* data for many reasons, including automated reporting and analysis of visits by factors such as age, severity of illness, and patient geography.

1.2. General objective

A principal interest in adopting the *ERU* source for surveillance lies in the variables that are available for analyses, such as age, triage score, and disposition information. However, the value of these variables, except for age, has been subjected to very little assessment in the literature. The main objective of this work is therefore **to evaluate the potential utility of age, triage scores, and disposition data for enhanced monitoring and prediction of the burden of severe influenza cases in Montreal, using the *ERU* database as a source of ILI ED visit counts.**

1.2.1. Usefulness

This study will help identify variables that may be useful for enhancing influenza surveillance in Montreal and elsewhere. Judiciously choosing data sources and variables to be used in a surveillance system is important, considering that the information available is constantly growing, but that resources for analysis are limited. In this respect, even negative results – that age or severity markers contained in *ERU* do not appear associated with influenza-related hospitalization – will be useful, in that they will influence decisions regarding what data to include when building a surveillance system using this data source.

Monitoring severe illness, in addition to the burden of symptomatic, less severe illness, is warranted, especially in a context of limited resources. Not all seasonal epidemics have the same severity or affect the same group of individuals, in terms of hospitalization and mortality rates (Thompson *et al.* 2006). Timely identification of the most severe ones may influence the timing and intensity of public health measures, such as vaccination promotion and communications with clinicians for enhanced awareness of influenza circulation, and may contribute to the planning of heath care resources.

A timely indication of the burden of severe illness may be particularly warranted during an influenza pandemic. During a pandemic period, care-seeking behavior may change, in part due to messages relayed by the media, and it is possible that more individuals with benign symptoms present to the ED. It would therefore be of interest to distinguish those with a more severe presentation, which are more likely to reflect the burden of severe disease in the population. Timely knowledge of the severity of a pandemic may guide decisions regarding the need to implement measures beyond those used for seasonal influenza, for example the opening of influenza clinics. On the other hand, the absence or limited number of severe cases may be used for public reassurance.

Chapter 2: Review of literature

This review of the literature contains four sections: 1) a review ILI syndrome definitions that were developed or tested, in order to orient the choice of a definition for this work; 2) a short overview of the use and methods of measurement of influenza-related hospitalizations and mortality, to inform the choice of an indicator of severe influenza burden for this study; 3) a review of studies reporting the relationship between ED-based influenza syndromic surveillance data and influenza-related hospitalizations and deaths – with a section on studies evaluating the use age, triage scores, and disposition as indicators of interest; and 4) methodological considerations for modeling time-series.

2.1. ILI syndrome definition

2.1.1. Overview

Based on emergency department chief complaints and discharge diagnoses, various syndrome definitions have been suggested for influenza – as illustrated in Tables 2-I to 2-III. When the data are coded, ILI definitions typically consist of a list of codes, such as ICD-9 or ICD-10 codes. When the data are in free-text form, the syndrome definition can consist of a list of findings (typically signs and symptoms), with or without combination rules; a free-text classifier is then required to apply the definition, taking into account synonyms, acronyms, abbreviations and misspellings (Chapman *et al.* 2010; Dara *et al.* 2008). In addition, statistical classifiers can be developed from a labeled training set (Olszewski 2003).

There are also various clinical definitions used for sentinel surveillance of ILI, consisting of clinical symptoms, signs, or history elements that a patient must have in order to meet the definition. Although not identical, they tend to be similar among surveillance systems (Thursky *et al.* 2003). For instance, the Center for Disease Control and Prevention (CDC) definition for ILI is fever ≥37.8°C with cough or sore throat, in the absence of known cause other than influenza (Center for Disease Control and Prevention 2011). In Canada, it is defined as acute respiratory illness with fever and cough and one or more of sore throat, arthralgia, myalgia, or prostration, which is likely due to influenza (Public Health Agency of Canada 2012).

Here, we distinguish between "clinical case definition", where a health care professional directly assessing a patient applies the case definition – such as general practioners participating in sentinel surveillance – from "syndromic case definition", applied to data already taken out of the clinical context – such as ED chief complaints and diagnoses. This is mainly for clarity's sake: although the terms "clinical case definition" (Boivin *et al.* 2000; Carrat *et al.* 1999) and "syndrome definition" (Cadieux *et al.* 2011; Chapman *et al.* 2010) have been used, we have not found this distinction made explicitly in the literature.

In this review, we include studies testing syndrome definitions based on electronically recorded 1) diagnoses, 2) chief complaints, or 3) both, in an outpatient setting – either community-based physician visit or ED visit. The studies included validate one (or more) syndrome definition(s) against a clinical ILI case definition or influenza laboratory test results as a gold standard, or compare definitions according to other criteria such as detection of influenza season. The studies included are summarized in Tables 2-I to 2-III. Most of these validation studies are ecological, comparing time series of ILI ED visits against time series of positive influenza tests (or another influenza-related event), thus precluding conclusions regarding the validity of the syndrome definition at the case level. Associations observed in time series studies may be due to the seasonal or secular variation of measured or unmeasured ecological confounders. Were the association with these confounders to change, the validity of the ILI syndrome may be affected. Record-level studies, on the other hand, allow for individual-level assessment of a syndrome definition's validity. However, a valid definition at the individual level may not directly translate into the most sensitive or specific definition at the population level, and may not provide for the most timely monitoring of influenza activity.

Table 2-I. Studies evaluating ILI syndrome definitions based on ED diagnoses

Study	Setting	Data source	Syndrome definitions	Comparator	Methodology	Main findings
Zheng *et al*. (2007)	New South Wales (Australia) EDs (75% coverage) 2001-2005	ICD-9/ICD-10 ED diagnoses	Diagnosis of influenza (coded ICD-9 487 or ICD-10 J10-11)	Influenza virological data	Poisson regression model Cross-correlation of residuals	Cross-correlation of residuals for ED influenza diagnoses and influenza laboratory counts diagnoses, maximum at lag -3 days (r = 0.06, p = 0.01).
Marsden-Haug *et al*. (2007)	U.S. military treatment facilities 2000-2004	ICD-9 diagnoses	"ILI-large" definition, which includes 10 relatively common diagnostic codes, "ILI-small" definition, which includes 4 less frequent diagnostic codes [1]	Influenza virological data	Correlations	Correlation coefficients of 0.71 and 0.86, p<0.0001, for ILI-large and ILI-small respectively.
Schindeler *et al*. (2009)	South-Eastern Sydney (Australia) EDs 2001-2006	ICD-9/ICD-10 ED diagnoses	Five different respiratory syndrome definitions; included an ILI syndrome defined as a diagnosis of influenza (coded ICD-9 487 or ICD-10 J10-11)	Influenza virological data	Semi-parametric generalized additive model	Association between influenza laboratory counts and all five syndrome definitions, strongest association with the ILI syndrome (1-week lag, risk ratio 1.047).
Cadieux *et al*. (2011)	Quebec (Canada) outpatient visits 2005-2007	Physician billing claim diagnoses	"ILI-large" definition and "ILI-small" definition as defined by Marsden-Haug *et al*. (2007)	ILI diagnoses, signs, and symptoms recorded in the chart	Measures of sensitivity, specificity, predictive values	High specificity for both definitions (small: 1.00, large 0.98); ILI-small lower sensitivity (0.18 vs. 0.38), lower PPV (0.29 vs. 0.77) and NPV (0.99 vs. 0.88).
Moore *et al*. (2011)	Two hospitals from Victoria (Australia) 2001-2009	ICD-10 ED diagnoses	No pre-supposed syndrome definition; codes tested individually	Influenza virological data	Correlations	5 codes moderately and significantly correlated (J11 Influenza virus not identified, J06 Acute upper respiratory infection multiple and unspecified sites, J22 Unspecified acute lower respiratory infection, B34 Viral infection, unspecified site, J18 Pneumonia organism unspecified).

[1] ILI-large: 079.99 viral infection NOS, 382.9 otitis media NOS, 460 nasopharyngitis, acute, 461.9 acute sinusitis, unspecified, 465.9 infectious upper respiratory, multiple sites, acute NOS, 466.0 bronchitis, acute, 486 pneumonia, organism NOS, 490 bronchitis NOS, 780.6 fever, 786.2 cough
ILI-small: 465.0 laryngopharyngistis, acute, 487.0 influenza with pneumonia, 487.1 influenza with respiratory manifestations NEC, 487.8 influenza with manifestation NEC

Table 2-II. Studies evaluating ILI syndrome definitions based on ED chief complaints

Study	Setting	Data source	Syndrome definitions	Comparator	Methodology	Main findings
Oslon *et al*. (2007)	New-York City (U.S.) EDs 2001-2006	ED chief complaints	''fever and respiratory'': combination of ''respiratory,'' ''fever/flu,'' ''common cold,'' and ''sepsis'' syndromes[1] narrow ILI definition: influenza keyword OR (fever-related keyword AND (cough OR sore throat))	Influenza virological data	Cross-correlation of weekly counts	Broad definition correlates and coincides with virological influenza data. Specific definition represent 11% of broad "fever and respiratory" syndrome. The two definitions highly correlated ($r^2 = 0.96$) except during 2 tree-pollen dominant periods.
Pendarvis *et al*. (2007)	Boston (U.S.) surveillance data 2005-2006 season	ED chief complaints	ILI 1 (fever OR cough OR cold OR sore throat) ILI2 (ILI 1 OR respiratory infections) ILI 3 (fever AND (cough OR cold OR sore throat))	National trends of reported cases	Comparison of trends	ILI1 and ILI2 had nearly identical trends, except in the elderly. ILI3 allowed comparison with national trends.
Paladini *et al*. (2008)	Boston and New York city surveillance data 2005-2008	ED chief complaints	Boston narrow and broad definitions, New-York city narrow and broad definitions	Influenza virological data	Correlations	Narrow definitions better correlated with virological isolates than broad definitions, and even more so when stratified by age.
Lemay *et al*. (2008)	3 EDs in Ottawa (Canada) 1998-2003	ED chief complaints	ILI symptom categories: fever, cough, respiratory symptoms, headache, sore throat, and myalgia[2]	Influenza virological data	ARIMA models Cross-correlation of residuals	Significant correlations in all ages.
Burkom *et al*. (2011)	6 ED (U.S.) 2006-2010	ED chief complaints	Influenza keyword OR (fever-related keyword AND (cough OR sore throat))	Local ILI definitions	Comparison of signal-to-noise ratio and epidemic detection	Slightly higher signal-to-noise ratios and detection performance for preferred definitions, but dependent on the site.

[1] ''sepsis'': sepsis, bacteremia, cardiac arrest, unresponsive, unconscious, or dead on arrival, ''common cold'': stuffy nose or nasal or cold symptoms, ''respiratory'': pneumonia, shortness of breath, bronchitis, upper respiratory tract infection, difficulty breathing, pleurisy, croup, cough, dyspnea, and chest cold, ''fever/flu'': fever, chills, malaise, body aches, viral syndrome, and influenza, excluding acute gastroenteritis, enteritis, or diarrhea.

[2] Fever: febrile, fever, temperature, hot, shiver, feeling hot, elevated temperature, high temperature, chills, shakes, rigors; cough: cough; respiratory symptoms: pneumonia, pneumonitis, difficulty breathing, diff. breathing, trouble breathing, shortness of breath, sob, dyspnoea, short of breath, flu, flulike illness, influenza, bronchitis, bronchiolitis, wheezing, wheeze, respiratory infection, respiratory illness; headache: headache, head ache, migraine; sore throat: sore throat, throat ache, throat pain; myalgia: muscle pain, muscle ache, body ache, body pain, prostration, weak, weakness, malaise, tired, fatigue

Table 2-III. Studies evaluating ILI syndrome definitions based on ED diagnoses and chief complaints

Study	Setting	Data source	Syndrome definitions	Comparator	Methodology	Main findings
Cochrane *et al*. (2008)	4 New-York City (U.S.) EDs retrospective cohort 2005-2007	ED chief complaints and ICD-9 diagnoses	Chief complaint of flu or an ICD9 final diagnosis of flu	Adapted CDC clinical definition of ILI, through chart review	Measures of predictive values	PPV for ILI symptoms through chart review: 23% and 60% for chief complaint and final diagnosis respectively.
Musumba *et al*. (2008)	One facility of North Dakota (U.S.) 2005-2008	ED chief complaints and ICD-9 diagnoses	ILI chief complaints, diagnoses with ICD9 code 487	Influenza virological data	Comparison of trends	Peaks obtain from chief complaint, diagnoses, and virological data well correlated
May *et al*. (2010)	One academic hospital ED 2005-2006	ED chief complaints and ICD-9 diagnoses	Chief complaint groupings: upper respiratory infection, asthma exacerbation, viral illness, malaise and myalgias, fever, and pneumonia. Diagnosis groupings: bronchitis, pneumonia, upper respiratory infection, acute sinusitis, pharyngitis, fever, and myalgias	CDC sentinel data for ILI	Outbreak detection with univariate and multivariate statistical algorithm	Univariate statistical algorithm: upper respiratory tract (URT) chief complaints flagged the outbreak more consistently then diagnoses. Multivariate statististical algorithm: a combination of URT, viral, and pneumonia diagnoses flagged the outbreak earlier, more consistently, and more clearly than the corresponding chief complaints.

2.1.2. Syndrome definition based on diagnosis

Schindeler *et al*. (2009) tested five different respiratory syndrome definitions using data from emergency departments in South-Eastern Sydney, Australia, over the 2001 to 2006 influenza seasons. The syndrome tested included an ILI syndrome defined as a diagnosis of influenza (coded ICD-9 487 or ICD-10 J10-11). Although there was an association between influenza laboratory counts and all five syndrome definitions, the strongest association was with the ILI syndrome defined above, with a 1-week lag (syndrome preceding virological data) and a risk ratio of 1.047 (95% CI 1.042-1.052). Using that same ILI syndrome definition and data from approximately three quarters of New South Wales ED data, Zheng *et al*. (2007) found a weak but statistically significant cross-correlation of residuals for ED influenza diagnoses and influenza laboratory counts diagnoses, with a maximum at lag -3 days ($r = 0.06$, $p = 0.01$), and with a cluster of positive correlations at minus 2-5 days.

Others have developed and tested syndrome definitions. Marsden-Haug *et al*. (2007) started with a set of 29 ICD-9 codes for ILI surveillance used by ESSENCE – a surveillance system initially developed by the U.S. Department of Defense (Lewis *et al.* 2002). For each code, using U.S. military treatment facilities data from 2000 to 2004, they assessed: 1) positive predictive value (PPV) for positive influenza laboratory test (through linked data from 2002-2004, in an individual level study design); 2) correlations with laboratory counts (ecological); 3) and a measure of signal-to-noise ratio. Using the results of these analyses, they created two ILI syndrome definitions: one “ILI-large” definition, which includes 10 relatively common diagnostic codes, and one “ILI-small” definition, which includes 4 less frequent diagnostic codes. The correlation with weekly virological counts was 0.71 and 0.86 ($p<0.0001$) for the ILI-large and ILI-small definitions, respectively. The ILI-small definition was most correlated with the CDC sentinel data.

Cadieux *et al*. (2011) used Québec outpatient physician billing claim diagnoses from 2005-2007 to validate these "large" and "small" syndromic definitions of ILI against phone physician-assisted chart reviews (N=1,098). They validated the syndromic definitions against corresponding diagnoses and signs and symptoms recorded in the chart, and found high specificity for both definitions (small: 1.00, large 0.98; 95% CI within 0.01); ILI-small had lower sensitivity (0.18, CI 0.12-0.26 vs. 0.38, CI 0.35-0.41), lower positive predictive value (PPV) (0.29, CI 0.16-0.41 vs. 0.77, CI 0.73-0.81), and higher negative predictive value (NPV) (0.99, CI 0.99-0.99 vs. 0.88, CI 0.87-0.89).

Moore *et al*. (2011) developed a syndrome definition without any a-priori assumptions. They assessed correlation of all ED ICD-10 coded diagnoses in two hospitals from Victoria, Australia, and mandatorily reported virological data, from 2001-2009. The diagnostic codes correlated with a coefficient greater than 0.3 were kept in the definition, which in its final version included 5 codes (J11 Influenza virus not identified, J06 Acute upper respiratory infection multiple and unspecified sites, J22 Unspecified acute lower respiratory infection, B34 Viral infection, unspecified site, J18 Pneumonia organism unspecified).

2.1.3. Syndrome definition based on chief complaint

Lemay *et al*. (2008) used a syndrome definition derived from the Canadian clinical ILI definition, including fever, cough, respiratory symptoms, headache, sore throat, and myalgia. They applied this definition to chief complaints from 3 EDs in Ottawa, Canada, from 1998-2003, fitted an ARIMA model to both ILI counts and influenza laboratory counts, and performed cross-correlation of residuals. They performed age-stratified analyses, and found significant correlations in all age groups. In children, the sub-classifications fever, cough, and respiratory symptoms were also correlated with virological data in many seasons.

Olson *et al*. (2007) used a broad syndrome definition, applied to New-York city EDs' chief complaints during the 2001-2002 to 2005-2006 seasons, which they termed ''fever and respiratory'' syndrome, and which is composed of the hierarchical and mutually exclusive syndromes ‘‘respiratory,’’ ‘‘fever/flu,’’ ‘‘common cold,’’ and ‘‘sepsis’’. Counts using this definition correlated and coincided with virological influenza data. They found that the narrow ILI definition “influenza keyword” OR (“fever-related keyword” AND (cough OR sore throat)) represented 11% of the broad “fever and respiratory” syndrome. The two definitions were highly correlated ($r^2 = 0.96$) except during tree-pollen dominant periods.

Burkom *et al*. (2011) compared this narrow standardized definition to the application of local “preferred” definitions in the Distribute project participating sites, from 2005 to 2009. Distribute was a North American effort to demonstrate the feasibility of a collaborative influenza surveillance network (Olson *et al.* 2011). Overall, the preferred definitions yielded more cases and stronger signals, but also produced more background noise. In terms of signal-to-noise ratio and detection performance, the balance was slightly in favour of preferred definitions, although it depended on the hospital. However, the standardized definition allowed obtaining comparable ratios of ILI/total visits across hospitals. Of note, contribution of each component (fever/cough or fever/sore throat or flu) varied according to site, age group, and season.

Pendarvis *et al*. (2007) compared 3 definitions using the Boston surveillance data during the 2005-2006 season: ILI 1 (fever OR cough OR cold OR sore throat) and ILI2 (ILI 1 OR respiratory infections) had nearly identical trends, except in the elderly; ILI 3 (fever AND (cough OR cold OR sore throat)) allowed comparison with national trends. Comparing the Boston narrow and broad definitions, as well as the New-York City narrow and broad definitions, from 2005 to 2008, Paladini *et al*. (2008) found that narrow definitions were better correlated with virological isolates than broad definitions, and even more so when stratified by age.

2.1.4. Comparison of ED diagnosis vs. chief complaint

May *et al*. (2010) compared the performance of chief complaints and diagnoses at time of disposition from one academic hospital ED to detect the onset of influenza epidemic for the 2005-2006 season. Diagnosis was the same as the chief complaint 29% and 24% of the time, for respiratory and viral chief complaints, respectively. "Upper respiratory tract" (URT) chief complaints (URT symptoms or "flu") followed the ILI trends from the CDC sentinel network better than URT diagnoses, and, using a univariate statistical algorithm, flagged the outbreak more consistently. On the other hand, in a multivariate statististical algorithm, a combination of URT, viral, and pneumonia diagnoses flagged the outbreak earlier, more consistently, and more clearly than the corresponding URT, viral, and pneumonia chief complaints.

Cochrane *et al*. (2008) compared visits in 4 New-York City EDs with a chief complaint of flu or an ICD9 final diagnosis of flu, to an adapted CDC clinical definition of ILI through chart review. PPV for ILI symptoms through chart review were 23% (95% CI 18-28%) and 60% (95% CI 51-69%) for chief complaint and final diagnosis respectively. Out of 512 visits with either flu chief complaint or diagnosis, 19 had both.

Using ED visits from one facility of North Dakota over 3 seasons, Musumba *et al*. (2008) found that ILI chief complaints, diagnoses with ICD9 code 487, and influenza positive test results had peaks that were well correlated.

2.1.5. General considerations

Overall, more sensitive syndromic definitions of ILI (sometimes including respiratory syndrome elements) tend to be well correlated with more specific syndromic definitions of ILI (that are closer to the clinical definitions) (Olson *et al.* 2007; Pendarvis *et al.* 2007). Specific definitions might be more correlated with virological isolates (Marsden-Haug *et al.* 2007; Paladini *et al.* 2008; Schindeler *et al.* 2009) and with sentinel surveillance data (Marsden-Haug *et al.* 2007).

2.2. Influenza-related hospitalizations and mortality – An overview

Outcomes often used to assess the burden of an influenza epidemic or pandemic are the rates of hospitalization or mortality due to influenza (Simonsen *et al.* 1997; Thompson *et al.* 2004; Zhou *et al.* 2012). However, hospitalizations and deaths due to influenza cannot usually be measured directly, because 1) patients with influenza can have various cardiovascular and respiratory presentations and many will never undergo virological testing, 2) tests performed after a certain time in the progression of the disease will be negative, and 3) hospitalisations and deaths are often due to secondary complications of influenza, or to underlying conditions exacerbated by influenza, and in such cases influenza is not likely to be written on the discharge summary or death certificate (Brammer *et al.* 2009; Thompson *et al.* 2006). Many methods have therefore been developed to model and estimate the burden of influenza.

One simple way that has been used to estimate hospitalizations or deaths due to influenza is the rate difference method, where rates during a period of influenza circulation are compared to rates during periods of no circulation; the difference is attributed to influenza (Beard *et al.* 2006; Chiu *et al.* 2002; Izurieta *et al.* 2000; Neuzil *et al.* 2000). Another approach is to use Serfling-type models, which serve to estimate the excess of hospitalisations or deaths due to influenza, as compared to a modeled seasonal baseline (Serfling 1963; Simonsen *et al.* 1997). Statistically significant excesses are said to be above epidemic threshold. Others yet have used multivariate modeling approaches, including generalized linear regression models and autoregressive integrated moving average (ARIMA) models (Hardelid *et al.* 2012; Mangtani *et al.* 2006; Nicholson 1996; Nunes *et al.* 2011; Thompson *et al.* 2004; Upshur *et al.* 1999; Wong *et al.* 2006; Zhou *et al.* 2012).

Estimates of influenza-related hospitalizations or deaths may vary according to the method used. Studies that compared rate difference, Serfling, generalized linear regression (with Poisson or negative binomial distributions), and/or ARIMA methods to estimate influenza-attributable hospitalizations or mortality found either moderate (Thompson *et al.* 2009) or important inter-method differences (Gilca *et al.* 2009; Newall *et al.* 2010; Yang *et al.* 2011). These differences stress the need to validate statistical methods against epidemiological data. One study compared rate difference and Poisson regression methods, and validated the results against rates of laboratory confirmed cases in a prospectively recruited pediatric population hospitalized with acute respiratory disease (Yang *et al.* 2011). They found Poisson regression to outperform the rate difference method.

In addition to the choice of method, the choice of health outcome will impact the estimate of the influenza-attributable burden of hospitalizations and mortality. An outcome commonly chosen to represent influenza-related hospitalizations and/or mortality is pneumonia and influenza (P&I) diagnoses (Berenbaum *et al.* 2007; Chan *et al.* 2011; Das *et al.* 2007; Muscatello *et al.* 2008; Olson *et al.* 2007; Schanzer *et al.* 2011; Sebastian *et al.* 2008; Simonsen *et al.* 1997; Tsui *et al.* 2001). However, some have suggested that P&I mortality is an underestimate of excess mortality due to influenza (Brammer *et al.* 2009; Simonsen *et al.* 1997). Simonsen *et al*. (1997) suggest that excess in overall mortality is a more accurate measure of the burden of influenza. Alternatively, excess overall mortality might be an overestimate of the impact of influenza, and respiratory and cardiovascular deaths might be a better measure (Brammer *et al.* 2009). A similar reasoning would apply to influenza-related hospitalizations, whereby P&I hospitalizations might be an underestimate of influenza-related hospitalizations. However, it remains a common measure of influenza-related hospitalizations (Berenbaum *et al.* 2007; Chan *et al.* 2011; Das *et al.* 2007; Olson *et al.* 2007; Sebastian *et al.* 2008; Tsui *et al.* 2001), thus allowing inter-study comparisons.

2.3. Relationship between ILI emergency department visits and influenza-related hospitalizations and mortality

This review of the literature includes studies that evaluate the association between ILI ED visits (measured with chief complaint or diagnosis) and influenza-related hospitalizations or mortality. Studies are included that look at overall ILI ED visits as well as ILI ED visits grouped by age, triage score, or disposition. Measures of interest include measures of association, prediction, timeliness, and validity (sensitivity, specificity and predictive value), at the ecological or individual level. Tables 2-IV to 2-VI summarize the studies that were included in this review of the literature.

Table 2-IV. Studies evaluating the association between overall ILI ED visits and influenza-related hospitalizations and mortality

Study	Setting	Syndrome tested	Comparator	Methodology	Main findings
Olson *et al.* (2007)	New York City (U.S.) EDs (coverage: 79-90%) 2001-2005	Broad "fever and respiratory" syndrome (fever/flu or respiratory)	P&I hospitalizations and P&I mortality (ICD-9 480–487; ICD-10 J10.0–J11.8, J12.0–J18.9)	Serfling method applied to both syndromic data and P&I hospitalizations to detect influenza epidemics; Cross-correlation functions	Serfling: ED visits 1 to 3-week ahead of hospitalizations and 2 to 3 weeks ahead of deaths Cross-correlations: ED visits and P&I hospitalizations concurrent with virological data, deaths 2 weeks after
Das *et al.* (2007)	New York City (U.S.) EDs (coverage: approximately 90%) 2001-2004	Broad "fever and respiratory" syndrome (fever/flu or respiratory)	P&I hospitalizations, primary or secondary diagnosis (ICD9 code 480-487)	Serfling method, ratios of ED visits to P&I hospitalizations excesses	Ratio of ED/hospitalization excesses 7:1 in 2002-2003 and 15:1 in 2003-2004; no hospitalization excess in 2002-2003.
Tsui *et al.* (2001)	One ED 1999 -2000	"respiratory" set (RS) and "influenza" set (IS) from ICD-9 coded chief complaints	P&I hospitalizations	Serfling method applied to both syndromic data and P&I hospitalizations to detect influenza epidemics; Cross-correlation functions	RS: 100% sensitivity; 50% PPV IS: 100% sensitivity, 25% PPV Serfling: 1-week lead time Cross-correlations: 2-week lead time

Table 2-V. Studies evaluating the association between age-stratified ILI ED visits and influenza-related hospitalizations and mortality

Study	Setting	Syndrome tested	Comparator	Methodology	Main findings
Chan *et al.* (2011)	ILI visits (community-based or emergency department) in Québec (Canada) 1998-2003	Set of ICD-9 codes based on ILI groupings validated by Marsden-Haug *et al*. (2007)	P&I hospitalizations, primary diagnosis (ICD-9 codes 480–487)	ARIMA modeling - cross-correlation functions of residuals	Highest correlation with P&I hospitalizations for ED visits by ≥65 yo age group. Greatest lead time, for peak correlation, for children 5-12 and 13-17 yo in the ED (2 weeks) and children 2-4, 5-12 and 13-17 yo in community-based settings (2 weeks).
Sebastian *et al.* (2008)	Medical visits for influenza (community-based or emergency department) in British-Columbia (Canada) 1998-2004	ICD-9 codes for influenza (487)	Population-wide P&I hospitalizations (primary diagnosis) and mortality (ICD-9 code for influenza (487) or pneumonia (480–486) or ICD-10 code for influenza (J108, J100, J101, J110, J111, J118) or pneumonia (J13-4, J120-2, J128-9, J150-60, J168, J180-1, J188-9, A403, A491, G001))	Timeliness of peaks Poisson regression: percent deviance explained	Visits in the 5-9 and 10-19 yo occurred earliest (5.3 days before hospitalizations). No significant difference between age groups in their predictive ability (percent deviance explained) for signaling P&I hospitalizations and mortality.
Olson *et al.* (2007)	New York City (U.S.) EDs (coverage: 79-90%) 2001-2005	Broad "fever and respiratory" syndrome (fever/flu or respiratory)	P&I hospitalizations and P&I deaths (ICD-9 480–487; ICD-10 J10.0–J11.8, J12.0–J18.9).	Serfling method applied to both syndromic data and P&I hospitalizations to detect influenza epidemics; Cross-correlation functions	Excess ED visits greatest in children. ED visits reached epidemic threshold earlier in children, exact age pattern season dependent. Cross-correlation functions: ED visits from children 2-17 yo leading virological isolates (and overall P&I hospitalizations) by 1 week; 18-64 y and < 2 yo coincident with viral isolates; ≥65 yo were lagging by 1 week.
Das *et al.* (2007)	New York City (U.S.) EDs (coverage: approximately 90%) 2001-2004	Broad "fever and respiratory" syndrome (fever/flu or respiratory)	P&I hospitalizations, primary or secondary diagnosis (ICD9 code 480-487)	Ratios of ED visits to P&I hospitalizations	Ratio of excess "fever/flu or respiratory" ED visits to excess P&I hospitalizations highest among children 0-4 yo (102:1) and lowest in adults ≥60 yo (0.3:1). Correlations between ED visits and P&I hospitalizations highest for young children and adults, lower in children 5-17 yo.
Brownstein *et al.* (2005)	4 emergency departments (pediatric, adult ED, community ED, and general ED), one ambulatory care setting and sentinel ILI visits for Massachusetts, U.S. 2000-2004	Respiratory illness syndrome	P&I mortality in New England	Cross-spectral analysis Poisson regression: percent deviance explained	3-4 yo: greatest lead time (34.0 days), followed by the <3 yo and 11-17 yo. Children < 3 yo best predictive value for overall P&I mortality, explaining on average 40.8% of the deviance, followed by children 3-4 yo, explaining 36.8% of the deviance.

Table 2-VI. Studies evaluating the use of ED disposition data for ILI/respiratory syndrome surveillance

Study	Setting	Syndrome tested	Comparator	Methodology	Main findings
Murray *et al.* (2008)	14 EDs in New-York City (U.S.) 2007-2008	ILI admissions from ED (complaints of fever and cough or sore throat, or mention of "flu")	Influenza virological data	Pearson correlation	ILI admissions well correlated with influenza isolates (ρ=0.76) and with all ILI visits (ρ=0.89)
Berenbaum *et al.* (2007)	Large tertiary hospital in Vermont (U.S.) 2003-2006	"Respiratory category" of inpatients (one or more respiratory signs, symptoms, or diagnoses in the chief complaint, impression diagnosis, or admission diagnosis) P&I admission diagnoses (ICD-9 480-487)	Hospitalizations with a discharge diagnosis of P&I (ICD-9 480-487)	Sensitivity, specificity, PPV	"Respiratory category": sensitivity, specificity and PPV of 55.6%, 94.7%, and 41% P&I admissions: sensitivity, specificity and PPV of 40.1%, 98.9% and 71%.
Townes *et al.* (2004)	ED information system used for surveillance by the Oregon Department of Human services (U.S.) 2001	Admission diagnosis of pneumonia	Hospitalizations with a discharge diagnosis of pneumonia	Sensitivity, specificity, PPV	Sensitivity 62% , specificity 98%, PPV 59%.

2.3.1. Overall ILI ED visits

Tsui *et al.* (2001) applied the Serfling method to counts of ICD-9 coded chief complaints, using a “respiratory” set (RS) and an “influenza” set (IS), as a method to detect influenza epidemics. As a gold standard, they used pneumonia and influenza (P&I) to which they also applied the Serfling method. Over a one year period (December 1999 – December 2000), RS signaled 3 times and IS 4 times. When evaluated against the P&I signals, both RS and IS had a 100% sensitivity; RS had a 50% PPV while IS had a 25% PPV. Both RS and IS signaled 1 week earlier than P&I; when measured with cross-correlation functions, the lead time was 2 weeks.

Olson *et al*. (2007) used a similar method applied to ED visits in participating New York City (NYC) hospitals with a broad “fever and respiratory” syndrome, NYC P&I hospitalizations and P&I deaths (ICD-9 480–487; ICD-10 J10.0–J11.8, J12.0–J18.9). Coverage was 79-90% of NYC for the ED data. During the 2001-2002 and 2003-2004 seasons, detection using the Serfling method on ED visits identified epidemics 1 week before P&I hospitalizations and 3 weeks before P&I deaths. In 2002-2003, ED visits signaled 2 weeks before deaths. In 2004-2005, ED visits signaled 3 weeks before P&I hospitalizations. Using cross correlation function on the most severe 2003-2004 season, they found ED visits and P&I hospitalizations to have highest correlation with virological data at lag 0, with high correlation coefficient for ED visits; P&I deaths were correlated with a 2-week lag (deaths occurring after virological data). Ratios of excess ED visits (fever/flu or respiratory) to excess P&I hospitalizations in NYC were also reported elsewhere (Das *et al.* 2007). These ratios were 7:1 in 2002-2003 and 15:1 in 2003-2004; there were no hospitalization excesses in 2002-2003.

2.3.2. Age-stratified ILI ED visits

In their study using NYC “fever and respiratory” ED visits, P&I hospitalizations, and P&I deaths, cited earlier, Olson *et al*. (2007) also assessed impact on, and timeliness of ED visits per age group. They found that in general, the burden of excess ED visits was greatest in children, and ED visits reached epidemic threshold earlier in children then in other age groups, although the exact age pattern was season dependent. The age group whose ED visits reached epidemic threshold first varied according to the season: < 2 and 2-4 year-olds in 2001-2002; 13-17 year-olds in 2003-2004 and; 2-4, 5-12, 13-17 year-olds in 2004-2005. Using cross-correlation functions on the 2003-2004 season, ED visits from children aged 2-4, 5-12 and 13-17 years were leading virological isolates and P&I hospitalizations by 1 week; visits from adults aged 18-39 and 40-64 years and from children aged < 2 years were coincident with viral isolates; and visits from adults aged ≥65 years were lagging by 1 week. Das *et al*. (2007) report that the ratio of excess "fever/flu or respiratory" ED visits to excess P&I hospitalizations is highest among children aged 0-4 years (102:1) and lowest in adults aged ≥60 years (0.3:1). Correlations between ED visits and P&I hospitalizations were highest in seasons 2001-2002 and 2003-2004 for young children and adults ($r^2 > 0.90$). It was lower in children aged 5-17 years ($r^2 = 0.56$) and weakest during the mild 2002-2003 season.

Sebastian *et al*. (2008) examined the relationship between medical visits for influenza (community-based or ED) per age group with P&I hospitalizations and mortality. They used data from the province of British-Columbia, Canada, over the 1998-1999 to 2003-2004 seasons. They found the 10-19 year-olds group to have the lowest rates of influenza medical visit, P&I hospitalization, and P&I mortality. Children aged <2 years and adults aged ≥65 years had the highest hospitalization rate, followed by children aged 2-4 years. Children aged <6 months and adults aged ≥65 years had the highest mortality rate. They assessed the timeliness of the peak of influenza medical visits per age group with respect to population-wide P&I hospitalizations. They found peak in visits for the 5-9 and 10-19 year-olds to occur earliest (5.3 days before hospitalizations), followed by those aged 2-4 years (3.5 days), 6-24 months, 20-49 years and 50-64 years (1.8 days), <6 months (0 days) and ≥65 years (-1.8 days). Using a regression model with Poisson distribution, they found no significant difference between age groups in their predictive ability (percent deviance explained) for signaling P&I hospitalizations and mortality.

Chan *et al*. (2011) used cross-correlation functions to assess the relationship between ILI visits, per age group and per setting (community-based or ED), with overall P&I hospitalizations, in the province of Québec, Canada, from 1998 to 2003. The highest correlation with P&I hospitalizations was for ED visits by ≥65 years-olds. The greatest lead time for peak correlation, where ED visits preceded hospitalizations, was for children aged 5-12 and 13-17 years in the ED (2 week lead time) and children aged 2-4, 5-12 and 13-17 years in community-based settings (2 week lead time). The earliest significant correlation occurred at 3 weeks for ED visits for the 5-12 year-olds and for community-based settings for the 2-4 and 13-17 year-olds. The peak correlation for ED visits for the <2, 2-4, 18-39, 40-64 and ≥65 year age groups occurred at a lag of 0; the earliest significant correlation varied between 1 and 2 weeks. In community-based setting, peak correlation occurred at 1 week before hospitalizations for the <2 and 18-39 year-olds, and at 0 week for the 40-64 and ≥65 year-olds; the earliest significant correlation was between 1 and 2 weeks. The age group with the greatest lead time differed from year to year, being most often the 2-4, 5-12 and 13-17 year age groups.

Brownstein *et al*. (2005) studied timeliness of visits with respiratory illness syndrome from different age groups and their predictive value for P&I mortality. They used visits at 4 emergency departments (pediatric, adult ED, community ED, and general ED), one ambulatory care setting, and sentinel ILI visits for Massachusetts, over 2 to 4 years depending on the setting, and assessed those counts against overall P&I mortality in New England between 2000 and 2004. Using cross-spectral analysis, they found visits by the 3-4 year-olds to have the greatest lead time (34.0 days, 95% CI 14.5-53.5), followed by the <3 and 11-17 year-olds (27.5 days, 95% CI 13.6-41.3 and 22.2-32.8 respectively) and the 5-10 year-olds (23.0 days, 95% CI 2.9-43). Children aged < 3 years had the best predictive value for overall P&I mortality, explaining on average 40.8% of the deviance (95% CI 20.1-61.5), followed by children aged 3-4 years, explaining 36.8% of the deviance (95% CI 14.4-56.1), although 95% confidence intervals overlapped.

2.3.3. Triage category-stratified ILI ED visits

Triage systems are used in the ED to prioritize patients based on the urgency of their condition. The Canadian Triage and Acuity Scale (CTAS) is used throughout Canada (Christ *et al.* 2010). CTAS scores were found to be predictive of individual patient outcomes, such as admission, length of stay, resource utilization, and mortality (Dong *et al.* 2007; Jimenez *et al.* 2003).

Information on triage category is being used by some public health practitioners for the purpose of enhancing syndromic surveillance systems. For instance, in New-South-Wales, they include sub-analyses by age, sex, triage category, and discharge status in their daily reports (Zheng *et al.* 2007). However, the added value of such sub-analyses has not been reported. Similarly, the Kingston, Frontenac and Lennox & Addington (KFL&A) Public Health jurisdiction (Ontario, Canada) used CTAS as part of their pilot syndromic surveillance system. They found it generally useful to monitor for unusual severity of illness; however, specifics on how it was useful (for instance how it may influence decision making) has not been reported (Moore *et al.* 2008).

The review of the literature has not revealed any study validating or evaluating the use of triage category information for enhancing surveillance of influenza.

2.3.4. Disposition-stratified ILI ED visits

Following an ED medical encounter, patients may be discharged home, admitted to the hospital, transferred to another facility, or die. No study was identified that explicitly stratified patients according to disposition; however, a few studies focused on patients admitted from the ED. Among those, none strictly fulfilled the initial inclusion criteria for this review, that is, studies that evaluate the association between ILI ED visits (measured with chief complaint or diagnosis, with stratification by disposition) and influenza-related hospitalizations or mortality. Therefore, inclusion criteria were loosened to allow studies looking at any respiratory syndrome and studies using virological data as a gold standard.

The review of literature identified two studies that tested the use of admission data (a combination of ED syndromic and diagnositic data, and disposition data) to monitor for influenza or respiratory related hospitalization (Berenbaum *et al.* 2007; Townes *et al.* 2004). Both studies used hospital discharge diagnosis as a "gold standard". One study tested admission data against virological data in an ecological design (Murray 2008). The rationale behind using ED disposition/admission data for surveillance, as opposed to hospital discharge data, is that there can be an important reporting lags for the latter (Berenbaum *et al.* 2007; Murray 2008).

Townes *et al*. (2004) describe the ED information system used for surveillance by the Oregon Department of Human services, in which they use discharge disposition as a variable of "severity of illness". Among variables of "severity of illness" (blood pressure, temperature, pulse, respiratory rate, oximetry, disposition and type of ward), disposition was the only one that was always recorded. They compared ED discharge disposition data with hospital discharge data considered as a "gold standard". Over the year of 2001, ED visits with an admission diagnosis of pneumonia were 62% sensitive and 98% specific for hospitalizations with a discharge diagnosis of pneumonia; the PPV was 59%.

Berenbaum *et al*. (2007) used a combination of ED and disposition data to evaluate a potential source of prospective surveillance of influenza-related hospitalizations. Using admission and discharge records from a large tertiary hospital in Vermont, from 2003-2006, they evaluated a "respiratory category" of inpatients and a category comprised of P&I admission diagnoses, against a gold standard of hospitalizations with a discharge diagnosis of P&I. They defined the "respiratory category" of inpatients as those with one or more respiratory signs, symptoms, or diagnoses in the chief complaint, impression diagnosis or admission diagnosis. The respiratory category had a sensitivity, specificity and PPV of 55.6%, 94.7%, and 41% for hospitalizations with P&I diagnosis. P&I admissions had a sensitivity, specificity and PPV of 40.1%, 98.9% and 71% for hospitalizations with P&I diagnosis.

Murray *et al*. (2008) used ED disposition data to compare ILI admissions with ED and virological data, for 14 EDs in NYC from 2007-2008. They found ILI hospitalizations to be well correlated with influenza isolates (ρ=0.76) and with all ILI visits (ρ=0.89).

No study has been identified that evaluates the predictive value of disposition data for influenza-related hospitalizations on a population basis – in particular, its added value over the use of all visits with ILI/respiratory chief complaints or diagnoses for prediction of hospitalization counts with varying lead times.

2.4. Methodological considerations

To evaluate the association between counts of ILI ED visits (overall or stratified) and counts of influenza-related hospitalizations or mortality, studies identified in this review have looked at 1) timeliness, 2) strength of association, or 3) predictive value, and have used a variety of methods. To look at timeliness of association, without a measure of strength of association, the relative timeliness of peaks of counts has been used (Sebastian *et al.* 2008). To assess timeliness of epidemic detection, the Serfling method has been used to generate signals, with sensitivity, specificity and predictive values as measures of performance (Olson *et al.* 2007; Tsui *et al.* 2001). Others have used cross-spectral analysis as a more complex approach to timeliness (Brownstein *et al.* 2005). Cross-correlations of time series have been used to obtain a measure of both timeliness and strength of association: either cross-correlations of the original time series (Olson *et al.* 2007; Tsui *et al.* 2001) or cross-correlation of residuals after applying an autoregressive integrated moving average (ARIMA) model to each time series (Chan *et al.* 2011). To obtain a measure of predictive value, Poisson regression has been used to obtain percent deviance explained (Brownstein *et al.* 2005; Sebastian *et al.* 2008). In the statistics literature, a popular approach to assess the predictive value of models is to use the Akaike Information Criterion (AIC) (Shmueli 2010), although this approach has not been used in the influenza surveillance studies identified in this literature review.

In this work, we are interested in using a modeling approach to evaluate the association between counts of ILI ED visits (overall or stratified) and counts of influenza-related hospitalizations. The following section highlights elements to consider in choosing the specific approach to time-series modeling.

2.4.1. Time-series modeling

The two most common approaches to time-series modeling are regression approaches using generalized linear models (GLMs), and ARIMA models (Tsui *et al.* 2008; Zeger *et al.* 2006). Both have been used to model influenza-related hospitalizations, as described in sections 2.2 and 2.3; they have also been used to model other time-series relevant to influenza surveillance, including virological counts and counts of respiratory or ILI syndrome (Bourgeois *et al.* 2006; Olson *et al.* 2007; Schindeler *et al.* 2009; Soebiyanto *et al.* 2010; van den Wijngaard *et al.* 2008; Zheng *et al.* 2007). Among GLMs, the specific model used has varied, including linear regression (Nicholson 1996; Olson *et al.* 2007; van den Wijngaard *et al.* 2008), Poisson and quasi-Poisson regression (Bourgeois *et al.* 2006; Hardelid *et al.* 2012; Mangtani *et al.* 2006; Schindeler *et al.* 2009; Thompson *et al.* 2004; Wong *et al.* 2006; Zheng *et al.* 2007), and negative binomial regression (Hardelid *et al.* 2012; Zhou *et al.* 2012).

The reason for using time-series methods is that data composed of repeated observations of a rate violate an important assumption of standard regression, namely, that observations should be independent. In a time-series, we expect that observations close to each other in time would be correlated, because of a number of measurable and non-measureable factors that tend to not change rapidly. Ignoring this autocorrelation while using standard regression would lead to biased error estimates (Zeger *et al.* 2006). ARIMA models are designed to model this autocorrelation. GMLs may also be used, but autocorrelation needs to be taken into account. An approach that has been taken is to first model secular trends and seasonal variation, as a way to model away long-term trends and associations, as well as account for autocorrelation. The residuals are then tested for autocorrelation (van den Wijngaard *et al.* 2008; Zheng *et al.* 2007). If autocorrelation remains, it is taken into account by including previous counts of the dependent variable in the model, as predictors of current counts. (Bourgeois *et al.* 2006; Mangtani *et al.* 2006; Schindeler *et al.* 2009; Wong *et al.* 2006)

Secular trends have been modeled using year indicators (Mangtani *et al.* 2006; Nicholson 1996), polynomial functions of various degrees (Hardelid *et al.* 2012; Nicholson 1996; Olson *et al.* 2007; Thompson *et al.* 2004; Wong *et al.* 2006; Zhou *et al.* 2012), or spline functions (Schindeler *et al.* 2009; Zheng *et al.* 2007). Seasonal variation has been modeled with month or time period indicators (Bourgeois *et al.* 2006; Mangtani *et al.* 2006; Nicholson 1996), sinusoidal terms with various number of harmonics (Olson *et al.* 2007; Thompson *et al.* 2004; van den Wijngaard *et al.* 2008; Wong *et al.* 2006; Zhou *et al.* 2012), or spline functions (Hardelid *et al.* 2012; Schindeler *et al.* 2009; Zheng *et al.* 2007). If using an ARIMA framework, seasonal ARIMA (SARIMA) models allow modeling of seasonal variation (Suhartono 2011).

Another consideration in time-series modeling is that there may be a time lag between the predictor variable (for instance, laboratory counts or syndromic surveillance counts) and the outcome of interest (for instance, hospitalizations and mortality). Most studies approached this issue by testing the inclusion of the predictor variable(s) at several lags (Hardelid *et al.* 2012; Mangtani *et al.* 2006; Schindeler *et al.* 2009; van den Wijngaard *et al.* 2008; Wong *et al.* 2006; Zhou *et al.* 2012).

Finally, especially for daily time series, day-of-week effect and holiday effect (where counts of the outcome variable are expected to differ) are taken into account using indicator variables (Mangtani *et al.* 2006; Zheng *et al.* 2007).

An advantage of GLMs over ARIMA models is that their interpretation can be more intuitive for health researchers. They may be favored, for instance, by public health professionals who use research results to guide their practice. Among GLMs, a Poisson regression model was found to provide good estimates of virologically confirmed influenza-related hospitalizations (Yang *et al.* 2011). Negative binomial regression is a generalized form of Poisson regression that accounts for overdispersion of data by introducing a mean parameter that has a gamma distribution; comparison of negative binomial and Poisson models have yielded inconsistent results (Gilca *et al.* 2009; Yang *et al.* 2011).

2.5. Gaps in knowledge and specific objective

The review of studies evaluating the association between ILI ED visits (overall or stratified by age, triage score, or disposition) and counts of severe influenza cases (including influenza-related hospitalizations) has identified very few studies. Studies with overall ILI ED visits and ILI ED visits stratified by age have focused mainly on timeliness, and little on predictive value. Studies using disposition data were mainly concerned with using admission diagnosis as a surveillance indicator of hospitalizations with a discharge diagnosis of interest. No study was identified that looked at triage score. To address these gaps, the **specific objective** of this study is:

Using a regression approach, to evaluate whether stratification of ILI ED visits by age, triage score, and disposition contributes to improved predictive models for overall counts of influenza-related hospitalizations.

Chapter 3: Methodology

3.1. Study setting

The study setting and databases were described in the introductory chapter of this work. The data sources used and their characteristics are summarized in Table 3-I.

3.1.1. Regional Emergency Departments Warehouse (*Entrepôt Régional des Urgences - ERU*)

The *ERU* database was used to derive counts of ED visits with ILI. At the time of this work, there were 8 non-psychiatric EDs contributing to the database: 1 pediatric ED, 4 general EDs seeing both adults and children, and 3 adult tertiary centers, covering approximately 41 percent of all non-psychiatric ED visits in the Montreal region. Dates of entry into the database varied, as indicated in Table 3-II. Date of entry was defined as the date where the ED started recording chief complaints into the *ERU* database consistently.

To derive counts of ILI, chief complaints were chosen over diagnoses since, because of the structure of the system, they appeared to be richer in information and were more rapidly available. In the *ERU* system, triage nurses select chief complaints for each visit using a drop-down menu. One or more codes may be selected for each visit. Each code may describe one or more symptoms, and may provide context (for instance, “immunosuppressed”, or “recent surgery”).

The *ERU* database was also used to derive information on age, triage score, and disposition. The triage urgency for each visit is recorded in the database using the Canadian Triage and Acuity Scale (CTAS). The CTAS categories are 1 (Resuscitation – needs immediate care), 2 (Emergent, - needs physician assessment within 15 minutes), 3 (Urgent – 30 minutes), 4 (Semi-urgent – 1 hour), and 5 (Non-urgent – 2 hours).

Table 3-I. Comparison of data sources

Data source	Description	Data	Coverage	Access by the Public Health Department
Regional Emergency Departments Warehouse (*Entrepôt Régional des Urgences* - *ERU*)	Database containing electronic records for every ED visit in participating hospitals	Visit/patient level information (demographic, clinical, and administrative)	Participating hospitals: variable coverage over time, up to 41% of non-psychiatric ED visits	Direct access to the database; database updated daily
Daily Report on Emergency Department and Hospital Situation (*Relevé quotidien de la situation à l'urgence et au centre hospitalier – RQSUCH*)	Established system of reporting pre-determined health indicators relevant for surveillance, by EDs/hospitals to the public health department	Manual counts only (e.g. number of ED visits, number of ED visits with ILI)	All acute care hospitals in Montreal	Daily reports
Hospitalization registry *Med-écho*	Electronic records for every hospitalization in the province of Québec	Hospitalization level information (demographic, clinical – including ICD 9 or 10 diagnoses – and administrative)	All acute care hospital in the province of Quebec	Access after approximately 1 year delay

3.1.2. Daily Report on Emergency Department and Hospital Situation (*Relevé quotidien de la situation à l'urgence et au centre hospitalier – RQSUCH*)

The daily counts of ED ILI visits from *RQSUCH* were used as a comparator for counts obtained using *ERU*, to assist in choosing an *ERU*-based ILI syndrome definition. Each hospital in the Montreal region is required to report the number of patients registering to the ED who present with ILI, defined as fever and cough, and those are the counts transmitted to the DSP. However, the way the definition is applied, by whom (healthcare professional or support staff), and from which source, is left to the discretion of each ED. This system has been in operation since May 2008, with nearly 100% coverage of acute care hospitals at the start, and 100% coverage since May 2009.

Table 3-II. Date of entry into *ERU* and *RQSUCH* systems, per ED

Emergency department	Date of entry in *ERU*/chief complaint available	Starting date of reporting ILI visits through RQSUCH
Pediatric	2009-09-21	2008-05-01
General 1	2006-04-01	2008-05-07
General 2	2006-04-01	2008-05-01
General 3	2009-05-11	2009-05-01
General 4	2007-04-01	2008-05-01
Tertiary 1	2006-06-24	2008-05-01
Tertiary 2	2006-06-24	2008-05-01
Tertiary 3	2006-06-24	2008-05-01

3.1.3. *Med-Écho* hospitalization registry

Hospitalization data from *Med-Écho* were used to address the main objective of the study. Data were available for hospitalizations in Québec with a discharge date up to March 31, 2011. However, diagnosis data were missing for hospitalizations with admission date before this date, but discharged later. Using the data set from April 1, 2006 to March 31, 2011, restricted to P&I hospitalizations in the study hospitals, it was estimated that 82.3% of hospitalizations have a length of stay of less than 1 month, and 94.3% have a length of stay of less than 2 months. Consequently, data were considered to be nearly complete for hospitalizations with admission dates up to January 31, 2011.

3.1.4. Study period

The full study period was from April 1, 2006 to November 14, 2011. Some analyses use a shorter study period, due to unavailability of data. Analyses involving *RQSUCH* data use the period from May 7, 2008 to November 14, 2011. Modeling of influenza-related hospitalizations – to address the main objective of this work – uses the period from June 25, 2006 to January 29, 2011.

3.2. ED ILI-visits: choice of syndrome definitions

Because the review of the literature did not identify a unique, universally accepted syndrome definition for ILI, a preliminary part of this work was to choose and test an ILI syndrome definition adapted to the data.

There were 3 steps in choosing and testing an ILI syndrome definition:

1. Choosing initial definitions based on the literature, and adapting them to the structure of the data.
2. Testing each syndrome definition, in terms of the proportion of ED visits captured, and in terms of the seasonal variation of the time-series produced.
3. Comparing the counts of ILI visits obtained with each syndrome definition, with the counts of ILI reported by each ED via *RQSUCH*.

The objective was to provide a basic assessment of whether syndrome definitions derived from the literature can be adapted to the *ERU* system, and whether one can be readily chosen for use in the following steps of this work.

3.2.1. Choosing and adapting definitions

Two definitions were chosen to reflect the WHO and CDC definition of ILI (Center for Disease Control and Prevention 2011; World Health Organization 2006), and to be comparable to definitions described in the literature. A specific ILI syndrome (ILI-Sp) was defined as:

ILI-Sp = (fever + cough) OR (fever + sore throat) OR influenza-related keyword,

identical to New-York City's narrow definition (Olson *et al.* 2007) and very similar to Boston's narrow definition (Pendarvis *et al.* 2007). A sensitive syndrome (ILI-Se) was defined as:

ILI-Se = fever OR cough OR sore throat OR influenza-related keyword,

also very similar to Boston's wide definition (Pendarvis *et al.* 2007).

For each hospital, the chief complaint drop down menu labels were searched for keywords indicating the presence of symptoms included in these definitions. An initial keyword set was generated, loosely based on a set of synonyms and related concepts for each symptom previously suggested (Chapman *et al.* 2010). In addition, the labels of the codes under the headings "respiratory", "general", "pediatrics", "infection", "ear-nose-throat", "pandemic", and "special" were all examined to look for codes missed with the initial keyword set. This search allowed identifying abbreviations that would otherwise have been missed. Table 3-III presents the keywords included in the symptom definitions.

"Chills" and "dysphagia" (difficulty swallowing) were included as proxies for "fever" and "sore throat". Of note, "dysphagia" appeared to be often misused as "pain on swallowing" or "sore throat", as evidenced by the code label "dysphagia without difficulty swallowing" and the fact that some hospitals use codes labelled "dysphagia" under the heading of "flu-like illness", without the presence of a "sore throat" code. Dysphagia-labelled codes under the headings of "abdomen/digestive system" and "allergy/allergic reaction" were not included. The labels resulting from the keyword search were all examined to eliminate those that expressed negation of a symptom, generating a final code set.

Table 3-III. Keywords for ILI syndrome definitions

Symptom/concept	Keywords used (in French in the system)
Fever	fever (*fièvre*), hyperthermia (*hyperthermie*), temperature (*température*), chills (*frissons*), febrile (*fébrile*), *T > 38*
Cough	cough (*toux*), coughs (*tousse*)
Sore throat	dysphagia (*dysphagie*), sore/pain + throat (*mal /douleur* + *gorge*)
Influenza	Influenza, flu (*grippe*), flu-like (*grippal, grippale*), ILI (*S.A.G.* - *syndrome d'allure grippale*)

3.2.2. Testing definitions using the *ERU* data

For this section of the work, all available data were used from April 1, 2006 to November 14, 2011. Analyses involving *RQSUCH* data used the period from May 7, 2008 to November 14, 2011.

<u>Descriptive statistics: ED visits and system utilisation</u>

Daily counts of ED visits were obtained using the *ERU* database. The daily percentage of visits with a chief complaint recorded, and the number of chief complaint codes per visit (among those with at least one chief complaint recorded) were also obtained. Averages were computed, overall and stratified by ED and by year. Counts of ED visits reported by *RQSUCH* were also obtained for each ED and compared to the *ERU* data, in terms of percent agreement.

Descriptive statistics and time-series: ILI

Using the chief complaint, daily counts of visits meeting each definition (ILI-Sp or ILI-Se) were obtained for each of the 8 participating hospitals. The proportion of ILI visits was defined as the ratio of ILI visits to all ED visits with non-missing chief complaint. When graphing time series, ratios were used, as opposed to absolute counts, to 1) control for the upward trend in ED visits due to addition of hospitals, and to 2) isolate the seasonal variability due to influenza and influenza-like illnesses and control for effects such as changes in utilization during holidays. To facilitate identification of longer-term trends, the data were smoothed using lowess smoothing, where each data point is replaced by a value obtained from locally weighted regression. Local weighting was done using Cleveland's (1979) tricube weighting function, with a bandwidth of 7 days. A smoothed time series of the proportion of ILI visits was graphed for each syndrome definition, for each ED as well as for all visits.

ILI counts reported via *RQSUCH* were considered as another measure of ILI ED visits, referred to as ILI-R. ILI-R might not be a gold standard for ILI visits (it has not been validated as such), but it is the only readily available external measure against which to compare counts obtained via *ERU*. Although they are available for all hospital EDs in the Montreal region, *RQSUCH* ILI-R counts were obtained for the hospitals participating to the *ERU* database, in order to allow for comparison with the *ERU* counts. For the *RQSUCH* data, ratios of ILI ED visits were computed using all ED visits also reported via *RQSUCH* as the denominator. Proportion of ILI visits and times series obtained with the *ERU* data were compared to those obtained with ILI-R from *RQSUCH*.

Correlations with ILI-R

Correlations were estimated between counts of ILI-Sp, ILI-Se, and ILI-R across all EDs and by ED. Pearson’s correlations were calculated at the aggregate level. A non-parametric method (Spearman’s *rho*) was chosen at the ED level due to low counts and non-normal distributions – Spearman’s *rho* was also obtained at the aggregate level to allow for comparison of coefficients. In addition, ILI syndromes were further decomposed into their components (“fever”, “cough”, “sore throat”, “fever + cough”, “fever + sore throat” ”, and “influenza keyword”), and these components were correlated with ILI-R for each ED.

Outliers

Both *ERU* and *RQSUCH* data were examined for outliers, prior to analyses. However, because of the expected important seasonal variation, and because of the large number of data points, quantitative cut offs (such as, for example, greater than 3 standard deviations away from the mean) were not used.

For total ED visits, scatter plots were created comparing *ERU* and *RQSUCH* data. Points that clearly did not agree between the two sources (expected to be a straight line) were identified as outliers. Whether the *ERU* or *RQSUCH* value was more likely to be aberrant was determined by examining their respective univariate distributions. For ILI-Sp, ILI-Se, and ILI-R visits, outliers were identified on the univariate distributions.

Outliers were removed for the analyses above, because they were thought to be the result of erroneous data entry, and because they can have a large effect on averages and moving averages. In a manual surveillance system such as *RQSUCH*, aberrant data are quickly identified as such, and the reason (often erroneous data entry) quickly determined; the data are then usually corrected.

3.3. Value of age, triage score, and disposition data for predicting influenza-related hospitalizations

3.3.1. Study period

For this part of the study, the data used spanned from June 25, 2006 to January 29, 2011. For analyses purposes, the H1N1 pandemic year was defined as the 52 weeks between April 12, 2009 to April 10, 2010. This period was thus defined to cover both H1N1 waves (Helferty *et al.* 2010), to be of exactly one year duration, and to correspond to the CDC and Canadian surveillance weeks (week 15 2009 to week 14 2010 inclusively) (Center for Disease Control and Prevention 2011; Public Health Agency of Canada 2012). Separate analyses were run for the non-pandemic and pandemic periods, because the pandemic year did not exhibit the usual influenza seasonality.

For this study period, complete data were available for 5 hospitals (2 general and 3 tertiary centers) providing an approximate coverage of 28% of the ED visits in non-psychiatric, non-pediatric hospitals of the Montreal region. Other hospitals were excluded because they had missing data for a significant portion of the study period.

The unit of analysis was chosen to be the week, rather than the day, because of the low daily counts of the dependent variable (P&I hospitalizations).

3.3.2. ILI visits

Weekly ILI counts were obtained from the *ERU* database using both ILI-Sp and ILI-Se as defined above, based on date of ED registration, and aggregated over the 5 hospitals with complete data. In the manuscript (chapter 4), ILI-Sp is referred to as ILI, and ILI-Se is mentioned only in the sensitivity analysis.

Subgroups presenting to ED with ILI were defined based on age, triage category, and disposition status. Categorization was made to allow for a sufficient number of ILI visits in each group. For age, visits were categorized into <18, 18-64 and ≥65 year-olds groups. A "severe" triage category was defined as triage scores of 1 to 3. For disposition categories, "admission", "transfer (to another facility)" or "death" were grouped together into a "severe" disposition category. For ILI counts based on disposition, the counts were based on the date of discharge from the ED (as opposed to the date of registration).

3.3.3. Influenza-related hospitalizations

Hospitalization data for the 5 hospitals in the study were obtained from the *Med-Écho* registry. Influenza-related hospitalizations were defined as hospitalizations with a primary or secondary diagnosis of pneumonia and influenza

(P&I) (ICD10 J09-J18). This measure was chosen to allow for comparisons with other studies. Weekly counts were tabulated, based on date of admission.

3.3.4. Statistical model

Weekly counts of P&I hospitalizations were modeled using negative binomial regression. A GLM approach was chosen over an ARIMA approach, because the interpretation of the results, expressed in terms of incidence rate ratios, is more intuitive. Negative binomial models, which account for overdispersion of data, have been used before to model influenza-related outcomes (Gilca *et al.* 2009; Hardelid *et al.* 2012; Yang *et al.* 2011; Zhou *et al.* 2012).

Secular trends were modeled with polynomial terms and seasonal trends with sine and cosine terms, an approach that has been used by others (Hardelid *et al.* 2012; Nicholson 1996; Olson *et al.* 2007; Thompson *et al.* 2004; Wong *et al.* 2006; Zhou *et al.* 2012). The number of polynomial terms and harmonics were chosen based on the Akaike Information Criterion (AIC), which takes into account both goodness of fit and parsimony, a lower AIC suggesting a better predictive model (Bozdogan 1987). The AIC was chosen over the Baysian Information Criterion (BIC), since some authors favor the use of the AIC to assess predictive accuracy and the use of the BIC to assess the goodness of fit of explanatory models (Shmueli 2010).

After modeling secular and seasonal trends, the presence or absence of residual auto-correlation was verified. P&I hospitalizations counts from previous weeks were included as independent variables, when necessary, to eliminate this residual auto-correlation.

This baseline model was fitted separately for non-pandemic and pandemic years. Weekly ILI-Sp counts were added to the baseline model, testing lead times of up to 5 weeks (ILI ED visits occurring before the P&I hospitalization count date). Weekly counts for all ED visits were also included as a potential predictor of hospitalizations and confounder of the effect of interest, with lead times corresponding to those for ILI-Sp. The analyses were repeated using ILI-Se instead of ILI-Sp.

Total ILI counts were replaced by counts from subgroups presenting to ED with ILI, defined based on age, triage category, and disposition status. The informative potential of models was compared using the AIC. In all models, the dependent variable remained the overall weekly counts of P&I hospitalizations.

Statistical analyses were done using STATA 10 (StataCorp LP, College Station, Texas). The study was approved by the Research Ethics Committee of the Montreal Regional Health and Social Services Agency.

Chapter 4: The potential utility of age, triage score, and disposition data to improve emergency department-based surveillance of influenza-like illness in Montréal, Canada: a time series analysis from 2006 to 2011

This manuscript addresses the main objective of this work, namely, to evaluate the potential utility of age, triage scores, and disposition data for enhanced monitoring of the burden of severe influenza cases, using the *ERU* database available for syndromic surveillance, and using influenza-related hospitalizations as a measure of the burden of severe influenza cases.

As a main author, I planned the study, performed all analyses, interpreted the results, and wrote the manuscript. At each step, my supervisor, David Buckeridge, and my co-supervisors, Robert Allard and Lucie Bédard, provided comments and suggestions. They also critically reviewed and commented the manuscript.

This manuscript is intended for the journal *Eurosurveillance*, and its form follows the journal requirements, except for the numbering system for sections, tables, and figures that follow the structure of this thesis. The supplementary material is not intended for the journal, but is included here as it provides the results of the sensitivity analysis mentioned in the manuscript, the numerical data presented as figures in the manuscript, and the raw outputs from the regression models.

The results of the descriptive statistics and analyses that were involved in choosing a syndrome definition are presented in Chapter 5: Additional results.

The potential utility of age, triage score, and disposition data to improve emergency department-based surveillance of influenza-like illness in Montréal, Canada: a time series analysis from 2006 to 2011

Noémie Savard MD,[1*] Lucie Bédard MSc,[1,2] Robert Allard MD MSc FRCPC,[2,3] David L. Buckeridge MD PhD FRCPC[2,3]

[1] Department of Social and Preventive Medicine, University of Montréal, Montréal, Québec, Canada

[2] Direction de santé publique de Montréal, Montréal, Québec, Canada

[3] Department of biostatistics, epidemiology and occupational health, McGill University, Montréal, Canada

*Corresponding author

4.1. Abstract

Demographic data and markers of illness severity are increasingly captured in emergency department electronic systems, but their value for surveillance has not been evaluated. This study evaluates the potential value of age, triage score, and disposition data contained in emergency department electronic records for predicting counts of influenza-related hospitalizations. From June 25, 2006 to January 29, 2011, weekly counts of pneumonia and influenza hospitalizations in 5 participating hospitals of the Montreal region were modeled using negative binomial regression. Weekly counts of emergency department visits with influenza-like illness were included as the main predictor, correcting for secular trends, seasonality, and autocorrelation. Counts of overall influenza-like illness visits were then replaced by counts stratified by age, triage score, and disposition, and models were compared using Akaike's information criterion. Visits from the ≥65 year-olds in the non-pandemic years, visits from the <18 year-olds and those with high priority triage scores during the H1N1 pandemic year, and visits resulting in admission/transfer/death during both non-pandemic and H1NI periods, provided small improvement to predictive models for overall P&I hospitalizations, compared to overall influenza-like illness emergency department visits. Future directions should include prospective evaluation of the practical utility of these covariates in an influenza surveillance system.

KEYWORDS: Age; Disposition; Emergency department; Influenza; Surveillance, syndromic; Time series analysis; Triage score.

4.2. Background

Influenza remains a disease of public health importance due to the morbidity and mortality that result from annual epidemics and periodic pandemics [1]. This burden is partly preventable through vaccination and other control measures [1]. The application of influenza control measures relies upon information from surveillance systems, which can detect epidemics, monitor their evolution, and identify shifts in disease burden, virulence, or epidemiological characteristics. This information can guide decisions about infection control measures, such as the composition of vaccines, vaccination programs, and anti-viral drug policies [2].

In Montreal, Canada, syndromic surveillance is increasingly used as part of a strategy to monitor influenza. In this context, syndromic surveillance refers to the monitoring of health-related events or outcomes with an emphasis on little or no delay between the event and the availability of the data for analysis [3]. Reasons to conduct syndromic surveillance of influenza and influenza-like illness (ILI) include monitoring disease burden and detecting shifts in virulence [4]. This objective could be achieved, for example, by prospectively monitoring severe events due to influenza, such as influenza-related hospitalizations or mortality. However, hospitalization or mortality data are not always available to public health departments in a timely manner.

Another approach would be to monitor other influenza-related events that are predictive of hospitalization or morality burden. Emergency department (ED) visits with ILI are an example of such events commonly monitored in surveillance systems. However, due to factors such as accessibility and care seeking behavior, people present to an ED with a range of disease severity. This range of illness severity is however captured in electronic systems, for example, with standardized triage score and disposition information. It can be hypothesized that among those presenting to EDs with ILI, a subset of patients with more “severe” disease, as identified by triage score or disposition, could form a sentinel population for detecting and monitoring influenza epidemics with a high burden of severe disease. There has been little published on the utility of such markers of severity for disease surveillance purposes. A few studies suggest that a combination of ED clinical and disposition data could be used for estimation and real-time monitoring of influenza-related hospitalizations [5, 6]. As for triage score, although its use in surveillance systems has been reported, [7, 8], its value for surveillance has not been evaluated.

Demographic data, including age, are also captured routinely by ED electronic systems and are used for stratified analyses in surveillance systems. Although not directly a marker of disease severity, age-stratified analyses may enhance detection and monitoring of influenza epidemics with a high burden of severe disease. Children and young adults with ILI have been identified as a sentinel population heralding the occurrence of epidemics, as measured by virological isolates, influenza-related hospitalizations, or influenza-related mortality, although the exact age group providing the earliest lead time varied across studies or seasons [9-14]. ILI visits from the older adults [11] and the youngest children [12] were most strongly associated with overall influenza-related hospitalizations or mortality. The predictive value of age-stratified ILI visits has not, to our knowledge, been compared to the predictive value of visits stratified by other variables.

The objective of this study was to evaluate the potential utility of age, triage scores, and disposition data contained in ED electronic records, to enhance surveillance of severe influenza in the Montreal Health Region. Influenza-related hospitalizations were used as a marker of the burden of severe disease, and the data from ED systems were assessed in terms of their predictive value for hospitalizations.

4.3. Methods

Study setting

The Montreal Public Health Department, responsible for a population of 1.85 million, conducts routine influenza surveillance [15]. Data available for surveillance include detailed records of ED visits for a subset of the hospitals in Montreal, via the Regional Emergency Department Warehouse (*Entrepôt Régional des Urgences - ERU)*. This database contains records from each ED visit to a participating hospital, including chief complaint, age, triage category, and disposition. Hospitals transmit records once daily to the database, which the Public Health Department accesses for surveillance. Complete data were available for 5 hospitals, including 3 tertiary centers, covering approximately 28% of the ED visits to non-psychiatric, non-pediatric hospitals of the Montreal region.

The triage urgency for each visit is recorded in the database using the Canadian Triage and Acuity Scale (CTAS). CTAS is used throughout Canada [16]. It has been validated as a predictor of individual patient outcomes, including admission, length of stay, resource utilization, and mortality [17, 18]. The CTAS categories are 1 (Resuscitation – needs immediate care), 2 (Emergent - needs physician assessment within 15 minutes), 3 (Urgent – 30 minutes), 4 (Semi-urgent – 1 hour), and 5 (Non-urgent – 2 hours).

The Public Health Department also has access to detailed information on all hospitalizations in acute care hospitals in the province of Quebec, Canada, in a registry called *Med-echo*. However, these data are available with approximately a one-year delay after the date of discharge and are not suitable for real-time surveillance.

The study period spanned from June 25, 2006 to January 29, 2011. For analysis purposes, the H1N1 pandemic year was defined as the 52 weeks between April 12, 2009 to April 10, 2010, covering both H1N1 waves. This research was approved by the Research Ethics Committee of the Montreal Regional Health and Social Services Agency.

ILI ED visits

Weekly ILI counts were obtained from the Regional Emergency Departments Warehouse. Visits were classified using the chief complaint, which triage nurses select for each visit using a drop-down menu. One or more symptoms may be selected for each visit. A record was classified as an ILI syndrome if the chief complaint met the following condition: "(fever + cough) OR (fever + sore throat) OR influenza-related keyword". This definition was chosen to be consistent with the WHO and CDC definitions of ILI [19, 20], and to be comparable to what has been used elsewhere [9, 21]. Weekly counts were used, based on date of registration to the ED.

In sensitivity analyses, a more sensitive ILI definition was used. A record was classified as a sensitive ILI syndrome (ILI-Se) if the chief complaint met the following condition: "fever OR cough OR sore throat OR influenza-related keyword".

Influenza-related hospitalizations

Hospitalization data for the 5 hospitals in the study were obtained from the *Med-echo* registry. Influenza-related hospitalizations were defined as hospitalizations with a primary or secondary diagnosis of pneumonia and influenza (P&I) (International Classification of Disease 10th revision J09-J18). P&I hospitalizations have been used elsewhere to estimate influenza-related hospitalizations [5, 9-11, 22-24]. Weekly counts were tabulated, based on date of admission. For better data visualization, a lowess-smoothed time series was obtained, where each data point is replaced by a value obtained from locally weighted regression. Local weighting was done using Cleveland's tricube weighting function [25], with a bandwidth of 4 weeks.

Statistical model

Weekly counts of P&I hospitalizations were modeled using negative binomial regression. Negative binomial models, which account for overdispersion of data, have been used before to model influenza-related outcomes [26-29]. Secular trends were modeled with polynomial terms, and seasonal trends with sine and cosine terms. The number of polynomial terms and harmonics were chosen based on the Akaike information criterion (AIC), which takes into account both goodness of fit and parsimony, a lower AIC suggesting a better predictive model [30]. P&I hospitalization counts from previous weeks were included as independent variables, when necessary, to eliminate residual auto-correlation. This baseline model was fit separately for non-pandemic and pandemic years, because the pandemic year did not exhibit the usual influenza seasonality.

Weekly ILI counts were added to the baseline model, testing lead times up to 5 weeks (ILI ED visits occurring before the P&I hospitalization count date). Weekly counts for all ED visits were also included as a potential predictor and confounder, with lead times corresponding to those for ILI counts.

Total ILI counts were then replaced by counts from subgroups presenting to the ED with ILI, defined based on age, triage category, and disposition status. Age groups tested were <18, 18-64 and ≥65 year-olds. The triage scores were grouped into a "severe" (scores 1 to 3) and "non-severe" (4 and 5) categories. For disposition categories, "admission", "transfer (to another facility)" or "death" were grouped together into a "severe" disposition category. For ILI counts based on disposition, the counts were based on the date of discharge from the ED (as opposed to the date of registration). The informative potential of models was compared using the AIC. In all models, the dependent variable remained the overall weekly counts of P&I hospitalizations.

Statistical analyses were done using STATA 10 (StataCorp LP, College Station, Texas).

4.4. Results

There were on average 3634 ED visits per week over the study period. 98% of visits had a chief complaint recorded. 2.1% and 3.5% of these ED visits met the ILI definition during the non-pandemic and the H1N1 periods, respectively. The mean weekly counts of P&I hospitalizations were 39.9 during the non-H1N1 period and 43.3 during the H1N1 period.

Table 4-I shows the distribution of visits by age group, triage category, and disposition, in non-pandemic and pandemic years. There was an important

increase in ILI visits during the H1N1 period for almost all subgroups. Figure 4-1 illustrates the time series of ED visits with ILI and P&I hospitalizations. ILI visits, and to a lesser extent P&I hospitalizations, display clear seasonal variation, in addition to peaks corresponding to each H1N1 wave.

Table 4-I. Mean number of weekly influenza-like illness emergency department visits according to visit characteristics, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

	Weekly mean (95% confidence interval)	
	Non-pandemic period (N=188)	Pandemic year[a] (N=52)
Age (years)		
<18	16 (14-17)	27 (21-33)
18-64	49 (46-53)	86 (72-99)
≥65	10 (9-11)	13 (12-15)
Triage score		
1- Resuscitation	0.1 (0.0-0.1)	0.1 (0.0-0.2)
2- Emergent	3.0 (2.7-3.3)	4.9 (3.8-6.0)
3- Urgent	25 (23-27)	38 (31-44)
4- Semi-urgent	39 (36-42)	71 (60-83)
5- Non-urgent	8.1 (7.5-8.7)	12 (10.2-14.3)
Disposition		
Home/residence	71 (67-76)	121 (102-139)
Admission	3.3 (2.9-3.6)	4.8 (3.8-5.7)
Transfer	0.4 (0.3-0.5)	0.7 (0.4-1.0)
Death	0.02 (0.00-0.04)	0.00 (0.00-0.00)
Total	75 (70-80)	126 (106-146)

[a]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

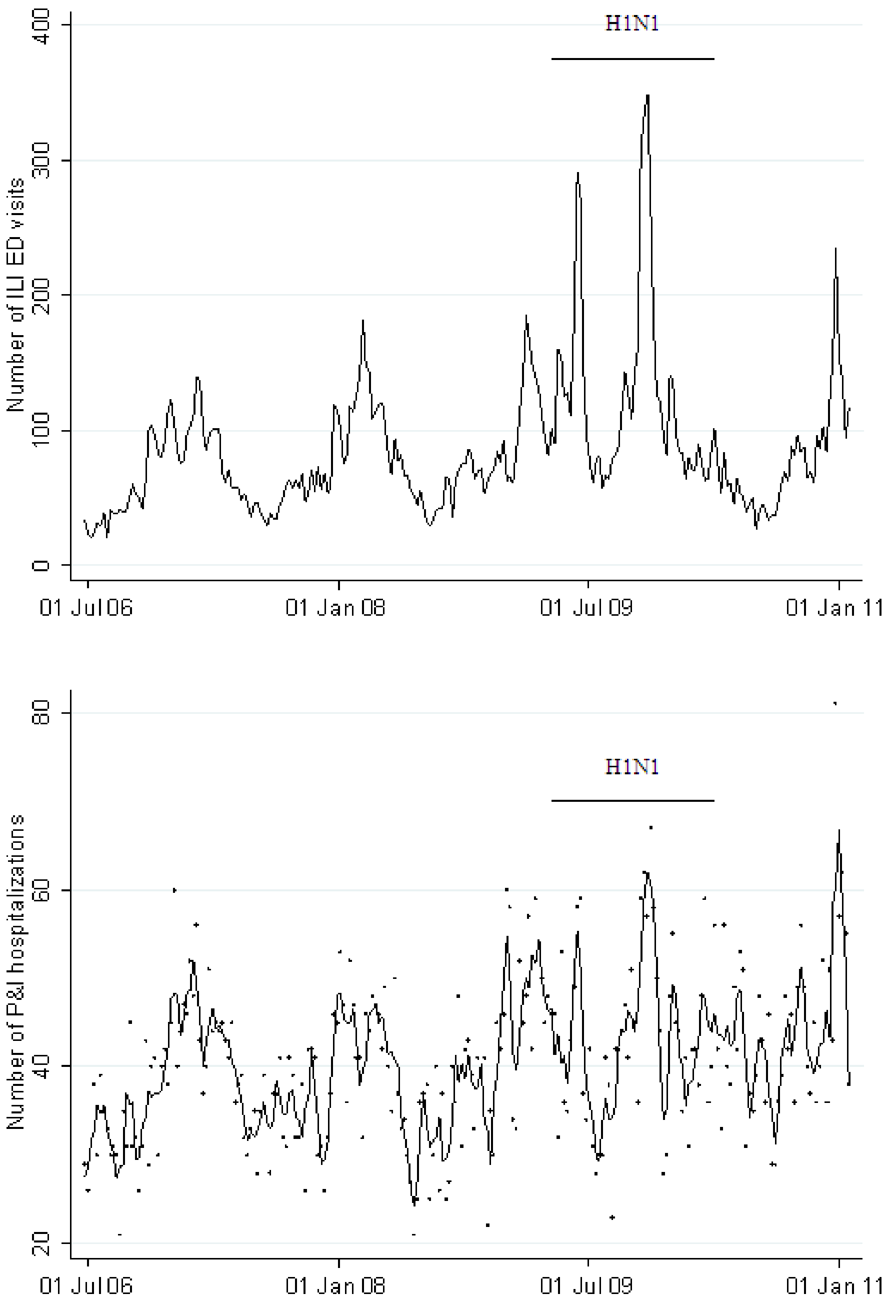

Figure 4-1: Weekly emergency department (ED) visits with influenza-like illness (ILI) and pneumonia and influenza (P&I) hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011
Upper pane: weekly ILI ED visits. Lower pane: weekly P&I hospitalization counts (dots) and lowess-smoothed trend (line).

The model included linear and quadratic terms and sine-cosine terms up to the second harmonic. Residual autocorrelation remained at 4 weeks, thus P&I hospitalizations counts from the 4 previous weeks were included in the model. The baseline model was as follows:

$$\text{Log } Y_i = ß_0 + ß_1(t) + ß_2(t^2) + ß_3\sin 2\pi t/(52.18) + ß_4\cos 2\pi t/(52.18) + ß_5\sin 4\pi t/(52.18) + ß_6\cos 4\pi t/(52.18) + ß_7 Y_{i-1} + ß_8 Y_{i-2} + ß_9 Y_{i-3} + ß_{10} Y_{i-4}$$

where Y_i is the number of P&I hospitalizations at week i, t is the time elapsed in weeks from a time t_0 arbitrarily set at the beginning of the study period, and 52.18 represents the average number of weeks per year. Figure 4-2 illustrates the baseline model fit, graphed against the lowess-smoothed time-series of P&I hospitalizations for better visualization.

Table 4-II presents incidence risk ratios (IRR) of overall P&I hospitalizations for each standard deviation (SD) increase in ILI ED visits, overall and according to age, triage score, or disposition. During the non-pandemic period, there was a positive association between overall ILI ED visits and P&I hospitalizations occurring the same week (lead time 0), with each SD increase in ILI visits (35 visits) being associated with a 4.5% increase in P&I hospitalizations (95% CI 0.3%-8.8%). During the H1N1 period, the associations between ILI and P&I hospitalizations were positive with lead times from 0 to 3 weeks, with a peak association at 1 week, where each SD increase in ILI visits (73 visits) was associated with a 15.2% (95% CI 5.4%-25.9%) increase in P&I hospitalizations.

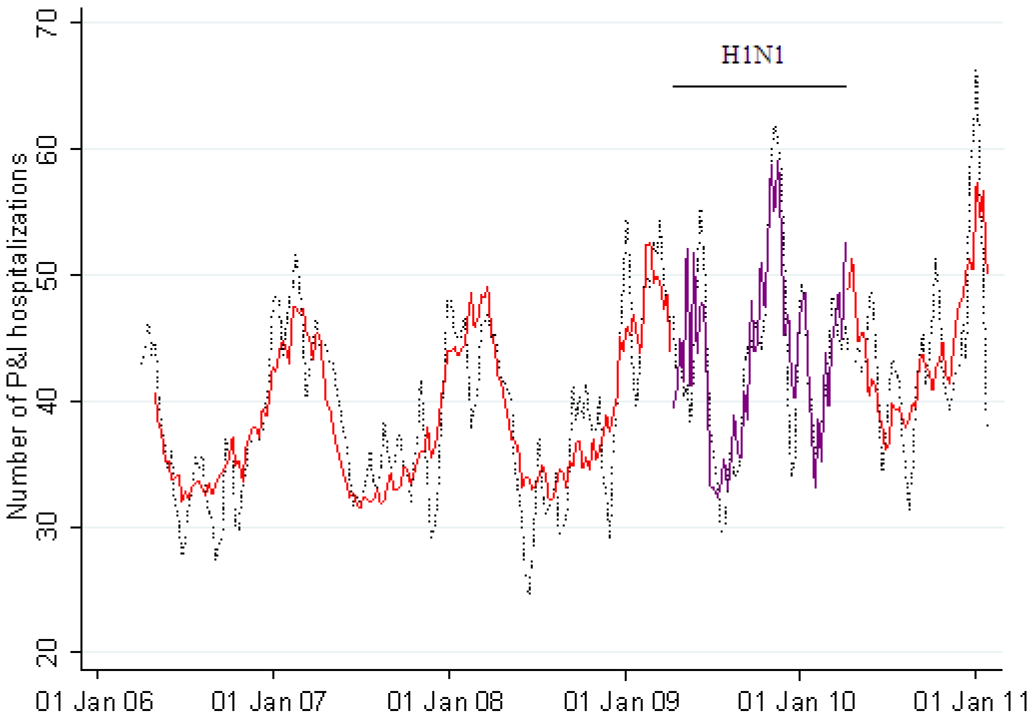

Figure 4-2. Baseline model of weekly pneumonia and influenza (P&I) hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

Lowess-smoothed time series of weekly counts (dotted line), and predicted counts from the non-pandemic years (red) and pandemic year (purple) models.

Table 4-II. IRR of overall P&I hospitalizations, for each SD increase in ILI visits, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

		Incidence risk ratio (95% confidence interval)					
		Lead time (weeks)					
		0	1	2	3	4	5
Non-pandemic period							
All ILI visits		1.04 (1.00-1.09)	1.03 (0.99-1.08)	1.02 (0.98-1.07)	1.02 (0.98-1.07)	1.01 (0.97-1.06)	1.02 (0.98-1.08)
Age (years)	<18	1.00 (0.97-1.03)	1.03 (0.99-1.06)	1.01 (0.97-1.04)	1.01 (0.98-1.05)	1.02 (0.99-1.05)	1.00 (0.97-1.04)
	18-64	1.04 (1.00-1.08)	1.01 (0.97-1.06)	1.03 (0.98-1.07)	1.03 (0.99-1.08)	1.01 (0.97-1.06)	1.02 (0.98-1.07)
	≥65	1.05 (1.02-1.09)	1.04 (1.01-1.08)	1.01 (0.98-1.05)	0.97 (0.94-1.01)	0.98 (0.95-1.02)	1.02 (0.98-1.05)
Triage: 1-3		1.02 (0.99-1.06)	1.02 (0.98-1.06)	1.03 (0.99-1.07)	1.02 (0.98-1.06)	1.03 (0.99-1.07)	1.02 (0.98-1.06)
Disposition: A/T/D		1.02 (1.00-1.05)	1.04 (1.01-1.07)	1.00 (0.97-1.03)	1.01 (0.98-1.04)	1.00 (0.97-1.03)	1.02 (0.99-1.05)
Pandemic year[a]							
All ILI visits		1.06 (0.97-1.16)	1.15 (1.05-1.26)	1.08 (0.97-1.20)	1.15 (1.02-1.28)	0.99 (0.88-1.12)	0.93 (0.83-1.03)
Age (years)	<18	1.06 (0.99-1.13)	1.13 (1.05-1.21)	1.08 (0.99-1.17)	1.15 (1.05-1.25)	1.07 (0.97-1.18)	0.96 (0.87-1.05)
	18-64	1.04 (0.95-1.13)	1.11 (1.01-1.21)	1.04 (0.94-1.15)	1.10 (0.99-1.22)	0.96 (0.87-1.07)	0.94 (0.85-1.03)
	≥65	1.05 (0.97-1.13)	1.11 (1.02-1.21)	1.07 (0.98-1.17)	0.95 (0.87-1.05)	0.97 (0.88-1.06)	0.96 (0.88-1.06)
Triage: 1-3		1.04 (0.96-1.12)	1.11 (1.03-1.20)	1.10 (1.00-1.20)	1.14 (1.04-1.25)	1.00 (0.90-1.11)	0.89 (0.81-0.97)
Disposition: A/T/D		1.06 (1.00-1.13)	1.13 (1.06-1.20)	1.01 (0.93-1.09)	0.98 (0.90-1.07)	0.92 (0.85-1.00)	0.97 (0.90-1.05)

Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. Effect size for one standard deviation increase in influenza-like illness (ILI) ED visits, or a subset thereof.

IRR: incidence rate ratio; P&I: pneumonia and influenza; SD: standard deviation; Triage score 1-3: requiring urgent to immediate care; Disposition A/T/D: admission, transfer, or death.

[a]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

During the non-pandemic period, visits with ILI among ≥ 65 year-olds were significantly associated with overall P&I hospitalizations the same week and the following week. These models also had a lower AIC than the model with all ILI visits, suggesting a better predictive value (Figure 4-3). Visits with ILI among 18-64 year-olds were also significantly associated with P&I hospitalizations the same week, but did not provide better predictive value than total ILI visits. Visits from the <18 year-olds were not significantly associated with the outcome at any lead time. Counts of admissions/transfers/deaths with ILI were also associated with P&I hospitalizations the following week, resulting in a lower AIC than the models with all ILI visits. No significant effect was observed at any lead-time for the severe triage categories.

During the pandemic (H1N1) year, ILI visits from the ≥65 and 18-64 year-olds were significantly associated with P&I hospitalizations only at a lead time of 1 week, and did not provided better predictive value than total ILI visits at any lead time. On the other hand, the model including ILI visits from <18 year-olds had a lower AIC than models with all ILI visits, at all lead times, and the association with P&I hospitalizations, positive from leads of 0 to 4 weeks, reached statistical significance at 1 and 3-week lead times. ILI visits with severe triage category were significantly associated with P&I hospitalizations at 2 and 3-week lead times, and those with admissions/transfers/deaths at 0 and 1-week lead times. These models with triage or disposition data had lower AICs than those with total ILI visits.

Using ILI-Se to assess the value of age, triage score, and disposition status to predict hospitalizations led to similar results (data not shown).

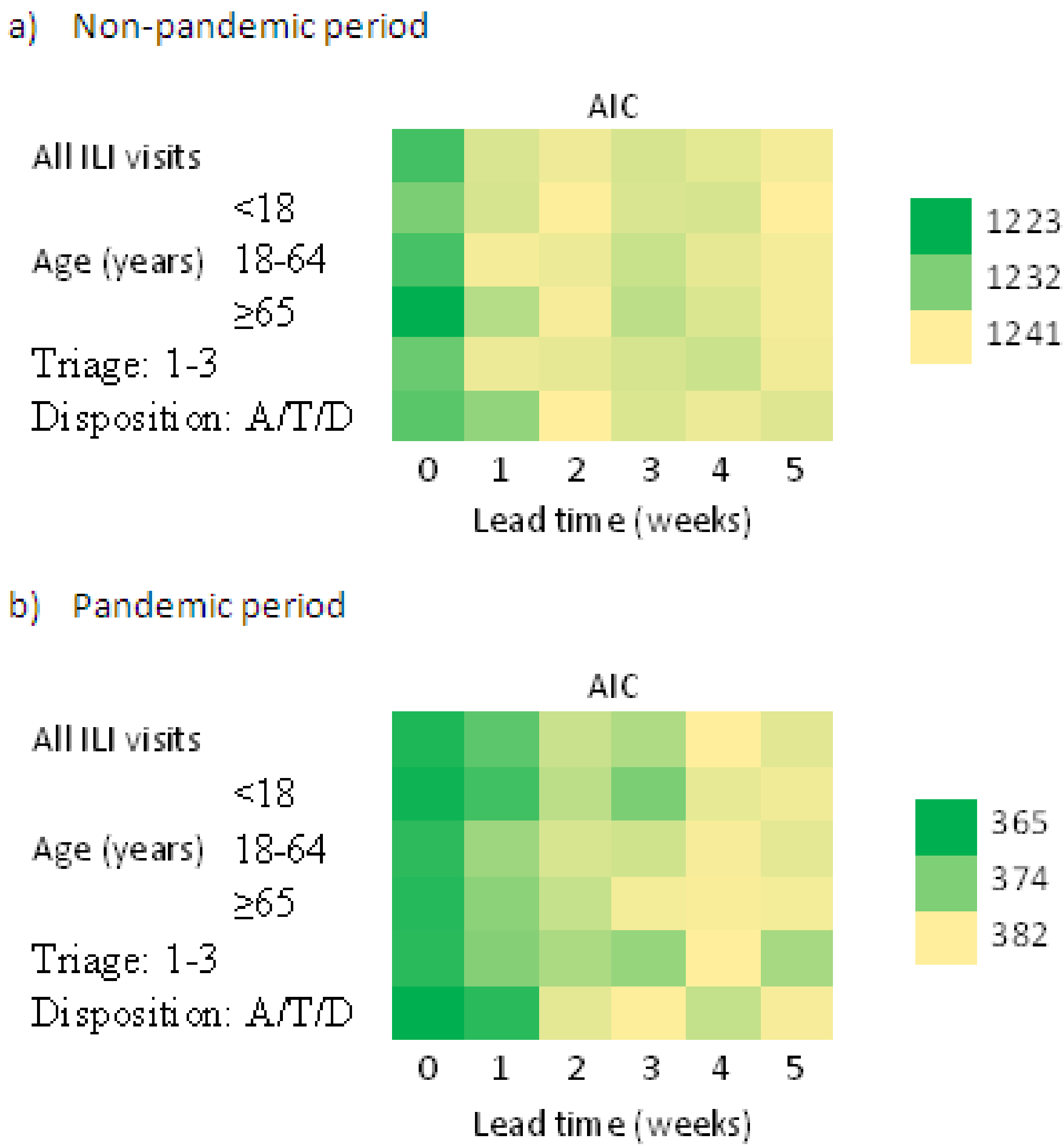

Figure 4-3. Akaike's information criterion (AIC) of predictive models for pneumonia and influenza hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

Pandemic (H1N1) period: April 12, 2009 to April 10, 2010. Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. AIC for models containing all influenza-like illness (ILI) ED visits, or a subset thereof. Triage score 1-3: requiring urgent to immediate care. Disposition A/T/D: admission, transfer, or death.

4.5. Discussion

During non-pandemic years, ED visits with ILI chief complaints were found to be associated with P&I hospitalizations during the same week. There was 4.5% more P&I hospitalizations for every one standard deviation increase in ILI ED visits (35 visits). This association was observed after correcting for long term trends and seasonality, and it therefore reflects a short term association. During the H1N1 year, the association was found with longer lead times and larger effect sizes.

Age-stratified ILI visits, notably visits from the ≥65 year-olds in the non-pandemic years and visits from the <18 year-olds during the H1N1 year, provided small additional predictive value to models for overall P&I hospitalizations predictions. This difference in the effect of age between the non-pandemic and the H1N1 periods may be due to a combination of factors, such as differences in age-specific rates of infection and symptomatic disease, perceptions of risk, and care-seeking behavior during the pandemic versus non-pandemic years.

These findings suggest that age data provide some value for monitoring influenza epidemics. The older age group may be a sentinel population for trends in hospitalizations during seasonal influenza, and similarly for the younger age group during pandemic influenza, although our data is restricted to the 2009 H1N1 pandemic. However, age-stratified information on ILI ED visits can also be useful beyond improving prediction of hospitalizations and heralding epidemic trends. It may allow detecting shifts in age-specific attack rates associated with new/pandemic strains. Furthermore, timely knowledge on how different age groups are affected in a given epidemic or pandemic may inform decisions such as which age group to prioritize for vaccination, and whether to initiate control measures such as closing schools.

As for disposition data, ILI ED visits resulting in admission/transfer/death were consistently associated with P&I hospitalizations with a 1-week lead time, during both non-pandemic and pandemic periods. Similarly, ILI visits with "severe" triage category (requiring urgent to immediate care) improved prediction for P&I hospitalizations, although only during the H1N1 year. Counts of ILI visits with "severe" disposition status (those admitted, transferred, or deceased) or "severe" triage score may be a marker of the severity of an influenza epidemic in the community, rising earlier than counts of hospitalizations with a discharge diagnosis of P&I. Thus, monitoring them could potentially be useful for timely surveillance of influenza epidemic severity. It is not clear why triage category improved hospitalization prediction during the H1N1 year only. It is conceivable that during the pandemic, ILI visit counts reflected, in addition to the incidence of influenza in the population, care-seeking behaviors influenced by the mediatisation of the pandemic. ILI visits with "severe" triage categories may have been less associated with social factors and more reflective of the burden of severe disease.

An association of ILI visits in the ≥65 year-olds with overall P&I hospitalizations, as found during the non-H1N1 period, is consistent with at least one other study, where the authors compared ILI visits from different age groups and in different settings [11]. They found that ED visits from the ≥65 year-olds were correlated with overall P&I hospitalizations, with higher correlation coefficients than for other age groups. However, this relationship has not been observed consistently. Some studies have reported no significant difference in predictive value of different age groups for influenza-related hospitalizations [10], while others have found the youngest age groups (<3 and 3-4 year-olds) to provide the best predictive value, although for P&I mortality rather than hospitalizations [12].

The difference in lead times provided by the ≥65 and <18 year-olds is also consistent with what has been reported in the literature. Some studies found that the youngest age groups present earliest with ILI to emergency departments: either school age children and adolescents [10, 11], the youngest children [12], or older or younger children depending on the season [9]. Looking at virologial data, others have found older children and young adults to be driving epidemics [13, 14].

A decrease in the importance of the ≥65 year-olds and an increase in the importance of the <18 year-olds in predictive value for P&I hospitalizations during the H1N1 period, compared to the non-pandemic period, is consistent with the different age-specific attack rates during H1N1 reported in the literature. In one study, the greatest increase of ILI visits to sentinel physicians was observed for school age children, adolescents, and young adults in the United-States, when compared to seasonal influenza; the lowest increase was for the ≥65 year-olds. As for influenza-related hospitalizations, the greatest increase was in young and middle-age adults, followed by school-age children and adolescents; the lowest increase being in the ≥65 and <4 year-olds [31]. Another study found the proportion of 10-19 and 20-29 year-olds affected by H1N1 to be greater than the proportion usually affected by seasonal influenza [14].

A few studies assessed the use of ED disposition data to predict influenza-related hospitalizations. The use of ED data (signs and symptoms, chief complaints, ED or admission diagnosis) allowed prediction of hospitalizations with a discharge diagnosis of P&I (or pneumonia) with moderate sensitivity (40-62%), high specificity (94-99%) and moderate positive predictive value (41-71%)[5, 6]. To our knowledge, however, no study has previously reported the disposition of ED visits for ILI to be a leading indicator of P&I hospital admissions.

Finally, although the use of triage category in surveillance systems has been reported in the literature [7, 8] and has been deemed useful [8], performance metrics, association measures, or other quantitative analyses have not been previously reported.

One limitation of our study is the small size of the population, and the possibly biased sampling fraction resulting from the catchment areas of the hospitals with available data. Another limitation is the absence of a pediatric hospital in the data set for the study period, significantly limiting results for the pediatric population. However, these limitations reflect real life surveillance practice, where all the relevant data are often not available.

Another limitation is that neither ILI nor P&I are specific for influenza, and both can be due to other respiratory viruses, such as respiratory syncytial virus, to bacterial infections, and to non-infectious causes. However, P&I hospitalizations have often been used as a measure of influenza-related hospitalizations [9-11, 13, 32, 33], thus allowing for comparability of results. Furthermore, our results were generally robust to choice of ILI definition.

Importantly, measures of association and goodness of fit do not guarantee practical utility. One next step would be to test the predictive value of these models on hold-out data not used for model fitting. There would then still be a need for evaluating whether adding these covariates into a surveillance system leads to better public health practice, such as earlier and improved planning of infection control measures and hospital resources, improved understanding of the current epidemic, or improved communication with the public and decision makers.

4.6. Conclusion

ILI ED visits stratified by age group, triage score, and disposition status provided small improvement in predictive models for overall P&I hospitalizations, as compared to overall ILI ED visits. Our findings suggest it may be valuable to integrate these covariates into an ED-based ILI surveillance system. Future directions should include the evaluation of the practical utility of using these covariates, in terms of informing decision making and implantation of influenza control measures, in the context of actual surveillance systems.

Authors' contribution

All authors contributed to conception and design of the study. NS analyzed and interpreted the data with contributions from DLB, RA, and LB. NS drafted the manuscript, and all coauthors revised it critically for important intellectual content. All authors approved of the final version.

4.7. References

1. Nicholson KG, Wood JM, Zambon M. Influenza. The Lancet. 2003;362(9397):1733-45.

2. Brammer L, Budd A, Cox N. Seasonal and pandemic influenza surveillance considerations for constructing multicomponent systems. Influenza Other Respir Viruses. 2009;3(2):51-8.

3. Buehler JW, Sonricker A, Paladini M, Soper P, Mostashari F. Syndromic Surveillance Practice in the United States: Findings from a Survey of State, Territorial, and Selected Local Health Departments. Advances in Disease Surveillance. 2008;6(3):1-20.

4. van den Wijngaard CC, van Pelt W, Nagelkerke NJ, Kretzschmar M, Koopmans MP. Evaluation of syndromic surveillance in the Netherlands: its added value and recommendations for implementation. Euro Surveill. 2011;16(9).

5. Berenbaum P, Gibson M, Blevins LZ. Accuracy versus Timeliness for Influenza Detection: A Comparison of Hospital Syndromic Surveillance Data with Discharge Data. Advances in Disease Surveillance. 2007;2(93).

6. Townes JM, Kohn MA, Southwick KL, Bangs CA, Zechnich AD, Magnuson JA, *et al*. Investigation of an electronic emergency department information system as a data source for respiratory syndrome surveillance. J Public Health Manag Pract. 2004 Jul-Aug;10(4):299-307.

7. Zheng W, Aitken R, Muscatello DJ, Churches T. Potential for early warning of viral influenza activity in the community by monitoring clinical diagnoses of influenza in hospital emergency departments. BMC Public Health. 2007;7:250.

8. Moore KM, Edgar BL, McGuinness D. Implementation of an automated, real-time public health surveillance system linking emergency departments and health units: rationale and methodology. 2008. 2008;10(2):114-9.

9. Olson DR, Heffernan RT, Paladini M, Konty K, Weiss D, Mostashari F. Monitoring the impact of influenza by age: emergency department fever and

respiratory complaint surveillance in New York City. PLoS Med. 2007 Aug;4(8):e247.

10. Sebastian R, Skowronski DM, Chong M, Dhaliwal J, Brownstein JS. Age-related trends in the timeliness and prediction of medical visits, hospitalizations and deaths due to pneumonia and influenza, British Columbia, Canada, 1998-2004. Vaccine. 2008 Mar 4;26(10):1397-403.

11. Chan EH, Tamblyn R, Charland KML, Buckeridge DL. Outpatient physician billing data for age and setting specific syndromic surveillance of influenza-like illnesses. J Biomed Inform. 2011;44(2):221-8.

12. Brownstein JS, Kleinman KP, Mandl KD. Identifying pediatric age groups for influenza vaccination using a real-time regional surveillance system. Am J Epidemiol. 2005 Oct 1;162(7):686-93.

13. Schanzer D, Vachon J, Pelletier L. Age-specific Differences in Influenza A Epidemic Curves: Do Children Drive the Spread of Influenza Epidemics? Am J Epidemiol. 2011 May 20, 2011.

14. Timpka T, Eriksson O, Spreco A, Gursky EA, Strömgren M, Holm E, *et al*. Age as a Determinant for Dissemination of Seasonal and Pandemic Influenza: An Open Cohort Study of Influenza Outbreaks in Östergötland County, Sweden. PLoS ONE. 2012;7(2):e31746.

15. Agence de la santé et des services sociaux de Montréal. Espace montréalais d'information sur la santé. Gouvernement du Québec; 2011; Available from: http://emis.santemontreal.qc.ca/. (Accessed on August 19, 2011).

16. Christ M, Grossmann F, Winter D, Bingisser R, Platz E. Modern triage in the emergency department. Dtsch Arztebl Int. 2010 Dec;107(50):892-8.

17. Dong SL, Bullard MJ, Meurer DP, Blitz S, Akhmetshin E, Ohinmaa A, *et al*. Predictive validity of a computerized emergency triage tool. Acad Emerg Med. 2007 Jan;14(1):16-21.

18. Jimenez JG, Murray MJ, Beveridge R, Pons JP, Cortes EA, Garrigos JB, *et al*. Implementation of the Canadian Emergency Department Triage and Acuity Scale (CTAS) in the Principality of Andorra: Can triage parameters serve as emergency department quality indicators? CJEM. 2003 Sep;5(5):315-22.

19. Center for Disease Control. Overview of Influenza Surveillance in the United States. 2011; Available from: http://www.cdc.gov/flu/weekly/overview.htm. (Accessed on May 22, 2012).

20. World Health Organization. WHO Recommended Surveillance Standards, 2nd edn. 2006; Available from: http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_CSR_ISR_99_2_EN/en/. (Accessed on April 4, 2012).

21. Pendarvis J, Gunn J, Smith AK, Donovan M, Barry A. Sneezes vs. Wheezes: Syndrome Definitions for Influenza-like Illness. Advances in Disease Surveillance. 2007;2(115):1.

22. Thompson WW, Comanor L, Shay DK. Epidemiology of seasonal influenza: use of surveillance data and statistical models to estimate the burden of disease. J Infect Dis. 2006 Nov 1;194 Suppl 2:S82-91.

23. Tsui FC, Wagner MM, Dato V, Chang CC. Value of ICD-9 coded chief complaints for detection of epidemics. Proc Amia Symp. 2001:711-5.

24. Das D, Olson D, Heffernan R. Estimating Hospital Admissions for Influenza Using Emergency Department (ED) Syndromic Surveillance Data, New York City. Advances in Disease Surveillance. 2007;2(150).

25. Cleveland, WS. Robust locally weighted regression and smoothing scatterplots. Journal of the American Statistical Association, 1979;74:829-836.

26. Yang L, Chiu SS, Chan K-P, Chan K-H, Wong WH-S, Peiris JSM, *et al*. Validation of Statistical Models for Estimating Hospitalization Associated with Influenza and Other Respiratory Viruses. PLoS ONE. 2011;6(3):e17882.

27. Gilca R, De Serres G, Skowronski D, Boivin G, Buckeridge DL. The Need for Validation of Statistical Methods for Estimating Respiratory Virus–Attributable Hospitalization. Am J Epidemiol. 2009 October 1, 2009;170(7):925-36.

28. Zhou H, Thompson WW, Viboud CG, Ringholz CM, Cheng P-Y, Steiner C, *et al*. Hospitalizations Associated With Influenza and Respiratory Syncytial Virus in the United States, 1993–2008. Clin Infect Dis. 2012 April 10, 2012.

29. Hardelid P, Pebody R, Andrews N. Mortality caused by influenza and respiratory syncytial virus by age group in England and Wales 1999-2010. Influenza Other Respi Viruses. 2012 Mar 9.
30. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika. 1987;52(3):345-70.
31. Karageorgopoulos DE, Vouloumanou EK, Korbila IP, Kapaskelis A, Falagas ME. Age distribution of cases of 2009 (H1N1) pandemic influenza in comparison with seasonal influenza. PLoS ONE. 2011;6(7):e21690.
32. Muscatello DJ, Morton PM, Evans I, Gilmour R. Prospective surveillance of excess mortality due to influenza in New South Wales: feasibility and statistical approach. Commun Dis Intell. 2008 Dec;32(4):435-42.
33. Simonsen L, Clarke MJ, Williamson GD, Stroup DF, Arden NH, Schonberger LB. The impact of influenza epidemics on mortality: introducing a severity index. Am J Public Health. 1997 Dec;87(12):194.

4.8. Supplementary material

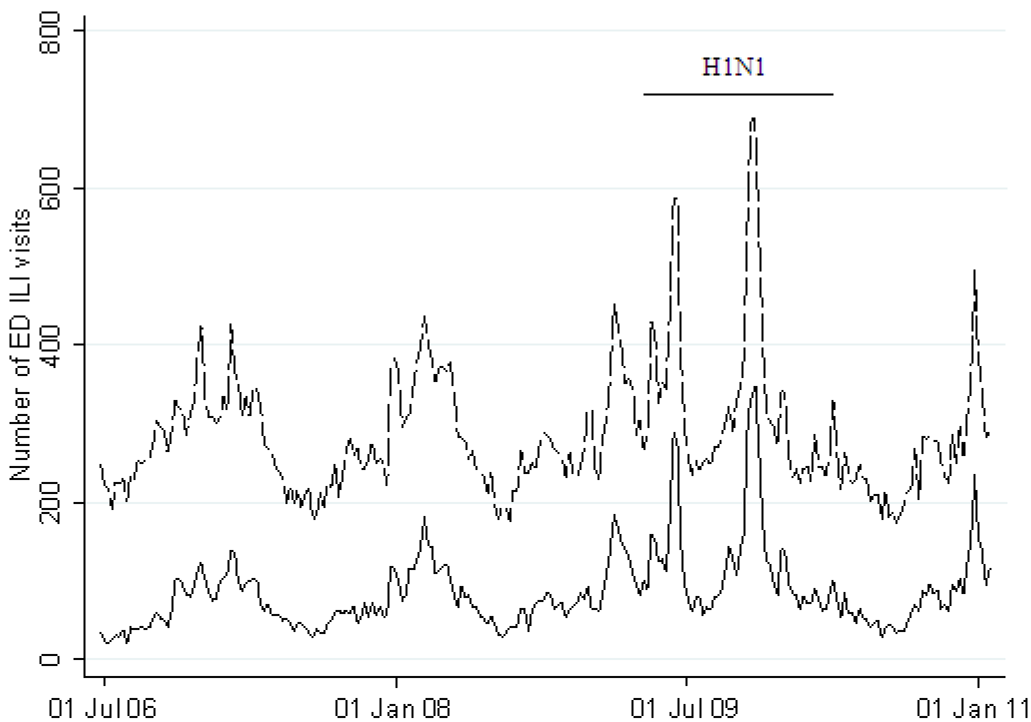

Figure 4-4. Weekly emergency department (ED) visits with influenza-like illness (ILI), hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

Continuous line: ILI-specific definition ((fever AND cough) OR (fever AND sore throat) OR influenza-related keyword). Dotted line: ILI-sensitive definition (fever OR cough OR sore throat OR influenza-related keyword).

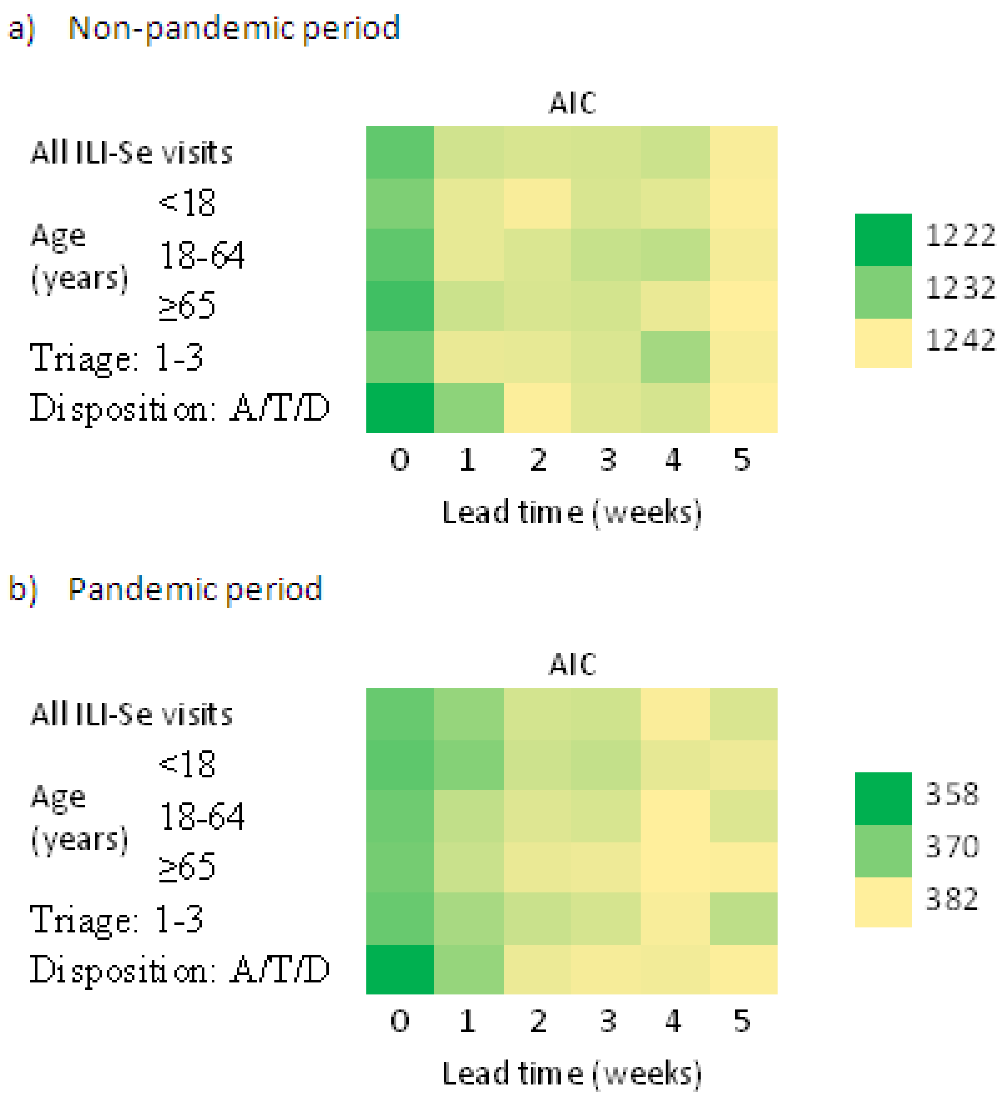

Figure 4-5. Akaike's information criterion (AIC) of predictive models for pneumonia and influenza hospitalizations, using ILI-Se[a] visits, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011
Pandemic (H1N1) period: April 12, 2009 to April 10, 2010. Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. AIC for models containing all influenza-like illness (ILI) ED visits, or a subset thereof. Triage score 1-3: requiring urgent to immediate care. Disposition A/T/D: admission, transfer, or death.
[a]Influenza-like illness – sensitive definition (fever OR cough OR sore throat OR influenza-related keyword)

Table 4-III. Mean number of weekly influenza-like illness – sensitive definition[a] - emergency department visits, according to visit characteristics, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

		Weekly mean (95% confidence interval)	
		Non-pandemic period (N=188)	Pandemic year[b] (N=52)
Age (years)			
	<18	38 (36-40)	46 (38-53)
	18-64	188 (182-194)	237 (214-261)
	≥65	50 (48-52)	50 (47-54)
Triage score			
	1- Resuscitation	0,4 (0,3-0,5)	0,4 (0,2-0,6)
	2- Emergent	28 (27-29)	30 (28-33)
	3- Urgent	129 (125-133)	139 (127-151)
	4- Semi-urgent	91 (87-95)	132 (116-148)
	5- Non-urgent	27 (26-28)	32 (29-35)
Disposition			
	home/residence	244 (235-252)	301 (270-332)
	admission	28 (27-29)	29 (27-31)
	transfer	3,1 (2,9-3,4)	3,9 (3,3-4,5)
	death	0,1 (0,1-0,2)	0,1 (0,0-0,1)
Total		275 (266-284)	333 (301-365)

[a]ILI-Se: fever OR cough OR sore throat OR influenza-related keyword
[b]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

.

Table 4-IV. IRR of overall P&I hospitalizations, for each unit increase in ILI visits (specific definition), hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

		Incidence risk ratio (95% confidence interval)					
		Lead time (weeks)					
		0	1	2	3	4	5
ILI-Sp[a] - non-pandemic period							
All ILI-Sp visits		1,0012 (1,0001-1,0024)	1,0010 (0,9997-1,0022)	1,0007 (0,9994-1,0019)	1,0006 (0,9993-1,0018)	1,0005 (0,9992-1,0017)	1,0007 (0,9993-1,0021)
Age (years)	<18	1,0003 (0,9972-1,0034)	1,0026 (0,9995-1,0058)	1,0005 (0,9973-1,0038)	1,0014 (0,9981-1,0046)	1,0021 (0,9989-1,0054)	1,0005 (0,9972-1,0039)
	18-64	1,0018 (1,0001-1,0035)	1,0006 (0,9987-1,0025)	1,0011 (0,9993-1,0029)	1,0013 (0,9994-1,0031)	1,0006 (0,9987-1,0024)	1,0010 (0,9989-1,0031)
	≥65	1,0083 (1,0030-1,0135)	1,0066 (1,0009-1,0123)	1,0021 (0,9962-1,0081)	0,9950 (0,9890-1,0011)	0,9966 (0,9904-1,0029)	1,0032 (0,9967-1,0097)
Triage: 1-3		1,0017 (0,9990-1,0044)	1,0014 (0,9986-1,0043)	1,0019 (0,9990-1,0047)	1,0013 (0,9984-1,0041)	1,0022 (0,9994-1,0051)	1,0017 (0,9986-1,0048)
Disposition: A/T/D		1,0088 (0,9984-1,0193)	1,0151 (1,0046-1,0258)	1,0005 (0,9895-1,0117)	1,0034 (0,9924-1,0145)	1,0005 (0,9892-1,0119)	1,0094 (0,9978-1,0212)
ILI-Sp[a] - pandemic year[b]							
All ILI-Sp visits		1,0008 (0,9996-1,0020)	1,0019 (1,0007-1,0032)	1,0010 (0,9995-1,0025)	1,0019 (1,0003-1,0034)	0,9999 (0,9982-1,0015)	0,9989 (0,9974-1,0005)
Age (years)	<18	1,0027 (0,9996-1,0058)	1,0057 (1,0024-1,0090)	1,0034 (0,9994-1,0075)	1,0065 (1,0024-1,0107)	1,0031 (0,9984-1,0078)	0,9980 (0,9936-1,0024)
	18-64	1,0008 (0,9991-1,0025)	1,0020 (1,0003-1,0038)	1,0008 (0,9988-1,0029)	1,0019 (0,9998-1,0040)	0,9993 (0,9971-1,0014)	0,9987 (0,9967-1,0007)
	≥65	1,0085 (0,9937-1,0235)	1,0201 (1,0042-1,0362)	1,0124 (0,9954-1,0296)	0,9913 (0,9734-1,0094)	0,9939 (0,9761-1,0121)	0,9930 (0,9758-1,0105)
Triage: 1-3		1,0015 (0,9985-1,0044)	1,0040 (1,0010-1,0071)	1,0035 (1,0001-1,0070)	1,0050 (1,0014-1,0086)	0,9999 (0,9959-1,0039)	0,9953 (0,9915-0,9990)
Disposition: A/T/D		1,0144 (1,0000-1,0290)	1,0281 (1,0130-1,0434)	1,0013 (0,9824-1,0205)	0,9961 (0,9768-1,0158)	0,9808 (0,9627-0,9993)	0,9940 (0,9760-1,0124)

Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. Effect size for all influenza-like illness (ILI) ED visits, or a subset thereof.
IRR: incidence rate ratio; P&I: pneumonia and influenza; SD: standard deviation; Triage score 1-3: requiring urgent to immediate care; Disposition A/T/D: admission, transfer, or death.
[a]ILI-specific definition: (fever AND cough) OR (fever AND sore throat) OR influenza-related keyword
[b]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

Table 4-V. IRR of overall P&I hospitalizations, for each unit increase in ILI visits (sensitive definition), hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

		Incidence risk ratio (95% confidence interval)					
		Lead time (weeks)					
		0	1	2	3	4	5
ILI-Se[a] - non-pandemic period							
All ILI-Se visits		1,0006 (0,9999-1,0014)	1,0007 (0,9999-1,0014)	1,0007 (0,9999-1,0014)	1,0004 (0,9996-1,0012)	1,0006 (0,9998-1,0014)	1,0003 (0,9994-1,0011)
Age (years)	<18	0,9993 (0,9971-1,0015)	1,0012 (0,9990-1,0034)	1,0003 (0,9981-1,0026)	1,0010 (0,9987-1,0032)	1,0009 (0,9986-1,0031)	1,0005 (0,9982-1,0028)
	18-64	1,0009 (0,9998-1,0021)	1,0007 (0,9995-1,0018)	1,0009 (0,9998-1,0021)	1,0009 (0,9997-1,0020)	1,0011 (0,9999-1,0023)	1,0005 (0,9992-1,0018)
	≥65	1,0027 (1,0004-1,0050)	1,0023 (0,9999-1,0047)	1,0021 (0,9996-1,0046)	0,9987 (0,9961-1,0012)	1,0002 (0,9976-1,0028)	0,9998 (0,9972-1,0025)
Triage: 1-3		1,0007 (0,9993-1,0020)	1,0007 (0,9993-1,0021)	1,0009 (0,9995-1,0023)	1,0004 (0,9990-1,0019)	1,0017 (1,0003-1,0031)	1,0006 (0,9991-1,0021)
Disposition: A/T/D		1,0069 (1,0027-1,0111)	1,0066 (1,0021-1,0110)	1,0002 (0,9955-1,0049)	0,9996 (0,9949-1,0043)	1,0030 (0,9983-1,0077)	1,0004 (0,9958-1,0051)
ILI-Se[a] - pandemic year[b]							
All ILI-Se visits		1,0004 (0,9997-1,0012)	1,0012 (1,0004-1,0019)	1,0007 (0,9998-1,0017)	1,0011 (1,0001-1,0021)	1,0003 (0,9993-1,0013)	0,9991 (0,9981-1,0000)
Age (years)	<18	1,0019 (0,9994-1,0043)	1,0042 (1,0017-1,0067)	1,0027 (0,9997-1,0058)	1,0040 (1,0008-1,0072)	1,0028 (0,9993-1,0062)	0,9979 (0,9945-1,0013)
	18-64	1,0004 (0,9995-1,0013)	1,0011 (1,0001-1,0021)	1,0007 (0,9996-1,0018)	1,0012 (1,0000-1,0023)	1,0001 (0,9988-1,0013)	0,9989 (0,9978-1,0001)
	≥65	1,0004 (0,9951-1,0057)	1,0054 (0,9997-1,0112)	1,0012 (0,9952-1,0073)	0,9961 (0,9902-1,0022)	1,0002 (0,9940-1,0064)	0,9992 (0,9934-1,0051)
Triage: 1-3		1,0009 (0,9993-1,0024)	1,0021 (1,0005-1,0037)	1,0018 (0,9999-1,0036)	1,0020 (1,0001-1,0039)	1,0008 (0,9987-1,0028)	0,9975 (0,9956-0,9994)
Disposition: A/T/D		1,0131 (1,0055-1,0207)	1,0133 (1,0047-1,0220)	0,9991 (0,9889-1,0093)	0,9953 (0,9847-1,0060)	0,9943 (0,9837-1,0050)	1,0007 (0,9918-1,0097)

Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. Effect size for all influenza-like illness (ILI) ED visits, or a subset thereof.
IRR: incidence rate ratio; P&I: pneumonia and influenza; SD: standard deviation; Triage score 1-3: requiring urgent to immediate care; Disposition A/T/D: admission, transfer, or death.
[a]ILI-sensitive definition: fever OR cough OR sore throat OR influenza-related keyword
[b]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

Table 4-VI. IRR of overall P&I hospitalizations, for each SD increase in ILI-Se[a] visits, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

		Incidence risk ratio (95% confidence interval)					
		Lead time (weeks)					
		0	1	2	3	4	5
Non-pandemic period							
All ILI-Se visits		1,04 (0,99-1,09)	1,04 (0,99-1,10)	1,04 (0,99-1,10)	1,02 (0,97-1,08)	1,04 (0,99-1,09)	1,02 (0,97-1,07)
Age (years)	<18	0,99 (0,96-1,02)	1,02 (0,99-1,05)	1,00 (0,97-1,04)	1,01 (0,98-1,05)	1,01 (0,98-1,05)	1,01 (0,97-1,04)
	18-64	1,04 (0,99-1,09)	1,03 (0,98-1,08)	1,04 (0,99-1,09)	1,04 (0,99-1,09)	1,05 (1,00-1,10)	1,02 (0,97-1,07)
	≥65	1,04 (1,01-1,07)	1,03 (1,00-1,07)	1,03 (0,99-1,07)	0,98 (0,95-1,02)	1,00 (0,97-1,04)	1,00 (0,96-1,03)
Triage: 1-3		1,02 (0,98-1,07)	1,02 (0,98-1,07)	1,03 (0,98-1,08)	1,01 (0,97-1,06)	1,06 (1,01-1,10)	1,02 (0,97-1,07)
Disposition: A/T/D		1,05 (1,02-1,07)	1,04 (1,01-1,07)	1,00 (0,97-1,03)	1,00 (0,97-1,03)	1,02 (0,99-1,05)	1,00 (0,97-1,03)
Pandemic year[b]							
All ILI-Se visits		1,05 (0,96-1,15)	1,15 (1,05-1,25)	1,09 (0,98-1,21)	1,13 (1,01-1,27)	1,04 (0,92-1,17)	0,90 (0,81-1,00)
Age (years)	<18	1,05 (0,98-1,13)	1,12 (1,05-1,20)	1,08 (0,99-1,17)	1,11 (1,02-1,22)	1,08 (0,98-1,18)	0,94 (0,86-1,03)
	18-64	1,04 (0,95-1,12)	1,10 (1,01-1,20)	1,06 (0,96-1,17)	1,11 (1,00-1,23)	1,01 (0,90-1,12)	0,91 (0,83-1,01)
	≥65	1,00 (0,95-1,07)	1,06 (1,00-1,13)	1,01 (0,95-1,08)	0,96 (0,89-1,02)	1,00 (0,94-1,07)	0,99 (0,93-1,06)
Triage: 1-3		1,05 (0,97-1,13)	1,11 (1,03-1,21)	1,09 (1,00-1,20)	1,11 (1,00-1,22)	1,04 (0,94-1,16)	0,88 (0,80-0,97)
Disposition: A/T/D		1,11 (1,04-1,18)	1,11 (1,04-1,19)	0,99 (0,91-1,08)	0,96 (0,88-1,05)	0,96 (0,88-1,04)	1,01 (0,94-1,08)

Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. Effect size for one standard deviation increase in influenza-like illness (ILI) ED visits, or a subset thereof. IRR: incidence rate ratio; P&I: pneumonia and influenza; SD: standard deviation; Triage score 1-3: requiring urgent to immediate care; Disposition A/T/D: admission, transfer, or death.

[a]ILI – sensitive definition: fever OR cough OR sore throat OR influenza-related keyword [b]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

Table 4-VII. Akaike's information criterion (AIC) of predictive models for pneumonia and influenza hospitalizations, hospitals participating to *ERU*, June 25, 2006 to January 29, 2011

		AIC					
		Lead time (weeks)					
		0	1	2	3	4	5
ILI-Sp[a] - non-pandemic period							
All ILI-Sp visits		1227,6	1238,6	1240,2	1238,4	1239,4	1240,6
	<18	1231,8	1238,4	1241,2	1238,6	1238,4	1241,4
Age (years)	18-64	1227,8	1240,6	1240,0	1237,4	1239,6	1240,6
	≥65	1222,6	1236,0	1240,8	1236,6	1238,8	1240,6
Triage: 1-3		1230,4	1240,0	1239,6	1238,4	1237,6	1240,4
Disposition: A/T/D		1229,2	1233,4	1241,4	1238,8	1240,0	1239,0
ILI-Sp[a] - pandemic year[c]							
All ILI-Sp visits		367,2	371,4	378,8	377,0	382,4	380,4
	<18	366,2	369,6	378,0	373,6	380,8	381,4
Age (years)	18-64	368,2	375,8	379,8	379,2	381,8	380,6
	≥65	367,8	374,6	378,6	381,6	382,0	381,6
Triage: 1-3		368,0	374,2	376,8	375,4	382,4	376,4
Disposition: A/T/D		365,2	368,0	380,6	382,2	378,4	381,8
ILI-Se[b] - non-pandemic period							
All ILI-Se visits		1229,4	1238,0	1238,6	1238,4	1237,6	1241,2
	<18	1231,6	1239,8	1241,2	1238,6	1239,4	1241,4
Age (years)	18-64	1229,2	1239,8	1238,8	1237,2	1236,6	1240,8
	≥65	1226,8	1237,6	1238,6	1238,2	1240,0	1241,6
Triage: 1-3		1231,0	1240,0	1239,8	1238,8	1234,6	1241,0
Disposition: A/T/D		1221,8	1232,8	1241,4	1239,2	1238,4	1241,6
ILI-Se[b] - pandemic year[c]							
All ILI-Se visits		367,8	372,2	378,2	377,8	382,0	378,8
	<18	366,8	370,6	377,6	376,6	380,0	380,8
Age (years)	18-64	368,4	376,4	379,2	378,6	382,4	379,0
	≥65	369,0	377,2	380,4	380,8	382,4	382,2
Triage: 1-3		367,8	374,0	377,2	378,4	381,8	376,0
Disposition: A/T/D		357,6	372,2	380,6	381,6	381,2	382,2

Models adjusted for secular trends, seasonality, all-cause emergency department (ED) visits, and autocorrelation. AIC for models with all ILI ED visits, or a subset thereof. Triage score 1-3: requiring urgent to immediate care. Disposition A/T/D: admission, transfer, or death.

[a]ILI-specific definition: (fever AND cough) OR (fever AND sore throat) OR influenza-related keyword

[b]ILI-sensitive definition: fever OR cough OR sore throat OR influenza-related keyword

[c]Pandemic (H1N1) year: April 12, 2009 to April 10, 2010

Chapter 5: Additional results

Prior to performing the analyses described in the manuscript, it was necessary to understand and describe the data, their structure, and how they were generated, and to develop syndrome definitions. The results of this preliminary work are presented here, since they provide context for the main results presented in the manuscript, and they allow a better understanding of their significance for public health practice.

5.1. Descriptive statistics: number of ED visits and use of the electronic system

ERU

Over the whole study period, from April 1, 2006 to November 14, 2011, there were on average 702 ED visits per day recorded in the *ERU* (standard deviation (SD) = 193), of which 96.8% had a chief complaint recorded. The average number of visits increased as additional hospitals participated in the database, going from 443 visits per day in the first year to 874 visits per day in the last year of the study. Differences between hospitals in *ERU* system utilization are presented in

Table **5-**I. The proportion of visits with chief complaint recorded was high in every ED, ranging from 89% to 100%. There were important differences between EDs in the average number of chief complaint codes assigned per visits, ranging from 1.4 to 6.2.

For the period between May 7, 2008 to November 14, 2011 (period used for comparisons with *RQSUCH* data), there were on average 799 ED visits per day (the pediatric and general 3 hospitals being included starting on their respective entry dates). Table A1-I, Table A1-II and Table A1-III, in Appendix 1, represent an extension of Table 5-I, with descriptive statistics for each time window used for analyses in this project. Figure A1-1, Figure A1-2, and Figure A1-3 present the results per year. Number of ED visits, proportion of visits with chief complaint recorded, and average number of chief complaint codes per visit changed very little according to time window or year.

Table 5-I. Number of emergency department (ED) visits, proportion with chief complaint, and number of chief complaint per visit in *ERU*, from date of entry to November 14, 2011

Emergency department	Date[1] of entry in *ERU*	Mean number of ED visits per day (95% CI)	Proportion of visits with chief complaint recorded (95% CI)	Mean number of chief complaint codes recorded per visit (95% CI)
Pediatric	2009-09-21	210.7 (208.3-213.0)	89.2% (88.5%-89.9%)	4.04 (4.02-4.06)
General 1	2006-04-01	100.4 (99.9-100.9)	99.9% (99.9%-99.9%)	2.48 (2.47-2.49)
General 2	2006-04-01	106.8 (106.3-107.4)	89.1% (88.8%-89.4%)	1.46 (1.46-1.46)
General 3	2007-04-01	117.2 (116.3-118.1)	97.8% (97.7%-97.9%)	4.64 (4.63-4.66)
General 4	2009-05-11	78.9 (78.4-79.3)	99.9% (99.9%-99.9%)	6.23 (6.21-6.24)
Tertiary 1	2006-06-24	115.8 (115.1-116.4)	99.7% (99.7%-99.8%)	1.50 (1.49-1.50)
Tertiary 2	2006-06-24	112.5 (111.8-113.1)	100.0% (99.9%-100.0%)	1.44 (1.44-1.44)
Tertiary 3	2006-06-24	81.3 (80.8-81.9)	100.0% (100.0%-100.0%)	1.53 (1.53-1.54)
Total[2]	-	701.8 (693.5-710.2)	96.7% (96.6%-96.8%)	2.59 (2.59-2.59)

[1]YYYY-MM-DD

[2] Each ED included starting on its entry date

CI: confidence interval

RQSUCH

During the period from May 7, 2008 to November 14, 2011 (for which ILI data are available in *RQSUCH*), there was a mean of 798 ED visits per day (SD = 157) reported by *RQSUCH*.

The number of visits reported via *RQSUCH* was identical to that obtained from *ERU* on 78.8 to 99.4% of days, depending on the ED, and was within 1 visit in 92.6 to 99.9% of cases. 0.40% of the *RQSUCH* counts were identified as aberrant, versus none of the *ERU* counts. Mean numbers of daily visits did not differ significantly between *RQSUCH* and *ERU*. Detailed comparisons of *ERU* and *RQSUCH* are presented in Appendix 1, Table A1-IV.

5.2. Descriptive statistics: ILI visits

There were no outliers among the counts of ILI-Sp and ILI-Se visits, and 0.02% (2 data points) among the counts of ILI-R.

Overall, among visits with a chief complaint recorded in *ERU*, 3.2% (SD = 2.2%) met the ILI-Sp definition, and 10.9% (SD = 4.1%) met the ILI-Se definition. For the period starting May 7, 2008, with the pediatric and general 3 hospitals being included starting on their respective entry dates, the proportion was slightly higher for both definitions (3.7% and 12.2% for ILI-Sp and ILI-Se respectively).

Using *RQSUCH* data, for the same period, the mean daily number of visits with ILI-R reported was 36 (SD = 31), corresponding to 4.1% of visits. Descriptive statistics on proportion of ILI visits per data source, ED, and window of time are presented in Appendix 1, Table A1-V, Table A1-VI, and Table A1-VII.

There were important differences across emergency departments for the proportion of visits with ILI-Sp, ILI-Se, and ILI-R. Figure 5-1 illustrates the differences between emergency departments, for ILI-Sp, ILI-Se, and ILI-R, for the May 7, 2008 to November 14, 2011 period. Proportions per ED and data source are detailed in Appendix 1, Table A1-VIII. For the proportion of visits with ILI-Sp, there was an almost 9-fold difference between the tertiary ED with the lowest proportion, and the general ED with the highest proportion; there was a 16-fold difference with the pediatric ED. For ILI-Se, differences were present with a similar pattern, but proportionally less important. The proportion of visits with ILI-R tended to follow, or be inferior to, the proportion of visits with ILI-Sp – except for the pediatric hospital, where proportion of visits with ILI-R was almost 19.4%.

The same pattern of differences was seen when using data after September 20, 2009, when all EDs were participating (data not shown).

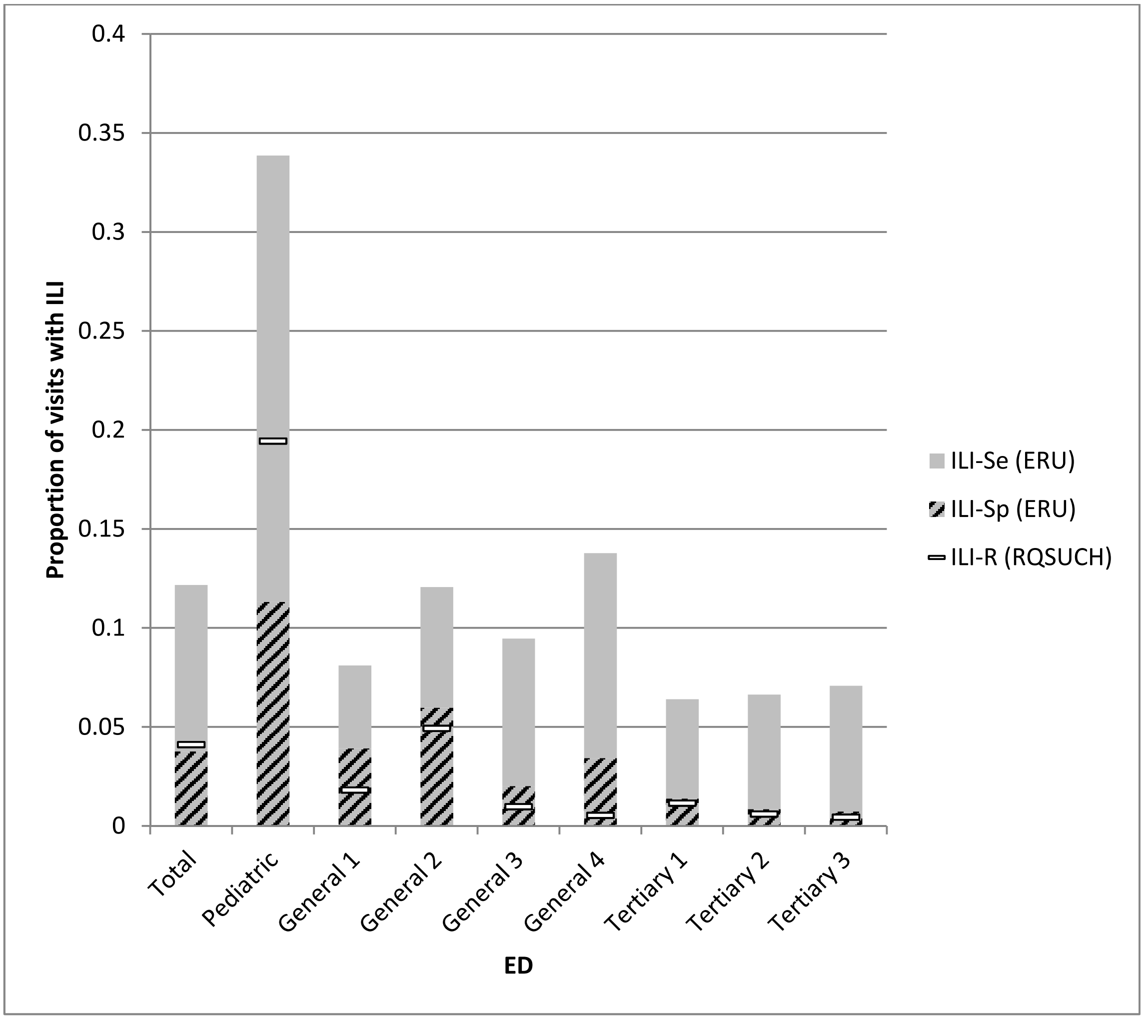

Figure 5-1. Proportion of emergency department (ED) visits with influenza-like illness (ILI), according to emergency department, data source, and syndrome definition

Mean of daily proportions, from May 7, 2008 to November 14, 2011 (Pediatric ED starting September 21, 2009; General 3 ED starting May 11, 2009)

Time-series

For all EDs aggregated, times series of both ILI-Sp and ILI-Se exhibited clear seasonal variation: yearly peaks were visible, as well as a peak for each wave of the H1N1 pandemic, as illustrated in the upper pane of Figure 5-2. ILI-Se exhibited both higher amplitude of variation and higher baseline than ILI-Sp. ILI-R tended to follow the trend of ILI-Sp. There were important differences across EDs. The lower pane of Figure 5-2 illustrates the time series for the two EDs (other than pediatric) with the highest and lowest proportions of ILI-Sp. Time series for all EDs are presented in Appendix 1, Figure A1-4. EDs with a higher proportion of ILI visits appeared to have larger seasonal variation compared to the background noise; this was not, however, tested with quantitative assessment.

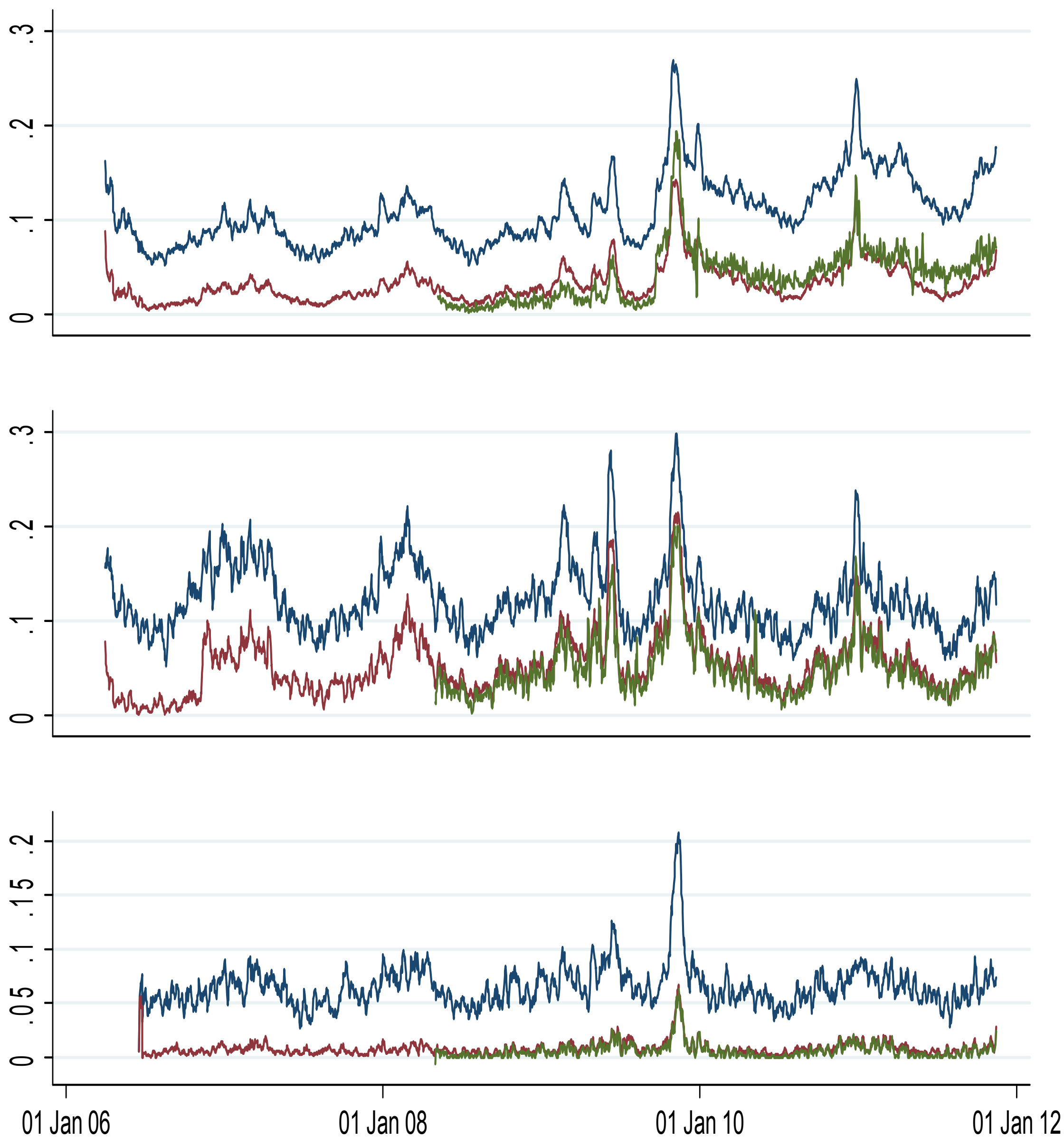

Figure 5-2. Lowess-smoothed time series of daily proportion of emergency department (ED) visits with influenza-like illness (ILI), total and selected EDs, 2006 to 2011

Total (top), general ED 2 (middle), tertiary center ED 2 (bottom)
Red: ILI-Sp, blue: ILI-Se, green: ILI-R

5.3. Correlations

The Pearson correlation between daily count of ILI-Sp and ILI-Se, aggregated over all EDs, was 0.90 (95% CI 0.89-0.91); it was 0.88 (95% CI: 0.86-0.89) between ILI-Sp and ILI-R, and 0.91 (95% CI: 0.90-0.91) between ILI-Se and ILI-R. Using Spearman's rho led to similar results. At the ED-level, Spearman's rho ranged from 0.34 to 0.78 for ILI-Sp versus ILI-Se, from 0.40 to 0.94 for ILI-Sp versus ILI-R, and from 0.28 to 0.70 for ILI-Se versus ILI-R (all different from zero with $p < 0.0001$).

Figure 5-3 illustrates the correlations between each syndrome component and counts of ILI-R. The "influenza-key word" portion of ILI-Sp or ILI-Se was perfectly correlated with ILI-R counts in one of the tertiary EDs (ρ_s =1.0000), almost perfectly correlated for the other two tertiary EDs (ρ_s=0.998, 95% CI 0.998-0.998 and ρ_s=0.992, 95% CI 0.991-0.993), and very highly correlated in one of the general EDs (ρ_s=0.95, 95% CI 0.95-0.96). Low to moderate correlations were observed for other EDs. The lowest correlations were observed for the "sore throat" and "fever + sore throat" components across EDs.

	Correlation with ILI-R (*RQSUCH*) - Spearman's *rho*							
	ERU-derived syndromes		*ERU*- derived syndrome components					
ED	ILI-Sp	ILI-Se	Fever	Cough	Sore throat	Influenza keyword	Fever + cough	Fever + sore throat
Pediatric	0.62	0.63	0.60	0.63	0.11	0.25	0.62	0.13
General 1	0.54	0.40	0.33	0.44	0.13	0.59	0.40	0.10
General 2	0.94	0.70	0.48	0.79	0.47	0.95	0.63	0.41
General 3	0.49	0.44	0.44	0.47	0.26	0.26	0.52	0.29
General 4	0.41	0.28	0.33	0.31	0.18	0.64	0.43	0.23
Tertiary 1	0.91	0.48	0.27	0.23	0.13	1.00	0.16	0.10
Tertiary 2	0.81	0.40	0.21	0.22	0.16	1.00	0.17	0.09
Tertiary 3	0.74	0.33	0.23	0.11	0.17	0.99	0.12	0.09

Figure 5-3. Correlation between *ERU*-derived syndrome components and *RQSUCH*-obtained influenza-like illness (ILI) counts

Underlying heat-map: green = high correlation, red = low correlation. $p < 0.0001$, except for cough in tertiary ED 3, sore throat in pediatric ED, and fever + sore throat in pediatric, general 1, tertiary 1, 2, and 3 EDs ($p < 0.01$). Correlations between daily counts from May 7, 2008 to November 14, 2011 (Pediatric ED starting September 21, 2009; General 3 ED starting May 11, 2009). ED: emergency department

Chapter 6: Discussion

6.1. Results, implications, and limits

Using a regression approach, we found that the use of age-, triage score-, and disposition-stratified ILI ED visits improved predictive models for P&I hospitalizations, compared to total ILI ED visits, with variable lead times. These results, their comparison with the literature, and their limitations were already discussed in the manuscript (chapter 4). A few additional points will be brought up in this chapter regarding the implication of our results for surveillance practice.

Our results suggest that integrating age, triage score, and disposition data in the influenza surveillance system for the Montreal region may assist in early detection of pandemics or epidemics with unusual severity, potentially allowing for early outbreak response and implementation of control measures, such as communications with clinicians for enhanced influenza circulation awareness, launching of a vaccination campaign and/or its extension to age groups not usually covered, opening of influenza clinics, and health care resources planning. In addition, information on age groups most affected would further inform some of these decisions, such as which age groups to prioritize for vaccination.

The lead-time provided by ILI ED visits stratified by age groups, triage score, and disposition (1 to 3 weeks), as compared to hospitalizations, makes these data available for early decision support. However, the strength of association that was found, which is at best moderate, makes it unlikely that these ILI ED data would be heavily relied upon to make important decisions regarding intervention implementation. It would be more likely that they be used in combination with other indicators to contribute to decision making.

Our results may not, however, directly translate into improved surveillance practice, due to a number of data- and method-related limitations. Some of these limitations were mentioned in the manuscript, and others are listed here. One limit is that, due to a small sample size, analysis was done with weekly data, as opposed to daily data. In addition, the EDs in the study might not be representative of all EDs deserving the population of the Montreal region. Furthermore, a small percentage of visits are not captured by the chief complaint, and might differ in terms of reason for visit and/or severity. However, this percentage remained small and fairly constant over time, and should not affect our results significantly. Finally, from a prediction perspective, the scope of this study was limited to the initial modeling step. A next step would be to test those predictive models on new data not used for model fitting. There would then still be a need to assess whether using covariates such as age, triage score, or disposition in a surveillance system actually leads to improved or timelier decision making, in terms of control measures and communications.

6.2. System limitations

In addition to the limitations of the study *per se*, there are also limitations to the use of the *ERU* database for surveillance, in particular pertaining to the choice of syndrome definition. The validity of age-, triage score-, and disposition-stratified ILI data depends to some extent on the validity of the ILI syndrome definition.

The proportions of ED visits with ILI, both specific and sensitive definitions, varied widely across EDs. Similarly, the seasonal variability of ILI visits was highly ED-dependent. Notably, the three tertiary center EDs exhibited very low proportion of ILI-Sp visits, and ILI-Sp time series with very little variation. This aspect should be considered in choosing a syndrome definition, since a time series with so few counts and so little variation is likely to lack informative potential. On the other hand, some of the general EDs had a high proportion of ILI-Sp visits, and an ILI-Sp time series with high seasonal variability. This is also an important consideration for syndrome definition selection: in those cases, the specific definition may be most appropriate, and a sensitive definition may only add to the background noise.

One likely explanation for these differences in ILI visit proportions and time series is the differences in patient characteristics such as age. The pediatric ED had, by far, the highest proportion of ILI visits, while the adult tertiary centers had the lowest. The general EDs, which are open to all age groups, displayed intermediate ILI visit ratios.

Another likely explanation is that there were important differences between EDs in the way the chief complaint was entered. In some EDs, an average of 1.4 codes was entered for each visit, in contrast to up to 6.2 on average in one of the general hospital EDs. This difference is likely to affect the proportion of visits meeting the ILI definition, especially the specific definition. If only one code (which often corresponds to only one symptom) is entered, visits are not likely to meet the "fever + cough" or "fever + sore throat" portions of the definition. This was likely the case for the three tertiary center EDs, which exhibited very low proportion of ILI-Sp visits, and ILI-Sp time series with very little variation.

On the other hand, one of the general hospital EDs, despite using 1.5 codes per visit, had a high proportion of ILI-Sp visits, and an ILI-Sp time series with high seasonal variability. This finding suggests the general hospital EDs either have a different patient population from the adult tertiary centers, different chief complaint coding practices, or both. In terms of coding practices, the staff in a given ED may be instructed, or have the habit, to preferentially select codes like "flu", or codes containing more than one symptom (such as "cough with fever"), as opposed to codes such as "fever" or "cough". Coding practices have not been investigated in this study, but it may be relevant to do so if such an investigation could inform the choice of a syndrome definition for surveillance purposes.

Another challenge in choosing a syndrome definition is the difficulty in obtaining a gold standard against which to assess the studied definitions. In our study, counts of both ILI-Sp and ILI-Se were highly correlated with counts of ILI reported by EDs via *RQSUCH* (ILI-R). ILI-R itself is based on the clinical definition "fever + cough". It is not surprising then that the "sore throat" component from the *ERU* chief complaints, with or without "fever", was least correlated with ILI-R counts.

Fever and cough have been identified in a number of clinical studies as the most common symptoms in patients with laboratory-proven influenza (Babcock *et al.* 2006; Boivin *et al.* 2000; Monto *et al.* 2000; Thursky *et al.* 2003), potentially making ILI-R, if not a gold standard for ILI visits, at least a good comparator. However, we do not know of the way this clinical definition is applied locally in each ED, that is, whether ILI-R counts truly reflect the counts of patients with fever and cough. It would thus be worth investigating the way ILI-R counts are obtained and reported in each ED, and evaluate whether they could be used as a gold standard against which to validate ILI definitions applied to the *ERU* data. If ILI-R counts are deemed to be an appropriate gold standard for ILI visits, then the correlations at the ED level between ILI-R and each symptom derived from *ERU* (such as illustrated in Figure 5-3) may be used to identify syndrome definitions that would be most appropriate for each ED.

Despite these limitations, however, our results on the predictive value of age, triage score, and disposition data appeared to be robust to the choice of ILI syndrome definition.

6.3. Recommendations

Our study leads us to make a few recommendations regarding the future use of the *ERU* database for ILI surveillance, in terms of choice of syndrome definition and integration of age, triage score, and disposition as covariates; many of these are also generalizable to other surveillance systems.

Our first recommendation, which should apply to any surveillance system, is to gain a thorough understanding of all the steps involved in generating surveillance data, starting at the data collection level. Knowledge of these metadata is important for choosing syndrome definitions and for interpreting surveillance data from the system.

Our second recommendation is to standardize, as much as possible, the way manual reporting and electronic record systems are used at the ED level. However, this might not always be feasible, in Montreal or elsewhere. In the event where standardization of local practices is not feasible, our recommendation is to either 1) use one syndrome definition that performs best at the aggregated (regional) level, acknowledging that it might not be ideal at the ED level or 2) keep more than one syndrome definition in the surveillance system.

Performance at the aggregated level may be assessed against a gold standard. ILI-R counts from RQSUCH may be deemed, after investigation on how they are obtained, to be a sufficiently adequate comparator. Alternatively, virological data could be used as a gold standard against which to compare candidate definitions. This is the most common approach in studies validating ILI syndrome definitions (Marsden-Haug *et al.* 2007; Moore *et al.* 2011; Olson *et al.* 2007; Paladini *et al.* 2008; Schindeler *et al.* 2009; Zheng *et al.* 2007).

The second option – to keep more than one syndrome definition in the surveillance system – may be a valid option in Montreal, especially if inter-hospital differences in the way they use the electronic record system are expected to persist, in order to keep at least one definition that would be appropriate for each ED. Using more than one influenza syndrome definitions in parallel within the same surveillance system has been proposed by others, although their stated objective was to improve characterization of the situation, rather than account for inter-hospital differences (Pendarvis *et al.* 2007). Options 1) and 2) may also be combined, keeping one definition performing best at the aggregated (regional) level, and local definitions for individual or subsets of EDs.

Once it is deemed feasible to use *ERU* for ILI surveillance, age, triage score, and disposition data may be integrated into the system. However, their usefulness should be evaluated concomitantly. First, the predictive models obtained in this study should be tested against new data collected. This would allow validation – or invalidation – of the predictive value of age-, triage-, or disposition-specific ILI counts for P&I hospitalizations. Their practical, day-to-day utility should also be evaluated. Qualitative and/or quantitative aspects may be included, addressing the central question of whether, and how, adding age, triage score, and disposition data changs influenza surveillance practice, related decision-making, and intervention implementation. Ultimately, the objective of applying the results of this study to public health practice is to decrease influenza-related morbidity and mortality at the population level. It would be unrealistic at this point to aim at measuring population-level effects on morbidity and attributing them to the addition of markers in the surveillance system. Nonetheless, having an effect on the practice of surveillance is an intermediate objective that can, and should, be documented.

Chapter 7: Conclusion

In this study, we found that adding age, triage score, and disposition data to ILI counts from ED electronic records improved prediction for P&I hospitalizations. We conclude that these data may be useful in a surveillance system for influenza, with a focus on severe illness. They would allow monitoring rates of ILI ED visits with more severe presentations or outcomes, and ILI ED visit rates in age subgroups that predict later hospitalizations counts. In either case, they would provide a real-time marker of influenza activity with an emphasis on severe cases.

Use of these covariates in Montreal is feasible, as they are available through the *ERU* electronic record database. However, there are practical challenges that must first be addressed, notably the standardization of the way the system is used and the choice of a syndrome definition appropriate at the ED level. Furthermore, an important step in implementation would be to test their practical utility, since the goal of integrating information into an influenza surveillance system, in Montreal or elsewhere, is to assist public health practioners in their decision making, communications, and interventions, and, ultimately, to improve health outcomes related to influenza in the population they serve.

References

Agence de la santé et des services sociaux de Montréal. (2011). Espace montréalais d'information sur la santé Retrieved August 19, 2011, from http://emis.santemontreal.qc.ca/

Babcock, H. M., Merz, L. R., & Fraser, V. J. (2006). Is influenza an influenza-like illness? Clinical presentation of influenza in hospitalized patients. *Infection Control and Hospital Epidemiology, 27*(3), 266-270.

Beard, F., McIntyre, P., Gidding, H., & Watson, M. (2006). Influenza related hospitalisations in Sydney, New South Wales, Australia. *Archives of Disease in Childhood, 91*(1), 20-25.

Berenbaum, P., Gibson, M., & Blevins, L. Z. (2007). Accuracy versus Timeliness for Influenza Detection: A Comparison of Hospital Syndromic Surveillance Data with Discharge Data. *Advances in Disease Surveillance, 2*(93).

Boivin, G., Hardy, I., Tellier, G., & Maziade, J. (2000). Predicting Influenza Infections during Epidemics with Use of a Clinical Case Definition. *Clinical Infectious Diseases, 31*(5), 1166-1169.

Bourgeois, F. T., Olson, K. L., Brownstein, J. S., McAdam, A. J., & Mandl, K. D. (2006). Validation of syndromic surveillance for respiratory infections. *Annals of Emergency Medicine, 47*(3), 265 e261.

Bozdogan, H. (1987). Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. *Psychometrika, 52*(3), 345-370.

Brammer, L., Budd, A., & Cox, N. (2009). Seasonal and pandemic influenza surveillance considerations for constructing multicomponent systems. *Influenza and Other Respiratory Viruses, 3*(2), 51-58.

Brownstein, J. S., Kleinman, K. P., & Mandl, K. D. (2005). Identifying pediatric age groups for influenza vaccination using a real-time regional surveillance system. *American Journal of Epidemiology, 162*(7), 686-693.

Buckeridge, D. L. (2011). Comments on ‘Some methodological issues in biosurveillance’. *Statistics in Medicine, 30*(5), 420-422.

Buehler, J. W., Sonricker, A., Paladini, M., Soper, P., & Mostashari, F. (2008). Syndromic Surveillance Practice in the United States: Findings from a Survey of State, Territorial, and Selected Local Health Departments. *Advances in Disease Surveillance, 6*(3), 1-20.

Buehler, J. W., Whitney, E. A., Smith, D., Prietula, M. J., Stanton, S. H., & Isakov, A. P. (2009). Situational uses of syndromic surveillance. *Biosecur Bioterror, 7*(2), 165-177.

Burkom, H., Olson, D., Paladini, M., Baer, A., Revere, D., & McIntyre, A. (2011). *Analytic evaluation of a standardization effort for the Distribute emergency department surveillance project.* Paper presented at the Joint Statistical Meetings, Miami, Florida.

Burkom, H. S. (2011). Comments on 'some methodological issues in biosurveillance'. *Statistics in Medicine, 30*(5), 426-429; discussion 434-441.

Cadieux, G., Buckeridge, D., Jacques, A., Libman, M., Dendukuri, N., & Tamblyn, R. (2011). Accuracy of syndrome definitions based on diagnoses in physician claims. *BMC Public Health, 11*(1), 17.

Carrat, F., Tachet, A., Rouzioux, C., Housset, B., & Valleron, A.-J. (1999). Evaluation of Clinical Case Definitions of Influenza: Detailed Investigation of Patients During the 1995–1996 Epidemic in France. *Clinical Infectious Diseases, 28*(2), 283-290.

Center for Disease Control and Prevention. (2011). Overview of Influenza Surveillance in the United States Retrieved May 22, 2012, from http://www.cdc.gov/flu/weekly/overview.htm

Chan, E. H., Tamblyn, R., Charland, K. M. L., & Buckeridge, D. L. (2011). Outpatient physician billing data for age and setting specific syndromic surveillance of influenza-like illnesses. *Journal of Biomedical Informatics, 44*(2), 221-228.

Chapman, W. W., Dowling, J. N., Baer, A., Buckeridge, D. L., Cochrane, D., Conway, M. A., . . . Lober, B. (2010). Developing syndrome definitions based on consensus and current use. *Journal of the American Medical Informatics Association, 17*(5), 595-601.

Chiu, S. S., Lau, Y. L., Chan, K. H., Wong, W. H., & Peiris, J. S. (2002). Influenza-related hospitalizations among children in Hong Kong. *New England Journal of Medicine, 347*(26), 2097-2103.

Christ, M., Grossmann, F., Winter, D., Bingisser, R., & Platz, E. (2010). Modern triage in the emergency department. *Dtsch Arztebl Int, 107*(50), 892-898.

Cleveland, W. S. (1979). Robust locally weighted regression and smoothing scatterplots. *Journal of the American Statistical Association, 74*(368), 829-836.

Cochrane, D. G., Allegra, J. R., McCarthy, C., Luk, J., Chang, H.-G., & Chen, J.-H. (2008). The Utility of Patient Chief Complaint and ICD 9 Classifiers for the Influenza Sub-syndrome. *Advances in Disease Surveillance, 5*(15).

Dailey, L., Watkins, R. E., & Plant, A. J. (2007). Timeliness of data sources used for influenza surveillance. [Article]. *Journal of the American Medical Informatics Association, 14*(5), 626-631.

Dara, J., Dowling, J. N., Travers, D., Cooper, G. F., & Chapman, W. W. (2008). Evaluation of preprocessing techniques for chief complaint classification. *J Biomed Inform, 41*(4), 613-623.

Das, D., Olson, D., & Heffernan, R. (2007). Estimating Hospital Admissions for Influenza Using Emergency Department (ED) Syndromic Surveillance Data, New York City. *Advances in Disease Surveillance, 2*(150).

Dong, S. L., Bullard, M. J., Meurer, D. P., Blitz, S., Akhmetshin, E., Ohinmaa, A., . . . Rowe, B. H. (2007). Predictive validity of a computerized emergency triage tool. *Academic Emergency Medicine, 14*(1), 16-21.

Fricker, R. D. (2011). Some methodological issues in biosurveillance. *Statistics in Medicine, 30*(5), 403-415.

Gilca, R., De Serres, G., Skowronski, D., Boivin, G., & Buckeridge, D. L. (2009). The Need for Validation of Statistical Methods for Estimating Respiratory

Virus–Attributable Hospitalization. *American Journal of Epidemiology, 170*(7), 925-936.

Hanni, K. D. (2011). Comments on 'Some methodological issues in biosurveillance'. *Statistics in Medicine, 30*(5), 423-425.

Hardelid, P., Pebody, R., & Andrews, N. (2012). Mortality caused by influenza and respiratory syncytial virus by age group in England and Wales 1999-2010. *Influenza Other Respi Viruses*.

Helferty, M., Vachon, J., Tarasuk, J., Rodin, R., Spika, J., & Pelletier, L. (2010). Incidence of hospital admissions and severe outcomes during the first and second waves of pandemic (H1N1) 2009. *Canadian Medical Association Journal, 182*(18), 1981-1987.

Izurieta, H. S., Thompson, W. W., Kramarz, P., Shay, D. K., Davis, R. L., DeStefano, F., . . . Fukuda, K. (2000). Influenza and the rates of hospitalization for respiratory disease among infants and young children. *New England Journal of Medicine, 342*(4), 232-239.

Jimenez, J. G., Murray, M. J., Beveridge, R., Pons, J. P., Cortes, E. A., Garrigos, J. B., & Ferre, M. B. (2003). Implementation of the Canadian Emergency Department Triage and Acuity Scale (CTAS) in the Principality of Andorra: Can triage parameters serve as emergency department quality indicators? *CJEM, 5*(5), 315-322.

Lemay, R., Mawudeku, A., Shi, Y., Ruben, M., & Achonu, C. (2008). Syndromic surveillance for influenzalike illness. *Biosecur Bioterror, 6*(2), 161-170.

Lewis, M. D., Pavlin, J. A., Mansfield, J. L., O'Brien, S., Boomsma, L. G., Elbert, Y., & Kelley, P. W. (2002). Disease outbreak detection system using syndromic data in the greater Washington DC area. *American Journal of Preventive Medicine, 23*(3), 180-186.

Mangtani, P., Hajat, S., Kovats, S., Wilkinson, P., & Armstrong, B. (2006). The association of respiratory syncytial virus infection and influenza with emergency admissions for respiratory disease in London: an analysis of routine surveillance data. *Clinical Infectious Diseases, 42*(5), 640-646.

Marsden-Haug, N., Foster, V. B., Gould, P. L., Elbert, E., Wang, H., & Pavlin, J. A. (2007). Code-based syndromic surveillance for influenzalike illness by International Classification of Diseases, Ninth Revision. *Emerging Infectious Diseases, 13*(2), 207-216.

May, L. S., Griffin, B. A., Bauers, N. M., Jain, A., Mitchum, M., Sikka, N., . . . Stoto, M. A. (2010). Emergency department chief complaint and diagnosis data to detect influenza-like illness with an electronic medical record. *West J Emerg Med, 11*(1), 1-9.

Monto, A. S., Gravenstein, S., Elliott, M., Colopy, M., & Schweinle, J. (2000). Clinical signs and symptoms predicting influenza infection. *Archives of Internal Medicine, 160*(21), 3243-3247.

Moore, K., Black, J., Rowe, S., & Franklin, L. (2011). Syndromic surveillance for influenza in two hospital emergency departments. Relationships between ICD-10 codes and notified cases, before and during a pandemic. *BMC Public Health, 11*, 338.

Moore, K. M., Edgar, B. L., & McGuinness, D. (2008). Implementation of an automated, real-time public health surveillance system linking emergency departments and health units: rationale and methodology. *2008, 10*(2), 114-119.

Murray, E. L. (2008). Using Emergency Department Disposition Data to Monitor Hospitalizations for Influenza-like Illness. *Advances in Disease Surveillance, 5*(183), 1.

Muscatello, D. J., Morton, P. M., Evans, I., & Gilmour, R. (2008). Prospective surveillance of excess mortality due to influenza in New South Wales: feasibility and statistical approach. *Communicable Diseases Intelligence, 32*(4), 435-442.

Musumba, A., Feist, M., Kubischta, L., Miller, T., & Goplin, J. (2008). Evaluation of ILI data use to augment traditional Influenza Surveillance. *Advances in Disease Surveillance, 5*(120).

Neuzil, K. M., Mellen, B. G., Wright, P. F., Mitchel, E. F., Jr., & Griffin, M. R. (2000). The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. *New England Journal of Medicine, 342*(4), 225-231.

Newall, A. T., Viboud, C., & Wood, J. G. (2010). Influenza-attributable mortality in Australians aged more than 50 years: a comparison of different modelling approaches. *Epidemiology and Infection, 138*(6), 836-842.

Nicholson, K. G. (1996). Impact of influenza and respiratory syncytial virus on mortality in England and Wales from January 1975 to December 1990. *Epidemiology and Infection, 116*(1), 51-63.

Nicholson, K. G., Wood, J. M., & Zambon, M. (2003). Influenza. *The Lancet, 362*(9397), 1733-1745.

Nunes, B., Viboud, C., Machado, A., Ringholz, C., Rebelo-de-Andrade, H., Nogueira, P., & Miller, M. (2011). Excess mortality associated with influenza epidemics in Portugal, 1980 to 2004. *PLoS ONE, 6*(6), e20661.

Olson, D. R., Heffernan, R. T., Paladini, M., Konty, K., Weiss, D., & Mostashari, F. (2007). Monitoring the impact of influenza by age: emergency department fever and respiratory complaint surveillance in New York City. *PLoS Medicine, 4*(8), e247.

Olson, D. R., Paladini, M., Lober, W. B., & Buckeridge, D. L. (2011). Applying a New Model for Sharing Population Health Data to National Syndromic Influenza Surveillance: DiSTRIBuTE Project Proof of Concept, 2006 to 2009. *PLoS Curr, 3*, RRN1251.

Olszewski, R. T. (2003). Bayesian classification of triage diagnoses for the early detection of epidemics. In A. Cohn & K. Ford (Eds.), *Proceedings of the FLAIRS Conference*. Menlo Park, CA AAAI Press.

Paladini, M., Pendarvis, J., Murray, E. L., Gunn, J., & Olson, D. (2008). A Comparison of Locally Developed Influenza-like Syndrome Definitions Using Electronic Emergency Department Data in Boston and New York City. *Advances in Disease Surveillance, 5*(50), 1.

Pendarvis, J., Gunn, J., Smith, A. K., Donovan, M., & Barry, A. (2007). Sneezes vs. Wheezes: Syndrome Definitions for Influenza-like Illness. *Advances in Disease Surveillance, 2*(115), 1.

Public Health Agency of Canada. (2012). Flu Watch Retrieved June 18, 2012, from http://www.phac-aspc.gc.ca/fluwatch/11-12/def11-12-eng.php

Schanzer, D., Vachon, J., & Pelletier, L. (2011). Age-specific Differences in Influenza A Epidemic Curves: Do Children Drive the Spread of Influenza Epidemics? *American Journal of Epidemiology*.

Schindeler, S. K., Muscatello, D. J., Ferson, M. J., Rogers, K. D., Grant, P., & Churches, T. (2009). Evaluation of alternative respiratory syndromes for specific syndromic surveillance of influenza and respiratory syncytial virus: a time series analysis. *BMC Infectious Diseases, 9*, 190.

Sebastian, R., Skowronski, D. M., Chong, M., Dhaliwal, J., & Brownstein, J. S. (2008). Age-related trends in the timeliness and prediction of medical visits, hospitalizations and deaths due to pneumonia and influenza, British Columbia, Canada, 1998-2004. *Vaccine, 26*(10), 1397-1403.

Serfling, R. E. (1963). Methods for current statistical analysis of excess pneumonia-influenza deaths. *Public Health Reports, 78*(6), 494-506.

Shmueli, G. (2010). To explain or to predict. *Statistical Science, 25*(3), 289-310.

Shmueli, G., & Burkom, H. (2010). Statistical Challenges Facing Early Outbreak Detection in Biosurveillance. *Technometrics, 52*(1), 39-51.

Simonsen, L., Clarke, M. J., Williamson, G. D., Stroup, D. F., Arden, N. H., & Schonberger, L. B. (1997). The impact of influenza epidemics on mortality: introducing a severity index. *Am J Public Health, 87*(12), 1944-1950.

Soebiyanto, R. P., Adimi, F., & Kiang, R. K. (2010). Modeling and predicting seasonal influenza transmission in warm regions using climatological parameters. *PLoS ONE, 5*(3), e9450.

Suhartono. (2011). Time Series Forecasting by using Seasonal Autoregressive Integrated Moving Average: Subset, Multiplicative or Additive Model. *Journal of Mathematics and Statistics, 7*(1), 20-27.

Thompson, W. W., Comanor, L., & Shay, D. K. (2006). Epidemiology of seasonal influenza: use of surveillance data and statistical models to estimate the burden of disease. *Journal of Infectious Diseases, 194 Suppl 2*, S82-91.

Thompson, W. W., Shay, D. K., Weintraub, E., Brammer, L., Bridges, C. B., Cox, N. J., & Fukuda, K. (2004). Influenza-associated hospitalizations in the United States. *JAMA, 292*(11), 1333-1340.

Thompson, W. W., Weintraub, E., Dhankhar, P., Cheng, P. Y., Brammer, L., Meltzer, M. I., . . . Shay, D. K. (2009). Estimates of US influenza-associated deaths made using four different methods. *Influenza Other Respi Viruses, 3*(1), 37-49.

Thursky, K., Cordova, S. P., Smith, D., & Kelly, H. (2003). Working towards a simple case definition for influenza surveillance. *Journal of Clinical Virology, 27*(2), 170-179.

Townes, J. M., Kohn, M. A., Southwick, K. L., Bangs, C. A., Zechnich, A. D., Magnuson, J. A., & Jui, J. (2004). Investigation of an electronic emergency department information system as a data source for respiratory syndrome surveillance. *Journal of Public Health Management and Practice, 10*(4), 299-307.

Tsui, F. C., Wagner, M. M., Dato, V., & Chang, C. C. (2001). Value of ICD-9 coded chief complaints for detection of epidemics. *Proceedings / Amia Symposium*, 711-715.

Tsui, K.-L., Chiu, W., Gierlich, P., Goldsman, D., Liu, X., & Maschek, T. (2008). A Review of Healthcare, Public Health, and Syndromic Surveillance. *Quality Engineering, 20*(4), 435-450.

Upshur, R. E., 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. *American Journal of Epidemiology, 149*(1), 85-92.

van den Wijngaard, C., van Asten, L., van Pelt, W., Nagelkerke, N. J., Verheij, R., de Neeling, A. J., . . . Koopmans, M. P. (2008). Validation of syndromic surveillance for respiratory pathogen activity. *Emerging Infectious Diseases, 14*(6), 917-925.

van den Wijngaard, C. C., van Pelt, W., Nagelkerke, N. J., Kretzschmar, M., & Koopmans, M. P. (2011). Evaluation of syndromic surveillance in the

Netherlands: its added value and recommendations for implementation. *Euro Surveill, 16*(9).

Wong, C. M., Yang, L., Chan, K. P., Leung, G. M., Chan, K. H., Guan, Y., . . . Peiris, J. S. (2006). Influenza-associated hospitalization in a subtropical city. *PLoS Medicine, 3*(4), e121.

World Health Organization. (2006). WHO Recommended Surveillance Standards, 2nd edn. Retrieved April 4, 2012, from http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_CSR_ISR_99_2_EN/en/

Yang, L., Chiu, S. S., Chan, K.-P., Chan, K.-H., Wong, W. H.-S., Peiris, J. S. M., & Wong, C.-M. (2011). Validation of Statistical Models for Estimating Hospitalization Associated with Influenza and Other Respiratory Viruses. *PLoS ONE, 6*(3), e17882.

Zeger, S. L., Irizarry, R., & Peng, R. D. (2006). On time series analysis of public health and biomedical data. *Annual Review of Public Health, 27*(1), 57-79.

Zheng, W., Aitken, R., Muscatello, D. J., & Churches, T. (2007). Potential for early warning of viral influenza activity in the community by monitoring clinical diagnoses of influenza in hospital emergency departments. *BMC Public Health, 7*, 250.

Zhou, H., Thompson, W. W., Viboud, C. G., Ringholz, C. M., Cheng, P.-Y., Steiner, C., . . . Shay, D. K. (2012). Hospitalizations Associated With Influenza and Respiratory Syncytial Virus in the United States, 1993–2008. *Clinical Infectious Diseases*.

Appendix 1: Descriptive statistics and time series

Table A1-I. Number of emergency department (ED) visits: daily mean per period of analysis, *ERU*

	ED visits, daily mean (95% confidence interval)		
ED	date of entry[1] – Nov 14, 2011	May 7, 2008 - Nov 14, 2011	June 25, 2006 – Jan 29, 2011
Pediatric	210.7 (208.3-213.0)	-	-
General 1	100.4 (99.9-100.9)	98.9 (98.2-99.5)	100.8 (100.2-101.3)
General 2	106.8 (106.3-107.4)	102.5 (101.9-103.2)	108.2 (107.6-108.8)
General 3	117.2 (116.3-118.1)	-	-
General 4	78.9 (78.4-79.3)	77.6 (77.1-78.1)	-
Tertiary 1	115.8 (115.1-116.4)	116.4 (115.6-117.2)	115.7 (115.0-116.4)
Tertiary 2	112.5 (111.8-113.1)	112.1 (111.3-112.9)	112.8 (112.1-113.6)
Tertiary 3	81.3 (80.8-81.9)	80.4 (79.7-81.1)	81.3 (80.7-81.9)
Total	701.8 (693.5-710.2)[2]	587.8 (584.9-590.8)[3]	518.9 (516.5-521.2)[3]

[1]Pediatric: November 20, 2009; General 1 and 2: April 1, 2006; General 3: May 11, 2009; General 4: April 1, 2007; Tertiary 1 to 3: June 24, 2006
[2] Each ED included starting on its entry date
[3] Includes EDs with complete data for analysis period

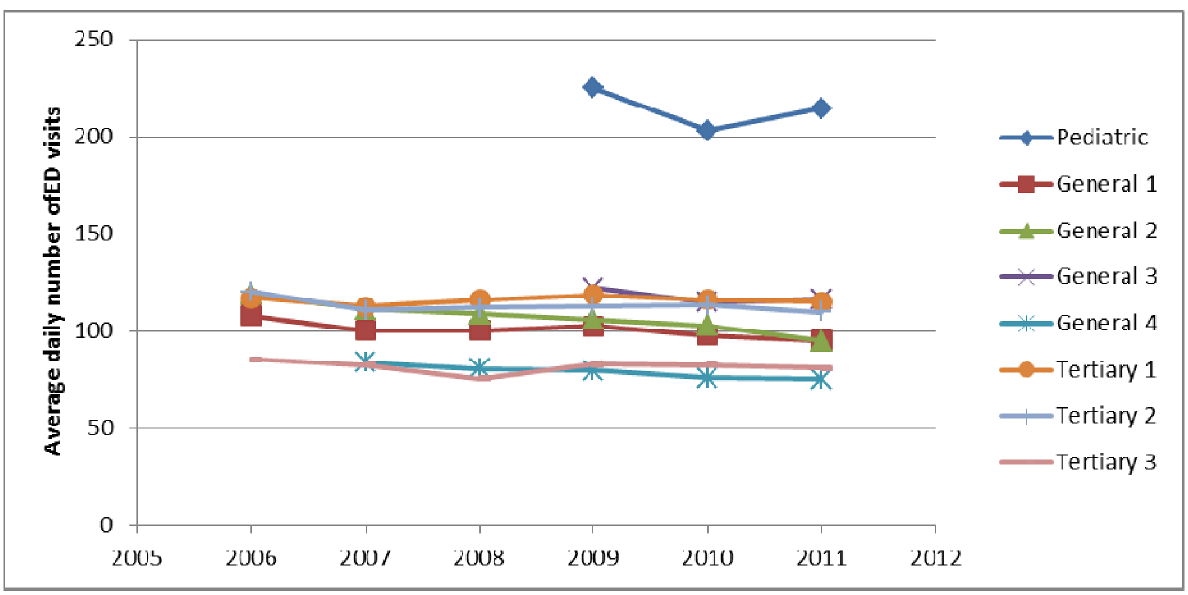

Figure A1-1. Average daily number of emergency department (ED) visits, stratified per year and ED, 2006 to 2011

Table A1-II. Proportion of emergency department (ED) visits with chief complaints recorded: daily mean per period of analysis, *ERU*

	Proportion of visits with chief complaint recorded, daily mean (95% confidence interval)		
ED	date of entry[1] – Nov 14, 2011	May 7, 2008 - Nov 14, 2011	June 25, 2006 – Jan 29, 2011
Pediatric	89.2% (88.5%-89.9%)	-	-
General 1	99.9% (99.9%-99.9%)	99.8% (99.8%-99.9%)	99.9% (99.9%-100.0%)
General 2	89.1% (88.8%-89.4%)	91.5% (91.3%-91.8%)	89.3% (88.9%-89.6%)
General 3	97.8% (97.7%-97.9%)	-	-
General 4	99.9% (99.9%-99.9%)	99.9% (99.9%-99.9%)	-
Tertiary 1	99.7% (99.7%-99.8%)	99.8% (99.7%-99.8%)	99.7% (99.7%-99.7%)
Tertiary 2	100.0% (99.9%-100.0%)	100.0% (99.9%-100.0%)	100.0% (99.9%-100.0%)
Tertiary 3	100.0% (100.0%-100.0%)	100.0% (100.0%-100.0%)	100.0% (100.0%-100.0%)
Total	96.7% (96.6%-96.8%)[2]	98.4% (98.4%-98.5%)[3]	97.7% (97.6%-97.7%)[3]

[1]Pediatric: November 20, 2009; General 1 and 2: April 1, 2006; General 3: May 11, 2009; General 4: April 1, 2007; Tertiary 1 to 3: June 24, 2006
[2] Each ED included starting on its entry date
[3] Includes EDs with complete data for analysis period

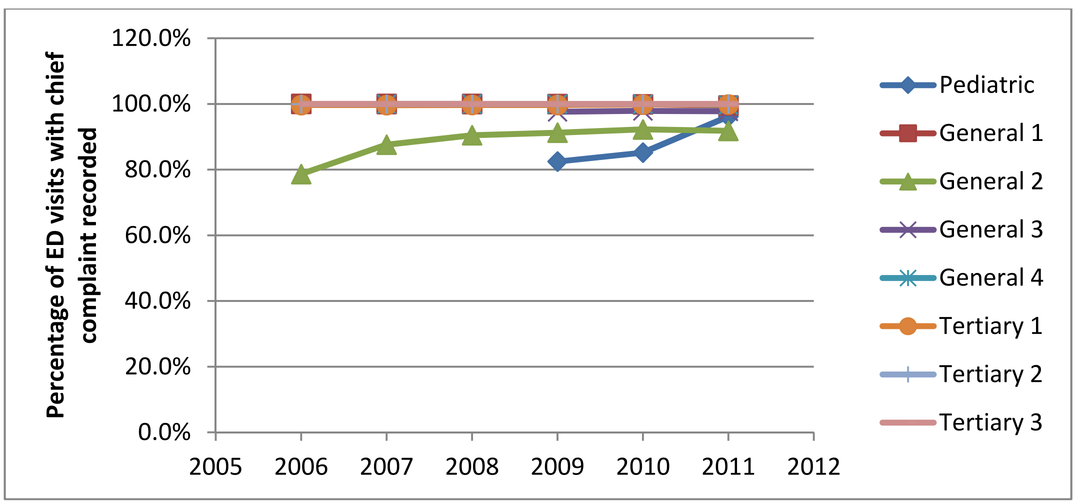

Figure A1-2. Proportion of emergency department (ED) visits with chief complaint recorded: daily mean stratified per year and ED, 2006 to 2011

Table A1-III. Mean number of chief complaint codes per emergency department (ED) visits, per period of analysis

	Number of chief complaint codes recorded per visit, mean (95% confidence interval)		
ED	date of entry[1] – Nov 14, 2011	May 7, 2008 - Nov 14, 2011	June 25, 2006 – Jan 29, 2011
Pediatric	4.04 (4.02-4.06)	-	-
General 1	2.48 (2.47-2.49)	2.40 (2.38-2.41)	2.42 (2.41-2.42)
General 2	1.46 (1.46-1.46)	1.45 (1.45-1.46)	1.44 (1.44-1.45)
General 3	4.64 (4.63-4.66)	-	-
General 4	6.23 (6.21-6.24)	6.32 (6.30-6.34)	-
Tertiary 1	1.50 (1.49-1.50)	1.50 (1.49-1.50)	1.49 (1.49-1.50)
Tertiary 2	1.44 (1.44-1.44)	1.43 (1.43-1.44)	1.44 (1.44-1.45)
Tertiary 3	1.53 (1.53-1.54)	1.57 (1.56-1.57)	1.52 (1.52-1.53)
Total	2.59 (2.59-2.59)[2]	2.29 (2.28-2.29)[3]	1.66 (1.66-1.66)[3]

[1]Pediatric: November 20, 2009; General 1 and 2: April 1, 2006; General 3: May 11, 2009; General 4: April 1, 2007; Tertiary 1 to 3: June 24, 2006
[2] Each ED included starting on its entry date
[3] Includes EDs with complete data for analysis period

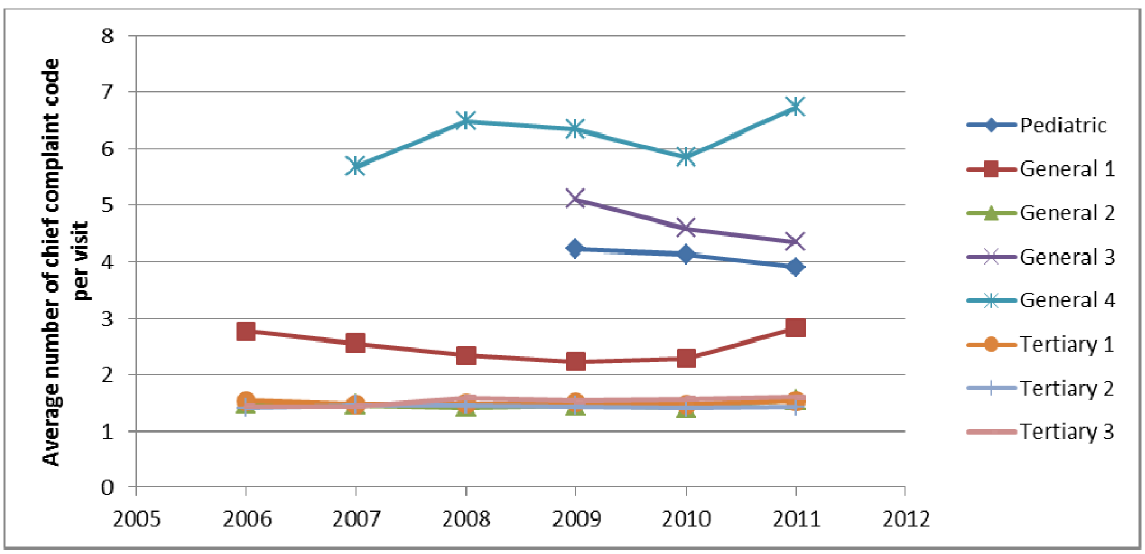

Figure A1-3. Mean number of chief complaint codes per emergency department (ED) visits, stratified per year and ED

Table A1-IV. Number of emergency department (ED) visits obtained from *ERU* and *RQSUCH*: daily mean, percent agreement, and outliers

ED	Period[1]	N (days)	Number of ED visits daily mean (95% CI)		Percent agreement		Percent outliers - *RQSUCH*	Number of ED visit, daily mean (95% CI) – *RQSUCH,* outliers removed
			ERU	*RQSUCH*	perfect	within 1 visit		
Pediatric	2009/09/20-2011/11/14	785	210.7 (208.3-213.0)	210.9 (208.6-213.3)	94.5%	95.9%	0.00%	210.9 (208.6-213.3)
General 1	2008/05/07-2011/11/14	1287	98.9 (98.2-99.5)	98.4 (97.7-99.1)	95.7%	98.5%	0.54%	98.9 (98.2-99.5)
General 2	2008/05/07-2011/11/14	1287	102.5 (101.9-103.2)	101.9 (101.2-102.7)	92.7%	98.5%	0.78%	102.6 (101.9-103.2)
General 3	2009/05/11-2011/11/14	918	117.2 (116.3-118.1)	116.9 (115.9-117.9)	80.2%	93.5%	0.44%	117.3 (116.4-118.3)
General 4	2008/05/07-2011/11/14	1287	77.6 (77.1-78.1)	77.1 (76.4-77.8)	78.8%	92.6%	1.24%	78.0 (77.4-78.5)
Tertiary 1	2008/05/07-2011/11/14	1287	116.4 (115.6-117.2)	116.4 (115.6-117.2)	99.4%	99.9%	0.00%	116.4 (115.6-117.2)
Tertiary 2	2008/05/07-2011/11/14	1287	112.1 (111.3-112.9)	112.2 (111.4-113.0)	92.8%	99.1%	0.00%	112.2 (111.4-113.0)
Tertiary 3	2008/05/07-2011/11/14	1287	80.4 (79.7-81.1)	80.5 (79.8-81.1)	98.8%	99.5%	0.08%	80.4 (79.7-81.1)
Total	2008/05/07-2011/11/14[2]	1287	799.9 (791.4-808.5)	798.5 (789.9-807.1)	91.9%[3]	97.4%[3]	0.40%[3]	801.0 (792.3-809.7)

[1] YYYY/MM/DD
[2] Pediatric ED included starting September 21, 2009; General 3 ED included starting May 11, 2009
[3] Average over all EDs, weighted for the number of days participating
CI: confidence interval

Table A1-V. Proportion of emergency department (ED) visits with ILI-Sp: daily mean per period of analysis, *ERU*

	Proportion of ED visits with ILI-Sp, daily mean (95% confidence interval)		
ED	date of entry[1] – Nov 14, 2011	May 7, 2008 - Nov 14, 2011	June 25, 2006 – Jan 29, 2011
Pediatric	11.3% (10.9%-11.7%)	-	-
General 1	3.8% (3.7%-3.9%)	3.9% (3.8%-4.1%)	3.9% (3.8%-4.0%)
General 2	5.3% (5.2%-5.5%)	6.0% (5.7%-6.2%)	5.6% (5.4%-5.8%)
General 3	2.0% (1.9%-2.2%)	-	-
General 4	3.5% (3.4%-3.7%)	3.4% (3.3%-3.6%)	-
Tertiary 1	1.3% (1.2%-1.3%)	1.4% (1.3%-1.5%)	1.3% (1.2%-1.4%)
Tertiary 2	0.8% (0.7%-0.8%)	0.9% (0.8%-0.9%)	0.8% (0.7%-0.8%)
Tertiary 3	0.7% (0.6%-0.7%)	0.7% (0.7%-0.8%)	0.7% (0.7%-0.8%)
Total	3.2% (3.1%-3.3%)[2]	2.7% (2.6%-2.8%)[3]	2.4% (2.4%-2.5%)[3]

[1]Pediatric: November 20, 2009; General 1 and 2: April 1, 2006; General 3: May 11, 2009; General 4: April 1, 2007; Tertiary 1 to 3: June 24, 2006
[2] Each ED included starting on its entry date
[3] Includes EDs with complete data for analysis period

Table A1-VI. Proportion of emergency department (ED) visits with ILI-Se: daily mean per period of analysis, *ERU*

	Proportion of ED visits with ILI-Se, daily mean (95% confidence interval)		
ED	date of entry[1] – Nov 14, 2011	May 7, 2008 - Nov 14, 2011	June 25, 2006 – Jan 29, 2011
Pediatric	33.9% (33.4%-34.4%)	-	-
General 1	8.2% (8.1%-8.4%)	8.1% (7.9%-8.3%)	8.4% (8.2%-8.6%)
General 2	12.4% (12.1%-12.6%)	12.1% (11.8%-12.4%)	12.7% (12.4%-12.9%)
General 3	9.5% (9.2%-9.8%)	-	-
General 4	14.0% (13.7%-14.2%)	13.8% (13.5%-14.1%)	-
Tertiary 1	6.3% (6.1%-6.4%)	6.4% (6.2%-6.6%)	6.3% (6.2%-6.5%)
Tertiary 2	6.5% (6.4%-6.6%)	6.6% (6.5%-6.8%)	6.5% (6.4%-6.7%)
Tertiary 3	7.1% (7.0%-7.3%)	7.1% (6.9%-7.3%)	7.2% (7.0%-7.3%)
Total	10.9% (10.7%-11.1%)[2]	8.8% (8.6%-8.9%)[3]	8.2% (8.0%-8.3%)[3]

[1]Pediatric: November 20, 2009; General 1 and 2: April 1, 2006; General 3: May 11, 2009; General 4: April 1, 2007; Tertiary 1 to 3: June 24, 2006
[2] Each ED included starting on its entry date
[3] Includes EDs with complete data for analysis period

Table A1-VII. Proportion of emergency department (ED) visits with ILI-R: daily mean per period of analysis, *RQSUCH*

	Proportion of ED visits with ILI-R, daily mean (95% confidence interval)	
Emergency department	date of entry[1] – Nov 14, 2011	May 7, 2008 - Nov 14, 2011
Pediatric	19.4% (19.0%-19.9%)	20% (19%-20%)
General 1	-	1.8% (1.7%-1.9%)
General 2	-	4.9% (4.7%-5.1%)
General 3	1.0% (0.9%-1.1%)	-
General 4	-	0.5% (0.5%-0.6%)
Tertiary 1	-	1.2% (1.1%-1.2%)
Tertiary 2	-	0.6% (0.5%-0.7%)
Tertiary 3	-	0.4% (0.4%-0.5%)
Total	-	6.5% (6.3%-6.6%)[2]

[1] Date of entry in *ERU:* Pediatric: September 20, 2009; General 3: May 11, 2009
[2] Includes EDs with complete data for analysis period

Table A1-VIII. Proportion of emergency department (ED) visits with influenza-like illness (ILI), according to data source and syndrome definition

ED	Period[1]	N (days)	Proportion of ED visits with ILI, daily mean (95% confidence interval) ILI-Sp	ILI-Se	ILI-R
Pediatric	2009/09/20-2011/11/14	785	11.3% (10.9%-11.7%)	33.9% (33.4%-34.4%)	19.4% (19.0%-19.9%)
General 1	2008/05/07-2011/11/14	1287	3.9% (3.8%-4.1%)	8.1% (7.9%-8.3%)	1.8% (1.7%-1.9%)
General 2	2008/05/07-2011/11/14	1287	6.0% (5.7%-6.2%)	12.1% (11.8%-12.4%)	4.9% (4.7%-5.1%)
General 3	2009/05/11-2011/11/14	918	2.0% (1.9%-2.2%)	9.5% (9.2%-9.8%)	1.0% (0.9%-1.1%)
General 4	2008/05/07-2011/11/14	1287	3.4% (3.3%-3.6%)	13.8% (13.5%-14.1%)	0.5% (0.5%-0.6%)
Tertiary 1	2008/05/07-2011/11/14	1287	1.4% (1.3%-1.5%)	6.4% (6.2%-6.6%)	1.2% (1.1%-1.2%)
Tertiary 2	2008/05/07-2011/11/14	1287	0.9% (0.8%-0.9%)	6.6% (6.5%-6.8%)	0.6% (0.5%-0.7%)
Tertiary 3	2008/05/07-2011/11/14	1287	0.7% (0.7%-0.8%)	7.1% (6.9%-7.3%)	0.4% (0.4%-0.5%)
Total	2008/05/07-2011/11/14[2]	1287	3.8% (3.6%-3.9%)	12.2% (11.9%-12.4%)	4.1% (3.9%-4.3%)

[1] YYYY/MM/DD
[2] Pediatric ED included starting September 21, 2009; General 3 ED included starting May 11, 2009

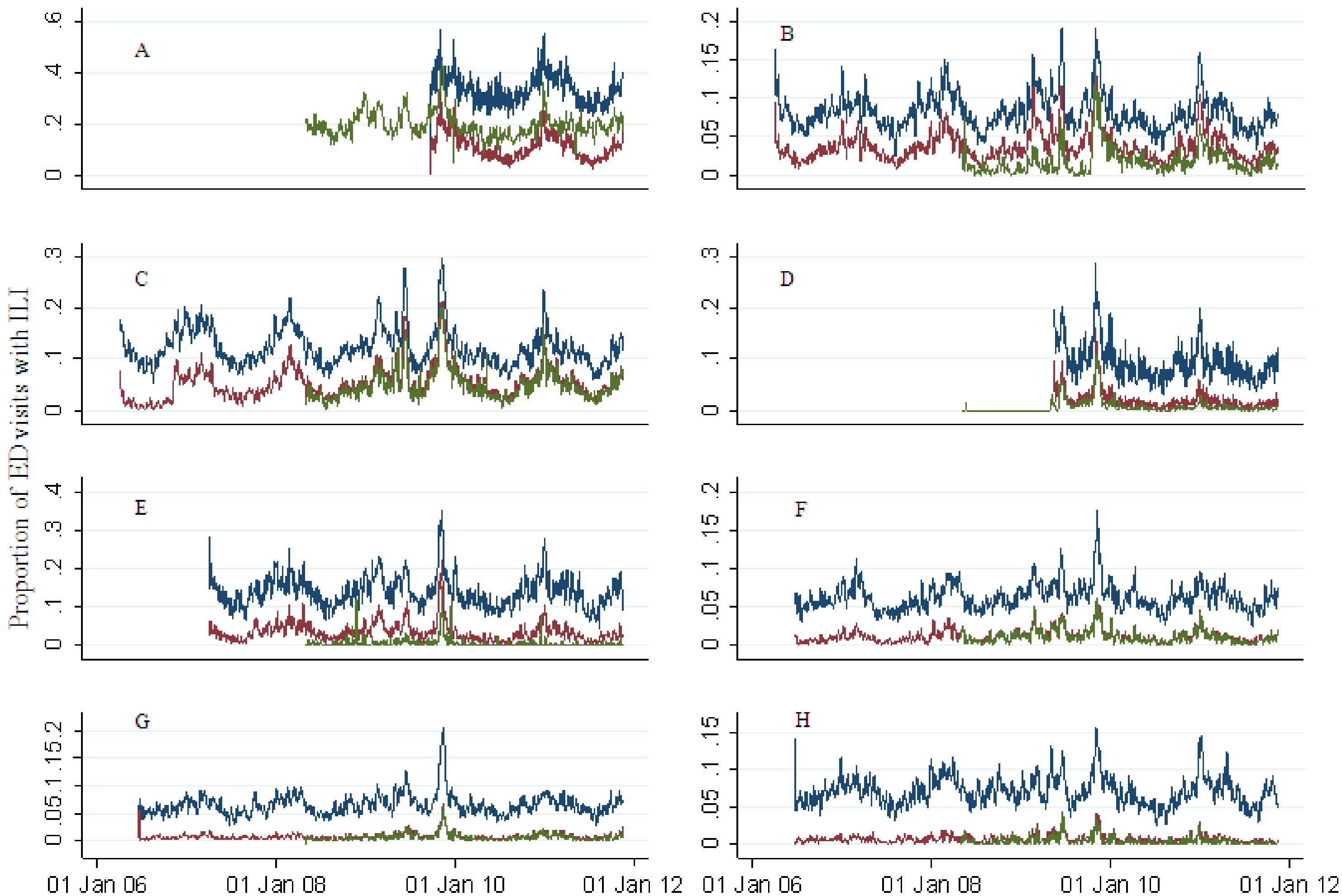

Figure A1-4. Smoothed time series of daily proportion of emergency department (ED) visits with influenza-like illness (ILI), 2006 to 2011

Pediatric ED (A), general ED 1 (B), general ED 2 (C), general ED 3 (D), general ED 4 (E), tertiary ED 1 (F), tertiary ED 2 (G), and tertiary ED 3 (H)
Red: ILI-Sp, blue: ILI-Se, green: ILI-R