Assessing and improving the accuracy of surveillance case definitions using administrative data

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Abstract

Background

Monitoring infectious diseases is a continuously evolving challenge, and constant advances in surveillance methods and infrastructure are necessary to keep pace with rapidly evolving demands. A promising new surveillance methodology is syndromic surveillance, where health department staff, assisted by automated data acquisition and generation of statistical alerts, monitor human health indicators, including pre-diagnostic and diagnostic data, in real-time or near real-time. This novel approach is used increasingly for detecting disease outbreaks rapidly, and, more recently, for 'situation awareness' or guiding efforts to control recognized public health threats in real-time. There are many syndromic surveillance systems in place throughout the world, and several of these systems use diagnoses captured in administrative databases. Because diagnoses in physician claims are not audited, variations in coding are expected. The influence of this variation on the accuracy of surveillance case definitions is not known. Furthermore, in practice, high false-positive rates undermine the usefulness of existing syndromic surveillance systems. Attempts to reduce the false-positive rate by improving statistical detection algorithms have had limited success. However, almost no effort has been made to reduce the false-positive rate by improving the positive predictive value (PPV) of the diagnostic data used in syndromic surveillance.

Objectives

1) To evaluate the feasibility of identifying syndromes using diagnoses from physician claims.

2) To assess the accuracy of syndrome definitions based on diagnostic codes in physician claims.

3) To identify physician, billing, patient, and encounter characteristics associated with the PPV of syndrome definitions based on diagnoses in physician claims.

Methods & Results

Study 1: We focused on a subset of diagnoses from a single syndrome (respiratory), for which we compared cases and non-cases identified from physician claims to medical charts. A convenience sample of 9 family physicians concurrently enrolled in the MOXXI e-Rx trial agreed to participate. 3,526 visits among 729 patients were abstracted from medical charts and linked to a physician claim in the Quebec provincial health insurance database. Episodes of common cold, influenza, laryngitis, unspecified acute upper respiratory infection, pharyngitis, acute bronchitis, pneumonia, otitis media, and sinusitis were investigated. Sensitivity and specificity estimates were adjusted for sampling a larger fraction of cases relative to non-cases. The sensitivity and PPV of physician claims for identifying episodes of respiratory infection were 0.49, 95% CI (0.45, 0.53) and 0.93, 95% CI (0.91, 0.94). This pilot work demonstrated the feasibility of the proposed methods and generated estimates of sensitivity and PPV, which were crucial to planning and obtaining funding for a full-scale, population-based validation of several case definitions used in syndromic surveillance.

Study 2: We focused on 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory, including influenza-like illness) because of their relevance to public health. We selected a random sample of 3,600 physicians who practiced in the fee-for-service system in the province of Quebec, Canada in 2005-2007. We randomly selected 10 visits per physician from their claims, stratifying on syndrome type and presence, diagnosis, and month. Double-blinded chart reviews were conducted by telephone with consenting physicians to obtain information on patient diagnoses for all sampled visits. The sensitivity, specificity, PPV and negative predictive value (NPV) of physician claims were estimated by comparison to chart review. 1,098 (30.5%) physicians completed the chart review. A chart entry on the date of the corresponding claim was found for 10,529 (95.9%) visits. The sensitivity of syndrome definitions based on diagnoses in physician claims was low, ranging from 0.11, 95%CI (0.10, 0.13) for fever syndrome to 0.44, 95%CI (0.41, 0.47) for respiratory syndrome. The specificity and NPV were very high for all

syndromes. The PPV was moderate to high, ranging from 0.59, 95%CI (0.55, 0.64) for fever syndrome, to 0.85, 95%CI (0.83, 0.88) for respiratory syndrome.

Study 3: The same syndrome definitions as in study 2 were used. We focused on the 4,330 visits with a syndrome-positive diagnosis in the claims (i.e., the cases) of the 1,098 physicians who participated in study 2. We estimated the association between claim-chart agreement on syndrome and physician, patient, encounter, and billing characteristics using multivariate logistic regression analyses. The likelihood of the medical chart agreeing with the physician claim about the presence of a syndrome was higher when the treating physician had billed many visits for the same syndrome recently ($RR_{\text{per 10 visits for the same syndrome}}$, 1.05; 95% CI, 1.01-1.08), had a lower workload on the day of the visit ($RR_{\text{per 10 claims}}$, 0.93; 95% CI, 0.90-0.97), and when the patient was younger ($RR_{\text{per 5 years}}$, 0.96; 95% CI, 0.94-0.97) and less socially deprived ($RR_{\text{most versus least deprived quintile}}$, 0.76; 95% CI, 0.60-0.95). We also found that syndrome-positive physician claims produced by billing software that abstracted the billing diagnosis from the electronic medical record in an automated manner were more likely to be confirmed as syndrome-positive by the medical chart than claims produced by software that required the manual input of billing diagnoses.

Conclusions

This was the first large-scale, population-based investigation of the accuracy of syndrome definitions based on diagnoses in physician claims. We found that the sensitivity of syndrome definitions based on diagnoses in physician claims was low, the PPV was moderate to high, and the specificity and NPV were near-perfect. We identified several physician, patient, encounter, and billing characteristics associated with the PPV of syndrome definitions based on diagnoses in physician claims. Many of the predictors of syndrome definition accuracy that we identified are readily accessible to public health departments and other organizations that routinely perform syndromic surveillance, such as the US Department of Defense (ESSENCE) and some health maintenance organizations. These predictors could be used to reduce the false-positive rate of

syndromic surveillance systems, either by focusing on the diagnostic data most likely to be correct, or by adjusting the observed data for known biases in diagnostic coding and performing surveillance using the adjusted values.

Résumé

Contexte

La surveillance des maladies infectieuses est un défi en constante évolution, et un progrès continu au niveau des méthodes et des infrastructures est nécessaire pour répondre à la demande. Une nouvelle approche méthodologique prometteuse est la surveillance syndromique. La surveillance syndromique est une approche par laquelle le personnel des départements de santé, assisté de systèmes automatisés de collecte de données et de génération d'alertes statistiques, surveille des indicateurs de santé en temps réel ou quasi-réel. Cette nouvelle méthodologie est utilisée de façon croissante pour la détection rapide des épidémies, et plus récemment, pour guider, en temps réel, les interventions de santé publique cherchant à contrôler des menaces connues. Plusieurs systèmes de surveillance syndromique sont utilisés à travers le monde, et nombre d'entre eux s'appuient sur les codes de diagnostics enregistrés dans les bases de données administratives. Étant donné que ces codes ne font pas l'objet d'audits, des variations au niveau du codage sont probables. L'effet de ces variations sur l'exactitude des définitions de cas syndromiques n'est pas connu. De plus, en pratique, l'utilité des systèmes de surveillance syndromique existants est également réduite par leurs taux élevés de faux positifs. Par le passé, des chercheurs ont tenté de réduire ces taux en améliorant les algorithmes de détection statistiques, mais ces tentatives ont rencontré un succès limité. Toutefois, peu d'efforts ont été consentis afin d'améliorer le coefficient de prédiction positif des codes de diagnostics utilisés par les systèmes de surveillance syndromiques, une approche qui permettrait de réduire leurs taux de faux-positifs.

Objectifs

1) Évaluer la faisabilité d'identifier des syndromes en utilisant les codes de diagnostics provenant des services facturés par les médecins.

2) Évaluer l'exactitude de définitions syndromiques basées sur les codes de diagnostics provenant des services facturés par les médecins.

3) Identifier les caractéristiques des médecins, du mode de facturation, des patients, et de la rencontre médecin-patient qui sont associées au coefficient de prédiction positif des définitions syndromiques basées sur les codes de diagnostics provenant des services facturés par les médecins.

Méthodes & Résultats

Étude 1: Cette étude portait sur un sous-ensemble de codes de diagnostics associés à un seul syndrome (respiratoire). Pour ce syndrome, nous avons comparés les cas positifs et négatifs, identifiés à partir des codes de diagnostics provenant des services facturés par les médecins (données administratives), aux données contenues dans les dossiers médicaux des patients. Un échantillon de convenance, composé de 9 médecins de famille, a été constitué à partir du groupe de médecins faisant partie de l'étude clinique MOXXI; une étude portant sur la prescription électronique. Les codes de diagnostics associés à 3 526 visites médicales, effectuées par 729 patients, ont été extraits des dossiers médicaux de ces patients, et reliées aux services médicaux correspondants dans la base de données administrative provinciale du Québec. Les épisodes de rhume, de grippe (influenza), de laryngite, d'infection non-précisée des voies respiratoires supérieures, de pharyngite, de bronchite aigue, de pneumonie, d'otite moyenne et de sinusite ont été examinés. La sensibilité et la spécificité ont ensuite été estimées, puis ajustées de façon à tenir compte du sur-échantillonnage des codes de diagnostics d'intérêt. La sensibilité et le coefficient de prédiction positif, associés à l'identification d'épisodes d'infection respiratoire à partir de codes de diagnostics issus des services facturés par les médecins, étaient 0.49, 95% IC (0.45, 0.53) et 0.93, 95% IC (0.91, 0.94) respectivement. Cette étude pilote a démontré la faisabilité des méthodes proposées, et a généré des estimés de la sensibilité et du coefficient de prédiction positif qui ont contribué à la planification et à l'obtention du financement pour une étude à grande-échelle portant sur la validation de plusieurs définitions syndromiques.

Étude 2: Cette étude portait sur 5 syndromes (fièvre, gastro-intestinal, neurologique, cutané, et respiratoire, incluant le syndrome d'allure grippale), sélectionnés en raison

de leur importance pour la santé publique. Nous avons sélectionné un échantillon aléatoire de 3 600 médecins de première ligne ayant été rémunérés à l'acte, entre 2005 et 2007, dans la province de Québec (Canada). Utilisant la base de données administrative provinciale du Québec, nous avons par la suite échantillonné aléatoirement 10 visites, parmi l'ensemble des services facturés par chacun de ces médecins, et ce en stratifiant en fonction de quatre paramètres : 1) le type de syndrome, 2) la présence ou de l'absence de ce syndrome, 3) le code de diagnostic utilisé et, 4) le mois où la visite a été facturée. Pour chacune des visites échantillonnées, une révision de dossier à double insu a par la suite été conduite par téléphone, avec les médecins consentants, et ce afin d'obtenir les diagnostics notés dans les dossiers médicaux. La sensibilité, la spécificité et les coefficients prédictifs positif et négatif des définitions syndromiques basées sur des codes de diagnostics ont été estimés en comparant les données administratives aux données contenues dans les dossiers médicaux. Un total de 1 098 (30.5%) médecins ont pris part aux entrevues téléphonique, et l'information pertinente à l'étude a été retrouvée dans le dossier médical pour 10,529 (95.3%) visites. La sensibilité des définitions syndromiques était faible, allant de 0.11, 95%CI (0.10, 0.13) pour le syndrome fièvre à 0.44, 95%CI (0.41, 0.47) pour le syndrome respiratoire. La spécificité et le coefficient prédictif négatif étaient très élevés pour tous les syndromes. Le coefficient prédictif positif variait de moyen à élevé, allant de 0.59, 95%CI (0.55, 0.64) pour le syndrome fièvre à 0.85, 95%CI (0.83, 0.88) pour le syndrome respiratoire.
Étude 3: Nous avons utilisé les définitions syndromiques de l'étude 2. Nous avons restreint notre échantillon aux 4 330 visites avec un diagnostic positif pour l'un ou l'autre des syndromes à l'étude, et aux 1 098 médecins ayant participé à l'étude 2. Nous avons utilisé une régression logistique multi-variée afin d'estimer le degré d'association entre les caractéristiques du médecin traitant, du mode de facturation, du patient, et de la rencontre médecin-patient (variables indépendantes) et l'exactitude des données administratives quant à la présence de ce syndrome, telle que vérifiée par comparaison avec les données contenues dans le dossier médical du patient (variable dépendante). La probabilité que le dossier médical confirme la présence d'un syndrome, tel que suggéré

par les données administratives, était plus élevée lorsque le médecin traitant avait facturé plusieurs visites pour le même syndrome récemment ($RR_{\text{par 10 visites pour le même syndrome}}$, 1.05; 95% IC, 1.01-1.08), lorsque le médecin avait une charge de travail moindre le jour de la visite ($RR_{\text{par 10 services médicaux}}$, 0.93; 95% IC, 0.90-0.97) et lorsque le patient était plus jeune ($RR_{\text{par 5 ans}}$, 0.96; 95% IC, 0.94-0.97) et provenait d'un milieu moins socialement défavorisé ($RR_{\text{quintile le plus défavorisé comparé au moins défavorisé}}$, 0.76; 95% IC, 0.60-0.95). Nous avons aussi découvert que les données administratives suggérant la présence d'un syndrome ont de meilleures chances d'être confirmées par le dossier médical lorsqu'un logiciel de facturation génère automatiquement les codes de diagnostics d'intérêt à partir d'un dossier médical informatisé, que lorsque qu'il requiert l'entrée manuelle de ces codes.

Conclusions

Cette étude fut la première investigation à grande-échelle à examiner l'exactitude de définitions syndromiques qui sont basées sur des codes de diagnostics provenant des services facturés par les médecins. Nous avons découvert que la sensibilité de ces définitions était faible, que le coefficient prédictif positif variait de moyen à élevé et que la spécificité et le coefficient prédictif négatif étaient près de 100%. Nous avons identifiés plusieurs caractéristiques du médecin, du mode de facturation, du patient et de la rencontre médecin-patient associées au coefficient de prédiction positif des définitions syndromiques. Plusieurs de ces caractéristiques peuvent être facilement obtenues par les départements de santé publique et les organisations qui font de la surveillance syndromique, dont le Département de la Défense des États-Unis (ESSENCE) et certains organismes d'assurance maladie. Ces caractéristiques pourraient être utilisées afin de réduire les taux de faux-positifs des systèmes de surveillance syndromique; soit en identifiant les données ayant le meilleur coefficient prédictif positif; soit en ajustant, dans un premier temps, les données observées de façon à tenir compte des principaux biais de codification des diagnostics, et en s'appuyant, dans un deuxième temps, sur les données ajustées afin de faire la surveillance.

Statement of originality

Syndromic surveillance systems are currently being used around the world to monitor population health. However, existing systems are plagued by high false-alert rates that limit their usefulness. The work contained in this thesis is an original and important contribution to the improvement of public health surveillance methods. First, it assesses the accuracy of case definitions used in syndromic surveillance. Whereas a few other studies also attempted to do this, they suffered from important methodological limitations. The present research was the first to assess the accuracy of syndrome definitions in a large representative sample of community healthcare settings; a larger volume of syndrome cases present to community healthcare settings than to emergency departments, and some studies suggest that monitoring visits to community healthcare settings enables timelier influenza detection than monitoring emergency department visits. This work was also the first to correct for verification bias introduced at the sampling stage; to date, all other published estimates of syndrome definition sensitivity are highly inaccurate due verification bias induced by sampling a larger fraction of cases relative to non-cases. Additionally, we were the first to provide estimates of positive predictive value at the level of the individual ICD-9 code, which lends empirical support to ongoing work to modify syndrome definitions; others have only reported accuracy at the syndrome level. Finally, to our knowledge, the present research was the first to attempt to remedy the high false-alert rate of existing syndromic surveillance systems by identifying physician, billing, patient, and encounter characteristics associated with the positive predictive value of case definitions used in syndromic surveillance.

With the help and guidance of my thesis supervisors and committee members, I generated the research questions, reviewed the relevant literature, developed the methods, performed the statistical analyses, and wrote each manuscript. The medical chart data used in this thesis was collected by me with the help of others, using a methodology I developed, specifically for the purpose of answering the research

questions posed in this thesis. The physician claims data used in this thesis was obtained from the *Régie de l'assurance maladie du Québec* (RAMQ); however, the predictor variables used in this thesis were operationalized and produced by me, using RAMQ data.

Contribution of authors

Manuscript 1: Cadieux, G.; Tamblyn, R. Accuracy of physician billing claims for identifying acute respiratory infections in primary care. *Health Services Research* 2008; 43(6): 2223-38.

Manuscript 2: Cadieux, G; Buckeridge, D.L.; Jacques, A.; Libman, M.; Dendukuri, N. Tamblyn, R. Assessing the accuracy of syndrome definitions based on diagnoses in physician claims. *BMC Public Health* 2011; 11: 1-10.

Manuscript 3: Cadieux, G; Buckeridge, D.L.; Jacques, A.; Libman, M.; Dendukuri, N. Tamblyn, R. Predictors of accuracy of syndrome definitions based on diagnoses in physician claims. Submitted to *Health Services Research*.

Whereas the manuscripts were co-authored, they were developed, executed and written primarily by the PhD student, Geneviève Cadieux. With guidance and feedback provided by my supervisors and the members of my thesis committee, I generated the research questions, developed the study protocols, performed statistical analyses, interpreted the findings, conducted literature reviews, and was lead author on all manuscripts.

Robyn Tamblyn is a James McGill Chair, and a Professor in the Department of Medicine and the Department of Epidemiology, Biostatistics and Occupational Health at McGill University. She is the founder and scientific director of the Clinical and Health Informatics Research Group at McGill University. As thesis supervisor, she oversaw all aspects of protocol development, was actively involved in the interpretation of the results, and provided editorial feedback on all three manuscripts.

David Buckeridge holds a Canada Research Chair in Public Health Informatics, and is an Assistant Professor in the Department of Epidemiology, Biostatistics and Occupational Health at McGill University. He is also a medical consultant to the Montreal Public Health Department and the Quebec National Public Health Institute. As thesis co-supervisor, he oversaw all aspects of protocol development (studies 2 and 3), was actively involved in the interpretation of the results, and provided editorial feedback on all three manuscripts.

Nandini Dendukuri is an experienced biostatistician and Assistant Professor in the Department of Epidemiology, Biostatistics and Occupational Health at McGill University. Dr. Dendukuri provided input on specific statistical and methodological considerations in the protocol design stage and in the execution of the analyses (studies 2 and 3); she also provided editorial feedback on manuscripts 2 and 3.

André Jacques is the Director of the Practice Improvement Division of the Québec College of Physicians. He contributed his expertise to the protocol design, and was instrumental in enabling the data collection for studies 2 and 3. He also provided editorial feedback on manuscripts 2 and 3.

Michael Libman is an experienced infectious diseases specialist, and the Director of the Division of Infectious Diseases of the McGill University Health Centre. He contributed his expertise to the design of the studies 2 and 3, and provided advice on how to interpret findings; he also provided editorial feedback on manuscripts 2 and 3.

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I am grateful to my thesis co-supervisor, David Buckeridge, for providing me with a window into public health practice. Through his joint appointments at McGill University, the *Direction de la santé publique de Montréal*, and the *Institut national de santé publique du Québec*, and through his many collaborations with American researchers in the field of syndromic surveillance, David always had his 'finger on the pulse' of public health surveillance. His unique perspective helped inform and ensured the relevance of my Ph.D. research from its inception and at every step along the way.

I would like to thank the members of my thesis committee for their important contributions. Many thanks to Nandini Dendukuri for suggesting creative solutions to account for a very complex sampling strategy. Thanks also to André Jacques for leveraging the resources of the Quebec College of Physicians to ensure the successful completion of my project. Thanks to Michael Libman, whose considerable experience and expertise in infectious diseases helped inform my research design and shed light on some findings.

Many thanks to the staff of the Clinical and Health Informatics Research Group. In particular, I would like to thank Jimmy for his 24/7 IT support and incomparable

database design and management, Rosalba for attending to all financial matters related to the project, and Pat for providing much needed clerical support. Special thanks to my three physician interviewers – Louise, Milva, and Isabelle – for their great patience and perseverance in contacting busy primary care physicians and reliably completing so many chart reviews. Thanks also to Aman for his work mapping Statistics Canada's 2006 census data for the province of Quebec to 6-digit postal codes. Many thanks to the members of the Peer Pressure Writing Club, whose insightful comments helped shape all three manuscripts included in this thesis. I would also like to thank the staff of the Quebec College of Physicians for their efforts recruiting physicians to our study, and for tolerating any inconvenience created by our project, which lasted longer than anticipated.

I would like to thank the 1,098 primary care physicians from across the province of Quebec who, in spite of extremely busy work schedules, graciously accepted to take part in our study. I would also like to thank the *Commission d'accès à l'information du Québec* and the *Régie de l'assurance maladie du Québec* for repeatedly challenging us to improve our study design to better address evolving privacy concerns, and for granting us access to the administrative data necessary to this project.

I would like to acknowledge the gracious financial support I received throughout my studies, including M.D.-Ph.D. studentships from the *Fonds de la Recherche en Santé du Québec* (2005-2007) and the Canadian Institutes of Health Research (2007-2010). I would also like to thank the Research Institute of the McGill University Health Center and the Canadian Institutes of Health Research for granting us the operational funding necessary to carry out the research described in manuscripts 2 and 3. Additional resources and research support were provided by the Clinical and Health Informatics Research Group and the McGill University M.D.-Ph.D. program.

Thanks also to the McGill University M.D.-Ph.D. program for their guidance during these many years. In particular, I would like to thank my fellow M.D.-Ph.D. students for their shared understanding of the difficulties of this joint degree program, and for their continued encouragement. I am also very grateful to the Faculty of Medicine for acknowledging the many delays and obstacles I faced in carrying out my Ph.D. research, and for granting me two 1-year extensions, without which I could not have completed this thesis.

Finally, I would like to thank my friends and family for their unwavering support and their belief in me. In particular, I am deeply grateful to my mom, who helped me work through the many obstacles and frustrations I encountered, and tirelessly cheered me on these many years.

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Chapter 1. Introduction

Monitoring infectious diseases: a continuously evolving challenge

Since the US Surgeon General declared victory over infectious diseases in 1967 (1), we have witnessed the emergence of many new pathogens (e.g., *Legionella*, HIV, *Borrelia*) (2;3), and the re-emergence, fuelled in part by antimicrobial drug resistance, of infections previously thought to be under control (e.g., tuberculosis, cholera, dengue fever) (3;4). Infectious diseases continue to be a leading cause of healthcare expenditure in North America, accounting for about one fifth (5) to one quarter (6) of all outpatient visits in the US each year, and with annual direct and indirect costs totalling more than $120 billion dollars in the US (6). The healthcare burden of infectious disease increases sharply during epidemics; for example, the direct and indirect costs of the 2003 epidemic of severe acute respiratory syndrome (SARS) were estimated at approximately $2 billion in Canada alone (7).

Recent outbreaks of SARS in Toronto (8;9), West Nile Virus in New York City (10), *Clostridium difficile* in Quebec (11;12), and influenza A (H1N1) in Mexico and around the world (13;14) have brought infectious diseases back to the forefront of public consciousness in North America, and exposed shortcomings in surveillance and control. In the current context of increasing globalization and converging disease ecologies (3), tracking emerging infectious diseases presents a continuously evolving challenge. Public health agencies recognize that traditional surveillance methods and infrastructure are insufficient to meet rapidly evolving demands.

Traditional surveillance relies on routine or ad hoc reporting of counts or individual cases of disease by clinicians and laboratories to local health departments, where staff aggregate and examine reported data for unusual patterns of occurrence. Because most traditional approaches monitor previously known diseases, outbreaks of emerging infections are almost always recognized by astute clinicians, who notice and report

suspicious clusters of cases to health departments (15;16). For example, the 1993 Four Corners outbreak of hantavirus pulmonary syndrome was first recognized by medical personnel at the Indian Health Service, and the SARS outbreak was first reported by physicians in Asia (15). Even when used to monitor previously known diseases, the usefulness of the traditional disease surveillance approach for the detection of outbreaks is severely limited by delays in obtaining data. Delays occur because case reporting is still done by mail or fax in many jurisdictions, and because of delays inherent to laboratory confirmation of a suspected diagnosis. As a result, public health agencies are generally not aware of cases from an outbreak until days or weeks after cases occur (17-19), especially in situations where outbreaks involve cases spread over a wide area (20). For example, a retrospective analysis of hospital admissions and emergency department visits for gastroenteritis suggested that the drinking water caused significant waterborne cryptosporidiosis in Milwaukee well before the massive documented outbreak of April 1993, and that earlier identification of these cases of infection could have prevented the larger outbreak (21).

Timely surveillance information is essential for effective public health action. Early detection of outbreaks is important to hasten public health response to limit transmission, thereby reducing outbreak size and incidence of infection in high-risk individuals. Providing timely and accurate surveillance information to public health practitioners requires novel surveillance methods enabling outbreak detection on a time scale consistent with incubation periods, and allowing the characterization of ongoing outbreaks to guide focussed and effective interventions (22).

Syndromic surveillance: a promising new approach

One promising approach for improving public health surveillance is syndromic surveillance. Syndromic surveillance is a surveillance methodology where health department staff, assisted by automated data acquisition and generation of statistical

alerts, monitor human health indicators, including pre-diagnostic and diagnostic data, in real-time or near real-time. This novel approach is used increasingly for detecting disease outbreaks rapidly (23), and, more recently, for 'situation awareness' or guiding efforts to control recognized public health threats in real-time (24). Health indicators monitored by syndromic surveillance systems reflect either health services utilization, such as visits to clinics and emergency departments with a chief complaint or diagnosis corresponding to a syndrome under surveillance (e.g., influenza-like illness), or health-related behaviours, such as purchase of over-the-counter medications for respiratory or gastrointestinal symptom relief (e.g., oral rehydration salts), and school/work absenteeism (25).

To provide a more timely and accurate description of population health, syndromic surveillance systems use pre-diagnostic data that are available electronically, and rely on automated data transfer, processing, and analysis. Pre-diagnostic data are data generated before laboratory confirmation of a suspected diagnosis (26). These data may reveal anomalous patterns earlier in the course of an outbreak than laboratory-confirmed diagnoses, and therefore provide more timely results than traditional surveillance systems. For example, assuming a population of infected persons (Figure 1), a majority of cases are expected to self-treat (27-29), at least initially, and some may purchase over-the-counter symptom-relief medication. A smaller proportion of cases are expected to present to primary care walk-in clinics (27), likely later in the course of the illness, and an even smaller number may find their way to a hospital emergency department. Laboratory testing may be requested for a small number of those who presented to a clinic or an emergency department. For most infections (except hemorrhagic fevers and other rare infections with fulminant onset), monitoring clinic visits will yield a greater volume of cases and may yield more timely detection than monitoring emergency department visits.

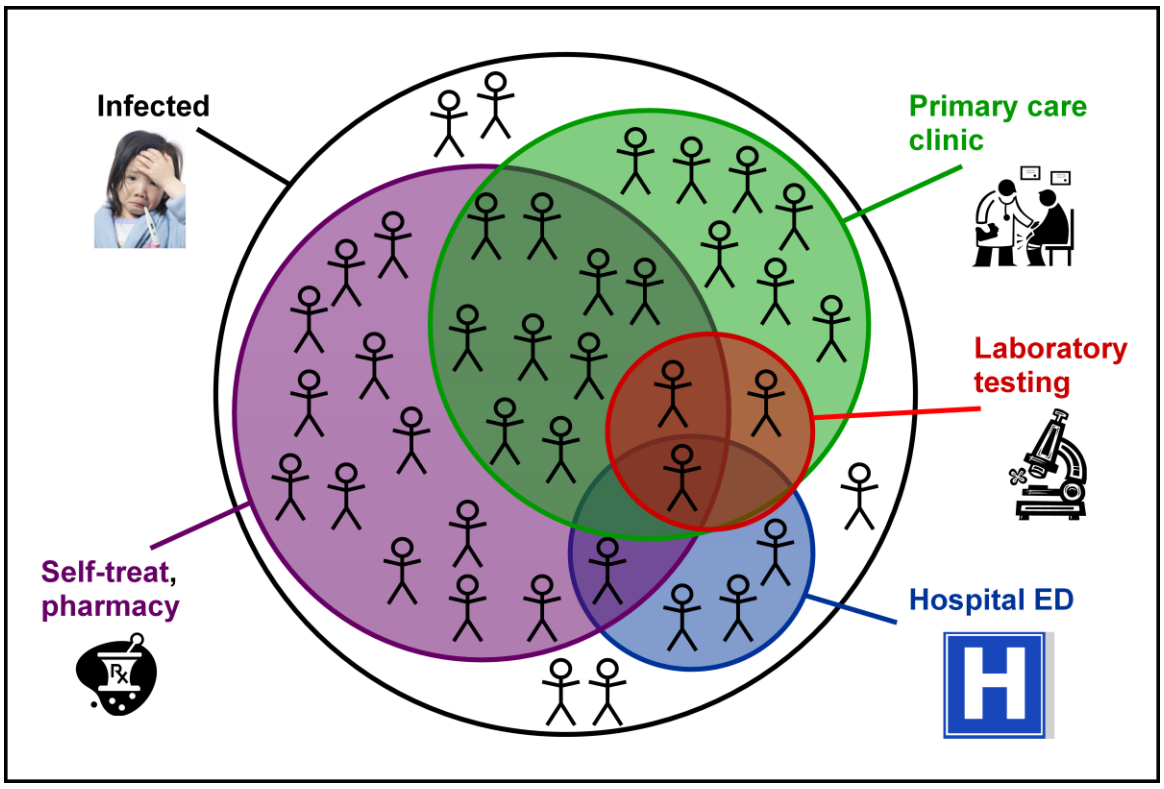

Figure 1. Opportunities for case detection

Data used in syndromic surveillance are also expected to reflect changes in population health due to conditions that are not under routine surveillance, such as newly emerging infectious diseases. This is because syndromic surveillance monitors groups of related clinical presentations, which are more sensitive and less specific than laboratory-confirmed diagnoses because they aggregate many similar clinical presentations into syndromes. For example, surveillance for respiratory syndrome would have been expected to identify cases of SARS, even before its etiology was discovered, because its clinical presentation overlapped with the case definition for respiratory syndrome.

Secondary use of existing data for surveillance purposes

Surveillance systems that require healthcare providers to enter additional data to report a suspicious case using a parallel system, independent and unrelated to care delivery, are becoming less common due to the many limitations of this approach (Table 1).

Parallel reporting of suspicious cases by healthcare professionals requires extra time and offers little incentive for timely and exhaustive reporting. For this reason, the information obtained from parallel reporting is likely to present a dated and biased account of a developing outbreak, thereby limiting the use of surveillance systems that

Table 1. Data sources used in surveillance: parallel reporting versus secondary use of existing data

	Parallel reporting of cases		Case identification from existing data	
	Notifiable diseases surveillance	**Sentinel surveillance**	**Administrative data**	**Electronic medical record data**
Diseases under surveillance	· Typically 50-100 diseases · Previously known diseases only	· Typically one or a few case definitions · Previously established case definitions only	· Unlimited number of case definitions · Data can be queried for any case definition	· Unlimited number of case definitions · Data can be queried for any case definition
Data type	· Individual cases · Potential for detailed clinical information	· Usually, weekly counts of cases · Potential for detailed clinical information	· Diagnostic codes · Procedure codes · Characteristics of the insured (e.g., age, sex, area of residence)	· Triage chief complaint · Physician diagnosis · Full clinical notes · Laboratory and imaging reports
Data entry	· Parallel data entry system with associated implementation and maintenance costs · Transmission is typically done by telephone, fax, mail, or, in some jurisdictions, electronically	· Parallel data entry system with associated implementation and maintenance costs · Transmission is typically done electronically	· Existing computerized billing system · Centralized data repository (payer)	· Requires pre-existing electronic medical record system in local clinical settings (e.g., community clinics) · Issues associated with meaningful aggregation of data from different sites and systems
Timeliness	· Poor, because lack of incentive for timely reporting and delay inherent to method of reporting	· Poor, because lack of incentive for timely reporting and delay inherent to method of reporting (e.g., weekly)	· Timely, because information is tied to physician payment cycle	· Timely, because information is tied to patient care
Population coverage	· Population coverage tends to be poor	· Sentinel sites only	· Complete population coverage	· To date, few sites (mostly hospitals, few community clinics)
Validity	· Sporadic and selective reporting, because reporting increases physician workload	· Sporadic and selective reporting, because reporting increases physician workload	· Avoids reporting biases when information is tied to physician payment	· Avoids reporting biases when information is tied to patient care
Examples	· Treating physicians report diagnosed cases of notifiable diseases to their local public health agency by telephone, fax, or mail · Laboratories report positive tests for notifiable diseases to their local public health agency electronically.	· Volunteer sentinel physicians report weekly counts of patients that met the case definition for influenza-like illness (ILI) to public health (US Influenza Sentinel Provider Surveillance Network). · Physicians practicing in 49 sentinel travel health clinics report individual cases of travel-related morbidity to the GeoSentinel system electronically.	· Physician billing data from a health maintenance organisation is queried for ICD-9 coded diagnoses that may reflect measles-like illness (30).	· Electronic medical records from a network of community health centers are queried for chief complaints, diagnoses, and laboratory testing results that meet the criteria for ILI or infectious gastroenteritis (31).

rely on this type of information (32). Also, surveillance systems that rely on parallel reporting of suspicious cases by healthcare professionals typically have poor population coverage. For example, a review of previous evaluations of US notifiable disease surveillance found that the completeness of reporting was as low as 9% for some diseases (33). Despite these many limitations of parallel reporting, its main advantage is the potential for collecting detailed information (e.g., symptoms, contacts, exposures).

In contrast, making secondary use of existing data for surveillance does not add to the healthcare provider's burden. Furthermore, when electronic documentation of the reason for a medical visit is tied to provider payment or patient care, timely and complete capture of cases is ensured, thereby avoiding biases inherent to parallel reporting (34). Administrative data offer the broadest population coverage, i.e., the large territory served by the health administrative authority. To date, surveillance systems that rely on electronic medical record data offer variable population coverage, depending on the number of hospitals and clinics that share information with public health, and their respective catchment areas. Broader population coverage and greater representativeness are expected to increase the sensitivity of surveillance and outbreak detection systems by enabling more cases to be captured, as opposed to capturing only cases that seek care at sentinel sites. Systems with broad population coverage that monitor populations across geo-political boundaries (e.g., health administrative regions) are more likely to detect outbreaks involving a few cases spread over a wide area (20), such as outbreaks associated with foods not produced locally. Whereas, at present, administrative data offer the broadest population coverage, they contain the least clinical detail: most administrative health databases are limited to one primary diagnosis or symptom, usually represented by an International Classification of Disease, 9th revision (ICD-9) code.

Because administrative data offer broader population coverage than parallel sentinel reporting and electronic medical records, many syndromic surveillance systems

currently in place in North America use diagnoses from administrative data, including the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) of the US Department of Defense (DoD) and ESSENCE II (35). These syndromic surveillance systems use groups of ICD-9 diagnostic codes to define syndromes of interest for surveillance. Using groups of codes, instead of individual codes, is expected to increase the sensitivity of detection, and is motivated by the concern that individual codes are too fine-grained for outbreak detection. Many diseases can initially present with overlapping symptoms that may not raise clinical suspicion; therefore grouping cases into syndromes is expected to provide earlier evidence of an outbreak. Grouping similar ICD-9 codes into syndromes is also expected to improve coding accuracy by minimizing inter-coder variability and within-coder variability over time. For example, pneumonias (ICD-9 codes 480-486), and influenza (487) are grouped under respiratory syndrome.

Whereas administrative data offer great promise for population surveillance by allowing access to diagnostic information from many geographically-dispersed community healthcare settings, concerns about administrative data quality arise because, unlike procedure codes, diagnostic codes are not audited by health administrative authorities. This is expected to result in differences in diagnostic coding practices between physicians and between institutions. Therefore, before we evaluate how accurately syndrome definitions based on diagnostic codes in physician claims can detect outbreaks, we should first determine how accurately these codes capture the reason for the clinical encounter.

The development of syndromic surveillance case definitions based on diagnoses in administrative data

To harness the potential of administrative data for syndromic surveillance, clinical case definitions must be mapped to diagnostic codes. To this end, a multi-agency working

group under the auspices of the US Centers for Disease Control and Prevention (CDC) was given the mandate of developing case definitions for the syndromic surveillance of diseases associated with critical bioterrorism-associated agents, which were published in 2003. The expert panel settled on 11 syndromes (Table 2). For each syndrome, the experts first articulated a conceptual definition, taking care to exclude any chronic conditions with similar clinical presentations. Then, the experts selected the International Classification of Disease, 9th revision, Clinical Modification (ICD-9-CM) codes that most closely corresponded to the conceptual definition. Each ICD-9-CM code was ranked based on expert consensus, from 1 (highest consensus) to 3 (lowest consensus). These definitions were later adopted by the US Department of Defense (DoD) for use in their syndromic surveillance system.

Table 2. Eleven syndrome definitions developed and published by the US Center for Disease Control and Prevention in 2003

Syndrome	Conceptual definition	Examples of corresponding ICD-9-CM codes
Botulism-like	ACUTE condition that may represent exposure to botulinum toxin ACUTE paralytic conditions consistent with botulism: cranial nerve VI (lateral rectus) palsy, ptosis, dilated pupils, decreased gag reflex, media rectus palsy. ACUTE descending motor paralysis (including muscles of respiration) ACUTE symptoms consistent with botulism: diplopia, dry mouth, dysphagia, difficulty focusing to a near point.	005.1 Botulism 344.9 Paralysis 368.2 Diplopia 342.9 Hemiparesis/hemiplegia, unspecified 784.3 Aphasia 784.5 Speech disturbance 037 Tetanus
Fever	ACUTE potentially febrile illness of origin not specified INCLUDES fever and septicemia not otherwise specified INCLUDES unspecified viral illness even though unknown if fever is present EXCLUDE entry in this syndrome category if more specific diagnostic code is present allowing same patient visit to be categorized as respiratory, neurological or gastrointestinal illness syndrome	020.2 Plague, septicemic 020.8 Plague, other 020.9 Plague, unspecified 038.9 Septicemia, unspecified 780.6 Fever 790.7 Bacteremia 790.8 Viremia, unspecified
Gastro-intestinal	ACUTE infection of the upper and/ or lower gastrointestinal (GI) tract SPECIFIC diagnosis of acute GI distress such as Salmonella gastroenteritis ACUTE non-specific symptoms of GI distress such as nausea, vomiting, or diarrhea EXCLUDES any chronic conditions such as inflammatory bowel syndrome	005.9 Food poisoning, unspecified 008.5 Bacterial enteritis, other 008.8 Viral enteritis, unspecified 535.0 Acute gastritis 787.91 Diarrhea 787.01 Nausea and vomiting
Hemorrhagic illness	SPECIFIC diagnosis of any virus that causes viral hemorrhagic fever (VHF): yellow fever, dengue, Rift Valley fever, Crimean-Congo HF, Kyasanur Forest disease, Omsk HF, Hantaan, Junin, Machupo, Lassa, Marburg, Ebola ACUTE condition with multiple organ involvement that may be consistent with exposure to any virus that causes VHF ACUTE blood abnormalities consistent with VHF: leucopenia, neutropenia, thrombocytopenia, decreased clotting factors, albuminuria	287.1 Platelet disorder 287.2 Nonthrombocytopenic purpura 287.9 Hemorrhagic condition, unspecified 511.8 Hemothorax 459.0 Hemorrhage, unspecified 578.0 Hematemesis

Table 2 (continued). Eleven syndrome definitions developed and published by the US Center for Disease Control and Prevention in 2003

Syndrome	Conceptual definition	Examples of corresponding ICD-9-CM codes
Lymphadenitis	ACUTE regional lymph node swelling and/ or infection (painful bubo- particularly in groin, axilla or neck)	020.0 Plague, bubonic 075 Mononucleosis 289.3 Lymphadenitis, unspecified 785.6 Lymph node enlargement
Localized cutaneous lesion	SPECIFIC diagnosis of localized cutaneous lesion/ ulcer consistent with cutaneous anthrax or tularemia ACUTE localized edema and/ or cutaneous lesion/ vesicle, ulcer, eschar that may be consistent with cutaneous anthrax or tularemia INCLUDES insect bites EXCLUDES any lesion disseminated over the body or generalized rash EXCLUDES diabetic ulcer and ulcer associated with peripheral vascular disease	020.0 Plague, bubonic 022.0 Anthrax, cutaneous 680.9 Boil, unspecified 682.9 Cellulitis, unspecified 919.4 Insect bite, non-venomous, unspecified site 078.3 Cat-scratch disease
Neurological	ACUTE neurological infection of the central nervous system (CNS) SPECIFIC diagnosis of acute CNS infection such as pneumococcal meningitis, viral encephalitis ACUTE non-specific diagnosis of CNS infection such as meningitis not otherwise specified (NOS), encephalitis NOS, encephalopathy NOS ACUTE non-specific symptoms of CNS infection such as meningismus, delirium EXCLUDES any chronic, hereditary or degenerative conditions of the CNS such as obstructive hydrocephalus, Parkinson's, Alzheimer's	047.9 Viral meningitis, unspecified 320.9 Bacterial meningitis, unspecified 322.9 Meningitis, unspecified 348.3 Encephalopathy, unspecified 323.9 Encephalitis, unspecified 781.6 Meningismus 784.0 Headache 784.3 Aphasia
Rash	ACUTE condition that may present as consistent with smallpox (macules, papules, vesicles predominantly of face/arms/legs) SPECIFIC diagnosis of acute rash such as chicken pox in person > XX years of age (base age cut-off on data interpretation) or smallpox ACUTE non-specific diagnosis of rash compatible with infectious disease, such as viral exanthem EXCLUDES allergic or inflammatory skin conditions such as contact or seborrheic dermatitis, rosacea EXCLUDES rash NOS, rash due to poison ivy, sunburn, and eczema	050.9 Smallpox, unspecified 052.9 Varicella, unspecified 057.9 Viral exanthema, unspecified 695.9 Erythematous condition, unspecified 692.9 Dermatitis, unspecified 782.1 Rash/nonspecific skin eruption
Respiratory	ACUTE infection of the upper and/ or lower respiratory tract (from the oropharynx to the lungs, includes otitis media) SPECIFIC diagnosis of acute respiratory tract infection (RTI) such as pneumonia due to parainfluenza virus ACUTE non-specific diagnosis of RTI such as sinusitis, pharyngitis, laryngitis ACUTE non-specific symptoms of RTI such as cough, stridor, shortness of breath, throat pain EXCLUDES chronic conditions such as chronic bronchitis, asthma without acute exacerbation, chronic sinusitis, allergic conditions (Note: INCLUDE *acute exacerbation* of chronic illnesses.)	460 Acute nasopharyngitis 462 Acute pharyngitis 463 Acute tonsilitis 464.0 Acute laryngitis, without obstruction 465.9 Acute upper respiratory infection, unspecified 466.0 Acute bronchitis 480.9 Viral pneumonia, unspecified 486 Pneumonia, organism unspecified
Severe illness or death potentially due to infectious disease	ACUTE onset of shock or coma from potentially infectious causes EXCLUDES shock from trauma INCLUDES SUDDEN death, death in emergency room, intrauterine deaths, fetal death, spontaneous abortion, and still births EXCLUDES induced fetal abortions, deaths of unknown cause, and unattended deaths	780.01 Coma 780.50 Shock, unspecified 780.59 Shock, unspecified, without trauma 799.9 Mortality, cause unknown
Specific infection	ACUTE infection of known cause not covered in other syndrome groups, usually has more generalized symptoms (i.e., not just respiratory or gastrointestinal) INCLUDES septicemia from known bacteria INCLUDES other febrile illnesses such as scarlet fever	Not specified

There have been few attempts to validate these syndrome definitions, which were developed based on expert consensus, using diagnostic data from medical visits. Published validations have focused on the syndromes with the highest prevalence, have involved small convenience samples of one or a few healthcare sites, and have suffered from several methodological limitations. As a result, prior estimates of the accuracy of these syndrome case definitions vary widely. A thorough discussion of these studies is found in the next chapter.

More recently, investigators involved with the US DoD's ESSENCE system developed a definition for another syndrome of great importance for population surveillance: influenza-like illness (ILI). A set of 29 ICD-9-CM diagnostic codes potentially corresponding to ILI was first identified by experts, and then pruned using empirical methods in a 2-step process. In the first step, using a sample of 6,236 medical visits with a diagnostic code included in the ILI set and where a respiratory specimen was collected and tested for influenza, the investigators calculated, for each ICD-9-CM diagnostic code, the proportion of medical visits in which the patient tested positive for influenza virus A or B. In the next step, in a DoD-wide sample, investigators evaluated the correlation between a time-series of weekly counts of positive influenza isolates and a time-series of weekly counts of medical visits with a diagnostic code included in the ILI set, for each diagnostic code individually. Combining results from these two assessments, investigators then selected the ICD-9-CM diagnostic codes most likely to reflect 'true' cases of ILI, yielding a sensitive 'large-group' definition of ILI (14 codes) and a specific 'small-group' definition of ILI (4 codes).

Limitations of existing systems and the expanding uses of syndromic surveillance

Syndromic surveillance systems were adopted rapidly in the wake of the terrorist attacks of September 11, 2001 to address concerns of bioterrorism. The primary purpose of these systems was to detect disease outbreaks and bioterrorism events rapidly. To

ensure that no outbreak would be missed, syndromic surveillance systems were initially designed to generate alerts at very low thresholds. A consequence of this design was high rates of false-positive alerts (36), which have limited syndromic surveillance systems' ability to correctly identify outbreaks. Indeed, because of the prohibitive cost of investigating every alert, many public health practitioners have adopted a 'wait-and-see' response to alerts, thereby detracting from a main advantage of syndromic surveillance systems over traditional public health surveillance systems, namely the ability to provide a timelier portrait of population health. Attempts to reduce false-positive rates by improving statistical detection algorithms used in syndromic surveillance (37-39) have had limited success. Partly because of these limitations, and partly because of the absence of bioterrorist attacks since 2001 (40), the focus of syndromic surveillance has begun to shift away from outbreak detection towards population health monitoring or situation awareness (24). Syndromic surveillance systems are now being used to describe the course of seasonal illnesses (e.g., influenza) as they sweep across communities, and to monitor unintentional disease outbreaks (e.g., food contamination), adverse health effects of natural and other disasters (e.g., wild fires, heat waves), and non-infectious conditions (e.g., exposures to toxic chemicals) (24).

Syndromic surveillance systems are now being tailored to suit these novel uses. Whereas outbreak detection sought to identify and alert on every suspicious increase in the incidence of cases, maintaining situation awareness entails gathering data about the current state of population health, analyzing and interpreting these data, and projecting the likely evolution of the current state (41). Accurate case definitions are critical for monitoring population health and maintaining situation awareness, but to date, almost no attempts have been made to improve the accuracy of the case definitions used in syndromic surveillance (42-44). Identifying properties of surveillance data associated with higher positive predictive value of case definitions used in syndromic surveillance

will improve individual case detection and situation awareness, and will likely also lead to improved outbreak detection.

Improving the accuracy of syndromic surveillance case definitions using covariates

Several properties of surveillance data, such as who generated them (healthcare provider characteristics), how they were reported (reporting/billing system characteristics), who they describe (patient characteristics), and where and in what context they arose (clinical encounter characteristics), are likely to influence case definition accuracy. Characteristics of the healthcare provider that are associated with practice style or coding accuracy may influence the positive predictive value of diagnostic data. For example, two studies have found that greater experience was associated with lower diagnostic coding accuracy (45) and lower billing diagnosis accuracy (46). Reporting/billing practices, including who enters the diagnosis in the system and how the diagnosis is entered (e.g., direct entry of diagnostic codes, searchable list of diagnoses that the software then maps to codes, automated abstraction of the billing diagnosis from an electronic medical record) are likely to influence the positive predictive value of diagnostic data. The context for the clinical encounter, which influences how much time and what resources are available for reporting/billing, is also likely to impact diagnostic data accuracy. For example, higher physician workloads were associated with lower billing diagnosis accuracy in one study (46). Treating more complex patients likely requires more working memory and increases physician cognitive load (47), therefore diagnostic coding errors may be more likely to occur for complex patients. For this reason, indicators of patient complexity, such as age, comorbidity, socioeconomic status, and health services utilization (48), may impact the positive predictive value of diagnostic data.

Research objectives

The purpose of my thesis work was to evaluate the accuracy of administrative data for use in population-based syndromic surveillance. The specific objectives were:

1) To evaluate the feasibility of identifying syndromes using diagnoses from physician claims.
2) To assess the accuracy of syndrome definitions based on diagnostic codes in physician claims from community healthcare settings.
3) To identify predictors of accuracy of syndrome definitions based on diagnostic codes in physician claims from community healthcare settings.

Organization of the dissertation

This thesis is organized around three core research manuscripts. The next chapter provides further background for these manuscripts by reviewing published validations of syndrome case definition accuracy, relevant methodological issues, and studies that sought to identify covariates associated with the accuracy of case definitions based on diagnoses in administrative data. Chapter 3 describes the data sources, sampling strategy, and data collection methods used in manuscripts 2 and 3, as well as the statistical methods used to account for the complex sampling strategy in manuscript 2. The core chapters (4-6) present research that directly addresses each specific thesis objective, respectively. Chapter 4 describes an evaluation of the feasibility of identifying syndromes using diagnoses from physician claims, and was published in *Health Services Research* under the title "Accuracy of physician billing claims for identifying acute respiratory infections in primary care." Chapter 5 presents an assessment of the accuracy of syndrome definitions based on diagnostic codes in physician claims; this manuscript was published in *BMC Public Health* under the title "Accuracy of syndrome definitions based on diagnoses in physician claims." Chapter 6 identifies physician,

billing, patient, and encounter characteristics associated with the positive predictive value of syndrome definitions based on diagnoses in physician claims in a manuscript titled “Predictors of accuracy of syndrome definitions based on diagnoses in physician claims.” Finally, the last chapter summarizes the most important findings from the three studies, highlights their strengths and limitations, discusses the public health implications of the findings, and suggests potential research avenues for improving infectious disease monitoring through syndromic surveillance.

Chapter 2. Background

In the previous chapter, we advocated that syndromic surveillance is a promising new approach for detecting disease outbreaks rapidly and for guiding efforts to control recognized public health threats in real-time. We also argued that the most useful surveillance systems are those that make use of pre-diagnostic data that are already available electronically, gather data from many healthcare sites that cover a large representative sample of the population, and rely on automated data transfer, processing, and analysis. We briefly mentioned that there have been numerous efforts to develop surveillance case definitions based on administrative data, and that attempts to validate these case definitions had been plagued with methodological limitations that impeded the interpretation of their results. Finally, we suggested that the accuracy of surveillance case definitions may be improved by taking into account other variables that are associated with case definition accuracy and that are readily accessible to public health departments.

In this chapter, we provide a more thorough critique of the published validations of syndromic surveillance case definitions based on administrative data. Because several of these published validations suffered from verification bias, we provide a detailed discussion of how this bias arises, what effect it has on the results, and how to correct for it. Finally, we look to studies outside the realm of syndromic surveillance for evidence that case definitions based on diagnoses in administrative data are associated with, and can be improved by the addition of, covariates.

Validity of syndromic surveillance case definitions based on administrative data

Many syndromic surveillance systems rely on health-related data collected for administrative purposes because of the advantages of using existing data for surveillance, compared to implementing parallel case reporting. However, because

administrative data are not collected for surveillance purposes, public health users need to assess the accuracy of these data for use in syndromic surveillance. Studies to assess the accuracy of administrative data for syndromic surveillance can be grouped in two large categories based on methodology: ecological studies and 'direct' validation of individual cases.

Many validation studies of administrative data used in syndromic surveillance have relied on an ecological (correlation) approach. In this approach, a time-series of (daily or weekly) counts of cases identified from administrative data is compared to a time-series of counts of cases identified using another data source. The two time-series are compared using some statistical method (e.g., cross-correlations at different lags), and a judgement is made about how closely the time-series obtained from administrative data resembles the time-series obtained from the other data source. Several validation studies of syndrome case definitions published in the literature have used this approach (Table 3).

Whereas the ecological validation approach can provide some general assurance that case counts based on administrative data yield similar seasonal variation as case counts from another data source, the accuracy of the data source being used as a comparison often has not been convincingly established. Also, by virtue of this approach being ecological, it does not enable us to examine whether a given individual case identified from administrative data is indeed a case, based on other information. Furthermore, the ecological approach does not permit the estimation of the sensitivity, specificity, positive predictive value, and negative predictive value of the case definition, which are very important parameters for public health to consider when implementing a syndromic surveillance system and when interpreting alerts from an existing syndromic surveillance system.

Table 3. Studies that have assessed the validity of syndromic surveillance case definitions based on administrative data using an ecological approach

Study	Syndrome under surveillance	Administrative data being validated (format)	Data used as comparison (format)	Study population and validation methodology	Findings
Hripcsak *et al*., 2009 (31)	Influenza-like illness Gastrointestinal	Electronic health record (EHR) from 13 community health centers in NYC: 1) Structured EHR data: diagnoses (ICD-9 codes), coded reason for visit, temperature, and respiratory rate 2) Narrative EHR data: Outpatient internal medicine notes (free text)	1) ED chief complaint recorded by triage nurse (free text) from 47 EDs throughout NYC 2) Laboratory tests positive for influenza A or B (daily counts) from the US WHO collaborating laboratories in NYC	July 1, 2004 to June 30, 2005 (1 year of data) Manhattan and the Bronx 124,568 visits to the 13 community health centers with a temperature recording 3.4 million ED chief complaints Lagged (daily) cross-correlations between time-series	*For influenza-like illness:* Structured EHR data: 0.89 correlation with lab data 0.84 correlation with ED data Narrative EHR data: 0.93 correlation with lab data 0.89 correlation with ED data *For gastrointestinal syndrome:* Structured EHR data: 0.81 correlation with ED data Narrative EHR data: 0.47 correlation with ED data
Marsden-Haug *et al*., 2007 (49)	Influenza-like illness	Outpatient visit diagnoses (ICD-9 code) from all US military treatment facilities in the US and abroad	Laboratory tests positive for influenza A or B, or any viral respiratory pathogen (weekly counts) from all US military treatment facilities in the US and abroad	October 2000 to December 2004 (almost 4 years) All US military treatment facilities (in the US and abroad) Lagged (weekly) cross-correlations between time-series and signal-to-noise analysis for each ICD-9 code separately	Influenza-like illness, *small*-group definition (ICD-9 codes with a significant correlation and a high signal-to-noise ratio): 465.9, 487.0, 487.1, 487.8. Influenza-like illness, *large*-group definition (ICD-9 codes with a significant correlation but a lower signal-to-noise ratio): 79.99, 382.9, 460, 461.9, 465.9, 466.0, 486, 490, 780.6, 786.2.
May *et al*., 2010 (50)	Upper respiratory infection (URI) URI and sinusitis Viral illness Pneumonia	From a single academic hospital in Washington, DC: 1) ED chief complaint (free text or pull-down menu) 2) ED discharge diagnoses (ICD-9 codes)	Cases (weekly counts) reported by sentinel physicians and laboratories from the US CDC Influenza Sentinel Provider Surveillance Network for the South Atlantic region	June 2005 to May 2006 (1 year) Washington, DC Time-series modeling No cross-correlations computed	ED complaints of URI peaked at week 10 of the influenza season, whereas the CDC data peaked at week 7. ED chief complaints of URI began to rise earlier than ED diagnoses of URI.
Lemay *et al*., 2008 (51)	Influenza-like illness	ED chief complaint recorded by triage nurse (free text) from 3 hospitals in the Ottawa region, Canada	Laboratory tests positive for influenza A or B (weekly counts) from the provincial Reporting Disease Information System	1998-2003 (5 influenza seasons) Ottawa region, Canada 892,674 ED visits Data were stratified by age group and aggregated by week Time-series modeling Box-Jenkins lagged (weekly) cross-correlations	194,816 (21%) visits for influenza-like illness For children aged 5 and under: Cross-correlation of ED chief complaint data and laboratory data were statistically significant in each influenza season (except 2002-2003), but at different lags

ED: emergency department. ICD: International Classification of Disease. NYC: New York City. WHO: World Health Organisation. US DoD: US Department of Defense. US CDC: US Centers for Disease Control and Prevention.

Table 3 (continued). Studies that have assessed the validity of syndromic surveillance case definitions based on administrative data using an ecological approach

Study	Syndrome under surveillance	Administrative data being validated (format)	Data used as comparison (format)	Study population and validation methodology	Findings
Caudle *et al*., 2009 (52)	Gastrointestinal	ED discharge diagnoses (ICD-10-CA code) from the National Ambulatory Care Reporting System (NACRS), which receives data from all hospitals in Ontario, Canada	Patient disposition from calls to Telehealth Ontario (nurse-assigned syndrome groups)	June 1, 2004 to March 31, 2006 (almost 2 years of data) Ontario province, Canada 184,904 calls and 34,499 ED visits for gastrointestinal illness Lagged (weekly) cross-correlations between time-series Spearman rank tests	0.90 ($p<0.0001$) correlation coefficient at lag 0 between ED discharge diagnoses from NACRS and Telehealth Ontario calls
Van Dijk *et al.*, 2008 (53)	Respiratory	Patient disposition from calls to Telehealth Ontario (nurse-assigned syndrome group)	ED discharge diagnosis (ICD-10-CA codes) from the from the National Ambulatory Care Reporting System (NACRS), which receives data from all hospitals in Ontario, Canada	July 4, 2004 to March 31, 2006 (almost 2 years of data) Ontario province, Canada 216,105 Telehealth Ontario calls for respiratory complaints 819,832 ED discharge diagnoses of respiratory illness Lagged (weekly) cross-correlations between time-series Spearman rank tests	0.97 ($p<0.0001$) correlation coefficient at lag 0 between Telehealth Ontario calls and ED discharge diagnoses from NACRS
Van Dijk *et al.*, 2009 (54)	Respiratory	ED chief complaint recorded by triage nurse (free text) from the Emergency Department Surveillance System (EDSS), which receives data from 7 hospitals in Southeastern Ontario, Canada	1) ED discharge diagnosis (ICD-10-CA codes) from the from the National Ambulatory Care Reporting System (NACRS), which receives data from all hospitals in Ontario, Canada 2) Patient disposition from calls to Telehealth Ontario (nurse-assigned syndrome group)	July 4, 2004 to March 31, 2006 (almost 2 years of data) Southeastern region of Ontario province, Canada 29,668 ED chief complaints of respiratory disease 19,315 ED discharge diagnoses of respiratory disease 4,247 Telehealth Ontario calls about respiratory disease Lagged (weekly) cross-correlations between time-series Spearman rank tests	0.98 ($p<0.0001$) correlation coefficient at lag 0 between ED chief complaints from EDSS and ED discharge diagnoses from NACRS 0.91 ($p<0.0001$) correlation coefficient at lag 0 between ED chief complaints from EDSS and Telehealth Ontario calls
Brabazon *et al*., 2010 (55)	Influenza-like illness	Patient self-reported reason for call (free text) to the general practitioner out-of-hours (GP OOH) telehealth system in Ireland, UK (7-9.5% population coverage)	Cases (weekly counts) reported by sentinel physicians to the Irish Sentinel GP influenza surveillance system (54 GPs, 5% population coverage)	2003-2009 (6 influenza seasons) Ireland, UK 539,732 calls to the GP OOH, of which 17,062 (3.2%) were for influenza-like illness Time-series modeling Spearman's rank correlation	Correlation between GP OOH calls for influenza-like illness and visits to sentinel physicians for influenza-like illness ranged from 0.68 to 0.90 over the 6 influenza seasons, and all were statistically significant

ED: emergency department. ICD: International Classification of Disease.

Table 3 (continued). Studies that have assessed the validity of syndromic surveillance case definitions based on administrative data using an ecological approach

Study	Syndrome under surveillance	Administrative data being validated (format)	Data used as comparison (format)	Study population and validation methodology	Findings
Cooper *et al*., 2007 (56)	Respiratory	Patient disposition from calls to NHS Direct health information telephone line (nurse-assigned syndrome group), available in England and Wales	Laboratory tests positive for respiratory viruses and *Strep. pneumoniae* (weekly counts) from the Health Protection Agency Centre for Infections, which collects reports from about 400 laboratories in England, Wales, and Northern Ireland	October 2002 to October 2004 (2 years of data) England and Wales, UK 601,454 NHS Direct calls for respiratory syndrome 49,652 laboratory reports positive for respiratory pathogens Looked at different ages categories: all ages vs. 0-4 years Multiple linear regression models to estimate the weekly proportion of NHS Direct calls (dependent variable) attributable to respiratory pathogens in laboratory reports (independent variable)	Respiratory viruses, notably influenza and respiratory syncytial virus (RSV) were responsible for at least 50% of the seasonal variation in NHS Direct calls. During the 2 influenza seasons, influenza was estimated to account for 25-51% of cold/flu calls (all ages), and 17-41% of fever calls (0-4 years).
Yih *et al*., 2009 (57)	Influenza-like illness	Patient disposition (nurse-assigned syndrome group) from calls to the Optum national managed-care nurse telephone triage service	From the US CDC Influenza Sentinel Provider Surveillance Network: 1) Laboratory tests positive for respiratory viruses and *Strep. pneumoniae* (weekly counts) 2) Cases reported by sentinel physicians (weekly counts)	October 3, 2004 to April 16, 2005 (1 influenza season) 17 US states with at least 500,000 residents eligible to use the nurse telephone triage service by virtue of their health insurance plan Analyses stratified by US state Pairwise lagged (weekly) correlations Pearson correlation test	For the 17 states, the median correlation coefficient between Optum calls and laboratory isolates was 0.65 (range 0.35-0.83) at lag 0; only 4 states had a correlation coefficient ≥0.75. For the 17 states, the median correlation coefficient between Optum calls and visits to sentinel physicians was 0.74 (range 0.34-0.83) at lag 0; and 8 states had a correlation coefficient ≥0.75.
Lazarus *et al*., 2001 (58)	Lower respiratory	Ambulatory care visit diagnoses (ICD-9 codes) and temperature from the electronic medical record used by Harvard Vanguard Medical Associates (10% population coverage of Eastern Massachusetts)	Mortality due to pneumonia or influenza (ICD-10 codes) in 122 US cities obtained from the US CDC	October 1996 to October 1999 (3 years of data) Eastern Massachusetts 152,435 visits for lower respiratory illness in the electronic medical record Time-series modeling Visual inspection only	Seasonal variation in visits for lower respiratory illness in the electronic medical record was similar to seasonal variation in mortality due to pneumonia or influenza. For most winters the counts of lower respiratory illness rise shortly before the peaks in mortality.

ED: emergency department. ICD: International Classification of Disease. US CDC: US Centers for Disease Control and Prevention.

Table 3 (continued). Studies that have assessed the validity of syndromic surveillance case definitions based on administrative data using an ecological approach

Study	Syndrome under surveillance	Administrative data being validated (format)	Data used as comparison (format)	Study population and validation methodology	Findings
Lazarus *et al*., 2002 (59)	Lower respiratory	Ambulatory care visit diagnoses (ICD-9 codes) and temperature from the electronic medical record used by Harvard Vanguard Medical Associates (10% population coverage of Eastern Massachusetts)	Hospitalisation discharge diagnoses (ICD-9 codes) from the Massachusetts Division of Healthcare Finance and Policy	October 1996 to October 1999 (3 years of data) Eastern Massachusetts Time-series modeling Spearman rank lagged (weekly) correlations	Correlation between the hospital discharge data and the ambulatory care data was: 0.89 at lag 0 0.90 at lag -1 week 0.92 at lag -2 weeks 0.89 at lag -3 weeks 0.85 at lag -4 weeks 0.85 at lag -5 weeks 0.80 at lag -6 weeks These results suggests that the hospital discharge data lagged behind the ambulatory care data
Van den Wijngaard *et al*., 2008 (60)	Respiratory	1) Hospitalisation discharge diagnoses (ICD-9-CM codes) from the Dutch National Medical Register (99% population coverage) 2) Mortality due to respiratory causes (ICD-10 codes) from Statistics Netherlands (100% population coverage) 3) Electronic medical record diagnoses for visits to general practitioners (IPCP codes) from the Netherlands Information Network of General Practice (1-2% population coverage) 4) Work absenteeism from Statistics Netherlands (80% coverage of the working population) 5) Laboratory test requests from the Dutch National Infectious Diseases Information System (16% coverage)	1) Laboratory tests positive for respiratory viruses (weekly counts) from the Weekly Sentinel Surveillance System of the Dutch Working Group in Clinical Virology (38-73% population coverage) 2) Laboratory tests positive for *Strep. pneumoniae* from 6 regional public health laboratories (24% population coverage) 3) Reports of pertussis to the national notifiable disease surveillance system	1999-2004 (5 years), or less for some data sources The Netherlands All data were aggregated by week Time-series modeling Pearson correlation coefficients Linear regression analyses with the number of syndrome cases as the dependent variable and the number of positive laboratory isolates as the independent variable, with lags of -5 to +5 weeks	Earliest syndrome elevations were observed in absenteeism data, followed by hospital data (+1 week), visits to general practitioners (+2 weeks), and mortality/laboratory test requests (+3 weeks). 86% of variation in syndrome counts was explained by the number of positive laboratory isolates.

ED: emergency department. ICD: International Classification of Disease. ICPC: International Classification of Primary Care.

Rigorous attempts to validate individual syndrome cases identified using diagnostic codes in administrative data against information on the same case from another data source have been few (Table 4). All have relied on small convenience samples of one or a few healthcare sites, bringing into question the generalizability of their findings. With the possible exception of Marsden-Haug *et al*. (49), all of these validation studies focused exclusively on emergency departments visits, yet there is evidence to suggest that visits to community healthcare settings offer potential for earlier outbreak detection (43;44). Also, many of these studies suffered from methodological limitations, which may explain the large differences in sensitivity estimates for the same syndromes in different studies; the specificity and negative predictive value of syndrome definitions were high in a majority of the studies.

In the next paragraphs, I review validation studies of case definitions from two large syndromic surveillance systems currently in use in North America: the University of Pittsburgh's Real-time Outbreak and Disease Surveillance System (RODS) and the US DoD's ESSENCE system. I provide a detailed discussion of the methodological limitations of these two studies, and I explain how these limitations may have biased the results.

Chapman *et al*. (61) performed a validation study of the syndrome case definitions used by the RODS system (Appendix B). They validated 7 syndrome case definitions (botulinic, constitutional, gastrointestinal, hemorrhagic, neurological, rash, and respiratory) consisting of ICD-9 coded diagnoses from hospital emergency department reports. They sampled only one site, the University of Pittsburgh Medical Center Presbyterian Hospital emergency department. A total of 1,557 hospital charts were reviewed by trained internists for the presence of none, one, or many of the syndromes under study, and the syndrome(s) abstracted from the chart were compared to the syndrome(s) obtained from the ICD-9 coded diagnosis in the emergency department report. Whereas the RODS study findings challenged some of the scepticism about using administrative data for surveillance purposes, the sampling of only 1 hospital emergency department

Table 4. Studies that have assessed the validity of syndrome definitions based on diagnostic codes through direct comparison of data on individual cases

Study	Syndrome under surveillance	Administrative data being validated (format)	Data used as comparison (format)	Study population and sampling	Accuracy of syndrome definitions based on ICD-9 codes	Limitations
Espino *et al*., 2001 (62)	Acute respiratory illness	1) ED chief complaint recorded by triage nurse (ICD-9 code) 2) ED discharge diagnoses (ICD-9 code)	Chart review of ED reports	University of Pittsburgh Medical Center Health System 9 hospital EDs Simple random sample of 800 visits July-October 2000 (4 months)	Prevalence based on chart review: 4.9% Chief complaint: Sn: 0.44 ± 0.15 Sp: 0.97 ± 0.01 PPV: 0.44 ± 0.15 NPV: 0.97 ± 0.01 Discharge diagnosis: Sn: 0.43 ± 0.15 Sp: 0.97 ± 0.01 PPV: 0.45 ± 0.16 NPV: 0.97 ± 0.04	Excluded 131 (16.4%) ED visit due to missing discharge diagnosis or chief complaint, therefore agreement may have been overestimated.
Bourgeois *et al*., 2007 (63)	7 syndromes, including: Fever Respiratory Gastrointestinal Dermatologic Neurological	1) ED chief complaint recorded by triage nurse (free text) 2) ED discharge diagnoses (ICD-9 code) 3) Patient/parent self-report survey (free text)	Chart review of ED reports	Children's Hospital Boston 1 hospital ED Patients aged 22 years or younger eligible February 2004-March 2005 (1 year) 85% participation rate during 'recruitment periods' 936 patients enrolled	Discharge diagnosis: Fever: Sn: 0.21, Sp: 0.99 Respiratory: Sn: 0.52, Sp: 99 Gastrointestinal: Sn: 0.75, Sp: 99 Dermatologic: Sn: 0.41, Sp: 0.99 Neurological: Sn: 0.67, Sp: 0.99	No description of 'recruitment periods', and annual census for that ED is approx. 51,000 patients, therefore difficult to assess the sampling strategy and population coverage. No estimates of PPV or NPV, and no confidence intervals provided.
Guasticchi *et al*., 2009 (64)	13 syndromes, including: Respiratory infection with fever Gastroenteritis Febrile illness with rash Meningitis-like	ED chief complaint recorded by triage nurse (syndrome category) and ED discharge diagnoses (ICD-9-CM code)	To estimate PPV, chart review of ED reports To estimate sensitivity, free-text physician diagnosis from ED report, present in only 40% of all ED reports	34 hospital EDs (of 61 in the Lazio region of Italy) All ED visits in 2004 (1 year) were eligible To estimate PPV, random sample of 300 cases for each of the 13 syndromes selected based on chief complaint and discharge diagnosis (jointly). To estimate sensitivity, used capture-recapture method	Chief complaint and discharge diagnosis (jointly): Respiratory infection with fever: PPV: 0.99, 95% CI (0.98, 1.00) Sn: 0.79, 95% CI (0.77, 0.81) Gastroenteritis: PPV: 0.94, 95% CI (0.92, 96.3) Sn: 0.76, 95% CI (0.74, 0.78) Febrile illness with rash: PPV: 0.98, 95% CI (0.97, 1.00) Sn: 0.77, 95% CI (0.76, 0.78) Meningitis-like : PPV: 0.37, 95% CI (0.32, 0.41) Sn: 0.32, 95% CI (0.26, 0.40)	Agreement overestimated because used a modified version of the capture-recapture methodology, but with two different data fields from the same data source (i.e., the data sources were not independent).

ED: emergency department. ICD: International Classification of Disease. Sn: sensitivity. Sp: specificity. PPV: positive predictive value. NPV: negative predictive value. ICPC: International Classification of Primary Care.

Table 4 (continued). Studies that have assessed the validity of syndrome definitions based on diagnostic codes through direct comparison of data on individual cases

Study	Syndrome under surveillance	Administrative data being validated (format)	Data used as comparison (format)	Study population and sampling	Accuracy of syndrome definitions based on ICD-9 codes	Limitations
May *et al*., 2010 (50)	Influenza-like illness Gastrointestinal Viral illness	ED discharge diagnoses (ICD-9 code)	ED chief complaint recorded by triage nurse (free text or pull-down menu)	1 hospital ED in Washington, DC June 2005-May 2006 (1 year) Sampled all visits with either an ED chief complaint or an ED discharge diagnosis corresponding to one of the syndrome definitions 5,682 ED visits sampled	Influenza-like illness: % agreement: 71% Gastrointestinal: % agreement: 61% Viral illness: % agreement: 76%	Cannot estimate Sn or PPV because no 'syndrome-negative' ED visits (based on either source of information) were sampled.
Betancourt *et al*., 2007 (65)	CDC-ESSENCE syndrome definitions (66): Fever Gastrointestinal Respiratory	ED discharge diagnoses (ICD-9 code)	Chart review of ED reports	3 military hospital EDs September 1999-August 2000 (1 year) Random sample of ED visits, stratified on syndrome status based on ED discharge diagnosis (case to non-case ratio of 1:2)	Fever (N=465): Sn: 0.69, Sp: 0.96, PPV: 0.81, NPV: 0.92 Gastrointestinal (N=875): Sn: 0.89, Sp: 0.96, PPV: 0.93, NPV: 0.94 Respiratory (N=454): Sn: 0.66, Sp: 0.96, PPV: 0.81, NPV: 0.91	Sensitivity overestimated and specificity underestimated due to verification bias introduced by sampling strategy stratified on syndrome status based on ED discharge diagnosis. No 95% confidence intervals provided for the estimates.
Marsden-Haug *et al*., 2007 (49)	Influenza-like illness	Military treatment facility outpatient visit diagnoses (ICD-9 code)	Laboratory tests positive for influenza A or B	US Air Force military treatment facilities June 2002-June 2004 (2 years) All 6,236 outpatient visits where a respiratory specimen was collected and tested for viral pathogens	% visits with a test positive for influenza A or B is reported for each ICD-9 code separately, with the highest (75%) being for influenza with pneumonia (ICD-9 487.0), and the lowest (0%) for acute tonsilitis (ICD-9 463)	Collection of respiratory specimens at the discretion of the treating physician (convenience sample). Whereas definitions of influenza-like illness consisting of ICD-9 codes are suggested based on viral positivity, their Sn, Sp, PPV, and NPV are not estimated.
Chapman *et al*., 2005 (61)	7 syndromes, including : Constitutional Respiratory Gastrointestinal Neurological Rash	ED discharge diagnoses (ICD-9 code)	Chart review of ED reports	University of Pittsburgh Medical Center Presbyterian Hospital (1 hospital ED) December1990-September 2003 (14 years) Random sample of 1,557 ED visits, stratified on syndrome type (7) and ICD-9 code within syndrome	Constitutional: Sn: 0.24, PPV: 0.43 Respiratory: Sn: 0.38, PPV: 0.74 Gastrointestinal: Sn: 0.30, PPV: 0.86 Neurological: Sn: 0.29, PPV: 0.79 Rash: Sn: 0.66, PPV: 0.48	PPV likely underestimated because of sampling strategy (i.e., the stratification on ICD-9 code within syndrome) was not taken into account. Sensitivity affected by sampling strategy as above, and also subject to verification bias.

ED: emergency department. ICD: International Classification of Disease. Sn: sensitivity. Sp: specificity. PPV: positive predictive value. NPV: negative predictive value. ICPC: International Classification of Primary Care.

raises concerns about the generalizability of results. Also, the investigators sampled equal numbers of charts for each ICD-9 diagnostic code that comprise the 7 syndrome definitions. Consequently, the final chart review sample did not reflect the true frequency distribution of diagnostic codes. Because infrequent diagnostic codes are more likely to result from coding errors (67;68), the reported sensitivity and positive predictive value estimates were likely biased downward. Also, the analysis did not adjust for the verification bias induced by the relative difference in the sampling fraction for cases (ED visits with a diagnosis corresponding to the syndrome of interest) and non-cases (ED visits with a diagnosis corresponding to any other syndrome); verification bias results in an over-estimation of sensitivity and underestimation of specificity (69). The use of ED visits with a diagnosis corresponding to any other syndrome as 'non-cases' is also problematic, because, as the authors themselves report, fever (ICD-9 code: 780.6), which is included in the case definition of constitutional syndrome, is often present among cases of other syndromes as well (e.g., gastrointestinal, respiratory, neurological). The use of cases of other syndromes as controls may have led to an underestimation of sensitivity: due to overlapping case definitions, chart review would have shown that a portion of the ED visits originally classified as non-cases for a given syndrome were really cases of that syndrome.

Two years later, Betancourt *et al*. (65) published a validation of the syndrome definitions developed by the US CDC (66) and used by the US DoD's ESSENCE system. In that study, the accuracy of ICD-9 codes in ED reports for identifying 3 syndromes (fever, gastrointestinal, and respiratory) was assessed as compared to hospital chart diagnoses. The investigators sampled only 3 military treatments facilities, and they reported substantial variation in sensitivity and positive predictive value between sites, which raises questions about the generalizability of their results. For greater data collection efficiency, the fraction of syndrome-positive ED reports sampled was larger than the fraction of syndrome-negative ED reports sampled. However, analyses were not adjusted for this sampling strategy, which resulted in verification bias (69;70), and led to

a large overestimation of sensitivity and underestimation of specificity. Furthermore, syndrome-negative ED visits were not matched to syndrome-positive ED visits on season. Because most syndromes follow seasonal variation, this sampling strategy may have resulted in seasonal bias if the seasonal distribution of the syndrome-negative ED visits was different from that of the syndrome-positive ED visits. For example, if respiratory syndrome cases occurred predominantly in winter, and non-cases were sampled predominantly from the summer months, then sensitivity would be overestimated because, due to the lower prevalence of respiratory syndrome in summer, fewer summer non-cases than winter non-cases would turn out to be false-negatives after chart review.

In summary, a majority of validation studies of syndrome case definitions based on administrative data have relied on an ecological approach, whereby two time-series of case counts are compared using cross-correlations. Fewer studies involved a 'direct' validation of individual syndrome cases identified from administrative data against a 'gold standard', most often medical chart review. Of those studies that validated individual syndrome cases, a majority relied on small convenience samples of one or a few healthcare sites, and all suffered from methodological limitations that impeded the interpretation and comparison of their findings. A common methodological limitation was verification bias, which resulted from the use of a stratified sampling strategy whereby the proportion of cases validated was higher relative to the proportion of non-cases validated. We provide a detailed explanation of how verification bias arises, its impact on results, and how to correct for it in the next section of this chapter.

Verification bias: source, effect, and correction

Verification bias was first described in relation to diagnostic test evaluation (69). It referred to the situation in which patients are first tested with test A (e.g., fecal occult blood test), and then, based on the clinician's interpretation of the results from test A in

the context of other relevant factors (e.g., other signs, symptoms, family history), some patient are selected to undergo test B (e.g., colonoscopy). Verification bias arises in the estimation of the sensitivity and specificity of test A when a non-representative sample of patients who underwent test A are selected to undergo test B. For example, for a screening test, a larger fraction of patients who tested positive on the screening test A will typically be selected to undergo the diagnostic test B, as compared to the fraction of patient who tested negative on test A who may be asked to undergo the diagnostic test B (based on the full clinical picture available at the time). Failure to account for the mechanism whereby patients are selected to undergo test B (i.e., the 'verification' test) when estimating the sensitivity and specificity of test A results in verification bias, the consequence of which is that the sensitivity of test A is overestimated and the specificity of test A is underestimated.

Verification bias in diagnostic testing

		Diagnostic Test B		
		Positive	Negative	
Screening Test A	Positive	TP	FP	Typically, a larger fraction of patients who tested positive on the screening test will be asked to undergo the diagnostic test, as compared to patients who tested negative on the screening test.
	Negative	FN	TN	Some patients who tested negative on the screening test may still be asked to undergo the diagnostic test, based on other relevant information.

Whereas verification bias was first described for diagnostic tests, it also arises in any validation study based on a stratified random sample where the sampling fractions differ between the 'positive' (cases) and 'negative' (non-cases) strata. This stratified sampling strategy is often used to validate case definitions of diseases that have low population prevalence, because the alternative – validating a simple random sample large enough to include a sufficient number of cases – is often infeasible. Therefore, for diseases that have low population prevalence, investigators usually sample a larger fraction of the cases than the non-cases, i.e., they select a relatively larger random sample in the case stratum than in the non-case stratum.

Syndromes monitored by syndromic surveillance systems typically have a low population prevalence; for example, one study (62) reported a prevalence of 4.9% for respiratory syndrome. For this reason, validation studies of case definitions used by two large syndromic surveillance systems in North America, RODS (61) and ESSENCE (65), both used such a stratified random sampling strategy. However, neither corrected their sensitivity and specificity estimates for the verification bias caused by their sampling strategy. The example below, based on the validation study of ESSENCE case definitions by Betancourt *et al.* (65), illustrates how verification bias arises from the use of this type of stratified random sampling.

Stratified random sample of ESSENCE reports

		Chart review (gold standard)		
		Fever-positive	Fever-negative	Total
ESSENCE reports	Fever-positive	378	87	465
	Fever-negative	167	1,842	2,009
	Total	545	1,929	2,474

Sensitivity = 0.69 (overestimated)
Specificity = 0.95 (underestimated)
Positive predictive value = 0.81
Negative predictive value = 0.92
Prevalence of fever-positive ESSENCE reports in this study sample = 0.19

Simple random sample of ESSENCE reports

		Chart review (gold standard)		
		Fever-positive	Fever-negative	Total
ESSENCE reports	Fever-positive	378	87	465
	Fever-negative	3,683	42,352	46,035
	Total	4,061	42,439	46,500

Sensitivity = 0.09
Specificity = 1.00
Positive predictive value = 0.81
Negative predictive value= 0.92
Prevalence of fever-positive ESSENCE reports in the entire system= 0.01

In this example, there were 465 fever-positive and 2,009 fever-negative ESSENCE reports sampled, for a sample prevalence of fever-positive ESSENCE reports of 19%. Assuming that the prevalence of fever syndrome in ESSENCE reports is similar to the prevalence of fever syndrome in billing claims from primary care physicians practicing in the province of Quebec (71), the true prevalence of fever-positive reports in ESSENCE should be about 10 per 1,000 reports or 1%. Because estimating sensitivity and specificity involves summing fever-positive and fever-negative ESSENCE reports (i.e., summing numbers from different sampling strata), failure to adjust for the different sampling fractions in

each stratum leads to verification bias. Verification bias does not affect the positive predictive value or the negative predictive value because positive predictive value is estimated within the sampling stratum of fever-positive ESSENCE reports, and negative predictive value is estimated within the sampling stratum of fever-negative ESSENCE reports (i.e., each is estimated within its own sampling stratum, not across sampling strata).

Another way of explaining verification bias is to compare the ratio of fever-positive to fever-negative ESSENCE reports in the study sample, which is 465 to 2,009 (about 1:4), to the same ratio for the entire population of ESSENCE reports, which is 465 to 46,035 (about 1:99). Verification bias arises because the ratio of fever-positive to fever-negative ESSENCE reports is not the same in the sample and in the population. By manipulating the ratio of fever-positive to fever-negative ESSENCE reports in the sample (and not adjusting for the resulting verification bias), sensitivity is artificially inflated and specificity is underestimated.

A method for correcting for verification bias was published by Begg and Greenes (69). It involves taking into account the relative difference in sampling fractions between the syndrome-positive stratum and the syndrome-negative stratum in the estimation of sensitivity and specificity. The larger the relative difference in sampling fractions between strata, the bigger the change in sensitivity and specificity when the verification bias correction is applied. For syndrome definitions based on diagnoses in administrative data, which usually have low prevalence and very high specificity, the impact of the verification bias correction is usually greater for sensitivity estimates, as compared to specificity estimates. In the example above, the sensitivity is reduced drastically, from 0.69 to 0.09, and the specificity is slightly increased, from 0.95 to 1.00.

Predictors of accuracy of case definitions based on administrative data

There have been a few attempts to improve the accuracy of syndromic surveillance systems by modifying statistical outbreak detection algorithms (37-39) or by using different data sources (42;72). Only one study has attempted to improve the accuracy of a case definition used in syndromic surveillance by taking into account covariates. DeLisle *et al.* (73), sought to improve the accuracy of a case definition of acute respiratory infection based on ICD-9 diagnostic codes from the Veteran's Affairs Healthcare system by also considering other structured data from the electronic medical record (vital signs, test orders, imaging requests, and symptom-relief or antimicrobial drug prescriptions) and respiratory symptoms (e.g., cough) extracted from the free-text clinical notes. They found that algorithms including ICD-9 diagnostic codes performed significantly better than those that did not include them, suggesting that ICD-9 diagnostic codes represent an invaluable source of data for syndromic surveillance systems. They also found that adding prescriptions for cough remedies and elevations in body temperature to the case definition based on ICD-9 codes significantly improved its sensitivity, but decreased its specificity and positive predictive value. Adding symptoms extracted from free-text analysis further increased sensitivity, but caused a large decline in positive predictive value.

In areas outside syndromic surveillance, diagnostic codes in administrative data are commonly used to identify disease cases. Many studies have attempted to identify covariates associated with the accuracy of case definitions based on diagnostic codes in administrative data. Most of these studies have focused on improving the identification of chronic disease cases using diagnoses in administrative databases.

In order to identify potential covariates that may influence the accuracy of case definitions based on diagnostic codes in administrative data, an understanding of the mechanism whereby diagnostic codes are entered on physician claims is necessary.

Figure 2 illustrates the steps commonly involved in physician billing for outpatient visits in a fee-for-service healthcare system. First, the physician meets with the patient, takes the patient's medical history and performs the relevant physical examination(s). Then, the physician documents his observations in the medical chart and fills out a billing slip. Figure 3 is an example of the physician billing slip used in the province of Quebec; of note, only one 4-digit ICD-9 diagnostic code can be entered per billing slip. The information on the billing slip is then entered into billing software; this step may be accomplished by the physician, a secretary or clerk at the clinic, or by an off-site billing agency. The claim is then submitted to the Quebec provincial health agency electronically. Fax or mail submission of paper billing slips is rare, because a penalty of $0.50 is levied on each billing slip not submitted electronically. Although physicians have up to 3 months from the date of the visit to submit a claim to the Quebec provincial health agency, claims submission generally follows the biweekly physician reimbursement cycle.

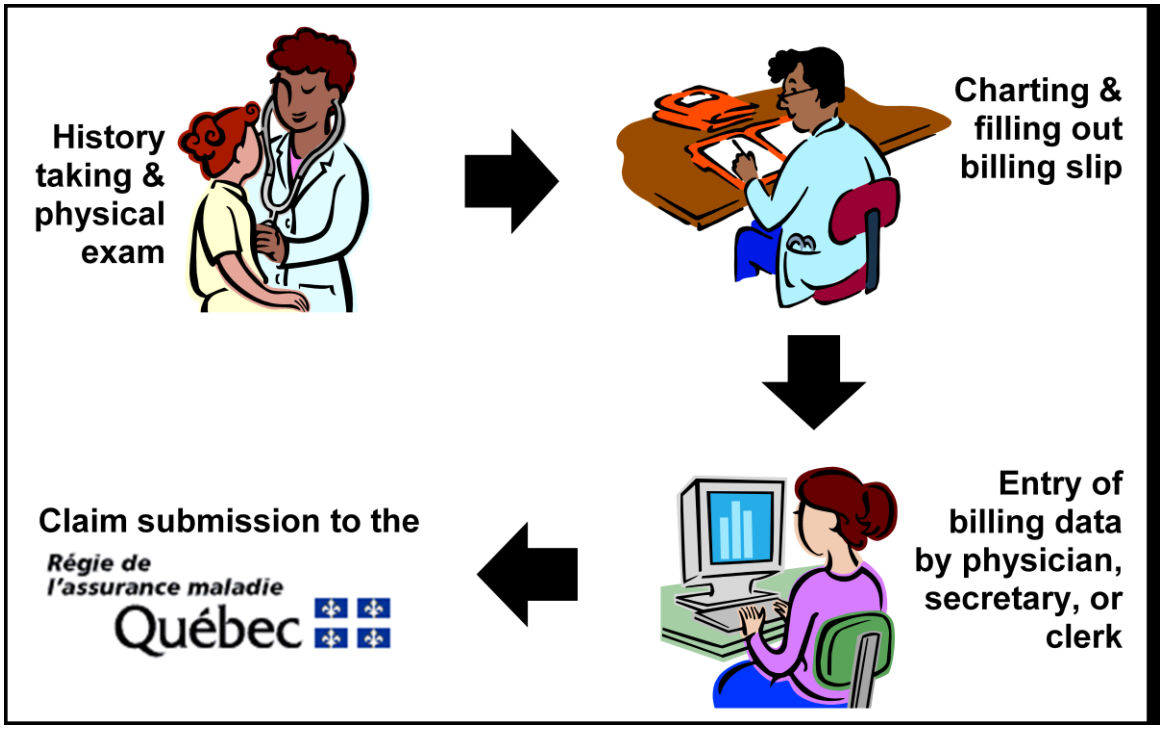

Figure 2. Typical process of physician billing for outpatient visits in fee-for-service healthcare system

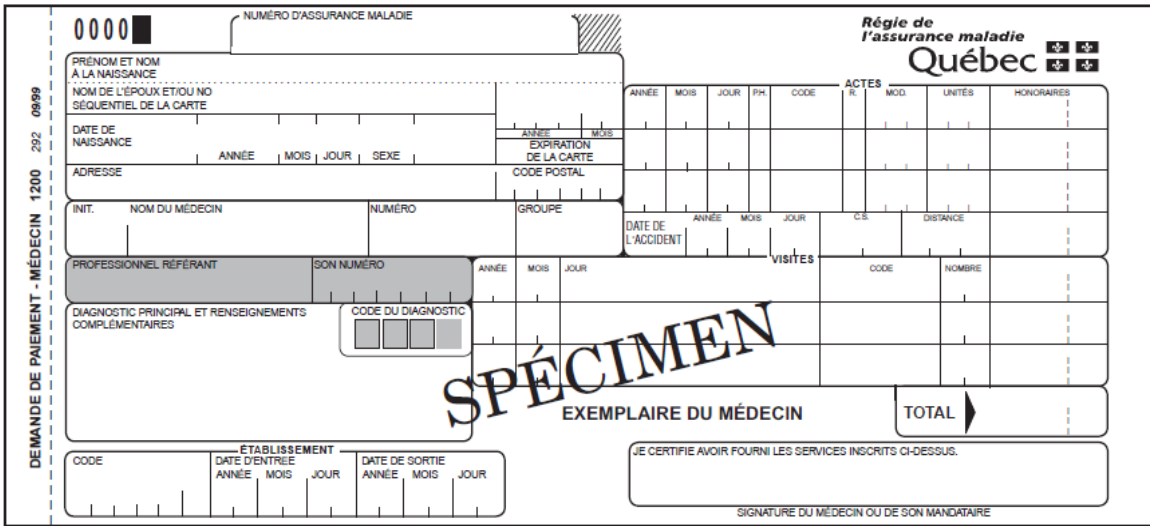

Figure 3. Physician billing slip used in the province of Quebec; only one 4-digit ICD-9 diagnostic code can be entered per billing slip

In keeping with what is known about the physician billing process, previous attempts to improve the identification of chronic disease cases using diagnoses in administrative databases have investigated the effect of covariates such as the characteristics of the physician, patient, encounter or hospitalisation, and healthcare site (Table 5).

Whereas diagnoses in administrative databases are often assigned by physicians, especially for visits to community clinics, few studies have investigated the impact of physician characteristics on the accuracy of diagnostic codes in administrative data. Studney *et al*. (46) reported that physician workload, as measured by both gross income and the number of patients seen per day, was significantly and negatively associated with billing diagnosis accuracy. A study by Farzandipour *et al*. (45) reported that errors in ICD-10 principal diagnosis coding were more common among coders with more years of experience and among those who coded from memory instead of using reference materials. Whereas the Farzandipour *et al*. study involved hospitalisations for which ICD-10 coding was performed by professional medical records coders, its findings are likely to also apply to physicians, when working in clinical settings where they perform their own diagnostic coding. Finally, a study by Peabody *et al*. (74) reported that the physician error rate in primary diagnosis varied by healthcare site and by condition, with

Table 5. Studies that have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data

Study	Disease(s) under study	Administrative data being validated (format)	Data used as comparison (format)	Covariate data source	Study population and sampling	Statistical analysis	Findings
Farzandipour *et al*., 2010 (45)	No specific disease targeted	Hospital discharge diagnoses (ICD-10 codes)	Blinded expert recoding of discharge diagnoses (ICD-10 codes)	Original coder's experience and education were obtained from personnel files Coding practice was assessed through direct observation	Stratified random sample of 370 hospitalisations to 4 teaching hospitals in Kashan, Iran in 2007-2008	Outcome: errors in principal diagnosis coding Bivariate analyses Chi-squared tests	Errors were present in principal diagnosis coding in 84 (22.7%) medical records. Less experienced coders made fewer errors ($p < 0.0001$) As compared to memory-based coding, using reference materials was associated with fewer coding errors ($p<0.0001$).
Studney *et al*., 1981 (46)	No specific disease targeted	Billing diagnoses on account cards (in words, not coded)	Medical record review	Average patients seen per day was computed from day sheets for the study period Gross income was based on gross billing for the study period	Sample of 1,215 visits to 12 physicians from 1 clinic located in British Columbia, Canada over a 3-month period in 1976	Outcome: % agreement between billing diagnosis and medical record diagnosis Bivariate analyses Pearson's correlation coefficients	Disagreement on principal diagnosis was present in 40% of visits. Agreement was significantly ($p<0.01$) and negatively associated with physician workload, as measured by both average patients seen per day ($r = -0.73$) and gross income ($r=-0.75$).
Peabody *et al*., 2004 (74)	Diabetes, COPD, vascular disease, depression	1) Diagnoses in computerized administrative records (format not described) 2) Diagnoses on administrative encounter forms	Medical record review	Disease was assigned to each standardized patient Training was categorized as 2nd year resident, 3rd year resident, or attending physician	348 visits by 45 standardized patients at 3 outpatient clinics in San Francisco, CA between March-July 2002	Outcome: % agreement between diagnoses in administrative data and medical record diagnoses Bivariate analyses Chi-squared tests	Administrative data contained the correct diagnosis in 57% of visits. Agreement was significantly ($p<0.05$) different for different diseases and clinics. Agreement was not significantly associated with physician training (R2, R3, or attending).
Kostylova *et al*., 2005 (75)	Head injury, probable head injury, orthopedic injury	Physician claims diagnoses from the *Régie de l'assurance maladie du Québec* (ICD-9 codes)	Canadian Hospitals Injury research and Prevention Program (CHIRPP) database	Patient age and sex was obtained from the CHIRPP database	3,145 children aged 1-18 years who sought care for an injury in 2000-2001 at either of the two Montreal pediatric hospitals emergency departments	Outcome: agreement between physician claims diagnosis and CHIRPP data Bivariate analyses	Good agreement (Kappa, 0.66) Mean age of children whose claim diagnosis disagreed with CHIRPP diagnosis (6.6 years) was significantly lower than that of children whose claim diagnosis agreed with the CHIRPP diagnosis (8.5 years) ($p<0.001$).

ICD: International Classification of Disease. COPD: chronic obstructive pulmonary disease.

Table 5 (continued). Studies that have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data

Study	Disease(s) under study	Administrative data being validated (format)	Data used as comparison (format)	Covariate data source	Study population and sampling	Statistical analysis	Findings
Andrade *et al*., 2002 (76)	Peptic ulcer, upper gastro-intestinal bleeding	Hospital discharge diagnoses (ICD-9-CM codes)	Diagnosis confirmed by surgery, endoscopy, x-ray or autopsy documented in the hospital chart	Patient age and gender were obtained from the health maintenance organization database	8 large US health maintenance organizations 1,152 hospitalisations with a hospital discharge diagnosis of peptic ulcer or upper gastrointestinal bleeding in 1994-1997 The hospital chart was located for 884 (76.7%) hospitalisations	Outcome: PPV of hospital discharge diagnoses Bivariate analyses Chi-squared test	The discharge diagnosis was confirmed for 207 (23.4%) hospitalisations. The proportion of confirmed discharge diagnoses was higher among patients aged less than 60 years (32%) as compared to those 80 years and older (19%) ($p = 0.01$). Site-specific diagnostic codes had higher positive predictive values than nonspecific codes.
Losina et al., 2003 (77)	Rheumatoid arthritis, avascular necrosis, osteoathritis	Hospital and surgeons' Medicare claim diagnoses (ICD-9-CM codes)	Medical record review	Hospitals were categorized as low- and high-volume based on a cut-off of 25 total hip replacements per year (median of the sample)	A stratified random sample of 922 Medicare beneficiaries who received total hip replacement in 1995 in Ohio, Pennsylvania, and Colorado	Outcomes: sensitivity and PPV of the Medicare claim diagnoses Bivariate analyses Chi-squared test ($p<0.05$)	Sensitivity ranged from 0.54 (95% CI, 0.42-0.66) for avascular necrosis to 0.96 (95% CI, 0.95-0.98) for osteoathritis. PPV did not differ by disease (range, 0.86-0.89). Sensitivity was higher for rheumatoid arthritis and lower for avascular necrosis in low-volume hospitals as compared to high-volume ones. No relationship between PPV and hospital volume.
Jollis *et al*., 1993 (78)	12 prognostic factors in patients with ischemic heart disease	Medicare claims diagnoses (ICD-9-CM codes)	Hospital clinical information system	Patient age and sex were obtained from the hospital clinical information system	All 12,937 Medicare patients who underwent inpatient cardiac catheterization at Duke Medical Center in 1985-1990	Outcome: Sensitivity of Medicare claims diagnoses Bivariate analyses Chi-squared test	The sensitivity of Medicare claims diagnoses ranged from 0.83 for diabetes to 0.14 for unstable angina and tobacco use. Sensitivity of Medicare claims diagnoses was significantly higher for patients aged less than 65 years as compared to patients aged 65 years and older.

ICD: International Classification of Disease. PPV: positive predictive value.

Table 5 (continued). Studies that have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data

Study	Disease(s) under study	Administrative data being validated (format)	Data used as comparison (format)	Covariate data source	Study population and sampling	Statistical analysis	Findings
Katzman-McClish *et al*., 1997 (79)	Breast, colorectal, lung, and prostate cancers	Medicare claims diagnoses (ICD-9-CM codes)	Virginia Cancer Registry	Patient age, gender, and comorbidity were obtained from the Medicare database Income and education were obtained from the 1990 Census Cancer stage was obtained from the Virginia Cancer Registry	All Virginia residents aged 65 years and older with a breast (N=3,690), colorectal (N=4,690), lung (N=5,781), or prostate (N=4,495) cancer diagnosis in the Virginia Cancer Registry in 1986-1989	Outcome: case not identified by Medicare claims (yes/no) Multivariate logistic regression analyses stratified by type of cancer	Medicare claims diagnoses identified between 73% (prostate cancer) and 83% (breast and lung cancers) of cases in the registry. Patient characteristics associated with Medicare claims data missing a case included age 65-75 years (vs. 75+ years), male gender, urban area of residence, higher education and income, in situ disease, and lack of comorbidity.
Ostbye *et al*., 2008 (80)	Dementia	Medicare claims diagnoses (ICD-9-CM codes)	Self- or proxy-reported cognitive status from the Asset and Health Dynamics among the Oldest Old (AHEAD) national survey	Patient age, gender, and education (data source not described)	7,974 cases of dementia were identified from the AHEAD study Of those, 80% consented to share their Medicare claims data with the researchers	Outcome: agreement (yes/no) Multivariate logistic regression analyses with	Agreement between Medicare claims and survey data was poor (Cohen's Kappa, 0.23; 95% CI, 0.17-0.30). Agreement between Medicare claims and survey data was more likely among older ($OR_{per\ year\ of\ age}$, 0.94; 95% CI, 0.93-0.96) and more educated respondents ($OR_{per\ year\ od\ education}$ 1.05; 95% CI, 1.02-1.07).
Muhajarine *et al*., 1997 (34)	Hypertension	Physician claims data from the Manitoba Health Insurance Plan (ICD-9-CM codes)	Manitoba Heart Health Survey: 1) patient self-report 2) clinical measurement of blood pressure	Patient sex, age, education, income, employment, and marital status, smoking, obesity, cholesterol levels, physical activity, diabetes, and cardiac medications were obtained from the survey	Stratified random sample of 2,792 non-institutionalized adults aged 18-74 years residing in Manitoba 2,339 (84%) completed the clinical visit 2,275 (97.3%) had a physician claim in the 2 years before the survey	Outcome: Disagreement (yes/no) Multivariate logistic regression analyses	Disagreement between claims and clinical measurement was more likely among homemakers (OR, 1.78; 95% CI, 1.11-2.84), 1.62-2.79), obese patients (OR, 2.13; 95% CI, 1.62-2.79), older patients ($OR_{55+\ vs.\ 18-34\ y.o.}$, 2.92; 95% CI, 1.84-4.61), patients with hypercholesterolemia (OR, 1.35; 95% CI 1.02-1.79), and patients on medication for heart disease (OR, 1.66; 95% CI 1.13-2.43).

ICD: International Classification of Disease.

Table 5 (continued). Studies that have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data

Study	Disease(s) under study	Administrative data being validated (format)	Data used as comparison (format)	Covariate data source	Study population and sampling	Statistical analysis	Findings
MacIntyre *et al*., 1997 (67)	Australian national diagnosis-related groups (ANDRG)	Victorian In-Patient Minimum Database (ICD-9-CM codes)	Medical record audit	Hospital location (rural or urban), admission type (emergency or other), length of stay, death, ANDRG frequency, and type of ANDRG (medical or other) were obtained from the Victorian In-Patient Minimum Database	7,013 cases from 63 (54%) Victorian hospitals in the year 1993-1994 were randomly selected and audited	Outcome: disagreement on principal diagnosis Multivariate logistic regression analyses	Disagreement was present in 1,565 (22%) cases. Disagreement was more likely among hospitalizations longer than 5 days (OR, 1.95; 95% CI, 1.69-2.25), involving emergency admission (OR, 1.14; (% CI, 1.02-1.28), and resulting in death (OR, 1.90; 95% CI 1.19-3.00). Likelihood of discrepancy increased with increasing rarity of ANDRG.
Taylor *et al*., 2002 (81)	Alzheimer's disease	ICD-9 codes in Medicare claims (ICD-9 codes)	Clinical diagnosis of Alzheimer's disease in the Consortium to Establish a Registry for Alzheimer's Disease (CERAD)	Patient age, education, marital status, and Alzheimer's disease severity, were obtained from CERAD Number of visits was ascertained from Medicare claims	417 patients with a clinical diagnosis of Alzheimer's disease in CERAD	Outcome: Alzheimer's disease diagnosis in Medicare claims (among patient so diagnosed in CERAD) Multivariate Cox proportional hazards analyses	A diagnosis of Alzheimer's in Medicare claims was more likely among males (HR, 1.27; $p<0.05$), younger patients ($HR_{per\ year}$, 0.97; $p<0.05$), patients with less severe disease (HR_{stage}, 0.65; $p<0.01$). The likelihood of a diagnosis of Alzheimer's in Medicare claims increased with the number of visits ($HR_{per\ visit}$, 1.09; $p<0.001$).
Singh *et al*., 2009 (82)	Arthritis	Diagnosis in the Veteran's Affairs administrative data (ICD-9 -CM codes)	Patient self-reported physician diagnosis from the Prior Veterans' Quality of Life (Vet-QoL) survey	Patient sex, education, comorbidity, activity limitation, tobacco use, and health status (SF-36) were obtained from the survey database	Of 70,334 veterans contacted for the survey, 34,440 (49.0%) answered the question on arthritis	Outcome: Discordance between administrative and survey data Multivariate logistic regression analyses	Poor agreement (Kappa, 0.25) Discordance more likely among infrequent healthcare users ($OR_{lowest\ vs.\ highest\ tertile}$, 1.11; 95% CI, 1.03-1.19), with no prior hospitalization ($OR_{1+\ vs.\ 0}$, 0.88; 95% CI, 0.80-0.96), older veterans ($OR_{65+\ vs.\ <50\ y.o.}$, 1.38; 95% CI, 1.26-1.52), with more comorbidities ($OR_{3+\ vs.\ 0}$, 1.54; 95% CI, 1.40-1.69), and worse physical health ($OR_{highest\ vs.\ lowest\ PCS\ score\ tertile}$, 0.83; 95% CI, 0.76-0.91).

ICD: International Classification of Disease.

Table 5 (continued). Studies that have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data

Study	Disease(s) under study	Administrative data being validated (format)	Data used as comparison (format)	Covariate data source	Study population and sampling	Statistical analysis	Findings
Lix *et al*., 2008 (83)	Osteoporosis	Physician claims diagnoses from the Manitoba Health Insurance Plan (ICD-9-CM codes)	BMD test results in the Manitoba Bone Density Program database	Patient age, region of residence, income quintile, comorbidity, osteoporosis prescriptions were obtained from administrative databases	5,527 patients with at least one BMD test in the Manitoba Bone Density Program database during the fiscal year 2000-2001	Outcome: osteoporosis based on BMD test result Multivariate logistic regression analyses	Likelihood of osteoporosis based on BMD test increased with an ICD-9 diagnostic code for osteoporosis in physician claims (OR, 2.74; p <0.0001), a prescription for an osteoporosis-specific medication (OR, 5.13; p<0.0001), and older age ($OR_{per\ year\ of\ age}$: 1.06; p<0.0001).
Gabriel *et al*., 1996 (84)	Osteoarthritis	Diagnoses from the Olmsted County, Minnesota computerized database (ICD-9 code)	Medical record review	Patient age and sex were obtained from the computerized database	Random sample of 400 patients with a diagnosis of osteoarthritis in the computerized database in1975-1987 The medical record was available for 387 (96.8%) patients	Outcome: positive predictive value of the computerized database Recursive partitioning analysis	Positive predictive value of the computerized database: 60% (232/387). Older patients were more likely to be true-positives.
Love *et al*., 2010 (85)	Psoriatic arthritis	Physician billing diagnostic codes (ICD-9) in the Research Patient Data Registry (RDPR)	Rheumatologist-diagnosed psoriatic arthritis ascertained by a review of the RDPR	Coded data from the RDPR Information extracted from the full text visit notes from the RDPR Laboratory values from the RDPR	2,318 patients with a physician billing diagnostic code for psoriatic arthritis in 1995-2007 were identified from the RDPR of the Brigham and Women's Hospital and its outpatient clinics (Boston, MA) A random sample of 550 (23.7%) patient records were reviewed	Outcome: rheumatologist-diagnosed psoriatic arthritis Random forest analysis (an extension of recursive partitioning)	The sensitivity of coded data (e.g., number of psoriatic arthritis diagnostic codes) for identifying rheumatologist-diagnosed psoriatic arthritis was improved by the addition of variables extracted from the medical record using natural language processing (e.g., the number of rheumatology and clinic notes mentioning psoriatic arthritis) and laboratory values (e.g., highest erythrocyte sedimentation rate).

ICD: International Classification of Disease. BMD: bone mineral density.

Table 5 (continued). Studies that have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data

Study	Disease(s) under study	Administrative data being validated (format)	Data used as comparison (format)	Covariate data source	Study population and sampling	Statistical analysis	Findings
Szumski *et al*., 2009 (86)	Parkinson's disease	Diagnoses from Veteran's Affairs administrative data (ICD-9-CM codes)	Medical record review	Patient age, sex, number of diagnostic codes for Parkinson's disease, number of visits to neurology clinic, and number of visits to movement disorder clinic were obtained from the Veteran's Affairs database	577 patients with a diagnosis of Parkinson's disease in the Veteran's Affairs administrative database between October 1, 2001 and September 30, 2002	Outcome: sensitivity, specificity, PPV and NPV of administrative data as compared to the chart Two-sample test of proportion (α=0.05) used to compare outcome estimates across algorithms	Medical record review determined 436 (75.6%) patients to have Parkinson's disease. PPV of administrative data was improved by giving greater weight to diagnostic codes from specialists over non-specialists, and by taking into account prescriptions for Parkinson's disease-related medications.
Van Walraven *et al*., 2010 (87)	Kidney disease	Diagnoses in the Ottawa Hospital Data Warehouse (ICD-10)	Serum creatinine measurements from the from the Ottawa Hospital Data Warehouse	Patient age, sex, and comorbidity were obtained from the Ottawa Hospital Data Warehouse Hospitalization-level characteristics: admission urgency, admitting service, ICU stay, surgical procedures, hospital survival, and length of stay were obtained from the Ottawa Hospital Data Warehouse	A random sample of 100,000 adult admissions to the Ottawa Hospital in 2002-2008 was selected from the Ottawa Hospital Data Warehouse	Outcome: kidney disease based on serum creatinine measurements Multivariate logistic regression	Kidney disease was confirmed by serum creatinine in 20,713 (20.7%) patients. The most powerful predictor of kidney disease based on serum creatinine was a diagnostic code for kidney disease (RR: 34.4). Other variables were associated with kidney disease based on serum creatinine, including patient characteristics (e.g., age, gender, comorbidities) and hospitalization characteristics (e.g., length of stay, ICU stay, dialysis).

ICD: International Classification of Disease. ICU: intensive care unit. PPV: positive predictive value. NPV: negative predictive value.

errors being less common for diabetes and more common for chronic obstructive pulmonary disease and vascular disease. That study found no association between physician experience and diagnostic coding errors, but a very uninformative measure of experience was used: physicians were categorized as 2nd year resident, 3rd year resident, or attending physician, with the latter category likely encompassing a wide range of years of experience.

Several studies have attempted to identify patient characteristics associated with the accuracy of case definitions based on diagnoses in administrative data. For chronic diseases that are typically first diagnosed among the elderly (e.g., dementia, osteoporosis, osteoarthritis, renal failure), accuracy of case definitions based on diagnoses in administrative data was higher among older patients (79;80;83;84;87). Patient comorbidity was negatively associated with accuracy of case definitions based on diagnoses in administrative data (34;82;87); a likely explanation for this finding is that the selection of a single principal diagnosis for a medical encounter is complicated by the presence of concurrent illness(es). The studies reviewed in Table 5 do not show a clear trend between accuracy of case definitions based on diagnoses in administrative data and patient income, education, or geographic area of residence.

Few studies have assessed the impact of visit- or site-specific characteristics on the accuracy of case definitions based on diagnoses in administrative data. Losina *et al*. (77) reported that the sensitivity of case definitions based on diagnoses in Medicare claims was higher among low-volume hospitals than high-volume hospitals; this finding is similar to that of a study by Studney *et al*. (46), in which diagnostic coding accuracy was higher among physicians with lower workloads, as compared to those with higher workloads. Two studies (67;87) have assessed the impact of length of stay and emergency admission on the accuracy of case definitions based on hospital discharge diagnoses, and they report opposite findings.

To summarize, we found only one published study (73) in which the investigators attempted to improve the accuracy of syndrome definitions based on diagnoses in administrative data by taking into account covariates, and the covariates investigated were limited to characteristics of the presentation and medical management of the illness itself, i.e., symptoms, signs, laboratory test orders, imaging requests, and medications prescribed. In contrast, in areas outside syndromic surveillance, many studies have identified covariates associated with the accuracy of case definitions based on diagnoses in administrative data (67;74-78;81;82;87), and a few studies have even shown that the accuracy of case definitions can be improved substantially by taking into account such covariates (83-86). Whereas some of the covariates identified by these studies may be disease-specific (e.g., older age in identifying diseases more prevalent among the elderly), and therefore may not be directly applicable to syndromic surveillance, these studies nonetheless provide clues as to what type of covariates may influence the accuracy of syndrome case definitions. Specifically, based on findings from these studies, we should investigate the impact of physician, patient, encounter, and healthcare site characteristics on the accuracy of syndrome case definitions based on diagnoses in administrative data.

Chapter 3. Methods

In the previous chapter, we discussed the methodological limitations of published validations of syndrome case definitions based on diagnoses in administrative data. In particular, we drew attention to the fact that most published validations were based on a convenience sample of one or a few healthcare sites, and we showed how verification bias led to a large overestimation of sensitivity in some of these studies. We also described findings from studies outside the realm of syndromic surveillance that suggested types of covariates that may be associated with case definition accuracy, namely physician, patient, encounter, and healthcare site characteristics.

In this chapter, we provide a detailed explanation of the methodology we used to obtain data for our large-scale, population-based validation of syndrome case definitions based on diagnostic codes in physician claims (manuscript 2), and our study on the predictors of syndrome definition accuracy (manuscript 3). (Of note, our approach to the methodology used in manuscripts 2 and 3 was guided by our pilot work experience and the findings published in manuscript 1). We first describe the administrative data used in this thesis, including the physician claims whose diagnoses were validated in manuscript 2, and the various data sources used to generate many of the potential predictors of syndrome case definition accuracy investigated in manuscript 3. We then provide a detailed explanation of the sampling strategy we used to select physician claims for validation in manuscript 2, and how this strategy insured population representativeness and guarded against biases. Next, we describe how we collected data from the medical chart (i.e., the 'gold standard'), and the various safeguards that were put in place to ensure high data quality. Finally, we explain the statistical analyses we used to estimate the accuracy of syndrome case definitions based on diagnostic codes in RAMQ physician claims, taking into account our complex stratified sampling strategy.

Administrative databases used in this thesis

The work contained in this thesis was conducted in the province of Quebec, Canada, where universal health coverage is provided through the provincial health insurance plan. Each Canadian province maintains a population-based registry of insured persons and claims for all physician visits remunerated on a fee-for-service basis. All claims record unique physician and patient identifiers that can be used to create longitudinal histories of healthcare use. In the province of Quebec, 99% of residents have provincial health insurance and 85-95% of medical visits are remunerated on a fee-for-service basis (88). In 2006, there were more than 7.6 million inhabitants in Quebec (89), and 18,908 active registered physicians (90). The availability of diagnostic information for nearly all medical visits to Quebec physicians represented an invaluable opportunity for assessing the validity of using diagnostic codes in physician claims for population-based surveillance.

Three databases from the provincial healthcare agency, the *Régie de l'assurance maladie du Québec* (RAMQ), were used in this thesis. Patient age and gender, as well as an anonymized unique patient identifier, were obtained from the *beneficiary database*. The *physician claims database* provided the treating physician identifier, patient identifier, date of visit, medical procedure code, ICD-9 diagnostic code, type of clinic (private clinic, community health center, ambulatory hospital-based clinic), and geographic location of clinic (urban, rural) for all visits billed on a fee-for-service basis. The *physician demographics database* provided the physician identifier and the physician gender, language (French or English), and specialty. The Quebec medical regulatory authority, the *Collège des Médecins du Québec* (CMQ), provided physicians' year of licensure.

Statistics Canada's 2006 census data for the province of Quebec was mapped to 6-digit postal codes by the research team; a high degree of spatial precision was achieved by mapping the 6-digit postal code centroids (i.e., geometric centers) to the corresponding

census dissemination area, which was the smallest available census area. The RAMQ then linked the census data to the *beneficiary database* using the patient's 6-digit residential postal code. Census variables provided to the research team included geographic location of residence (urban, rural), average household income in the 6-digit postal code area (in thousands of dollars), and proportion of persons with a university degree in the 6-digit postal code area. Material and social deprivation indices developed by the Quebec National Public Health Institute (91;92) were computed by the RAMQ for each patient using Statistics Canada's 2006 census data. The material deprivation index summarizes information on the proportion of persons who have no high school diploma, the proportion of persons employed, and the average income in the patient's 6-digit postal code area of residence. The social deprivation index summarizes information on the proportion of single-parent families, the proportion of persons living alone, and the proportion of persons separated, divorced, or widowed in the patient's 6-digit postal code area of residence.

Sampling of physician claims to be validated (for manuscripts 2 and 3)

The accuracy of case definitions based on diagnoses in physician claims for identifying syndromes was assessed by comparison to clinical information in the corresponding medical chart. To ensure representativeness, we used a population-based, 3-stage stratified random sample of 36,000 visits (Figure 4), for which we made the necessary statistical adjustments in the analyses so as to avoid verification bias. In the first stage (Figure 4, Stage 1), the RAMQ identified all physicians who were eligible to be included in our study. To be eligible, physicians had to be a general practitioner, pediatrician, internist, geriatrician or general surgeon who practiced in the fee-for-service system in a private clinic, community health center, or hospital-based ambulatory care clinic during the 2-year study period (October 1, 2005 to September 30, 2007). Internists and general surgeons were included in our sample because, especially in rural-remote and underserved areas, these physicians may provide first-contact care and act as patients'

family physician. From the 8,700 eligible physicians identified, the provincial health insurance agency selected a random sample of 3,600 (41.4%) physicians.

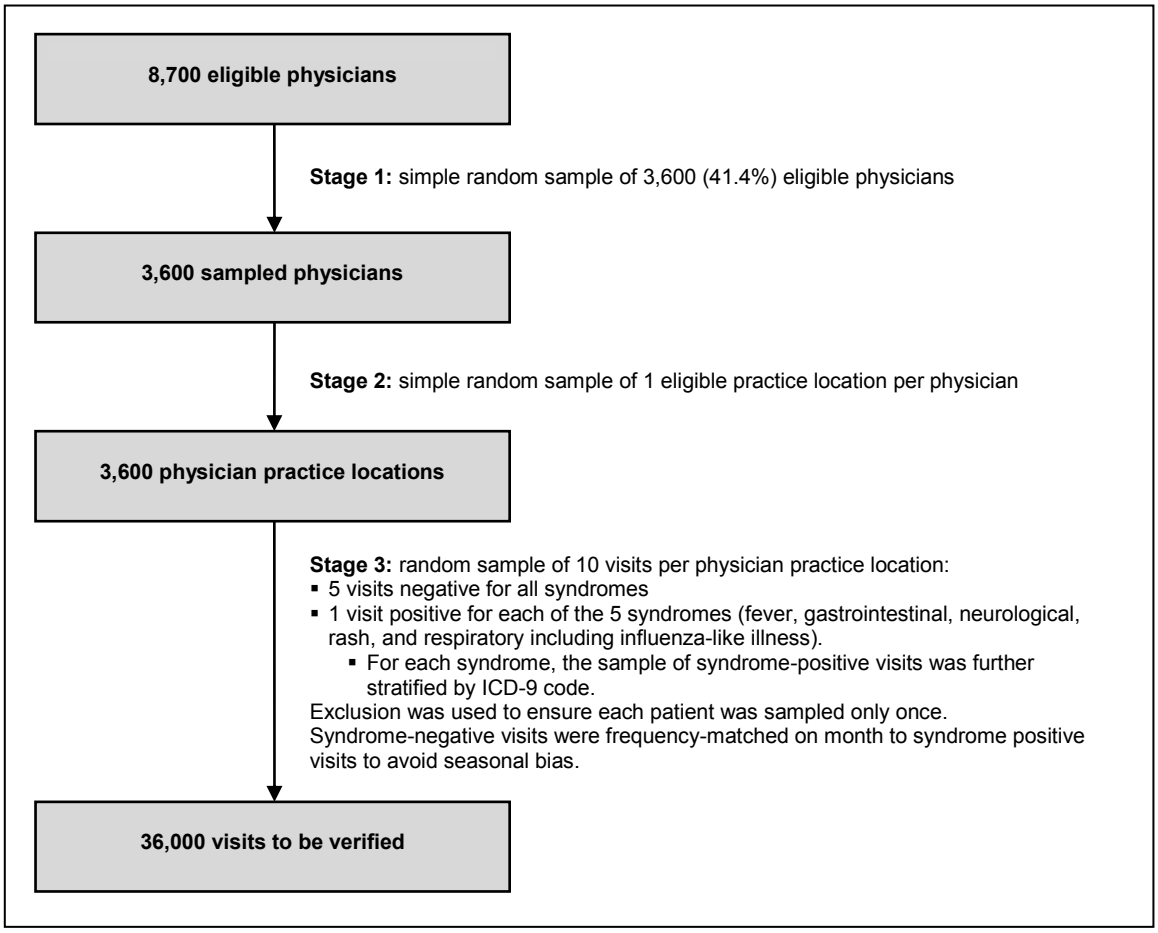

Figure 4. Population-based, 3-stage stratified random sample of ambulatory visits to all physicians working in community healthcare settings in the province of Quebec in 2005-2007

In the second stage (Figure 4, Stage 2), to facilitate chart retrieval for review, the RAMQ randomly selected one eligible community practice location for each physician. The RAMQ then sent the research team an anonymized file containing all physician claims billed by the 3,600 physicians from their respective selected community practice location during the 2-year study period.

In the third stage (Figure 4, Stage 3), the research team randomly selected 5 syndrome-positive visits, i.e., 1 visit for each of fever, gastrointestinal, neurological, rash, and

respiratory syndrome (including influenza-like illness), and 5 visits negative for all syndromes. A visit was considered syndrome-positive if the ICD-9 code on the physician claim for the visit was included in the syndrome definition. Because syndromes have low population prevalence, to maximize data collection efficiency (69;70), syndrome-positive visits were over-sampled relative to syndrome-negative ones, so as to yield 5 syndrome-positive visits and 5 syndrome-negative visits per physician. When sampling syndrome-positive claims, to maximize the number of syndrome-positive ICD-9 codes verified, we further stratified on ICD-9 code. Because two or more syndromes can occur concurrently in the same patient (61), syndrome-negative visits were negative for *all* syndromes. Syndrome-negative visits were also frequency-matched to syndrome-positive visits on calendar month to avoid bias due to syndrome seasonality (Figure 5). To avoid bias due to visits being clustered within patients, restriction was used to ensure that each patient was only sampled once. The number of syndrome-positive visits, per syndrome, in the sampling frame and in the final sample of 36,000 visits is shown in Table 6.

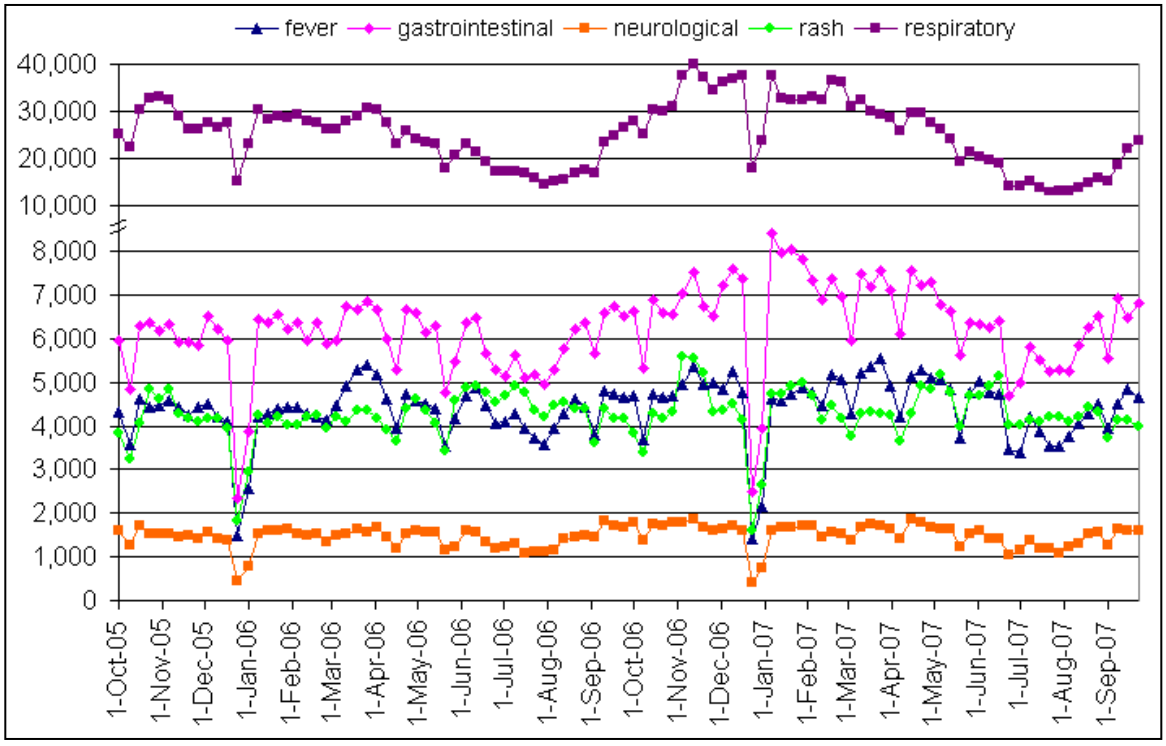

Figure 5. Weekly counts of syndrome-positive claims (CDC syndrome definitions) among all physician claims billed by the 3,600 physicians from their selected practice location from October1, 2005 to September 30, 2007

Table 6. Number and prevalence of syndrome-positive visits, per syndrome, among all physician claims billed by the 3,600 physicians from their selected practice location from October1, 2005 to September 30, 2007, and number of syndrome-positive visits, per syndrome, in the sample of 36,000 visits to be validated

	In the sampling frame		In the sample
Syndrome	**No. visits**	**Prevalence[1] (per 1,000 visits)**	**No. visits**
CDC-DoD ESSENCE definitions (66) :			
Fever	241,705	11.9	1,966
Gastrointestinal	471,491	23.2	2,868
Neurological	114,046	5.6	3,172
Rash	351,270	17.3	2,991
Respiratory	2,555,164	125.7	3,600
ESSENCE definitions[3] (49) :			
Influenza-like illness, large group	1,751,828	86.2	2,218
Influenza-like illness, small group	93,300	4.6	160
RODS definitions[4] (61) :			
Fever	453,990	22.3	2,817
Gastrointestinal	429,933	21.2	2,347
Neurological	103,688	5.1	2,876
Rash	158,949	7.8	2,698
Respiratory	1,355,757	66.7	2,263
None of the syndromes above	16,469,389	810.2	19,557

[1] There were a total of 20,326,404 visits among all physician claims billed by the 3,600 physicians from their selected practice location between October1, 2005 and September 30, 2007.
[2] A total of 36,000 visits (10 visits per physician x 3,600 physicians) were sampled for validation.
[3] Each of the diagnostic codes in the influenza-like illness definitions are included in the respiratory and/or fever syndrome definitions; influenza-like illness did not required separate sampling.
[4] For the same syndrome, there is some overlap between the diagnostic codes included in the CDC-DoD ESSENCE definitions and the RODS definition. When we selected the sample of 36,000 visits to validate, we pooled the CDC-DoD ESSENCE and RODS definitions by syndrome, and attempted to select 3,600 syndrome-positive visits per syndrome.

The list of 10 sampled visits was enumerated for each of the 3,600 physicians, and an anonymized unique identifier, the study number, was assigned to each sampled visit by the research team.

Medical chart data retrieval (for manuscripts 2 and 3)

Medical chart data retrieval methodology

The accuracy of syndrome case definitions based on diagnoses in physician claims was assessed by comparison to clinical information from medical charts. Because we used a province-wide sampling frame, physician-facilitated chart reviews were deemed

superior to both in-office chart abstraction and mail or web-based self-report. Chart abstraction would have involved prohibitive travel costs and required patient consent, the latter increasing the complexity of recruitment and further contributing to non-response bias. Alternatively, mail or web-based self-report would have yielded poorer data quality (93), and increased the potential for measurement error by having as many raters as physicians.

Validation of the medical chart data retrieval methodology

To avoid biasing responses in a particular direction, the interview was semi-structured and questions were open-ended. The questionnaire was pre-tested to ensure accurate capture of all relevant information in the patient medical record by comparing physician-facilitated chart review to chart abstraction (by the thesis author). A convenience sample of 6 physicians concurrently enrolled in the MOXXI electronic prescribing trial (94) was used, and 8 visits were validated per physician. After consent was obtained, I telephoned each physician and performed the physician-facilitated chart review. Physicians then faxed me a copy of the medical chart entry corresponding to each sampled visit; to preserve patient anonymity, the physician was asked to black-out any patient identifiers and add a visit number to the medical chart copy before faxing it. Agreement between the physician-facilitated chart review and the medical chart was very high for 5 of the 6 physicians: 50 diagnoses were common to the physician-facilitated chart review and the paper chart abstraction, 2 diagnoses were obtained only from the physician-facilitated chart review (not found verbatim in the paper chart), and 1 diagnosis was found in the paper chart but not mentioned during the physician-facilitated chart review. One physician's charts were almost entirely illegible, which highlighted the advantage of having the physician interpret his own writing.

Overview of the data collection procedure

Figure 6 provides an overview of how the medical chart data was collected. To preserve physician and patient anonymity, the health insurance agency sent the list of physicians and visits sampled by the research team to the medical regulatory authority (Figure 6,

Step 3). The medical regulatory authority has the legal right to access confidential physician and patient information, therefore the list it received included physicians' name and mailing address, as well as patients' name, insurance number, sex, and date of birth. The medical regulatory authority acted as a trusted third party and recruited physicians to the study on behalf of the research team; it also sent each physician the list of 10 sampled visits (Figure 6, Step 4). Lists sent to physicians included patients' first and last names, sex, date of birth, health insurance number, date of the visit to be verified, and the 'study number' assigned to each visit.

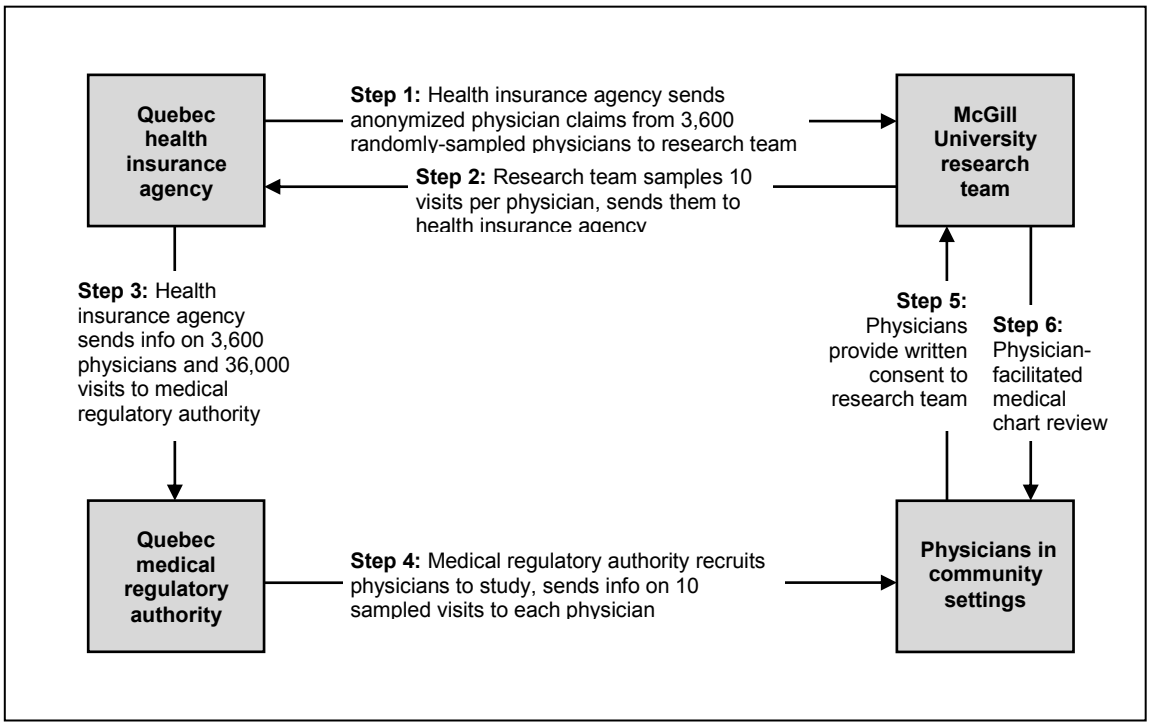

Figure 6. Overview of data collection

Because the lists sent to physicians contained both patient information and study numbers, it enabled physicians to retrieve the relevant medical charts, and researchers to link the information collected through chart review to the anonymized physician claims file. Interested physicians mailed their written consent and contact information to the research team (Figure 6, Step 5). Non-responding physicians were sent up to five reminders. To maximize participation, physicians were offered $50 compensation for

their participation and a summary of study findings. Using a previously published methodology (95), trained interviewers contacted consenting physicians by telephone to perform the chart review (Figure 6, Step 6). During the chart review, interviewers and physicians referred to each visit using only the study number and visit date, thereby preserving patient anonymity.

Physician recruitment and participation

Efforts to recruit physicians to our study began in September 2008 and ended in August 2009. The Quebec medical regulatory authority made up to 5 attempts to recruit each physician, for a total of 13,840 recruitment packages mailed. Physician response after each mailing is shown in Table 7. On average, obtaining physician consent required 2 mailings (median, 2; range, 1-5).

Table 7. Physician response after each mailing

	Mailings					Total
	1st	2nd	3rd	4th	5th	
No. letters sent	3,600	2,863	2,556	2,434	2,387	13,840
No. physicians with incorrect addresses	172	0	0	0	0	172
No. physicians who refused	29	37	105	36	11	218
No. physicians who consented	536	270	201	86	36	1,129
% physicians who consented[1]	14.9	9.4	7.9	3.5	1.5	8.2

[1] The % consent was calculated as the (no. physicians who consented * 100) / no. letters sent.

Figure 7 provides a detailed breakdown of physician eligibility and participation. The Quebec provincial health agency had an inaccurate billing address for 172 (5%) physicians, which suggests that these physicians were not being reimbursed on a fee-for-service basis; we considered these physicians to be ineligible to participate in the study. Another 170 (5%) physicians contacted the research team but were determined to be ineligible to participate, most often because they were no longer working in an eligible community-based practice setting, had retired, were on sick/maternity leave, or had moved their practice to another Canadian province. Of the remaining 3,258 (90%) potentially eligible physicians, 218 (7%) refused to participate in the study; the two most

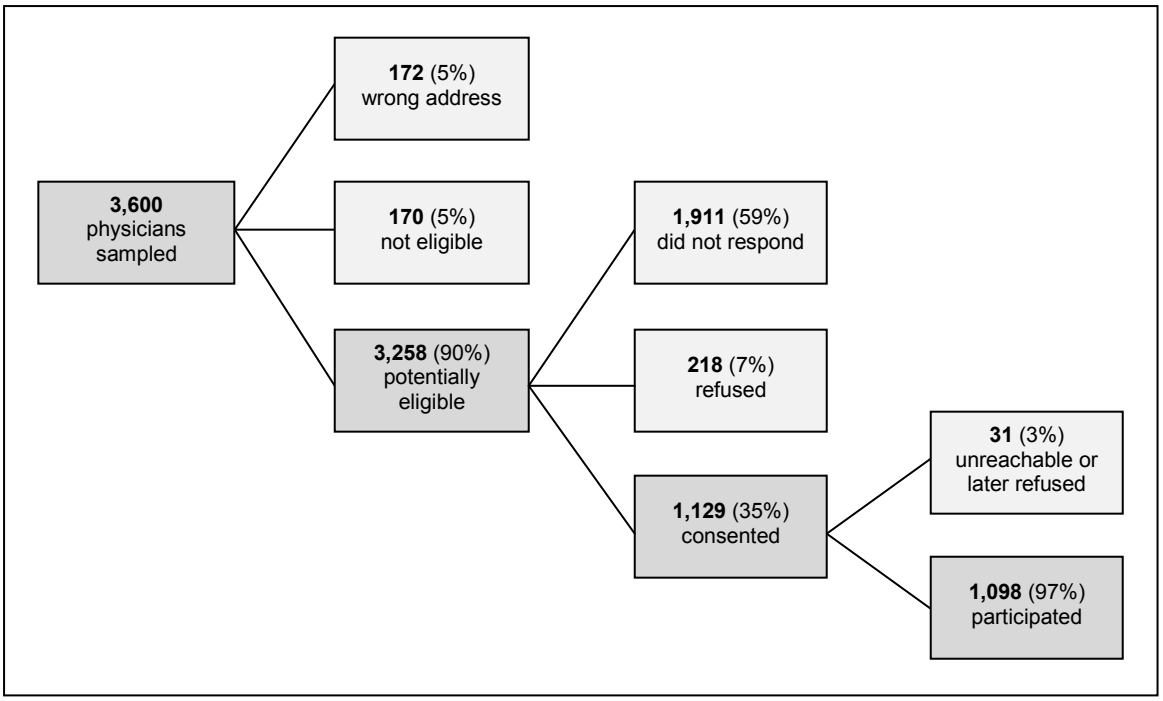

Figure 7. Physician eligibility and participation

common reasons for refusal were lack of time to participate and lack of interest in the study. Of 1,129 physicians who consented to participate in our study, 31 (3%) later refused or were not reached. A total of 1,098 physicians participated in the study, for a participation rate of 33.7% (1,098/3,258). After the research team received physicians' written consent via business-reply mail, it took an average of 5.4 (median, 4; range, 1-35) telephone calls to schedule and complete the physician-facilitated chart review. An average of 20 days (median, 13; range, 0-326) elapsed between the date when the physician's consent form was received and the date when the physician-facilitated chart review was completed. Of the 1,129 physicians who consented to participate in the study, 100 (8.9%) physicians were not available to complete the telephone chart review at the scheduled time at least once, for a total of 138 missed/rescheduled telephone chart reviews.

Physician-facilitated chart reviews

Physician-facilitated medical chart reviews began in September 2008 and ended in December 2009. For each of the 10 sampled visits, the interviewer asked the physician

to list all diagnoses. For each diagnosis corresponding to a syndrome definition, the interviewer asked the physician about the signs, symptoms, and key findings recorded in the medical chart, as well as the most likely etiology for the diagnosis (based solely on information available at the time of the visit). The interviewer entered physician responses directly into an Oracle database using an Access data entry form (Figures 8-11). Diagnoses were selected from a searchable list of diagnoses (mapped to ICD-9 codes) or, if the physician had recorded the ICD-9 code in the medical chart, the ICD-9 code was entered directly. For each syndrome-positive diagnosis, a list of syndrome-specific signs and symptoms (Table 8) was elicited, and the interviewer selected from a drop-down list whether the symptom had been present, absent, or not recorded in the medical chart. Symptoms or signs not in the list and other key findings, such as contacts with other diagnosed cases (e.g., siblings or children with diagnosed Strep throat) or links to known outbreaks (e.g., salmonella outbreak among employees on a chicken farm), were recorded as free text in separate fields. The data collection tool was translated to French for use with French-speaking physicians, and back-translated to English to ensure comparability of data collection. To minimize data entry errors, the database was pre-populated with the physician identifier, visit identifier and visit date. Logical limits were placed on date fields (e.g., physician consent date) to insure that dates entered manually fell within a reasonable time interval.

At the time of the chart review, the physician and the interviewer were both blinded to the ICD-9 code in the physician claim and the syndrome-positive or syndrome-negative status of the visit. To minimize measurement error due to inter-rater differences, interviewers were trained to use the data collection tool. Inter-rater reliability was assessed at baseline by having interviewers perform 2 simulated physician interviews of 10 visits each (for a total of 20 visits). To maintain data quality, interviewers underwent quality assurance monitoring every 3 months. Each assessment was comprised of 2 simulated physician interviews of 10 visits each (for a total of 20 visits). Agreement between interviewers was perfect (ICC=1.00) on all assessments of inter-rater reliability;

all interviewers agreed on all items on the first two assessments (at baseline and 3 months later), one interviewer recorded 1 item incorrectly on the third assessment (6 months after baseline), and two interviewers recorded 1 and 2 items incorrectly on the last assessment (9 months after baseline). Of note, only the author of this thesis performed physician-facilitated chart reviews during the first 1.5 months of data collection (i.e., gradual roll-out period, before the interviewers were hired and trained) and the last 4.5 months of the study (i.e., winding-down period, after attempts to recruit physicians had stopped).

Table 8. Signs and symptoms recorded during the physician-facilitated chart review

Syndrome[1]	Signs and symptoms[2]
Fever	Fever Chills Rapid breathing Increased heart rate Low blood pressure Altered level of consciousness
Gastrointestinal	Fever Nausea Vomiting Diarrhea Bloody diarrhea
Neurological	Fever Headache Nuchal rigidity / stiff neck Vomiting Altered level of consciousness
Rash	Fever Pruritis What type of rash was it predominantly? (drop-down list) Macular/papular Vesicular Nodular Ulcerating Hives Other (free text entry) Not recorded
Respiratory	Fever Throat pain Cough Increased sputum production Abnormal lung sounds on auscultation Shortness of breath

[1] The pooled RODS and CDC-DoD ESSENCE definitions were applied to the 'diagnosis' and 'potential cause' ICD-9 codes entered during the physician-assisted chart review to determine which list(s) of symptoms needed to be asked by the interviewer.
[2] The question asked by the interviewer was "Based on your notes for this visit only, did the patient have or report...' The physician's answer was recorded as 'present', 'absent', or 'not recorded' (unless otherwise specified).

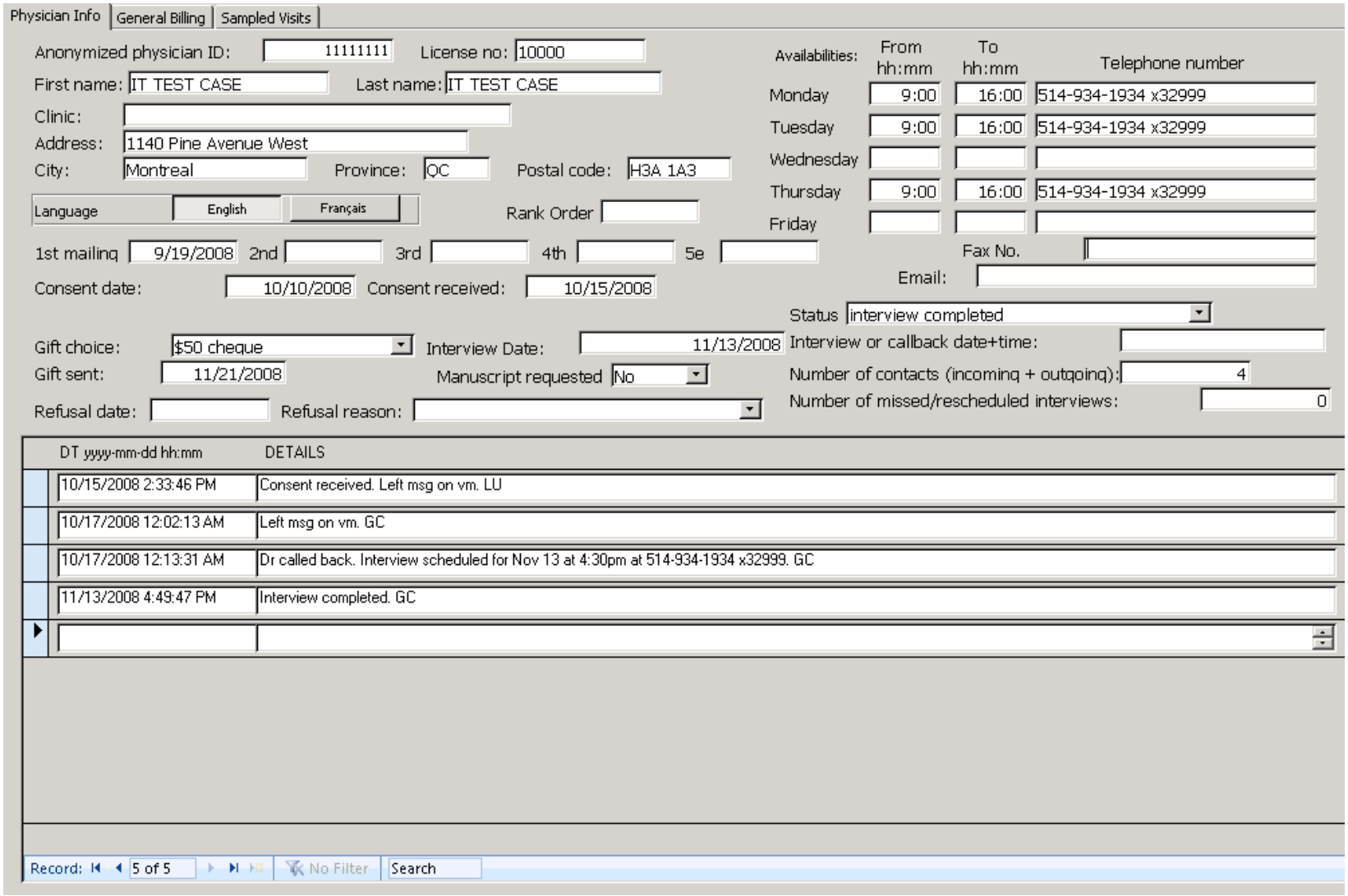

Figure 8. Screenshot of the Access data entry form used during the physician-facilitated chart review: physician contact information and call tracking / interview scheduling

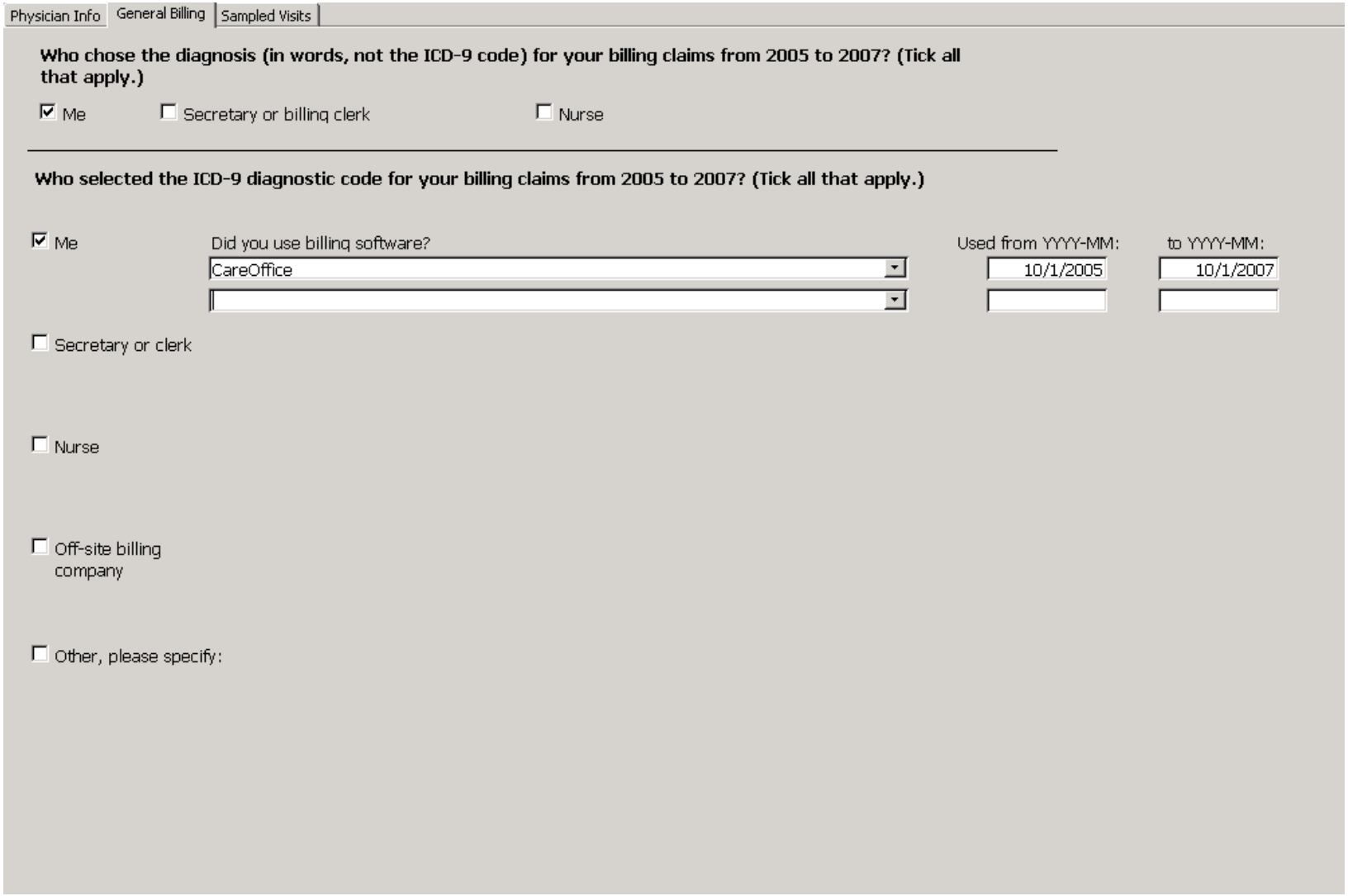

Figure 9. Screenshot of the Access data entry form used during the physician-facilitated chart review: questions about physician billing practices

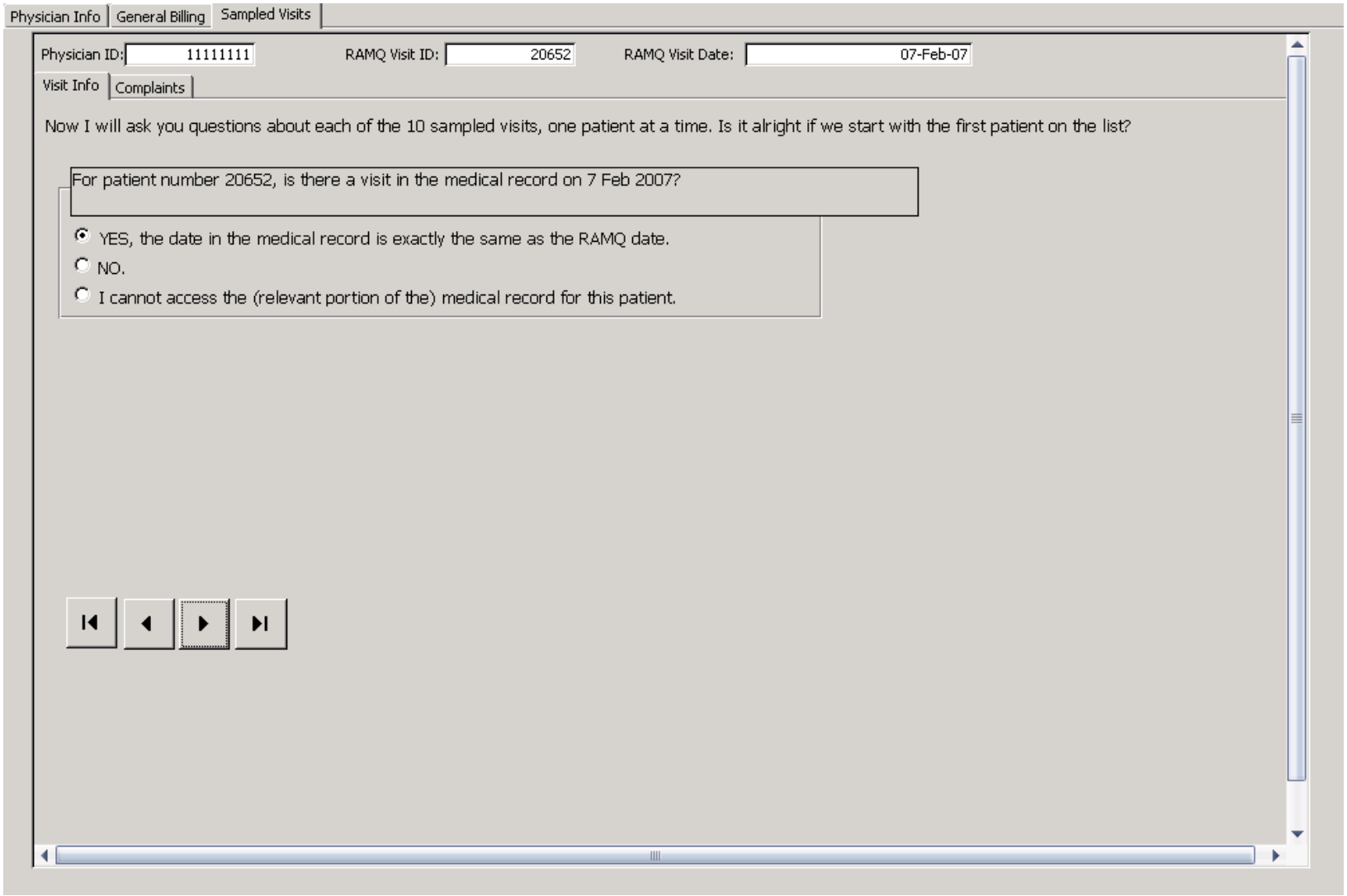

Figure 10. Screenshot of the Access data entry form used during the physician-facilitated chart review: questions about date agreement between the claims and the medical chart

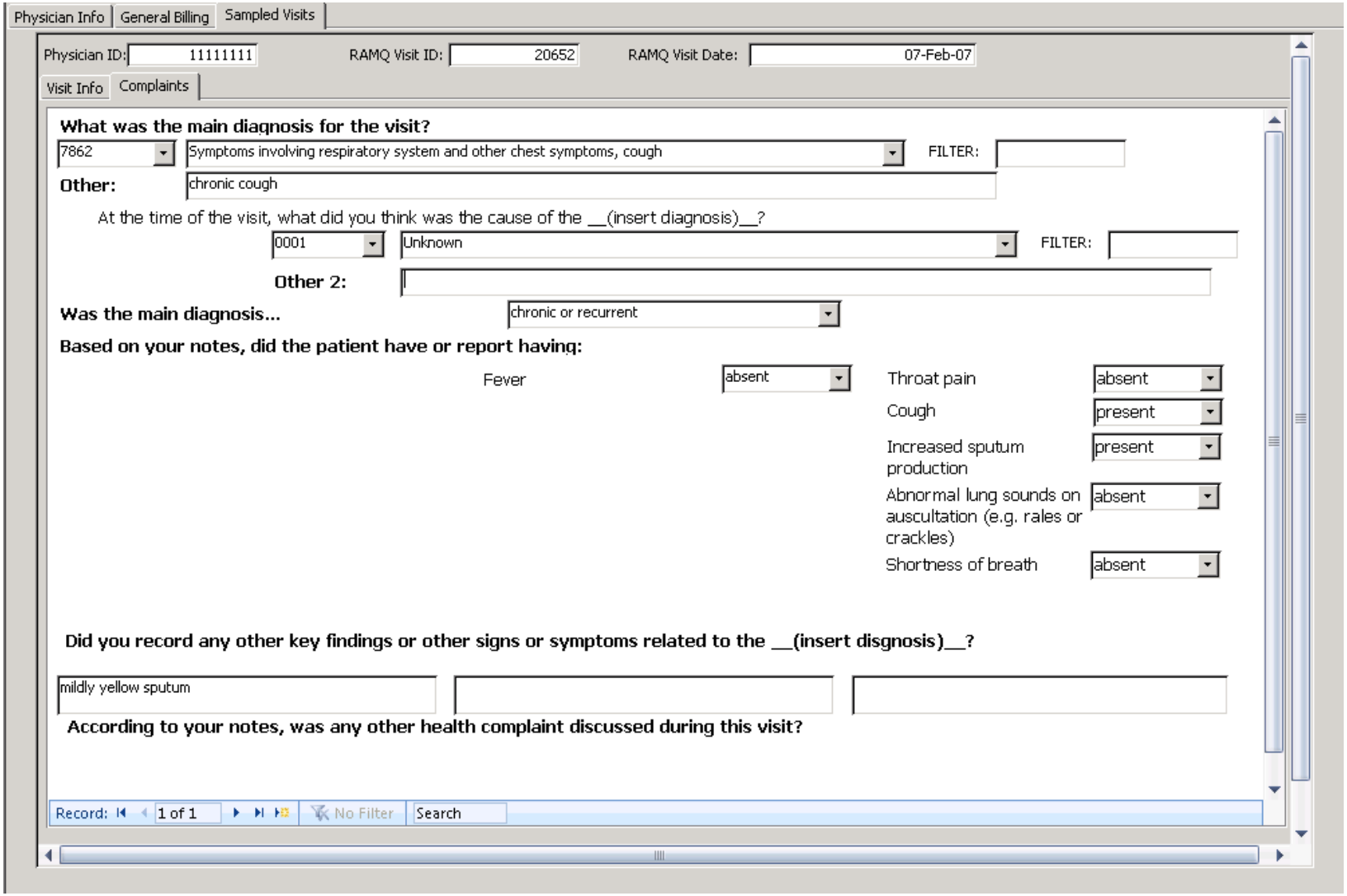

Figure 11. Screenshot of the Access data entry form used during the physician-facilitated chart review: questions about the diagnosis, suspected cause, signs, symptoms, and other key findings for the visit (1 form per diagnosis, unlimited number of diagnoses per visit)

Ethics

The research described in manuscript 1 was included in the MOXXI III research program; copies of ethics certificates from the McGill Institutional Review Board and the provincial privacy commission, the *Commission d'accès à l'information du Québec* (CAI), pertaining to the MOXXI III research program and relevant to the time period covered in manuscript 1 can be found in Appendix D. Data collection for manuscript 1 was performed in 2004-2005, among physicians and patients who had previously consented to participate in the MOXXI III research program.

Copies of ethics certificates pertaining to the research described in manuscripts 2 and 3 from the McGill Institutional Review Board, the CAI, and the legal department of the RAMQ can be found in Appendix E. It should be noted that, due to issues at the CAI unrelated to our project, we faced an unexpected delay of several months in obtaining initial ethics approval for the research in manuscripts 2 and 3 (jointly). Furthermore, although there was approval from both the CAI and the RAMQ on the data access request for manuscript 3, the RAMQ later refused to honour that agreement because of concerns about the size of the dataset. As a result, we had to make major modifications to our data request to suit all concerned parties, and seek further approval from the CAI and from the RAMQ's legal department, which took nearly a year. The data necessary for the completion of manuscript 3 was finally received in September 2010.

Statistical analyses

Comparison of the characteristics of participating and non-participating physicians

The analyses in manuscripts 2 and 3 are based on visits billed by participating physicians. Based on other large-scale studies of primary care physicians, we expected the physician participation rate to be low. We tested the statistical significance at the $p<0.05$ level of any differences between participating and non-participating physicians using a

multivariate logistic regression model where the dependent variable was participation and the independent variables were all available physician and practice characteristics (see manuscript 2, Table 1).

Statistical adjustment for our complex stratified sampling strategy

In manuscript 2, we used a complex stratified sampling strategy (Figure 3). Because of the low prevalence of syndrome-positive visits, we validated a larger sampling fraction of syndrome-positive visits relative to syndrome-negative visits. Because of large variation in prevalence between individual syndrome-positive ICD-9 codes within a given syndrome definitions we stratified our sample of syndrome-positive visits by ICD-9 code to maximize the number of different diagnostic codes validated. To avoid biasing our results, we took into account the sampling strategy used in our estimation of sensitivity, specificity, positive predictive value, and negative predictive value.

Re-sampling of syndrome-negative visits to avoid seasonal bias

In our initial sample of 36,000 visits, syndrome-positive visits (based on the physician claim) were frequency-matched on calendar month to syndrome-negative visits (based on the physician claim) (Figure 4). However, low physician participation and our inability to validate some visits among participating physicians (e.g., because some charts were not accessible) led to imbalances in seasonal distribution between syndrome-positive and syndrome-negative visits in the final sample of 10,529 validated visits. To ensure that the seasonal distribution of syndrome-negative visits (based on the physician claim) was identical to that of the syndrome-positive visits (based on the physician claim), we re-sampled the syndrome-negative visits (based on the physician claim) at the analysis stage. To do so, for each syndrome, we calculated the proportion of all visits positive for that syndrome (based on the physician claim) that took place in each of the 12 calendar months. Then, among the 5,564 validated visits that were negative for all syndromes (based on the physician claim), we randomly sampled as many syndrome-negative visits as possible while ensuring that the proportional distribution of syndrome-negative visits

over the 12 months was identical to that of the syndrome-positive visits (see example in Table 9).

Estimation of positive predictive value and negative predictive value

The negative predictive value of each syndrome case definition was estimated directly from the data for that syndrome. Because we stratified syndrome-positive visits by ICD-9 code, we had to use an adjustment based on Bayes Theorem (69) to estimate the PPV of each syndrome definition. The PPV was estimated as a weighted average of each ICD-9 code's PPV, the weight being the number of visits with a given ICD-9 code among participating physicians' claims, divided by the total number of visits positive for that syndrome among participating physicians' claims.

Table 9. Example of the re-sampling of syndrome-negative visits at the analysis stage to avoid seasonal bias (respiratory syndrome, CDC definition)

	Validated visits positive for the CDC's respiratory syndrome based on the physician claim (N=1,049)		Validated visits negative for all syndromes based on the physician claim			
			Among all 10,529 validated visits		In the month-matched random sample used in the analyses	
Month	**No.**	**%**	**No.**	**%**	**No.**	**%**
January	123	11.7	453	8.1	453	11.7
February	100	9.5	498	9.0	368	9.5
March	97	9.2	525	9.4	357	9.2
April	93	8.9	461	8.3	343	8.9
May	88	8.4	494	8.9	324	8.4
June	80	7.6	520	9.3	295	7.6
July	63	6.0	393	7.1	232	6.0
August	55	5.2	442	7.9	203	5.3
September	71	6.8	435	7.8	261	6.8
October	75	7.1	341	6.1	276	7.1
November	121	11.5	562	10.1	446	11.5
December	83	7.9	440	7.9	306	7.9
Total	1,049	100.0	5,564	100.0	3,864	100.0

Estimation of sensitivity and specificity and the correction for verification bias

Because we validated a larger fraction of syndrome-positive visits than syndrome-negative ones, direct estimation of the sensitivity and specificity of syndrome case definitions using our data would lead to verification bias: sensitivity would be

overestimated, and specificity underestimated (69). However, because validated claims were randomly sampled within syndrome-positive and syndrome-negative strata, unbiased estimation of these parameters was achieved by re-weighting for the different sampling fractions (69). Therefore, to estimate the sensitivity and specificity of each syndrome definition from the PPV and NPV (96), while correcting for verification bias (69), we used the following equations (where is the prevalence of syndrome-positive visits in the physician claims):

$$Sensitivity = \frac{PPV \times p}{\left((PPV \times p) + (1 - NPV)\right) \times (1 - p)}$$

$$Specificity = \frac{NPV \times (1 - p)}{\left((NPV \times (1 - p)) + (1 - PPV)\right) \times p}$$

We estimated the 95% confidence intervals (CI) for the bias-corrected sensitivity and specificity using the methods described by Begg and Greenes (69).

Chapter 4. Accuracy of diagnoses in physician billing claims for identifying acute respiratory infections in primary care

Preamble to Manuscript 1

The purpose of the pilot work described in manuscript 1 was to demonstrate the feasibility of using groups of ICD-9 diagnostic codes in RAMQ physician claims to identify episodes of acute respiratory infection. The impetus for manuscript 1 was to assess whether diagnoses in physician claims accurately reflected treatment indication, for the purpose of evaluating antibiotic prescribing for acute respiratory infections. The respiratory infection diagnoses validated in manuscript 1 (Table 10) overlap with the definitions of respiratory syndrome developed by the CDC (66) and RODS (61) syndromic surveillance systems.

Table 10. Respiratory infection diagnoses and their corresponding ICD-9 diagnostic codes

Diagnoses	Corresponding ICD-9 diagnostic codes
Infections of likely viral etiology:	
Acute unspecified upper respiratory infection	465-465.9
Common cold	460-460.9
Laryngitis	464-464.9, 476-476.9
Influenza	487-487.9
Infections of potentially bacterial etiology:	
Pharyngitis	34.0, 462-462.9, 463-463.9, 472-472.9
Otitis media	381-381.9, 382-382.9
Sinusitis	461-461.9, 473-473.9
Bronchitis	466-466.9, 490-490.9
Pneumonia	481-481.9, 482-482.9, 483-483.9, 485-485.9, 486-486.9

The pilot work described in manuscript 1 allowed us to generate estimates of sensitivity and positive predictive value for acute respiratory infections, and these estimates were crucial to planning and obtaining funding for a full-scale, population-based validation of definitions of respiratory and other syndromes. However, the respiratory infection diagnoses validated in manuscript 1, as a group, would be expected to have higher specificity than either the CDC's or the RODS system's definition of respiratory

syndrome, because the definitions of respiratory syndrome also include many ICD-9 codes for respiratory symptoms not specific to respiratory infection (e.g., cough, dyspnea).

Title Page

The accuracy of physician billing claims for identifying acute respiratory infections in primary care

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Abstract

Objective: To assess the accuracy of physician billing claims for identifying acute respiratory infections in primary care.

Study setting: Nine primary care physician practices in Montreal, Canada (2002-2005).

Study design: A validation study was carried out to compare diagnoses in 3,526 physician billing claims to diagnoses documented in the corresponding patient medical records.

Data collection: In-office medical record abstraction.

Principal findings: Claims had a high PPV, NPV, and specificity for identifying respiratory infections; however, their sensitivity was below 50%. Large variation in sensitivity and PPV was observed among physicians.

Conclusions: Because claims data are now routinely used to monitor antibiotic prescribing in primary care, future research should determine if acute respiratory infections diagnoses are missing from claims at random, or if bias is present.

Introduction

Several randomized, placebo-controlled trials of antibiotic use have shown that antibiotics do not provide clinical benefit to children or adults with upper respiratory tract infections (97-103), and fail to prevent complicated bacterial infections (104;105). Yet 75% of oral antibiotics prescribed to ambulatory patients are for pharyngitis, otitis media, sinusitis, bronchitis, common cold, and unspecified upper respiratory tract infection of likely viral etiology (106), and 22-49% are estimated to be unnecessary (107;108). Inappropriate use of antibiotics for respiratory infections promotes antibiotic resistance (109-111), increases health services utilization and costs (112), and increases the risk of preventable drug-related adverse events (113). To enable the development of effective interventions to reduce inappropriate antibiotic use in primary care, determinants of inappropriate antibiotic prescribing and accurate methods for monitoring antibiotic use need to be identified.

Monitoring antibiotic prescribing in primary care is challenging because well developed measures of antibiotic prescribing are scarce, often inaccurate, and may not reflect real prescribing practices. Studies of antibiotic prescribing in primary care have relied on physician self-reported prescribing (114-116), chart review or audit (117-119), or prescription claims (107;108;120-124). Self-reported antibiotic prescribing was shown to underestimate actual antibiotic prescribing by about 30% (117) and the cost of chart review is too high for wide scale use. Prescription claims data avoid self-report bias, do not require additional data collection, and because they involve financial transactions, prescription claims are carefully audited by payers and have been found to be highly accurate (125). Due to these advantages, prescription claims are now used routinely to monitor antibiotic prescribing for respiratory infections in primary care (107;108;120-124;126).

However, an important limitation of using prescription claims to monitor antibiotic prescribing is that treatment indication is not recorded on prescription claims. Treatment indication is required to determine the appropriateness of antibiotic prescribing; therefore it must be inferred from other sources of information, such as physician billing claims for patient visits. If prescription claims are to be used to monitor antibiotic prescribing, then the accuracy of using diagnostic information in physician billing claims to infer the indication for antibiotic treatment needs to be assessed.

Two previous studies have assessed the accuracy of physician billing claims for identifying respiratory infection diagnoses, and both have shown promising results. The first was a study of administrative claims data from 7 health insurance providers in Colorado, and it found that 79% of bronchitis diagnoses and 83% of pharyngitis diagnoses in administrative claims had a corresponding diagnosis in the written medical record (PPV) (127). However, this study did not investigate what proportion of bronchitis and pharyngitis diagnoses documented in patient medical records were accurately documented in physician billing claims (sensitivity and specificity). The second study assessed the accuracy of Research Patient Data Repository (RPDR) claims from 9 primary care clinics in the Brigham and Women's Primary Care Practice-Based Research Network in Boston, and reported that 86% of respiratory infection diagnoses in RPDR claims had a corresponding diagnosis in the electronic health record (128). However, sensitivity and specificity estimates were not corrected for the verification bias introduced by over-sampling claims with a diagnosis of respiratory infection relative to claims without such a diagnosis (i.e., the study design inflated the prevalence of respiratory infection in the sample, relative to the true population prevalence) (69;70).

The objective of this study was to assess the accuracy of physician billing claims for identifying episodes of acute respiratory infection in primary care. In particular, we sought to estimate the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of physician billing claims.

Methods

Study design and population

A validation study was carried out to assess the sensitivity, specificity, positive predictive value, and negative predictive value of physician billing claims for identifying episodes of respiratory infection, as compared to the patient medical record. The study population was comprised of 34 Montreal-region family physicians and 17,002 of their patients who were participating in the MOXXI electronic medication management trial (129) in 2002-2005. All patients participating in the MOXXI trial had previously consented to share their medical records and provincial health insurance (RAMQ) data with researchers. These data were available for a period starting 1 year prior to patient enrolment date (2001 or later) until 2005, when the present study was conducted. From the available physician billing claims, we identified those with a diagnostic code (International Classification of Disease, 9th Revision, or ICD-9) for laryngitis/tracheitis (464), common cold (460), influenza (480, 487), acute unspecified upper respiratory infection (465), pharyngitis/tonsillitis (462, 463, 034), otitis media (381, 382), sinusitis (461), acute bronchitis (466), or bacterial pneumonia (481-486) (all decimal place suffixes of these ICD-9 codes were included). We purposefully selected 10 physicians who had been enrolled in the MOXXI trial for at least 2 years and had the most MOXXI-consenting patients (and therefore also had the most physician billing claims available for research purposes), and requested their consent.

Sample of physician billing claims

Among the 10 physicians selected, we identified all MOXXI-consenting patients who had at least one physician billing claim with a diagnosis of acute respiratory infection during the study period, and randomly sampled 635 of those patients. We also identified all patients without any physician billing claim with a diagnosis of acute respiratory

infection during the study period, and randomly sampled 94 of those patients. To improve the efficiency of data collection, we over-sampled patients with at least one diagnosis of acute respiratory infection, relative to those with no diagnosis of acute respiratory infection (69;70). For each of the 729 patients sampled, we identified all physician billing claims generated during the study period (i.e., from 2001 or later, depending on enrolment date, until 2005) and validated each one against the paper-based patient medical record. Information available in the physician billing claims included the patient's lifelong RAMQ personal identifier, physician license number, visit date, and ICD-9 diagnostic code.

Medical record abstraction

Once the physician billing claims had been sampled, a list of sampled patients' names and RAMQ personal identifiers was generated and faxed to each consenting physician's office. The selected patients' paper-based medical records were retrieved by office staff, and reviewed by one of the authors (GC). For each sampled physician billing claim, the corresponding visit was identified in the medical record, the date of the visit was recorded, and the presence or absence of all acute respiratory infections under study was ascertained from the clinical notes. At the time of the medical record abstraction, the reviewer was blinded to the ICD-9 code in the corresponding physician billing claim. Information abstracted from patient medical records was entered directly in an electronic, structured chart abstraction form and stored in a MS Access database, which had been pre-populated with participating physicians' license numbers, sampled patients' RAMQ identifiers, and visit dates according to physician billing claims. Intra-rater reliability was measured on 25 randomly selected visits that were reviewed a second time, and the percent agreement between the first and second review was 100%.

Linkage of physician billing claims and data abstracted from medical records

Data retrieved from patient medical records were linked directly to physician billing claims using the patient's lifelong RAMQ personal identifier, physician license number, and visit date +/- one day.

Analyses

For each type of acute respiratory infection under study, a 2x2 table of diagnoses abstracted from patient medical records versus diagnoses obtained from the corresponding physician billing claims was generated using SAS statistical software (Version 9.3, SAS Institute Inc., Cary, NC). Information retrieved from the patient medical record was treated as a gold standard. The prevalence, PPV, and NPV of physician billing claims for identifying acute respiratory infections were estimated. Sensitivity and specificity estimates were corrected for the over-sampling of claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (69) using MS Excel 2003 (Version 5.1). To investigate between-physician variation in physician billing claim diagnosis accuracy, these analyses were repeated for each physician individually, combining all 9 types of acute respiratory infection under study (because each physician contributed too few of each type of acute respiratory infection to analyze each type individually).

Because we sampled several claims (and medical record visits) per patient, we conducted a sensitivity analysis to assess the effect of clustering of claims within patients on our estimates of sensitivity, specificity, PPV, and NPV. We did this by generating 100 random samples of 1 claim per patient (n= 729 claims) from our total sample of 3,526 claims, and averaging the estimates of sensitivity, specificity, PPV, and NPV over all 100 random samples, which is similar to bootstrapping methodology (130).

Results

Ten physicians participating in the MOXXI trial were purposefully selected for this study, and 9 agreed to participate. Among these 9 physicians' patients enrolled in the MOXXI trial, we randomly selected 635 patients who had at least one claim with a diagnosis of acute respiratory infection, and 94 patients without any claims with a diagnosis of acute respiratory infection. These 729 patients made 3,526 visits to their respective MOXXI physician during the study period (duration of 1-5 years, depending on the date of enrolment), for an average of 4.8 visits per patient. The medical records of all 729 sampled patients were abstracted, and written documentation for each of the 3,526 visits identified from physician billing claims was found in the corresponding patient's medical record. In all, 1,173 (33.3%) of sampled claims were positive for respiratory infection. Sixty-six percent of sampled patients were women, and the mean age of sampled patients was 47.6 (SD 21.0, range <1 to 90 years). The characteristics of patients enrolled in the MOXXI trial, as compared to those of the general population, have been discussed previously (131).

The agreement between the diagnosis in the medical record and the ICD-9 code in the physician billing claim is shown in Table 1, where shaded areas indicate concordant diagnoses. For example, there were 63 physician billing claims with a diagnosis of laryngitis, and for all 63 claims, a diagnosis of laryngitis was also documented in the medical record at the corresponding date; however an additional 16 diagnoses of laryngitis were documented in medical records that were not documented in physician billing claims. The overall percent agreement for the presence of any acute respiratory infection was 72.5%, which is the sum of all diagnoses of respiratory infection present in the physician billing claim and the corresponding medical record (969) divided by the sum of all diagnoses of respiratory infection documented in medical records (1,337). The proportion of physician billing claims with a diagnosis of acute respiratory infection confirmed in the patient medical record (PPV) was 0.93, 95% CI (0.91, 0.94) for all acute

respiratory infection combined, and 0.84, 95% CI (0.81, 0.88) for respiratory infections of likely viral etiology (Table 2). The PPV for acute respiratory infections of potentially bacterial etiology was 0.89, 95% CI (0.87, 0.92), and ranged from 0.72, 95% CI (0.67, 0.78) for acute bronchitis to 0.91, 95% CI (0.85, 0.97) for bacterial pneumonia. Sensitivity of physician billing claims for all acute respiratory infections combined was 0.49, 95% CI (0.45, 0.53). With the exception of influenza, sensitivity was markedly lower for viral respiratory infections than for bacterial ones. Specificity was 0.99 or higher for all types of acute respiratory infection studied.

The prevalence of acute respiratory infection diagnoses in physician billing claims varied between physicians from 19.5 to 111.4 per 1,000 claims (Table 3). Sensitivity and PPV varied between physicians from 1.00, 95% CI (1.00, 1.00) to 0.19, 95% CI (0.06, 0.47), and from 0.98, 95% CI (0.96, 1.00) to 0.70, 95% CI (0.53, 0.87), respectively. The accuracy of physician billing claims for identifying acute respiratory infections did not appear to be higher among physicians who diagnosed more acute respiratory infections.
Our sensitivity analysis using only 1 claim per patient yielded estimates for sensitivity (0.55, 95% CI 0.45, 0.64), specificity (0.99, 95% CI 0.99, 1.00), PPV (0.93, 95% CI 0.90, 0.96) and NPV (0.94, 95% CI 0.91, 0.97) that were similar to the estimates obtained when all visits were used. The confidence intervals from the sensitivity analysis are wider because the sample size is smaller: 729 claims (1 per patient) were used instead of all 3,526. This shows that the effect of within-patient clustering of claims on sensitivity, specificity, PPV, and NPV estimates is small.

Discussion

The PPV of physician billing claims was high for all types of acute respiratory infection studied. Our study was the first to estimate the prevalence, sensitivity, and specificity of physician billing claims for identifying chart-documented acute respiratory infections in primary care. For all but one type of acute respiratory infection investigated, our

sensitivity estimates were below 0.50. Our study was also the first to look at between-physician variation in physician billing claim diagnosis accuracy. We found that prevalence of respiratory infections in physician billing claims varied widely between primary care physicians. We also observed large unexplained between-physician variation in sensitivity and PPV of physician billing claims for identifying acute respiratory infections.

If physician billing claims had many false-positive diagnoses of respiratory infection, they would not be a useful data source for monitoring antibiotic prescribing. Therefore, a high PPV, or a high likelihood that diagnoses of respiratory infection in physician billing claims are also present in the corresponding patient medical record, provides support for using health administrative data for monitoring antibiotic prescribing. For most of the acute respiratory infection diagnoses investigated, our estimates of PPV were similar to those previously reported in the literature (127;128). However, our PPV estimate for influenza (0.66, 95% CI 0.58, 0.74) was much higher than the 0.20 reported by Linder et al, but the latter was aberrantly low as compared to other PPV estimates in the same study (128).

Previous studies have emphasized the high PPV of health administrative data for identifying episodes of respiratory infection, but have overlooked the importance of sensitivity (127;128). A high sensitivity is desirable because it suggests that the data capture a majority of visits for respiratory infections. A low sensitivity is problematic because it suggests that several visits for respiratory infections are not documented in health administrative data. Non-documentation of visits for respiratory infections may or may not be associated with antibiotic prescribing, which may result in bias when using health administrative data to monitor antibiotic prescribing.

Our study estimated the sensitivity of physician billing claims for identifying acute respiratory infections. Our sensitivity estimates were below 0.50 for all types of acute

respiratory infection studied except acute bronchitis, which raises concerns about the potential for bias. Whereas one previous study estimated the sensitivity of claims for identifying respiratory infections (128), the authors did not correct their sensitivity estimate for the verification bias introduced by over-sampling claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (69;70); consequently they greatly overestimated sensitivity. For example, if we had not corrected our estimates for verification bias, our estimate of the sensitivity of physician billing claims for identifying laryngitis would have been 0.80, as compared to the corrected sensitivity estimate of 0.20.

We were first to investigate between-physician variation in physician billing claim diagnosis accuracy for acute respiratory infections. We found almost 6-fold variation between physicians in the prevalence of respiratory infection. We observed similar between-physician variation in the sensitivity and PPV of physician billing claims for identifying acute respiratory infection. We expected that claims submitted by physician who diagnosed more acute respiratory infections would be more accurate for identifying acute respiratory infections, but we found that neither frequency nor prevalence of acute respiratory infection seemed to be related to physician billing claim diagnosis accuracy. This finding suggests that other factors are likely responsible for the observed between-physician variation in physician billing claim diagnosis accuracy.

A limitation of our study is that medical records may not represent a true gold standard for identifying acute respiratory infections diagnosed in primary care. The use of a single rater was also a limitation of our study, and systematic misclassification of acute respiratory infection diagnoses may have occurred as a result. Another limitation of our study was its small convenience sample of primary care physicians. Whereas physicians participating in the MOXXI trial are generally similar to other eligible physicians in the Montreal region, they tend to be younger than MOXXI non-participants. If physician billing claim diagnosis accuracy is related to physician age or practice experience, then

our study results may not be applicable to older or more-experienced physicians. Also, the MOXXI trial involves physicians practicing in urban and suburban areas, and our results may not be generalizable to physicians practicing in rural areas. Furthermore, patients enrolled in the MOXXI trial tend to differ from non-participating patients in that they are generally older, with more complex health status, and more visits to the MOXXI physician (131). Younger, healthier patients may be under-represented in our study sample. Future research should involve a large random sample of primary care physician from both urban and rural areas, and a stratified random sample of patients from each physician's practice population.

Because physician billing claims and prescription claims are now routinely used to monitor antibiotic prescribing for acute respiratory infections in primary care (107;108;120-124), it is important for future research to determine whether half of all acute respiratory infections diagnoses are missing from physician billing claims at random, or whether bias is present. If bias is present, future research should also focus on identifying determinants of physician billing claim diagnosis accuracy, so that appropriate corrections for the resulting bias can be developed and applied when physician billing claims are used to infer treatment indication for antibiotic prescribing. As suggested by the large between-physician variation observed in this study, physician characteristics may be associated with physician billing claim diagnosis accuracy. The effect of physician characteristics, as well as patient, encounter, practice, and billing characteristics, on physician billing claim diagnosis accuracy should be assessed in future research.

Table 1. Concordance of diagnoses in physician billing claims and patient medical records (shaded areas indicate concordance)

		Number of visits in patient medical records										
		Laryngitis	Common cold	Influenza	Unspecified acute upper respiratory infection	Pharyngitis	Otitis Media	Sinusitis	Acute bronchitis	Pneumonia	No respiratory infection	Total
Number of physician billing claims	Laryngitis	63	0	0	0	0	0	0	0	0	0	63
	Common cold	1	66	1	0	2	0	0	0	0	4	74
	Influenza	2	1	85	7	1	1	6	6	5	15	129
	Unspecified acute upper respiratory infection	0	1	1	154	3	0	2	4	0	22	187
	Pharyngitis	2	1	1	2	93	1	1	0	0	6	107
	Otitis Media	0	0	0	5	1	116	1	0	1	8	132
	Sinusitis	1	1	1	0	0	0	138	3	0	9	153
	Acute bronchitis	6	3	1	11	3	3	15	173	9	15	239
	Pneumonia	0	0	0	0	0	0	2	2	81	4	89
	No respiratory infection	4	29	5	28	12	28	19	28	11	2,189	2,353
	Total	79	102	95	207	115	149	184	216	107	2,272	3,526
	Uncorrected sensitivity*	0.80	0.65	0.89	0.74	0.81	0.78	0.75	0.80	0.76		

* The uncorrected sensitivity estimate is inflated due to the purposeful over-sampling of physician billing claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (69;70).

Table 2. Sensitivity, specificity, and positive and negative predictive values of the RAMQ physician billing claims for identifying episodes of acute respiratory infection

	RAMQ physician billing claims				
	Prevalence per 1,000 (95% CI)	Sensitivity[1] (95% CI)	Specificity[1] (95% CI)	PPV[2] (95% CI)	NPV[3] (95% CI)
All respiratory infections	**67.3 (65.6, 69.0)**	**0.49 (0.45, 0.53)**	**0.99 (0.99, 1.00)**	**0.93 (0.91, 0.94)**	**0.93 (0.92, 0.94)**
All likely viral respiratory infections	*16.4 (15.6, 17.3)*	*0.30 (0.26, 0.34)*	*1.00 (1.00, 1.00)*	*0.84 (0.81, 0.88)*	*0.97 (0.96, 0.97)*
Laryngitis / tracheitis	1.2 (0.9, 1.4)	0.20 (0.13, 0.30)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (0.99, 1.00)
Common cold	1.4 (1.2, 1.7)	0.11 (0.08, 0.15)	1.00 (1.00, 1.00)	0.89 (0.82, 0.96)	0.99 (0.99, 0.99)
Influenza	3.6 (3.2, 4.0)	0.45 (0.30, 0.60)	1.00 (1.00, 1.00)	0.66 (0.58, 0.74)	1.00 (1.00, 1.00)
Unspecified acute upper respiratory infection	10.2 (9.6, 10.9)	0.35 (0.29, 0.42)	1.00 (1.00, 1.00)	0.82 (0.77, 0.88)	0.98 (0.98, 0.99)
All potentially bacterial respiratory infections	*50.9 (49.4, 52.3)*	*0.51 (0.47, 0.56)*	*0.99 (0.99, 0.99)*	*0.89 (0.87, 0.92)*	*0.95 (0.95, 0.96)*
Pharyngitis / tonsilitis	5.3 (4.9, 5.8)	0.42 (0.32, 0.53)	1.00 (1.00, 1.00)	0.87 (0.81, 0.93)	0.99 (0.99, 1.00)
Otitis Media	8.6 (7.9, 9.2)	0.44 (0.35, 0.53)	1.00 (1.00, 1.00)	0.88 (0.82, 0.93)	0.99 (0.99, 0.99)
Sinusitis	12.5 (11.7, 13.2)	0.46 (0.38, 0.53)	1.00 (1.00, 1.00)	0.90 (0.85, 0.95)	0.99 (0.98, 0.99)
Acute bronchitis	19.5 (18.6, 20.4)	0.52 (0.46, 0.59)	0.99 (0.99, 0.99)	0.72 (0.67, 0.78)	0.99 (0.98, 0.99)
Pneumonia	5.0 (4.5, 5.5)	0.38 (0.28, 0.47)	1.00 (1.00, 1.00)	0.91 (0.85, 0.97)	0.99 (0.99, 1.00)

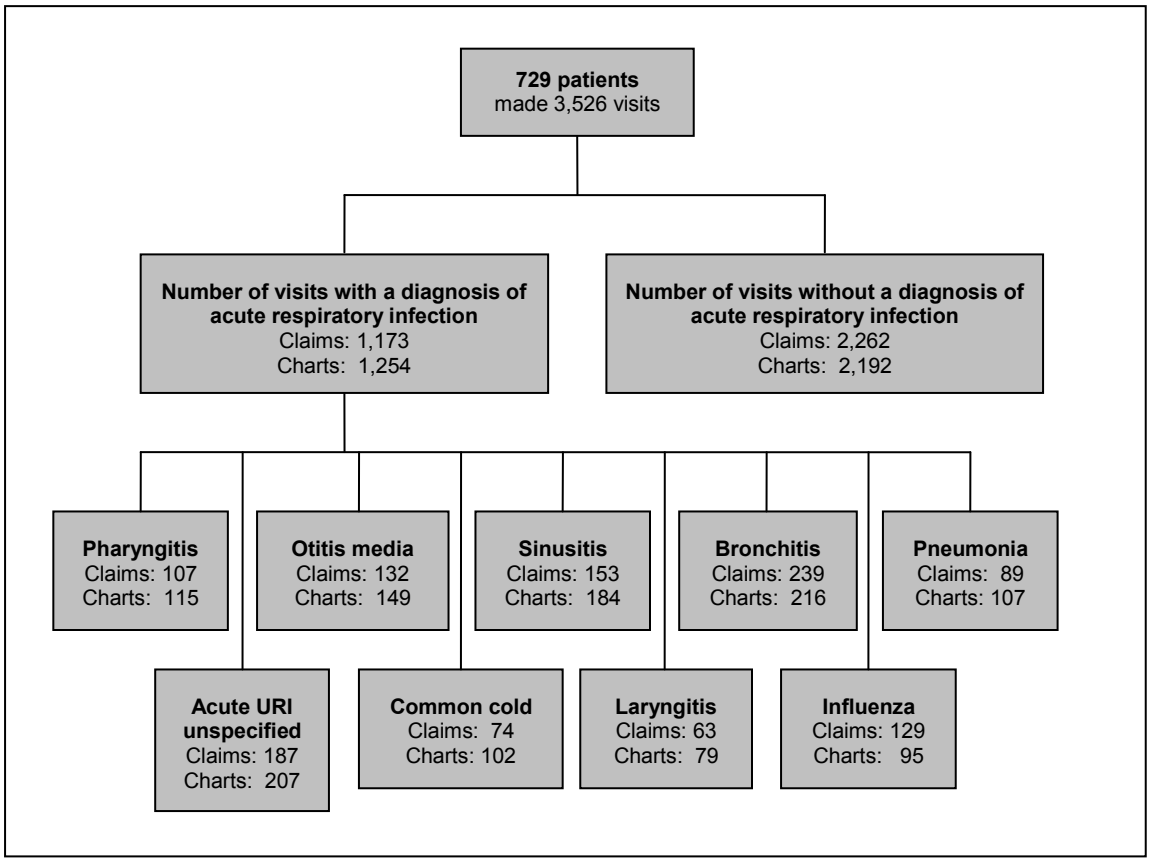
[1] Adjusted for over-sampling of physician billing claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (69;70).
[2] Positive predictive value.
[3] Negative predictive value.

Table 3. Sensitivity, specificity, and positive and negative predictive values of the RAMQ physician billing claims database for identifying all acute respiratory infections combined, *by study physician*

	RAMQ physician billing claims						
Study physician	No. claims with a diagnosis of acute RI[1]	No. claims	Prevalence per 1,000 (95% CI)	Sensitivity[2] (95% CI)	Specificity[2] (95% CI)	PPV[3] (95% CI)	NPV[4] (95% CI)
1	1,324	16,264	81.4 (77.1, 85.6)	0.85 (0.78, 0.91)	1.00 (0.99, 1.00)	0.96 (0.94, 0.98)	0.99 (0.98, 1.00)
2	2,041	18,319	111.4 (106.9, 116.0)	0.39 (0.33, 0.44)	0.98 (0.98, 0.99)	0.89 (0.86, 0.92)	0.82 (0.78, 0.86)
3	522	4,815	108.4 (99.6, 117.2)	0.42 (0.35, 0.49)	1.00 (0.99, 1.00)	0.97 (0.95, 1.00)	0.84 (0.80, 0.88)
4	356	9,614	37.0 (33.3, 40.8)	0.34 (0.24, 0.47)	1.00 (1.00, 1.00)	0.98 (0.96, 1.00)	0.93 (0.90, 0.96)
5	163	5,553	29.4 (24.9, 33.8)	0.37 (0.22, 0.56)	1.00 (0.99, 1.00)	0.89 (0.81, 0.97)	0.95 (0.92, 0.99)
6	159	6,905	23.0 (19.5, 26.6)	0.57 (0.16, 0.90)	0.99 (0.99, 1.00)	0.77 (0.64, 0.90)	0.99 (0.98, 1.00)
7	752	6,754	111.3 (103.8, 118.8)	0.72 (0.45, 0.89)	0.98 (0.96, 1.00)	0.82 (0.66, 0.98)	0.96 (0.92, 1.00)
8	94	4,815	19.5 (15.6, 23.4)	1.00 (1.00, 1.00)	0.99 (0.99, 1.00)	0.70 (0.53, 0.87)	1.00 (1.00, 1.00)
9	365	18,319	19.9 (17.9, 21.9)	0.19 (0.06, 0.47)	1.00 (0.99, 1.00)	0.97 (0.95, 1.00)	0.92 (0.84, 1.00)

[1] RI: respiratory infection.
[2] Adjusted for over-sampling of respiratory infections relative to other diagnoses (69;70).
[3] Positive predictive value.
[4] Negative predictive value.

Figure 1. Diagnoses from the sampled physician billing claims and corresponding patient medical records



Chapter 5. Assessing the accuracy of syndrome definitions based on diagnoses in physician claims

Preamble to Manuscript 2

Findings from manuscript 1 provided encouraging preliminary evidence that ICD-9 coded diagnoses in RAMQ physician claims could be used to identify episodes of acute respiratory infection. These results also pointed to the presence of considerable variation between physicians in the accuracy of diagnostic coding and in the prevalence of acute respiratory infections. Previous validations of syndrome definitions based on ICD-9 coded diagnoses in administrative data were based on small convenience samples of one or a few healthcare sites (50;61-63;65); therefore their results likely did not reflect the true breath of syndrome prevalence and diagnostic coding accuracy. Therefore, a large representative sample of healthcare sites was needed to generate unbiased estimates of the accuracy of syndrome definitions based on diagnoses in administrative data.

Previous studies of the accuracy of syndrome definitions based on diagnoses in administrative data focused exclusively on diagnoses from emergency departments (50;61-65). However, community-based clinics (as a group) offer broader population coverage and treat a larger volume of patients than emergency departments. Also, two studies suggested that diagnoses from community healthcare settings could detect seasonal influenza earlier than those from emergency departments (43;44).

The purpose of the research described in manuscript 2 was to perform a large-scale, population-based validation of several syndrome definitions based on diagnoses in RAMQ physician claims from community healthcare settings. A province-wide random sample of physicians likely to provide first-contact care was drawn, and the accuracy of syndrome definitions based on diagnoses in their claims was evaluated against information in the corresponding medical chart.

Title page

Accuracy of syndrome definitions based on diagnoses in physician claims

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ABSTRACT

BACKGROUND: Community clinics offer potential for timelier outbreak detection and monitoring than emergency departments. However, the accuracy of syndrome definitions used in surveillance has never been evaluated in community settings. This study's objective was to assess the accuracy of syndrome definitions based on diagnostic codes in physician claims for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory including influenza-like illness) in community clinics.

METHODS: We selected a random sample of 3,600 community-based primary care physicians who practiced in the fee-for-service system in the province of Quebec, Canada in 2005-2007. We randomly selected 10 visits per physician from their claims, stratifying on syndrome type and presence, diagnosis, and month. Double-blinded chart reviews were conducted by telephone with consenting physicians to obtain information on patient diagnoses for each sampled visit. The sensitivity, specificity, and positive predictive value (PPV) of physician claims were estimated by comparison to chart review.

RESULTS: 1,098 (30.5%) physicians completed the chart review. A chart entry on the date of the corresponding claim was found for 10,529 (95.9%) visits. The sensitivity of syndrome definitions based on diagnostic codes in physician claims was low, ranging from 0.11(fever) to 0.44 (respiratory), the specificity was high, and the PPV was moderate to high, ranging from 0.59 (fever) to 0.85 (respiratory). We found that rarely used diagnostic codes had a higher probability of being false-positive, and that more commonly used diagnostic codes had a higher PPV.

CONCLUSIONS: Future research should identify physician, patient, and encounter characteristics associated with the accuracy of diagnostic codes in physician claims. This would enable public health to improve syndromic surveillance, either by focusing on physician claims whose diagnostic code is more likely to be accurate, or by using all

physician claims and weighting each according to the likelihood that its diagnostic code is accurate.

INTRODUCTION

Syndromic surveillance is used widely by public health departments to detect and monitor unusual disease activity in the population by extracting nonspecific clinical data from information systems in clinical settings (24;25;132;133). Whereas much syndromic surveillance practice (24) and research (134) has focused on visits to emergency departments (ED), visits to community clinics offer another promising source of data. Syndromes followed in practice, such as influenza-like-illness (ILI), typically involve earlier, milder stages of disease, and most affected persons are likely to self-treat (28;135;136), at least initially, or present to walk-in clinics (135). In fact, researchers have demonstrated that excess ILI activity can be detected earlier using data from clinics as compared to data from EDs (137-139). The accuracy of data from community clinics has not, however, been established.

Many syndromic surveillance systems use International Classification of Disease , 9th revision (ICD-9) diagnostic codes in administrative databases to monitor syndrome occurrence (140). For this purpose, expert panels have generated groupings of ICD-9 codes corresponding to conceptual syndrome definitions (66). Administrative databases offer great promise for population-based surveillance by providing access to diagnostic information from many sites, including community healthcare settings. However, unlike medical procedure codes, ICD-9 diagnostic codes are not usually linked to healthcare provider payment, and therefore are not audited by health administrative authorities. Because of this, variation in diagnostic coding between physicians and between institutions is expected.

In a pilot study (141), we evaluated the accuracy of diagnostic codes in physician claims for identifying acute respiratory infections in nine Montreal-area physicians. We abstracted the diagnosis from the medical chart for the 3,526 visits made by 729 sampled patients in 2002-2005, and compared the medical chart diagnosis to the ICD-9

code on the corresponding physician claim. For all acute respiratory infections combined, we found a sensitivity of 0.49, 95% CI (0.45, 0.53), and a positive predictive value (PPV) of 0.93, 95% CI (0.91, 0.94). These pilot study results are promising, but there is a need for a large-scale, population-based investigation of the accuracy of diagnostic codes used in syndromic surveillance.

The objective of the present study was to assess the accuracy of syndrome definitions based on diagnostic codes from a representative sample of physician claims for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory including influenza-like illness (ILI)) in community healthcare settings. These syndromes were selected for their relevance to public health and the likelihood of being first detected among patients presenting to community healthcare settings.

METHODS

Context

This study was conducted in the province of Quebec, Canada, where universal health coverage is provided through the provincial health insurance plan. Each Canadian province maintains a population-based registry of insured persons and claims for all physician visits remunerated on a fee-for-service basis. Physician claims include information on the diagnosis (ICD-9 coded), medical procedure, visit date, location, and cost of service. All claims also record unique physician and patient identifiers that can be used to create longitudinal histories of healthcare use. In the province of Quebec, 99% of residents have provincial health insurance and 85-95% of medical visits are remunerated on a fee-for-service basis (88). In 2006, there were more than 7.6 million inhabitants in Quebec (89), and 18,908 active registered physicians (90). The availability of diagnostic information for nearly all medical visits to Quebec physicians represents an invaluable opportunity for assessing the validity of using diagnostic codes in physician claims for population-based surveillance, including syndromic surveillance.

Study design and sampling

The accuracy of diagnostic codes in physician claims for identifying syndromes was assessed by comparison to clinical information in the corresponding medical chart. To ensure representativeness, we used a population-based, 3-stage stratified random sample of 36,000 visits (Figure 1). In the first stage (Figure 1, Stage 1), the provincial health insurance agency identified all physicians who were eligible to be included in our study. To be eligible, physicians had to be a general practitioner, pediatrician, internist, geriatrician or general surgeon who practiced in the fee-for-service system in a private clinic, community health center, or hospital-based ambulatory care clinic during the 2-year study period (October 1, 2005 to September 30, 2007). Internists and general surgeons were included in our sample because, especially in rural-remote and underserved areas, these physicians may provide first-contact care and act as patients' family physician. From the 8,700 eligible physicians identified, the provincial health insurance agency selected a random sample of 3,600 (41.4%) physicians.

In the second stage (Figure 1, Stage 2), to facilitate chart retrieval for review, the health insurance agency randomly selected one eligible community practice location for each physician. The health insurance agency then sent the research team an anonymized file containing all physician claims billed by the 3,600 physicians from their respective selected community practice location during the 2-year study period (Figure 2, Step 1).

In the third stage (Figure 1, Stage 3), the research team randomly selected 5 syndrome-positive visits, i.e., 1 visit for each of fever, gastrointestinal, neurological, rash, and respiratory syndrome (including ILI), and 5 visits negative for all syndromes. Visits were classified as positive for a syndrome if a physician claim for the visit had an ICD-9 code that was part of the syndrome definition. Because syndromes have low population prevalence, to maximize data collection efficiency (70), syndrome-positive visits were over-sampled relative to syndrome-negative ones, so as to yield 1 syndrome-positive

visit per syndrome per physician and 5 syndrome-negative visits per physician. When sampling syndrome-positive claims, to maximize the number of syndrome-positive ICD-9 codes verified, we further stratified on ICD-9 code. Because two or more syndromes can occur concurrently in the same patient (61), syndrome-negative visits were negative for *all* syndromes. Syndrome-negative visits were also matched to syndrome-positive visits on calendar month to avoid bias due to syndrome seasonality. To avoid bias due to visits being clustered within patients, restriction was used to ensure that each patient was only sampled once. The list of 10 sampled visits was enumerated for each of the 3,600 physicians, for a total of 36,000 visits. An anonymized unique identifier, the study number, was assigned to each sampled visit by the research team. The list of 36,000 sampled visits was then sent to the health insurance agency (Figure 2, Step 2).

Syndrome definitions

We verified two sets of definitions for the 5 syndromes under study: the definitions developed and published by the US Centers for Disease Control and Prevention (CDC) in 2003 (66), and used by the US Department of Defense's (DoD) Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE), as well as the corresponding definitions in the University of Pittsburgh's Real-time Outbreak and Disease Surveillance (RODS) system (61). For ILI, we used the large-group (sensitive) and small-group (specific) definitions developed for the DoD ESSENCE system (49). These definitions are similar to the consensus syndrome definitions being developed by representatives from the 10 syndromic surveillance systems in place in the US (142), which have not yet been mapped to ICD-9 codes.

Physician recruitment

To preserve physician and patient anonymity, the health insurance agency sent the list of 3,600 physicians and 36,000 visits sampled by the research team to the medical regulatory authority (Figure 2, Step 3). The medical regulatory authority has the legal right to access confidential physician and patient information, therefore the list it

received included physician names and mailing addresses, as well as patient names, insurance numbers, and dates of birth. The medical regulatory authority acted as a trusted third party and recruited physicians to the study on behalf of the research team; it also provided physicians with information on the 10 sampled visits (Figure 2, Step 4). Interested physicians mailed their written consent and contact information to the research team (Figure 2, Step 5). Non-responding physicians were sent up to five reminders. Physician recruitment began in September 2008 and ended in August 2009. To maximize participation, physicians were offered $50 compensation for their participation and a summary of study findings.

Physician-facilitated medical chart review

The medical regulatory authority sent each physician the list of 10 sampled visits (Figure 2, Step 3). Lists sent to physicians included patients' first and last names, date of birth, health insurance number, and date of the visit to be verified, as well as the study number for each visit. Because the lists sent to physicians contained both patient information and study numbers, it enabled physicians to retrieve the relevant medical charts, and researchers to link the information collected through chart review to the anonymized physician claims file. During the chart review, interviewers and physicians referred to each visit using only the study number and visit date, thereby preserving patient anonymity.

Physician-facilitated medical chart reviews began in September 2008 and ended in December 2009. Using a previously published methodology (95), trained interviewers contacted consenting physicians by telephone to perform the chart review (Figure 2, Step 6). For each of the 10 sampled visits, the interviewer asked the physician to list all diagnoses. For each diagnosis corresponding to a syndrome definition, the interviewer asked the physician about the signs, symptoms, and key findings recorded in the medical chart, as well as the most likely etiology for the diagnosis (based solely on information available at the time of the visit).

Physician responses were entered directly into a database by the interviewer. Diagnoses were selected from a searchable list of diagnoses (mapped to ICD-9 codes) or, if the physician had recorded the ICD-9 code in the medical chart, the ICD-9 code was entered directly. For each syndrome-positive diagnosis, a list of syndrome-specific signs and symptoms was elicited, and the interviewer recorded whether the sign or symptom had been present, absent, or not recorded in the medical chart. Symptoms or signs not in the list and other key findings, such as epidemiologic links to other diagnosed cases or known outbreaks, were recorded as free text in separate fields. The data collection tool was translated to French for use with French-speaking physicians, and back-translated to English to ensure comparability of data collection.

At the time of the chart review, the physician and the interviewer were both blinded to ICD-9 code in the physician claim and the syndrome-positive or syndrome-negative status of the claim. To minimize measurement error due to inter-rater differences, interviewers were trained to use the data collection tool. Inter-rater reliability was assessed at baseline by having interviewers perform 2 simulated physician interviews of 10 visits each (for a total of 20 visits). To maintain data quality, interviewers underwent quality assurance monitoring every 3 months. Each assessment was comprised of 2 simulated physician interviews of 10 visits each (for a total of 20 visits). Agreement between raters was measured using the intraclass correlation coefficient (ICC).

Linkage of the medical chart review data to the physician claims data

The database containing the medical chart review data was linked to the physician claims file using the study number, physician identifier, and visit date. In our pilot study (141), we found that the visit date in the chart sometimes differed slightly from the visit date on the claim. We considered the chart and the claim to refer to the same visit if the visit date in the chart was within 0 (identical date) to 3 days from the visit date in the claim.

Physician characteristics that may influence participation

Physician gender, preferred language, specialty, practice setting, and geographic location were obtained from the health insurance agency. Physician year of licensure was obtained from the medical regulatory authority. The number of days worked per year was calculated as the number of days when at least one claim was submitted by the physician to the health insurance agency. The number of patients seen per day worked was calculated as the number of distinct patients for which one or more claim was submitted by the physician per day worked. The number and prevalence of syndrome-positive visits were calculated for each physician using claims generated from the selected practice location during the 2-year study period.

Statistical methods

For each visit, we assessed if the ICD-9 code in the physician claim and the diagnosis in the corresponding medical chart agreed as to the presence of each of the 5 syndromes and ILI. For example, if the diagnosis in the claim was cough (786.2) and the diagnosis in the corresponding medical chart was acute bronchitis (466.0), then both the claim diagnosis and the chart diagnosis were positive for respiratory syndrome, therefore the claim was a true-positive for respiratory syndrome. If the diagnosis in the claim was cough (786.2) and the diagnoses in the chart were hypertension (401.9) and diabetes (250.0), then the claim diagnosis was positive for respiratory syndrome and the chart diagnoses were not, therefore the claim was a false-positive for respiratory syndrome.

The negative predictive value (NPV) of a syndrome definition was estimated directly from the data for each of the 5 syndromes and ILI. Because we stratified syndrome-positive visits by ICD-9 code, we had to use an adjustment based on Bayes Theorem (69) to estimate the PPV of each syndrome. The PPV was estimated as a weighted average of each ICD-9 code's PPV, the weight being the number of visits with a given ICD-9 code divided by the total number of visits positive for that syndrome among participating physicians.

Because we verified more syndrome-positive visits than syndrome-negative ones, direct estimation of physician claims sensitivity and specificity using our data would lead to verification bias: sensitivity would be overestimated, and specificity underestimated (69). Because verified claims were randomly sampled within syndrome-positive and syndrome-negative strata, unbiased estimation of these parameters was achieved by re-weighting for the verification fractions (69). The sensitivity and specificity of physician claims for identifying each syndrome was estimated from the PPV and NPV (96) using the correction for verification bias (69), re-weighting for the different sampling fractions. We estimated the 95% CI for the bias-corrected sensitivity and specificity using the methods described by Begg and Greenes (69).

Ethics review

The research protocol for this study was reviewed and approved by the McGill University Institutional Review Board, the Quebec privacy commission, the Quebec health insurance agency, and the Quebec medical regulatory authority.

RESULTS

Between October 1, 2005 and September 30, 2007, the 3,600 study physicians billed for over 20 million visits by 4.8 million patients (61% of the province's population) from their randomly selected community practice.

Physician participation

Of 3,600 physicians contacted, 172 (4.8%) had an incorrect address on file with the health insurance agency, and 170 (4.7%) were discovered to be ineligible (recently deceased, retired, on sick/maternity leave, no longer practicing at the selected practice location). Of the 3,258 remaining physicians, 1,129 (34.7%) physicians consented to participate in the study, 218 (6.7%) refused, and 1,911 (58.7%) did not respond. Of the 1,129 consenting physicians, 1,098 (97.3%) completed the physician-facilitated medical

chart review, and 31 (2.7%) were unreachable or withdrew consent prior to interview. Participating and non-participating physicians were similar on all measured variables except two (Table 1): as compared to non-participants, participants had been in practice longer and had worked more days during the study period. Syndrome prevalence was similar among participating and non-participating physicians, and ranged from 5 per 1,000 visits for neurological syndrome and ILI small-group, to 126 per 1,000 visits for respiratory syndrome.

Inter-rater agreement

Agreement between raters was measured using simulated physician interviews shortly before the start of data collection and every 3 months thereafter. Agreement was perfect on all assessments (ICC=1.00).

Date agreement between the claim and the medical chart

Of the 10,980 visits selected for verification (10 visits per participating physician), physicians were able to access the corresponding medical chart for 10,669 (97.2%). The most common reasons for being unable to access the chart were inability to locate the medical chart (151 charts) and medical chart in storage with retrieval fee (140 charts). For 10,465 (98.1%) of the sampled visits, the visit date in the medical chart was identical to the visit date on the claim. Allowing for potential date transcription errors during billing, an additional 64 (0.6%) visits that had a date in the medical chart that was within 1-3 days of the visit date on the claim were identified, for a total of 10,529 visits for which both the medical chart and the claim was available and the visit dates were in agreement (within the 3 day time window).

Syndrome agreement between the claim ICD-9 code and the medical chart diagnosis

Table 2 shows the accuracy of ICD-9 codes in physician claims for identifying syndromes, as compared to the medical chart. The sensitivity of ICD-9 codes in physician claims for identifying syndromes was low, ranging from 0.11, 95% CI (0.10, 0.13) for fever

syndrome to 0.44, 95% CI (0.41, 0.47) for respiratory syndrome. The PPV of ICD-9 codes in physician claims for identifying syndromes was moderate to high, ranging from 0.59, 95% CI (0.55, 0.64) for fever syndrome to 0.85, 95% CI (0.83, 0.88) for respiratory syndrome. Both the specificity and NPV of ICD-9 codes in physician claims were near-perfect for all syndromes studied.

The additional file (excerpted in Table 3) shows the PPV of physician claims for identifying syndromes for each verified ICD-9 code individually. There was wide variation in PPV between different ICD-9 codes in a given syndrome. ICD-9 codes that were very rarely used by physicians, for example tularemia (ICD-9 code: 21.9), had a high probability of being false-positive, and therefore a very low PPV. ICD-9 codes that represent a common symptom, for example fever (ICD-9 code: 780.6), had a lower probability of being false-positive, and a higher PPV. ICD-9 codes that represent a common diagnosis, for example acute bronchitis (ICD-9 code: 466.0), had the lowest probability of being a false-positive, and the highest PPV.

DISCUSSION

This study was the first large-scale, population-based investigation of the accuracy of syndrome definitions based on diagnostic codes in physician claims from community healthcare settings. We found that the sensitivity of syndrome definitions based on diagnostic codes in physician claims for identifying syndromes was low, the PPV was moderate to high, and the specificity and NPV were near-perfect. Even though our sensitivity estimates were low for all syndromes definitions, these syndrome definitions may still be useful for monitoring syndrome occurrence when there are large numbers of cases (e.g., seasonal influenza). Respiratory syndrome had the highest prevalence and was the most accurately reported in physician claims. Unexpectedly, ILI small-group had the lowest PPV of all syndromes definitions studied, much lower than previously reported by others (49). The small-group definition of ILI is made up of only four ICD-9

codes: influenza with pneumonia (487.0), influenza with other respiratory manifestations (487.1), influenza with other manifestations (487.8), and acute upper respiratory infection, other multiple sites (465.8). Based on our interviews of over a thousand community physicians, we think that the poor accuracy of the ILI small-group definition reflects the common usage of the word 'flu' to describe a vague illness or a combination of non-specific symptoms. In addition to observing variation in physician claim accuracy between syndromes, we also found large variation in accuracy and prevalence between diagnostic codes within syndromes. Diagnostic codes with a very low prevalence were generally more likely to be false-positive; conversely, diagnostic codes with a higher prevalence were generally less likely to be false-positive, especially if they represented a diagnosis, as opposed to a symptom. This suggests that physicians are more likely to know the correct diagnostic code for a frequently diagnosed ailment, as compared to a rare one.

Rigorous attempts to assess the accuracy of ICD-9 codes used in syndromic surveillance as compared to the medical chart have been few, and they have relied on small convenience samples of emergency departments. In one such study, the accuracy of ICD-9 codes in ED reports for identifying 3 syndromes (fever, gastrointestinal, and respiratory) was assessed as compared to hospital chart diagnoses in the context of the US DoD ESSENCE surveillance system (65). For greater data collection efficiency, syndrome-positive ED reports were over-sampled relative to syndrome-negative ones; however, analyses were not adjusted for this differential sampling strategy, resulting in verification bias (69), and leading to a large overestimation of sensitivity and underestimation of specificity. To illustrate, the proportion of fever-positive visits in the sample was 0.19, whereas the proportion of fever-positive visits in the population is approximately 0.01 (based on our study). The authors reported sensitivity of 0.69 and specificity of 0.95. However, adjusting for verification bias, the estimates would be approximately 0.09 for sensitivity and 1.00 for specificity, which is similar to our results. In another study, the accuracy of ICD-9 codes in ED reports for identifying 7 syndrome

definitions (botulinic, constitutional, gastrointestinal, hemorrhagic, neurological, rash, and respiratory) was assessed against hospital chart diagnoses in the context of the RODS surveillance system (61). To maximize the quantity of syndrome-positive ICD-9 codes verified, the investigators selected a random sample of syndrome-positive visits from ED reports, stratified on syndrome-positive ICD-9 code, such that an equal number of syndrome-positive visits was sampled for each ICD-9 code in a syndrome. For example, fever (780.6) and bubonic plague (020.0), both corresponding to constitutional syndrome, contributed the same number of cases. However, the prevalence and accuracy of each ICD-9 code in a syndrome is different, and because the analyses were not adjusted for the uniform sampling strategy used, the reported estimates of sensitivity, specificity, PPV and NPV are biased. In a third study (62), the accuracy of ICD-9 coded physician diagnoses from 9 hospital EDs for identifying 'acute respiratory illness' was assessed by comparison to medical chart review. A simple random sample was used; therefore the results were not subject to verification bias. The authors reported a sensitivity of 0.43, 95% CI (0.28-0.58) , which is almost identical to our sensitivity estimate for respiratory syndrome; their estimates of NPV and specificity were also similar to ours, but their PPV estimate of 0.45, 95% CI (0.29-0.61) is much lower than ours.

Our study had several strengths and limitations. We used a large population-based random sample of all physicians working in the fee-for-service system in community healthcare settings in the province of Quebec in 2005-2007, thereby capturing potential ICD-9 coding differences between physicians, institutions, and regions. Not only did we estimate the accuracy of syndrome definitions, as others have done, but our study design enabled us to estimate the PPV for individual diagnostic codes within each syndrome definition. Matching syndrome-negative visits to syndrome-positive visit on calendar month ensured that our results were not affected by seasonal bias. Because two or more syndromes can occur concurrently in the same person (61), our requirement that syndrome-negative visits be negative for all 5 syndromes and ILI

ensured that we did not overestimate false-negatives and underestimate sensitivity and NPV. Our participation rate, though low, was consistent with that of other large population-based studies of Canadian physicians (143;144). Participating and non-participating physicians were similar on nearly all measured variables. The physician participation rate was significantly lower among recently licensed physicians than among their more experienced counterparts; recently licensed physicians may have been less likely to participate in our study because they tend to experience greater practice mobility (145) and report more impediments to practice (146) than their more experienced counterparts. Unfortunately, the accuracy of very rare syndrome-positive ICD-9 codes, such as cutaneous and pulmonary anthrax (22.0 and 22.1), could not be estimated because, as expected, they were not present in any of the 1,098 participating physicians' claims during the 2-year study period.

CONCLUSIONS

We found that diagnostic codes in physician claims from community healthcare settings have low sensitivity, moderate to high PPV, and near-perfect specificity and NPV for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory including ILI). Future research should evaluate the practical implications of our findings on decision-making in response to alerts from existing syndromic surveillance systems. Future research should also identify physician, patient, and encounter characteristics associated with better accuracy of diagnostic codes in physician claims. This would enable public health to improve syndromic surveillance, either by focusing on physician claims whose diagnostic code is more likely to be accurate, or by using all physician claims and weighting each according to the likelihood that its diagnostic code is accurate. We also estimated the prevalence and PPV of individual diagnostic codes within each syndrome. We found that rarely used diagnostic codes had a higher probability of being false-positive, and that more commonly used diagnostic codes had a higher PPV. These findings may be useful to the ongoing development of sensitive and

specific consensus syndrome definitions, as either a sensitive or a specific definition may be more useful depending on the surveillance objective.

Table 1. Characteristics of participating and non-participating physicians (N=3,258 eligible physicians)

	Participating physicians (N=1,098)		Non-participating physicians (N=2,160)	
Physician characteristics	**No.**	**(%)**	**No.**	**(%)**
Gender:				
Female	411	37.4	823	38.1
Male	687	62.6	1,337	61.9
Preferred language:				
French	1,006	91.6	1,937	89.7
English	92	8.4	223	10.3
Specialty:				
General practice	993	90.4	1,932	89.4
Internal medicine	13	1.2	41	1.9
Pediatrics	62	5.6	102	4.7
General surgery	30	2.7	85	3.9
Geriatrics	0	0	0	0
Type of setting selected:[1]				
Private clinic	1,060	96.5	2,044	94.6
Community health center	5	0.5	9	0.4
Hospital-based ambulatory clinic	33	3.0	107	5.0
Geographic location of selected setting:[1,3]				
Urban	921	83.9	1,867	86.4
Rural	177	16.1	293	13.6
	Mean	**SD**	**Mean**	**SD**
Years since licensure	24.2	9.7	22.3	10.5
No. days worked per year[1]	157.0	55.0	143.2	59.8
No. patients seen per day worked[1]	21.2	13.4	21.0	13.3
Syndrome frequency based on claim ICD-9 code	**No. visits[1,2]**	**Prevalence per 1,000 visits[1]**	**No. visits[1,2]**	**Prevalence per 1,000 visits[1]**
CDC and DoD-GEIS ESSENCE				
Fever	80,884	11	160,821	12
Gastrointestinal	162,282	22	309,209	24
Neurological	40,236	5	73,810	6
Rash	126,900	17	224,370	17
Respiratory	911,924	125	1,643,240	126
RODS				
Fever	162,000	22	291,990	22
Gastrointestinal	146,355	20	283,578	22
Neurological	36,344	5	67,344	5
Rash	55,251	8	103,698	8
Respiratory	478,201	65	877,556	67
Influenza-like illness				
Large-group	622,046	85	1,129,782	87
Small-group	32,173	4	61,127	5

[1]As per our study design, for each physician, a single practice location was randomly selected to facilitate the validation process. The information in this table is based on claims generated from the selected practice location during the 2-year study period.

[2] There were a total of 7,315,994 visits to the 1,098 participating physicians, and 13,010,410 visits to the 2,160 eligible non-participating physicians at the selected practice location during the 2-year study period.

[3] We tested the statistical significance (at the $p<0.05$ level) of any differences between participating and non-participating physicians using a multivariate logistic regression model where the dependent variable was participation and the independent variables were all characteristics in Table 1. Due to overlap between CDC, RODS, and ILI syndrome definitions, to avoid collinearity, we used separate models for each set of syndrome definitions. As compared to non-participating physicians, participating physicians had been in practice longer (odds ratio $(OR)_{\text{per 10 years since licensure}}$, 1.15; 95% CI, 1.05-1.25), and had worked more days ($OR_{\text{per 50 days}}$, 1.18; 95% CI, 1.09-1.28) during the 2-year study period.

Table 2. Accuracy of ICD-9 coded diagnoses in physician claims, as compared to ICD-9 coded diagnoses from physician-facilitated medical chart review, for identifying constitutional, gastrointestinal, neurological, rash, and respiratory syndrome, as well as influenza-like illness (ILI) (N=10,529 visits with matched claim-record pair)

Syndrome definition	No. visits in verified claims	No. visits in verified charts	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
CDC and DoD-GEIS ESSENCE						
Fever	601	656	0.11 (0.10, 0.13)	0.99 (0.99, 0.99)	0.59 (0.55, 0.64)	0.94 (0.93, 0.95)
Gastrointestinal	855	888	0.23 (0.20, 0.26)	0.99 (0.99, 0.99)	0.71 (0.66, 0.75)	0.94 (0.94, 0.95)
Neurological	971	693	0.17 (0.14, 0.21)	1.00 (1.00, 1.00)	0.67 (0.64, 0.70)	0.98 (0.98, 0.98)
Rash	897	905	0.20 (0.18, 0.23)	0.99 (0.99, 0.99)	0.66 (0.62, 0.70)	0.95 (0.95, 0.96)
Respiratory	1,049	1,779	0.44 (0.41, 0.47)	0.97 (0.96, 0.98)	0.85 (0.83, 0.88)	0.84 (0.83, 0.85)
RODS						
Fever	873	961	0.14 (0.12, 0.16)	0.99 (0.99, 0.99)	0.60 (0.56, 0.64)	0.91 (0.90, 0.92)
Gastrointestinal	703	834	0.20 (0.18, 0.23)	0.99 (0.99, 0.99)	0.68 (0.63, 0.73)	0.94 (0.94, 0.95)
Neurological	874	523	0.16 (0.13, 0.20)	1.00 (1.00, 1.00)	0.52 (0.48, 0.55)	0.99 (0.98, 0.99)
Rash	814	718	0.12 (0.10, 0.14)	1.00 (1.00, 1.00)	0.63 (0.59, 0.66)	0.96 (0.96, 0.97)
Respiratory	665	1,209	0.29 (0.26, 0.32)	0.98 (0.98, 0.98)	0.74 (0.70, 0.79)	0.87 (0.86, 0.88)
Influenza-like illness						
Large-group	653	1,232	0.38 (0.35, 0.41)	0.98 (0.98, 0.98)	0.77 (0.73, 0.81)	0.88 (0.87, 0.89)
Small-group	53	49	0.18 (0.12, 0.26)	1.00 (1.00, 1.00)	0.29 (0.16, 0.41)	0.99 (0.99, 0.99)

PPV: positive predictive value. NPV: negative predictive value.

Table 3. Example of diagnostic codes with the highest and lowest positive predictive value (excerpted from the Appendix)

Example of diagnostic codes with the HIGHEST positive predictive value (PPV)			
Syndrome definition	**ICD-9 code**	**Diagnostic label**	**PPV (95% CI)**
CDC fever	82.8	Tick-borne rickettsiosis not elsewhere classified	1.00 (1.00, 1.00)
	88.8	Other specified arthropod-borne diseases	1.00 (1.00, 1.00)
CDC gastrointestinal	7.1	Giardiasis	1.00 (1.00, 1.00)
	5.9	Food poisoning not otherwise specified	1.00 (1.00, 1.00)
CDC neurological	323.0	Encephalitis in viral disease classified elsewhere	1.00 (1.00, 1.00)
	784.3	Aphasia	1.00 (1.00, 1.00)
CDC rash	53.8	Herpes zoster with unspecified complication	1.00 (1.00, 1.00)
	695.2	Erythema nodosum	1.00 (1.00, 1.00)
CDC respiratory	33.0	*Bordetella pertussis*	1.00 (1.00, 1.00)
	462.9	Pharyngitis, acute not otherwise specified	1.00 (1.00, 1.00)
ILI large-group	487.0	Influenza with pneumonia	1.00 (1.00, 1.00)
	486.0	Pneumonia, organism not otherwise specified	1.00 (1.00, 1.00)
Example of diagnostic codes with the LOWEST positive predictive value (PPV)			
Syndrome definition	**ICD-9 code**	**Diagnostic label**	**PPV (95% CI)**
CDC fever	88.0	Bartonellosis	0.00 (0.00, 0.00)
	78.2	Sweating fever	0.00 (0.00, 0.00)
CDC gastrointestinal	555.0	Regional enteritis, small intestine	0.00 (0.00, 0.00)
	1.1	Cholera due to *Vibrio cholerae* El Tor	0.00 (0.00, 0.00)
CDC neurological	323.2	Encephalitis in protozoal disease classified elsewhere	0.00 (0.00, 0.00)
	53.0	Herpes zoster with meningitis	0.00 (0.00, 0.00)
CDC rash	51.0	Cowpox	0.00 (0.00, 0.00)
	55.8	Measles complications not otherwise specified	0.00 (0.00, 0.00)
CDC respiratory	20.4	Secondary pneumonic plague	0.00 (0.00, 0.00)
	79.8	Hantavirus infection	0.00 (0.00, 0.00)
ILI large-group	490.0	Bronchitis not otherwise specified	0.00 (0.00, 0.00)
	465.8	Acute upper respiratory infection, other multiple sites	0.36 (0.08, 0.65)

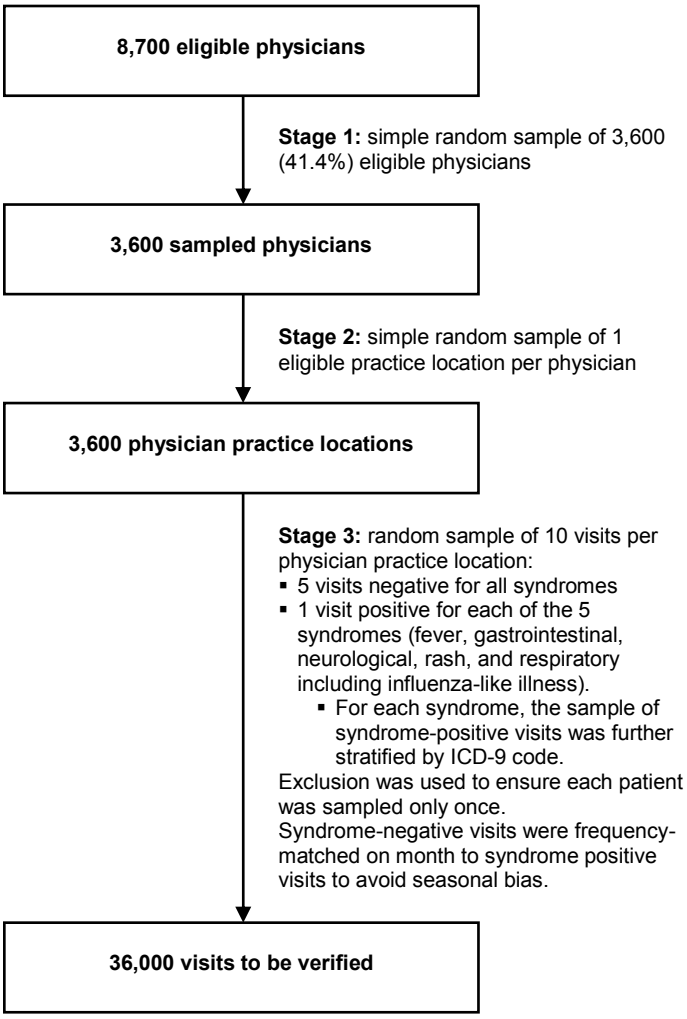

Figure 1. Population-based, 3-stage stratified random sample of visits to all community physicians in the province of Quebec

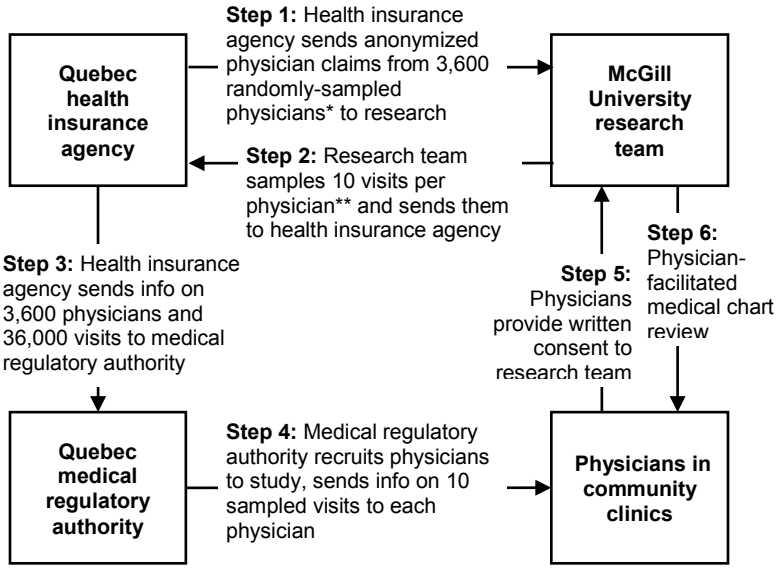

Figure 2. Overview of data collection
* Physician sampling by the Quebec health insurance agency is described in Figure 1, Stages 1 and 2.
** Visit sampling by the research team is described in Figure 1, Stage 3.

Appendix – Table 1. FEVER syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
2.0	TYPHOID FEVER	48	2	0.50	0.00	1.00
2.1	PARATYPHOID FEVER A	5	2	0.00	0.00	0.00
2.2	PARATYPHOID FEVER B	0	0	.	.	.
2.3	PARATYPHOID FEVER C	1	1	0.00	0.00	0.00
2.9	PARATYPHOID FEVER NOS	9	0	.	.	.
3.1	SALMONELLA SEPTICEMIA	5	2	0.00	0.00	0.00
20.2	PLAGUE, SEPTICEMIC	297	1	0.00	0.00	0.00
20.8	OTHER TYPES OF PLAGUE	0	0	.	.	.
20.9	PLAGUE NOS	1	0	.	.	.
21.8	TULAREMIA NEC	0	0	.	.	.
21.9	TULAREMIA NOS	2	2	0.00	0.00	0.00
22.3	ANTHRAX, SEPTICEMIA	0	0	.	.	.
22.8	ANTHRAX, OTHER SPECIFIED	0	0	.	.	.
22.9	ANTHRAX, UNSPECIFIED	0	0	.	.	.
23.0	BRUCELLA MELITENSIS	2	0	.	.	.
23.1	BRUCELLA ABORTUS	0	0	.	.	.
23.2	BRUCELLA SUIS	6	3	0.33	0.00	0.87
23.3	BRUCELLA CANIS	0	0	.	.	.
23.8	BRUCELLOSIS NEC	1	0	.	.	.
23.9	BRUCELLOSIS, UNSPECIFIED	14	6	0.33	0.00	0.71
24.9	GLANDERS	6	0	.	.	.
25.9	MELOIDOSIS	10	0	.	.	.
27.0	LISTERIOSIS	3	2	0.00	0.00	0.00
34.1	SCARLET FEVER	2,552	42	0.81	0.69	0.93
38.0	SEPTICEMIA STAPHYLOCOCCAL	5	4	0.25	0.00	0.67
38.1	SEPTICEMIA STAPHYLOCOCCAL	0	0	.	.	.
38.2	PNEUMOCOCCAL SEPTICEMIA	0	0	.	.	.
38.3	ANAEROBES SEPTICEMIA	0	0	.	.	.
38.4	GRAM-NEGATIVE SEPTICEMIA	22	5	0.20	0.00	0.55
38.8	SEPTICEMIAS, OTHER SPECIF	0	0	.	.	.
38.9	SEPTICEMIA, NOS	111	6	0.50	0.10	0.90
54.5	HERPETIC SEPTICEMIA	2	1	0.00	0.00	0.00
60.0	YELLOW FEVER, SYLVATIC	115	1	0.00	0.00	0.00
60.1	YELLOW FEVER, URBAN	3	1	0.00	0.00	0.00
60.9	YELLOW FEVER, UNSPEC	35	0	.	.	.
66.0	PHLEBOTOMUS FEVER	5	0	.	.	.
66.1	TICK-BORNE FEVER	0	0	.	.	.
66.2	VENEZUELAN EQUINE FEVER	0	0	.	.	.
66.3	MOSQUITO-BORNE FEVER NEC	0	0	.	.	.
66.8	ARTHROPOD VIRUS NEC	0	0	.	.	.
66.9	ARTHROPOD VIRUS NOS	306	1	0.00	0.00	0.00
78.2	SWEATING FEVER	10	5	0.00	0.00	0.00
79.8	VIRAL INFECTION OTHER S	154	4	0.00	0.00	0.00
79.9	VIRAL INFECTIONS UNSPECIFIED	5,551	30	0.30	0.14	0.46
80.9	LOUSE-BORNE TYPHUS	2	0	.	.	.
81.0	MURINE TYPHUS	3	1	0.00	0.00	0.00
81.1	BRILL'S DISEASE	0	0	.	.	.
81.2	SCRUB TYPHUS	137	2	0.00	0.00	0.00
81.9	TYPHUS NOS	0	0	.	.	.

Appendix – Table 1. FEVER syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
82.8	TICK-BORNE RICKETTS NEC	4	1	1.00	1.00	1.00
82.9	TICK-BORNE RICKETTS NOS	9	4	0.00	0.00	0.00
83.0	Q FEVER	56	0	.	.	.
83.1	TRENCH FEVER	8	1	0.00	0.00	0.00
83.2	RICKETTSIALPOX	2	2	0.00	0.00	0.00
83.8	RICKETTSIOSES NEC	2	1	0.00	0.00	0.00
83.9	RICKETTSIOSIS	2	1	0.00	0.00	0.00
84.0	MALARIA, FALCIPARUM	46	5	0.20	0.00	0.55
84.1	VIVAX MALARIA	4	2	0.00	0.00	0.00
84.2	QUARTAN MALARIA	34	6	0.17	0.00	0.46
84.3	OVALE MALARIA	9	0	.	.	.
84.5	MIXED MALARIA	160	0	.	.	.
84.6	MALARIA UNSPECIFIED	37	19	0.32	0.11	0.52
86.2	CHAGA'S DISEASE WITHOUT MENTION OF ORG	2	2	0.00	0.00	0.00
86.3	TRYPANOSOMIASIS, GAMBIAN	1	0	.	.	.
86.4	TRYPANOSOMIASIS, RHODESIAN	0	0	.	.	.
86.5	TRYPANOSOMIASIS, AFRICAN	0	0	.	.	.
86.9	TRYPANOSOMIASIS, UNSPEC	19	1	0.00	0.00	0.00
87.0	LOUSE-BORNE RELAPS FEVER	64	0	.	.	.
87.1	TICK-BORNE RELAPS FEVER	5	0	.	.	.
87.9	RELAPSING FEVER NOS	54	1	0.00	0.00	0.00
88.0	BARTONELLOSIS	624	9	0.00	0.00	0.00
88.8	OTHER ARTHROPOD-BORNE	2	1	1.00	1.00	1.00
88.9	ARTHROPOD-BORNE DIS NOS	23	10	0.60	0.30	0.90
100.8	LEPTOSPIROSIS, OTHER	0	0	.	.	.
780.3	FEBRILE CONVULSIONS	653	19	0.63	0.41	0.85
780.6	FEVER	20,028	150	0.58	0.50	0.66
780.7	BACTEREMIA	49,102	232	0.65	0.59	0.71
780.8	VIREMIA NOS	511	10	0.40	0.10	0.70
Total		**80,884**	**601**	**0.59**	**0.55**	**0.64**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 2. GASTROINTESTINAL syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
1.0	CHOLERA D/T VIB CHOLERAE	13	10	0.00	0.00	0.00
1.1	CHOLERA D/T VIB EL TOR	24	11	0.00	0.00	0.00
1.9	CHOLERA NOS	21	6	0.17	0.00	0.46
3.0	SALMONELLA GASTROENTERITI	266	3	0.67	0.13	1.00
3.2	LOCAL SALMONELLA INF NOS	3	1	0.00	0.00	0.00
3.8	SALMONELLA INFECTION NEC	0	0	.	.	.
3.9	SALMONELLA INFECTION UNSP	30	12	0.75	0.51	1.00
4.0	SHIGELLA DYSENTERIAE	64	0	.	.	.
4.1	SHIGELLA FLEXNERI	0	0	.	.	.
4.2	SHIGELLA BOYDII	0	0	.	.	.
4.3	SHIGELLA SONNEI	2	2	0.00	0.00	0.00
4.8	SHIGELLA INFECTIONS OTHER	43	0	.	.	.
4.9	SHIGELLOSIS, UNSPECIFIED	4	1	1.00	1.00	1.00
5.0	STAPH FOOD POISONING	3	0	.	.	.
5.2	FOOD POIS D/T C. PERFRIN	102	1	0.00	0.00	0.00
5.3	FOOD POIS: CLOSTRID NEC	343	1	0.00	0.00	0.00
5.4	FOOD POIS: V. PARAHAEM	5	1	0.00	0.00	0.00
5.8	FOOD POISONING, OTHER BAC	0	0	.	.	.
5.9	FOOD POISONING NOS	175	4	1.00	1.00	1.00
6.0	AC AMEBIASIS W/O ABSCESS	9	3	0.33	0.00	0.87
6.8	AMEBIC INFECTION NEC	0	0	.	.	.
6.9	AMEBIASIS UNSPECIFIED	5	3	1.00	1.00	1.00
7.0	BALANTIDIASIS	23	9	0.00	0.00	0.00
7.1	GIARDIASIS	23	17	1.00	1.00	1.00
7.2	COCCIDIOSIS	7	2	0.00	0.00	0.00
7.3	INTEST TRICHOMONIASIS	0	0	.	.	.
7.4	CRYPTOSPORIDOSIS	0	0	.	.	.
7.5	CYCLOSPORIASIS	0	0	.	.	.
7.8	PROTOZOAL INTEST DIS NEC	4	1	0.00	0.00	0.00
7.9	PROTOZOAL INTEST DIS NOS	1	0	.	.	.
8.0	E COLI ENTERITIS	4	3	0.33	0.00	0.87
8.1	ARIZONA ENTERITIS	4	2	0.50	0.00	1.00
8.2	AEROBACTER ENTERITIS	1	0	.	.	.
8.3	PROTEUS ENTERITIS	0	0	.	.	.
8.4	INTEST. INFECT BY OTHER B	10	4	0.25	0.00	0.67
8.5	BACTERIAL ENTERITIS NOS	24	0	.	.	.
8.6	ENTERITIS VIRAL OTHER	11	5	0.60	0.17	1.00
8.8	ENTERITIS VIRAL NOS	343	3	1.00	1.00	1.00
9.0	ENTERITIS/COLITIS/GASTRO.	3,818	25	0.80	0.64	0.96
9.1	COLITIS ENTERIT,GASTRO,IN	1,920	21	0.71	0.52	0.91
9.2	DIARRHEA, INFECTIOUS NOS	371	2	0.50	0.00	1.00
9.3	DIARRHEA OF INFECT ORIG	342	4	0.50	0.01	0.99
21.1	TULAREMIA, ENTERIC	0	0	.	.	.
22.2	GASTROINTESTINAL ANTHRAX	22	6	0.33	0.00	0.71
78.8	EPIDEMIC VOMITING SYND	204	4	0.00	0.00	0.00
127.0	ASCARIASIS	9	9	0.89	0.68	1.00
127.1	ANISAKIASIS	1	0	.	.	.
127.3	STRONGYLOIDIASIS	0	0	.	.	.
127.3	TRICHURIASIS	6	2	0.50	0.00	1.00

Appendix – Table 2. GASTROINTESTINAL syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
127.4	ENTEROBIASIS	253	4	0.50	0.01	0.99
127.5	CAPILLARIASIS	0	0	.	.	.
127.6	TRICHOSTRONGYLIASIS	0	0	.	.	.
127.7	INTEST HELMINTHIASIS NEC	0	0	.	.	.
127.8	MIXED INTESTINE HELMINTH	0	0	.	.	.
127.9	INTESTINAL HELMINTHIASIS,	251	3	1.00	1.00	1.00
129.9	INTESTINAL PARASITISM UNS	86	1	1.00	1.00	1.00
535.0	GASTRITIS, ACUTE	7,439	54	0.78	0.67	0.89
535.4	GASTRITIS,OTH SPEC.	4,602	58	0.72	0.61	0.84
535.5	GASTRITIS/DUODENITIS UNS	12,534	88	0.73	0.63	0.82
535.6	DUODENITIS UNS	398	3	0.67	0.13	1.00
536.2	VOMITING PERSISTENT	90	3	0.33	0.00	0.87
555.0	ENTERITIS SMALL INTESTINE	759	16	0.00	0.00	0.00
555.1	REG ENTERITIS, LG INTEST	1,332	9	0.11	0.00	0.32
555.2	REG ENTERIT SM/LG INTEST	0	0	.	.	.
558.2	GASTROENTERITIS/COLITIS,	0	0	.	.	.
558.9	GASTROENTERITIS/COLITIS N	28,890	120	0.85	0.79	0.91
567.0	PERITONITIS IN INFEC DIS	1	1	1.00	1.00	1.00
567.1	PNEUMOCOCCAL PERITONITIS	2	1	0.00	0.00	0.00
567.2	PERITONITIS SUPPURATIVE	8	5	0.20	0.00	0.55
567.8	PERITONITIS, OTHER SPECIF	1	0	.	.	.
567.9	PERITONITIS NOS	43	0	.	.	.
568.9	PERITONEAL DISORDER NOS	231	3	0.67	0.13	1.00
569.9	INTESTINAL DISORDER NOS	523	9	0.56	0.23	0.88
578.0	HEMATEMESIS	102	3	0.67	0.13	1.00
787.0	NAUSEA AND/OR VOMITING	4,882	76	0.63	0.52	0.74
787.1	HEARTBURN/PYROSIS	572	8	0.50	0.15	0.85
787.2	DYSPHAGIA	1,918	40	0.60	0.45	0.75
787.3	FLATUL/ERUCTAT/GAS PAIN	434	8	0.50	0.15	0.85
787.4	PERISTALSIS, VISIBLE	3	2	0.00	0.00	0.00
787.9	DIARRHEA	2,787	14	0.79	0.57	1.00
789.0	ABDOMINAL PAIN,UNSPECIF.	82,851	125	0.69	0.61	0.77
789.6	ABDOMINAL TENDERNESS, UNS	0	0	.	.	.
789.9	ABDOMEN/PELVIS SYMPTOMS O	3,030	23	0.22	0.05	0.39
Total		**162,282**	**855**	**0.71**	**0.66**	**0.75**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.

**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.

***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 3. NEUROLOGICAL syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
3.2	SALMONELLA MENINGITIS	3	1	0.00	0.00	0.00
36.0	MENINGITIS (MENINGOCOCCAL	3	2	0.50	0.00	1.00
36.1	ENCEPHALITIS, MENINGOCOCCAL	8	5	0.60	0.17	1.00
36.2	MENINGOCOCCEMIA INFECTION	23	2	0.00	0.00	0.00
36.8	INFECTION, MENINGOCOCCAL NEC	0	0	.	.	.
36.9	INFECTION, MENINGOCOCCAL NOS	0	0	.	.	.
47.0	COXSACKIE DUE TO MENINGIT	10	6	0.00	0.00	0.00
47.1	MENINGITIS D/T ECHO VIRUS	0	0	.	.	.
47.8	MENINGITIS, VIRAL NEC	0	0	.	.	.
47.9	MENINGITIS VIRAL NOS	10	5	0.60	0.17	1.00
48.9	DIS ENTEROVIRAL OF CNS, NEC	3	0	.	.	.
49.0	CHORIOMENINGITIS, LYMPHOCYTIC	328	3	0.00	0.00	0.00
49.1	MENINGITIS, ADENOVIRUS	471	3	0.00	0.00	0.00
49.8	ENCEPHALITIS VIRAL OTHER	0	0	.	.	.
49.9	ENCEPHALITIS VIRAL NOS	58	1	0.00	0.00	0.00
52.0	POSTVARICELLA ENCEPHALIT	0	0	.	.	.
53.0	HERPES ZOSTER WITH MENINGITIS	396	13	0.00	0.00	0.00
53.1	HERPES ZOSTER W UNSPED NER S	42	2	0.00	0.00	0.00
54.3	HERPETIC MENINGOENCEPHALI	8	2	0.00	0.00	0.00
54.7	HSV, MENINGITIS	16	8	0.13	0.00	0.35
55.0	POSTMEASLES ENCEPHALITIS	10	1	0.00	0.00	0.00
56.0	RUBELLA, WITH NEURO COMPLI	4	4	0.00	0.00	0.00
61.9	DENGUE	2	0	.	.	.
62.0	ENCEPHALITIS, JAPANESE	7	1	0.00	0.00	0.00
62.1	ENCEPHALITIS, WESTERN EQUINE	0	0	.	.	.
62.2	ENCEPHALITIS, EASTERN EQUINE	0	0	.	.	.
62.3	ST.LOUIS ENCEPHALITIS	0	0	.	.	.
62.4	ENCEPHALITIS, AUSTRALIAN	0	0	.	.	.
62.5	ENCEPHALITIS, CALIFORNIA VIRUS	1	1	0.00	0.00	0.00
62.8	ENCEPHALITIS, MOSQUITO-BORNE NEC	0	0	.	.	.
62.9	ENCEPHALITIS, MOSQUITO-BORNE NOS	1	1	0.00	0.00	0.00
63.0	ENCEPHALITIS, RUSSIAN SPRING-SUMMER	1	0	.	.	.
63.1	LOUPING ILL	0	0	.	.	.
63.2	ENCEPHALITIS, CENTRAL EUROPEAN	0	0	.	.	.
63.8	ENCEPHALITIS, VIRAL, TICK-BORNE NEC	0	0	.	.	.
63.9	ENCEPHALITIS, TICK-BORNE VIRAL NOS	3	3	0.00	0.00	0.00
64.9	ENCEPHALITIS ARTHPD-BORNE VIRAL NEC	7	0	.	.	.
66.4	WEST NILE FEVER	0	0	.	.	.
71.9	RABIES	7	0	.	.	.
72.1	MUMPS MENINGITIS	7	4	0.00	0.00	0.00
72.2	MUMPS ENCEPHALITIS	0	0	.	.	.
84.9	MALARIA COMPLICATED NEC	16	1	0.00	0.00	0.00
86.2	CHAGA'S DISEASE WITHOUT	2	2	0.00	0.00	0.00

Appendix – Table 3. NEUROLOGICAL syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
	MENTION OF ORG					
86.3	TRYPANOSOMIASIS, GAMBIAN	1	0	.	.	.
86.4	TRYPANOSOMIASIS, RHODESIAN	0	0	.	.	.
86.5	TRYPANOSOMIASIS, AFRICAN	0	0	.	.	.
91.8	ACUTE SYPHIL MENINGITIS	4	2	0.00	0.00	0.00
98.8	GONOCCOCAL, MENINGITIS	34	12	0.00	0.00	0.00
100.8	LEPTOSPIRAL INFECTIONS,MENINGITIS (ASEPTIC)	0	0	.	.	.
114.2	COCCIDIODAL MENINGITIS	0	0	.	.	.
115.0	HISTOPLASMOSIS MENINGITIS	1	1	0.00	0.00	0.00
115.1	HISTOPLASMA DUBOISII, MENINGITIS	0	0	.	.	.
115.9	HISTOPLASMOSIS, UNSPEC, MENINGITIS	12	5	0.20	0.00	0.55
117.5	CRYPTOCOCCOSIS	0	0	.	.	.
130.0	TOXOPLASMOSIS, MENINGOENCEPHALITIS	0	0	.	.	.
136.2	SPECIFIC INF BY FREE LIVING AMOEBA	0	0	.	.	.
293.0	DELIRIUM, ACUTE	67	2	0.50	0.00	1.00
293.1	CONFUSIONAL STATE(del subacute)	9	4	0.25	0.00	0.67
307.8	TENSION HEADACHE	3,311	70	0.74	0.64	0.85
320.0	HEMOPHILUS MENINGITIS	0	0	.	.	.
320.1	MENINGITIS PNEUMOCOCCAL	0	0	.	.	.
320.2	MENINGITIS, STREPTOCOCCAL	1	0	.	.	.
320.3	MENINGITIS, STAPHYLOCOCCAL	0	0	.	.	.
320.7	MENG, IN OTH BCTRL DISEASE CE	4	1	0.00	0.00	0.00
320.8	BACTERIAL MENINGITIS OTHER	0	0	.	.	.
320.9	BACTERIAL MENINGITIS NOS	6	6	0.00	0.00	0.00
321.0	MENINGITIS, CRYPTOCOCCAL	0	0	.	.	.
321.1	MENINGITIS IN OTH. FUNGAL	1	1	0.00	0.00	0.00
321.2	Meningitis d/t viral diseases NEC	0	0	.	.	.
321.3	MENINGITIS D/T TRYPANOSOMIASIS	2	1	0.00	0.00	0.00
321.4	MENINGITIS IN SARCOIDOSIS	1	1	0.00	0.00	0.00
321.8	MENG D/T OTH NONBACT ORGANISM CE	2	0	.	.	.
322.0	MENINGITIS, NONPYOGENIC	18	5	0.20	0.00	0.55
322.1	MENINGITIS, EOSINOPHILIC	0	0	.	.	.
322.9	MENINGITIS NOS	240	3	0.67	0.13	1.00
323.0	ENCEPHALITIS IN VIRAL DISEASE CE	16	2	1.00	1.00	1.00
323.1	ENCEPHALITIS IN RICKETTSIAL DIS CE	0	0	.	.	.
323.2	ENCEPHALITIS IN PROTOZOAL DIS CE	18	12	0.00	0.00	0.00
323.4	ENCEPHALITIS, OTH D/T INFECTION CE	4	1	1.00	1.00	1.00
323.5	ENCEPHALITIS, POSTIMMUNIZATION	0	0	.	.	.
323.6	ENCEPHALITIS POSTINFECTIO	0	0	.	.	.
323.7	ENCEPHALITIS, TOXIC	1	1	0.00	0.00	0.00
323.8	OTHER CAUSES OF ENCEPHALI	0	0	.	.	.

Appendix – Table 3. NEUROLOGICAL syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
323.9	ENCEPHALITIS NOS	204	5	0.20	0.00	0.55
348.3	ENCEPHALOPATHY NOS	175	3	0.33	0.00	0.87
780.0	ALTERATION OF AWARENESS	1,603	47	0.02	0.00	0.06
780.3	CONVULSIONS	653	19	0.53	0.30	0.75
781.6	MENINGISMUS	21	11	0.18	0.00	0.41
784.0	HEADACHE	32,290	683	0.73	0.70	0.76
784.3	APHASIA	90	2	1.00	1.00	1.00
Total		**40,236**	**971**	**0.67**	**0.64**	**0.70**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 4. RASH syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
26.0	SPIRILLARY FEVER	0	0	.	.	.
26.1	STREPTOBACILLARY FEVER	1	1	0.00	0.00	0.00
26.9	RAT-BITE FEVER UNSPECIFIED	6	3	0.00	0.00	0.00
50.0	SMALL POX, VARIOLA MAJOR	3	3	0.00	0.00	0.00
50.1	SMALL POX, ALASTRIM	0	0	.	.	.
50.2	SMALL POX, MODIFIED	0	0	.	.	.
50.9	SMALLPOX NOS	2	2	0.50	0.00	1.00
51.0	COWPOX	3,730	20	0.00	0.00	0.00
51.1	PSEUDOCOWPOX	42	0	.	.	.
51.2	DERMATITIS PUSTULAR, CONT	44	1	1.00	1.00	1.00
51.9	PARAVACCINIA NOS	30	1	1.00	1.00	1.00
52.7	VARICELLA COMPLICAT NEC	0	0	.	.	.
52.8	VARICELLA W/UNSPECIFIED C	0	0	.	.	.
52.9	VARICELLA NOS	1,558	26	0.88	0.76	1.00
53.2	HERPES ZOSTER DERMATITIS E	229	4	1.00	1.00	1.00
53.7	HERPES ZOSTER WITH OTHER SPECIF COMPLIC	19	6	1.00	1.00	1.00
53.8	H.Z. W/ UNSPEC. COMPLICATION	17	8	1.00	1.00	1.00
53.9	HERPES ZOSTER NOS W/O COM	10,551	168	0.87	0.82	0.92
54.0	ECZEMA HERPETICUM	708	13	0.62	0.35	0.88
54.7	HERPES SIMPLEX W/OTH.SPEC	16	8	0.75	0.45	1.00
54.8	HERPES SIMPLEX, W/UNS.COM	5	4	0.50	0.01	0.99
54.9	HERPES SIMPLEX NOS	8,763	153	0.66	0.59	0.74
55.7	MEASLES COMPLICATION NEC	0	0	.	.	.
55.8	MEASLES COMPLICATION NOS	141	4	0.00	0.00	0.00
55.9	MEASLES UNCOMPLICATED	82	3	0.33	0.00	0.87
56.7	RUBELLA COMPLICATION NEC	2	1	0.00	0.00	0.00
56.8	RUBELLA COMPLICATION NOS	0	0	.	.	.
56.9	RUBELLA UNCOMPLICATED	172	1	0.00	0.00	0.00
57.0	ERYTHEMIA INFECT.(5TH DIS	238	2	1.00	1.00	1.00
57.8	EXANTHEMATA VIRAL OTHER S	619	9	0.56	0.23	0.88
57.9	EXANTHEM VIRAL, UNSPECIFI	1,440	15	0.40	0.15	0.65
74.3	HAND/FOOT AND MOUTH DISEA	49	1	1.00	1.00	1.00
78.0	MOLLUSCUM CONTAGIOSUM	3,323	43	0.84	0.73	0.95
82.0	ROCKY MOUNTAIN SPOTTED FE	2	2	0.50	0.00	1.00
83.2	RICKETTSIALPOX	2	2	0.00	0.00	0.00
692.9	DERMATITIS UNSPECIFIED CA	73,677	181	0.64	0.57	0.71
695.0	ERYTHEMA TOXIC	53	3	0.67	0.13	1.00
695.1	ERYTHEMA MULTIFORME	106	1	1.00	1.00	1.00
695.2	ERYTHEMA NODOSUM	135	5	1.00	1.00	1.00
695.3	ROSACEA	554	10	0.70	0.42	0.98
695.4	LUPUS ERYTHEMATOSUS	540	9	0.56	0.23	0.88
695.8	ERYTHEMATOUS CONDITIONS O	735	12	0.67	0.40	0.93
695.9	ERYTHEMATOUS CONDITION N	3,183	41	0.54	0.38	0.69
782.1	RASH/OTHER NONSPEC SKIN E	16,123	131	0.74	0.67	0.82
Total		**126,900**	**897**	**0.66**	**0.62**	**0.70**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 5. RESPIRATORY syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
3.2	SALMONELLA PNEUMONIA	3	1	0.00	0.00	0.00
20.3	PRIMARY PNEUMONIC PLAGUE	0	0	.	.	.
20.4	SECONDARY PNEUMON PLAGUE	7	3	0.00	0.00	0.00
20.5	PNEUMONIC PLAGUE NOS	0	0	.	.	.
21.2	PULMONARY TULAREMIA	0	0	.	.	.
22.1	PULMONARY ANTHRAX	0	0	.	.	.
31.0	MYCOBACTERIA, PULMONARY	7	3	0.33	0.00	0.87
31.8	MYCOBACTERIAL DIS NEC	6	1	0.00	0.00	0.00
31.9	MYCOBACTERIA DISEASES/UNS	15	5	0.20	0.00	0.55
32.0	FAUCIAL DIPHTHERIA	52	0	.	.	.
32.1	NASOPHARYNX DIPHTHERIA	8	5	0.60	0.17	1.00
32.2	ANT NASAL DIPHTHERIA	7	2	0.00	0.00	0.00
32.3	LARYNGEAL DIPHTHERIA	1	0	.	.	.
32.8	DIPHTHERIA NEC	0	0	.	.	.
32.9	DIPHTHERIA NOS	2	2	0.50	0.00	1.00
33.0	BORDETELLA PERTUSSIS	39	9	1.00	1.00	1.00
33.1	BORDETELLA PARAPERTUSSIS	0	0	.	.	.
33.8	WHOOPING COUGH NEC	5	1	1.00	1.00	1.00
33.9	WHOOPING COUGH(UNSPE.ORGA	325	0	.	.	.
34.0	STREP SORE THROAT	735	2	1.00	1.00	1.00
52.1	VARICELLA WITH PNEUMONIA	0	0	.	.	.
55.1	POSTMEASLES PNEUMONIA	8	3	0.67	0.13	1.00
55.2	POSTMEASLES OTITIS MEDIA	502	1	0.00	0.00	0.00
73.0	ORNITHOSIS, WITH PNEUMONIA	0	0	.	.	.
73.7	ORNITHOSIS, OTHER SPECIF COMPLIC	0	0	.	.	.
73.8	ORNITHOSIS, UNSPECIFIED COMPLIC	0	0	.	.	.
73.9	ORNITHOSIS, UNSPECIFIED	1	1	0.00	0.00	0.00
75.9	MONONUCLEOSIS, INFECTIOUS	2,373	2	1.00	1.00	1.00
79.0	ADENOVIRUS INFECT NOS	507	0	.	.	.
79.1	ECHO VIRUS INFECT NOS	3	0	.	.	.
79.2	COXSACKIE VIRUS	12	7	0.57	0.20	0.94
79.3	RHINOVIRUS INFECT NOS	2	1	1.00	1.00	1.00
79.6	RESPIRATORY SYNCYTIAL VIR	0	0	.	.	.
79.8	HANTAVIRUS INFECTION	154	4	0.00	0.00	0.00
98.6	GONOCCOCAL, INFECTION OF PHARYNX	4	1	1.00	1.00	1.00
114.5	PULM COCCIDIOIDOMYCOS,UN	0	0	.	.	.
114.9	COCCIDIOIDOMYCOSIS NOS	2	1	0.00	0.00	0.00
115.0	HISTOPLASMA CAPSULATUM NOS	1	1	0.00	0.00	0.00
115.1	HISTOPLASMA DUBOISII NOS	0	0	.	.	.
115.9	HISTOPLASMOSIS UNS	12	5	0.20	0.00	0.55
116.0	BLASTOMYCOSIS	5	1	0.00	0.00	0.00
116.1	PARACOCCIDIOIDOMYCOSIS	2	2	0.00	0.00	0.00
117.1	SPOROTRICHOSIS	1	1	0.00	0.00	0.00
117.3	PULMONARY ASPERGILLOSIS	15	6	0.50	0.10	0.90
117.5	CRYPTOCOCCOSIS	0	0	.	.	.

Appendix – Table 5. RESPIRATORY syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
130.4	TOXOPLASMA PNEUMONITIS	0	0	.	.	.
136.3	PNEUMOCYSTOSIS	1	0	.	.	.
381.0	OTITIS MEDIA NONSUP ACUTE	9,398	16	0.94	0.82	1.00
381.4	OTITIS MEDIA NONSUPPURATI	6,730	17	0.53	0.29	0.77
381.5	EUSTACHIAN SALPINGITIS	144	0	.	.	.
382.0	OM SUPPURATIVE & UNSPEC	6,326	17	0.88	0.73	1.00
382.4	OM SUPPURATIVE NOS	154	0	.	.	.
382.9	OTITIS MEDIA NOS	95,165	68	0.75	0.65	0.85
460.0	NASOPHARYNGITIS, ACUTE	1	0	.	.	.
460.9	NASOPHARYNGITIS, ACUTE NOS	20,179	11	1.00	1.00	1.00
461.0	MAXILLARY SINUSITIS, ACUT	4,234	5	1.00	1.00	1.00
461.1	SINUSITIS, FRONTAL-ACUTE	145	1	1.00	1.00	1.00
461.2	SINUSITIS, ETHMOIDAL	43	7	0.57	0.20	0.94
461.3	SINUSITIS,ACUTE SPHENOIDA	2	1	1.00	1.00	1.00
461.8	SINUSITIS, ACUTE, OTHER	1,466	5	0.40	0.00	0.83
461.9	SINUSITIS, ACUTE NOS	39,976	57	0.91	0.84	0.99
462.0	PHARYNGITIS, ACUTE	10	0	.	.	.
462.9	PHARYNGITIS, ACUTE NOS	39,695	24	1.00	1.00	1.00
463.0	TONSILLITIS, ACUTE	3	0	.	.	.
463.9	TONSILLITIS, ACUTE NOS	32,676	16	0.94	0.82	1.00
464.0	LARYNGITIS, ACUTE	12,319	27	0.81	0.67	0.96
464.1	TRACHEITIS, ACUTE	9,716	13	0.92	0.78	1.00
464.2	LARYNGOTRACHEITIS, ACUTE	1,214	1	1.00	1.00	1.00
464.3	EPIGLOTTITIS, ACUTE	32	16	0.69	0.46	0.91
464.4	CROUP	916	0	.	.	.
464.5	SUPRAGLOTTIS, UNS	0	0	.	.	.
465.0	LARYNGOPHARYNGITIS, ACUTE	4,679	3	0.67	0.13	1.00
465.8	URI, OTHER MULT. SITES	3,809	11	0.91	0.74	1.00
465.9	URI, ACUTE NOS	223,128	84	0.90	0.84	0.97
466.0	BRONCHITIS ACUTE	62,662	67	0.90	0.82	0.97
466.1	BRONCHIOLITIS ACUTE	5,006	10	0.90	0.71	1.00
478.9	RESPIRATORY TRACT DISEASE	85	0	.	.	.
480.0	ADENOVIRAL PNEUMONIA	636	2	1.00	1.00	1.00
480.1	PNEUMONIA,RESP.SYNCYTIAL	3	3	0.67	0.13	1.00
480.2	PARINFLUENZA VIRAL PNEUM	1	0	.	.	.
480.8	VIRAL PNEUMONIA NEC	1	1	1.00	1.00	1.00
480.9	PNEUMONIA, VIRAL	1,044	0	.	.	.
481.9	PNEUMOCOCCAL PNEUMONIA	837	1	1.00	1.00	1.00
482.0	PNEUMONIA-KLEBSIELLA PNEU	311	0	.	.	.
482.1	PNEUMONIA DUE TO PSEUDOMO	26	6	0.50	0.10	0.90
482.2	H.INFLUENZAE PNEUMONIA	8	4	1.00	1.00	1.00
482.3	STREPTOCOCCUS UNSPECIFIED	0	0	.	.	.
482.4	STAPH PNEUMONIA NOS	0	0	.	.	.
482.8	PNEUMONIA/ANAEROBES	25	4	1.00	1.00	1.00
482.9	PNEUMONIA, BACTERIAL NOS	2,915	2	0.50	0.00	1.00
483.0	PNEUMONIA MYCOPLASMA	0	0	.	.	.
483.1	PNEUMONIA DUE TO CHLAMYD	0	0	.	.	.
483.8	PNEUMONIA DUE TO ORGANISM NEC	0	0	.	.	.
484.1	PNEUM W CYTOMEG INCL DIS	10	4	0.50	0.01	0.99

Appendix – Table 5. RESPIRATORY syndrome, CDC definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
484.3	PNEUMONIA IN WHOOP COUGH	0	0	.	.	.
484.5	PNEUMONIA IN ANTHRAX	1	1	1.00	1.00	1.00
484.6	PNEUMONIA IN ASPERGILLOSI	0	0	.	.	.
484.7	PNEUM IN OTH SYS MYCOSES	0	0	.	.	.
484.8	PNEUM IN INFECT DIS NEC	1	1	1.00	1.00	1.00
485.9	BRONCHOPNEUMONIA ORGANISM	2,255	4	1.00	1.00	1.00
486.0	PNEUMONIA, ORGANISM NOS	4	1	1.00	1.00	1.00
486.9	PNEUMONIA, ORGANISM NOS	19,755	18	0.83	0.66	1.00
487.0	INFLUENZA WITH PNEUMONIA	278	1	1.00	1.00	1.00
487.1	INFLUENZA W/OTH. RESP. MA	28,029	41	0.88	0.78	0.98
487.8	INFLUENZA W/OTHR MANIFEST	57	0	.	.	.
490.0	BRONCHITIS NOS	7	1	0.00	0.00	0.00
490.9	BRONCHITIS NOS	60,126	44	0.89	0.79	0.98
493.0	ASTHMA, EXTRINSIC	3,265	10	0.90	0.71	1.00
493.1	ASTHMA, INTRINSIC	25	9	1.00	1.00	1.00
493.9	ASTHMA, UNSPEC	96,278	78	0.85	0.77	0.93
511.0	PLEURISY W/O EFFUSION	139	1	.	.	.
511.1	PLEURAL EFFUSION-VIRAL(NO	0	0	.	.	.
511.8	HEMOTHORAX	9	6	0.67	0.29	1.00
511.9	PLEURAL EFFUSION UNSPECIF	366	2	1.00	1.00	1.00
513.0	ABSCESS LUNG	21	7	0.71	0.38	1.00
513.1	ABSCESS OF MEDIASTINUM	1	1	0.00	0.00	0.00
514.9	EDEMA PULMONARY	101	0	.	.	.
518.0	PULMONARY COLLAPSE	143	2	0.50	0.00	1.00
518.4	EDEMA LUNG ACUTE NOS	246	1	0.00	0.00	0.00
518.8	RESPIRATORY FAILURE, ACUTE	2,572	11	0.36	0.08	0.65
519.2	MEDIASTINITIS	7	3	0.33	0.00	0.87
519.3	MEDIASTINUM, DISEASES NEC	11	6	0.17	0.00	0.46
769.9	RESPIRATORY DISTRESS SYND	24	1	0.00	0.00	0.00
782.5	CYANOSIS	42	0	.	.	.
784.1	PAIN IN THROAT	3,061	6	1.00	1.00	1.00
786.0	RESPIRATORY ABNORMALITY	24,392	69	0.30	0.20	0.41
786.1	STRIDOR	54	0	.	.	.
786.2	COUGH	43,291	69	0.90	0.83	0.97
786.3	HEMOPTYSIS	930	5	0.60	0.17	1.00
786.5	CHEST PAIN, UNSPECIFIED	33,582	67	0.69	0.58	0.80
786.7	ABNORMAL CHEST SOUNDS	30	0	.	.	.
786.9	RESP SYS/CHEST SYMP NEC	2,204	7	0.57	0.20	0.94
799.1	RESPIRATORY ARREST	70	2	0.50	0.00	1.00
Total		**911,924**	**1,050**	**0.85**	**0.83**	**0.88**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 6. FEVER syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
2.0	Typhoid/paratyphoid fever	48	2	0.50	0.00	1.00
2.1	Paratyphoid fever a	5	2	0.00	0.00	0.00
2.2	Paratyphoid fever b	0	0	.	.	.
2.3	Paratyphoid fever c	1	1	0.00	0.00	0.00
2.9	Paratyphoid fever nos	9	0	.	.	.
20.0	Bubonic plague	1	1	0.00	0.00	0.00
20.2	Septicemic plague	297	1	0.00	0.00	0.00
20.8	Other specified types of plague	0	0	.	.	.
20.9	Plague, unspecified	1	0	.	.	.
21.0	Ulceroglandular tularemia	0	0	.	.	.
21.3	Oculoglandular tularemia	0	0	.	.	.
21.8	Other specified tularemia	0	0	.	.	.
21.9	Unspecified tularemia	2	2	0.00	0.00	0.00
22.3	Anthrax septicemia	0	0	.	.	.
22.8	Other specified manifestations of anthrax	0	0	.	.	.
22.9	Anthrax, unspecified	0	0	.	.	.
23.0	Brucella melitensis	2	0	.	.	.
23.1	Brucella abortus	0	0	.	.	.
23.2	Brucella suis	6	3	0.33	0.00	0.87
23.3	Brucella canis	0	0	.	.	.
23.8	Other brucellosis	1	0	.	.	.
23.9	Brucellosis, unspecified	14	6	0.33	0.00	0.71
60.0	Sylvatic yellow fever	115	1	0.00	0.00	0.00
60.1	Urban yellow fever	3	1	0.00	0.00	0.00
60.9	Yellow fever, unspecified	35	0	.	.	.
66.3	Mosquito-borne viral fever, Chikungunya	0	0	.	.	.
73.7	Ornithosis with other specified complications	0	0	.	.	.
73.8	Ornithosis with unspecified complication	0	0	.	.	.
73.9	Ornithosis, unspecified	1	1	0.00	0.00	0.00
75.0	Infectious mononucleosis	0	0	.	.	.
78.3	Cat-scratch disease	14	4	0.00	0.00	0.00
78.5	Cytomegaloviral disease	30	4	0.50	0.01	0.99
79.0	Viral inf in oth dis/nos	507	0	.	.	.
79.1	Echo virus infection in conditions classified elsewhere and of unspecified site	3	0	.	.	.
79.2	Coxsackie virus infection in conditions classified elsewhere and of unspecified site	12	7	0.57	0.20	0.94
79.9	Viral infection nos	5,551	30	0.33	0.16	0.50
81.2	Scrub typhus	137	2	0.00	0.00	0.00
130.7	Toxoplasmosis of other specified sites	0	0	.	.	.
130.8	Multisystemic disseminated toxoplasmosis	0	0	.	.	.
130.9	Toxoplasmosis, unspecified	5	4	0.50	0.01	0.99
461.0	Acute maxillary sinusitis	4,234	5	0.40	0.00	0.83
461.1	Acute frontal sinusitis	145	1	1.00	1.00	1.00

Appendix – Table 6. FEVER syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
461.2	Acute ethmoidal sinusitis	43	7	0.57	0.20	0.94
461.3	Acute sphenoidal sinusitis	2	1	0.00	0.00	0.00
461.8	Other acute sinusitis	1,466	5	0.40	0.00	0.83
461.9	Acute sinusitis, unspecified	39,976	57	0.82	0.73	0.92
464.0	Acute laryngitis	12,319	27	0.48	0.29	0.67
464.5	Supraglottitis	0	0	.	.	.
472.1	Chronic pharyngitis	466	4	0.00	0.00	0.00
487.8	Influenza with other manifestations	57	0	.	.	.
780.4	Dizziness and giddiness	23,611	257	0.35	0.30	0.41
780.6	Fever	20,028	150	0.61	0.54	0.69
780.7	Malaise and fatigue	49,102	232	0.66	0.60	0.72
780.8	Hyperhidrosis	511	10	0.40	0.10	0.70
780.9	Other general symptoms	2,004	29	0.21	0.06	0.35
783.0	Anorexia	1,236	16	0.13	0.00	0.29
Total		**162,000**	**873**	**0.60**	**0.56**	**0.64**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 7. GASTROINTESTINAL syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
1.0	Cholera due to Vibrio cholerae	13	10	0.00	0.00	0.00
1.1	Cholera due to Vibrio cholerae el tor	24	11	0.00	0.00	0.00
1.9	Cholera, unspecified	21	6	0.17	0.00	0.46
3.0	Salmonella gastroenteritis	266	3	0.67	0.13	1.00
4.0	Shigella dysenteriae	64	0	.	.	.
4.1	Shigella flexneri	0	0	.	.	.
4.2	Shigella boydii	0	0	.	.	.
4.3	Shigella sonnei	2	2	0.00	0.00	0.00
4.8	Other specified shigella infections	43	0	.	.	.
4.9	Shigellosis, unspecified	4	1	1.00	1.00	1.00
5.0	Staphylococcal food poisoning	3	0	.	.	.
5.2	Food poisoning due to Clostridium perfringens (C. welchii)	102	1	0.00	0.00	0.00
5.3	Food poisoning due to other clostridia	343	1	0.00	0.00	0.00
5.4	Food poisoning due to vibrio parahaemolyticus	5	1	0.00	0.00	0.00
5.8	Other bacterial food poisoning	0	0	.	.	.
5.9	Food poisoning, unspecified	175	4	1.00	1.00	1.00
6.0	Acute amebic dysentery without mention of abscess	9	3	0.33	0.00	0.87
6.1	Chronic intestinal amebiasis without mention of abscess	7	2	0.00	0.00	0.00
7.0	Balantidiasis	23	9	0.00	0.00	0.00
7.1	Glardiasis	23	17	0.94	0.83	1.00
7.2	Coccidiosis	7	2	0.00	0.00	0.00
7.3	Intestinal trichomoniasis	0	0	.	.	.
7.4	Cryptosporidiosis	0	0	.	.	.
7.5	Cyclosporiasis	0	0	.	.	.
7.8	Other specified protozoal intestinal diseases	4	1	0.00	0.00	0.00
7.9	Unspecified protozoal intestinal disease	1	0	.	.	.
8.0	Intestinal infection due to escherichia coli [e. Coli]	4	3	0.33	0.00	0.87
8.1	Intestinal infection due to arizona group of paracolon bacilli	4	2	0.50	0.00	1.00
8.2	Intestinal infection due to aerobacter aerogenes	1	0	.	.	.
8.3	Intestinal infection due to proteus (mirabilis) (morganii)	0	0	.	.	.
8.4	Intestinal infection due to other specified bacteria	10	4	0.00	0.00	0.00
8.5	Bacterial enteritis nos	24	0	.	.	.
8.6	Enteritis due to specified virus	11	5	0.60	0.17	1.00
8.8	Intestinal infection due to other organism, not elsewhere classified	343	3	1.00	1.00	1.00
9.0	Infectious colitis, enteritis, and gastroenteritis	3,818	25	0.76	0.59	0.93
9.1	Colitis, enteritis, and gastroenteritis of presumed infectious origin	1,920	21	0.90	0.78	1.00
9.2	Infectious diarrhea	371	2	0.50	0.00	1.00
9.3	Diarrhea of presumed infectious origin	342	4	0.50	0.01	0.99
21.1	Enteric tularemia	0	0	.	.	.

Appendix – Table 7. GASTROINTESTINAL syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
22.2	GI anthrax	22	6	0.33	0.00	0.71
32.8	Diphtheritic peritonitis	0	0	.	.	.
535.0	Acute gastritis	7,439	54	0.67	0.54	0.79
536.2	Persistent vomiting	90	3	0.33	0.00	0.87
555.0	Regional enteritis of small intestine	759	16	0.44	0.19	0.68
555.1	Regional enteritis of large intestine	1,332	9	0.78	0.51	1.00
555.2	Regional enteritis of small intestine with large intestine	0	0	.	.	.
555.9	Regional enteritis of unspecified site	6,993	95	0.88	0.82	0.95
556.0	Ulcerative (chronic) enterocolitis	0	0	.	.	.
556.1	Ulcerative (chronic) ileocolitis	0	0	.	.	.
556.2	Ulcerative (chronic) proctitis	0	0	.	.	.
556.3	Ulcerative (chronic) proctosigmoiditis	0	0	.	.	.
556.4	Pseudopolyposis of colon	0	0	.	.	.
556.5	Left-sided ulcerative (chronic) colitis	0	0	.	.	.
556.6	Universal ulcerative (chronic) colitis	0	0	.	.	.
556.8	Other ulcerative colitis	0	0	.	.	.
556.9	Ulcerative colitis, unspecified	2,154	32	0.88	0.76	0.99
558.0	Other and unspecified noninfectious gastroenteritis and colitis	0	0	.	.	.
558.1	Gastroenteritis and colitis due to radiation	0	0	.	.	.
558.2	Toxic gastroenteritis and colitis	0	0	.	.	.
558.3	Allergic gastroenteritis and colitis	0	0	.	.	.
558.9	Other and unspecified noninfectious gastroenteritis and colitis	28,890	120	0.86	0.80	0.92
569.8	Ulceration of intestine	162	4	1.00	1.00	1.00
787.0	Nausea and vomiting	4,882	76	0.62	0.51	0.73
787.9	Diarrhea	2,787	14	0.50	0.24	0.76
789.0	Abdominal pain	82,851	125	0.61	0.52	0.69
789.4	Abdominal rigidity	7	6	0.33	0.00	0.71
Total		**146,355**	**703**	**0.68**	**0.63**	**0.73**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 8. NEUROLOGICAL syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
13.0	Tuberculous meningitis	4	1	0.00	0.00	0.00
13.6	Tuberculous encephalitis or myelitis	0	0	.	.	.
13.8	Other specified tuberculosis of CNS	0	0	.	.	.
13.9	Unspecified tuberculosis of CNS	0	0	.	.	.
36.0	Meningococcal meningitis	3	2	0.50	0.00	1.00
36.1	Meningococcal encephalitis	8	5	0.60	0.17	1.00
36.2	Meningococcemia	23	2	0.00	0.00	0.00
36.8	Meningococcal infect nec	0	0	.	.	.
36.9	Meningococcal infect nos	0	0	.	.	.
47.0	Coxsackie virus meningitis	10	6	0.00	0.00	0.00
47.1	Echo virus meningitis	0	0	.	.	.
47.8	Viral meningitis nec	0	0	.	.	.
47.9	Viral meningitis nos	10	5	0.60	0.17	1.00
48.0	Oth enteroviral cns dis	0	0	.	.	.
49.0	Lymphocytic choriomeningitis	328	3	0.00	0.00	0.00
49.1	Adenoviral meningitis	471	3	0.00	0.00	0.00
49.8	Viral encephalitis nec	0	0	.	.	.
49.9	Viral encephalitis nos	58	1	0.00	0.00	0.00
52.0	Postvaricella encephalitis	0	0	.	.	.
54.3	Herpetic meningoencephalitis	8	2	0.00	0.00	0.00
54.7	Herpes simplex meningitis	16	8	0.00	0.00	0.00
55.0	Postmeasles encephalitis	10	1	0.00	0.00	0.00
56.0	Encephalomyelitis due to rubella	4	4	0.00	0.00	0.00
62.0	Japanese encephalitis	7	1	0.00	0.00	0.00
62.1	Western equine encephalitis	0	0	.	.	.
62.2	Eastern equine encephalitis	0	0	.	.	.
62.3	St. Louis encephalitis	0	0	.	.	.
62.4	Australian encephalitis	0	0	.	.	.
62.5	California virus encephalitis	1	1	0.00	0.00	0.00
62.8	Other specified mosquito-borne viral encephalitis	0	0	.	.	.
62.9	Mosquito-borne viral encephalitis, unspecified	1	1	0.00	0.00	0.00
63.0	Russian spring-summer (taiga) encephalitis	1	0	.	.	.
63.1	Louping ill	0	0	.	.	.
63.2	Central European encephalitis	0	0	.	.	.
63.8	Other specified tick-borne viral encephalitis	0	0	.	.	.
63.9	Tick-borne viral encephalitis, unspecified	3	3	0.00	0.00	0.00
64.0	Viral encephalitis arthropod nec	0	0	.	.	.
66.2	Venezuelan equine fever (encephalitis)	0	0	.	.	.
66.4	West Nile fever (encephalitis)	0	0	.	.	.
71.0	Rabies	0	0	.	.	.
72.2	Mumps encephalitis	0	0	.	.	.
94.2	Syphilitic meningitis	10	5	0.00	0.00	0.00
94.8	Syphilitic encephalitis	1	1	0.00	0.00	0.00
100.8	Leptospiral meningitis	0	0	.	.	.
114.2	Coccidioidal meningitis	0	0	.	.	.

Appendix – Table 8. NEUROLOGICAL syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
115.0	Histoplasma capsulatum meningitis	1	1	0.00	0.00	0.00
115.1	Histoplasma duboisii meningitis	0	0	.	.	.
115.9	Histoplasmosis meningitis	12	5	0.20	0.00	0.55
130.0	Meningoencephalitis due to toxoplasmosis	0	0	.	.	.
293.0	Acute delirium	67	2	0.50	0.00	1.00
293.1	Subacute delirium	9	4	0.25	0.00	0.67
320.0	Hemophilus meningitis	0	0	.	.	.
320.1	Pneumococcal meningitis	0	0	.	.	.
320.2	Streptococcal meningitis	1	0	.	.	.
320.3	Staphylococcal meningitis	0	0	.	.	.
320.7	Meningitis in oth bact dis	4	1	0.00	0.00	0.00
320.8	Bacterial meningitis nec	0	0	.	.	.
320.9	Bacterial meningitis nos	6	6	0.00	0.00	0.00
321.0	Cryptococcal meningitis	0	0	.	.	.
321.1	Meningitis in oth fungal dis	1	1	0.00	0.00	0.00
321.2	Meningitis in oth viral dis	0	0	.	.	.
321.3	Trypanosomiasis meningitis	2	1	0.00	0.00	0.00
321.8	Meningitis in oth nonbac dis	0	0	.	.	.
322.0	Nonpyogenic meningitis	18	5	0.20	0.00	0.55
322.1	Eosinophilic meningitis	0	0	.	.	.
322.9	Meningitis nos	240	3	0.67	0.13	1.00
323.0	Encephalitis in viral diseases classified elsewhere	16	2	1.00	1.00	1.00
323.1	Encephalitis in rickettsial diseases classified elsewhere	0	0	.	.	.
323.2	Encephalitis in protozoal diseases classified elsewhere	18	12	0.00	0.00	0.00
323.4	Other encephalitis due to infection classified elsewhere	4	1	1.00	1.00	1.00
323.5	Encephalitis following immunization procedures	0	0	.	.	.
323.6	Postinfectious encephalitis	0	0	.	.	.
323.7	Toxic encephalitis	1	1	0.00	0.00	0.00
323.8	Other causes of encephalitis	0	0	.	.	.
323.9	Unspecified cause of encephalitis	204	5	0.20	0.00	0.55
331.8	Reye's syndrome	8	2	0.00	0.00	0.00
348.3	Encephalopathy, unspecified	175	3	0.33	0.00	0.87
780.0	Coma and stupor	1,603	47	0.02	0.00	0.06
780.3	Convulsions	653	19	0.53	0.30	0.75
781.6	Meningismus	21	11	0.18	0.00	0.41
784.0	Headache	32,290	683	0.56	0.52	0.60
989.7	Aflatoxin and other mycotoxin (food contaminants)	1	1	0.00	0.00	0.00
998.0	Toxic effect of fish and shellfish (Saxitoxin)	10	3	0.00	0.00	0.00
Total		**36,342**	**874**	**0.52**	**0.48**	**0.55**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 9. RASH syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
20.1	Cellulocutaneous plague	6	2	0.00	0.00	0.00
22.0	Cutaneous anthrax	9	6	0.00	0.00	0.00
34.1	Scarlet fever	2,552	42	0.88	0.78	0.98
40.8	Toxic shock syndrome	4	2	0.50	0.00	1.00
50.0	Variola major	3	3	0.00	0.00	0.00
50.1	Alastrim (Variola minor)	0	0	.	.	.
50.2	Modified smallpox	0	0	.	.	.
50.9	Smallpox, unspecified	2	2	0.50	0.00	1.00
51.0	Cowpox	3,730	20	0.00	0.00	0.00
51.1	Pseudocowpox	42	0	.	.	.
51.2	Contagious pustular dermatitis	44	1	0.00	0.00	0.00
51.9	Paravaccinia, unspecified	30	1	1.00	1.00	1.00
52.0	Chickenpox	0	0	.	.	.
52.7	Chickenpox with other specified complications	0	0	.	.	.
52.8	Chickenpox with unspecified complication	0	0	.	.	.
52.9	Varicella without mention of complication	1,558	26	0.88	0.76	1.00
53.0	Herpes zoster with meningitis	396	13	0.92	0.78	1.00
53.1	Herpes zoster with other nervous system complications	42	2	0.50	0.00	1.00
53.2	Herpes zoster with ophthalmic complications	229	4	1.00	1.00	1.00
53.7	Herpes zoster with other specified complications	19	6	1.00	1.00	1.00
53.8	Herpes zoster with unspecified complication	17	8	1.00	1.00	1.00
53.9	Herpes zoster without mention of complication	10,551	168	0.89	0.84	0.93
54.0	Eczema herpeticum	708	13	0.46	0.19	0.73
54.4	Herpes simplex with ophthalmic complications	7	5	0.40	0.00	0.83
54.7	Herpes simplex with other specified complications	16	8	0.88	0.65	1.00
54.8	Herpes simplex with unspecified complication	5	4	0.50	0.01	0.99
54.9	Herpes simplex without mention of complication	8,763	153	0.65	0.57	0.72
55.0	Measles	10	1	0.00	0.00	0.00
55.7	Measles with other specified complications	0	0	.	.	.
55.8	Measles with unspecified complication	141	4	0.00	0.00	0.00
55.9	Measles without mention of complication	82	3	0.33	0.00	0.87
56.0	Rubella	4	4	0.50	0.01	0.99
56.7	Rubella with other specified complications	2	1	0.00	0.00	0.00
56.8	Rubella with unspecified complications	0	0	.	.	.
56.9	Rubella without mention of complication	172	1	0.00	0.00	0.00
57.0	Erythema infectiosum [fifth disease]	238	2	1.00	1.00	1.00
57.8	Other specified viral exanthemata	619	9	0.56	0.23	0.88
57.9	Viral exanthem, unspecified	1,440	15	0.33	0.09	0.57

Appendix – Table 9. RASH syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
74.3	Hand, foot mouth dis	49	1	1.00	1.00	1.00
80.0	Louse-borne (epidemic) typhus	0	0	.	.	.
81.0	Murine (endemic) typhus	3	1	0.00	0.00	0.00
81.9	Typhus, unspecified	0	0	.	.	.
82.0	Spotted fevers (Rocky mountain spotted fever)	2	2	0.50	0.00	1.00
82.1	Boutonneuse fever	14	2	0.00	0.00	0.00
82.2	North asian tick fever	2	1	0.00	0.00	0.00
82.3	Queensland tick typhus	3	2	0.00	0.00	0.00
82.8	Tick-borne ricketts nec	4	1	1.00	1.00	1.00
82.9	Tick-borne ricketts nos	9	4	0.00	0.00	0.00
83.2	Rickettsialpox	2	2	0.00	0.00	0.00
83.8	Rickettsioses nec	2	1	0.00	0.00	0.00
83.9	Rickettsiosis nos	2	1	0.00	0.00	0.00
91.3	Secondary syphilis skin	48	0	.	.	.
115.1	Infection by Histoplasma duboisii	0	0	.	.	.
287.0	Allergic purpura	66	2	1.00	1.00	1.00
287.1	Qualitative platelet defects	56	2	0.00	0.00	0.00
287.2	Other nonthrombocytopenic purpuras	389	11	0.36	0.08	0.65
287.8	Other specified hemorrhagic conditions	2	2	0.00	0.00	0.00
287.9	Unspecified hemorrhagic conditions	394	11	0.18	0.00	0.41
684.0	Impetigo	0	0	.	.	.
686.0	Pyoderma	752	13	0.15	0.00	0.35
686.1	Pyogenic granuloma	433	6	0.00	0.00	0.00
694.3	Impetigo herpetiformis	4	3	0.00	0.00	0.00
695.0	Toxic erythema	53	3	0.67	0.13	1.00
695.1	Erythema multiforme	106	1	1.00	1.00	1.00
695.2	Erythema nodosum	135	5	1.00	1.00	1.00
695.8	Other specified erythematous conditions	735	12	0.67	0.40	0.93
695.9	Unspecified erythematous condition	3,183	41	0.29	0.15	0.43
782.1	Rash and other nonspecific skin eruption	16,123	131	0.69	0.62	0.77
782.7	Spontaneous ecchymoses	1,239	24	0.33	0.14	0.52
Total		**55,251**	**814**	**0.63**	**0.59**	**0.66**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 10. RESPIRATORY syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
3.2	Salmonella pneumonia	3	1	0.00	0.00	0.00
10.0	Primary tuberculous infection	2	1	1.00	1.00	1.00
10.1	Tuberculous pleurisy in primary progressive tuberculosis	3	2	0.50	0.00	1.00
10.8	Other primary progressive tuberculosis	1	1	0.00	0.00	0.00
10.9	Primary tuberculous infection, unspecified type	16	6	0.33	0.00	0.71
11.0	Tuberculosis of lung, infiltrative	29	8	0.38	0.04	0.71
11.1	Tuberculosis of lung, nodular	20	8	0.13	0.00	0.35
11.2	Tuberculosis of lung with cavitation	32	0	.	.	.
11.3	Tuberculosis of bronchus	171	0	.	.	.
11.4	Tuberculous fibrosis of lung	2	1	0.00	0.00	0.00
11.5	Tuberculous bronchiectasis of lung	1	1	1.00	1.00	1.00
11.6	Tuberculous pneumonia (any form) of lung	2	1	0.00	0.00	0.00
11.7	Tuberculous pneumothorax of lung	7	2	0.00	0.00	0.00
11.8	Other specified pulmonary tuberculosis	4	0	.	.	.
11.9	Unspecified pulmonary tuberculosis	259	1	0.00	0.00	0.00
20.0	Plague	1	1	1.00	1.00	1.00
20.3	Primary pneumonic plague	0	0	.	.	.
20.4	Secondary pneumonic plague	7	3	0.33	0.00	0.87
20.5	Pneumonic plague, unspecified	0	0	.	.	.
21.2	Pulmonary tularemia	0	0	.	.	.
22.0	Anthrax	9	6	0.00	0.00	0.00
22.1	Pulmonary anthrax	0	0	.	.	.
24.0	Glanders	0	0	.	.	.
25.0	Melioidosis	0	0	.	.	.
32.0	Faucial diphtheria	52	0	.	.	.
32.1	Nasopharyngeal diphtheria	8	5	0.40	0.00	0.83
32.2	Anterior nasal diphtheria	7	2	0.00	0.00	0.00
32.3	Laryngeal diphtheria	1	0	.	.	.
32.8	Other specified diphtheria	0	0	.	.	.
32.9	Diphtheria, unspecified	2	2	0.50	0.00	1.00
33.0	Bordetella pertussis	39	9	1.00	1.00	1.00
33.1	Bordetella parapertussis	0	0	.	.	.
33.8	Whooping cough nec	5	1	1.00	1.00	1.00
33.9	Whooping cough nos	325	0	.	.	.
34.0	Strep sore throat	735	2	1.00	1.00	1.00
52.1	Varicella (hemorrhagic) pneumonitis	0	0	.	.	.
55.1	Postmeasles pneumonia	8	3	0.67	0.13	1.00
73.0	Ornithosis (Psittacoisis)	0	0	.	.	.
74.1	Epidemic pleurodynia	7	1	1.00	1.00	1.00
79.0	Adenovirus infection in conditions classified elsewhere and of unspecified site	507	0	.	.	.
79.3	Rhinovirus infection in conditions classified elsewhere and of unspecified site	2	1	0.00	0.00	0.00
79.6	Resp syncytial virus (rsv) infection in conditions classified elsewhere and of unspecified site	0	0	.	.	.

Appendix – Table 10. RESPIRATORY syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
79.8	Viral infection nec	154	4	0.00	0.00	0.00
83.0	Q fever	56	0	.	.	.
112.4	Candidiasis of lung	3	1	0.00	0.00	0.00
114.0	Primary coccidioidomycosis (pulmonary)	0	0	.	.	.
114.9	Coccidioidomycosis nos	2	1	0.00	0.00	0.00
115.0	Infection by Histoplasma capsulatum	1	1	0.00	0.00	0.00
115.1	Infection by Histoplasma duboisii	0	0	.	.	.
115.9	Histoplasmosis, unspecified	12	5	0.20	0.00	0.55
130.4	Pneumonitis due to toxoplasmosis	0	0	.	.	.
136.3	Pneumocystosis	1	0	.	.	.
460.0	Acute nasopharyngitis [common cold]	1	0	.	.	.
462.0	Acute pharyngitis	10	0	.	.	.
463.0	Acute tonsillitis	3	0	.	.	.
464.0	Acute laryngitis	12,319	27	0.74	0.58	0.91
464.1	Acute tracheitis	9,716	13	0.77	0.54	1.00
464.2	Acute laryngotracheitis	1,214	1	1.00	1.00	1.00
464.3	Acute epiglottitis	32	16	0.69	0.46	0.91
464.4	Croup	916	0	.	.	.
465.0	Acute laryngopharyngitis	4,679	3	0.67	0.13	1.00
465.8	Acute upper Resp infections of other multiple sites	3,809	11	0.64	0.35	0.92
465.9	Acute upper Resp infections of unspecified site	223,128	84	0.79	0.70	0.87
466.0	Acute bronchitis	62,662	67	0.81	0.71	0.90
466.1	Acute bronchiolitis	5,006	10	0.90	0.71	1.00
480.0	Pneumonia due to adenovirus	636	2	0.00	0.00	0.00
480.1	Pneumonia due to Resp syncytial virus	3	3	0.33	0.00	0.87
480.2	Pneumonia due to parainfluenza virus	1	0	.	.	.
480.8	Pneumonia due to other virus not elsewhere classified	1	1	1.00	1.00	1.00
480.9	Viral pneumonia, unspecified	1,044	0	.	.	.
481.0	Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]	0	0	.	.	.
482.0	Pneumonia due to Klebsiella pneumoniae	311	0	.	.	.
482.1	Pneumonia due to Pseudomonas	26	6	0.33	0.00	0.71
482.2	Pneumonia due to Hemophilus influenzae [H. influenzae]	8	4	1.00	1.00	1.00
482.3	Pneumonia due to Streptococcus	0	0	.	.	.
482.4	Pneumonia due to Staphylococcus	0	0	.	.	.
482.8	Pneumonia due to other specified bacteria	25	4	1.00	1.00	1.00
482.9	Bacterial pneumonia, unspecified	2,915	2	0.50	0.00	1.00
483.0	Pneumonia due to Mycoplasma pneumoniae	0	0	.	.	.
483.1	Pneumonia due to Chlamydia	0	0	.	.	.
483.8	Pneumonia due to other specified organism	0	0	.	.	.
484.0	Pneumonia in infectious diseases classified elsewhere	6	3	0.33	0.00	0.87

Appendix – Table 10. RESPIRATORY syndrome, RODS definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
484.1	Pneumonia in cytomegalic inclusion disease	10	4	0.50	0.01	0.99
484.3	Pneumonia in whooping cough	0	0	.	.	.
484.5	Pneumonia in anthrax	1	1	0.00	0.00	0.00
484.6	Pneumonia in aspergillosis	0	0	.	.	.
484.7	Pneumonia in other systemic mycoses	0	0	.	.	.
484.8	Pneumonia in other infectious diseases classified elsewhere	1	1	0.00	0.00	0.00
485.0	Bronchopneumonia, organism unspecified	0	0	.	.	.
486.0	Pneumonia, organism unspecified	1	1	1.00	1.00	1.00
487.0	Influenza with pneumonia	278	1	1.00	1.00	1.00
487.1	Influenza with other Resp manifestations	28,029	41	0.76	0.62	0.89
490.0	Bronchitis nos	2	1	0.00	0.00	0.00
491.0	Chronic bronchitis	1,452	0	.	.	.
491.1	Mucopurulent chronic bronchitis	90	0	.	.	.
491.2	Obstructive chronic bronchitis	578	1	0.00	0.00	0.00
491.8	Chronic bronchitis nec	795	3	0.67	0.13	1.00
491.9	Chronic bronchitis nos	8,098	16	0.44	0.19	0.68
507.0	Pneumonitis due to solids and liquids	24	11	0.45	0.16	0.75
507.1	Pneumonitis due to inhalation of oils and essences	0	0	.	.	.
507.8	Pneumonitis due to other solids and liquids	0	0	.	.	.
511.0	Pleurisy	139	0	.	.	.
511.1	Bact pleur/effus not tb	0	0	.	.	.
511.8	Pleural effus nec not tb	9	6	0.67	0.29	1.00
511.9	Pleural effusion nos	366	2	1.00	1.00	1.00
513.0	Abscess of lung	21	7	0.71	0.38	1.00
513.1	Abscess of mediastinum	1	1	0.00	0.00	0.00
518.0	Pulmonary collapse	143	2	0.50	0.00	1.00
518.4	Acute lung edema nos	246	1	0.00	0.00	0.00
518.8	Other diseases of lung	2,572	11	0.36	0.08	0.65
519.2	Mediastinitis	7	3	0.33	0.00	0.87
784.1	Throat pain	3,061	6	1.00	1.00	1.00
786.0	Dyspnea/Resp abn	24,392	69	0.28	0.17	0.38
786.1	Stridor	54	0	.	.	.
786.2	Cough	43,291	69	0.84	0.75	0.93
786.5	Painful respiration	33,582	67	0.67	0.56	0.78
795.3	Nonspecific positive findings for anthrax (Positive findings by nasal swab)	3	1	0.00	0.00	0.00
V018	Contact or exposure to anthrax (Other communicable diseases)	2	1	0.00	0.00	0.00
Total		**478,215**	**665**	**0.74**	**0.70**	**0.79**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 11. INFLUENZA-LIKE ILLNESS, large-group definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
79.9	VIRAL INFECTIONS UNSPECIFIED	5,551	30	0.63	0.46	0.81
382.9	OTITIS MEDIA NOS	95,165	68	0.54	0.43	0.66
460.0	NASOPHARYNGITIS, ACUTE	1	0	.	.	.
460.9	NASOPHARYNGITIS, ACUTE NOS	20,179	11	0.82	0.59	1.05
461.9	SINUSITIS, ACUTE NOS	39,976	57	0.74	0.62	0.85
465.8	URI, OTHER MULT. SITES	3,809	11	0.36	0.08	0.65
465.9	URI, ACUTE NOS	223,128	84	0.86	0.78	0.93
466.0	BRONCHITIS ACUTE	62,662	67	0.85	0.77	0.94
486.0	PNEUMONIA, ORGANISM NOS	4	1	1.00	1.00	1.00
486.9	PNEUMONIA, ORGANISM NOS	19,755	18	0.39	0.16	0.61
487.0	INFLUENZA WITH PNEUMONIA	278	1	1.00	1.00	1.00
487.1	INFLUENZA W/OTH. RESP. MA	28,029	41	0.78	0.65	0.91
487.8	INFLUENZA W/OTHR MANIFEST	57	0	.	.	.
490.0	BRONCHITIS NOS	7	1	0.00	0.00	0.00
490.9	BRONCHITIS NOS	60,126	44	0.86	0.76	0.97
780.6	FEVER	20,028	150	0.77	0.71	0.84
786.2	COUGH	43,291	69	0.81	0.72	0.90
Total		**622,046**	**653**	**0.77**	**0.73**	**0.81**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Appendix – Table 12. INFLUENZA-LIKE ILLNESS, small-group definition: positive predictive value of individual syndrome-positive ICD-9 diagnostic codes

ICD-9 code in claims*	Text label for ICD-9 code	No. visits in claims**	No. visits in verified claims***	PPV	95% CI	
					Lower limit	Upper limit
465.8	URI, OTHER MULT. SITES	3,809	11	0.09	0.00	0.26
487.0	INFLUENZA WITH PNEUMONIA	278	1	0.00	0.00	0.00
487.1	INFLUENZA W/OTH. RESP. MA	28,029	41	0.32	0.17	0.46
487.8	INFLUENZA W/OTHR MANIFEST	57	0	.	.	.
Total		**32,173**	**53**	**0.29**	**0.16**	**0.41**

*The Quebec provincial healthcare agency records ICD-9 diagnostic codes up to the first decimal position only. ICD-9 codes that are in the syndrome definition but do not appear in this table were not used in any of the 7,315,994 visits billed by the 1,098 participating physicians during the 2-year study period.
**Among the 7,315,994 visits to the 1,098 participating physicians during the 2-year study period.
***Among the 10,529 visits for which both the physician claim and the medical chart were available for verification.

Chapter 6. Predictors of accuracy of syndrome definitions based on diagnoses in physician claims

Preamble to Manuscript 3

Analyses for manuscript 2 revealed that, whereas the specificity and negative predictive value of syndrome definitions based on diagnoses in physician claims were extremely high, their sensitivity and positive predictive value could be improved. A potential method for improving the accuracy of syndrome definitions is to identify and take into account variables associated with syndrome definition accuracy. Our review of the literature suggested that this had only been attempted once in the context of syndromic surveillance. However, several studies in other fields, especially chronic diseases research, showed that the accuracy of case definitions based on diagnoses in administrative data was associated with covariates such as patient (34;75;76;78-82) and clinical encounter (67;74) characteristics, and could be improved by taking into account covariates (83-86). We hypothesized that several properties of surveillance data, including who generated them (i.e., healthcare provider characteristics), how the data were reported (i.e., reporting or billing system characteristics), who they describe (i.e., patient characteristics), and where and in what context they arose (i.e., clinical encounter characteristics), were likely to influence case definition accuracy.

When the research protocol for this thesis was developed, the main goal of syndromic surveillance was the early detection of outbreaks, and the emphasis was on maximizing the sensitivity of surveillance systems, often at the expense of specificity and positive predictive value. This resulted in frequent false-alerts, and ultimately limited the usefulness of syndromic surveillance for early detection. Partly because of these limitations, syndromic surveillance systems are increasingly being used to monitor population health for situation awareness. The expanding goal of syndromic surveillance requires better positive predictive value and fewer false-positives. Therefore, for

manuscript 3, we attempted to identify covariates associated with the positive predictive value of syndrome definitions based on diagnoses in physician claims.

Title page

Predictors of accuracy of syndrome definitions based on diagnoses in physician claims

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ABSTRACT

BACKGROUND: Case definition accuracy is an important determinant of surveillance system usefulness. We assessed whether physician, billing, patient, and encounter characteristics are associated with the positive predictive value of case definitions for 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory including influenza-like illness).

METHODS: We sampled 4,330 syndrome-positive visits from the claims of 1,098 randomly-selected physicians working in Quebec, Canada in 2005-2007. For each visit, we assessed whether the same syndrome was present in the medical chart through physician-facilitated chart review. We used multivariate logistic regression analyses to estimate the association between claim-chart agreement about the presence of a syndrome and physician, billing, patient, and encounter characteristics.

RESULTS: The likelihood of the medical chart agreeing with the physician claim about the presence of a syndrome was higher when the treating physician had billed many visits for the same syndrome recently ($OR_{\text{per 5 years since licensure}}$, 0.96; 95% CI, 0.92-1.00), had a lower workload ($OR_{\text{per 10 claims}}$, 0.93; 95% CI, 0.90-0.97), and when the patient was younger ($OR_{\text{per 5 years of age}}$, 0.96; 95% CI, 0.94-0.97), and less socially deprived ($OR_{\text{most versus least deprived}}$, 0.76; 95% CI, 0.60-0.95).

CONCLUSION: Many predictors of syndrome definition accuracy identified are accessible to public health and other organizations that routinely perform syndromic surveillance. These predictors can be used to reduce the false-positive rate of syndromic surveillance systems, either by focusing on the data most likely to be accurate, or by adjusting the observed data for known biases in diagnosis reporting and performing surveillance using the adjusted values.

INTRODUCTION

Syndromic surveillance systems were adopted rapidly in the wake of 9/11 amidst concerns of bioterrorism. The primary purpose of these systems was to detect disease outbreaks and bioterrorism events rapidly. To ensure that no outbreak would be missed, syndromic surveillance systems were initially designed to generate alerts at very low thresholds. A consequence of this design was high rates of false-positive alerts (36), which have limited syndromic surveillance systems' ability to correctly identify outbreaks. Indeed, because of the prohibitive cost of investigating every alert, many public health practitioners have adopted a 'wait-and-see' response to alerts, thereby detracting from a main advantage of syndromic surveillance systems over traditional public health surveillance systems, namely the ability to provide a timelier portrait of population health. Attempts to reduce false-positive rates by improving statistical detection algorithms used in syndromic surveillance (37-39) have had limited success.

Partly because of these limitations, the focus of syndromic surveillance has begun to shift away from outbreak detection towards population health monitoring or situation awareness (41;147). Syndromic surveillance systems are now being tailored to suit this novel use. Whereas outbreak detection sought to identify and alert on every suspicious increase in the incidence of cases, maintaining situation awareness entails gathering data about the current state of population health, analyzing and interpreting these data, and projecting the likely evolution of the current state (41). Accurate case definitions are critical for monitoring population health and maintaining situation awareness, but, to date, almost no attempts have been made to improve the accuracy of the case definitions used in syndromic surveillance (42-44). Identifying properties of surveillance data associated with higher positive predictive value (PPV) of case definitions used in syndromic surveillance will improve individual case detection and situation awareness, and will likely also lead to improved outbreak detection.

Several properties of surveillance data, such as who generated them (healthcare provider characteristics), how they were reported (reporting/billing system characteristics), who they describe (patient characteristics), and where and in what context they arose (clinical encounter characteristics), are likely to influence case definition accuracy. Characteristics of the healthcare provider that are associated with practice style or coding accuracy may influence the PPV of diagnostic data. For example, two studies have reported that greater experience was associated with lower diagnostic coding accuracy (45) and lower billing diagnosis accuracy (46). Reporting/billing practices, including who enters the diagnosis in the system and how the diagnosis is entered (e.g., direct entry of diagnostic codes, searchable list of diagnoses that the software then maps to codes, automated abstraction of the billing diagnosis from an electronic medical record) are likely to influence the PPV of the diagnostic data. The context for the clinical encounter, which influences how much time and what resources are available for reporting/billing, is also likely to impact diagnostic data accuracy. For example, higher physician workloads were associated with lower billing diagnosis accuracy in one study (46). Treating more complex patients likely requires more working memory and increases physician cognitive load (47), therefore diagnostic coding errors may be more likely to occur for complex patients. For this reason, indicators of patient complexity, such as age, comorbidity, socioeconomic status, and health services utilization(48), may impact the PPV of diagnostic data (67).

The objective of the present study was to identify physician, billing, patient, and encounter characteristics associated with the PPV of syndrome definitions based on diagnoses in physician claims. Because of their public health importance, our study focused on the following 5 syndromes: fever, gastrointestinal, neurological, rash, and respiratory (66), including influenza-like illness (ILI)(49).

METHODS

Context

This study was conducted in the province of Quebec, Canada, where universal health coverage is provided through the provincial health insurance plan. Similar to health maintenance organizations and medical provider networks, each Canadian province maintains a population-based registry of insured persons and claims for all physician visits remunerated on a fee-for-service basis. The registrant database includes patient sex, date of birth, and postal code, enabling linkage to census information. Physician claims include information on the diagnosis, medical procedure, visit date, and location. All claims also record unique physician and patient identifiers that can be used to create longitudinal histories of healthcare use. In the province of Quebec, 99% of residents have provincial health insurance, and 85-95% of medical visits are remunerated on a fee-for-service basis (148). In 2006, there were more than 7.6 million inhabitants in Quebec (89), and 18,908 active registered physicians (90).

Study design and population

In a prior study assessing the accuracy of syndrome definitions based on diagnoses in physician claims (71), we randomly selected a cohort of 3,600 physicians who were practicing in the fee-for-service system in the province of Quebec in 2005-2007, and who were likely to provide first-contact care. For each physician, we selected a stratified random sample of 5 visits with a syndrome-positive diagnosis in the claim (i.e., 1 visit for each of these 5 syndromes: fever, gastrointestinal, neurological, rash, and respiratory including ILI). Restriction was used to ensure that patients were only sampled once. The present study is based on the cohort of 1,098 physicians who consented to provide medical chart information (participation rate of 30.5%) and 4,330 of their visits with a syndrome-positive claim diagnosis (71).

Outcome measure

For each visit with a syndrome-positive diagnosis in the physician claim, we assessed whether the same syndrome was documented in the medical chart. Medical chart data was retrieved using a previously described physician-facilitated chart review methodology (71).

Potential predictors of the accuracy of syndrome definitions based on physician claim diagnoses

Physician characteristics

Physician gender is associated with several practice style indicators, including physician-patient communication (149-152), and it may be associated with billing diagnosis accuracy. Physician gender was obtained from the provincial health insurance agency. *Physician language* (French or English) likely affects communication with the patient, and may therefore impact billing diagnosis accuracy; physician language was obtained from the provincial health insurance agency. *Year since licensure* was calculated by subtracting the year of licensure, which was obtained from the provincial medical regulatory authority, from the year of the syndrome-positive visit. As compared to generalists, specialists see a narrower segment of the patient population for a subset of health conditions; therefore they likely use fewer diagnostic codes and may have better billing diagnosis accuracy. *Physician specialty* was obtained from the provincial health insurance agency.

Billing practices

Different billing softwares use different methods for entering diagnoses, which likely affect billing diagnosis accuracy. Billing software was obtained through a telephone interview with the physician (71). *Who enters the diagnostic code in the claim* was obtained through a telephone interview with the physician (71). We expect claim diagnosis accuracy to be highest when a physician does his own billing. Physicians'

annual billing volume is an indicator of practice style. Annual billing volume was calculated as the number of distinct claims billed by a physician during the study year when the syndrome-positive visit occurred. The *percent of visits with missing or unspecified diagnostic codes* is expected to reflect attention to diagnostic coding. It was calculated as the total number of visits without any diagnostic code or with a diagnostic code of 'V999' (unspecified), multiplied by 100, and divided by the total number of visits billed by the physician during the study year when the syndrome-positive visit occurred. The *number of distinct diagnostic codes used* likely reflects the scope of health conditions treated by a physician, and physicians who see a narrower scope of health conditions may be more likely to remember and assign the correct diagnostic code for these conditions. It was calculated as the number of distinct diagnostic codes used among all claims billed during the study year when the syndrome-positive visit occurred.

Patient characteristics

Patient gender is expected to influence communication during the visit (149-152), and it may influence physician documentation of patient complaints. Patient gender was obtained from the registrant database. Greater patient complexity, by taxing limited physician resources, is expected to reduce physician billing diagnosis accuracy (67). Patient complexity is associated with patient age, comorbidity, and socioeconomic status (48). *Patient age* on October 1st of the study year when the visit took place was obtained from the provincial health services agency. For each patient, The Charlson Comorbidity Index (153) was computed using diagnoses in claims billed by *all* physicians seen (not only study physicians) during the year preceding the visit. *Material and social deprivation indices* developed by the Quebec National Public Health Institute (91;92), are associated with health services utilization (154-156), and therefore may influence billing diagnosis accuracy. The material deprivation index summarizes information on the proportion of persons who have no high school diploma, the proportion of persons employed, and the average income in the patient's 6-digit postal code area of residence. The social deprivation index summarizes information on the proportion of single-parent

families, the proportion of persons living alone, and the proportion of persons separated, divorced, or widowed in the patient's 6-digit postal code area of residence. For each patient, the material and social deprivation indices were calculated by the provincial health services agency using Statistics Canada's 2006 census data. *Health services utilization* is expected to reflect patient complexity; it was calculated as the number of ambulatory care visits in the previous year.

Encounter characteristics

As reported in our previous study, different syndrome definitions have vastly different PPVs (71). Therefore s*yndrome type* is likely to influence claim diagnosis accuracy. Different resources for physician billing are likely to be available depending on the *type of clinic* and *geographic location of the clinic*, which may influence claim diagnosis accuracy. The type of clinic was obtained from the physician claim and categorized as private clinic, community health center, or hospital ambulatory care clinic. The geographic location of the clinic was categorized as urban or rural based on the clinic's 6-digit postal code. Because the majority of physicians do not schedule appointments on the weekend, a medical encounter during the weekend is more likely to be a 'walk-in' visit for a specific acute or urgent health complaint, such as an infectious syndrome. For this reason, we expect syndromes to be more accurately reported in the physician claim for a weekend encounter, as opposed to a weekday encounter. The *day of the week* on which the encounter took place was derived from the encounter date in the physician claim. In our previous study, we found that infrequent claim diagnoses are more likely to be erroneous than frequent ones (71). Therefore, we expect that the more frequently a syndrome is diagnosed, the more accurate the claim diagnosis is. As an indicator of syndrome frequency, the *number of visits for the same syndrome billed by the study physician in the previous 30 days* was calculated from each physician's claims. The occurrence of many syndromes undergoes seasonal variation, peaking in winter and plummeting in summer, therefore we expect that the season in which the encounter took place will influence the accuracy of claim diagnoses through a similar mechanism as

syndrome frequency. The *season* during which the encounter took place was derived from the encounter date in the physician claim. Higher *physician workload* may have a negative impact on record-keeping and billing practices, and may lead to poorer billing diagnosis accuracy. Workload was calculated as the number of physician claims on the day of the encounter, which reflects both the number of patients seen and the complexity of their care. Greater physician familiarity with a patient may increase the scope of health conditions discussed during the clinical encounter, thereby adding to the complexity of patient care. Therefore, the encounter is expected to be more focused, and claim diagnosis accuracy is expected to be better when physicians are not familiar with the patient. As an indicator of *physician familiarity with the patient,* we assessed whether or not the physician had treated the patient in the previous year, using the physicians' claims.

Statistical methods

Multivariable logistic regression analyses for clustered data were performed using generalized estimating equations (GEE) to estimate the association between the presence or absence of the syndrome in the medical chart (binary dependent variable) for a given visit with a syndrome-positive diagnosis in the physician claim, and physician characteristics, billing practices, patient characteristics, and encounter characteristics (SAS Version 9.2, SAS Institute Inc., Cary, NC). The visit was the unit of analysis, and visits were clustered within study physicians (there was only 1 visit per patient). Based on the assumption that physician diagnostic coding and billing patterns may change over time, visits were ordered chronologically, and a first-order autoregressive correlation structure of residuals was used to account for clustering. A 2-sided test with a p-value of 0.05 was used to assess statistical significance. In the main analyses, physician time since licensure, billing characteristics, and patient age, health services utilization, and Charlson comorbidity index were modelled as continuous variables, assuming the linearity of their association with the logit of the probability of the presence or absence of the syndrome in the medical chart. In sensitivity analyses, to account for possibly non-linear

relationships, continuous variables were categorized into quartiles and modelled through three dummy indicators with the lowest quartile as the reference; we also tested the statistical significance of the quadratic component.

Ethics review

The research protocol for this study was reviewed and approved by the McGill University Institutional Review Board, the Quebec privacy commission, the Quebec health insurance agency, and the Quebec medical regulatory authority.

RESULTS

Of 4,330 visits with a syndrome-positive diagnosis in the physician claim, 2,967 (68.5%) also had a syndrome-positive diagnosis in the medical chart.

Physician characteristics

The accuracy of claim diagnoses decreased by 4% with every 5 additional years since medical licensure ($OR_{per\ 5\ years}$, 0.96; 95% CI, 0.92-1.00) (Table 1). Whereas an effect of 4% may appear small, this is due to the scale used (i.e., per 5 years), and it implies a 20% difference between recently graduated physicians and those who have been in practice for 25 years, which was the average time elapsed since licensure among physicians in our sample. As compared to general practitioners, internists and general surgeons had 41% poorer claim diagnosis accuracy (OR, 0.59; 95% CI, 0.35-0.98). Physician gender and language were not significantly associated with the PPV of syndrome definitions based on physician claim diagnoses.

Billing practices

Several billing softwares were significantly associated with claim diagnosis accuracy (Table 2). Purkinje billing software, which abstracted the billing diagnosis from the electronic medical record in an automated manner, had higher claim diagnosis accuracy

than *Soft Informatique*, which required manual input of the billing diagnosis (OR, 1.29; 95% CI, 1.05-1.59). Surprisingly, who entered the ICD-9 diagnostic code on the billing claim was not significantly associated with claim diagnosis accuracy. Physician annual billing volume, proportion of visits billed with a missing or unspecified diagnostic code, and number of distinct diagnostic codes used were not significantly associated with claim diagnosis accuracy.

Patient characteristics

Claim diagnosis accuracy decreased by 4% with every additional 5 years of patient age ($OR_{per\ 5\ years}$, 0.96; 95% CI, 0.94-0.97), so that older patient had much poorer claim diagnosis accuracy than younger ones (Table 3). Whereas patient comorbidity, as measured by the Charlson Comorbidity Index, was significantly and negatively associated with claim diagnosis accuracy in bivariate analyses ($OR_{per\ 1\text{-}point\ increase}$, 0.92; 95% CI, 0.86-0.97), the association was no longer significant when the model was adjusted for patient age ($OR_{per\ 1\text{-}point\ increase}$, 0.98; 95% CI, 0.92-1.05). Similarly, health services utilization in the previous year was significantly and negatively associated with claim diagnosis accuracy ($OR_{per\ additional\ visit}$, 0.99; 95% CI, 0.98-0.99), but the association did not remain statistically significant in multivariate analyses. Patients in the highest quintile of social deprivation had significantly poorer claim diagnosis accuracy ($OR_{most\ versus\ least\ deprived}$, 0.76; 95% CI, 0.60-0.95), as compared to those in the least socially deprived quintile. Patient gender was not significantly associated with claim diagnosis accuracy.

Encounter characteristics

Gastrointestinal syndrome (OR, 1.72; 95% CI, 1.36-2.16), neurological syndrome (OR, 1.38; 95% CI, 1.11-1.72), rash syndrome (OR, 1.89; 95% CI, 1.51-2.37), respiratory syndrome (OR, 1.66; 95% CI, 1.29-2.14), and ILI large-group (OR, 2.68; 95% CI, 2.06-3.48), all had significantly higher claim diagnosis accuracy than fever syndrome (Table 4). With respect to physician workload, claim diagnosis accuracy decreased by 7% with

every 10 additional claims on the day of the encounter ($OR_{per\ 10\ claims}$, 0.93; 95% CI, 0.90-0.97). Claim diagnosis accuracy improved by 5% with every 10 visits billed by the study physician for the same syndrome in the previous month ($OR_{per\ 10\ same\text{-}syndrome\ positive\ visits}$, 1.05; 95% CI, 1.01-1.08). With respect to seasonality, claim diagnosis accuracy was significantly better in spring, as compared to winter (OR, 1.29; 95% CI, 1.07-1.57); this association seemed to be strongest for fever syndrome (Appendix 1). Type of clinic and geographic location of the clinic were not significantly associated with claim diagnosis accuracy.

DISCUSSION

To improve the accuracy of syndromic surveillance, we sought to identify physician, billing, patient, and encounter characteristics associated with the PPV of syndrome definitions based on diagnoses in physician claims. We identified several properties of surveillance data – healthcare provider, billing, patient, and encounter characteristics – associated with the PPV of syndrome definitions. Several of the predictors of syndrome definition accuracy that we identified (e.g., patient age, number of visits for the same syndrome in the last month) are readily accessible to public health departments and other organizations that routinely perform syndromic surveillance. These predictors can be used to reduce the false-positive rate of syndromic surveillance systems, either by focusing on the data most likely to be accurate, or by adjusting the observed data for known biases in diagnosis reporting and performing surveillance using the adjusted values.

Specifically, we found that visits with a syndrome-positive diagnosis in physician claims were more likely to be confirmed as syndrome-positive by the medical chart when the physician was recently licensed. This finding is similar to those of other, general studies of billing diagnosis accuracy and physician practice experience (45;46). A potential explanation for this finding is that younger physicians may be more likely to follow

guidelines and give greater attention to billing, whereas more experienced physicians may be more likely to 'code from memory', which has been associated with more frequent diagnostic coding errors, as compared to coding from reference materials (45), Similar to another study (46), we found that physicians with a higher workload on the day of the encounter had lower billing diagnosis accuracy. We also found that claims for less complex patients (i.e., younger and less socially deprived patients) were more likely to be confirmed as syndrome-positive by the medical chart, as compared to those of more complex patients. Higher physician workload and greater patient complexity may increase demands on limited physician resources – taxing working memory and increasing cognitive load – thereby increasing the likelihood of physician errors, including errors in billing diagnosis. Additionally, we found that visits with a syndrome-positive diagnosis in physician claims were more likely to be confirmed as syndrome-positive by the medical chart when the physician had billed many visits for the same syndrome recently. This finding agrees with our previous finding (71) that commonly used diagnoses are more likely to be accurate than rarely used ones. The observation that billing diagnosis accuracy increases with repeated use can be explained by widely accepted theories on the effect of repetition on recall (157).

We also found that billing software had a significant impact on the PPV of syndrome definitions based on diagnoses in physician claims: software that abstracted the billing diagnosis from the electronic medical record in an automated manner had higher claim diagnosis accuracy than software requiring the manual input of billing diagnoses. This finding has important implications for both clinical users and public health surveillance, given the ongoing transformation from a process where clinical practitioners manually submit case reports to a process where public health agencies automatically extract relevant data from clinical information systems. Indeed, the US federal government has allotted $39 billion to support the adoption and "meaningful use" of electronic health records, and software purchased using these funds must support automated submission of data to public health agencies for three public health uses, including syndromic

surveillance (158). This investment presents an opportunity to improve syndromic surveillance systems by having electronic health records capture and transmit information on highly influential predictors, such as indicators of patient complexity, to public health.

Our study had several strengths. It was based on a large representative sample of physicians and patients. We had access to many physician, billing, patient, and encounter characteristics, which enabled us to perform a comprehensive assessment of the impact of a variety of factors on the accuracy of syndrome definitions. Whereas some of our findings are specific to our study population, most of our findings are likely to be generalizable to other jurisdictions across North America because of similar physician and patient populations. A limitation of our study was that the number of visits per syndrome was too small to identify predictors of syndrome definition accuracy for each syndrome individually. Whereas most of the predictors of syndrome definition accuracy that we identified would be expected to impact all syndrome definitions in a similar manner (e.g., physician workload, patient complexity), some predictors may have a greater or lesser impact on syndrome definition accuracy depending on the syndrome (e.g., season).

In closing, we have demonstrated through a large random sample of physicians with chart validation that measurable elements of the medical visit determine the accuracy of a given syndrome report derived from physician claims. These elements include physician, billing, patient, and encounter characteristics, which public health departments can collect through surveillance and use to focus or adjust their analyses in order to enhance the accuracy of surveillance. The rich clinical data streams becoming accessible to public health should enable the implementation of surveillance strategies that incorporate our findings. As the volume and detail of clinical data continue to increase, future research should explore how public health can harness their full breadth to further enhance the accuracy of case detection.

Table 1. Physician characteristics associated with accuracy of syndrome definitions based on physician claims (OR>1.00 means the physician characteristic increased the PPV of the syndrome definition, OR<1.00 means the physician characteristic reduced the PPV)

	No. visits with a syndrome-positive physician claim						Bivariate regression analysis			Multivariate regression analysis[1]		
Physician characteristics	**Syndrome-positive in the chart (N=2,967)**		**Syndrome-negative in the chart (N=1,363)**		**Total (N=4,330)**		**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
	No.	**%**	**No.**	**%**	**No.**	**%**						
Gender:												
Female	1,164	39.2	523	38.4	1,687	39.0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Male	1,803	60.8	840	61.6	2,643	61.0	0.97	(0.83, 1.12)	0.64	1.13	(0.96, 1.33)	0.13
Preferred language:												
French	2,743	92.5	1,253	91.9	3,996	92.3	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
English	224	7.5	110	8.1	334	7.7	0.93	(0.69, 1.25)	0.63	0.94	(0.69, 1.26)	0.66
Specialty:												
General practice	2,721	91.7	1,246	91.4	3,967	91.6	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pediatrics	203	6.8	75	5.5	278	6.4	1.24	(0.88, 1.77)	0.22	0.83	(0.57, 1.20)	0.33
Internal medicine or general surgery	43	1.5	42	3.1	85	2.0	0.46	(0.31, 0.69)	<0.001	0.59	(0.35, 0.98)	0.04
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**						
Years since licensure (per 5 years)	22.9	9.2	23.7	9.6	23.1	9.4	0.95	(0.92, 0.99)	0.02	0.96	(0.92, 1.00)	0.04

[1] Multivariate analysis adjusted for all physician characteristics in Table 1, all patient characteristics in Table 3, and all encounter characteristics in Table 4.

Table 2. Billing characteristics associated with accuracy of syndrome definitions based on physician claims (OR>1.00 means the billing characteristic increased the PPV of the syndrome definition, OR<1.00 means the billing characteristic reduced the PPV)

	No. visits with a syndrome-positive physician claim						Bivariate regression analysis			Multivariate regression analysis[1]		
Billing practices	**Syndrome-positive in the chart (N=2,967)**		**Syndrome-negative in the chart (N=1,363)**		**Total (N=4,330)**		**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
	No.	**%**	**No.**	**%**	**No.**	**%**						
Who entered the diagnostic code in the claim?												
Physician	443	14.9	203	14.9	646	14.9	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Secretary or nurse	2,015	67.9	907	66.5	2,922	67.5	1.01	(0.82, 1.26)	0.91	0.93	(0.75, 1.15)	0.50
Off-site billing company or RAMQ (i.e., paper billing)	509	17.2	253	18.6	762	17.6	0.92	(0.71, 1.19)	0.52	0.81	(0.62, 1.06)	0.12
Billing software used:												
Soft Informatique	715	24.4	342	25.4	1,057	24.8	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Purkinje	721	24.7	264	19.6	985	23.1	1.30	(1.07, 1.60)	0.01	1.29	(1.05, 1.59)	0.02
ADN Medical	405	13.9	166	12.3	571	13.4	1.16	(0.90, 1.49)	0.24	1.17	(0.91, 1.50)	0.23
Omni-Med.com Caduceus	250	8.6	124	9.2	374	8.8	0.96	(0.74, 1.25)	0.77	0.94	(0.72, 1.24)	0.67
Medicus MED-WIN	123	4.2	67	5.0	190	4.5	0.87	(0.65, 1.17)	0.36	0.87	(0.64, 1.17)	0.35
Facturation.net	73	2.5	64	4.8	137	3.2	0.55	(0.35, 0.86)	0.01	0.54	(0.34, 0.85)	0.01
ANDX Xclaim	61	2.1	40	3.0	115	2.7	0.73	(0.47, 1.14)	0.17	0.70	(0.42, 1.15)	0.16
CareOffice	85	2.9	30	2.2	103	2.4	1.36	(0.84, 2.18)	0.21	1.32	(0.76, 2.27)	0.32
Médifiche	75	2.6	28	2.1	101	2.4	1.28	(0.81, 2.02)	0.29	1.24	(0.77, 1.98)	0.38
Toubib	52	1.8	43	3.2	95	2.2	0.58	(0.32, 1.05)	0.07	0.53	(0.29, 0.97)	0.04
FMP	57	2.0	16	1.2	73	1.7	1.71	(0.92, 3.19)	0.09	1.74	(0.90, 3.34)	0.10
Médicalc Inc.[2]	49	1.7	19	1.4	68	1.6	1.23	(0.61, 2.47)	0.57	1.27	(0.62, 2.62)	0.51
Param	47	1.6	18	1.3	65	1.5	1.24	(0.67, 2.29)	0.49	1.19	(0.66, 2.17)	0.56
ACL Systèmes Santé	43	1.5	20	1.5	63	1.5	1.03	(0.58, 1.84)	0.92	1.06	(0.56, 2.02)	0.85
Factura-Med	43	1.5	17	1.3	60	1.4	1.20	(0.79, 1.84)	0.39	1.24	(0.81, 1.89)	0.32
FmedX MED-Office	39	1.3	18	1.3	57	1.3	1.04	(0.48, 2.25)	0.92	0.99	(0.46, 2.13)	0.98
Sys-Thèmes	24	0.8	9	0.7	33	0.8	1.27	(0.54, 3.00)	0.59	1.24	(0.55, 2.77)	0.61
Gestimed	12	0.4	14	1.0	26	0.6	0.41	(0.21, 0.81)	0.01	0.45	(0.25, 0.84)	0.01

[1] Multivariate analysis adjusted for all billing practices in Table 2 and all physician characteristics in Table 1.
[2] Software developed and used solely by their namesake off-site billing company.
[3] Single-user billing software developed by individual physicians.
[4] In the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.

Table 2 (continued). Billing characteristics associated with accuracy of syndrome definitions based on physician claims (OR>1.00 means the billing characteristic increased the PPV of the syndrome definition, OR<1.00 means the billing characteristic reduced the PPV)

	No. visits with a syndrome-positive physician claim						Bivariate regression analysis			Multivariate regression analysis[1]		
Billing practices	**Syndrome-positive in the chart (N=2,967)**		**Syndrome-negative in the chart (N=1,363)**		**Total (N=4,330)**		**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
	No.	**%**	**No.**	**%**	**No.**	**%**						
Billing software used (continued):												
Salus	10	0.3	10	0.7	20	0.5	0.48	(0.18, 1.32)	0.16	0.45	(0.14, 1.44)	0.18
Logimedic	7	0.2	8	0.6	15	0.4	0.41	(0.16, 1.05)	0.06	0.39	(0.15, 1.03)	0.06
Medi-Go	2	0.1	6	0.5	8	0.2	0.16	(0.02, 1.68)	0.13	0.15	(0.01, 1.72)	0.13
Services de facturations médicales informatiques[2]	4	0.1	3	0.2	7	0.2	0.63	(0.40, 1.01)	0.06	0.65	(0.37, 1.16)	0.14
Other[3]	13	0.4	3	0.2	16	0.4	2.12	(0.71, 6.29)	0.18	1.94	(0.71, 5.28)	0.19
Unknown	15	0.5	17	1.3	32	0.8	0.41	(0.20, 0.86)	0.02	0.48	(0.24, 0.93)	0.03
RAMQ (i.e., paper billing)	42	1.4	17	1.2	59	1.4	1.18	(0.55, 2.57)	0.67	1.39	(0.63, 3.07)	0.41
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**						
Annual billing volume (per 1,000 claims)[4]	4,913	2,623	4,913	2,646	4,913	2,630	1.00	(0.97, 1.03)	0.94	1.00	(0.97, 1.04)	0.91
Percent of visits with a missing or unspecified diagnostic code[4]	2.5	5.7	2.5	5.1	2.5	5.5	1.00	(0.99, 1.02)	0.91	1.01	(0.99, 1.02)	0.34
No. distinct diagnostic codes used (per 100 codes)[4]	228	88	227	97	228	91	1.01	(0.94, 1.10)	0.76	1.02	(0.92, 1.12)	0.75

[1] Multivariate analysis adjusted for all billing practices in Table 2 and all physician characteristics in Table 1.
[2] Software developed and used solely by their namesake off-site billing company.
[3] Single-user billing software developed by individual physicians.
[4] In the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.

Table 3. Patient characteristics associated with accuracy of syndrome definitions based on physician claims (OR>1.00 means the patient characteristic increased the PPV of the syndrome definition, OR<1.00 means the patient characteristic reduced the PPV)

	No. visits with a syndrome-positive physician claim						Bivariate regression analysis			Multivariate regression analysis[1]		
Patient characteristics	**Syndrome-positive in the chart (N=2,967)**		**Syndrome-negative in the chart (N=1,363)**		**Total (N=4,330)**		**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Sex:	**No.**	**%**	**No.**	**%**	**No.**	**%**						
Female	1,810	61.0	824	60.5	2,634	60.8	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Male	1,157	39.0	539	39.5	1,696	39.2	0.98	(0.86, 1.12)	0.75	0.89	(0.77, 1.03)	0.11
Material deprivation index:[2]												
1st quintile (least deprived)	524	17.7	284	20.8	808	18.7	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
2nd quintile	584	19.7	270	19.8	854	19.7	1.16	(0.94, 1.42)	0.16	1.18	(0.95, 1.46)	0.14
3rd quintile	604	20.4	243	17.8	847	19.6	1.33	(1.08, 1.64)	0.01	1.44	(1.15, 1.81)	<0.01
4th quintile	581	19.6	261	19.1	842	19.4	1.21	(0.98, 1.49)	0.07	1.25	(1.01, 1.55)	0.04
5th quintile (most deprived)	545	18.4	255	18.7	800	18.5	1.16	(0.94, 1.43)	0.16	1.21	(0.97, 1.50)	0.09
Social deprivation index:[2]												
1st quintile (least deprived)	611	20.6	251	18.4	862	19.9	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
2nd quintile	574	19.3	263	19.3	837	19.3	0.90	(0.73, 1.10)	0.30	0.91	(0.74, 1.13)	0.41
3rd quintile	572	19.3	251	18.4	823	19.0	0.91	(0.74, 1.13)	0.41	0.97	(0.77, 1.21)	0.76
4th quintile	554	18.7	261	19.1	815	18.8	0.87	(0.70, 1.07)	0.19	0.88	(0.70, 1.10)	0.26
5th quintile (most deprived)	527	17.8	287	21.1	814	18.8	0.75	(0.61, 0.93)	0.01	0.76	(0.60, 0.95)	0.02
Deprivation indices missing:												
No	2,838	95.7	1,313	96.3	4,151	95.9	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	129	4.3	50	3.7	179	4.1	1.04	(0.73, 1.49)	0.83	1.06	(0.68, 1.64)	0.81
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**						
Age (per 5 years)[3]	36.4	24.9	43.2	24.0	38.5	24.8	0.95	(0.93, 0.96)	<0.0001	0.96	(0.94, 0.97)	<0.0001
Health services utilization (no. ambulatory visits in the previous year)[4]	9.0	10.1	10.6	12.7	9.5	11.0	0.99	(0.98, 0.99)	<0.0001	0.99	(0.99, 1.00)	0.08
Charlson comorbidity index (per 1-point increase in score)[4]	0.38	0.98	0.49	1.17	0.42	1.04	0.92	(0.86, 0.97)	<0.01	0.98	(0.92, 1.05)	0.58

[1] Multivariate analysis adjusted for all patient characteristics in Table 3, all physician characteristics in Table 1, and all encounter characteristics in Table 4.
[2] The material and social deprivation indices were calculated using Statistics Canada's 2006 census data. These indices were developed by the Quebec National Public Health Institute. The material deprivation index summarizes information on the proportion of persons who have no high school diploma, the proportion of persons employed, and the average income in the patient's 6-digit postal code area of residence. The social deprivation index summarizes information on the proportion of single-parent families, the proportion of persons living alone, and the proportion of persons separated, divorced, or widowed in the patient's 6-digit postal code area of residence.
[3] On October 1st of the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.
[4] Based on all medical services claims billed by all Quebec physicians (not only the 3,600 study physicians) in the year prior to the date of the syndrome-positive visit.

Table 4. Encounter characteristics associated with accuracy of syndrome definitions based on physician claims (OR>1.00 means the encounter characteristic increased the PPV of the syndrome definition, OR<1.00 means the encounter characteristic reduced the PPV)

	No. visits with a syndrome-positive physician claim						Bivariate regression analysis			Multivariate regression analysis[1]		
Encounter characteristics	**Syndrome-positive in the chart (N=2,967)**		**Syndrome-negative in the chart (N=1,363)**		**Total (N=4,330)**		**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
	No.	**%**	**No.**	**%**	**No.**	**%**						
Syndrome type:												
Fever	371	12.5	230	16.9	601	13.9	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Gastrointestinal	572	19.3	283	20.8	855	19.8	1.57	(1.25, 1.97)	<0.0001	1.72	(1.36, 2.16)	<0.0001
Neurological	608	20.5	363	26.6	971	22.4	1.29	(1.05, 1.60)	0.02	1.38	(1.11, 1.72)	<0.01
Rash	628	21.2	269	19.7	897	20.7	1.80	(1.44, 2.25)	<0.0001	1.89	(1.51, 2.37)	<0.0001
Respiratory	808	27.2	241	17.7	1049	24.2	1.72	(1.36, 2.17)	<0.0001	1.66	(1.29, 2.14)	<0.0001
ILI large-group	555	18.7	98	7.2	653	15.1	2.98	(2.32, 3.82)	<0.0001	2.68	(2.06, 3.48)	<0.0001
Type of clinic:												
Private clinic	2,916	98.3	1,320	96.9	4,236	97.8	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Community health center	10	0.3	8	0.6	18	0.4	0.58	(0.14, 2.35)	0.45	0.46	(0.11, 2.01)	0.30
Hospital-based ambulatory clinic	41	1.4	35	2.6	76	1.8	0.53	(0.30, 0.93)	0.03	0.75	(0.37, 1.53)	0.43
Geographic location of clinic:												
Urban	2,476	83.5	1,169	85.8	3,645	84.2	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rural	491	16.6	194	14.2	685	15.8	1.20	(0.99, 1.46)	0.07	1.19	(0.98, 1.45)	0.08
Physician familiarity with the patient (patient treated by the study physician in the previous year):												
No	1,199	40.4	475	34.9	1,674	38.7	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	1,768	59.6	888	65.1	2,656	61.3	0.79	(0.69, 0.91)	<0.001	0.95	(0.82, 1.11)	0.53
Day of the week:												
Weekday	2,797	94.3	1,308	96.0	4,105	94.8	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Weekend	170	5.7	55	4.0	225	5.2	1.42	(1.03, 1.95)	0.03	1.28	(0.92, 1.77)	0.15
Season:												
Winter (12/22-03/20)	737	24.8	339	24.9	1,076	24.9	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Spring (03/21-06/20)	855	28.8	317	23.3	1,172	27.1	1.22	(1.02, 1.47)	0.03	1.29	(1.07, 1.57)	0.01
Summer (06/21-09/22)	645	21.7	351	25.8	996	23.0	0.84	(0.70, 1.01)	0.06	0.91	(0.75, 1.10)	0.33
Fall (09/23-12/21)	730	24.6	356	26.1	1,086	25.1	0.94	(0.79, 1.12)	0.48	0.97	(0.81, 1.17)	0.79

[1] Multivariate analysis adjusted for all encounter characteristics in Table 4, all physician characteristics in Table 1, and all patient characteristics in Table 3.

Table 4 (continued). Encounter characteristics associated with accuracy of syndrome definitions based on physician claims (OR>1.00 means the encounter characteristic increased the PPV of the syndrome definition, OR<1.00 means the encounter characteristic reduced the PPV)

	No. visits with a syndrome-positive physician claim						Bivariate regression analysis			Multivariate regression analysis[1]		
Encounter characteristics	**Syndrome-positive in the chart (N=2,967)**		**Syndrome-negative in the chart (N=1,363)**		**Total (N=4,330)**		**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**						
No. syndrome-positive visits billed by the study physician in the previous 30 days, for the same syndrome as the verified visit (per 10 visits)	4.1	6.7	4.2	6.2	4.2	6.6	1.08	(0.95, 1.23)	0.25	1.05	(1.01, 1.08)	0.01
Physician workload: no. claims billed that day (per 10 claims)	35.1	17.4	36.5	21.0	35.5	18.6	0.96	(0.93, 1.00)	0.03	0.93	(0.90, 0.97)	<0.001

[1] Multivariate analysis adjusted for all encounter characteristics in Table 4, all physician characteristics in Table 1, and all patient characteristics in Table 3.

Appendix – Table 1. Physician characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the physician characteristic increased the PPV of the syndrome definition, OR<1.00 means the physician characteristic reduced the PPV)

	Fever syndrome (N=601 visits)				Gastrointestinal syndrome (N=855 visits)				Neurological syndrome (N=971 visits)				Rash syndrome (N=897 visits)			
Physician characteristics	**No. visits**	**OR**	**95% CI**	**P Value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P Value**	**No. visits**	**OR**	**95% CI**	**P value**
Gender:																
Female	249	Ref.	Ref.	Ref.	340	Ref.	Ref.	Ref.	371	Ref.	Ref.	Ref.	338	Ref.	Ref.	Ref.
Male	352	0.82	(0.60, 1.14)	0.25	515	0.83	(0.62, 1.11)	0.21	600	1.09	(0.83, 1.41)	0.54	559	1.37	(1.03, 1.84)	0.03
Preferred language:																
French	548	Ref.	Ref.	Ref.	784	Ref.	Ref.	Ref.	901	Ref.	Ref.	Ref.	830	Ref.	Ref.	Ref.
English	53	0.59	(0.33, 1.05)	0.07	71	0.79	(0.48, 1.30)	0.35	70	1.13	(0.68, 1.86)	0.64	67	1.22	(0.70, 2.14)	0.48
Specialty:																
General practice	539	Ref.	Ref.	Ref.	776	Ref.	Ref.	Ref.	899	Ref.	Ref.	Ref.	828	Ref.	Ref.	Ref.
Internal medicine	8	0.30	(0.06, 1.50)	0.14	12	0.18	(0.05, 0.68)	0.01	11	0.54	(0.16, 1.79)	0.31	8	0.72	(0.17, 3.02)	0.65
Pediatrics	51	1.51	(0.84, 2.73)	0.17	54	1.57	(0.84, 2.93)	0.16	56	1.00	(0.59, 1.75)	0.99	55	0.82	(0.46, 1.45)	0.49
General surgery	3	>999	infinity	0.98	13	0.34	(0.11, 1.06)	0.06	5	0.16	(0.02, 1.46)	0.10	6	0.22	(0.04, 1.18)	0.08
Years since licensure (per 5 years)	601	0.92	(0.84, 1.00)	0.05	855	0.91	(0.84, 0.98)	0.01	971	0.99	(0.92, 1.06)	0.76	897	0.97	(0.89, 1.04)	0.35

Appendix – Table 1 (continued). Physician characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the physician characteristic increased the PPV of the syndrome definition, OR<1.00 means the physician characteristic reduced the PPV)

	Respiratory syndrome (N=1,049 visits)				Influenza-like illness (N=653 visits)			
Physician characteristics	**No. visits**	**OR**	**95% CI**	**P Value**	**No. visits**	**OR**	**95% CI**	**P value**
Gender:								
Female	401	Ref.	Ref.	Ref.	255	Ref.	Ref.	Ref.
Male	648	0.72	(0.54, 0.98)	0.04	398	0.93	(0.64, 1.33)	0.67
Preferred language:								
French	973	Ref.	Ref.	Ref.	595	Ref.	Ref.	Ref.
English	76	0.85	(0.50, 1.44)	0.54	58	0.85	(0.47, 1.56)	0.61
Specialty:								
General practice	961	Ref.	Ref.	Ref.	575	Ref.	Ref.	Ref.
Internal medicine	11	3.16	(0.40, 24.83)	0.27	9	0.67	(0.17, 2.73)	0.58
Pediatrics	67	2.04	(1.00, 4.18)	0.05	65	1.49	(0.77, 2.87)	0.23
General surgery	10	0.32	(0.09, 1.10)	0.07	4	0.34	(0.05, 2.42)	0.28
Years since licensure (per 5 years)	1,049	0.93	(0.86, 1.01)	0.07	653	0.93	(0.84, 1.02)	0.12

Appendix - Table 2. Billing characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the billing characteristic increased the PPV of the syndrome definition, OR<1.00 means the billing characteristic reduced the PPV)

	Fever syndrome (N=601 visits)				Gastrointestinal syndrome (N=855 visits)				Neurological syndrome (N=971 visits)				Rash syndrome (N=897 visits)			
Billing practices	**No. visits**	**OR**	**95% CI**	**P Value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**
Who entered the diagnostic code in the claim?																
Physician	95	Ref.	Ref.	Ref.	133	Ref.	Ref.	Ref.	137	Ref.	Ref.	Ref.	130	Ref.	Ref.	Ref.
Secretary or nurse	407	1.51	(0.96, 2.37)	0.07	571	1.21	(0.82, 1.78)	0.33	659	1.17	(0.80, 1.70)	0.42	614	0.78	(0.51, 1.20)	0.26
Off-site billing company or RAMQ (i.e., paper billing)	99	1.34	(0.76, 2.35)	0.31	151	1.56	(0.96, 2.55)	0.08	175	0.87	(0.55, 1.36)	0.53	153	0.73	(0.44, 1.22)	0.23
Billing software used:																
Soft Informatique	126	Ref.	Ref.	Ref.	217	Ref.	Ref.	Ref.	241	Ref.	Ref.	Ref.	216	Ref.	Ref.	Ref.
Purkinje	135	1.21	(0.74, 1.97)	0.45	197	0.81	(0.54, 1.22)	0.31	222	1.93	(1.30, 2.85)	0.001	206	1.10	(0.72, 1.67)	0.67
ADN Medical	80	0.97	(0.56, 1.71)	0.92	100	1.04	(0.62, 1.75)	0.88	128	1.05	(0.68, 1.63)	0.82	122	1.19	(0.73, 1.94)	0.50
Omni-Med.com Caduceus	55	0.98	(0.52, 1.85)	0.96	70	1.04	(0.58, 1.87)	0.89	82	0.66	(0.40, 1.10)	0.11	80	1.03	(0.59, 1.80)	0.93
Medicus MED-WIN	27	0.95	(0.41, 2.18)	0.90	41	0.52	(0.26, 1.02)	0.06	43	0.67	(0.35, 1.28)	0.22	37	0.65	(0.32, 1.32)	0.23
Facturation.net	24	0.36	(0.14, 0.94)	0.04	25	0.35	(0.15, 0.81)	0.01	29	0.43	(0.19, 0.94)	0.03	32	0.84	(0.38, 1.84)	0.66
ANDX Xclaim	21	0.54	(0.21, 1.40)	0.21	21	0.73	(0.29, 1.83)	0.50	22	0.70	(0.29, 1.67)	0.42	17	0.39	(0.15, 1.06)	0.06
CareOffice	20	0.72	(0.28, 1.86)	0.50	21	0.89	(0.35, 2.31)	0.82	23	1.31	(0.53, 3.20)	0.56	26	1.85	(0.67, 5.11)	0.24
Médifiche	14	3.23	(0.86, 12.13)	0.08	19	0.77	(0.29, 2.03)	0.59	24	0.98	(0.42, 2.29)	0.96	19	0.61	(0.23, 1.57)	0.30
Toubib	13	0.39	(0.12, 1.38)	0.13	21	0.60	(0.24, 1.48)	0.26	20	0.70	(0.28, 1.74)	0.44	18	0.35	(0.13, 0.93)	0.04
Other[2] or unknown	86	1.35	(0.77, 2.35)	0.29	123	0.57	(0.36, 0.90)	0.02	137	1.01	(0.66, 1.55)	0.97	124	1.12	(0.69, 1.82)	0.65
Annual billing volume (per 1,000 claims)[1]	601	0.98	(0.92, 1.04)	0.44	855	0.97	(0.92, 1.02)	0.21	971	1.01	(0.96, 1.06)	0.85	897	1.02	(0.97, 1.08)	0.48
Percent of visits with a missing or unspecified diagnostic code[1]	601	1.01	(0.98, 1.04)	0.39	855	0.99	(0.97, 1.02)	0.55	971	0.98	(0.96, 1.01)	0.13	897	1.02	(0.99, 1.05)	0.29
No. distinct diagnostic codes used (per 100 codes)[1]	601	0.99	(0.84, 1.17)	0.93	855	1.01	(0.87, 1.18)	0.90	971	0.94	(0.81, 1.08)	0.35	897	1.03	(0.88, 1.20)	0.74

[1] In the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.
[2] The remaining billing softwares were aggregated under “other” because their numbers were too small to report individually in this analysis.

Appendix - Table 2 (continued). Billing characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the billing characteristic increased the PPV, OR<1.00 means the billing characteristic reduced the PPV)

	Respiratory syndrome (N=1,049 visits)				Influenza-like illness (N=653 visits)			
Billing practices	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**
Who entered the diagnostic code in the claim?								
Physician	158	Ref.	Ref.	Ref.	116	Ref.	Ref.	Ref.
Secretary or nurse	702	0.75	(0.48, 1.15)	0.18	431	1.11	(0.69, 1.78)	0.66
Off-site billing company or RAMQ (i.e., paper billing)	189	0.69	(0.41, 1.15)	0.16	106	0.93	(0.51, 1.68)	0.80
Billing software used:								
Soft Informatique	266	Ref.	Ref.	Ref.	132	Ref.	Ref.	Ref.
Purkinje	233	1.67	(1.11, 2.53)	0.02	139	1.65	(0.95, 2.87)	0.08
ADN Medical	144	1.83	(1.12, 3.00)	0.02	105	1.20	(0.68, 2.11)	0.54
Omni-Med.com Caduceus	91	1.25	(0.73, 2.15)	0.42	47	1.84	(0.81, 4.15)	0.14
Medicus MED-WIN	43	1.39	(0.66, 2.97)	0.39	38	1.22	(0.54, 2.74)	0.63
Facturation.net	28	1.27	(0.52, 2.10)	0.60	19	0.48	(0.18, 1.28)	0.14
ANDX Xclaim	25	2.22	(0.74, 6.67)	0.16	16	1.88	(0.51, 6.98)	0.34
CareOffice	28	1.06	(0.45, 2.50)	0.90	26	1.18	(0.46, 3.03)	0.73
Médifiche	29	2.64	(0.89, 7.84)	0.08	22	2.75	(0.77, 9.83)	0.12
Toubib	23	0.79	(0.32, 1.94)	0.61	11	4.34	(0.54, 35.06)	0.17
Other[2] or unknown	139	1.60	(0.99, 2.61)	0.06	98	1.42	(0.78, 2.58)	0.25
Annual billing volume (per 1,000 claims)[1]	1,049	1.01	(0.96, 1.07)	0.63	653	1.03	(0.97, 1.10)	0.36
Percent of visits with a missing or unspecified diagnostic code[1]	1,049	1.02	(0.99, 1.06)	0.17	653	1.00	(0.97, 1.03)	0.97
No. distinct diagnostic codes used (per 100 codes)[1]	1,049	1.06	(0.91, 1.24)	0.47	653	1.38	(1.12, 1.70)	<0.01

[1] In the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.
[2] The remaining billing softwares were aggregated under “other” because their numbers were too small to report individually in this analysis.

Table 3. Patient characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the patient characteristic increased the PPV of the syndrome definition, OR<1.00 means the patient characteristic reduced the PPV)

	Fever syndrome (N=601 visits)				Gastrointestinal syndrome (N=855 visits)				Neurological syndrome (N=971 visits)				Rash syndrome (N=897 visits)			
Patient characteristics	**No. visits**	**OR**	**95% CI**	**P Value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**
Sex:																
Female	366	Ref.	Ref.	Ref.	529	Ref.	Ref.	Ref.	642	Ref.	Ref.	Ref.	534	Ref.	Ref.	Ref.
Male	235	1.10	(0.79, 1.53)	0.56	326	0.95	(0.71, 1.27)	0.73	329	0.72	(0.55, 0.94)	0.02	363	0.85	(0.64, 1.13)	0.26
Material deprivation index:[1]	601	1.18	(1.05, 1.34)	<0.01	855	1.06	(0.96, 1.17)	0.28	971	1.03	(0.94, 1.13)	0.55	897	1.08	(0.97, 1.20)	0.14
1st quintile (least deprived)	107	Ref.	Ref.	Ref.	153	Ref.	Ref.	Ref.	177	Ref.	Ref.	Ref.	174	Ref.	Ref.	Ref.
2nd quintile	121	1.39	(0.83, 2.35)	0.21	152	1.41	(0.89, 2.24)	0.14	183	1.19	(0.78, 1.81)	0.42	196	1.29	(0.83, 1.96)	0.25
3rd quintile	129	1.53	(0.91, 2.56)	0.11	173	1.63	(1.04, 2.56)	0.03	196	1.52	(1.00, 2.31)	0.05	176	1.47	(0.94, 2.31)	0.09
4th quintile	121	1.54	(0.91, 2.60)	0.11	171	1.64	(1.05, 2.58)	0.03	181	1.19	(0.78, 1.82)	0.41	170	1.36	(0.87, 2.14)	0.18
5th quintile (most deprived)	92	2.26	(1.28, 4.00)	0.01	168	1.24	(0.79, 1.93)	0.35	203	1.16	(0.77, 1.75)	0.47	147	1.42	(0.88, 2.28)	0.15
Missing	31	2.78	(1.20, 6.48)	0.02	38	2.51	(1.11, 5.66)	0.03	31	0.96	(0.44, 2.06)	0.91	34	1.19	(0.54, 2.60)	0.67
Social deprivation index:[1]	601	0.98	(0.87, 1.11)	0.79	855	0.94	(0.85, 1.04)	0.21	971	0.97	(0.88, 1.06)	0.52	897	0.95	(0.85, 1.05)	0.27
1st quintile (least deprived)	106	Ref.	Ref.	Ref.	162	Ref.	Ref.	Ref.	192	Ref.	Ref.	Ref.	197	Ref.	Ref.	Ref.
2nd quintile	131	0.87	(0.52, 1.46)	0.60	163	1.01	(0.64, 1.60)	0.97	197	1.11	(0.74, 1.67)	0.61	170	0.61	(0.39, 0.95)	0.03
3rd quintile	117	0.97	(0.57, 1.64)	0.91	162	1.12	(0.70, 1.77)	0.64	202	1.16	(0.77, 1.74)	0.48	167	0.73	(0.46, 1.16)	0.19
4th quintile	109	1.27	(0.74, 2.18)	0.39	163	0.70	(0.45, 1.10)	0.12	169	1.12	(0.74, 1.72)	0.59	164	0.61	(0.38, 0.96)	0.03
5th quintile (most deprived)	107	0.75	(0.44, 1.29)	0.30	167	0.87	(0.56, 1.37)	0.55	180	0.86	(0.57, 1.29)	0.46	165	0.76	(0.48, 1.22)	0.25
Missing	31	1.81	(0.78, 4.20)	0.17	38	1.70	(0.75, 3.84)	0.20	31	0.83	(0.39, 1.78)	0.63	34	0.67	(0.31, 1.48)	0.33
Age (per 5 years):[2]	601	0.99	(0.98, 1.00)	<0.01	855	0.99	(0.98, 0.99)	<0.01	971	0.99	(0.99, 1.00)	0.01	897	1.00	(0.99, 1.01)	0.93
Healthcare services utilization (no. ambulatory visits in the previous year)[3]	601	0.99	(0.97, 1.01)	0.24	855	0.98	(0.97, 1.00)	0.01	971	1.00	(0.99, 1.01)	0.45	897	1.00	(0.98, 1.01)	0.50
Charlson comorbidity index (per 1-point score increase)[3]	601	0.88	(0.75, 1.04)	0.13	855	0.86	(0.77, 0.97)	<0.01	971	0.96	(0.83, 1.09)	0.50	897	0.96	(0.83, 1.11)	0.59

[1] The material and social deprivation indices, developed by the Quebec National Public Health Institute, were calculated using Statistics Canada's 2006 census data.
[2] On October 1st of the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.
[3] Based on all medical services claims billed by all Quebec physicians (not only the 3,600 study physicians) in the year prior to the date of the syndrome-positive visit.

Appendix - Table 3 (continued). Patient characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the patient characteristic increased the PPV, OR<1.00 means the patient characteristic reduced the PPV)

	Respiratory syndrome (N=1,049 visits)				Influenza-like illness (N=653 visits)			
Patient characteristics	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**
Sex:								
Female	585	Ref.	Ref.	Ref.	371	Ref.	Ref.	Ref.
Male	464	1.00	(0.75, 1.33)	0.98	282	1.45	(1.01, 2.10)	0.05
Material deprivation index:[1]	1,049	0.96	(0.87, 1.06)	0.43	653	1.18	(1.03, 1.34)	0.01
1st quintile (least deprived)	204	Ref.	Ref.	Ref.	140	Ref.	Ref.	Ref.
2nd quintile	213	0.88	(0.56, 1.38)	0.57	126	1.24	(0.73, 2.11)	0.43
3rd quintile	180	1.17	(0.71, 1.93)	0.53	115	1.42	(0.82, 2.48)	0.21
4th quintile	208	0.89	(0.57, 1.42)	0.63	130	1.67	(0.96, 2.89)	0.07
5th quintile (most deprived)	196	0.81	(0.51, 1.27)	0.35	109	1.92	(1.06, 3.48)	0.03
Missing	48	0.76	(0.37, 1.56)	0.46	33	1.70	(0.69, 4.22)	0.25
Social deprivation index:[1]	1,049	0.92	(0.83, 1.02)	0.13	653	0.94	(0.83, 1.07)	0.34
1st quintile (least deprived)	215	Ref.	Ref.	Ref.	130	Ref.	Ref.	Ref.
2nd quintile	184	1.22	(0.75, 1.99)	0.42	134	1.09	(0.62, 1.91)	0.78
3rd quintile	184	0.89	(0.56, 1.41)	0.62	102	1.01	(0.55, 1.84)	0.99
4th quintile	214	0.99	(0.63, 1.57)	0.98	133	1.17	(0.66, 2.08)	0.59
5th quintile (most deprived)	204	0.74	(0.48, 1.16)	0.19	121	0.71	(0.41, 1.24)	0.23
Missing	48	0.77	(0.38, 1.58)	0.48	33	1.21	(0.48, 3.06)	0.68
Age (per 5 years):[2]	1,049	0.98	(0.97, 0.98)	<0.01	653	1.00	(0.99, 1.00)	0.14
Healthcare services utilization (no. ambulatory visits in the previous year)[3]	1,049	0.97	(0.96, 0.98)	<0.01	653	0.98	(0.96, 1.00)	0.02
Charlson comorbidity index (per 1-point score increase)[3]	1,049	0.84	(0.74, 0.95)	<0.01	653	0.96	(0.83, 1.12)	0.63

[1] The material and social deprivation indices, developed by the Quebec National Public Health Institute, were calculated using Statistics Canada's 2006 census data.
[2] On October 1st of the study year when the visit took place. The study spanned 2 years: October 1, 2005 to September 30, 2006, and October 1, 2006 to September 30, 2007.
[3] Based on all medical services claims billed by all Quebec physicians (not only the 3,600 study physicians) in the year prior to the date of the syndrome-positive visit.

Appendix - Table 4. Encounter characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the encounter characteristic increased the PPV, OR<1.00 means the encounter characteristic reduced the PPV)

	Fever syndrome (N=601 visits)				Gastrointestinal syndrome (N=855 visits)				Neurological syndrome (N=971 visits)				Rash syndrome (N=897 visits)			
Encounter characteristics	**No. visits**	**OR**	**95% CI**	**P Value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**
Type of clinic:																
Private clinic	587	Ref.	Ref.	Ref.	831	Ref.	Ref.	Ref.	952	Ref.	Ref.	Ref.	880	Ref.	Ref.	Ref.
Community health center	3	1.70	(0.15, 18.89)	0.66	2	0.27	(0.03, 3.02)	0.29	4	0.65	(0.09, 4.61)	0.66	4	0.15	(0.02, 1.40)	0.10
Hospital-based ambulatory clinic	11	0.19	(0.04, 0.88)	0.03	31	0.50	(0.21, 1.18)	0.11	15	0.32	(0.11, 0.95)	0.04	13	0.70	(0.23, 2.15)	0.53
Geographic location of clinic:																
Urban	514	Ref.	Ref.	Ref.	720	Ref.	Ref.	Ref.	818	Ref.	Ref.	Ref.	751	Ref.	Ref.	Ref.
Rural	87	1.09	(0.69, 1.72)	0.72	135	1.34	(0.90, 1.99)	0.15	153	1.39	(0.96, 2.00)	0.08	146	1.26	(0.85, 1.87)	0.26
Patient treated by the study physician in the previous year:																
No	255	Ref.	Ref.	Ref.	307	Ref.	Ref.	Ref.	345	Ref.	Ref.	Ref.	371	Ref.	Ref.	Ref.
Yes	346	0.95	(0.69, 1.32)	0.77	548	0.80	(0.60, 1.08)	0.14	626	0.94	(0.72, 1.23)	0.67	526	0.83	(0.62, 1.11)	0.20
Season:																
Winter (12/22-03/20)	153	Ref.	Ref.	Ref.	211	Ref.	Ref.	Ref.	228	Ref.	Ref.	Ref.	193	Ref.	Ref.	Ref.
Spring (03/21-06/20)	157	1.73	(1.10, 2.72)	0.02	230	1.02	(0.68, 1.53)	0.92	266	1.35	(0.94, 1.93)	0.11	261	1.41	(0.94, 2.12)	0.10
Summer (06/21-09/22)	152	0.94	(0.60, 1.47)	0.77	214	0.61	(0.41, 0.90)	0.01	219	1.52	(1.04, 2.22)	0.03	220	0.95	(0.64, 1.44)	0.84
Fall (09/23-12/21)	139	1.26	(0.79, 1.99)	0.33	200	0.79	(0.53, 1.19)	0.26	258	1.20	(0.84, 1.72)	0.32	223	1.13	(0.75, 1.71)	0.56
Day of the week:																
Weekday	572	Ref.	Ref.	Ref.	805	Ref.	Ref.	Ref.	934	Ref.	Ref.	Ref.	849	Ref.	Ref.	Ref.
Weekend	29	1.70	(0.78, 3.72)	0.19	50	1.46	(0.78, 2.76)	0.24	37	1.39	(0.69, 2.80)	0.36	48	1.20	(0.63, 2.31)	0.58
No. same-syndrome positive visits billed by the study physician in the previous 30 days (per 10 visits)	601	1.03	(0.98, 1.09)	0.23	855	1.04	(0.87, 1.25)	0.67	971	0.78	(0.54, 1.12)	0.17	897	0.96	(0.80, 1.15)	0.66
Workload: no. claims billed that day (per 10 claims)	601	0.92	(0.84, 1.01)	0.08	855	0.99	(0.92, 1.07)	0.84	971	0.97	(0.90, 1.04)	0.41	897	0.92	(0.85, 0.99)	0.03

Appendix - Table 4 (continued). Encounter characteristics associated with accuracy of syndrome definitions based on physician claims: results from *bivariate* regression analyses for each syndrome individually (OR>1.00 means the encounter characteristic increased the PPV, OR<1.00 means the encounter characteristic reduced the PPV)

	Respiratory syndrome (N=1,049 visits)				Influenza-like illness (N=653 visits)			
Encounter characteristics	**No. visits**	**OR**	**95% CI**	**P value**	**No. visits**	**OR**	**95% CI**	**P value**
Type of clinic:								
Private clinic	1,026	Ref.	Ref.	Ref.	642	Ref.	Ref.	Ref.
Community health center	4	>999	infinity	0.98	3	>999	infinity	0.99
Hospital-based ambulatory clinic	19	0.66	(0.24, 1.76)	0.41	8	0.33	(0.08, 1.32)	0.12
Geographic location of clinic:								
Urban	880	Ref.	Ref.	Ref.	560	Ref.	Ref.	Ref.
Rural	169	0.95	(0.65, 1.39)	0.79	93	0.69	(0.43, 1.11)	0.13
Patient treated by the study physician in the previous year:								
No	411	Ref.	Ref.	Ref.	295	Ref.	Ref.	Ref.
Yes	638	0.45	(0.33, 0.62)	<0.01	358	0.81	(0.57, 1.17)	0.26
Season:								
Winter (12/22-03/20)	304	Ref.	Ref.	Ref.	184	Ref.	Ref.	Ref.
Spring (03/21-06/20)	268	1.17	(0.78, 1.75)	0.45	172	1.04	(0.63, 1.72)	0.87
Summer (06/21-09/22)	197	0.78	(0.52, 1.19)	0.25	125	0.65	(0.39, 1.09)	0.10
Fall (09/23-12/21)	280	0.83	(0.57, 1.22)	0.34	172	0.89	(0.55, 1.45)	0.63
Day of the week:								
Weekday	987	Ref.	Ref.	Ref.	606	Ref.	Ref.	Ref.
Weekend	62	1.86	(0.90, 3.83)	0.09	47	0.85	(0.44, 1.66)	0.64
No. same-syndrome positive visits billed by the study physician in the previous 30 days (per 10 visits)	1,049	1.06	(1.02, 1.10)	<0.01	653	1.03	(0.99, 1.07)	0.13
Workload: no. claims billed that day (per 10 claims)	1,049	0.95	(0.89, 1.02)	0.15	653	0.98	(0.90, 1.07)	0.63

Chapter 7. Discussion

Monitoring infectious diseases is a continuously evolving challenge, and constant advances in surveillance methods and infrastructure are necessary to keep pace with rapidly evolving demands. Syndromic surveillance is a promising new surveillance methodology where health department staff, assisted by automated data acquisition and generation of statistical alerts, monitor human health indicators, including pre-diagnostic and diagnostic data, in real-time or near real-time. This novel surveillance approach is used increasingly for detecting disease outbreaks rapidly (23), and, more recently, for 'situation awareness' or guiding efforts to control recognized public health threats in real-time (24). There are many syndromic surveillance systems in place throughout the world, and several of these systems use diagnoses captured from administrative databases. Because diagnoses in physician claims are generally not audited, variations in coding are expected. The influence of this variation on the accuracy of surveillance case definitions is not known. In practice, high false-positive rates undermine the usefulness of existing syndromic surveillance systems. Attempts to reduce the false-positive rate by improving statistical outbreak detection algorithms have had limited success. However, almost no effort has been made to reduce the false-positive rate by improving the positive predictive value (PPV) of the case definitions, or syndromes, used in this type of surveillance. The objectives of this thesis were to evaluate the feasibility of identifying syndromes using diagnoses from physician claims, to assess the accuracy of syndromic surveillance case definitions based on diagnoses in physician claims, and to identify physician, billing, patient, and encounter characteristics associated with the positive predictive value of these case definitions, which may then be used to improve the accuracy of surveillance case definitions.

Summary of findings

The goal of the first manuscript was to assess the feasibility of using diagnoses in physician billing claims to identify episodes of acute respiratory infections. We found that the positive predictive value of diagnoses in physician claims was high for all acute respiratory infections studied. However, for all but one acute respiratory infection (i.e., acute bronchitis), our sensitivity estimates were below 0.45. Even though we used a convenience sample of only 9 physicians, we found that the prevalence of acute respiratory infections in physician claims varied widely between physicians, and that the sensitivity and positive predictive value of physician claims for identifying acute respiratory infections also varied between physicians. This pilot work demonstrated the feasibility of using diagnoses from physician claims to identify episodes of acute respiratory infection, and generated estimates of sensitivity and positive predictive value that were crucial to planning and obtaining funding for the research described in manuscripts 2 and 3.

The second manuscript reports the results of a full-scale, population-based validation of several syndromic surveillance case definitions based on diagnoses in physician billing claims from community-based physicians. We focused on 5 syndromes: fever, gastrointestinal, neurological, rash, and respiratory (including influenza-like illness), because of their public health importance and prevalence in community healthcare settings. We found that the sensitivity of the case definitions for these syndromes was low, the specificity and negative predictive value were very high, and the positive predictive value was moderate to high. We also estimated the prevalence and PPV of individual diagnostic codes within each syndrome. We found that rarely used diagnostic codes had a high probability of being false-positives, and that more commonly used diagnostic codes had a higher PPV.

The objective of the third manuscript – to identify predictors of the positive predictive value of syndrome definitions based on diagnoses in physician claims – reflects the expanding use of syndromic surveillance from outbreak detection to situation awareness, and explores one potential avenue for reducing frequent false-alerts in existing syndromic surveillance systems. We found that the positive predictive value of syndrome definitions was influenced by several properties of the data; information on these properties could easily be obtained by public health departments to improve case definition accuracy in syndromic surveillance. Agreement between the medical chart and the physician claim about the presence of a syndrome was higher when the treating physician had billed many visits for the same syndrome recently, had a lower workload on the day of the visit, and when the patient was younger and less socially deprived. We also found that syndrome-positive physician claims produced by billing software that abstracted the billing diagnosis from an electronic medical record in an automated manner were more likely to agree with the medical chart than claims produced by software that required manual input of billing diagnoses.

Strengths and limitations

This thesis research had several strengths, as well as some limitations. The research described in manuscript 1 was pilot work, and as such, it was limited by the small convenience sample used. The research in manuscripts 2 and 3 was based on a large stratified random sample of all physicians working in the fee-for-service system in community healthcare settings in the province of Quebec during a 2-year period. Although the participation rate was low, there were no significant differences between the participating and non-participating physicians on all measured variables, except that participating physicians had been in practice longer and had worked more days during the study period than non-participating physicians. In manuscript 3, we found that physician practice experience was significantly and negatively associated with the positive predictive value of syndrome definitions based on diagnoses in physician claims

– therefore the presence of more experienced physicians in our sample may have led to an underestimation of the positive predictive value. Based on our and another study's (45) finding that diagnostic coding accuracy decreases with increasing experience, we hypothesize that other parameters (i.e., sensitivity, specificity, and negative predictive value) would also be underestimated.

A major strength of our research was that our estimates of sensitivity and specificity in manuscripts 1 and 2 took into account the stratified sampling strategy used, and therefore did not suffer from verification bias. In other published validation studies (61;65;128), sensitivity was overestimated and specificity underestimated as a result of not correcting for the verification bias introduced by the sampling.

Unlike other published validation studies of syndrome case definitions (61;65), our study design enabled us to estimate and report positive predictive value at the level of the individual ICD-9 diagnostic code. Unfortunately, we were not able to assess the accuracy of all the diagnostic codes in the syndrome case definitions, because some diagnostic codes were never used by the physicians in our sample (e.g., cutaneous and pulmonary anthrax; ICD-9 codes 22.0 and 22.1). Given our finding that infrequently used diagnostic codes had lower positive predictive value than frequently used ones, the absence of some diagnostic codes from our sample may have led to an overestimation of the positive predictive value of the case definition for the syndrome.

When estimating the sensitivity, specificity, and positive and negative predictive values of syndrome definitions based on diagnoses in physician claims, we treated the physician-facilitated medical chart review as a gold standard. However, the physician-facilitated medical chart review may not be a perfect gold standard. One solution that avoids considering either source of data a 'gold standard' is latent class analysis (159). But, with diffuse priors, latent class analysis would make the problem non-identifiable; the model would have more unknown parameters than degrees of freedom. Therefore,

informative prior distributions would need to be elicited on any two of the five unknown parameters (the sensitivity and specificity of the physician claims, the sensitivity and specificity of the chart review, and the syndrome prevalence) to obtain a meaningful solution. Eliciting informative priors would have been difficult because, as discussed in chapter 2, previously published estimates of the accuracy of syndrome definitions based on ICD-9 coded diagnoses vary widely due to methodological limitations and biases.

Physician-facilitated chart reviews and physician claims may be conditionally dependent due to an unmeasured factor, other than true syndrome status. For example, it is possible that syndrome severity may affect both physician-facilitated chart reviews and physician claims, with more severe syndromes being more likely to be identified correctly from both sources. This unmeasured variable, shared by both sources of information, would cause the apparent correlation. Failure to account for conditional dependence between physician-facilitated chart reviews and physician claims may have overestimated the agreement between these two sources of information. In future research, the analyses presented in this thesis may be extended by modeling the conditional dependence between the two sources of information using random effects (160), such that the sensitivities and specificities of each source of information would be modelled as functions of a latent visit-specific random variable.

Public health implications

Implications for public health surveillance

We found that diagnostic codes in physician claims from community healthcare settings have low sensitivity, moderate to high PPV, and near-perfect specificity and NPV for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory including influenza-like illness). Even though the sensitivity was below 0.45 for all 5 syndrome definitions studied in this thesis, these syndrome definitions are likely to still be useful for surveillance when there are large numbers of cases (e.g., influenza-like

illness). More research is needed to identify how the relationship between syndrome sensitivity and prevalence influences the value of monitoring syndromes for different public health purposes.

We also estimated the prevalence and positive predictive value of individual diagnostic codes within each syndrome. We found that rarely used diagnostic codes had a higher probability of being false-positive, and that more commonly used diagnostic codes had a higher positive predictive value. These findings may be useful to the ongoing development of sensitive and specific consensus syndrome definitions (142), as either a sensitive or a specific definition may be more useful depending on the surveillance objective. For example, if the objective is not to miss any case of a given syndrome or infection (e.g., anthrax), then the sensitive definition is the best suited one for that objective. In contrast, if the objective is situation awareness, then the specific definition may be more appropriate.

We found that characteristics of the provider and the patient influenced the positive predictive value of syndrome definitions based on diagnoses in physician claims. Some of these predictors of accuracy (e.g., patient age) are readily available to public health departments. Public health departments can apply our findings to improve the positive predictive value of syndrome definitions, either by focusing on physician claims where diagnostic codes are more likely to be accurate (e.g., claims among children), or by using all physician claims and weighting each according to the likelihood that its diagnostic code is accurate (e.g., weighting by the positive predictive value of each ICD-9 code).

Implications for physician billing

Because of the many difficulties involved in obtaining population-level morbidity information, there is growing interest in making secondary use of ICD-9 coded diagnoses in physician claims from community healthcare settings for purposes beyond healthcare administration, including assessment of health outcomes (161) and clinical comorbidities

(153;162;163), and surveillance of chronic diseases (164;165), injury (166;167), and infectious syndromes (43;44;49;58-60). Furthermore, until electronic health records are implemented in every community-based clinic in a given healthcare jurisdiction, ICD-9 coded diagnoses in physician claims represent a valuable source of information for use in reimbursement reform such as pay-for-performance physician reimbursement models. Indeed, ICD-9 coded diagnoses in physician claims have been used in combination with prescription claims and/or procedure codes to identify specific patient populations, such as patients with asthma (168;169), and to monitor clinical outcomes, such as asthma control (169). High diagnostic accuracy in physician claims is paramount if we are to use these data for public health monitoring or health research, or to assess physician performance.

Many of the physicians who participated in our study told us that they would pay more attention to diagnostic coding if they knew that their codes were being used. Also, we and others (45) found that the accuracy of diagnostic coding decreased with experience. A potential explanation for this phenomena was suggested by a few participating and non-participating physicians, who told us that their attentiveness to diagnostic coding decreased over time, as they became increasingly aware that their choice of diagnostic codes generally had no impact on their reimbursement. One physician even told us that he had recently started using the code 'V999' (unspecified) for all patients seen on a walk-in basis. Based on these observations, interventions to prevent the loss of diagnostic coding accuracy over time in practice could be as simple as informing physicians that diagnostic codes on their claims are a widely used and valuable source of information for public health monitoring and health services research. Alternatively, if the healthcare agency (payer) wanted to insure high accuracy of diagnostic codes in physician claims – for example, to use in a pay-for-performance reimbursement model – the agency could enact mechanisms to 1) ask physicians to provide accurate diagnoses in their claims, and 2) audit diagnostic codes in physician claims.

Implications for the timely transmission of data from clinical to public health settings

If diagnoses in physician claims are to be used for outbreak detection or situation awareness, their timeliness must be improved. In the fee-for-service system currently in place in the province of Quebec, physicians are reimbursed every 2 weeks. Because of this reimbursement schedule, many physicians cumulate their claims over the 2-week period then submit them to the payer before the deadline. In theory, the frequency of physician claim submission to the payer could be increased from once every 2 weeks to once a week (or even once a day) with only minor modifications to physician's billing practices.

In contrast, to enable real-time surveillance, substantial modifications to physician billing and reimbursement procedures would be required. One way to obtain physician claims data in real-time would be to implement an online adjudication system for physician claims, as is already in place for prescription claims. In such a system, the claim is submitted to the payer electronically, and the payer transmits its decision about the reimbursement of the claim in the same manner in just a few seconds. However, for the real-time submission of physician claims (i.e., during or immediately after the patient visit) to be feasible, the visit would most likely have to be documented using an electronic medical record, and the claim would have to be filled out and submitted in a mostly automated manner based on the information in the electronic medical record.

Implications for the design and implementation of electronic medical records

We found that billing software had a significant impact on the positive predictive value of syndrome definitions based on diagnoses in physician claims. Software that abstracted the billing diagnosis from the electronic medical record in an automated manner had higher claim diagnosis accuracy than software that required the manual input of billing diagnoses. This finding has important implications for both clinical users and public health surveillance, given the ongoing transformation of public health surveillance from a process where clinical practitioners manually submit case reports to

a process where public health agencies automatically extract relevant data from clinical information systems.

The US federal government has allotted $39 billion to support the adoption and "meaningful use" of electronic health records, and software purchased using these funds must support automated submission of data to public health agencies for three public health uses, including syndromic surveillance (158). This investment presents an opportunity to improve syndromic surveillance systems by having electronic health records capture and transmit information on highly influential predictors, such as indicators of patient complexity, to public health. The rich clinical data streams becoming accessible to public health should enable the implementation of surveillance strategies that incorporate our findings. As the volume and detail of electronically-available clinical data continue to increase, future research should explore how public health can harness their full breadth to further enhance the accuracy of case detection.

Future research priorities

Measuring the practical implications of our findings on the response to alerts

Future research should evaluate the practical implications of our findings on decision-making in response to alerts from existing syndromic surveillance systems. Using the sensitivity estimates we obtained, simulations should be used to evaluate the usefulness of different syndrome definitions as a function of syndrome prevalence. Such an evaluation would help determine whether some syndrome definitions, as they are currently formulated, are sufficiently sensitive for surveillance purposes.

Modifying syndrome definitions to better suit surveillance objectives

In this thesis, we estimated the agreement on the presence of a given syndrome between the diagnosis in the physician claim and the diagnosis in the chart. For example, if the diagnosis in the claim was headache (ICD-9 code: 784.0), which is

included in the definition for neurological syndrome, we evaluated if the chart diagnosis was also included in the neurological syndrome definition. However, given that few 'headache' diagnoses in physician claims would be expected to be associated with an infection, and given that 'headache' is highly prevalent in physician claims (i.e., its prevalence is several orders of magnitude higher than that of 'meningitis', for example), monitoring the incidence of 'headache' diagnoses in physician claims to detect neurological syndrome may yield a high rate of false-alerts.

A potential avenue for improving the accuracy of syndrome case definitions would be to estimate, for each ICD-9 code in a syndrome case definition individually, the sensitivity, specificity, positive predictive value, and negative predictive value of that ICD-9 code for identifying true episodes of infection. To determine whether or not a visit involved a 'true' episode of infection, we could use information such as the patient signs, symptoms, and other key findings we collected through physician-facilitated chart review (manuscript 2). Estimates of individual ICD-9 codes' sensitivity, specificity, positive predictive value, and negative predictive value for identifying true episodes of infection could then be used to tailor syndrome definitions to match surveillance objectives. For example, the false-positive rate of the case definition for neurological syndrome could be reduced by weighting each individual ICD-9 code by its positive predictive value to identify true episodes of infection; as a result, visits with the ICD-9 code for 'headache' would be given less weight than those with the diagnostic code for 'meningitis', and the positive predictive value of the case definition for neurological syndrome would be improved. Similarly, if our surveillance objective was not to miss any case of hemorrhagic syndrome, then we could weight each visit by the sensitivity of its ICD-9 code for identifying true episodes of infection. As an alternative to weighting, we could establish a minimum threshold for the sensitivity, specificity, positive predictive value, and/or negative predictive value of individual ICD-9 codes, and exclude from the syndrome case definition any ICD-9 code whose accuracy is below the desired threshold.

Evaluating different methods of incorporating predictors of syndrome definition accuracy in surveillance analyses

In this thesis, we propose two possible methods for incorporating predictors of syndrome definition accuracy in surveillance analyses. The first method is to use the predictors of syndrome definition accuracy to identify the subgroup of physician claims whose diagnosis is most likely to be a true-positive (i.e., with a positive predictive value above a certain threshold), and to apply detection algorithms to those claims only. The impact of using different thresholds of positive predictive value should be investigated. The other method is to use the predictors of syndrome definition accuracy to weight each physician claim by the likelihood that its diagnosis is a true-positive, and apply a detection algorithm to the weighted claims. Future research should compare the results obtained from these two methods, and evaluate their respective impact on decision-making in response to alerts.

Evaluating the impact of feeding syndromic surveillance information back to clinicians and healthcare administrators

In addition to the obvious utility of syndromic surveillance for public health prevention and control, information generated by syndromic surveillance systems may also be useful to inform clinical decisions. Future research is needed to assess the impact of feeding back information, at the point of care, about local and regional syndrome incidence on the medical management of patients susceptible to and/or presenting with a complaint consistent with a prevalent syndrome. For example, given the high rates of inappropriate antibiotic prescribing for respiratory infections of likely viral etiology among primary care physicians (107;122;170;171), it would be interesting to measure the impact on antibiotic prescribing of providing primary care physicians with information about local respiratory syndrome incidence, and prevalence of etiological agents isolated from respiratory specimens. Furthermore, feeding back syndromic surveillance information derived from physician claims to physicians would likely

improve the quality of diagnoses in physician claims; as end-users of that information, physicians would be more likely to provide accurate claim diagnoses.

The timely provision of up-to-date syndromic surveillance information may also be useful to plan healthcare delivery and improve healthcare resource allocation. For example, providing hospital administrators with a daily syndromic surveillance update, including local and regional trends in syndrome incidence as well as a detailed picture of syndrome-related healthcare services utilisation, may enable a systematic approach to planning healthcare staffing for emergency departments.

Conclusions

This was the first large-scale, population-based investigation of the accuracy of syndrome case definitions based on diagnoses in physician claims in community healthcare settings. We found that the sensitivity of syndrome case definitions based on diagnoses in physician claims was low, the positive predictive value was moderate to high, and the specificity and the negative predictive value were near-perfect. We identified several physician, billing, patient, and encounter characteristics associated with the positive predictive value of syndrome case definitions based on diagnoses in physician claims. Many of the predictors of syndrome case definition accuracy that we identified are readily accessible to public health departments and other organizations that routinely perform syndromic surveillance. These predictors could be used to reduce the false-positive rate of syndromic surveillance systems, either by focusing on the surveillance data most likely to be correct, or by adjusting the observed data for known biases in diagnostic coding and using the adjusted values to perform surveillance.

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Appendix A. CDC syndrome definitions based on ICD-9 diagnostic codes

Syndrome Definitions for Diseases Associated with Critical Bioterrorism-associated Agents

Participating Agencies:

National Center for Infectious Diseases and Epidemiology Program Office, Centers for Disease Control and Prevention, Atlanta, Georgia
Division of Preventive Medicine, Walter Reed Army Institute of Research, Silver Spring, Maryland
Emergency Medical Associates of New Jersey Research Foundation, Livingston, New Jersey
Bureau of Epidemiology Services, New York City Department of Health and Mental Hygiene, New York City, New York
Harvard Medical School and Harvard Pilgrim Health Care, Boston, Massachusetts

Introduction

Recent events, including the emergence of severe acute respiratory syndrome (SARS), West Nile virus, and monkeypox, have resulted in the implementation of alternate methods of disease surveillance that can potentially identify clusters of cases before traditional methods. Some surveillance systems utilize International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) coded health information from physician visit records or emergency department discharge data (1). Other systems abstract data from emergency department logs, 911 calls, or nurse call line data through analysis of text or other developed coding systems (2). Such surveillance methods are often referred to as syndromic surveillance since they typically monitor the non-specific clinical information that may indicate a bioterrorism-associated disease before specific diagnoses are made. Syndromic surveillance systems often utilize data sources that already exist but have not been designed specifically for public health surveillance purposes. Two data sources that may be available to augment a public health agency's surveillance activities are ICD-9-CM-coded discharge diagnoses for outpatient visits and emergency department visits.

ICD-9-CM codes were developed to allow assignment of codes to diagnoses and procedures associated with hospital utilization in the United States and are often used for third-party insurance reimbursement purposes. ICD-9-CM codes have been monitored in several settings to support public health surveillance (3-6). Syndromic surveillance using ICD-9-CM-coded health information may be considered because the codes are readily available for use by health care systems, are used in multiple clinical settings (e.g., outpatient, inpatient, emergency departments), are often available electronically, and can be shared easily between different information systems. However, prior to implementing surveillance based on the use of ICD-9-CM-coded health information, public health agencies should evaluate their usefulness with regard to the goals of the surveillance system (7, 8). For example, there may be a substantial delay in ICD-9-CM code assignment or the availability of that information in an electronic health information system. Since timeliness is a critical requirement, use of ICD-9-CM-coded information that is not timely may not be appropriate. Additionally, nonspecific ICD-9-CM codes may be used in an outpatient setting yielding low specificity for the outcome of interest. There may be bias in the use of the codes by some data providers (e.g., using codes for greater severity of illness to justify patient treatment). Use of a limited number of ICD-9-CM codes to describe a clinical encounter may limit appropriate interpretation. However, given the widespread availability and use of ICD-9-CM codes, it is prudent to provide some guidance regarding their use and to encourage the evaluation of their use for syndromic surveillance.

Beginning in 1999 to support several enhanced syndromic surveillance activities associated with high-profile community events (e.g., national political conventions), the Centers for Disease Control and Prevention (CDC) identified syndrome categories to be monitored that were indicative of the clinical presentations of several critical bioterrorism-associated conditions. The Department of Defense's ESSENCE program also developed broad syndrome groups using ICD-9-CM codes that approximate natural infectious disease outbreaks or bioterrorism. These syndrome groups are currently under routine surveillance at military medical treatment facilities (9). Other public health agencies have also developed syndrome-based definitions and code groupings specific to their data sources and surveillance goals. By combining our experiences, Department of Defense, CDC, and other investigators developed a suggested list of syndrome groups, definitions, and corresponding ICD-9-CM codes that can be used in syndromic surveillance programs.

A multi-agency working group was established to identify and define candidate syndrome groups. Eleven syndromes and corresponding code sets were selected based on a systematic selection process (Table). Definitions for each syndrome group were created by consensus. Individual ICD-9-CM codes were selected as candidates for inclusion in defined syndrome groups after an exhaustive search through all possible codes (Appendix). The codes were divided into three categories based on overall association with a syndrome or specific disease and by observed frequency of code usage in three clinical data sources (representing discharge diagnoses for outpatient visits and emergency department visits). The following categories within syndrome groups were defined:

> **Category 1** - Consists of codes that reflect general symptoms of the syndrome group and also include codes for the bioterrorism diseases of highest concern or those diseases highly approximating them.
>
> **Category 2** - Consists of codes that might normally be placed in the syndrome group, but daily volume could overwhelm or otherwise detract from the signal generated from the Category 1 code set alone.
>
> **Category 3** - Consists of specific diagnoses that fit into the syndrome category but occur infrequently or have very few counts. These codes may be excluded to simplify syndrome category code sets.

The working group also assessed the trends over time, frequency of code use, and subsequent contribution of selected codes to background 'noise' of the ICD-9-CM-coded syndrome groups using two large medical data sets: DoD outpatient visits and civilian emergency department visits. This analysis is ongoing but emphasized the need to evaluate the performance of the code sets in each data source.

These syndrome definitions and associated ICD-9-CM-coded syndrome groups can be used in syndromic surveillance systems to allow for comparability and evaluation among programs. However, analysis of the syndrome groups and subcategory distributions in individual data sources must be done as the frequency of code usage may vary by data source and will dictate which codes are best included for a particular surveillance program. Additional guidance from the working group will be forthcoming regarding statistical analysis methods that can be used to systematically choose ideal combinations of codes for syndrome groups. At this time, the working group wanted to share the syndrome groupings so that other public health agencies can have access to the results of their deliberations regarding defined syndrome groupings.

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Table: Text-based Syndrome Case Definitions and Associated Category A Conditions

Syndrome	Definition	Category A Condition
Botulism-like	ACUTE condition that may represent exposure to botulinum toxin ACUTE paralytic conditions consistent with botulism: cranial nerve VI (lateral rectus) palsy, ptosis, dilated pupils, decreased gag reflex, media rectus palsy. ACUTE descending motor paralysis (including muscles of respiration) ACUTE symptoms consistent with botulism: diplopia, dry mouth, dysphagia, difficulty focusing to a near point.	Botulism
Hemorrhagic Illness	SPECIFIC diagnosis of any virus that causes viral hemorrhagic fever (VHF): yellow fever, dengue, Rift Valley fever, Crimean-Congo HF, Kyasanur Forest disease, Omsk HF, Hantaan, Junin, Machupo, Lassa, Marburg, Ebola ACUTE condition with multiple organ involvement that may be consistent with exposure to any virus that causes VHF ACUTE blood abnormalities consistent with VHF: leukopenia, neutropenia, thrombocytopenia, decreased clotting factors, albuminuria	VHF
Lymphadenitis	ACUTE regional lymph node swelling and/ or infection (painful bubo- particularly in groin, axilla or neck)	Plague (Bubonic)
Localized Cutaneous Lesion	SPECIFIC diagnosis of localized cutaneous lesion/ ulcer consistent with cutaneous anthrax or tularemia ACUTE localized edema and/ or cutaneous lesion/ vesicle, ulcer, eschar that may be consistent with cutaneous anthrax or tularemia INCLUDES insect bites EXCLUDES any lesion disseminated over the body or generalized rash EXCLUDES diabetic ulcer and ulcer associated with peripheral vascular disease	Anthrax (cutaneous) Tularemia
Gastrointestinal	ACUTE infection of the upper and/ or lower gastrointestinal (GI) tract SPECIFIC diagnosis of acute GI distress such as Salmonella gastroenteritis ACUTE non-specific symptoms of GI distress such as nausea, vomiting, or diarrhea EXCLUDES any chronic conditions such as inflammatory bowel syndrome	Anthrax (gastrointestinal)

Syndrome Definitions for Diseases Associated with Critical Bioterrorism-associated Agents
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Syndrome	Definition	Category A Condition
Respiratory	ACUTE infection of the upper and/ or lower respiratory tract (from the oropharynx to the lungs, includes otitis media) SPECIFIC diagnosis of acute respiratory tract infection (RTI) such as pneumonia due to parainfluenza virus ACUTE non-specific diagnosis of RTI such as sinusitis, pharyngitis, laryngitis ACUTE non-specific symptoms of RTI such as cough, stridor, shortness of breath, throat pain EXCLUDES chronic conditions such as chronic bronchitis, asthma without acute exacerbation, chronic sinusitis, allergic conditions (Note: INCLUDE *acute exacerbation* of chronic illnesses.)	Anthrax (inhalational) Tularemia Plague (pneumonic)
Neurological	ACUTE neurological infection of the central nervous system (CNS) SPECIFIC diagnosis of acute CNS infection such as pneumoccocal meningitis, viral encephailitis ACUTE non-specific diagnosis of CNS infection such as meningitis not otherwise specified (NOS), encephailitis NOS, encephalopathy NOS ACUTE non-specific symptoms of CNS infection such as meningismus, delerium EXCLUDES any chronic, hereditary or degenerative conditions of the CNS such as obstructive hydrocephalus, Parkinson's, Alzheimer's	Not applicable
Rash	ACUTE condition that may present as consistent with smallpox (macules, papules, vesicles predominantly of face/arms/legs) SPECIFIC diagnosis of acute rash such as chicken pox in person > XX years of age (base age cut-off on data interpretation) or smallpox ACUTE non-specific diagnosis of rash compatible with infectious disease, such as viral exanthem EXCLUDES allergic or inflammatory skin conditions such as contact or seborrheaic dermatitis, rosacea EXCLUDES rash NOS, rash due to poison ivy, sunburn, and eczema	Smallpox
Specific Infection	ACUTE infection of known cause not covered in other syndrome groups, usually has more generalized symptoms (i.e., not just respiratory or gastrointestinal) INCLUDES septicemia from known bacteria INCLUDES other febrile illnesses such as scarlet fever	Not applicable

Syndrome Definitions for Diseases Associated with Critical Bioterrorism-associated Agents
(continued from previous page)

Syndrome	Definition	Category A Condition
Fever	ACUTE potentially febrile illness of origin not specified INCLUDES fever and septicemia not otherwise specified INCLUDES unspecified viral illness even though unknown if fever is present EXCLUDE entry in this syndrome category if more specific diagnostic code is present allowing same patient visit to be categorized as respiratory, neurological or gastrointestinal illness syndrome	Not applicable
Severe Illness or Death potentially due to infectious disease	ACUTE onset of shock or coma from potentially infectious causes EXCLUDES shock from trauma INCLUDES SUDDEN death, death in emergency room, intrauterine deaths, fetal death, spontaneous abortion, and still births EXCLUDES induced fetal abortions, deaths of unknown cause, and unattended deaths	Not applicable

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APPENDIX: ICD-9-CM CODES

Fever ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
020.2	PLAGUE, SEPTICEMIC	1
020.8	OTHER TYPES OF PLAGUE	1
020.9	PLAGUE NOS	1
021.8	TULAREMIA NEC	1
021.9	TULAREMIA NOS	1
022.3	ANTHRAX, SEPTICEMIA	1
022.8	ANTHRAX, OTHER SPECIFIED	1
022.9	ANTHRAX, UNSPECIFIED	1
038.3	ANAEROBES SEPTICEMIA	1
038.40	GRAM-NEGATIVE ORGANISM UN	1
038.49	SEPTICEMIA,OTHER GRAM-NEG	1
038.8	SEPTICEMIAS, OTHER SPECIF	1
038.9	SEPTICEMIA, NOS	1
079.89	VIRAL INFECTION OTHER S	1
079.99	VIRAL INFECTIONS UNSPECIFIED	1
780.31	FEBRILE CONVULSIONS	1
780.6	FEVER	1
790.7	BACTEREMIA	1
790.8	VIREMIA NOS	1
002.0	TYPHOID FEVER	3
002.1	PARATYPHOID FEVER A	3
002.2	PARATYPHOID FEVER B	3
002.3	PARATYPHOID FEVER C	3
002.9	PARATYPHOID FEVER NOS	3
003.1	Salmonella septicemia	3
023.0	BRUCELLA MELITENSIS	3
023.1	BRUCELLA ABORTUS	3
023.2	BRUCELLA SUIS	3
023.3	BRUCELLA CANIS	3
023.8	BRUCELLOSIS NEC	3
023.9	BRUCELLOSIS, UNSPECIFIED	3
024	GLANDERS	3
025	MELOIDOSIS	3
027.0	LISTERIOSIS	3
034.1	SCARLET FEVER	3
038.0	SEPTICEMIA STAPHYLOCOCCAL	3
038.10	SEPTICEMIA STAPHYLOCOCCAL	3
038.11	SEPTICEMIA STAPHYLOC. AUR	3
038.19	SEPTICEMIA STAPHYLOCOCCAL	3
038.2	PNEUMOCOCCAL SEPTICEMIA	3
038.41	SEPTICEMIA, HEMOPHILUS INFLUENZAE	3
038.42	SEPTICEMIA, E. COLI	3
038.43	PSEUDOMONAS	3

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Fever ICD-9-CM Code List, Cont'd

038.44	SEPTICEMIA SERRATIA	3
054.5	HERPETIC SEPTICEMIA	3
060.0	YELLOW FEVER, SYLVATIC	3
060.1	YELLOW FEVER, URBAN	3
060.9	YELLOW FEVER, UNSPEC	3
066.0	PHLEBOTOMUS FEVER	3
066.1	TICK-BORNE FEVER	3
066.2	VENEZUELAN EQUINE FEVER	3
066.3	MOSQUITO-BORNE FEVER NEC	3
066.8	ARTHROPOD VIRUS NEC	3
066.9	ARTHROPOD VIRUS NOS	3
078.2	SWEATING FEVER	3
080	LOUSE-BORNE TYPHUS	3
081.0	MURINE TYPHUS	3
081.1	BRILL'S DISEASE	3
081.2	SCRUB TYPHUS	3
081.9	TYPHUS NOS	3
082.8	TICK-BORNE RICKETTS NEC	3
082.9	TICK-BORNE RICKETTS NOS	3
083.0	Q FEVER	3
083.1	TRENCH FEVER	3
083.2	RICKETTSIALPOX	3
083.8	RICKETTSIOSES NEC	3
083.9	RICKETTSIOSIS	3
084.0	MALARIA, FALCIPARUM	3
084.1	VIVAX MALARIA	3
084.2	QUARTAN MALARIA	3
084.3	OVALE MALARIA	3
084.5	MIXED MALARIA	3
084.6	MALARIA UNSPECIFIED	3
086.2	CHAGA'S DISEASE WITHOUT MENTION OF ORG	3
086.3	TRYPANOSOMIASIS, GAMBIAN	3
086.4	TRYPANOSOMIASIS, RHODESIAN	3
086.5	TRYPANOSOMIASIS, AFRICAN	3
086.9	TRYPANOSOMIASIS, UNSPEC	3
087.0	LOUSE-BORNE RELAPS FEVER	3
087.1	TICK-BORNE RELAPS FEVER	3
087.9	RELAPSING FEVER NOS	3
088.0	BARTONELLOSIS	3
088.81	LYME DISEASE	3
088.82	BABESIOSIS	3
088.89	OTHER ARTHROPOD-BORNE	3
088.9	ARTHROPOD-BORNE DIS NOS	3
100.82	LEPTOSPIROSIS, OTHER	3

Hemr_ill ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
287.1	PLATELET DISORDER	1
287.2	NONTHROMBOCYTOPENIC PURPU	1
287.8	HEMORRHAGIC COND NEC	1
287.9	HEMORRHAGIC CONDITIONS UN	1
511.8	HEMOTHORAX	1
790.01	HEMATOCRIT, PRECIPITOUS D	1
790.92	ABNORMAL COAGULATION PROF	1
286.9	COAGULATION DEFECTS-UNSPE	2
287.3	THROMBOCYTOPENIA	2
287.4	THROMBOCYTOPENIA SECONDAR	2
287.5	THROMBOCYTOPENIA UNSPEC.	2
459.0	HEMORRHAGE NOS	2
578.0	HEMATEMESIS	2
578.1	MELENA	2
578.9	GASTROINTESTINAL HEMORRHA	2
782.7	ECCHYMOSIS,SPONTANEOUS,NO	2
784.7	EPISTAXIS	2
784.8	HEMORRHAGE FROM THROAT	2
786.3	HEMOPTYSIS	2
061	DENGUE	3
065.0	CRIMEAN HEMORRHAGIC FEV	3
065.1	OMSK HEMORRHAGIC FEVER	3
065.2	KYASANUR FOREST DISEASE	3
065.3	TICK-BORNE HEM FEVER NEC	3
065.4	MOSQUITO-BORNE HEM FEVER	3
065.8	ARTHROPOD HEM FEVER NEC	3
065.9	ARTHROPOD HEM FEVER NOS	3
077.4	EPIDEM HEM CONJUNCTIVIT	3
078.6	HEM NEPHROSONEPHRITIS	3
078.7	ARENAVIRAL HEM FEVER	3
084.8	BLACKWATER FEVER	3
100.0	LEPTOSPIROSIS, ICTOHEMORRHAGICA	3
283.11	HEMOLYTIC-UREMIC SYNDROME	3

Lesion ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
020.0	PLAGUE, BUBONIC	1
020.1	CELLULOCUTANEOUS PLAGUE	1
021.0	ULCEROGLANDUL TULAREMIA	1
022.0	CUTANEOUS ANTHRAX	1
680.0	CARBUNCLE FACE	1
680.1	CARBUNCLE NECK	1
680.2	CARBUNCLE TRUNK	1
680.3	CARBUNCLE ARM	1
680.4	CARBUNCLE HAND	1
680.5	CARBUNCLE BUTTOCK	1
680.6	CARBUNCLE LEG	1
680.7	FURUNCLE FOOT, HEEL, TOE	1
680.8	FURUNCLE HEAD/SCALP EXCEP	1
707.11	ULCER OF THIGH	1
707.12	ULCER OF CALF	1
707.13	ULCER OF ANKLE	1
707.14	ULCER OF HEEL AND MIDFOOT	1
707.19	ULCER OF LOWER LIMB,OTHER	1
680.9	BOIL NOS	2
681.00	CELLULITIS FINGER, NOS	2
681.01	FELON	2
681.02	ONYCHIA/PARONYCHIA OF FIN	2
681.11	ONYCHIA/PARONYCHIA OF TOE	2
681.9	CELLULITIS DIGIT, NOS	2
682.0	CELLULITIS FACE	2
682.1	CELLULITIS NECK	2
682.2	CELLUL/ABSCESS-TRUNK/ABDO	2
682.3	CELLULITIS/ABSCESS ARM	2
682.4	CELLULITIS/ABSCESS HAND/W	2
682.5	CELLULITIS BUTTOCK	2
682.6	CELLULITIS LEG	2
682.7	CELLULITIS FOOT	2
682.8	ABSCESS/CELLULITIS-HEAD/S	2
682.9	CELLULITIS NOS	2
707.10	ULCER OF LOWER LIMB, UNSP	2
707.15	ULCER OF FOOT, OTHER PART	2
027.1	ERYSIPELOTHRIX INFECTION	3
054.6	HERPETIC WHITLOW	3
081.2	SCRUB TYPHUS	3
082.1	BOUTONNEUSE FEVER	3
082.2	NORTH ASIAN TICK FEVER	3
082.3	QUEENSLAND TICK TYPHUS	3
085.1	LEISHMANIASIS, CUTANEOUS, URBAN	3

Lesion ICD-9-CM Code List, Cont'd

085.2	LEISHMANIASIS, CUTANEOUS, ASIAN DESERT	3
085.3	LEISHMANIASIS, ETHIOPIAN	3
085.4	LEISHMANIASIS, CUTANEOUS AMERICAN	3
085.5	LEISHMANIASIS, MUCOCUTANEOUS, AMERICAN	3
086.2	CHAGA'S DISEASE WITHOUT MENTION OF ORG	3
086.3	TRYPANOSOMIASIS, GAMBIAN	3
086.5	TRYPANOSOMIASIS, AFRICAN	3
091.2	SYPHILIS (PRIMARY NEC)	3
103.0	PINTA, PRIMARY LESIONS	3
103.9	PINTA, UNSPEC	3
114.0	PRIMARY COCCIDIOIDOMYCOS	3
117.1	SPOROTRICHOSIS	3
911.4	Superficial inj/trunk, insect bite non-veno, no infect	3
911.5	Superficial inj/trunk, insect bite non-veno, infection	3
912.4	Superficial inj/shoulder/upper arm, insect bite non-veno, no infect	3
912.5	Superficial inj/shoulder/upper arm, insect bite non-veno, infection	3
913.4	Superficial inj/elbow,forearm,wrist, insect bite non-veno, no infect	3
913.5	Superficial inj/elbow,forearm,wrist, insect bite non-veno, infection	3
915.4	Superficial inj/finger(s), insect bite non-veno, no infect	3
915.5	Superficial inj/finger(s) insect bite non-veno, infection	3
916.4	Superficial inj/hip,thigh,leg,ankle, insect bite non-veno, no infect	3
916.5	Superficial inj/hip,thigh,leg,ankle insect bite non-veno, infection	3
917.4	Superficial inj/foot, toe(s), insect bite non-veno, no infect	3
917.5	Superficial inj/foot, toe(s), insect bite non-veno, infection	3
918	Superficial inj/eyelids, periocular area, insect bite	3
919.4	Superficial inj/other,multiple,unspec insect bite non-veno, no infect	3
919.5	Superficial inj/other, multiple, unspec insect bite non-veno, infection	3
E906.4	Bite of non-venomous arthropod/insect bite NOS	3

Lymph ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
020.0	PLAGUE, BUBONIC	1
021.0	ULCEROGLANDUL TULAREMIA	1
021.3	TULAREMIA, OCULOGLANDULAR	1
075	MONONUCLEOSIS, INFECTIOUS	1
289.3	LYMPHADENITIS NOS	1
683	ADENITIS, GANGRENOUS, ACU	1
785.6	LYMPH NODE ENLARGEMENT	1
026.0	SPIRILLARY FEVER	3
027.2	PASTEURELLOSIS	3
078.3	CAT-SCRATCH DISEASE	3
081.2	SCRUB TYPHUS	3
082.1	BOUTONNEUSE FEVER	3
082.2	NORTH ASIAN TICK FEVER	3
082.3	QUEENSLAND TICK TYPHUS	3
083.2	RICKETTSIALPOX	3
085.0	LEISHMANIASIS, VISCERAL	3
086.2	CHAGA'S DISEASE WITHOUT MENTION OF ORG	3
086.3	TRYPANOSOMIASIS, GAMBIAN	3
086.5	TRYPANOSOMIASIS, AFRICAN	3
088.0	BARTONELLOSIS	3
091.4	SYPHILITIC ADENOPATHY	3
099.0	CHANCROIOD	3
099.1	LYMPHOGRANULOMA VENEREUM	3
117.1	SPOROTRICHOSIS	3
125.0	BANCROFTIAN FILARIASIS	3
125.1	MALAYAN FILARIASIS	3

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Bot_Like ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
005.1	BOTULISM	1
344.04	QUADRIPLE/QUADRIPA.C5-C7	1
344.09	QUADRIPLEGIA/QUADRIPARESI	1
344.2	DIPLEGIA OF UPPER LIMBS	1
344.89	PARALYTIC SYNDROME, OTHR	1
344.9	PARALYSIS	1
351.9	FACIAL NERVE DISORDER UNS	1
352.6	CRANIAL NERVE PALSIES,MUL	1
352.9	CRANIAL NERVE DISORDER, U	1
357.0	GUILLAIN-BARRE SYNDROME	1
368.2	DIPLOPIA	1
374.30	PTOSIS OF EYELID, UNSPECI	1
378.51	NERV PALSY 3RD OR OCULOMO, PARTIAL	1
378.52	NERV PALSY 3RD OR OCULOMO, TOTAL	1
378.53	NERV PALSY 4TH OR TROCHLEAR	1
378.54	SIXTH OR ABDUCENS NERVE P	1
378.55	RECTUS PALSY (MEDIAL)	1
342.90	HEMIPLEGIA/HEMIPARESIS UN	2
344.00	QUADRIPLEGIA, UNSPECIFIED	2
344.1	PARAPLEGIA	2
351.0	BELL'S PALSY	2
351.8	NEURALGIA FACIAL	2
358.0	MYASTHENIA GRAVIS	2
368.8	VISUAL DISTURBANCES ;SPEC	2
368.9	VISUAL DISTURBANCE UNSPEC	2
784.3	APHASIA	2
784.5	SPEECH DISTURBANCE	2
787.2	DYSPHAGIA	2
037	TETANUS	3
350.8	TRIGEMINAL NERVE DISORDER, OTHER SPECIFIED	3
350.9	TRIGEMINAL NERVE DISORDER, UNSPECIFIED	3
352.0	OLFACTORY (1ST) CN DISORDERS	3
352.1	GLOSSOPHARYNGEAL NEURALGI	3
352.2	GLOSSOPHARYNGEAL, OTHER DISORDERS	3
352.3	DISORD. PNEUMOGASTRIC 10T	3
352.4	ACCESSORY (11TH) DISORDERS	3
352.5	HYPOGLOSSAL NERVE (12TH) DISORDERS	3
374.31	PARALYTIC PTOSIS	3
378.50	PARALYTIC STRABISMUS, UNSPEC	3
378.56	EXTERNAL OPTHALMOPLEGIA	3
527.7	XEROSTOMIA (DRY MOUTH)	3

GI-Total ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus	U or L
005.89	FOOD POISONING, OTHER BAC	1	L
005.9	FOOD POISONING NOS	1	L
008.49	INTEST. INFECT BY OTHER B	1	L
008.5	BACTERIAL ENTERITIS NOS	1	L
008.69	ENTERITIS VIRAL OTHER	1	L
008.8	ENTERITIS VIRAL NOS	1	L
009.0	ENTERITIS/COLITIS/GASTRO.	1	L
009.1	COLITIS ENTERIT,GASTRO,IN	1	L
009.2	DIARRHEA, INFECTIOUS NOS	1	L
009.3	DIARRHEA OF INFECT ORIG	1	L
022.2	GASTROINTESTINAL ANTHRAX	1	L
078.82	EPIDEMIC VOMITING SYND	1	U
535.00	GASTRITIS, ACUTE	1	U
535.01	GASTRITIS, WITH HEMORRHAG	1	U
535.40	GASTRITIS,W/O HEM. OTHER	1	U
535.41	GASTRITIS,OTH SPEC. W/HEM	1	U
535.50	GASTRITIS/GASTRODUOD. W/O	1	U
535.51	ASTRITIS/DUODEN W/O HEMO	1	U
535.60	DUODENITIS W/O HEMORRHAGE	1	U
535.61	DUODENITIS W/ HEMORRHAGE	1	U
536.2	VOMITING PERSISTENT	1	U
555.0	ENTERITIS SMALL INTESTINE	1	L
555.1	REG ENTERITIS, LG INTEST	1	L
555.2	REG ENTERIT SM/LG INTEST	1	L
558.2	GASTROENTERITIS/COLITIS,	1	L
558.9	GASTROENTERITIS/COLITIS N	1	L
569.9	INTESTINAL DISORDER NOS	1	L
787.01	NAUSEA WITH VOMITING	1	U
787.02	NAUSEA ALONE	1	U
787.03	VOMITING ALONE	1	U
787.3	FLATUL/ERUCTAT/GAS PAIN	1	L
787.91	DIARRHEA	1	L
567.1	PNEUMOCOCCAL PERITONITIS	2	L
567.2	PERITONITIS SUPPURATIVE	2	L
567.8	PERITONITIS, OTHER SPECIF	2	L
567.9	PERITONITIS NOS	2	L
568.9	PERITONEAL DISORDER NOS	2	L
578.0	HEMATEMESIS	2	U
787.1	HEARTBURN/PYROSIS	2	U
787.2	DYSPHAGIA	2	U
789.00	ABDOMINAL PAIN,UNSPECIF.	2	L
789.01	ABDOMINAL PAIN,RIGHT UPPE	2	L
789.02	ABDOMINAL PAIN,LEFT UPPER	2	L
789.03	ABDOMINAL PAIN,RIGHT LOW	2	L
789.04	ABDOMINAL PAIN,LEFT LOWER	2	L

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GI-Total ICD-9-CM Code List, Cont'd

789.05	ABDOMINAL PAIN,PERIUMBILI	2	L
789.06	ABDOMINAL PAIN,EPIGASTRIC	2	L
789.07	ABDOMINAL PAIN,GENERALIZE	2	L
789.09	ABDOMINAL PAIN,OTHER SPEC	2	L
789.60	ABDOMINAL TENDERNESS, UNS	2	L
789.61	ABDOMINAL TENDERNESS,RUQ	2	L
789.62	ABDOMINAL TENDERNESS,LUQ	2	L
789.63	ABDOMINAL TENDERNESS.RLQ	2	L
789.64	ABDOMINAL TENDERNESS,LLQ	2	L
789.65	ABDOMINAL TENDERNESS PERI	2	L
789.66	ABDOMINAL TENDERNESS EPIG	2	L
789.67	ABDOMINAL TENDERNESS GENE	2	L
789.69	ABDOMINAL TENDERNESS,OT S	2	L
789.9	ABDOMEN/PELVIS SYMPTOMS O	2	L
001.0	CHOLERA D/T VIB CHOLERAE	3	L
001.1	CHOLERA D/T VIB EL TOR	3	L
001.9	CHOLERA NOS	3	L
003.0	SALMONELLA GASTROENTERITI	3	L
003.20	LOCAL SALMONELLA INF NOS	3	L
003.29	LOCAL SALMONELLA INF NEC	3	L
003.8	SALMONELLA INFECTION NEC	3	L
003.9	SALMONELLA INFECTION UNSP	3	L
004.0	SHIGELLA DYSENTERIAE	3	L
004.1	SHIGELLA FLEXNERI	3	L
004.2	SHIGELLA BOYDII	3	L
004.3	SHIGELLA SONNEI	3	L
004.8	SHIGELLA INFECTIONS OTHER	3	L
004.9	SHIGELLOSIS, UNSPECIFIED	3	L
005.0	STAPH FOOD POISONING	3	U
005.2	FOOD POIS D/T C. PERFRIN	3	L
005.3	FOOD POIS: CLOSTRID NEC	3	L
005.4	FOOD POIS: V. PARAHAEM	3	L
005.81	FOOD POISON-VIBRIO VULNIF	3	L
006.0	AC AMEBIASIS W/O ABSCESS	3	L
006.8	AMEBIC INFECTION NEC	3	L
006.9	AMEBIASIS UNSPECIFIED	3	L
007.0	BALANTIDIASIS	3	L
007.1	GIARDIASIS	3	L
007.2	COCCIDIOSIS	3	L
007.3	INTEST TRICHOMONIASIS	3	L
007.4	CRYPTOSPORIDOSIS	3	L
007.5	CYCLOSPORIASIS	3	L
007.8	PROTOZOAL INTEST DIS NEC	3	L
007.9	PROTOZOAL INTEST DIS NOS	3	L
008.00	E.COLI,UNSP.(ESCHERICHIA	3	L
008.01	ENTRPATHOGENIC E COLI	3	L
008.02	ENTEROTOXIGENIC E COLI	3	L

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GI-Total ICD-9-CM Code List, Cont'd

008.03	ENTEROINVASIVE E COLI	3	L
008.04	ENTEROHEMORRAGIE E COLI	3	L
008.09	OTHER E COLI ENTERITIS	3	L
008.1	ARIZONA ENTERITIS	3	L
008.2	AEROBACTER ENTERITIS	3	L
008.3	PROTEUS ENTERITIS	3	L
008.41	STAPHYLOCOCC ENTERITIS	3	L
008.43	CAMPYLOBACTER ENTERITIS	3	L
008.44	YERSINIA ENTEROCOLITICA	3	L
008.45	CLOSTRIDIUM DIFFICILE	3	L
008.46	INTESTINAL INF.DUE TO ANA	3	L
008.47	GRAM-NEG ENTERITIS NEC	3	L
008.61	ENTERITIS D/T ROTAVIRUS	3	L
008.62	ENTERITIS D/T ADENOVIRUS	3	L
008.63	ENTERITIS D/T NORWALK VIRUS	3	L
008.64	ENTERITIS D/T SMALL ROUND VIRUS NEC	3	L
008.65	ENTERITIS D/T CALCIVIRUS	3	L
008.66	ENTERITIS D/T ASTROVIRUS	3	L
008.67	ENTERITIS DUE TO ENTEROVIRUS NOT ELSEWHERE CLASSIFIED	3	L
021.1	TULAREMIA, ENTERIC	3	L
127.0	ASCARIASIS	3	L
127.1	ANISAKIASIS	3	L
127.2	STRONGYLOIDIASIS	3	L
127.3	TRICHURIASIS	3	L
127.4	ENTEROBIASIS	3	L
127.5	CAPILLARIASIS	3	L
127.6	TRICHOSTRONGYLIASIS	3	L
127.7	INTEST HELMINTHIASIS NEC	3	L
127.8	MIXED INTESTINE HELMINTH	3	L
127.9	INTESTINAL HELMINTHIASIS,	3	L
129	INTESTINAL PARASITISM UNS	3	L
567.0	PERITONITIS IN INFEC DIS	3	L
787.4	PERISTALSIS, VISIBLE	3	L

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GI-Lower ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus	Lower GI
005.89	FOOD POISONING, OTHER BAC	1	L
005.9	FOOD POISONING NOS	1	L
008.49	INTEST. INFECT BY OTHER B	1	L
008.5	BACTERIAL ENTERITIS NOS	1	L
008.69	ENTERITIS VIRAL OTHER	1	L
008.8	ENTERITIS VIRAL NOS	1	L
009.0	ENTERITIS/COLITIS/GASTRO.	1	L
009.1	COLITIS ENTERIT,GASTRO,IN	1	L
009.2	DIARRHEA, INFECTIOUS NOS	1	L
009.3	DIARRHEA OF INFECT ORIG	1	L
022.2	GASTROINTESTINAL ANTHRAX	1	L
555.0	ENTERITIS SMALL INTESTINE	1	L
555.1	REG ENTERITIS, LG INTEST	1	L
555.2	REG ENTERIT SM/LG INTEST	1	L
558.2	GASTROENTERITIS/COLITIS,	1	L
558.9	GASTROENTERITIS/COLITIS N	1	L
569.9	INTESTINAL DISORDER NOS	1	L
787.3	FLATUL/ERUCTAT/GAS PAIN	1	L
787.91	DIARRHEA	1	L
567.1	PNEUMOCOCCAL PERITONITIS	2	L
567.2	PERITONITIS SUPPURATIVE	2	L
567.8	PERITONITIS, OTHER SPECIF	2	L
567.9	PERITONITIS NOS	2	L
568.9	PERITONEAL DISORDER NOS	2	L
789.00	ABDOMINAL PAIN,UNSPECIF.	2	L
789.01	ABDOMINAL PAIN,RIGHT UPPE	2	L
789.02	ABDOMINAL PAIN,LEFT UPPER	2	L
789.03	ABDOMINAL PAIN,RIGHT LOW	2	L
789.04	ABDOMINAL PAIN,LEFT LOWER	2	L
789.05	ABDOMINAL PAIN,PERIUMBILI	2	L
789.06	ABDOMINAL PAIN,EPIGASTRIC	2	L
789.07	ABDOMINAL PAIN,GENERALIZE	2	L
789.09	ABDOMINAL PAIN,OTHER SPEC	2	L
789.60	ABDOMINAL TENDERNESS, UNS	2	L
789.61	ABDOMINAL TENDERNESS,RUQ	2	L
789.62	ABDOMINAL TENDERNESS,LUQ	2	L
789.63	ABDOMINAL TENDERNESS.RLQ	2	L
789.64	ABDOMINAL TENDERNESS,LLQ	2	L
789.65	ABDOMINAL TENDERNESS PERI	2	L
789.66	ABDOMINAL TENDERNESS EPIG	2	L
789.67	ABDOMINAL TENDERNESS GENE	2	L
789.69	ABDOMINAL TENDERNESS,OT S	2	L
789.9	ABDOMEN/PELVIS SYMPTOMS O	2	L
001.0	CHOLERA D/T VIB CHOLERAE	3	L

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GI-Lower ICD-9-CM Code List, Cont'd

001.1	CHOLERA D/T VIB EL TOR	3	L
001.9	CHOLERA NOS	3	L
003.0	SALMONELLA GASTROENTERITI	3	L
003.20	LOCAL SALMONELLA INF NOS	3	L
003.29	LOCAL SALMONELLA INF NEC	3	L
003.8	SALMONELLA INFECTION NEC	3	L
003.9	SALMONELLA INFECTION UNSP	3	L
004.0	SHIGELLA DYSENTERIAE	3	L
004.1	SHIGELLA FLEXNERI	3	L
004.2	SHIGELLA BOYDII	3	L
004.3	SHIGELLA SONNEI	3	L
004.8	SHIGELLA INFECTIONS OTHER	3	L
004.9	SHIGELLOSIS, UNSPECIFIED	3	L
005.2	FOOD POIS D/T C. PERFRIN	3	L
005.3	FOOD POIS: CLOSTRID NEC	3	L
005.4	FOOD POIS: V. PARAHAEM	3	L
005.81	FOOD POISON-VIBRIO VULNIF	3	L
006.0	AC AMEBIASIS W/O ABSCESS	3	L
006.8	AMEBIC INFECTION NEC	3	L
006.9	AMEBIASIS UNSPECIFIED	3	L
007.0	BALANTIDIASIS	3	L
007.1	GIARDIASIS	3	L
007.2	COCCIDIOSIS	3	L
007.3	INTEST TRICHOMONIASIS	3	L
007.4	CRYPTOSPORIDOSIS	3	L
007.5	CYCLOSPORIASIS	3	L
007.8	PROTOZOAL INTEST DIS NEC	3	L
007.9	PROTOZOAL INTEST DIS NOS	3	L
008.00	E.COLI,UNSP.(ESCHERICHIA	3	L
008.01	ENTRPATHOGENIC E COLI	3	L
008.02	ENTEROTOXIGENIC E COLI	3	L
008.03	ENTEROINVASIVE E COLI	3	L
008.04	ENTEROHEMORRAGIE E COLI	3	L
008.09	OTHER E COLI ENTERITIS	3	L
008.1	ARIZONA ENTERITIS	3	L
008.2	AEROBACTER ENTERITIS	3	L
008.3	PROTEUS ENTERITIS	3	L
008.41	STAPHYLOCOCC ENTERITIS	3	L
008.43	CAMPYLOBACTER ENTERITIS	3	L
008.44	YERSINIA ENTEROCOLITICA	3	L
008.45	CLOSTRIDIUM DIFFICILE	3	L
008.46	INTESTINAL INF.DUE TO ANA	3	L
008.47	GRAM-NEG ENTERITIS NEC	3	L
008.61	ENTERITIS D/T ROTAVIRUS	3	L
008.62	ENTERITIS D/T ADENOVIRUS	3	L
008.63	ENTERITIS D/T NORWALK VIRUS	3	L
008.64	ENTERITIS D/T SMALL ROUND VIRUS NEC	3	L
008.65	ENTERITIS D/T CALCIVIRUS	3	L

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GI-Lower ICD-9-CM Code List, Cont'd

008.66	ENTERITIS D/T ASTROVIRUS	3	L
008.67	ENTERITIS DUE TO ENTEROVIRUS NOT ELSEWHERE CLASSIFIED	3	L
021.1	TULAREMIA, ENTERIC	3	L
127.0	ASCARIASIS	3	L
127.1	ANISAKIASIS	3	L
127.2	STRONGYLOIDIASIS	3	L
127.3	TRICHURIASIS	3	L
127.4	ENTEROBIASIS	3	L
127.5	CAPILLARIASIS	3	L
127.6	TRICHOSTRONGYLIASIS	3	L
127.7	INTEST HELMINTHIASIS NEC	3	L
127.8	MIXED INTESTINE HELMINTH	3	L
127.9	INTESTINAL HELMINTHIASIS,	3	L
129	INTESTINAL PARASITISM UNS	3	L
567.0	PERITONITIS IN INFEC DIS	3	L
787.4	PERISTALSIS, VISIBLE	3	L

(continued from previous page)

GI-Upper ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus	Upper GI
078.82	EPIDEMIC VOMITING SYND	1	U
535.00	GASTRITIS, ACUTE	1	U
535.01	GASTRITIS, WITH HEMORRHAG	1	U
535.40	GASTRITIS,W/O HEM OTHER	1	U
535.41	GASTRITIS,OTH SPEC W/HEM	1	U
535.50	GASTRITIS/GASTRODUOD. W/O	1	U
535.51	.ASTRITIS/DUODEN W/O HEMO	1	U
535.60	DUODENITIS W/O HEMORRHAGE	1	U
535.61	DUODENITIS W/ HEMORRHAGE	1	U
536.2	VOMITING PERSISTENT	1	U
787.01	NAUSEA WITH VOMITING	1	U
787.02	NAUSEA ALONE	1	U
787.03	VOMITING ALONE	1	U
578.0	HEMATEMESIS	2	U
787.1	HEARTBURN/PYROSIS	2	U
787.2	DYSPHAGIA	2	U
005.0	STAPH FOOD POISONING	3	U

(continued from previous page)

Neuro ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
047.8	MENINGITIS, VIRAL NEC	1
047.9	MENINGITIS, VIRAL NOS	1
048	DIS ENTEROVIRAL OF CNS, NEC	1
049.0	CHORIOMENINGITIS, LYMPHOCYTIC	1
049.9	ENCEPHALITIS VIRAL NOS	1
320.9	BACTERIAL MENINGITIS NOS	1
321.2	MENINGITIS D/T VIRAL DISEASES NEC	1
322.0	MENINGITIS, NONPYOGENIC	1
322.1	MENINGITIS, EOSINOPHILIC	1
322.9	MENINGITIS NOS	1
323.8	OTHER CAUSES OF ENCEPHALI	1
323.9	ENCEPHALITIS NOS	1
348.3	ENCEPHALOPATHY NOS	1
781.6	MENINGISMUS	1
293.0	DELIRIUM, ACUTE	2
293.1	CONFUSIONAL STATE(DEL SUBACUTE)	2
307.81	TENSION HEADACHE	2
780.02	ALTERATION OF AWARENESS/T	2
780.09	ALTERATION OF AWARENESS	2
780.39	CONVULSIONS, OTHER	2
784.0	HEADACHE	2
784.3	APHASIA	2
003.21	SALMONELLA MENINGITIS	3
036.0	MENINGITIS (MENINGOCOCCAL)	3
036.1	ENCEPHALITIS, MENINGOCCAL	3
036.2	MENINGOCOCCEMIA INFECTION	3
036.89	INFECTION, MENINGOCCAL NEC	3
036.9	INFECTION, MENINGOCCAL NOS	3
047.0	COXSACKIE DUE TO MENINGIT	3
047.1	MENINGITIS D/T ECHO VIRUS	3
049.1	MENINGITIS, ADENOVIRUS	3
049.8	OTHER SPECIFIED NON-ARTHORPOD-BORNE VIRAL DIS	3
052.0	POSTVARICELLA ENCEPHALIT	3
053.0	HERPES ZOSTER WITH MENINGITIS	3
053.10	HERPES ZOSTER W UNSPED NER S	3
054.3	HERPETIC MENINGOENCEPHALI	3
054.72	HSV, MENINGITIS	3
055.0	POSTMEASLES ENCEPHALITIS	3
056.00	RUBELLA, UNSPEC NEURO COMPLIC	3
056.01	RUBELLA, ENCEPHALOMYELITIS	3
056.09	RUBELLA, OTHER NEURO COMPLI	3
061	DENGUE	3
062.0	ENCEPHALITIS, JAPANESE	3
062.1	ENCEPHALITIS, WESTERN EQUINE	3

(continued from previous page)

Neuro ICD-9-CM Code List, Cont'd

062.2	ENCEPHALITIS, EASTERN EQUINE	3
062.3	ST. LOUIS ENCEPHALITIS	3
062.4	ENCEPHALITIS, AUSTRALIAN	3
062.5	ENCEPHALITIS, CALIFORNIA VIRUS	3
062.8	ENCEPHALITIS, MOSQUITO-BORNE NEC	3
062.9	ENCEPHALITIS, MOSQUITO-BORNE NOS	3
063.0	ENCEPHALITIS, RUSSIAN SPRING-SUMME	3
063.1	LOUPING ILL	3
063.2	ENCEPHALITIS, CENTRAL EUROPEAN	3
063.8	ENCEPHALITIS, VIRAL, TICK-BORNE NEC	3
063.9	ENCEPHALITIS, TICK-BORNE VIRAL NOS	3
064	ENCEPHALITIS, ARTHPD-BORNE VIRAL NE	3
066.4	WEST NILE FEVER	3
071	RABIES	3
072.1	MUMPS MENINGITIS	3
072.2	MUMPS ENCEPHALITIS	3
084.9	MALARIA COMPLICATED NEC	3
086.2	CHAGA'S DISEASE W/O MENTION OF ORG	3
086.3	TRYPANOSOMIASIS, GAMBIAN	3
086.4	TRYPANOSOMIASIS, RHODESIAN	3
086.5	TRYPANOSOMIASIS, AFRICAN	3
091.81	ACUTE SYPHIL MENINGITIS	3
098.82	GONOCCOCAL, MENINGITIS	3
100.81	LEPTOSPIRAL INFECTION, MENG(ASEPTIC)	3
114.2	COCCIDIODAL MENINGITIS	3
115.01	HISTOPLASMOSIS MENINGITIS	3
115.11	HISTOPLASMA DUBOISII, MENINGITIS	3
115.91	HISTOPLASMOSIS, UNSPEC, MENINGITIS	3
117.5	CRYPTOCOCCOSIS	3
130.0	TOXOPLASMOSIS, MENINGOENCEPHALITIS	3
136.2	SPECIFIC INF BY FREE LIVING AMOEBA	3
320.0	HEMOPHILUS MENINGITIS	3
320.1	MENINGITIS, PNEUMOCOCCAL	3
320.2	MENINGITIS, STREPTOCOCCAL	3
320.3	MENINGITIS, STAPHYLOCCAL	3
320.7	MENG, IN OTH BCTRL DISEASE CE	3
320.81	MENINGITIS, D/T ANAEROBIC BACTERIA	3
320.82	MENINGITIS DUE TO GRAM-NE,	3
320.89	MENINGITIS DUE TO OTHER S	3
321	MENINGITIS, CRYPTOCCAL	3
321.1	MENINGITIS IN OTH FUNGAL,	3
321.3	MENINGITIS D/T TRYPANOSOMIASIS	3
321.4	MENINGITIS IN SARCOIDOSIS	3
321.8	MENG D/T OTH NONBACT ORGANISM CE	3
323.0	ENCEPHALITIS IN VIRAL DISEASE CE	3
323.1	ENCEPHALITIS IN RICKETTSIAL DIS CE	3
323.2	ENCEPHALITIS IN PROTOZOAL DIS CE	3

(continued from previous page)

Neuro ICD-9-CM Code List, Cont'd

323.4	ENCEPHALITIS, OTH D/T INFECTION CE	3
323.5	ENCEPHALITIS, POSTIMMUNIZATION	3
323.6	ENCEPHALITIS POSTINFECTIO	3
323.7	ENCEPHALITIS, TOXIC	3

(continued from previous page)

Rash ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
050.0	SMALL POX, VARIOLA MAJOR	1
050.1	SMALL POX, ALASTRIM	1
050.2	SMALL POX, MODIFIED	1
050.9	SMALLPOX NOS	1
051.0	COWPOX	1
051.1	PSEUDOCOWPOX	1
052.7	VARICELLA COMPLICAT NEC	1
052.8	VARICELLA W/UNSPECIFIED C	1
052.9	VARICELLA NOS	1
057.8	EXANTHEMATA VIRAL OTHER S	1
057.9	EXANTHEM VIRAL, UNSPECIFI	1
695.0	ERYTHEMA TOXIC	1
695.1	ERYTHEMA MULTIFORME	1
695.2	ERYTHEMA NODOSUM	1
695.89	ERYTHEMATOUS CONDITIONS O	1
695.9	ERYTHEMATOUS CONDITION N	1
692.9	DERMATITIS UNSPECIFIED CA	2
782.1	RASH/OTHER NONSPEC SKIN E	2
026.0	SPIRILLARY FEVER	3
026.1	STREPTOBACILLARY FEVER	3
026.9	RAT-BITE FEVER UNSPECIFIED	3
051.2	DERMATITIS PUSTULAR, CONT	3
051.9	PARAVACCINIA NOS	3
053.20	HERPES ZOSTER DERMATITIS E	3
053.79	HERPES ZOSTER WITH OTHER SPECIF COMPLIC	3
053.8	H.Z. W/ UNSPEC. COMPLICATION	3
053.9	HERPES ZOSTER NOS W/O COM	3
054.0	ECZEMA HERPETICUM	3
054.79	HERPES SIMPLEX W/OTH.SPEC	3
054.8	HERPES SIMPLEX, W/UNS.COM	3
054.9	HERPES SIMPLEX NOS	3
055.79	MEASLES COMPLICATION NEC	3
055.8	MEASLES COMPLICATION NOS	3
055.9	MEASLES UNCOMPLICATED	3
056.79	RUBELLA COMPLICATION NEC	3
056.8	RUBELLA COMPLICATION NOS	3
056.9	RUBELLA UNCOMPLICATED	3
057.0	ERYTHEMIA INFECT.(5TH DIS	3
074.3	HAND/FOOT AND MOUTH DISEA	3
078.0	MOLLUSCUM CONTAGIOSUM	3
082.0	ROCKY MOUNTAIN SPOTTED FE	3
083.2	RICKETTSIALPOX	3
695.3	ROSACEA	3
695.4	LUPUS ERYTHEMATOSUS	3

(continued from previous page)

Resp ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
020.3	PRIMARY PNEUMONIC PLAGUE	1
020.4	SECONDARY PNEUMON PLAGUE	1
020.5	PNEUMONIC PLAGUE NOS	1
021.2	PULMONARY TULAREMIA	1
022.1	PULMONARY ANTHRAX	1
460	NASOPHARYNGITIS, ACUTE	1
462	PHARYNGITIS, ACUTE NOS	1
463	TONSILLITIS, ACUTE	1
464.00	LARYNGITIS, AC.W/O OBSTRU	1
464.01	LARYNGITIS, AC.W/OBSTRUCT	1
464.10	TRACHEITIS W/O OBSTRUCTIO	1
464.11	AC TRACHEITIS W OBSTRUCT	1
464.20	LARYNGOTRACHEITIS W/O OBS	1
464.21	AC LARYNGOTRACH W OBSTR	1
464.30	EPIGLOTTITIS ACUTE W/O OB	1
464.31	AC EPIGLOTTITIS W OBSTR	1
464.4	CROUP	1
464.50	SUPRAGLOTTIS,UNS.W/O OBST	1
464.51	SUPRAGLOTTIS,UNS.W/ OBST	1
465.0	LARYNGOPHARYNGITIS, ACUTE	1
465.8	URI, OTHER MULT. SITES	1
465.9	URI, ACUTE NOS	1
466.0	BRONCHITIS ACUTE	1
466.11	BRONCHIOLITIS ACUTE DUE T	1
466.19	BRONCHIOLITIS DUE TO OT/I	1
478.9	RESPIRATORY TRACT DISEASE	1
480.8	VIRAL PNEUMONIA NEC	1
480.9	PNEUMONIA, VIRAL	1
482.9	PNEUMONIA, BACTERIAL NOS	1
483.8	PNEUMONIA D/T ORGANISM NEC	1
484.5	PNEUMONIA IN ANTHRAX	1
484.8	PNEUM IN INFECT DIS NEC	1
485	BRONCHOPNEUMONIA ORGANISM	1
486	PNEUMONIA, ORGANISM NOS	1
490	BRONCHITIS NOS	1
511.0	PLEURISY W/O EFFUSION	1
511.1	PLEURAL EFFUSION-VIRAL(NO	1
511.8	HEMOTHORAX	1
513.0	ABSCESS LUNG	1
513.1	ABSCESS OF MEDIASTINUM	1
518.4	EDEMA LUNG ACUTE NOS	1
518.84	RESPIRATORY FAILURE,ACUTE	1
519.2	MEDIASTINITIS	1
519.3	MEDIASTINUM, DISEASES NEC	1
769	RESPIRATORY DISTRESS SYND	1
786.00	RESPIRATORY ABNORMALITY	1

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Resp ICD-9-CM Code List, Cont'd

786.06	TACHYPNEA	1
786.1	STRIDOR	1
786.2	COUGH	1
786.3	HEMOPTYSIS	1
786.52	PAINFUL RESPIRAT./PLEUROD	1
799.1	RESPIRATORY ARREST	1
075	MONONUCLEOSIS, INFECTIOUS	2
381.00	OTITIS MEDIA NONSUP ACUTE	2
381.01	OTITIS MEDIA SEROUS ACUTE	2
381.03	OM, ACUTE SANGUINOS	2
381.04	OM, ACUTE ALLERGIC SEROUS	2
381.4	OTITIS MEDIA NONSUPPURATI	2
381.50	EUSTACHIAN SALPINGITIS, U	2
381.51	EUSTACHIAN SALPINGITIS AC	2
382	OM SUPPURATIVE & UNSPEC	2
382.0	OM, ACUTE SUPPURATIVE	2
382.00	OTITIS MEDIA SUPP. ACUTE	2
382.01	OTITIS MEDIA SUP.W/EARDRU	2
382.02	OTITIS MEDIA SUPP.ACUTE I	2
382.4	OM, SUPPURATIVE NOS	2
382.9	OTITIS MEDIA NOS	2
461.0	MAXILLARY SINUSITIS, ACUT	2
461.1	SINUSITIS, FRONTAL-ACUTE	2
461.2	SINUSITIS, ETHMOIDAL	2
461.3	SINUSITIS,ACUTE SPHENOIDA	2
461.8	SINUSITIS, ACUTE, OTHER	2
461.9	SINUSITIS, ACUTE NOS	2
493.00	ASTHMA EXTRINSIC W/O STAT	2
493.01	ASTHMA, EXTRINSIC W/ASTHM	2
493.02	ASTHMA,EXTRINSIC W/AC.EXA	2
493.10	ASTHMA, INTRINSIC W/O AST	2
493.11	ASTHMA, INTRINSIC W/ASTHM	2
493.12	ASTHMA INTRINSIC W/AC.EXA	2
493.90	ASTHMA W/O STATUS ASTHMAT	2
493.91	ASTHMA W/ STATUS ASTHMATI	2
493.92	ASTHMA UNSPEC.W/AC.EXACER	2
511.9	PLEURAL EFFUSION UNSPECIF	2
514	EDEMA PULMONARY	2
518.0	PULMONARY COLLAPSE	2
518.81	RESPIRATORY FAILURE, ACUT	2
518.82	PULMONARY INSUFFICIENCY	2
782.5	CYANOSIS	2
784.1	PAIN IN THROAT	2
786.05	SHORTNESS OF BREATH	2
786.07	WHEEZING	2
786.09	DYSPNEA/RESP.ABNORMALITIE	2
786.50	CHEST PAIN, UNSPECIFIED	2

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Resp ICD-9-CM Code List, Cont'd

786.51	PRECORDIAL PAIN	2
786.59	CHEST PAIN, OTHER	2
786.7	ABNORMAL CHEST SOUNDS	2
786.9	RESP SYS/CHEST SYMP NEC	2
003.22	SALMONELLA PNEUMONIA	3
031.0	MYCOBACTERIA, PULMONARY	3
031.8	MYCOBACTERIAL DIS NEC	3
031.9	MYCOBACTERIA DISEASES/UNS	3
032.0	FAUCIAL DIPHTHERIA	3
032.1	NASOPHARYNX DIPHTHERIA	3
032.2	ANT NASAL DIPHTHERIA	3
032.3	LARYNGEAL DIPHTHERIA	3
032.89	DIPHTHERIA NEC	3
032.9	DIPHTHERIA NOS	3
033.0	BORDETELLA PERTUSSIS	3
033.1	BORDETELLA PARAPERTUSSIS	3
033.8	WHOOPING COUGH NEC	3
033.9	WHOOPING COUGH(UNSPE.ORGA	3
034.0	STREP SORE THROAT	3
052.1	VARICELLA WITH PNEUMONIA	3
055.1	POSTMEASLES PNEUMONIA	3
055.2	POSTMEASLES OTITIS MEDIA	3
073.0	ORNITHOSIS, WITH PNEUMONIA	3
073.7	ORNITHOSIS, OTHER SPECIF COMPLIC	3
073.8	ORNITHOSIS, UNSPECIFIED COMPLIC	3
073.9	ORNITHOSIS, UNSPECIFIED	3
079.0	ADENOVIRUS INFECT NOS	3
079.1	ECHO VIRUS INFECT NOS	3
079.2	COXSACKIE VIRUS	3
079.3	RHINOVIRUS INFECT NOS	3
079.6	RESPIRATORY SYNCYTIAL VIR	3
079.81	HANTAVIRUS INFECTION	3
098.6	GONOCCOCAL, INFECTION OF PHARYNX	3
114.5	PULM COCCIDIOIDOMYCOS,UN	3
114.9	COCCIDIOIDOMYCOSIS NOS	3
115.00	HISTOPLASMOSIS, WITHOUT MENTION OF MANIFESTATION	3
115.05	HISTOPLASM CAPS PNEUMON	3
115.09	HISTOPLASMA CAPSULAT NEC	3
115.10	HISTOPLASMA DUBOISII NOS	3
115.15	HISTOPLASMA DUBOISII PNEUMONIA	3
115.90	HISTOPLASMOSIS,W/O MANIFE	3
115.95	HISTOPLASMOSIS PNEUMONIA	3
115.99	HISTOPLASMOSIS NEC	3
116.0	BLASTOMYCOSIS	3
116.1	PARACOCCIDIOIDOMYCOSIS	3
117.1	SPOROTRICHOSIS	3

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Resp ICD-9-CM Code List, Cont'd

117.3	PULMONARY ASPERGILLOSIS	3
117.5	CRYPTOCOCCOSIS	3
130.4	TOXOPLASMA PNEUMONITIS	3
136.3	PNEUMOCYSTOSIS	3
480.0	ADENOVIRAL PNEUMONIA	3
480.1	PNEUMONIA,RESP.SYNCYTIAL	3
480.2	PARINFLUENZA VIRAL PNEUM	3
481	PNEUMOCOCCAL PNEUMONIA (L	3
482.0	PNEUMONIA-KLEBSIELLA PNEU	3
482.1	PNEUMONIA DUE TO PSEUDOMO	3
482.2	H.INFLUENZAE PNEUMONIA	3
482.30	STREPTOCOCCUS UNSPECIFIED	3
482.31	PNEUMONIA/STREPTOC GPA	3
482.32	PHEUMONIA/STREPTO GPB	3
482.39	PNEUMONIA/OTHER STREPTOC	3
482.40	STAPH PNEUMONIA NOS	3
482.41	PNEUMONIA, STAPHYLOCOC. A	3
482.49	OTH STAPH PNEUMONIA	3
482.81	PNEUMONIA/ANAEROBES	3
482.82	PNEUMONIA/E COLI	3
482.83	PNEUMONIA/OTHER GNEG BAC	3
482.84	LEGIONNAIRES' DISEASE	3
482.89	PNEUMONIA/OTHER SPEC BAC	3
483.0	PNEUMONIA MYCOPLASMA	3
483.1	PNEUMONIA DUE TO CHLAMYD	3
484.1	PNEUM W CYTOMEG INCL DIS	3
484.3	PNEUMONIA IN WHOOP COUGH	3
484.6	PNEUMONIA IN ASPERGILLOSI	3
484.7	PNEUM IN OTH SYS MYCOSES	3
487.0	INFLUENZA WITH PNEUMONIA	3
487.1	INFLUENZA W/OTH. RESP. MA	3
487.8	INFLUENZA W/OTHR MANIFEST	3

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Severe Illness_Dth due to ID ICD-9-CM Code List

ICD9CM	ICD9DESCR	Consensus
780.01	COMA	1
785.50	SHOCK (UNSPECIFIED)	1
785.59	SHOCK, OTHER, W/O TRAUMA	1
798.1	DEATH INSTANTANEOUS	1
798.2	DEATH IN E.R.	1
798.9	DEATH UNATTENDED	1
799.9	MORTALITY, CAUSE UNKNOWN	1
656.40	INTRAUTERINE DEATH, UNSPE	3
656.41	INTRAUTERINE DEATH DEL.AN	3
656.43	FETAL DEATH, ANTEPARTUM	3
761.8	ABORTION OF FETUS, SPONTA	3
768.0	FETAL DEATH	3
779.9	STILLBIRTH	3
798.0	SUDDEN INFANT DEATH SYND	3

Appendix B. RODS syndrome definitions based on ICD-9 diagnostic codes

Appendix A

ICD-9 Codes for Selection of Potentially Positive Patients

Syndrome	ICD-9	ICD-9 Description
Botulinic	045	Acute poliomyelitis
Botulinic	005.1	Botulism
Botulinic	045.0	Acute paralytic poliomyelitis specified as bulbar
Botulinic	045.00	Acute paralytic poliomyelitis specified as bulbar, unspecified type of poliovirus
Botulinic	045.01	Acute paralytic poliomyelitis specified as bulbar, poliovirus type i
Botulinic	045.02	Acute paralytic poliomyelitis specified as bulbar, poliovirus type ii
Botulinic	045.03	Acute paralytic poliomyelitis specified as bulbar, poliovirus type iii
Botulinic	045.1	Acute poliomyelitis with other paralysis
Botulinic	045.10	Acute poliomyelitis with other paralysis, unspecified type of poliovirus
Botulinic	045.11	Acute poliomyelitis with other paralysis, poliovirus type i
Botulinic	045.12	Acute poliomyelitis with other paralysis, poliovirus type ii
Botulinic	045.13	Acute poliomyelitis with other paralysis, poliovirus type iii
Botulinic	045.9	Acute poliomyelitis, unspecified
Botulinic	045.90	Acute poliomyelitis, unspecified, poliovirus, unspecified type
Botulinic	045.91	Acute poliomyelitis, unspecified, poliovirus type i
Botulinic	045.92	Acute poliomyelitis, unspecified, poliovirus type ii
Botulinic	045.93	Acute poliomyelitis, unspecified, poliovirus type iii
Botulinic	344.1	Paraplegia nos
Botulinic	344.2	Diplegia of upper limbs
Botulinic	344.30	Monopleg low limb uns si
Botulinic	344.31	Monopleg low limb dom si
Botulinic	344.32	Monopleg low limb nondom
Botulinic	344.40	Monopleg up limb uns si
Botulinic	344.41	Monopleg up limb dom sit
Botulinic	344.42	Monopleg up limb nondom
Botulinic	344.89	Oth paralytic syndromes
Botulinic	344.9	Paralysis nos
Botulinic	350.8	Other specified trigeminal nerve disorder
Botulinic	350.9	Trigeminal nerve dis nos
Botulinic	351	Facial nerve disorders
Botulinic	351.0	Bell's palsy
Botulinic	351.1	Geniculate ganglionitis
Botulinic	351.8	Other facial nerve disorders

Botulinic	351.9	Facial nerve disorder, unspecified
Botulinic	352	Disorders of other cranial nerves
Botulinic	352.0	Olfactory nerve disorder
Botulinic	352.1	Glossopharyngeal neuralgia
Botulinic	352.2	Other disorders of glossopharyngeal [9th nerve]
Botulinic	352.3	Disorders of pneumogastric [10th nerve]
Botulinic	352.4	Disorders of accessory [11th nerve]
Botulinic	352.5	Disorders of hypoglossal [12th nerve]
Botulinic	352.6	Multiple cranial nerve palsies
Botulinic	352.9	Unspecified disorder of cranial nerves
Botulinic	357	Acute infective polyneuritis
Botulinic	358	Myoneural disorders
Botulinic	358.0	Myasthenia gravis
Botulinic	358.1	Myasthenic syndromes in diseases classified elsewhere
Botulinic	358.2	Toxic myoneural disorders
Botulinic	358.8	Other specified myoneural disorders
Botulinic	358.9	Myoneural disorders, unspecified
Botulinic	368.2	Diplopia
Botulinic	368.8	Visual disturbances nec
Botulinic	368.9	Visual disturbance nos
Botulinic	374.3	Ptosis of eyelid
Botulinic	374.30	Ptosis of eyelid nos
Botulinic	374.31	Paralytic ptosis
Botulinic	519.4	Disorders of diaphragm
Botulinic	527.7	Disturbance of salivary secretion
Botulinic	784.5	Speech disturbance nec
Botulinic	787.2	Dysphagia
Constitutional	002	Typhoid/paratyphoid fev
Constitutional	002.0	Typhoid fever
Constitutional	002.1	Paratyphoid fever a
Constitutional	002.2	Paratyphoid fever b
Constitutional	002.3	Paratyphoid fever c
Constitutional	002.9	Paratyphoid fever nos
Constitutional	020.0	Bubonic plague
Constitutional	020.2	Septicemic plague
Constitutional	020.8	Other specified types of plague
Constitutional	020.9	Plague, unspecified
Constitutional	021	Tularemia
Constitutional	021.0	Ulceroglandular tularemia
Constitutional	021.3	Oculoglandular tularemia
Constitutional	021.8	Other specified tularemia
Constitutional	021.9	Unspecified tularemia
Constitutional	022.3	Anthrax septicemia
Constitutional	022.8	Other specified manifestations of anthrax
Constitutional	022.9	Anthrax, unspecified
Constitutional	023	Brucellosis
Constitutional	023.0	Brucella melitensis
Constitutional	023.1	Brucella abortus
Constitutional	023.2	Brucella suis
Constitutional	023.3	Brucella canis

Constitutional	023.8	Other brucellosis
Constitutional	023.9	Brucellosis, unspecified
Constitutional	060	Yellow fever
Constitutional	060.0	Sylvatic yellow fever
Constitutional	060.1	Urban yellow fever
Constitutional	060.9	Yellow fever, unspecified
Constitutional	066.3	Mosquito-borne viral fever, Chikungunya
Constitutional	073.7	Ornithosis with other specified complications
Constitutional	073.8	Ornithosis with unspecified complication
Constitutional	073.9	Ornithosis, unspecified
Constitutional	075	Infectious mononucleosis
Constitutional	078.3	Cat-scratch disease
Constitutional	078.5	Cytomegaloviral disease
Constitutional	079	Viral inf in oth dis/nos
Constitutional	079.1	Echo virus infection in conditions classified elsewhere and of unspecified site
Constitutional	079.2	Coxsackie virus infection in conditions classified elsewhere and of unspecified site
Constitutional	079.9	Viral infection nos
Constitutional	079.98	Chlamydial infect unspec
Constitutional	079.99	Viral infection unspec
Constitutional	081.2	Scrub typhus
Constitutional	130.7	Toxoplasmosis of other specified sites
Constitutional	130.8	Multisystemic disseminated toxoplasmosis
Constitutional	130.9	Toxoplasmosis, unspecified
Constitutional	461.0	Acute maxillary sinusitis
Constitutional	461.1	Acute frontal sinusitis
Constitutional	461.2	Acute ethmoidal sinusitis
Constitutional	461.3	Acute sphenoidal sinusitis
Constitutional	461.8	Other acute sinusitis
Constitutional	461.9	Acute sinusitis, unspecified
Constitutional	464.00	Acute laryngitis without mention of obstruction
Constitutional	464.50	Supraglottitis, unspecified without mention of obstruction
Constitutional	472.1	Chronic pharyngitis
Constitutional	487.8	Influenza with other manifestations
Constitutional	780.4	Dizziness and giddiness
Constitutional	780.6	Fever
Constitutional	780.7	Malaise and fatigue
Constitutional	780.79	Other malaise and fatigue
Constitutional	780.8	Hyperhidrosis
Constitutional	780.9	Other general symptoms
Constitutional	780.91	Fussy infant (baby)
Constitutional	780.92	Excessive crying of infant (baby)
Constitutional	780.99	Other general symptoms
Constitutional	783.0	Anorexia
Gastrointestinal	001	Cholera
Gastrointestinal	001.0	Cholera due to Vibrio cholerae
Gastrointestinal	001.1	Cholera due to Vibrio cholerae el tor
Gastrointestinal	001.9	Cholera, unspecified
Gastrointestinal	003.0	Salmonella gastroenteritis

Gastrointestinal	004	Shigellosis
Gastrointestinal	004.0	Shigella dysenteriae
Gastrointestinal	004.1	Shigella flexneri
Gastrointestinal	004.2	Shigella boydii
Gastrointestinal	004.3	Shigella sonnei
Gastrointestinal	004.8	Other specified shigella infections
Gastrointestinal	004.9	Shigellosis, unspecified
Gastrointestinal	005	Other food poisoning (bacterial)
Gastrointestinal	005.0	Staphylococcal food poisoning
Gastrointestinal	005.2	Food poisoning due to Clostridium perfringens (C. welchii)
Gastrointestinal	005.3	Food poisoning due to other clostridia
Gastrointestinal	005.4	Food poisoning due to vibrio parahaemolyticus
Gastrointestinal	005.8	Other bacterial food poisoning
Gastrointestinal	005.81	Food pois-vibrio vulnif
Gastrointestinal	005.89	Oth bacterial food pois
Gastrointestinal	005.9	Food poisoning, unspecified
Gastrointestinal	006.0	Acute amebic dysentery without mention of abscess
Gastrointestinal	006.1	Chronic intestinal amebiasis without mention of abscess
Gastrointestinal	007	Other protozoal intestinal diseases
Gastrointestinal	007.0	Balantidiasis
Gastrointestinal	007.1	Gastrointestinalardiasis
Gastrointestinal	007.2	Coccidiosis
Gastrointestinal	007.3	Intestinal trichomoniasis
Gastrointestinal	007.4	Cryptosporidiosis
Gastrointestinal	007.5	Cyclosporiasis
Gastrointestinal	007.8	Other specified protozoal intestinal diseases
Gastrointestinal	007.9	Unspecified protozoal intestinal disease
Gastrointestinal	008	Intestinal infections due to other organisms
Gastrointestinal	008.0	Intestinal infection due to escherichia coli [e. Coli]
Gastrointestinal	008.00	Intestinal infection due to unspecified e. Coli
Gastrointestinal	008.01	Intestinal infection due to enteropathogenic e. Coli
Gastrointestinal	008.02	Intestinal infection due to enterotoxigenic e. Coli
Gastrointestinal	008.03	Intestinal infection due to enteroinvasive e. Coli
Gastrointestinal	008.04	Enterohemorrhagic E. coli (0157:H7)
Gastrointestinal	008.09	Other intestinal e. Coli infections
Gastrointestinal	008.1	Intestinal infection due to arizona group of paracolon bacilli
Gastrointestinal	008.2	Intestinal infection due to aerobacter aerogenes
Gastrointestinal	008.3	Intestinal infection due to proteus (mirabilis) (morganii)
Gastrointestinal	008.4	Intestinal infection due to other specified bacteria
Gastrointestinal	008.41	Intestinal infection due to staphylococcus
Gastrointestinal	008.42	Intestinal infection due to pseudomonas
Gastrointestinal	008.43	Intestinal infection due to campylobacter
Gastrointestinal	008.44	Intestinal infection due to yersinia enterocolitica

Gastrointestinal	008.45	Intestinal infection due to clostridium difficile
Gastrointestinal	008.46	Intestinal infection due to other anaerobes
Gastrointestinal	008.47	Intestinal infection due to other gram-negative bacteria
Gastrointestinal	008.49	Intestinal infection due to other specified bacteria
Gastrointestinal	008.5	Bacterial enteritis nos
Gastrointestinal	008.6	Enteritis due to specified virus
Gastrointestinal	008.61	Enteritis due to rotavirus
Gastrointestinal	008.62	Enteritis due to adenovirus
Gastrointestinal	008.63	Enteritis due to norwalk virus
Gastrointestinal	008.64	Enteritis due to other small round viruses [srv's]
Gastrointestinal	008.65	Enteritis due to calcivirus
Gastrointestinal	008.66	Enteritis due to astrovirus
Gastrointestinal	008.67	Enteritis due to enterovirus nec
Gastrointestinal	008.69	Enteritis due to other viral enteritis
Gastrointestinal	008.8	Intestinal infection due to other organism, not elsewhere classified
Gastrointestinal	009	Ill-defined intestinal infections
Gastrointestinal	009.0	Infectious colitis, enteritis, and gastroenteritis
Gastrointestinal	009.1	Colitis, enteritis, and gastroenteritis of presumed infectious origin
Gastrointestinal	009.2	Infectious diarrhea
Gastrointestinal	009.3	Diarrhea of presumed infectious origin
Gastrointestinal	021.1	Enteric tularemia
Gastrointestinal	022.2	Gastrointestinal anthrax
Gastrointestinal	032.83	Diphtheritic peritonitis
Gastrointestinal	535.00	Acute gastritis w/o hem
Gastrointestinal	536.2	Persistent vomiting
Gastrointestinal	555	Regional enteritis
Gastrointestinal	555.0	Regional enteritis of small intestine
Gastrointestinal	555.1	Regional enteritis of large intestine
Gastrointestinal	555.2	Regional enteritis of small intestine with large intestine
Gastrointestinal	555.9	Regional enteritis of unspecified site
Gastrointestinal	556	Ulcerative colitis
Gastrointestinal	556.0	Ulcerative (chronic) enterocolitis
Gastrointestinal	556.1	Ulcerative (chronic) ileocolitis
Gastrointestinal	556.2	Ulcerative (chronic) proctitis
Gastrointestinal	556.3	Ulcerative (chronic) proctosigmoiditis
Gastrointestinal	556.4	Pseudopolyposis of colon
Gastrointestinal	556.5	Left-sided ulcerative (chronic) colitis
Gastrointestinal	556.6	Universal ulcerative (chronic) colitis
Gastrointestinal	556.8	Other ulcerative colitis
Gastrointestinal	556.9	Ulcerative colitis, unspecified
Gastrointestinal	558	Other and unspecified noninfectious gastroenteritis and colitis
Gastrointestinal	558.1	Gastroenteritis and colitis due to radiation
Gastrointestinal	558.2	Toxic gastroenteritis and colitis
Gastrointestinal	558.3	Allergic gastroenteritis and colitis

Gastrointestinal	558.9	Other and unspecified noninfectious gastroenteritis and colitis
Gastrointestinal	569.82	Ulceration of intestine
Gastrointestinal	787.0	Nausea and vomiting
Gastrointestinal	787.01	Nausea with vomiting
Gastrointestinal	787.02	Nausea alone
Gastrointestinal	787.03	Vomiting alone
Gastrointestinal	787.91	Diarrhea
Gastrointestinal	789.0	Abdominal pain
Gastrointestinal	789.00	Abdominal pain, unspecified site
Gastrointestinal	789.01	Abdominal pain, right upper quadrant
Gastrointestinal	789.02	Abdominal pain, left upper quadrant
Gastrointestinal	789.03	Abdominal pain, right lower quadrant
Gastrointestinal	789.04	Abdominal pain, left lower quadrant
Gastrointestinal	789.05	Abdominal pain, periumbilic
Gastrointestinal	789.06	Abdominal pain, epigastric
Gastrointestinal	789.07	Abdominal pain, generalized
Gastrointestinal	789.09	Abdominal pain, other specified site; multiple sites
Gastrointestinal	789.4	Abdominal rigidity
Gastrointestinal	789.40	Abd rigidity unspe site
Gastrointestinal	789.41	Abd rigidity rt up quad
Gastrointestinal	789.42	Abd rigidity lt up quad
Gastrointestinal	789.43	Abd rigidity rt low quad
Gastrointestinal	789.44	Abd rigidity lt low quad
Gastrointestinal	789.45	Abd rigidity periumbili
Gastrointestinal	789.46	Abd rigidity epigastric
Gastrointestinal	789.47	Abd rigidity generalized
Gastrointestinal	789.49	Abd rigid oth spec site
Hemorrhagic	065	Arthropod hemorrhag fev
Hemorrhagic	065.0	Crimean hemorrhagic fev
Hemorrhagic	065.1	Omsk hemorrhagic fever
Hemorrhagic	065.2	Kyasanur forest disease
Hemorrhagic	065.3	Tick-borne hem fever nec
Hemorrhagic	065.4	Mosquito-borne hemorrhagic fever (Chikungunya hemorrhagic fever)
Hemorrhagic	065.8	Other specified arthropod-borne hemorrhagic fever
Hemorrhagic	065.9	Arthropod-borne hemorrhagic fever, unspecified
Hemorrhagic	078.6	Hemorrhagic nephrosonephritis (Junin virus)
Hemorrhagic	078.7	Arenaviral hemorrhagic fever (Korean)
Hemorrhagic	459.0	Hemorrhage, unspecified
Hemorrhagic	530.7	Gastroesophageal laceration-hemorrhage syndrome
Hemorrhagic	530.82	Esophageal hemorrhage
Hemorrhagic	531.0	Gastric ulcer- Acute with hemorrhage
Hemorrhagic	531.00	Acute with hemorrhage- without mention of obstruction
Hemorrhagic	531.01	Acute with hemorrhage- with obstruction
Hemorrhagic	531.2	Gastric ulcer- Acute with hemorrhage and perforation

Hemorrhagic	531.20	Acute with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	531.21	Acute with hemorrhage and perforation- with obstruction
Hemorrhagic	531.4	Gastric ulcer- Chronic or unspecified with hemorrhage
Hemorrhagic	531.40	Chronic or unspecified with hemorrhage- without mention of obstruction
Hemorrhagic	531.41	Chronic or unspecified with hemorrhage- with obstruction
Hemorrhagic	531.6	Gastric ulcer- Chronic or unspecified with hemorrhage and perforation
Hemorrhagic	531.60	Chronic or unspecified with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	531.61	Chronic or unspecified with hemorrhage and perforation- with obstruction
Hemorrhagic	532.0	Duodenal ulcer- Acute with hemorrhage
Hemorrhagic	532.00	Acute with hemorrhage- without mention of obstruction
Hemorrhagic	532.01	Acute with hemorrhage- with obstruction
Hemorrhagic	532.2	Duodenal ulcer- Acute with hemorrhage and perforation
Hemorrhagic	532.20	Acute with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	532.21	Acute with hemorrhage and perforation- with obstruction
Hemorrhagic	532.4	Duodenal ulcer- Chronic or unspecified with hemorrhage
Hemorrhagic	532.40	Chronic or unspecified with hemorrhage- without mention of obstruction
Hemorrhagic	532.41	Chronic or unspecified with hemorrhage- with obstruction
Hemorrhagic	532.6	Duodenal ulcer- Chronic or unspecified with hemorrhage and perforation
Hemorrhagic	532.60	Chronic or unspecified with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	532.61	Chronic or unspecified with hemorrhage and perforation- with obstruction
Hemorrhagic	533.0	Peptic ulcer, site unspecified- Acute with hemorrhage
Hemorrhagic	533.00	Acute with hemorrhage- without mention of obstruction
Hemorrhagic	533.01	Acute with hemorrhage- with obstruction
Hemorrhagic	533.2	Peptic ulcer, site unspecified- Acute with hemorrhage and perforation
Hemorrhagic	533.20	Acute with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	533.21	Acute with hemorrhage and perforation- with obstruction
Hemorrhagic	533.4	Peptic ulcer, site unspecified- Chronic or unspecified with hemorrhage

Hemorrhagic	533.40	Chronic or unspecified with hemorrhage- without mention of obstruction
Hemorrhagic	533.41	Chronic or unspecified with hemorrhage- with obstruction
Hemorrhagic	533.6	Peptic ulcer, site unspecified- Chronic or unspecified with hemorrhage and perforation
Hemorrhagic	533.60	Chronic or unspecified with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	533.61	Chronic or unspecified with hemorrhage and perforation- with obstruction
Hemorrhagic	534.0	Gastrojejunal ulcer- Acute with hemorrhage
Hemorrhagic	534.00	Acute with hemorrhage- without mention of obstruction
Hemorrhagic	534.01	Acute with hemorrhage- with obstruction
Hemorrhagic	534.2	Gastrojejunal ulcer- Acute with hemorrhage and perforation
Hemorrhagic	534.20	Acute with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	534.21	Acute with hemorrhage and perforation- with obstruction
Hemorrhagic	534.4	Gastrojejunal ulcer- Chronic or unspecified with hemorrhage
Hemorrhagic	534.40	Chronic or unspecified with hemorrhage- without mention of obstruction
Hemorrhagic	534.41	Chronic or unspecified with hemorrhage- with obstruction
Hemorrhagic	534.6	Gastrojejunal ulcer- Chronic or unspecified with hemorrhage and perforation
Hemorrhagic	534.60	Chronic or unspecified with hemorrhage and perforation- without mention of obstruction
Hemorrhagic	534.61	Chronic or unspecified with hemorrhage and perforation- with obstruction
Hemorrhagic	535.01	Acute gastritis w hem
Hemorrhagic	535.11	Atrophic gastritis- with hemorrhage
Hemorrhagic	535.21	Gastric mucosal hypertrophy- with hemorrhage
Hemorrhagic	535.31	Alcoholic gastritis- with hemorrhage
Hemorrhagic	535.41	Oth spec gastrit w/ hem
Hemorrhagic	535.51	Unspecified gastritis and gastroduodenitis- with hemorrhage
Hemorrhagic	535.61	Duodenitis- with hemorrhage
Hemorrhagic	537.83	Angiodysplasia of stomach and duodenum with hemorrhage
Hemorrhagic	562.02	Diverticulosis of small intestine with hemorrhage
Hemorrhagic	562.03	Diverticulitis of small intestine with hemorrhage
Hemorrhagic	562.12	Diverticulosis of colon with hemorrhage
Hemorrhagic	562.13	Diverticulitis of colon with hemorrhage
Hemorrhagic	569.3	Hemorrhage of rectum and anus
Hemorrhagic	569.85	Angiodysplasia of intestine with hemorrhage
Hemorrhagic	578	Gastrointestinal hemorrhage
Hemorrhagic	578.0	Hematemesis
Hemorrhagic	578.1	Blood in stool

Hemorrhagic	578.9	Gastrointest hemorr nos
Hemorrhagic	599.7	Hematuria
Hemorrhagic	626.6	Metrorrhagia
Hemorrhagic	626.8	Other disorders of menstruation and other abnormal bleeding from female genital tract
Hemorrhagic	626.9	Unspecified disorders of menstruation and other abnormal bleeding from female genital tract
Hemorrhagic	627.1	Postmenopausal bleeding
Hemorrhagic	784.7	Epistaxis
Hemorrhagic	784.8	Hemorrhage from throat
Hemorrhagic	786.3	Hemoptysis
Hemorrhagic	964.2	Poisoning by anticoagulants
Hemorrhagic	998.11	Hemorrhage complicating a procedure
Neurological	013	Tuberculosis of meninges and central nervous system
Neurological	013.0	Tuberculous meningitis
Neurological	013.00	Tuberculous meningitis, unspecified examination
Neurological	013.01	Tuberculous meningitis, bacteriological or histological examination not done
Neurological	013.02	Tuberculous meningitis, bacteriological or histological examination unknown (at present)
Neurological	013.03	Tuberculous meningitis, tubercle bacilli found (in sputum) by microscopy
Neurological	013.04	Tuberculous meningitis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Neurological	013.05	Tuberculous meningitis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Neurological	013.06	Tuberculous meningitis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods [inoculation of animals]
Neurological	013.6	Tuberculous encephalitis or myelitis
Neurological	013.60	Tuberculous encephalitis or myelitis, unspecified examination
Neurological	013.61	Tuberculous encephalitis or myelitis, bacteriological or histological examination not done
Neurological	013.62	Tuberculous encephalitis or myelitis, bacteriological or histological examination unknown (at present)
Neurological	013.63	Tuberculous encephalitis or myelitis, tubercle bacilli found (in sputum) by microscopy
Neurological	013.64	Tuberculous encephalitis or myelitis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Neurological	013.65	Tuberculous encephalitis or myelitis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically

Neurological	013.66	Tuberculous encephalitis or myelitis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods [inoculation of animals]
Neurological	013.8	Other specified tuberculosis of central nervous system
Neurological	013.9	Unspecified tuberculosis of central nervous system
Neurological	036	Meningococcal infection
Neurological	036.0	Meningococcal meningitis
Neurological	036.1	Meningococcal encephalitis
Neurological	036.2	Meningococcemia
Neurological	036.89	Meningococcal infect nec
Neurological	036.9	Meningococcal infect nos
Neurological	047	Enteroviral meningitis
Neurological	047.0	Coxsackie virus mening
Neurological	047.1	Echo virus meningitis
Neurological	047.8	Viral meningitis nec
Neurological	047.9	Viral meningitis nos
Neurological	048	Oth enteroviral cns dis
Neurological	049	Oth nonarthropod cns vir
Neurological	049.0	Lymphocytic choriomening
Neurological	049.1	Adenoviral meningitis
Neurological	049.8	Viral encephalitis nec
Neurological	049.9	Viral encephalitis nos
Neurological	052.0	Postvaricella encephalitis
Neurological	054.3	Herpetic meningoencephalitis
Neurological	054.72	H simplex meningitis
Neurological	055.0	Postmeasles encephalitis
Neurological	056.01	Encephalomyelitis due to rubella
Neurological	062	Mosquito-borne viral encephalitis
Neurological	062.0	Japanese encephalitis
Neurological	062.1	Western equine encephalitis
Neurological	062.2	Eastern equine encephalitis
Neurological	062.3	St. Louis encephalitis
Neurological	062.4	Australian encephalitis
Neurological	062.5	California virus encephalitis
Neurological	062.8	Other specified mosquito-borne viral encephalitis
Neurological	062.9	Mosquito-borne viral encephalitis, unspecified
Neurological	063	Tick-borne viral encephalitis
Neurological	063.0	Russian spring-summer (taiga) encephalitis
Neurological	063.1	Louping ill
Neurological	063.2	Central European encephalitis
Neurological	063.8	Other specified tick-borne viral encephalitis
Neurological	063.9	Tick-borne viral encephalitis, unspecified
Neurological	064	Vir enceph arthropod nec
Neurological	066.2	Venezuelan equine fever (encephalitis)
Neurological	066.4	West Nile fever (encephalitis)
Neurological	071	Rabies
Neurological	072.2	Mumps encephalitis
Neurological	094.2	Syphilitic meningitis

Neurological	94.81	Syphilitic encephalitis
Neurological	100.81	Leptospiral meningitis
Neurological	114.2	Coccidioidal meningitis
Neurological	115.01	Histoplasma capsulatum meningitis
Neurological	115.11	Histoplasma duboisii meningitis
Neurological	115.91	Histoplasmosis meningitis
Neurological	130.0	Meningoencephalitis due to toxoplasmosis
Neurological	293.0	Acute delirium
Neurological	293.1	Subacute delirium
Neurological	320	Bacterial meningitis
Neurological	320.0	Hemophilus meningitis
Neurological	320.1	Pneumococcal meningitis
Neurological	320.2	Streptococcal meningitis
Neurological	320.3	Staphylococc meningitis
Neurological	320.7	Mening in oth bact dis
Neurological	320.8	Bacterial meningitis nec
Neurological	320.81	Meningitis/anaerobic bac
Neurological	320.82	Memingitis/gram-neg bact
Neurological	320.89	Meningitis/bacteria nos
Neurological	320.9	Bacterial meningitis nos
Neurological	321	Oth organism meningitis
Neurological	321.0	Cryptococcal meningitis
Neurological	321.1	Mening in oth fungal dis
Neurological	321.2	Mening in oth viral dis
Neurological	321.3	Trypanosomiasis meningit
Neurological	321.8	Mening in oth nonbac dis
Neurological	322	Meningitis, unspecified
Neurological	322.0	Nonpyogenic meningitis
Neurological	322.1	Eosinophilic meningitis
Neurological	322.9	Meningitis nos
Neurological	323	Encephalitis, myelitis, and encephalomyelitis
Neurological	323.0	Encephalitis in viral diseases classified elsewhere
Neurological	323.1	Encephalitis in rickettsial diseases classified elsewhere
Neurological	323.2	Encephalitis in protozoal diseases classified elsewhere
Neurological	323.4	Other encephalitis due to infection classified elsewhere
Neurological	323.5	Encephalitis following immunization procedures
Neurological	323.6	Postinfectious encephalitis
Neurological	323.7	Toxic encephalitis
Neurological	323.8	Other causes of encephalitis
Neurological	323.9	Unspecified cause of encephalitis
Neurological	331.81	Reye's syndrome
Neurological	348.3	Encephalopathy, unspecified
Neurological	780.0	Coma and stupor
Neurological	780.01	Coma
Neurological	780.3	Convulsions
Neurological	781.6	Meningismus
Neurological	784.0	Headache

Neurological	989.7	Aflatoxin and other mycotoxin (food contaminents)
Neurological	998.0	Toxic effect of fish and shellfish (Saxitoxin)
Rash	020.1	Cellulocutaneous plague
Rash	022.0	Cutaneous anthrax
Rash	032.85	Cutaneous diphtheria
Rash	034.1	Scarlet fever
Rash	040.82	Toxic shock syndrome
Rash	050	Smallpox
Rash	050.0	Variola major
Rash	050.1	Alastrim (Variola minor)
Rash	050.2	Modified smallpox
Rash	050.9	Smallpox, unspecified
Rash	051	Cowpox and paravaccinia
Rash	051.0	Cowpox
Rash	051.1	Pseudocowpox
Rash	051.2	Contagious pustular dermatitis
Rash	051.9	Paravaccinia, unspecified
Rash	052	Chickenpox
Rash	052.7	Chickenpox with other specified complications
Rash	052.8	Chickenpox with unspecified complication
Rash	052.9	Varicella without mention of complication
Rash	053	Herpes zoster
Rash	053.0	Herpes zoster with meningitis
Rash	053.1	Herpes zoster with other nervous system complications
Rash	053.10	Herpes zoster with unspecified nervous system complication
Rash	053.11	Geniculate herpes zoster
Rash	053.19	Herpes zoster with other nervous system complications
Rash	053.2	Herpes zoster with ophthalmic complications
Rash	053.29	Herpes zoster with other ophthalmic complications
Rash	053.7	Herpes zoster with other specified complications
Rash	053.79	Herpes zoster with other specified complications
Rash	053.8	Herpes zoster with unspecified complication
Rash	053.9	Herpes zoster without mention of complication
Rash	054	Herpes simplex
Rash	054.0	Eczema herpeticum
Rash	054.4	Herpes simplex with ophthalmic complications
Rash	054.40	Herpes simplex with unspecified ophthalmic complication
Rash	054.49	Herpes simplex with other ophthalmic complications
Rash	054.7	Herpes simplex with other specified complications
Rash	054.79	Herpes simplex with other specified complications
Rash	054.8	Herpes simplex with unspecified complication
Rash	054.9	Herpes simplex without mention of complication

Rash	055	Measles
Rash	055.7	Measles with other specified complications
Rash	055.79	Measles with other specified complications
Rash	055.8	Measles with unspecified complication
Rash	055.9	Measles without mention of complication
Rash	056	Rubella
Rash	056.0	Rubella with neurological complications
Rash	056.00	Rubella with unspecified neurological complications
Rash	056.09	Rubella with other neurological complications
Rash	056.7	Rubella with other specified complications
Rash	056.71	Arthritis due to rubella
Rash	056.79	Rubella with other specified complications
Rash	056.8	Rubella with unspecified complications
Rash	056.9	Rubella without mention of complication
Rash	057	Other viral exanthemata
Rash	057.0	Erythema infectiosum [fifth disease]
Rash	057.8	Other specified viral exanthemata
Rash	057.9	Viral exanthem, unspecified
Rash	074.3	Hand, foot mouth dis
Rash	080	Louse-borne (epidemic) typhus
Rash	081	Other typhus
Rash	081.0	Murine (endemic) typhus
Rash	081.9	Typhus, unspecified
Rash	082	Tick-borne rickettsioses
Rash	082.0	Spotted fevers (Rocky mountain spotted fever)
Rash	082.1	Boutonneuse fever
Rash	082.2	North asian tick fever
Rash	082.3	Queensland tick typhus
Rash	082.8	Tick-borne ricketts nec
Rash	082.9	Tick-borne ricketts nos
Rash	083.2	Rickettsialpox
Rash	083.8	Rickettsioses nec
Rash	083.9	Rickettsiosis nos
Rash	091.3	Secondary syph skin
Rash	115.1	Infection by Histoplasma duboisii
Rash	115.10	Infection by Histoplasma duboisii, without mention of manifestation
Rash	287	Purpura and other hemorrhagic conditions
Rash	287.0	Allergic purpura
Rash	287.1	Qualitative platelet defects
Rash	287.2	Other nonthrombocytopenic purpuras
Rash	287.8	Other specified hemorrhagic conditions
Rash	287.9	Unspecified hemorrhagic conditions
Rash	684	Impetigo
Rash	686.0	Pyoderma
Rash	686.00	Pyoderma nos
Rash	686.01	Pyoderma gangrenosum
Rash	686.09	Oth pyoderma skin/subcu
Rash	686.1	Pyogenic granuloma
Rash	694.3	Impetigo herpetiformis

Rash	695	Erythematous conditions
Rash	695.0	Toxic erythema
Rash	695.1	Erythema multiforme
Rash	695.2	Erythema nodosum
Rash	695.8	Other specified erythematous conditions
Rash	695.81	Ritter's disease
Rash	695.89	Other specified erythematous conditions
Rash	695.9	Unspecified erythematous condition
Rash	782.1	Rash and other nonspecific skin eruption
Rash	782.7	Spontaneous ecchymoses
Respiratory	003.22	Salmonella pneumonia
Respiratory	010	Primary tuberculous infection
Respiratory	010.0	Primary tuberculous infection
Respiratory	010.00	Primary tuberculous infection, unspecified examination
Respiratory	010.01	Primary tuberculous infection, bacteriological or histological examination not done
Respiratory	010.02	Primary tuberculous infection, bacteriological or histological examination unknown (at present)
Respiratory	010.03	Primary tuberculous infection, tubercle bacilli found (in sputum) by microscopy
Respiratory	010.04	Primary tuberculous infection, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	010.05	Primary tuberculous infection, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	010.06	Primary tuberculous infection, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	010.1	Tuberculous pleurisy in primary progressive tuberculosis
Respiratory	010.10	Tuberculous pleurisy in primary progressive tuberculosis, unspecified examination
Respiratory	010.11	Tuberculous pleurisy in primary progressive tuberculosis, bacteriological or histological examination not done
Respiratory	010.12	Tuberculous pleurisy in primary progressive tuberculosis, bacteriological or histological examination results unknown (at present)
Respiratory	010.13	Tuberculous pleurisy in primary progressive tuberculosis, tubercle bacilli found (in sputum) by microscopy
Respiratory	010.14	Tuberculous pleurisy in primary progressive tuberculosis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture

Respiratory	010.15	Tuberculous pleurisy in primary progressive tuberculosis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	010.16	Tuberculous pleurisy in primary progressive tuberculosis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	010.8	Other primary progressive tuberculosis
Respiratory	010.80	Other primary progressive tuberculosis, unspecified examination
Respiratory	010.81	Other primary progressive tuberculosis, bacteriological or histological examination not done
Respiratory	010.82	Other primary progressive tuberculosis, bacteriological or histological examination unknown (at present)
Respiratory	010.83	Other primary progressive tuberculosis, tubercle bacilli found (in sputum) by microscopy
Respiratory	010.84	Other primary progressive tuberculosis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	010.85	Other primary progressive tuberculosis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	010.86	Other primary progressive tuberculosis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	010.9	Primary tuberculous infection, unspecified type
Respiratory	010.90	Primary tuberculous infection, unspecified type, unspecified examination
Respiratory	010.91	Primary tuberculous infection, unspecified type, bacteriological or histological examination not done
Respiratory	010.92	Primary tuberculous infection, unspecified type, bacteriological or histological examination unknown (at present)
Respiratory	010.93	Primary tuberculous infection, unspecified type, tubercle bacilli found (in sputum) by microscopy
Respiratory	010.94	Primary tuberculous infection, unspecified type, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	010.95	Primary tuberculous infection, unspecified type, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically

Respiratory	010.96	Primary tuberculous infection, unspecified type, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011	Pulmonary tuberculosis
Respiratory	011.0	Tuberculosis of lung, infiltrative
Respiratory	011.00	Tuberculosis of lung, infiltrative, unspecified examination
Respiratory	011.01	Tuberculosis of lung, infiltrative, bacteriological or histological examination not done
Respiratory	011.02	Tuberculosis of lung, infiltrative, bacteriological or histological examination unknown (at present)
Respiratory	011.03	Tuberculosis of lung, infiltrative, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.04	Tuberculosis of lung, infiltrative, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.05	Tuberculosis of lung, infiltrative, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.06	Tuberculosis of lung, infiltrative, tubercle bacilli not found bacteriological or histological examination, but tuberculosis confirmed by other methods(inoculation of animals)
Respiratory	011.1	Tuberculosis of lung, nodular
Respiratory	011.10	Tuberculosis of lung, nodular, unspecified examination
Respiratory	011.11	Tuberculosis of lung, nodular, bacteriological or histological examination not done
Respiratory	011.12	Tuberculosis of lung, nodular, bacteriological or histological examination unknown (at present)
Respiratory	011.13	Tuberculosis of lung, nodular, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.14	Tuberculosis of lung, nodular, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.15	Tuberculosis of lung, nodular, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.16	Tuberculosis of lung, nodular, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.2	Tuberculosis of lung with cavitation
Respiratory	011.20	Tuberculosis of lung with cavitation, unspecified examination
Respiratory	011.21	Tuberculosis of lung with cavitation, bacteriological or histological examination not done

Respiratory	011.22	Tuberculosis of lung with cavitation, bacteriological or histological examination unknown (at present)
Respiratory	011.23	Tuberculosis of lung with cavitation, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.24	Tuberculosis of lung with cavitation, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.25	Tuberculosis of lung with cavitation, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.26	Tuberculosis of lung with cavitation, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.3	Tuberculosis of bronchus
Respiratory	011.30	Tuberculosis of bronchus, unspecified examination
Respiratory	011.31	Tuberculosis of bronchus, bacteriological or histological examination not done
Respiratory	011.32	Tuberculosis of bronchus, bacteriological or histological examination unknown (at present)
Respiratory	011.33	Tuberculosis of bronchus, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.34	Tuberculosis of bronchus, tubercle bacilli not found (in sputum) by microscopy, but found in bacterial culture
Respiratory	011.35	Tuberculosis of bronchus, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.36	Tuberculosis of bronchus, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.4	Tuberculous fibrosis of lung
Respiratory	011.40	Tuberculous fibrosis of lung, unspecified examination
Respiratory	011.41	Tuberculous fibrosis of lung, bacteriological or histological examination not done
Respiratory	011.42	Tuberculous fibrosis of lung, bacteriological or histological examination unknown (at present)
Respiratory	011.43	Tuberculous fibrosis of lung, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.44	Tuberculous fibrosis of lung, tubercle bacilli not found (in sputum) by microscopy, but found in bacterial culture
Respiratory	011.45	Tuberculous fibrosis of lung, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically

Respiratory	011.46	Tuberculous fibrosis of lung, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.5	Tuberculous bronchiectasis
Respiratory	011.50	Tuberculous bronchiectasis, unspecified examination
Respiratory	011.51	Tuberculous bronchiectasis, bacteriological or histological examination not done
Respiratory	011.52	Tuberculous bronchiectasis, bacteriological or histological examination unknown (at present)
Respiratory	011.53	Tuberculous bronchiectasis, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.54	Tuberculous bronchiectasis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.55	Tuberculous bronchiectasis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.56	Tuberculous bronchiectasis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.6	Tuberculous pneumonia (any form)
Respiratory	011.60	Tuberculous pneumonia (any form), unspecified examination
Respiratory	011.61	Tuberculous pneumonia (any form), bacteriological or histological examination not done
Respiratory	011.62	Tuberculous pneumonia (any form) bacteriological or histological examination unknown (at present)
Respiratory	011.63	Tuberculous pneumonia (any form), tubercle bacilli found (in sputum) by microscopy
Respiratory	011.64	Tuberculous pneumonia (any form), tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.65	Tuberculous pneumonia (any form), tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.66	Tuberculous pneumonia (any form), tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.7	Tuberculous pneumothorax
Respiratory	011.70	Tuberculous pneumothorax, unspecified examination
Respiratory	011.71	Tuberculous pneumothorax, bacteriological or histological examination not done
Respiratory	011.72	Tuberculous pneumothorax, bacteriological or histological examination unknown (at present)

Respiratory	011.73	Tuberculous pneumothorax, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.74	Tuberculous pneumothorax, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.75	Tuberculous pneumothorax, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.76	Tuberculous pneumothorax, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.8	Other specified pulmonary tuberculosis
Respiratory	011.80	Other specified pulmonary tuberculosis, unspecified examination
Respiratory	011.81	Other specified pulmonary tuberculosis, bacteriological or histological examination not done
Respiratory	011.82	Other specified pulmonary tuberculosis, bacteriological or histological examination unknown (at present)
Respiratory	011.83	Other specified pulmonary tuberculosis, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.84	Other specified pulmonary tuberculosis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.85	Other specified pulmonary tuberculosis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
Respiratory	011.86	Other specified pulmonary tuberculosis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	011.9	Unspecified pulmonary tuberculosis
Respiratory	011.90	Unspecified pulmonary tuberculosis, unspecified examination
Respiratory	011.91	Unspecified pulmonary tuberculosis, bacteriological or histological examination not done
Respiratory	011.92	Unspecified pulmonary tuberculosis, bacteriological or histological examination unknown (at present)
Respiratory	011.93	Unspecified pulmonary tuberculosis, tubercle bacilli found (in sputum) by microscopy
Respiratory	011.94	Unspecified pulmonary tuberculosis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
Respiratory	011.95	Unspecified pulmonary tuberculosis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically

Respiratory	011.96	Unspecified pulmonary tuberculosis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
Respiratory	020	Plague
Respiratory	020.3	Primary pneumonic plague
Respiratory	020.4	Secondary pneumonic plague
Respiratory	020.5	Pneumonic plague, unspecified
Respiratory	021.2	Pulmonary tularemia
Respiratory	022	Anthrax
Respiratory	022.1	Pulmonary anthrax
Respiratory	024	Glanders
Respiratory	025	Melioidosis
Respiratory	032	Diphtheria
Respiratory	032.0	Faucial diphtheria
Respiratory	032.1	Nasopharyngeal diphtheria
Respiratory	032.2	Anterior nasal diphtheria
Respiratory	032.3	Laryngeal diphtheria
Respiratory	032.81	Conjunctival diphtheria
Respiratory	032.82	Diphtheritic myocarditis
Respiratory	032.84	Diphtheritic cystitis
Respiratory	032.89	Other specified diphtheria
Respiratory	032.9	Diphtheria, unspecified
Respiratory	033	Whooping cough
Respiratory	033.0	Bordetella pertussis
Respiratory	033.1	Bordetella parapertussis
Respiratory	033.8	Whooping cough nec
Respiratory	033.9	Whooping cough nos
Respiratory	034	Strep throat/scarlet fev
Respiratory	034.0	Strep sore throat
Respiratory	052.1	Varicella (hemorrhagic) pneumonitis
Respiratory	055.1	Postmeasles pneumonia
Respiratory	073	Ornithosis (Psittacoisis)
Respiratory	073.0	Ornithosis with pneumonia
Respiratory	074.1	Epidemic pleurodynia
Respiratory	079.0	Adenovirus infection in conditions classified elsewhere and of unspecified site
Respiratory	079.3	Rhinovirus infection in conditions classified elsewhere and of unspecified site
Respiratory	079.6	Respiratory syncytial virus (rsv) infection in conditions classified elsewhere and of unspecified site
Respiratory	079.8	Viral infection nec
Respiratory	079.81	Hantavirus infection
Respiratory	079.88	Oth spec chlamydial infe
Respiratory	079.89	Oth spec viral infection
Respiratory	083.0	Q fever
Respiratory	112.4	Candidiasis of lung
Respiratory	114.0	Primary coccidioidomycosis (pulmonary)
Respiratory	114.9	Coccidioidomycosis nos
Respiratory	115	Histoplasmosis
Respiratory	115.0	Infection by Histoplasma capsulatum

Respiratory	115.00	Infection by Histoplasma capsulatum, without mention of manifestation
Respiratory	115.02	Histoplasma capsulatum retinitis
Respiratory	115.03	Histoplasma capsulatum pericarditis
Respiratory	115.04	Histoplasma capsulatum endocarditis
Respiratory	115.05	Histoplasma capsulatum pneumonia
Respiratory	115.09	Infection by Histoplasma capsulatum, with mention of other manifestation
Respiratory	115.12	Histoplasma duboisii retinitis
Respiratory	115.13	Histoplasma duboisii pericarditis
Respiratory	115.14	Histoplasma duboisii endocarditis
Respiratory	115.15	Histoplasma duboisii pneumonia
Respiratory	115.19	Infection by Histoplasma duboisii with mention of other manifestation
Respiratory	115.9	Histoplasmosis, unspecified
Respiratory	115.90	Histoplasmosis, unspecified without mention of manifestation
Respiratory	115.92	Histoplasmosis retinitis
Respiratory	115.93	Histoplasmosis pericarditis
Respiratory	115.94	Histoplasmosis endocarditis
Respiratory	115.95	Histoplasmosis pneumonia
Respiratory	115.99	Histoplasmosis, unspecified with mention of other manifestation
Respiratory	130.4	Pneumonitis due to toxoplasmosis
Respiratory	136.3	Pneumocystosis
Respiratory	460	Acute nasopharyngitis [common cold]
Respiratory	462	Acute pharyngitis
Respiratory	463	Acute tonsillitis
Respiratory	464	Acute laryngitis and tracheitis
Respiratory	464.0	Acute laryngitis
Respiratory	464.1	Acute tracheitis
Respiratory	464.10	Acute tracheitis without mention of obstruction
Respiratory	464.11	Acute tracheitis with obstruction
Respiratory	464.2	Acute laryngotracheitis
Respiratory	464.20	Acute laryngotracheitis without mention of obstruction
Respiratory	464.21	Acute laryngotracheitis with obstruction
Respiratory	464.3	Acute epiglottitis
Respiratory	464.30	Acute epiglottitis without mention of obstruction
Respiratory	464.31	Acute epiglottitis with obstruction
Respiratory	464.4	Croup
Respiratory	465	Acute laryngopharyngitis
Respiratory	465.0	Acute upper respiratory infections of multiple or unspecified sites
Respiratory	465.8	Acute upper respiratory infections of other multiple sites
Respiratory	465.9	Acute upper respiratory infections of unspecified site
Respiratory	466	Acute bronchitis and bronchiolitis
Respiratory	466.0	Acute bronchitis
Respiratory	466.1	Acute bronchiolitis

Respiratory	466.11	Acute bronchiolitis due to respiratory syncytial virus (rsv)
Respiratory	466.19	Acute bronchiolitis due to other infectious organisms
Respiratory	480	Viral pneumonia
Respiratory	480.0	Pneumonia due to adenovirus
Respiratory	480.1	Pneumonia due to respiratory syncytial virus
Respiratory	480.2	Pneumonia due to parainfluenza virus
Respiratory	480.8	Pneumonia due to other virus not elsewhere classified
Respiratory	480.9	Viral pneumonia, unspecified
Respiratory	481	Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]
Respiratory	482	Other bacterial pneumonia
Respiratory	482.0	Pneumonia due to Klebsiella pneumoniae
Respiratory	482.1	Pneumonia due to Pseudomonas
Respiratory	482.2	Pneumonia due to Hemophilus influenzae [H. influenzae]
Respiratory	482.3	Pneumonia due to Streptococcus
Respiratory	482.30	Pneumonia due to Streptococcus, unspecified
Respiratory	482.31	Pneumonia due to Streptococcus Group A
Respiratory	482.32	Pneumonia due to Streptococcus Group B
Respiratory	482.39	Pneumonia due to other Streptococcus
Respiratory	482.4	Pneumonia due to Staphylococcus
Respiratory	482.40	Pneumonia due to Staphylococcus, unspecified
Respiratory	482.41	Pneumonia due to Staphylococcus aureus
Respiratory	482.49	Other Staphylococcus pneumonia
Respiratory	482.8	Pneumonia due to other specified bacteria
Respiratory	482.81	Pneumonia due to anaerobes
Respiratory	482.82	Pneumonia due to escherichia coli [E. coli]
Respiratory	482.83	Pneumonia due to other gram-negative bacteria
Respiratory	482.84	Legionnaires' disease
Respiratory	482.89	Pneumonia due to other specified bacteria
Respiratory	482.9	Bacterial pneumonia, unspecified
Respiratory	483	Pneumonia due to other specified organism
Respiratory	483.0	Pneumonia due to Mycoplasma pneumoniae
Respiratory	483.1	Pneumonia due to Chlamydia
Respiratory	483.8	Pneumonia due to other specified organism
Respiratory	484	Pneumonia in infectious diseases classified elsewhere
Respiratory	484.1	Pneumonia in cytomegalic inclusion disease
Respiratory	484.3	Pneumonia in whooping cough
Respiratory	484.5	Pneumonia in anthrax
Respiratory	484.6	Pneumonia in aspergillosis
Respiratory	484.7	Pneumonia in other systemic mycoses
Respiratory	484.8	Pneumonia in other infectious diseases classified elsewhere
Respiratory	485	Bronchopneumonia, organism unspecified
Respiratory	486	Pneumonia, organism unspecified
Respiratory	487	Influenza
Respiratory	487.0	Influenza with pneumonia
Respiratory	487.1	Influenza with other respiratory manifestations
Respiratory	490	Bronchitis nos
Respiratory	491	Chronic bronchitis
Respiratory	491.0	Simple chr bronchitis
Respiratory	491.1	Mucopurul chr bronchitis
Respiratory	491.20	Obstr chr bronc wo exac
Respiratory	491.21	Obstr chr bronc w/exac

Respiratory	491.8	Chronic bronchitis nec
Respiratory	491.9	Chronic bronchitis nos
Respiratory	507	Pneumonitis due to solids and liquids
Respiratory	507.0	Pneumonitis due to inhalation of food or vomitus
Respiratory	507.1	Pneumonitis due to inhalation of oils and essences
Respiratory	507.8	Pneumonitis due to other solids and liquids
Respiratory	511	Pleurisy
Respiratory	511.0	Pleurisy w/o effus or tb
Respiratory	511.1	Bact pleur/effus not tb
Respiratory	511.8	Pleural effus nec not tb
Respiratory	511.9	Pleural effusion nos
Respiratory	513	Lung/mediastinum abscess
Respiratory	513.0	Abscess of lung
Respiratory	513.1	Abscess of mediastinum
Respiratory	518	Other lung diseases
Respiratory	518.0	Pulmonary collapse
Respiratory	518.4	Acute lung edema nos
Respiratory	518.8	Other diseases of lung
Respiratory	518.81	Acute respiratory failur
Respiratory	518.82	Other pulm insuff - nec
Respiratory	518.84	Acute/chronic resp fail
Respiratory	518.89	Othr lung disease nec
Respiratory	519.2	Mediastinitis
Respiratory	784.1	Throat pain
Respiratory	786.0	Dyspnea/respiratory abn
Respiratory	786.00	Respiratory abnorm nos
Respiratory	786.05	Shortness of breath
Respiratory	786.06	Tachypnea
Respiratory	786.07	Wheezing
Respiratory	786.09	Respiratory abnorm nec
Respiratory	786.1	Stridor
Respiratory	786.2	Cough
Respiratory	786.52	Painful respiration
Respiratory	795.31	Nonspecific positive findings for anthrax (Positive findings by nasal swab)
Respiratory	V01.81	Anthrax (Other communicable diseases)

APPENDIX B

Classifying Patients into Syndromic Categories:
Physician Instructions

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1. Overall Goal of Project
Our goal is to detect outbreaks in their early stages – before the case has been culture-proven. Syndromic surveillance monitors patients based on the type of findings the patient presents with. We have designed seven syndromic categories we believe are useful to monitor. Because we monitor syndromes rather than diseases, the syndromic case definitions focus more on signs, symptoms, and findings consistent with relevant infectious diseases than on their etiology. To determine how well we can detect syndromic cases, we will compare our detection methods against a gold standard classification of patients made by physicians.

2. Your Task
Your task is to read the study patients' ED reports and to classify the patients into relevant syndromic categories. Your classifications will comprise a gold standard set of patients for evaluation of biosurveillance techniques. We have provided you with ED reports for patients you are assigned (section 2.1) and a data collection form for recording your classifications (section 2.2).

2.1. ED Reports
Every patient has been assigned a study ID that is printed in the top left-hand corner of the patient's report(s). If a patient visit generated more than one ED report – which is often the case in the Presby ED – you need to read all the reports before determining your answers. You should use information from the patient's entire ED record, including the past history, ED course, lab values, radiology findings, etc., to fill in the data collection form.

2.2. Data Collection Forms
For every patient you are assigned, fill in a single data collection form (Figure 1). If the patient meets the case definitions for any of the syndromes described on the form, check the box next to the syndrome and proceed to consider any case definitions nested under the syndrome. If you leave a box blank, it means the condition does not apply to that patient.

You can use electronic or paper data collection forms, or you can use a combination of the two. If you are using the paper data collection form, write in the patient study ID and check all boxes that apply to that patient. If you are using the electronic form, you can open the form in Microsoft Access (as shown in Figure 1) and check all relevant boxes with your mouse. Be aware that Access will always open to the first record you completed. If you have already

completed some records, click the right-hand arrow with line (shown in Figure 1) to go to the last record you completed, then click the single right arrow to begin a new record.

3. Syndromic Classifications
On the data collection form you will check all of the acute syndromic case definitions met by the patient, where acute is defined as ***within the last 2 weeks***. An acute syndromic presentation may be a new illness for the patient or could be acute exacerbation of a chronic problem (e.g., an acute asthma attack). A single patient can exhibit more than one syndrome, so mark all that apply.

If you check a syndrome, also consider any other case definitions nested under that syndrome. For example, if you check *Respiratory*, you must also consider whether any of the patient's respiratory symptoms are *Lower respiratory* and whether they are *Explained by a non-respiratory or non-infectious diagnosis*. If you check the *Lower respiratory* box, you must determine whether there is *Radiological evidence of an acute lower respiratory problem.*

3.1 Case Definitions

1. Respiratory
Signs, symptoms, or other evidence of an illness affecting the upper or lower respiratory tract, such as cough, decreased oxygen saturation, nasal congestion, sore throat, pneumonia, etc.

1.1 Lower respiratory
At least one of the patient's respiratory conditions occurs in the lower respiratory tract (defined as below the larynx), such as shortness of breath, physical findings of pneumonia, pleuritic chest pain, hypoxia, etc. A cough can be considered either upper or lower respiratory, depending on the patient's other characteristics.

1.1.1 Radiological evidence of acute lower respiratory problem
The report describes radiological evidence of an acute lower respiratory process, such as localized infiltrate, lobar mass, or widened mediastinum.

1.2 Explained by a non-respiratory or non-infectious diagnosis
Respiratory signs, symptoms, or findings are explained by a non-respiratory diagnosis, such as acute myocardial infarction, or a non-infectious diagnosis, such as congestive heart failure.

2. Gastrointestinal
Signs, symptoms, or other evidence of an illness affecting the gastrointestinal tract (defined as below and including the esophagus), such as nausea, vomiting, diarrhea, abdominal pain, or abdominal distension or swelling.

2.1 Has diarrhea
The patient has diarrhea.

2.2 Explained by a non-GI or non-infectious diagnosis

Signs, symptoms, or findings of GI illness are explained by a non-GI diagnosis, such as liver disease with ascites, or a non-infectious diagnosis, such as reaction to medication or chemotherapy.

3. Neurological
Non-psychiatric signs, symptoms, or other evidence of an illness affecting the neurological system, such as headache, facial pain, seizure, syncope, ataxia, altered mental status, vertigo, or stiff neck.

3.1 Meningoencephaltic
Neurological signs and symptoms are consistent with meningitis, encephalitis or meningoencephalitis.

4. Rash
Any rash that is not eczematous (i.e., macular, papular, vesicular, pustular, or hemorrhagic) or an ulcer with eschar.

5. Hemorrhagic
Bleeding from any site except the central nervous system or into the conjunctiva (e.g., bleeding from the lungs, GI tract, GU tract, nose, vagina, or skin). A patient bleeding from trauma or surgical incision should not be considered hemorrhagic.

6. Botulinic
Signs or symptoms consistent with a cranial nerve motor palsy (e.g., diplopia, blurred vision, mydriasis, ptosis, slurred speech, dysarthria, dysphagia, dry mouth) with or without symptoms or signs of a peripheral nerve motor palsy.

7. Constitutional
At least two non-localized (systemic) conditions, such as fever, chills, myalgia, weakness, fatigue, malaise, diaphoresis, non-cervical lymphadenopathy, anorexia, etc. Fever and chills can count as two separate conditions.

8. Fever
A measured temperature greater than 38.0 C (100.4 F) OR a report of recent fever or chills (report could come from the dictating physician, patient, family member, or referring institution).

9. No fever information given
The report does not provide the value of the patient's temperature and does not describe whether the patient is febrile. (This should never be checked if *Fever* is checked.)

3.1.1 Multiple Syndromic Classifications
Listed below are a few examples of cases that will require multiple syndromic classifications:
- If a patient presents with a hemorrhagic rash, classify her as both Hemorrhagic and Rash
- A patient with an upper respiratory infection, fever, and myalgia should be classified as Respiratory and Constitutional. You should also check the box for fever.

- If a patient has bloody stool, classify him as both GI and Hemorrhagic.
- A patient with hemoptysis should be classified as Respiratory and Hemorrhagic.
- A patient with hematemesis should be classified as GI and Hemorrhagic
- If a patient has a headache, fever, and light-headedness, you should check Neurological (for the headache) and Constitutional. You should also check the box for fever.
- A patient has a botulinic sign or symptom due to a neurological problem (e.g., slurred speech due to CVA), you should classify the patient as Botulinic (because he has at least one Botulinic symptom) and Neurological.
- If a patient has an upper respiratory infection, fever, and chills, you should check Respiratory and Constitutional, because fever and chills can count as two separate conditions. You should also check the box for fever.

3.1.2 Contradictory evidence in ED reports

There may be contradictions among different reports for the same patient visit. We are relying on your judgment and intuition as a physician to determine the best answers in the face of confusing or contradictory evidence.

If there is a conflict regarding the patient's fever status, use this guideline: If a patient has no fever on exam and if there is a believable report of fever or chills in the recent history, the patient should be considered Febrile. If the report of fever or chills is questionable (e.g., conflict between resident's and attending's notes), the measured temperature on exam should take precedence (i.e., the patient should be considered not Febrile).

Appendix C. Copy of published articles included in this thesis

Cadieux, G.; Tamblyn, R. Accuracy of physician billing claims for identifying acute respiratory infections in primary care. *Health Services Research* 2008; 43(6): 2223-38.

Cadieux, G.; Buckeridge D.L.; Jacques A.; Libman M.; Dendukuri N.; Tamblyn R. Accuracy of syndrome definitions based on diagnoses in physician claims. *BMC Public Health.* 2011: 11; 1-10.

DOI: 10.1111/j.1475-6773.2008.00873.x
RESEARCH BRIEF

Accuracy of Physician Billing Claims for Identifying Acute Respiratory Infections in Primary Care

Geneviève Cadieux and Robyn Tamblyn

Objective. To assess the accuracy of physician billing claims for identifying acute respiratory infections in primary care.
Study Setting. Nine primary care physician practices in Montreal, Canada (2002–2005).
Study Design. A validation study was carried out to compare diagnoses in 3,526 physician billing claims with diagnoses documented in the corresponding patient medical records.
Data Collection. In-office medical record abstraction.
Principal Findings. Claims had a high positive predictive value (PPV), negative predictive value, and specificity for identifying respiratory infections; however, their sensitivity was below 50 percent. Large variation in sensitivity and PPV was observed among physicians.
Conclusions. Because claims data are now routinely used to monitor antibiotic prescribing in primary care, future research should determine if acute respiratory infection diagnoses are missing from claims at random, or if bias is present.

Key Words. Validation studies, databases, health services, International Classification of Diseases, respiratory tract infections

Several randomized, placebo-controlled trials of antibiotic use have shown that antibiotics do not provide clinical benefit to children or adults with upper respiratory tract infections (Hoaglund et al. 1950; Cronk et al. 1954; Howie and Clark 1970; Stott and West 1976; Verheij, Hermans, and Mulder 1994; Kaiser et al. 1996; Arroll 2005) and fail to prevent complicated bacterial infections (Gadomski 1993; Heikkinen et al. 1995). Yet, 75 percent of oral antibiotics prescribed to ambulatory patients are for pharyngitis, otitis media, sinusitis, bronchitis, common cold, and unspecified upper respiratory tract infection of likely viral etiology (McCaig and Hughes 1995), and 22–49 percent are estimated to be unnecessary (Kozyrskyj et al. 2004; Cadieux et al. 2007).

Inappropriate use of antibiotics for respiratory infections promotes antibiotic resistance (Seppala et al. 1997; Austin, Kristinsson, and Anderson 1999; Pihlajamaki et al. 2001), increases health services utilization and costs (Little et al. 1997), and increases the risk of preventable drug-related adverse events (Classen et al. 1991). To enable the development of effective interventions to reduce inappropriate antibiotic use in primary care, determinants of inappropriate antibiotic prescribing and accurate methods for monitoring antibiotic use need to be identified.

Monitoring antibiotic prescribing in primary care is challenging because well-developed measures of antibiotic prescribing are scarce, often inaccurate, and may not reflect real prescribing practices. Studies of antibiotic prescribing in primary care have relied on physician self-reported prescribing (Mangione-Smith et al. 1999; Nash et al. 2002; Steinman, Landefeld, and Gonzales 2003), chart review or audit (Hueston, Jenkins, and Mainous 2000; Hutchinson et al. 2001; Mangione-Smith et al. 2002), or prescription claims (Mainous, Hueston, and Clark 1996; Majeed and Moser 1999; Wang et al. 1999; Steinke et al. 2000; Gill and Roalfe 2001; Kozyrskyj et al. 2004; Cadieux et al. 2007). Self-reported antibiotic prescribing was shown to underestimate actual antibiotic prescribing by about 30 percent (Mangione-Smith et al. 2002), and the cost of chart review is too high for wide-scale use. Prescription claims data avoid self-report bias, do not require additional data collection, and because they involve financial transactions, they are carefully audited by payers and have been found to be highly accurate (Tamblyn et al. 1995). Owing to these advantages, prescription claims are now used routinely to monitor antibiotic prescribing for respiratory infections in primary care (Mainous, Hueston, and Clark 1996; Majeed and Moser 1999; Wang et al. 1999; Steinke et al. 2000; Gill and Roalfe 2001; McCaig, Besser, and Hughes 2002; Kozyrskyj et al. 2004; Cadieux et al. 2007).

However, an important limitation of using prescription claims to monitor antibiotic prescribing is that treatment indication is not recorded on prescription claims. Treatment indication is required to determine the appropriateness of antibiotic prescribing; therefore, it must be inferred from other sources of information, such as physician billing claims for patient visits.

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If prescription claims are to be used to monitor antibiotic prescribing, then the accuracy of using diagnostic information in physician billing claims to infer the indication for antibiotic treatment needs to be assessed.

Two previous studies have assessed the accuracy of physician billing claims for identifying respiratory infection diagnoses, and both have shown promising results. The first was a study of administrative claims data from seven health insurance providers in Colorado, and it found that 79 percent of bronchitis diagnoses and 83 percent of pharyngitis diagnoses in administrative claims had a corresponding diagnosis in the written medical record (PPV; Maselli and Gonzales 2001). However, this study did not investigate what proportion of bronchitis and pharyngitis diagnoses documented in patient medical records was accurately documented in physician billing claims (sensitivity and specificity). The second study assessed the accuracy of Research Patient Data Repository (RPDR) claims from nine primary care clinics in the Brigham and Women's Primary Care Practice-Based Research Network in Boston and reported that 86 percent of respiratory infection diagnoses in RPDR claims had a corresponding diagnosis in the electronic health record (Linder et al. 2006). However, sensitivity and specificity estimates were not corrected for the verification bias introduced by over-sampling claims with a diagnosis of respiratory infection relative to claims without such a diagnosis (i.e., the study design inflated the prevalence of respiratory infection in the sample, relative to the true population prevalence; Begg and Greenes 1983; Irwig et al. 1994).

The objective of this study was to assess the accuracy of physician billing claims for identifying episodes of acute respiratory infection in primary care. In particular, we sought to estimate the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of physician billing claims.

METHODS

Study Design and Population

A validation study was carried out to assess the sensitivity, specificity, PPV, and NPV of physician billing claims for identifying episodes of respiratory infection, as compared with the patient medical record. The study population comprised 34 Montreal region family physicians and 17,002 of their patients who were participating in the MOXXI electronic medication management trial (Tamblyn et al. 2006) in 2002–2005. All patients participating in the MOXXI trial had

previously consented to share their medical records and provincial health insurance (RAMQ) data with researchers. These data were available for a period starting 1 year before patient enrollment date (2001 or later) until 2005, when the present study was conducted. From the available physician billing claims, we identified those with a diagnostic code (International Classification of Diseases, 9th Revision, or ICD-9) for laryngitis/tracheitis (464), common cold (460), influenza (480, 487), acute unspecified upper respiratory infection (465), pharyngitis/tonsillitis (462, 463, 034), otitis media (381, 382), sinusitis (461), acute bronchitis (466), or bacterial pneumonia (481–486); all decimal place suffixes of these ICD-9 codes were included. We purposefully selected 10 physicians who had been enrolled in the MOXXI trial for at least 2 years and had the most MOXXI-consenting patients (and therefore also had the most physician billing claims available for research purposes), and requested their consent.

Sample of Physician Billing Claims

Among the 10 physicians selected, we identified all MOXXI-consenting patients who had at least one physician billing claim with a diagnosis of acute respiratory infection during the study period, and randomly sampled 635 of those patients. We also identified all patients without any physician billing claim with a diagnosis of acute respiratory infection during the study period, and randomly sampled 94 of those patients. To improve the efficiency of data collection, we over-sampled patients with at least one diagnosis of acute respiratory infection, relative to those with no diagnosis of acute respiratory infection (Begg and Greenes 1983; Irwig et al. 1994). For each of the 729 patients sampled, we identified all physician billing claims generated during the study period (i.e., from 2001 or later, depending on the enrollment date, until 2005) and validated each one against the paper-based patient medical record. Information available in the physician billing claims included the patient's lifelong RAMQ personal identifier, physician license number, visit date, and ICD-9 diagnostic code.

Medical Record Abstraction

Once the physician billing claims had been sampled, a list of sampled patients' names and RAMQ personal identifiers was generated and sent to each consenting physician's office. The selected patients' paper-based medical records were retrieved by the office staff and reviewed by one of the authors (G. C.). For each sampled physician billing claim, the corresponding visit was identified in the medical record, the date of the visit was recorded, and

the presence or absence of all acute respiratory infections under study was ascertained from the clinical notes. At the time of the medical record abstraction, the reviewer was blinded to the ICD-9 code in the corresponding physician billing claim. Information abstracted from patient medical records was entered directly in an electronic, structured chart abstraction form and stored in an *MS Access* database, which had been prepopulated with participating physicians' license numbers, sampled patients' RAMQ identifiers, and visit dates according to physician billing claims. Intra-rater reliability was measured on 25 randomly selected visits that were reviewed a second time, and the percent agreement between the first and second review was 100 percent.

Linkage of Physician Billing Claims and Data Abstracted from Medical Records

Data retrieved from patient medical records were linked directly to physician billing claims using the patient lifelong RAMQ personal identifier, physician license number, and visit date $\pm$ 1 day.

Analyses

For each type of acute respiratory infection under study, a 2×2 table of diagnoses abstracted from patient medical records versus diagnoses obtained from the corresponding physician billing claims was generated using *SAS* statistical software (Version 9.3, SAS Institute Inc., Cary, NC). Information retrieved from the patient medical record was treated as a gold standard. The prevalence, PPV, and NPV of physician billing claims for identifying acute respiratory infections were estimated. Sensitivity and specificity estimates were corrected for the over-sampling of claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (Begg and Greenes 1983) using *MS Excel 2003* (Version 5.1). To investigate between-physician variation in physician billing claim diagnosis accuracy, these analyses were repeated for each physician individually, combining all nine types of acute respiratory infection under study (because each physician contributed too few of each type of acute respiratory infection to analyze each type individually).

Because we sampled several claims (and medical record visits) per patient, we conducted a sensitivity analysis to assess the effect of clustering of claims within patients on our estimates of sensitivity, specificity, PPV, and NPV. We did this by generating 100 random samples of one claim per patient ($n = 729$ claims) from our total sample of 3,526 claims, and averaging the estimates of sensitivity, specificity, PPV, and NPV over all 100 random samples, which is similar to bootstrapping methodology (Efron and Tibshirani 1994).

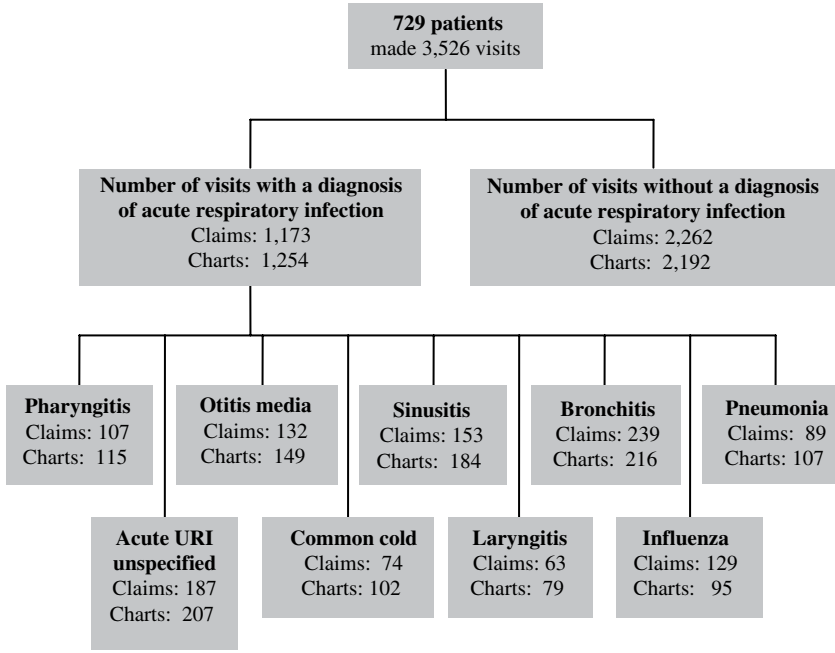
RESULTS

Ten physicians participating in the MOXXI trial were purposefully selected for this study, and nine agreed to participate. Among these nine physicians' patients enrolled in the MOXXI trial, we randomly selected 635 patients who had at least one claim with a diagnosis of acute respiratory infection, and 94 patients without any claims with a diagnosis of acute respiratory infection. These 729 patients made 3,526 visits to their respective MOXXI physicians during the study period (duration of 1–5 years, depending on the date of enrollment), for an average of 4.8 visits per patient. The medical records of all 729 sampled patients were abstracted, and written documentation for each of the 3,526 visits identified from physician billing claims was found in the corresponding patient's medical record. In all, 1,173 (33.3 percent) of sampled claims were positive for respiratory infection (Figure 1). Sixty-six percent of sampled patients were women, and the mean age of sampled patients was 47.6 (SD 21.0, range $<$1–90 years). The characteristics of patients enrolled in the MOXXI trial, as compared with those of the general population, have been discussed previously (Bartlett et al. 2005).

The agreement between the diagnosis in the medical record and the ICD-9 code in the physician billing claim is shown in Table 1, where shaded areas indicate concordant diagnoses. For example, there were 63 physician billing claims with a diagnosis of laryngitis, and for all 63 claims, a diagnosis of laryngitis was also documented in the medical record at the corresponding date; however, an additional 16 diagnoses of laryngitis were documented in medical records that were not documented in physician billing claims. The overall percent agreement for the presence of any acute respiratory infection was 72.5 percent, which is the sum of all diagnoses of respiratory infection present in the physician billing claim and the corresponding medical record (969) divided by the sum of all diagnoses of respiratory infection documented in medical records (1,337).

The proportion of physician billing claims with a diagnosis of acute respiratory infection confirmed in the patient medical record (PPV) was 0.93, 95 percent CI (0.91, 0.94), for all acute respiratory infection combined, and 0.84, 95 percent CI (0.81, 0.88), for respiratory infections of likely viral etiology (Table 2). The PPV for acute respiratory infections of potentially bacterial etiology was 0.89, 95 percent CI (0.87, 0.92), and ranged from 0.72, 95 percent CI (0.67, 0.78), for acute bronchitis to 0.91, 95 percent CI (0.85, 0.97), for bacterial pneumonia. Sensitivity of physician billing claims for all acute respiratory infections combined was 0.49, 95 percent CI (0.45, 0.53).

Figure 1: Diagnoses from the Sampled Physician Billing Claims and Corresponding Patient Medical Records.



With the exception of influenza, sensitivity was markedly lower for viral respiratory infections than for bacterial ones. Specificity was 0.99 or higher for all types of acute respiratory infection studied.

The prevalence of acute respiratory infection diagnoses in physician billing claims varied between physicians from 19.5 to 111.4 per 1,000 claims (Table 3). Sensitivity and PPV varied between physicians from 1.00, 95 percent CI (1.00, 1.00), to 0.19, 95 percent CI (0.06, 0.47), and from 0.98, 95 percent CI (0.96, 1.00), to 0.70, 95 percent CI (0.53, 0.87), respectively. The accuracy of physician billing claims for identifying acute respiratory infections did not appear to be higher among physicians who diagnosed more acute respiratory infections.

Our sensitivity analysis using only one claim per patient yielded estimates for sensitivity (0.55, 95 percent CI 0.45, 0.64), specificity (0.99, 95 percent CI 0.99, 1.00), PPV (0.93, 95 percent CI 0.90, 0.96), and NPV (0.94, 95 percent CI 0.91, 0.97) that were similar to the estimates obtained when all visits were used. The confidence intervals from the sensitivity analysis are wider because the sample size is smaller: 729 claims (one per patient) were

Table 1: Concordance of Diagnoses in Physician Billing Claims and Patient Medical Records

	Number of Visits in Patient Medical Records										
Number of Physician Billing Claims	*Laryngitis*	*Common Cold*	*Influenza*	*Unspecified Acute URI*	*Pharyngitis*	*Otitis Media*	*Sinusitis*	*Acute Bronchitis*	*Pneumonia*	*No Respiratory Infection*	*Total*
Laryngitis	63	0	0	0	0	0	0	0	0	0	63
Common cold	1	66	1	0	2	0	0	0	0	4	74
Influenza	2	1	85	7	1	1	6	6	5	15	129
Unspecified acute URI	0	1	1	154	3	0	2	4	0	22	187
Pharyngitis	2	1	1	2	93	1	1	0	0	6	107
Otitis media	0	0	0	5	1	116	1	0	1	8	132
Sinusitis	1	1	1	0	0	0	138	3	0	9	153
Acute bronchitis	6	3	1	11	3	3	15	173	9	15	239
Pneumonia	0	0	0	0	0	0	2	2	81	4	89
No respiratory infection	4	29	5	28	12	28	19	28	11	2,189	2,353
Total	79	102	95	207	115	149	184	216	107	2,272	3,526
Uncorrected sensitivity*	0.80	0.65	0.89	0.74	0.81	0.78	0.75	0.80	0.76		

Note: Shaded numbers indicate concordance.

*The uncorrected sensitivity estimate is inflated due to the purposeful over-sampling of physician billing claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (Begg and Greenes 1983; Irwig et al. 1994).

URI, upper respiratory infection.

Table 2: Sensitivity, Specificity, and Positive and Negative Predictive Values of the RAMQ Physician Billing Claims for Identifying Episodes of Acute Respiratory Infection

	RAMQ Physician Billing Claims				
	Prevalence per 1,000 (95% CI)	*Sensitivity* (95% CI)*	*Specificity* (95% CI)*	*PPV† (95% CI)*	*NPV‡ (95% CI)*
All respiratory infections	67.3 (65.6, 69.0)	0.49 (0.45, 0.53)	0.99 (0.99, 1.00)	0.93 (0.91, 0.94)	0.93 (0.92, 0.94)
All likely viral respiratory infections	16.4 (15.6, 17.3)	0.30 (0.26, 0.34)	1.00 (1.00, 1.00)	0.84 (0.81, 0.88)	0.97 (0.96, 0.97)
Laryngitis/tracheitis	1.2 (0.9, 1.4)	0.20 (0.13, 0.30)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (0.99, 1.00)
Common cold	1.4 (1.2, 1.7)	0.11 (0.08, 0.15)	1.00 (1.00, 1.00)	0.89 (0.82, 0.96)	0.99 (0.99, 0.99)
Influenza	3.6 (3.2, 4.0)	0.45 (0.30, 0.60)	1.00 (1.00, 1.00)	0.66 (0.58, 0.74)	1.00 (1.00, 1.00)
Unspecified acute URI	10.2 (9.6, 10.9)	0.35 (0.29, 0.42)	1.00 (1.00, 1.00)	0.82 (0.77, 0.88)	0.98 (0.98, 0.99)
All potentially bacterial respiratory infections	50.9 (49.4, 52.3)	0.51 (0.47, 0.56)	0.99 (0.99, 0.99)	0.89 (0.87, 0.92)	0.95 (0.95, 0.96)
Pharyngitis/tonsillitis	5.3 (4.9, 5.8)	0.42 (0.32, 0.53)	1.00 (1.00, 1.00)	0.87 (0.81, 0.93)	0.99 (0.99, 1.00)
Otitis media	8.6 (7.9, 9.2)	0.44 (0.35, 0.53)	1.00 (1.00, 1.00)	0.88 (0.82, 0.93)	0.99 (0.99, 0.99)
Sinusitis	12.5 (11.7, 13.2)	0.46 (0.38, 0.53)	1.00 (1.00, 1.00)	0.90 (0.85, 0.95)	0.99 (0.98, 0.99)
Acute bronchitis	19.5 (18.6, 20.4)	0.52 (0.46, 0.59)	0.99 (0.99, 0.99)	0.72 (0.67, 0.78)	0.99 (0.98, 0.99)
Pneumonia	5.0 (4.5, 5.5)	0.38 (0.28, 0.47)	1.00 (1.00, 1.00)	0.91 (0.85, 0.97)	0.99 (0.99, 1.00)

*Adjusted for over-sampling of physician billing claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (Begg and Greenes 1983; Irwig et al. 1994).

†Positive predictive value.

‡Negative predictive value.

URI, upper respiratory infection.

Table 3: Sensitivity, Specificity, and Positive and Negative Predictive Values of the RAMQ Physician Billing Claims Database for Identifying All Acute Respiratory Infections Combined, by Study Physician

	RAMQ Physician Billing Claims						
Study Physician	*Number of Claims with a Diagnosis of Acute RI*	*Total Number of Claims*	*Prevalence per 1,000 (95% CI)*	*Sensitivity* (95% CI)*	*Specificity* (95% CI)*	*PPV† (95% CI)*	*NPV‡ (95% CI)*
1	1,324	16,264	81.4 (77.1, 85.6)	0.85 (0.78, 0.91)	1.00 (0.99, 1.00)	0.96 (0.94, 0.98)	0.99 (0.98, 1.00)
2	2,041	18,319	111.4 (106.9, 116.0)	0.39 (0.33, 0.44)	0.98 (0.98, 0.99)	0.89 (0.86, 0.92)	0.82 (0.78, 0.86)
3	522	4,815	108.4 (99.6, 117.2)	0.42 (0.35, 0.49)	1.00 (0.99, 1.00)	0.97 (0.95, 1.00)	0.84 (0.80, 0.88)
4	356	9,614	37.0 (33.3, 40.8)	0.34 (0.24, 0.47)	1.00 (1.00, 1.00)	0.98 (0.96, 1.00)	0.93 (0.90, 0.96)
5	163	5,553	29.4 (24.9, 33.8)	0.37 (0.22, 0.56)	1.00 (0.99, 1.00)	0.89 (0.81, 0.97)	0.95 (0.92, 0.99)
6	159	6,905	23.0 (19.5, 26.6)	0.57 (0.16, 0.90)	0.99 (0.99, 1.00)	0.77 (0.64, 0.90)	0.99 (0.98, 1.00)
7	752	6,754	111.3 (103.8, 118.8)	0.72 (0.45, 0.89)	0.98 (0.96, 1.00)	0.82 (0.66, 0.98)	0.96 (0.92, 1.00)
8	94	4,815	19.5 (15.6, 23.4)	1.00 (1.00, 1.00)	0.99 (0.99, 1.00)	0.70 (0.53, 0.87)	1.00 (1.00, 1.00)
9	365	18,319	19.9 (17.9, 21.9)	0.19 (0.06, 0.47)	1.00 (0.99, 1.00)	0.97 (0.95, 1.00)	0.92 (0.84, 1.00)

*Adjusted for over-sampling of respiratory infections relative to other diagnoses (Begg and Greenes 1983; Irwig et al. 1994).

†Positive predictive value.

‡Negative predictive value.

RI, respiratory infection.

used instead of all 3,526. This shows that the effect of within-patient clustering of claims on sensitivity, specificity, PPV, and NPV estimates is small.

DISCUSSION

The PPV of physician billing claims was high for all types of acute respiratory infection studied. Our study was the first to estimate the prevalence, sensitivity, and specificity of physician billing claims for identifying chart-documented acute respiratory infections in primary care. For all but one type of acute respiratory infection investigated, our sensitivity estimates were below 0.50. Our study was also the first to look at between-physician variation in physician billing claim diagnosis accuracy. We found that prevalence of respiratory infections in physician billing claims varied widely between primary care physicians. We also observed large unexplained between-physician variation in sensitivity and PPV of physician billing claims for identifying acute respiratory infections.

If physician billing claims had many false-positive diagnoses of respiratory infection, they would not be a useful data source for monitoring antibiotic prescribing. Therefore, a high PPV, or a high likelihood that diagnoses of respiratory infection in physician billing claims are also present in the corresponding patient medical record, provides support for using health administrative data for monitoring antibiotic prescribing. For most of the acute respiratory infection diagnoses investigated, our estimates of PPV were similar to those previously reported in the literature (Maselli and Gonzales 2001; Linder et al. 2006). However, our PPV estimate for influenza (0.66, 95 percent CI 0.58, 0.74) was much higher than the 0.20 reported by Linder et al. (2006), but the latter was aberrantly low as compared with other PPV estimates in the same study.

Previous studies have emphasized the high PPV of health administrative data for identifying episodes of respiratory infection, but have overlooked the importance of sensitivity (Maselli and Gonzales 2001; Linder et al. 2006). A high sensitivity is desirable because it suggests that the data capture a majority of visits for respiratory infections. A low sensitivity is problematic because it suggests that several visits for respiratory infections are not documented in health administrative data. Nondocumentation of visits for respiratory infections may or may not be associated with antibiotic prescribing, which may result in bias when using health administrative data to monitor antibiotic prescribing.

Our study estimated the sensitivity of physician billing claims for identifying acute respiratory infections. Our sensitivity estimates were below 0.50 for all types of acute respiratory infection studied except acute bronchitis, which

raises concerns about the potential for bias. Whereas one previous study estimated the sensitivity of claims for identifying respiratory infections (Linder et al. 2006), the authors did not correct their sensitivity estimate for the verification bias introduced by over-sampling claims with a diagnosis of acute respiratory infection relative to claims without such a diagnosis (Begg and Greenes 1983; Irwig et al. 1994); consequently, they greatly overestimated sensitivity. For example, if we had not corrected our estimates for verification bias, our estimate of the sensitivity of physician billing claims for identifying laryngitis would have been 0.80, as compared with the corrected sensitivity estimate of 0.20.

We were first to investigate between-physician variation in physician billing claim diagnosis accuracy for acute respiratory infections. We found almost a sixfold variation between physicians in the prevalence of acute respiratory infections. We observed similar between-physician variation in the sensitivity and PPV of physician billing claims for identifying acute respiratory infections. We expected that claims submitted by physicians who diagnosed more acute respiratory infections would be more accurate for identifying acute respiratory infections, but we found that neither frequency nor prevalence of acute respiratory infections seemed to be related to physician billing claim diagnosis accuracy. This finding suggests that other factors are likely responsible for the observed between-physician variation in physician billing claim diagnosis accuracy.

A limitation of our study is that medical records may not represent a true gold standard for identifying acute respiratory infections diagnosed in primary care. The use of a single rater was also a limitation of our study, and systematic misclassification of acute respiratory infection diagnoses may have occurred as a result. Another limitation of our study was its small convenience sample of primary care physicians. Whereas physicians participating in the MOXXI trial are generally similar to other eligible physicians in the Montreal region, they tend to be younger than MOXXI nonparticipants. If physician billing claim diagnosis accuracy is related to physician age or practice experience, then our study results may not be applicable to older or more experienced physicians. Also, the MOXXI trial involves physicians practicing in urban and suburban areas, and our results may not be generalizable to physicians practicing in rural areas. Furthermore, patients enrolled in the MOXXI trial tend to differ from nonparticipating patients in that they are generally older, with more complex health status, and have more visits to the MOXXI physician (Bartlett et al. 2005). Younger, healthier patients may be underrepresented in our study sample. Future research should involve a large random sample of primary care physician from both urban and rural areas, and a stratified random sample of patients from each physician's practice population.

Because physician billing claims and prescription claims are now routinely used to monitor antibiotic prescribing for acute respiratory infections in primary care (Mainous, Hueston, and Clark 1996; Majeed and Moser 1999; Wang et al. 1999; Steinke et al. 2000; Gill and Roalfe 2001; Kozyrskyj et al. 2004; Cadieux et al. 2007), it is important for future research to determine whether half of all acute respiratory infections diagnoses are missing from physician billing claims at random, or whether bias is present. If bias is present, future research should also focus on identifying determinants of physician billing claim diagnosis accuracy, so that appropriate corrections for the resulting bias can be developed and applied when physician billing claims are used to infer treatment indication for antibiotic prescribing. As suggested by the large between-physician variation observed in this study, physician characteristics may be associated with physician billing claim diagnosis accuracy. The effect of physician characteristics, as well as patient, encounter, practice, and billing characteristics, on physician billing claim diagnosis accuracy should be assessed.

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SUPPLEMENTARY MATERIAL

The following supplementary material for this article is available online:

Appendix SA1: Verification Bias Correction.

Appendix SA2: Author Matrix.

This material is available as part of the online article from http://www.blackwell-synergy.com/doi/abs/10.1111/j.1475-6773.2008.00873.x (this link will take you to the article abstract).

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RESEARCH ARTICLE Open Access

Accuracy of syndrome definitions based on diagnoses in physician claims

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Abstract

Background: Community clinics offer potential for timelier outbreak detection and monitoring than emergency departments. However, the accuracy of syndrome definitions used in surveillance has never been evaluated in community settings. This study's objective was to assess the accuracy of syndrome definitions based on diagnostic codes in physician claims for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory including influenza-like illness) in community clinics.

Methods: We selected a random sample of 3,600 community-based primary care physicians who practiced in the fee-for-service system in the province of Quebec, Canada in 2005-2007. We randomly selected 10 visits per physician from their claims, stratifying on syndrome type and presence, diagnosis, and month. Double-blinded chart reviews were conducted by telephone with consenting physicians to obtain information on patient diagnoses for each sampled visit. The sensitivity, specificity, and positive predictive value (PPV) of physician claims were estimated by comparison to chart review.

Results: 1,098 (30.5%) physicians completed the chart review. A chart entry on the date of the corresponding claim was found for 10,529 (95.9%) visits. The sensitivity of syndrome definitions based on diagnostic codes in physician claims was low, ranging from 0.11 (fever) to 0.44 (respiratory), the specificity was high, and the PPV was moderate to high, ranging from 0.59 (fever) to 0.85 (respiratory). We found that rarely used diagnostic codes had a higher probability of being false-positives, and that more commonly used diagnostic codes had a higher PPV.

Conclusions: Future research should identify physician, patient, and encounter characteristics associated with the accuracy of diagnostic codes in physician claims. This would enable public health to improve syndromic surveillance, either by focusing on physician claims whose diagnostic code is more likely to be accurate, or by using all physician claims and weighing each according to the likelihood that its diagnostic code is accurate.

Background

Syndromic surveillance is used widely by public health departments to detect and monitor unusual disease activity in the population by extracting nonspecific clinical data from information systems in clinical settings [1-4]. Whereas much syndromic surveillance practice [3] and research [5] has focused on visits to emergency departments (ED), visits to community clinics offer another promising source of data. Syndromes followed in practice, such as influenza-like-illness (ILI), typically involve earlier, milder stages of disease, and most affected persons are likely to self-treat [6-8], at least initially, or present to walk-in clinics [6]. In fact, researchers have demonstrated that excess ILI activity can be detected earlier using data from clinics as compared to data from EDs [9-11]. The accuracy of diagnostic data from community clinics has not, however, been established.

Many syndromic surveillance systems use International Classification of Disease, 9th revision (ICD-9) diagnostic codes in administrative databases to monitor syndrome occurrence [12]. For this purpose, expert panels have generated groupings of ICD-9 codes corresponding to conceptual syndrome definitions [13]. Administrative databases offer great promise for population-based surveillance by providing access to diagnostic

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information from many sites, including community healthcare settings. However, unlike medical procedure codes, ICD-9 diagnostic codes are not usually linked to healthcare provider payment, and therefore are not audited by health administrative authorities. Because of this, variation in diagnostic coding between physicians and between institutions is expected.

In a pilot study [14], we evaluated the accuracy of diagnostic codes in physician claims for identifying acute respiratory infections in nine Montreal-area community-based physicians. We abstracted the diagnosis from the medical chart for the 3,526 visits made by 729 sampled patients in 2002-2005, and compared the medical chart diagnosis to the ICD-9 code on the corresponding physician claim. For all acute respiratory infections combined, we found a sensitivity of 0.49, 95% CI (0.45, 0.53), and a positive predictive value (PPV) of 0.93, 95% CI (0.91, 0.94). These pilot study results are promising, but there is a need for a large-scale, population-based investigation of the accuracy of diagnostic codes used in syndromic surveillance.

The objective of the present study was to assess the accuracy of syndrome definitions based on diagnostic codes from a representative sample of physician claims for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory, including influenza-like illness (ILI)) in community healthcare settings. These syndromes were selected for their relevance to public health and the likelihood of being first detected among patients presenting to community healthcare settings.

Methods

Context

This study was conducted in the province of Quebec, Canada, where universal health coverage is provided through the provincial health insurance plan. Each Canadian province maintains a population-based registry of insured persons and claims for all physician visits remunerated on a fee-for-service basis. Physician claims include information on the diagnosis (recorded as an ICD-9 code), medical procedure, visit date, location, and cost of service. All claims also record unique physician and patient identifiers that can be used to create longitudinal histories of healthcare use. In the province of Quebec, 99% of residents have provincial health insurance and 85-95% of medical visits are remunerated on a fee-for-service basis [15]. In 2006, there were more than 7.6 million inhabitants in Quebec [16], and 18,908 active registered physicians [17]. The availability of diagnostic information for nearly all medical visits to Quebec physicians represents an invaluable opportunity for assessing the validity of using diagnostic codes in physician claims for population-based surveillance, including syndromic surveillance.

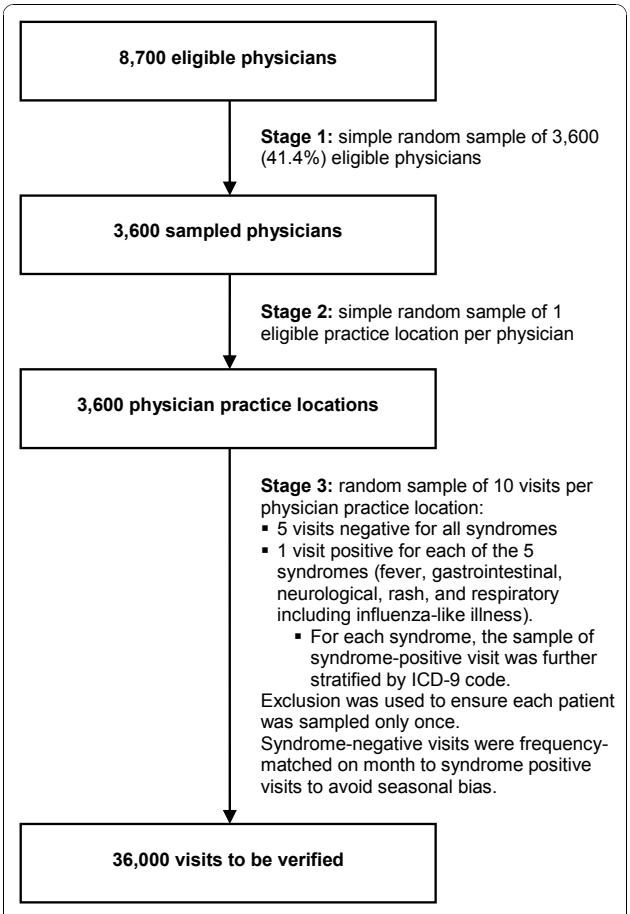

Figure 1 Population-based, 3-stage stratified random sample of visits to all community physicians in the province of Quebec.

Study design and sampling

The accuracy of diagnostic codes in physician claims for identifying syndromes was assessed by comparison to clinical information in the corresponding medical chart. To ensure representativeness, we used a population-based, 3-stage stratified random sample of 36,000 visits (Figure 1). In the first stage (Figure 1 Stage 1), the provincial health insurance agency identified all physicians who were eligible to be included in our study. To be eligible, physicians had to be a general practitioner, pediatrician, internist, geriatrician or general surgeon who practiced in the fee-for-service system in a private clinic, community health center, or hospital-based ambulatory care clinic during the 2-year study period (October 1, 2005 to September 30, 2007). Internists and general surgeons were included in our sample because, especially in rural-remote and underserved areas, these physicians may provide first-contact care and act as patients' family physician. From the 8,700 eligible physicians identified, the provincial health insurance agency selected a random sample of 3,600 (41.4%) physicians.

In the second stage (Figure 1 Stage 2), to facilitate chart retrieval for review, the health insurance agency randomly selected one eligible community practice location for each physician. The health insurance agency then sent the research team an anonymized file containing all physician claims billed by the 3,600 physicians from their respective selected community practice location during the 2-year study period (Figure 2 Step 1).

In the third stage (Figure 1 Stage 3), the research team randomly selected 5 syndrome-positive visits, i.e., 1 visit for each of fever, gastrointestinal, neurological, rash, and respiratory syndrome (including ILI), and 5 visits negative for all syndromes. Visits were classified as positive for a syndrome if a physician claim for the visit had an ICD-9 code that was part of the syndrome definition. Because syndromes have low population prevalence, to maximize data collection efficiency [18], syndrome-positive visits were over-sampled relative to syndrome-negative ones, so as to yield 1 syndrome-positive visit per syndrome per physician and 5 syndrome-negative visits per physician. When sampling syndrome-positive claims, to maximize the number of syndrome-positive ICD-9 codes verified, we further stratified on ICD-9 code. Because two or more syndromes can occur concurrently in the same patient [19], syndrome-negative visits were negative for *all* syndromes. Syndrome-negative visits were also matched to syndrome-positive visits on calendar month to avoid bias due to syndrome seasonality. To avoid bias due to visits being clustered within patients, restriction was used to ensure that each patient was only sampled once. The list of 10 sampled visits was enumerated for each of the 3,600 physicians, for a total of 36,000 visits. An anonymized unique identifier, the study number, was assigned to each sampled visit by the research team. The list of 36,000 sampled visits was then sent to the health insurance agency (Figure 2 Step 2).

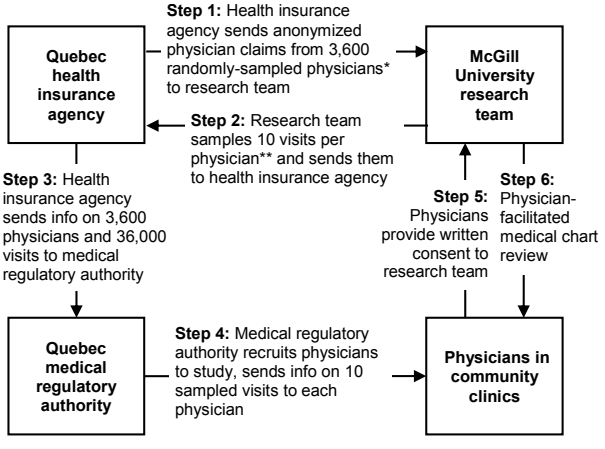

Figure 2 Overview of data collection * Physician sampling by the Quebec health insurance agency is described in Figure 1, Stages 1 and 2. ** Visit sampling by the research team is described in Figure 1, Stage 3.

Syndrome definitions

We verified two sets of definitions for the 5 syndromes under study: the definitions developed and published by the US Centers for Disease Control and Prevention (CDC) in 2003 [13], and used by the US Department of Defense's (DoD) Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE), as well as the corresponding definitions in the University of Pittsburgh's Real-time Outbreak and Disease Surveillance (RODS) system [19]. For ILI, we used the large-group (sensitive) and small-group (specific) definitions developed for the DoD ESSENCE system [20]. These definitions are similar to the consensus syndrome definitions being developed by representatives from the 10 syndromic surveillance systems in place in the US [21], which have not yet been mapped to ICD-9 codes.

Physician recruitment

To preserve physician and patient anonymity, the health insurance agency sent the list of 3,600 physicians and 36,000 visits sampled by the research team to the medical regulatory authority (Figure 2 Step 3). The medical regulatory authority has the legal right to access confidential physician and patient information, therefore the list it received included physician names and mailing addresses, as well as patient names, insurance numbers, and dates of birth. The medical regulatory authority acted as a trusted third party and recruited physicians to the study on behalf of the research team; it also provided physicians with information on the 10 sampled visits (Figure 2 Step 4). Interested physicians mailed their written consent and contact information to the research team (Figure 2 Step 5). Non-responding physicians were sent up to four reminders. Physician recruitment began in September 2008 and ended in August 2009. To maximize participation, physicians were offered $50 compensation for their participation and a summary of study findings.

Physician-facilitated medical chart review

The medical regulatory authority sent each physician the list of 10 sampled visits (Figure 2 Step 3). Lists sent to physicians included patients' first and last names, date of birth, health insurance number, and date of the visit to be verified, as well as the study number for each visit. Because the lists sent to physicians contained both patient information and study numbers, it enabled physicians to retrieve the relevant medical charts, and researchers to link the information collected through chart review to the anonymized physician claims file. During the chart review, interviewers and physicians

referred to each visit using only the study number and visit date, thereby preserving patient anonymity.

Physician-facilitated medical chart reviews began in September 2008 and ended in December 2009. Using a previously published methodology [22], trained interviewers contacted consenting physicians by telephone to perform the chart review (Figure 2 Step 6). For each of the 10 sampled visits, the interviewer asked the physician to list all diagnoses. For each diagnosis corresponding to a syndrome definition, the interviewer asked the physician about the signs, symptoms, and key findings recorded in the medical chart, as well as the most likely etiology for the diagnosis (based solely on information available at the time of the visit).

Physician responses were entered directly into a database by the interviewer. Diagnoses were selected from a searchable list of diagnoses (mapped to ICD-9 codes) or, if the physician had recorded the ICD-9 code in the medical chart, the ICD-9 code was entered directly. For each syndrome-positive diagnosis, a list of syndrome-specific signs and symptoms was elicited, and the interviewer recorded whether the sign or symptom had been present, absent, or not recorded in the medical chart. Symptoms or signs not in the list and other key findings, such as epidemiologic links to other diagnosed cases or known outbreaks, were recorded as free text in separate fields. The data collection tool was translated to French for use with French-speaking physicians, and back-translated to English to ensure comparability of data collection.

At the time of chart review, the physician and interviewer were both blinded to the ICD-9 code in the physician claim and the syndrome-positive or syndrome-negative status of the claim. To minimize measurement error due to inter-rater differences, interviewers were trained to use the data collection tool. Inter-rater reliability was assessed at baseline by having interviewers perform 2 simulated physician interviews of 10 visits each (for a total of 20 visits). To maintain data quality, interviewers underwent quality assurance monitoring every 3 months. Each assessment was comprised of 2 simulated physician interviews of 10 visits each (for a total of 20 visits). Agreement between raters was measured using the intraclass correlation coefficient (ICC).

Linkage of the medical chart review data to the physician claims data

The database containing the medical chart review data was linked to the physician claims file using the study number, physician identifier, and visit date. In our pilot study [14], we found that the visit date in the chart sometimes differed slightly from the visit date on the claim. We considered the chart and the claim to refer to the same visit if the visit date in the chart was within 0 (identical date) to 3 days from the visit date in the claim.

Physician characteristics that may influence participation

Physician gender, preferred language (French or English), specialty, practice setting, and geographic location were obtained from the health insurance agency. Physician year of licensure was obtained from the medical regulatory authority. The number of days worked per year was calculated as the number of days when at least one claim was billed by the physician to the health insurance agency. The number of patients seen per day worked was calculated as the number of distinct patients for which one or more claim was billed by the physician per day worked. The number and prevalence of syndrome-positive visits were calculated for each physician using claims billed from the selected practice location during the 2-year study period.

Statistical methods

For each visit, we assessed if the ICD-9 code in the physician claim and the diagnosis in the corresponding medical chart agreed as to the presence of each syndromes and ILI. For example, if the diagnosis in the claim was cough (786.2) and the diagnosis in the corresponding medical chart was acute bronchitis (466.0), then both the claim diagnosis and the chart diagnosis were positive for respiratory syndrome, therefore the claim was a true-positive for respiratory syndrome. If the diagnosis in the claim was cough (786.2) and the diagnoses in the chart were hypertension (401.9) and diabetes (250.0), then the claim diagnosis was positive for respiratory syndrome and the chart diagnoses were not, therefore the claim was a false-positive for respiratory syndrome.

The negative predictive value (NPV) of each syndrome definition was estimated directly from the data. Because we stratified syndrome-positive visits by ICD-9 code, we had to use an adjustment based on Bayes Theorem [23] to estimate the PPV of each syndrome. The PPV was estimated as a weighted average of each ICD-9 code's PPV, the weight being the number of visits with a given ICD-9 code divided by the total number of visits positive for that syndrome among participating physicians.

Because we verified more syndrome-positive visits than syndrome-negative ones, direct estimation of sensitivity and specificity using our data would lead to verification bias: sensitivity would be overestimated, and specificity underestimated [23]. Because verified claims were randomly sampled within syndrome-positive and syndrome-negative strata, unbiased estimation of these parameters was achieved by re-weighting for the verification fractions [23]. The sensitivity and specificity of physician claims for identifying each syndrome was

estimated from the PPV and NPV [24] using the correction for verification bias [23], re-weighting for the different sampling fractions. We estimated the 95% CI for the bias-corrected sensitivity and specificity using the methods described by Begg and Greenes [23].

Ethics review

The research protocol for this study was reviewed and approved by the McGill University Institutional Review Board, the Quebec privacy commission (Commission d'accès à l'information du Québec), the legal department of the Quebec health insurance agency (Régie de l'assurance maladie du Québec), and the Quebec medical regulatory authority (Collège des médecins du Québec).

Results

Between October 1, 2005 and September 30, 2007, the 3,600 study physicians billed for over 20 million visits by 4.8 million patients (61% of the province's population) from their randomly selected community practice.

Physician participation

Of 3,600 physicians contacted, 172 (4.8%) had an incorrect address on file with the health insurance agency, and 170 (4.7%) were discovered to be ineligible (recently deceased, retired, on sick/maternity leave, no longer practicing at the selected practice location). Of the 3,258 remaining physicians, 1,129 (34.7%) physicians consented to participate in the study, 218 (6.7%) refused, and 1,911 (58.7%) did not respond. Of the 1,129 consenting physicians, 1,098 (97.3%) completed the physician-facilitated medical chart review, and 31 (2.7%) were unreachable or withdrew consent prior to interview. Participating and non-participating physicians were similar on all measured variables except two (Table 1): as compared to non-participants, participants had been in practice longer and had worked more days during the study period. Syndrome prevalence was similar among participating and non-participating physicians, and ranged from 5 per 1,000 visits for neurological syndrome and ILI small-group, to 126 per 1,000 visits for respiratory syndrome.

Inter-rater agreement

Agreement between raters was measured using simulated physician interviews shortly before the start of data collection and every 3 months thereafter. Agreement was perfect on all assessments (ICC = 1.00).

Date agreement between the claim and the medical chart

Of the 10,980 visits selected for verification (10 visits per participating physician), physicians were able to access the corresponding medical chart for 10,669 (97.2%). The most common reasons for being unable to access the chart were inability to locate the medical chart (151 charts) and medical chart in storage with retrieval fee (140 charts). For 10,465 (98.1%) of the sampled visits, the visit date in the medical chart was identical to the visit date on the claim. Allowing for potential date transcription errors during billing, an additional 64 (0.6%) visits with a date in the medical chart that was within 1-3 days of the visit date on the claim were identified, for a total of 10,529 visits for which both the medical chart and the claim was available and the visit dates were in agreement (within the 3 day time window).

Syndrome agreement between the claim ICD-9 code and the medical chart diagnosis

Table 2 shows the accuracy of ICD-9 codes in physician claims for identifying syndromes, as compared to the medical chart. The sensivity of ICD-9 codes in physician claims for identifying syndromes was low, ranging from 0.11, 95% CI (0.10, 0.13) for fever syndrome to 0.44, 95% CI (0.41, 0.47) for respiratory syndrome. The PPV of ICD-9 codes in physician claims for identifying syndromes was moderate to high, ranging from 0.59, 95% CI (0.55, 0.64) for fever syndrome to 0.85, 95% CI (0.83, 0.88) for respiratory syndrome. Both the specificity and NPV of ICD-9 codes in physician claims were near-perfect for all syndromes studied.

Additional file 1 (excerpted in Table 3) shows the PPV of physician claims for identifying syndromes for each ICD-9 code individually. There was wide variation in PPV between different ICD-9 codes in a given syndrome. ICD-9 codes that were very rarely used by physicians, for example tularemia (ICD-9 code: 21.9), had a high probability of being false-positives, and therefore a very low PPV. ICD-9 codes for common symptoms, for example fever (ICD-9 code: 780.6), had a lower probability of being false-positives, and a higher PPV. ICD-9 codes that represent common diagnoses, for example acute bronchitis (ICD-9 code: 466.0), had the lowest probability of being false-positives, and the highest PPV.

Discussion

This study was the first large-scale, population-based investigation of the accuracy of syndrome definitions based on diagnostic codes in physician claims from community healthcare settings. We found that the sensitivity of syndrome definitions based on diagnostic codes in physician claims for identifying syndromes was low, the PPV was moderate to high, and the specificity and NPV were near-perfect. Even though our sensitivity estimates were low for all syndromes definitions, these syndrome definitions may still be useful for monitoring syndrome occurrence when there are large numbers of cases (e.g., seasonal influenza). Respiratory syndrome had the highest prevalence and was the most accurately

Table 1 Characteristics of participating and non-participating physicians

	Participating physicians (N = 1,098)		Non-participating physicians (N = 2,160)	
Physician characteristics	**No.**	**(%)**	**No.**	**(%)**
Gender:				
Female	411	37.4	823	38.1
Male	687	62.6	1,337	61.9
Preferred language:				
French	1,006	91.6	1,937	89.7
English	92	8.4	223	10.3
Specialty:				
General practice	993	90.4	1,932	89.4
Internal medicine	13	1.2	41	1.9
Pediatrics	62	5.6	102	4.7
General surgery	30	2.7	85	3.9
Geriatrics	0	0	0	0
Type of setting selected:[1]				
Private clinic	1,060	96.5	2,044	94.6
Community health center	5	0.5	9	0.4
Hospital-based ambulatory clinic	33	3.0	107	5.0
Geographic location of selected setting:[1,3]				
Urban	921	83.9	1,867	86.4
Rural	177	16.1	293	13.6
	Mean	**SD**	**Mean**	**SD**
Years since licensure	24.2	9.7	22.3	10.5
No. days worked per year[1]	157.0	55.0	143.2	59.8
No. patients seen per day worked[1]	21.2	13.4	21.0	13.3
Syndrome frequency based on claim ICD-9 code	**No. visits[1,2]**	**Prevalence per 1,000 visits[1]**	**No. visits[1,2]**	**Prevalence per 1,000 visits[1]**
CDC and DoD ESSENCE[4]				
Fever	80,884	11	160,821	12
Gastrointestinal	162,282	22	309,209	24
Neurological	40,236	5	73,810	6
Rash	126,900	17	224,370	17
Respiratory	911,924	125	1,643,240	126
RODS[5]				
Fever	162,000	22	291,990	22
Gastrointestinal	146,355	20	283,578	22
Neurological	36,344	5	67,344	5
Rash	55,251	8	103,698	8
Respiratory	478,201	65	877,556	67
Influenza-like illness[6]				
Large-group	622,046	85	1,129,782	87
Small-group	32,173	4	61,127	5

[1] As per our study design, for each physician, a single practice location was randomly selected to facilitate the validation process. The information in this table is based in claims generated from the selected practice location during the 2-year study period.

[2] There were a total of 7,315,994 visits to the 1,098 participating physicians, and 13,010,410 visits to the 2,160 eligible non-participating physicians at the selected practice location during the 2-year study period.

[3] We tested the statistical significance (at the $p < 0.05$ level) of any differences between participating and non-participating physicians using a multivariate logistic regression model where the dependent variable was participation and the independent variables were all characteristics in Table 1. Due to overlap between CDC, RODS, and ILI syndrome definitions, to avoid collinearity, we used separate models for each set of syndrome definitions. As compared to non-participating physicians, participating physicians had been in practice longer (odds ratio $(OR)_{per\ 10\ years\ since\ licensure}$, 1.15; 95% CI, 1.05-1.25), had worked more days ($OR_{per\ 50\ days}$, 1.18; 95% CI, 1.09-1.28) during the 2-year study period.

[4] Syndrome case definitions developed and published by the US Centers for Disease Control and Prevention (CDC) in 2003, and used by the US Department of Defense's Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE).

[5] Syndrome case definitions developed in the context of the University of Pittsburgh's Real-time Outbreak and Disease Surveillance (RODS) system.

[6] Syndrome case definitions developed in the context of the US Department of Defense's Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE).

Table 2 Accuracy of ICD-9 coded diagnoses in physician claims, as compared to ICD-9 coded diagnoses from physician-facilitated medical chart review, for identifying constitutional, gastrointestinal, neurological, rash, and respiratory syndrome, as well as influenza-like illness (ILI) (N = 10,529 visits with matched claim-record pair)

Syndrome definition	No. visits in verified claims	No. visits in verified charts	Sensivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
***CDC and DoD ESSENCE*[1]**						
Fever	601	656	0.11 (0.10, 0.13)	0.99 (0.99, 0.99)	0.59 (0.55, 0.64)	0.94 (0.93, 0.95)
Gastrointestinal	855	888	0.23 (0.20, 0.26)	0.99 (0.99, 0.99)	0.71 (0.66, 0.75)	0.94 (0.94, 0.95)
Neurological	971	693	0.17 (0.14, 0.21)	1.00 (1.00, 1.00)	0.67 (0.64, 0.70)	0.98 (0.98, 0.98)
Rash	897	905	0.20 (0.18, 0.23)	0.99 (0.99, 0.99)	0.66 (0.62, 0.70)	0.95 (0.95, 0.96)
Respiratory	1,049	1,779	0.44 (0.41, 0.47)	0.97 (0.96, 0.98)	0.85 (0.83, 0.88)	0.84 (0.83, 0.85)
***RODS*[2]**						
Fever	873	961	0.14 (0.12, 0.16)	0.99 (0.99, 0.99)	0.60 (0.56, 0.64)	0.91 (0.90, 0.92)
Gastrointestinal	703	834	0.20 (0.18, 0.23)	0.99 (0.99, 0.99)	0.68 (0.63, 0.73)	0.94 (0.94, 0.95)
Neurological	874	523	0.16 (0.13, 0.20)	1.00 (1.00, 1.00)	0.52 (0.48, 0.55)	0.99 (0.98, 0.99)
Rash	814	718	0.12 (0.10, 0.14)	1.00 (1.00, 1.00)	0.63 (0.59, 0.66)	0.96 (0.96, 0.97)
Respiratory	665	1,209	0.29 (0.26, 0.32)	0.98 (0.98, 0.98)	0.74 (0.70, 0.79)	0.87 (0.86, 0.88)
***Influenza-like illness*[3]**						
Large-group	653	1,232	0.38 (0.35, 0.41)	0.98 (0.98, 0.98)	0.77 (0.73, 0.81)	0.88 (0.87, 0.89)
Small-group	53	49	0.18 (0.12, 0.26)	1.00 (1.00, 1.00)	0.29 (0.16, 0.41)	0.99 (0.99, 0.99)

[1] Syndrome case definitions developed and published by the US Centers for Disease Control and Prevention (CDC) in 2003, and used by the US Department of Defense's Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE).

[2] Syndrome case definitions developed in the context of the University of Pittsburgh's Real-time Outbreak and Disease Surveillance (RODS) system.

[3] Syndrome case definitions developed in the context of the US Department of Defense's Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE).

reported in physician claims. Unexpectedly, ILI small-group had the lowest PPV of all syndromes definitions studied, much lower than previously reported by others [20]. The small-group definition of ILI is made up of only four ICD-9 codes: influenza with pneumonia (487.0), influenza with other respiratory manifestations (487.1), influenza with other manifestations (487.8), and acute upper respiratory infection, other multiple sites (465.8). Based on our interviews of over a thousand community physicians, we think that the poor accuracy of the ILI small-group definition reflects the common usage of the word 'flu' to describe a vague illness or a combination of non-specific symptoms. In addition to observing variation in physician claim accuracy between syndromes, we also found large variation in accuracy and prevalence between diagnostic codes within syndromes. Diagnostic codes with a very low prevalence were generally more likely to be false-positives; conversely, diagnostic codes with a higher prevalence were generally less likely to be false-positives, especially if they represented a diagnosis, as opposed to a symptom. This suggests that physicians are more likely to know the correct diagnostic code for a frequently diagnosed ailment, as compared to a rare one.

Rigorous attempts to assess the accuracy of ICD-9 codes used in syndromic surveillance as compared to the medical chart have been few, and they have relied on small convenience samples of emergency departments. In one such study, the accuracy of ICD-9 codes in ED reports for identifying 3 syndromes (fever, gastrointestinal, and respiratory) was assessed as compared to hospital chart diagnoses in the context of the US DoD ESSENCE surveillance system [25]. For greater data collection efficiency, syndrome-positive ED reports were over-sampled relative to syndrome-negative ones; however, analyses were not adjusted for this differential sampling strategy, resulting in verification bias [23], and leading to a large overestimation of sensivity and underestimation of specificity. To illustrate, the proportion of fever-positive visits in the sample was 0.19, whereas the proportion of fever-positive visits in the population is approximately 0.01 (based on our study). The authors reported a sensitivity of 0.69 and a specificity of 0.95. However, adjusting for verification bias, the estimates would be approximately 0.09 for sensivity and 1.00 for specificity, which is similar to our results. In another study, the accuracy of ICD-9 codes in ED reports for identifying 7 syndrome definitions (botulinic, constitutional, gastrointestinal, hemorrhagic, neurological, rash, and respiratory) was assessed against hospital chart diagnoses in the context of the RODS surveillance system [19]. To maximize the quantity of syndrome-positive ICD-9 codes verified, the investigators selected a random sample of syndrome-positive visits from ED reports, stratified on

Table 3 Example of diagnostic codes with the highest and lowest positive predictive value (excerpted from additional file 1)

Example of diagnostic codes with the HIGHEST positive predictive value (PPV)			
Syndrome	**ICD-9 code**	**Diagnostic label**	**PPV (95% CI)**
Fever[1]	82.8	Tick-borne rickettsiosis not elsewhere classified	1.00 (1.00, 1.00)
	88.8	Other specified arthropod-borne diseases	1.00 (1.00, 1.00)
Gastrointestinal[1]	7.1	Giardiasis	1.00 (1.00, 1.00)
	5.9	Food poisoning not otherwise specified	1.00 (1.00, 1.00)
Neurological[1]	323.0	Encephalitis in viral disease classified elsewhere	1.00 (1.00, 1.00)
	784.3	Aphasia	1.00 (1.00, 1.00)
Rash[1]	53.8	Herpes zoster with unspecified complication	1.00 (1.00, 1.00)
	695.2	Erythema nodosum	1.00 (1.00, 1.00)
Respiratory[1]	33.0	*Bordetella pertussis*	1.00 (1.00, 1.00)
	462.9	Pharyngitis, acute not otherwise specified	1.00 (1.00, 1.00)
ILI large-group[2]	487.0	Influenza with pneumonia	1.00 (1.00, 1.00)
	486.0	Pneumonia, organism not otherwise specified	1.00 (1.00, 1.00)
Example of diagnostic codes with the LOWEST positive predictive value (PPV)			
Syndrome	**ICD-9 code**	**Diagnostic label**	**PPV (95% CI)**
Fever[1]	88.0	Bartonellosis	0.00 (0.00, 0.00)
	78.2	Sweating fever	0.00 (0.00, 0.00)
Gastrointestinal[1]	555.0	Regional enteritis, small intestine	0.00 (0.00, 0.00)
	1.1	Cholera due to *Vibrio cholerae* El Tor	0.00 (0.00, 0.00)
Neurological[1]	323.2	Encephalitis in protozoal disease classified elsewhere	0.00 (0.00, 0.00)
	53.0	Herpes zoster with meningitis	0.00 (0.00, 0.00)
Rash[1]	51.0	Cowpox	0.00 (0.00, 0.00)
	55.8	Measles complications not otherwise specified	0.00 (0.00, 0.00)
Respiratory[1]	20.4	Secondary pneumonic plague	0.00 (0.00, 0.00)
	79.8	Hantavirus infection	0.00 (0.00, 0.00)
ILI large-group[2]	490.0	Bronchitis not otherwise specified	0.00 (0.00, 0.00)
	465.8	Acute upper respiratory infection, other multiple sites	0.36 (0.08, 0.65)

[1] Syndrome case definitions developed and published by the US Centers for Disease Control and Prevention (CDC) in 2003, and used by the US Department of Defense's Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE).

[2] Syndrome case definition developed in the context of the US Department of Defense's Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE).

syndrome-positive ICD-9 code, such that an equal number of syndrome-positive visits was sampled for each ICD-9 code in a syndrome. For example, fever (780.6) and bubonic plague (020.0), both corresponding to constitutional syndrome, contributed the same number of cases. However, the prevalence and accuracy of each ICD-9 code in a syndrome is different, and because the analyses were not adjusted for the uniform sampling strategy used, the reported estimates of sensitivity, specificity, PPV and NPV are biased. In a third study [26], the accuracy of ICD-9 coded physician diagnoses from 9 hospital EDs for identifying 'acute respiratory illness' was assessed by comparison to medical chart review. A simple random sample was used; therefore the results were not subject to verification bias. The authors reported a sensitivity of 0.43, 95% CI (0.28-0.58) for acute respiratory illness, which is almost identical to our sensitivity estimate for respiratory syndrome; their estimates of NPV and specificity were also similar to ours, but their PPV estimate of 0.45, 95% CI (0.29-0.61) is much lower than ours.

Our study had several strengths and limitations. We used a large population-based random sample of all physicians working in the fee-for-service system in community healthcare settings in the province of Quebec in 2005-2007, thereby capturing potential ICD-9 coding differences between physicians, institutions, and regions. Not only did we estimate the accuracy of syndrome definitions, as others have done, but our study design enabled us to estimate the PPV of individual diagnostic codes within each syndrome definition. Matching syndrome-negative visits to syndrome-positive visit on calendar month ensured that our results were not affected by seasonal bias. Because two or more syndromes can occur concurrently in the same person [19], our requirement that syndrome-negative visits be negative for all syndromes ensured that we did not overestimate false-

negatives and underestimate sensitivity and NPV. Our participation rate, though low, was consistent with that of other large population-based studies of Canadian physicians [27,28]. Participating and non-participating physicians were similar on nearly all measured variables. The participation rate was significantly lower among recently licensed physicians; recently licensed physicians may have been less likely to participate in our study because they tend to experience greater practice mobility [29] and report more impediments to practice [30] than their more experienced counterparts. Unfortunately, the accuracy of very rare syndrome-positive ICD-9 codes, such as cutaneous and pulmonary anthrax (22.0 and 22.1), could not be estimated because, as expected, they were not present in any of the 1,098 participating physicians' claims during the 2-year study period.

Conclusions

We found that diagnostic codes in physician claims from community healthcare settings have low sensitivity, moderate to high PPV, and near-perfect specificity and NPV for identifying 5 syndromes (fever, gastrointestinal, neurological, rash, and respiratory, including ILI). Future research should evaluate the practical implications of our findings on decision-making in response to alerts from existing syndromic surveillance systems. Future research should also identify physician, patient, and encounter characteristics associated with better accuracy of diagnostic codes in physician claims. This would enable public health to improve syndromic surveillance, either by focusing on physician claims whose diagnostic code is more likely to be accurate, or by using all physician claims and weighing each according to the likelihood that its diagnostic code is accurate. We also estimated the prevalence and PPV of individual diagnostic codes within each syndrome. We found that rarely used diagnostic codes had a higher probability of being false-positives, and that more commonly used diagnostic codes had a higher PPV. These findings may be useful to the ongoing development of sensitive and specific consensus syndrome definitions, as either a sensitive or a specific definition may be more useful depending on the surveillance objective.

Additional material

Additional file 1: Positive predictive value of individual ICD-9 codes within each syndrome case definition. For all 12 syndrome case definitions investigated, the positive predictive value of diagnoses in physician claims is provided for each individual ICD-9 code.

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Authors' contributions

All authors read and approved the final manuscript. GC collected the data, performed the data analysis, and is the primary author of the manuscript. AJ helped develop the methods and collect the data, and provided useful comments on the manuscript. ML helped develop the methods and provided useful comments on the manuscript. ND helped develop the methods, supervised the analysis, and provided useful comments on the manuscript. RT and DLB provided access to claims data and study subjects, helped develop the methods, oversaw the analysis, and provided useful comments on the manuscript.

Competing interests

The authors declare that they have no competing interests.

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