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Development of a risk prediction model of potentially avoidable readmission for patients hospitalized with community-acquired pneumonia: Study Protocol and Population.

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Abstract

Introduction: 30-day readmission rate is considered an adverse outcome reflecting suboptimal quality of care during index hospitalization for community-acquired pneumonia (CAP). However, potentially avoidable readmission would be a more relevant metric than all-cause readmission for tracking quality of hospital care for CAP. The objectives of this study are 1) to estimate potentially avoidable 30-day readmission rate and 2) to develop a risk prediction model intended to identify potentially avoidable readmissions for CAP.

Methods and analysis: The study population consists of consecutive patients admitted in two hospitals from the community or nursing home setting with pneumonia. To qualify for inclusion, patients must have a primary discharge diagnosis code of pneumonia or a secondary discharge diagnosis code of pneumonia with a primary diagnosis code of respiratory failure, sepsis, or pneumonia related-symptoms. Data sources include routinely collected administrative claims data as part of diagnosis-related group prospective payment system and structured chart reviews. The main outcome measure is potentially avoidable readmission within 30 days of discharge from index hospitalization. The likelihood that a readmission is potentially avoidable will be quantified using latent class analysis based on independent structured reviews performed by four panelists. We will use a two-stage approach to develop a claims data-based model intended to identify potentially avoidable readmissions. The first stage implies deriving a clinical model based on data collected through retrospective chart review only. In the second stage, the predictors comprising the medical record model will be translated into ICD-10 discharge diagnosis codes in order to obtain a claim data-based risk model.

Population: The study sample consists of 1150 hospital stays with a diagnosis of CAP. The median age for all patients is 78 years, 63.5% were in Pneumonia Severity Index risk classes IV-V on index hospital admission. 30-day index hospital readmission rate was 17.5%.

Ethics and dissemination: The protocol was reviewed by the Comité de Protection des Personnes Sud Est V (IRB 6705), prior to study initiation. The study database was approved by the French Data Agency (Commission Nationale Informatique et Liberté).

Registration: The protocol has been registered in Clinicaltrials.gov (NCT02833259).

Key Words

pneumonia; hospital readmission; prediction model,

Article Summary:

Strengths and limitations of this study

Potentially avoidable readmission within 30 days of index hospitalization is a more relevant quality metric than all-cause readmission for patients with community-acquired pneumonia.

Yet, implicit assessment of readmission avoidability is highly subjective and unreliable.

In this study, the likelihood that a readmission is potentially avoidable will be quantified using latent class analysis based on independent structured reviews by four panelists.

Limitation: This study does not track readmissions that occur at non-index hospital.

Introduction

Community-acquired pneumonia (CAP) is a leading infectious cause of adult hospitalization in Europe and North America,[1, 2] contributing to 250,000 hospital admissions in France each year.[3] CAP is also a serious and potentially-life threatening illness: it ranks as the first cause of death from infectious diseases in Western countries, with reported short-term mortality rates ranging from 5% to 14% for adult patients hospitalized with this illness.[4]

Because of the associated adverse outcomes and related costs, CAP has been a focus for quality improvement efforts for the past two decades. From 10% to 21% of adult patients hospitalized with CAP are readmitted within 30 days of discharge.[5, 6] Short-term readmission following CAP-related hospitalization poses significant problems for the patient and hospital. First, unplanned readmission is an undesirable outcome which matters for patients and families and negatively alters patient quality of life. Second, readmission exposes patient to unnecessary risk for hospital-acquired infections and venous thromboembolism. Third, readmission is associated with increased costs and resource utilization.

Readmission rates can be easily computed and tracked from computerized hospital discharge data. As part of the Hospital Readmission Reduction Program (HRRP) effective in fiscal year 2013, United States hospitals with higher than expected 30-day readmission rates after pneumonia hospitalization have been subject to financial penalties from the Center for Medicare and Medicaid Services (CMS).[7, 8] The underlying logic of the HRRP is based upon the notion that short-term readmission is often a preventable adverse outcome, reflecting suboptimal quality of care during index hospitalization. Yet, published evidence suggests that less than one in four all-cause readmissions are deemed avoidable.[9, 10] Because only avoidable readmissions can be influenced by interventions designed to decrease readmission rates, avoidable readmission is a more relevant metric than all-cause readmission for tracking quality of hospital care for pneumonia.

The suboptimal quality of care may relate to the management of pneumonia, the management of comorbid conditions present at the time of the index hospitalization, the continuity of care after the discharge, or ambulatory care after discharge. Causes and factors that contribute to avoidable readmission can be classified into 4 categories, including social context, patient health status, care organization and patient behavior.[11] Socioeconomic features include lower education level, lower income, the lack of occupational activity,[12-15] and health insurance status.[16] Markers of the patient's health status include age greater than 65 years,[17-19] multiple hospitalizations within the previous year,[20] frailty, sensory deficiencies, and the presence of comorbidities with higher Charlson index.[12, 17, 21] Care organization-related factors include early discharge,[22, 23] clinical instability on discharge,[24, 25] and poor discharge processes (e.g., lack of medication reconciliation, patient education regarding continuity of care, and follow-up processes).[17, 22, 24-28] Patient behavioral risk factors for readmission are poor adherence to treatment, alcoholism, drug addiction,[29, 30] psychosocial problems (e.g., housing instability, homeless), psychiatric disorders and depressive states.[17, 24, 26, 29, 31]

Although numerous risk prediction models of hospital readmission for CAP patients have been developed,[15, 32-35] only few focused on potentially avoidable readmission. A systematic review of 11 models found moderate predictive accuracy in terms of discrimination (*C* statistic ranging from 0.59 to 0.77).[34] More recently published models included various risk factors for readmission including comorbidities, pneumonia severity, clinical instability on discharge, number of previous hospitalizations, index length of stay and various clinical and biological data.[15, 20, 24, 32, 35]

The broad objective of this study is to develop an administrative claims-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP. The specific aims of this project are:

- to assess the accuracy of ICD-10 discharge diagnosis codes for CAP using a retrospective structured chart review as the reference method.
- to estimate the rate of all-cause readmissions in the same hospital within 30 days and one year of discharge for patients.
- to estimate the percentages of CAP patients who die within 30 days and one year of discharge without hospital readmission.
- to estimate the percentage of unplanned readmissions for patients hospitalized with CAP using a retrospective structured chart review.
- to describe pneumonia-related and –unrelated reasons for readmissions for patients hospitalized with CAP using a retrospective structured chart review.
- to quantify the probability that an unplanned readmission is avoidable using latent class analysis based on independent chart reviews performed by four medical panelists.
- to investigate the distribution of potentially avoidable readmission according to time from index hospitalization discharge.
- to identify the characteristics abstracted from medical record that are independently associated with potentially avoidable readmission.
- to derive and internally validate a medical record-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP.
- to identify administrative claims data that are independently associated with potentially avoidable readmission.
- to derive and internally validate an administrative claims-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP.
- to compare the overall accuracy, discrimination, and calibration for the administrative claims data-based versus medical record data-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP.

- to externally validate published risk prediction models of 30-day readmission of patients hospitalized with CAP.

Methods

I. Study design

This risk prediction model development study will be conducted according to current guidelines.[36-38] The present protocol describes the inclusion criteria, explains how data collection is undertaken, data will be analyzed and findings will be interpreted.

II. Participating study centers and setting

The study will be conducted in a university-affiliated hospital and a general hospital in France. With a capacity of 1,362 acute care beds, Grenoble university hospital (GUH) serves a predominantly urban population of 675,000 inhabitants and reported 135,999 stays in 2014. Annecy Genevois general hospital (AGH) has a capacity of 896 acute care beds and reported 70,651 stays in 2014.

III. Patients

The study population consists of consecutive patients admitted from the community or nursing home setting with pneumonia. To qualify for inclusion, patients must have a primary discharge diagnosis code of pneumonia or a secondary discharge diagnosis code of pneumonia with a primary diagnosis code of respiratory failure, sepsis, or pneumonia related-symptoms. The specific ICD-10 codes used to define the study cohort are listed in Table 1.

Although nursing home-acquired pneumonia has been termed “healthcare-associated pneumonia”,[39] it remains controversial whether nursing home-acquired pneumonia more closely resembles hospital-acquired pneumonia than CAP. Because nursing home-acquired pneumonia accounts for a limited proportion of CAP-related hospitalizations,[40] it will not be an exclusion criterion for this study. In contrast, patients with hospital-acquired or ventilator-associated pneumonia will be excluded. Hospital-acquired pneumonia is defined as pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission. Ventilator-associated pneumonia is defined as pneumonia occurring more than 48 hours after endotracheal intubation.

Patients will be excluded if they were admitted from another acute care facility, subsequently transferred to another acute care facility, or admitted in a day care unit. Death during index hospitalization will be collected and analyzed, but these patients will not be eligible for readmission analysis.

Consistent with Lindenauer et al.,[33] additional pneumonia admissions within 1 year of discharge from an index pneumonia hospitalization will be considered as readmissions and excluded as index admissions: a single admission cannot be counted both as an index admission and as a readmission for another index admission.

Patient and Public Involvement

No patient involved

IV. Data sources

Data sources include routinely collected hospital administrative claims data and retrospective structured chart reviews.

Administrative claims data. As part of the French diagnosis-related group (DRG)-based prospective payment system, computerized hospital discharge data include patient and hospital stay identifiers, admission and discharge dates, age, gender, length of stay, discharge location, primary and secondary ICD-10 discharge diagnosis codes for both index admission and readmission. ICD-10 coding complies with national guidelines and is done by trained technicians or physicians, depending on the hospital. Coders usually abstract diagnoses from physician notes, admission notes, daily progress notes, consultation reports, diagnostic imaging, and treatments that are routinely recorded in the medical chart. Discharge diagnosis data are externally audited by reabstracting a random sample of hospital stays every year.

Structured chart review. Two clinical research assistants will perform structured retrospective chart review using a computerized data collection instrument. The following variables will be recorded for

index hospitalizations: patient and hospital stay identifiers; baseline patient characteristics, including demographics, preexisting comorbid condition, pneumonia severity index (PSI) risk class, physical examination and laboratory findings on admission, X-ray or CT-scan findings within 48 hours of admission, initial microbiological work-up; in hospital antibiotic therapy and associated treatments, index hospital admission course, intensive care unit (ICU) admission, pneumonia-related and -unrelated complications, physical examination and laboratory findings at discharge; discharge plan and treatments.

The following variables will be recorded for the first hospital readmission within one year of discharge: patient and hospital stay identifiers, time from discharge to readmission, length of stay, physical examination and laboratory findings on readmission, X-ray or CT-scan findings within 48 hours of readmission, hospital readmission course (ICU admission, pneumonia-related and -unrelated complications, in-hospital mortality), and primary and secondary reasons for readmissions.

To account for competing risk of death,[41] out-of-hospital mortality will be recorded. Patient vital status will be retrieved using online obituaries.[42]

ED visits that do not result in hospital readmission within 30 days after discharge will be recorded. Similar to hospital readmission measure, only the first post-discharge ED visit will be counted in patients with multiple ED visits.[43]

Data management. To ensure optimal quality, all data collected retrospectively by chart review will be entered electronically by clinical research assistants using a personal identification code and a password-protected web-based data collection system. The clinical research assistants will receive formal training in the methods of data abstraction and recording. An operation manual that includes definitions and acceptable data sources for all variables will be distributed. Reliability of data abstraction will be assessed by randomly selecting cases for independent collection by a practicising physician.

V. Accuracy of ICD-10 discharge diagnosis codes for CAP

The discharge diagnosis codes used in claims databases do not distinguish between community and hospital-acquired pneumonia, two distinct clinical entities.[44] Consistent with previous studies, the accuracy of ICD-10 discharge diagnosis codes will be assessed using three reference methods:

1. Medical record and/or discharge letter notation of CAP diagnosis
2. Medical record notation of ≥ 1 respiratory symptom (cough, sputum production, dyspnea, tachypnea, or pleuritic pain), and ≥ 1 auscultation finding (rales or crepitations), and ≥ 1 sign of infection (temperature >38°c, shivering, or white blood cell count >10,000/µL or <4,000/µL), and a new infiltrate on chest radiography or CT-scan performed within 48 hours of admission.
3. A composite of #1 and/or #2

Positive predictive value point estimate along with 95% confidence interval (CI) will be reported for the three reference methods, separately.

VI. Physician review

A convenience sample of nine board-certified physicians with clinical experience in managing CAP was recruited, including three infectious disease specialists, three pulmonologists and three clinical epidemiology specialists. All readmission cases will be reviewed by four panelists, including at least one infectious disease specialist, one pulmonologist, and one epidemiologist (i.e., the fourth panelist will be either an infectious disease specialist, a pulmonologist, or an epidemiologist). The panelists will independently review medical records for both index hospitalization and readmission.

Consistent with Jasti et al.,[12] each panelist will use predefined criteria to categorize the primary reason for rehospitalization as:

1. pneumonia-related worsening of signs or symptoms
2. new or worsening comorbid condition(s) independent of pneumonia
3. any combination of pneumonia-related and comorbidity-related reasons.

The panelists will assign the primary reason for readmission, using 11 mutually exclusive categories [45]: 1) unforeseen readmission for a new affection, 2) complication of surgical care, 3) complication of nonsurgical care, 4) drug-related adverse event, 5) premature discharge, 6) discharge with a missing or erroneous diagnosis or therapy, 7) other inadequate discharge, 8) failure of post-discharge follow-up care, 9) inadequate patient behavior, 10) relapse or aggravation of a previously known condition, 11) social readmission.

Consistent with van Walraven et al.,[46] the panelists will use a 6-point ordinal scale to rate whether the readmission is an adverse event and whether the readmission could be avoided. A readmission with a rating above three in both domains will be classified as potentially avoidable. The panelists will indicate the factors contributing to the readmission among 7 non-exclusive categories: medication-related readmission, procedure-related readmission, nosocomial infection, diagnostic error, management error, system error, surgical complication.

VII. Outcome measure

The primary outcome measure is potentially avoidable readmission within 30 days of discharge from index hospitalization. The likelihood that a readmission is potentially avoidable will be quantified using latent class analysis based on the independent reviews by four panelists. A readmission will be considered potentially avoidable if the probability exceeds 0.50.[46]

VIII. Statistical analysis

Baseline characteristics. Descriptive summary statistics will be used for reporting continuous (mean and standard deviation or median and 25^{th}-75^{th} percentiles) and categorical (numbers and percentages) variables. Patient stay characteristics will be compared between study subgroups using the χ^2 test or Fisher exact test where appropriate for categorical variables and the Student *t*-test or non-parametric Wilcoxon test for continuous variables.

Model development overview. The model development sample will consist of eligible patients who have been readmitted within 30 days of discharge. A flow-chart will present graphically patient flow throughout the study. We will use a two-stage approach to develop an administrative claims-based model intended to identify potentially avoidable readmissions. The first stage implies deriving a medical record-based model with the use of data collected through retrospective chart review only. In the second stage, the predictors included in the resulting medical record-based model will be translated into ICD-10 discharge diagnosis codes in order to obtain an administrative claims-based model.

Medical record-based model development. Derivation and internal validation will be conducted according to current standards.[38] The medical record-based model will be derived using multivariable logistic regression for binary dependent variable. Candidate predictors will be identified among both hospital index admission and readmission variables based on the findings from a systematic review and significant relationship with avoidability. We will assess the log-linearity assumption for continuous variables using fractional polynomial regression. Missing values will be replaced by multiple imputation. In internal validation, the potential for statistical over-fitting will be quantified using bootstrapping.

The resulting medical record-based model predictive performance will be evaluated using overall, calibration, and discrimination measures.[36] Overall model performance will be quantified using pseudo-R^2 and Brier score. Discrimination, which refers to the ability of the model to distinguish individuals with and without potentially avoidable readmission, will be quantified by the concordance *C* statistic. Calibration, which refers to the agreement between avoidability likelihood predicted by the model and observed avoidability frequency, will be assessed by calibration slope.

Administrative claims-based model development. Two physicians with expertise in discharge diagnosis coding will independently translate relevant predictors comprising the resulting medical record-based model into ICD-10 diagnosis codes. A single model will be obtained after a reconciliation meeting of the two physicians. The candidate variables include age, sex, diagnosis

codes, Charlson's comorbidity index, length of stay, ED readmission, and time from discharge to readmission. The resulting administrative claims-based model predictive performance will be evaluated using overall, calibration, and discrimination measures.

Competing prediction models. External validation of competing prediction models will consist in applying their inherent predictors and parameter coefficients on our study dataset. The predictive performance of the models will be evaluated in terms of both calibration and discrimination.

All statistical analyses will be performed using Stata Special Edition version 15 or higher (Stata Corporation, College Station, TX, USA). Additional software may be used for the production of graphics and for statistical methodology not provided by this software package.

IX. Ethics and dissemination

The protocol for this study was approved by the Comité de Protection des Personnes Sud-Est V, Grenoble, France (IRB#6705). The consent for data collection through chart review and the use of corresponding administrative claims data will be sought under a regime of "non-opposition" (opt-out): after appropriate written information is delivered by regular mail, data will be collected unless the patient opposes. Computerized study data will be processed at Grenoble Alpes University Hospital, in compliance with French data protection regulations.

Efforts will be made to reduce the interval between the completion of data collection and the release of the primary study results. It is expected that 6 months will be necessary for the writing committee to compile the primary study results before manuscript submission to an appropriate journal. No later than 3 years after final acceptance of the primary study paper, de-identified data will be available upon request from the corresponding author for sharing purpose.

Study sample

From 1 January 2014 to 31 December 2014, 1,523 hospital stays with a ICD 10 diagnosis code of pneumonia were identified (Figure 1). After excluding 186 hospital stays because of the discovery of an exclusion criterion and 187 hospital stays with a diagnosis other than CAP, our analytical sample consisted of 1150 index hospital stays. Overall, 98 (8.5%) patients died in hospital and 184 were readmitted within 30 days of discharge, representing an early readmission rate of 17.5% (i.e., 184/1052, 95% CI, 15.2% to 19.9%). The medical records for both index hospitalizations and readmissions of these 184 CAP patients will be independently reviewed by the panelists for assigning the primary reason for readmission and rating the avoidability of readmission. The median age for all patients was 78 years, 56% were of male gender, and 15% were nursing home residents (Table 2). All patients had clinical or biological signs of infection. Median C-reactive protein was 114mg/L. Hypoxemia was common and more than one-third of patients (41%) required oxygen supplementation. Overall, 63.5% of patients were in PSI risk classes IV-V.

Most patients had pre-existing comorbidities, including arterial hypertension (49.8%), neurological conditions (36.9%), underlying respiratory disease (24.5%), cardiac arrhythmia (23.3%), diabetes mellitus (22.5%), coronary artery disease (20.1%), and kidney failure (15.8%) (Table 3). Fifteen percent of patients had one or more causes of immune depression. Charlson's comorbidity index ranged from 0 to 12 with a median of 2 (25^{th}-75^{th} percentile, 1 to 3). The median duration of the index stay was 8 days. A total of 168 (14.6%) patients were admitted to the ICU, 42 (25.1%) underwent invasive mechanical ventilation and 50 (29.9%) received inotropic or vasopressor support.

Blood was obtained for culturing from 817 patients (71.0%), and an urine sample for urinary antigen detection from 583 patients (50.7%). A pathogen was detected in 311 patients, including one or more viruses in 57 (5.0%) patients, one or more bacteria in 252 (21.9%), both bacterial and viral pathogens in 15 (1.3%), and fungi or mycobacteria in 22 (1.9%). The most common bacteria detected were *S. Pneumoniae* (6.9%), *Haemophilus influenzae* (2.8%) and *Legionella pneumophila (2.3%).*

Discussion

In this study, the 30-day readmission rate is 17.5% for patients hospitalized with CAP. This result is consistent with previous estimates, ranging from 7.3% to 25%. Thus, the rate of readmission varied from 13.6% to 25% in the studies of Makam et al.[35] and of Hatipoglu et al.[32], from 7.3% to 20.1% in the study of Prescott et al.[6] and from 11.8% to 20.8% with a median of 17.3% for Weinreich et al.[34]

Compared with previous reports, the patients enrolled in our study are older (median age, 78 years), more likely to present with severe pneumonia (prevalence of PSI risk classes IV-V, 63.5%) and have more comorbidities (prevalence of Charlson's comorbidity index ≥2, 53%). The 24% rate of patients with identified pathogens is lower than previously reported.[2] The potential explanations for such a low micro-organism detection rate include the lack of testing for known pathogens, antibiotic use before specimen collection, and non-infectious causes. Of notice, our study was observational in design and therefore microbiological diagnostic test ordering was left at the discretion of admitting physicians. Polymerase chain reaction (PCR) assay was rarely performed for the detection of respiratory viruses, which could have led to underestimating the prevalence of viral etiologies. Consistent with previous reports, the most commonly detected bacteria was *Streptococcus pneumoniae*. With the exception of viruses, the distribution of other micro-organisms was the same as reported in the literature.[1, 47, 48]

Various approaches have been used for assessing whether a readmission is potentially avoidable, including implicit assessment, explicit assessment, and latent class analysis. Implicit assessment based on unstructured chart review is the most common approach although its validity and reliability are questioned.[49] The lack of standardization in criteria might explain variations in percentages of potentially avoidable readmissions across primary studies.[49] Yet, implicit assessment may be improved by the use of two independent reviewers, resolution of disagreement by discussion between the two reviewers or by a third reviewer, and by interviews with the physicians in charge of the patient and with the patient.[50, 51]

Explicit assessment based on structured chart review by one or more reviewers has been used in various contexts. Halfon et al.[45] categorized readmissions as planned, unplanned for a new condition, and unplanned for a condition known at index hospitalization. Then, reviewers are asked to assign a root cause for readmission using 11 exclusive categories. This approach has been implemented throughout the «Striving for Quality Level and Analysing of Patient Expense» (SQLape) algorithm for use with administrative claims data.[52]

Van Walraven et al. have refined the explicit assessment approach by quantifying the likelihood that a readmission is potentially avoidable using a latent class analysis based on independent reviews by multiple panelists. We are planning to use the same approach, which is a strength of the present study.

The limitations of our study deserve mention. First, our study tracks index hospital readmissions only. Indeed, previous studies reported that one in five 30-day readmissions may occur at non-index hospitals.[53] Second, the effective sample size for model development is relatively limited with the potential for overfitting. As a rule of thumb, there will be a minimum of five potentially avoidable readmission cases per candidate predictor considered for inclusion in our multivariable logistic regression model. Third, our study is conducted in two hospitals in France and our findings may not apply to other settings or regions.

To conclude, we will develop an administrative claims-based model for identifying potentially avoidable 30-day readmissions of CAP patients, using latent class analysis of explicit assessment by independent panelists as the reference method. Our study will also provide the unique opportunity to estimate the accuracy of competing models in predicting potentially avoidable readmission in an external validation sample.

Author Contributions:

All authors reviewed the manuscript and contributed to its improvement.

All authors were involved in study population development.

Anne-Laure Mounayar : literature analysis and manuscript writing.

Patrice François : protocol development, literature analysis and manuscript writing.

Magali Bouisse : statistical analysis.

José Labarère : supervision of data collection, statistical analysis.

Arnaud Seigneurin : protocol development, statistical analysis.

Patricia Pavese, Elodie Sellier, Jacques Gaillat, Boubou Camara, Bruno Degano, Mylène Maillet : structured medical chart review for avoidability assessment.

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Figure 1: Flow-chart of study population
Abbreviations: CAP = community-acquired pneumonia, GUH = Grenoble University Hospital, AGH = Annecy Genevois general hospital

Table 1. ICD-10 codes that define pneumonia.

ICD-10	Description
Primary diagnosis code of pneumonia	
B01.2	Varicella pneumonia
B20.6	HIV disease resulting in Pneumocystis jirovecii pneumonia
B25.0	Cytomegaloviral pneumonitis
B59	Pneumocystosis
J10.0	Influenza with pneumonia, seasonal influenza virus identified
J11.0	Influenza with pneumonia, virus not identified
J12.x	Viral pneumonia, not elsewhere classified
J13	Pneumonia due to Streptococcus pneumoniae
J14	Pneumonia due to Haemophilus influenzae
J15.x	Bacterial pneumonia, not elsewhere classified
J16.x	Pneumonia due to other infectious organisms, not elsewhere classified
J17.x	Pneumonia in diseases classified elsewhere
J18.x	Pneumonia, organism unspecified
J69.0	Pneumonitis due to inhalation of food and vomit
Primary diagnosis code of sepsis, respiratory failure, or compatible symptoms with a secondary diagnosis code of pneumonia	
A40.x	Streptococcal sepsis
A41.x	Other sepsis
D65	Disseminated intravascular coagulation (defibrination syndrome)
E86.x	Volume depletion
E87.x	Other disorders of fluid, electrolyte and acid-base balance
J80	Adult respiratory distress syndrome
J81	Pulmonary edema
J85.1	Abscess of lung with pneumonia
J90	Pleural effusion, not elsewhere classified
J91	Pleural effusion in conditions classified elsewhere
J96.x	Respiratory failure, not elsewhere classified
O99.5	Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium
R04.2	Haemoptysis
R06.0	Abnormalities of breathing
R07.1	Chest pain on breathing
R07.2	Precordial pain
R07.3	Other chest pain
R07.4	Chest pain, unspecified
R41.0	Disorientation, unspecified
R50.9	Fever, unspecified
R57.1	Hypovolaemic shock
R57.2	Septic shock
R57.9	Shock, unspecified
R91	Abnormal findings on diagnostic imaging of lung

Table 2. Baseline Patient Characteristics (n=1150)

Characteristics*		
Demographics		
Male gender, *n (%)*	651	(56.6)
Age, median (IQR), *y*	77.8	(62.7-86.4)
Nursing home resident, *n (%)*	169	(14.7)
Index hospital stay		
Length of stay, median (IQR), *d*	8	(4-13)
Admission via emergency department, *n (%)*	1001	(87.0)
Physical examination findings		
Altered mental status, *n (%)*	230	(20.0)
Systolic blood pressure, median (IQR), *mmHg*	117	(102-132)
Pulse rate, median (IQR), *per min*	98	(85-113)
Respiratory rate, median (IQR), *per min*	26	(21-31)
Temperature, median (IQR), °C	37.8	(37.0-38.5)
Abnormal auscultation findings, *n (%)†*	931	(81.0)
Laboratory findings		
Arterial hypoxemia, *n (%)‡*	261	(22.7)
Hematocrit, median (IQR), %	38	(35-42)
Blood urea nitrogen, median (IQR), *mmol/L*	8.1	(5.5-11.6)
Serum sodium, median (IQR), *mEq/L*	137	(135-140)
Glucose, median (IQR), *mmol/L*	6.6	(5.6-8.5)
C-reactive protein, median (IQR), *mg/L*	114.0	(49.0-202.3)
White blood cell count, median (IQR), Giga/L	11.4	(8.4-15.5)
Pneumonia severity index, *n (%)*		
Class I	73	6.4
Class II	135	11.7
Class III	212	18.4
Class IV	457	39.7
Class V	273	23.7

Abbreviations: IQR = interquartile range (i.e., 25-75th percentiles)

* Values were missing for systolic blood pressure (n = 8), pulse rate (n = 8), respiratory rate (n = 627), temperature (n=8), arterial hypoxemia (n=29), hematocrit (n = 21), blood urea nitrogen

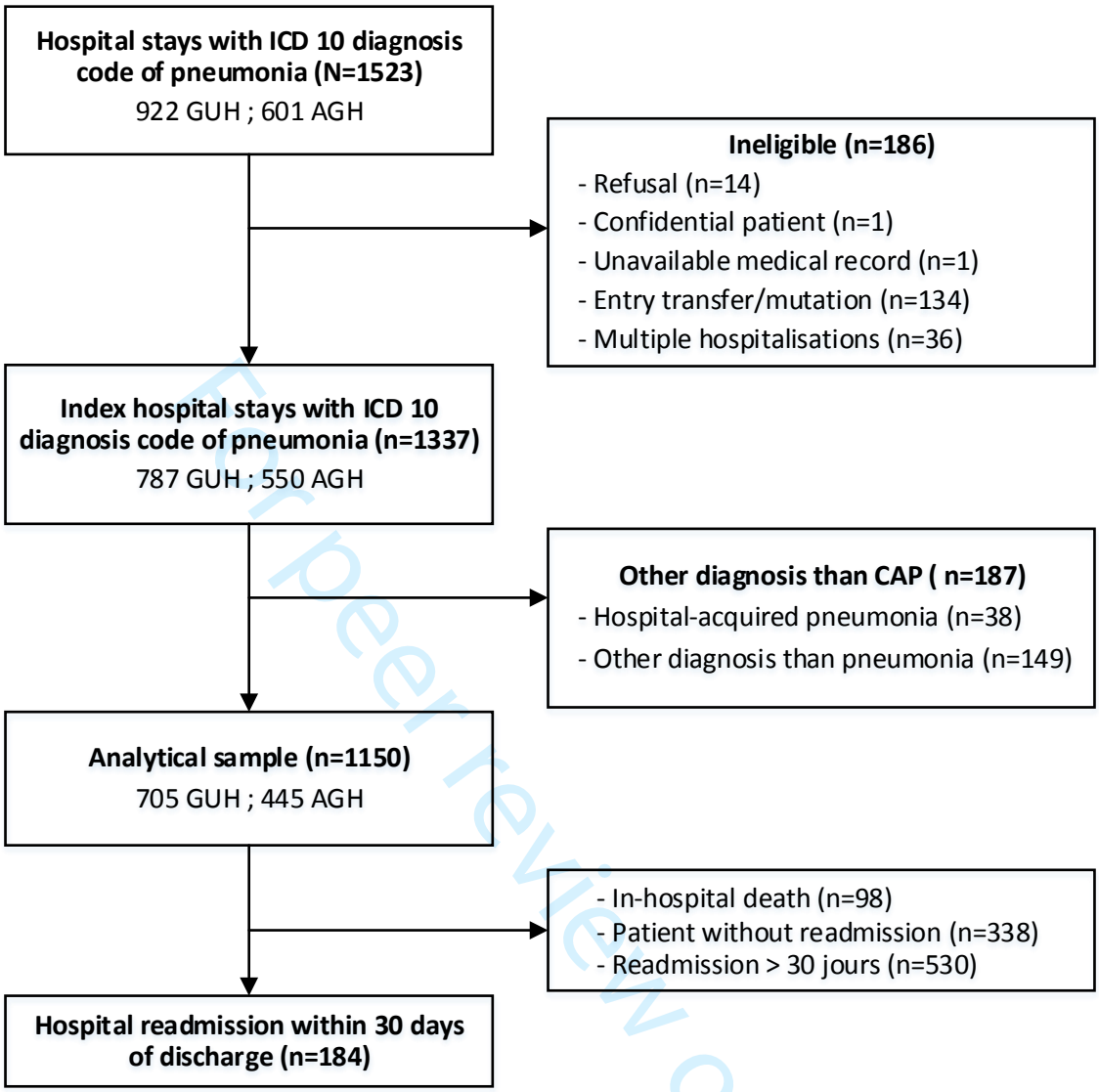
(n = 30), serum sodium (n = 19), glucose (n = 207), C-reactive protein (n = 18), white blood cell count (n = 13),

† Abnormal auscultation findings included rales and crepitations.

‡ Arterial hypoxemia was defined by O_2 saturation <90% or arterial PO_2<60 mm Hg using pulse oximetry or arterial blood gas.

Table 3. Pre-existing comorbid conditions (n=1150)

Preexisting comorbid conditions	**n**	**(%)**
Cardiovascular disease	754	(65.6)
Arterial hypertension	*573*	*(49.8)*
Congestive heart failure	*150*	*(13.0)*
Peripheral vascular disease	*127*	*(11.0)*
Coronary artery disease	*231*	*(20.1)*
Heart dysrhythmia	*268*	*(23.3)*
Respiratory disease	282	(24.5)
Chronic obstructive pulmonary disease	*204*	*(17.7)*
Other	*109*	*(9.5)*
Active cancer	93	(8.1)
Liver disease (moderate or severe)	32	(2.8)
Renal disease	182	(15.8)
Neurologic and psychiatric disease	424	(36.9)
Cerebrovascular disease	*164*	*(14.3)*
Dementia or Alzheimer's disease	*133*	*(11.6)*
Psychiatric illness	*143*	*(12.4)*
Others	*211*	*(18.3)*
Diabetes mellitus	259	(22.5)
Charlson Index		
0	274	(23.8)
1	263	(22.9)
2	204	(17.7)
>2	409	(35.6)



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Development of a risk prediction model of potentially avoidable readmission for patients hospitalized with community-acquired pneumonia: Study Protocol and Population.

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Development of a risk prediction model of potentially avoidable readmission for patients hospitalized with community-acquired pneumonia: Study Protocol and Population.

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Abstract

Introduction: 30-day readmission rate is considered an adverse outcome reflecting suboptimal quality of care during index hospitalization for community-acquired pneumonia (CAP). However, potentially avoidable readmission would be a more relevant metric than all-cause readmission for tracking quality of hospital care for CAP. The objectives of this study are 1) to estimate potentially avoidable 30-day readmission rate and 2) to develop a risk prediction model intended to identify potentially avoidable readmissions for CAP.

Methods and analysis: The study population consists of consecutive patients admitted in two hospitals from the community or nursing home setting with pneumonia. To qualify for inclusion, patients must have a primary or secondary discharge diagnosis code of pneumonia. Data sources include routinely collected administrative claims data as part of diagnosis-related group prospective payment system and structured chart reviews. The main outcome measure is potentially avoidable readmission within 30 days of discharge from index hospitalization. The likelihood that a readmission is potentially avoidable will be quantified using latent class analysis based on independent structured reviews performed by four panelists. We will use a two-stage approach to develop a claims data-based model intended to identify potentially avoidable readmissions. The first stage implies deriving a clinical model based on data collected through retrospective chart review only. In the second stage, the predictors comprising the medical record model will be translated into ICD-10 discharge diagnosis codes in order to obtain a claim data-based risk model.

The study sample consists of 1150 hospital stays with a diagnosis of CAP. 30-day index hospital readmission rate is 17.5%.

Ethics and dissemination: The protocol was reviewed by the Comité de Protection des Personnes Sud Est V (IRB 6705). Efforts will be made to release the primary study results within 6 months of data collection completion.

Registration: The protocol has been registered in Clinicaltrials.gov (NCT02833259).

Key Words

pneumonia; hospital readmission; prediction model;

Article Summary:

Strengths and limitations of this study

Potentially avoidable readmission within 30 days of index hospitalization is a more relevant quality metric than all-cause readmission for patients with community-acquired pneumonia.

Yet, implicit assessment of readmission avoidability is highly subjective and unreliable.

In this study, the likelihood that a readmission is potentially avoidable will be quantified using latent class analysis based on independent structured reviews by four panelists.

Limitation: This study does not track readmissions that occur at non-index hospital.

Introduction

Community-acquired pneumonia (CAP) is a leading infectious cause of adult hospitalization in Europe and North America,[1, 2] contributing to 250,000 hospital admissions in France each year.[3] CAP is also a serious and potentially-life threatening illness: it ranks as the first cause of death from infectious diseases in Western countries, with reported short-term mortality rates ranging from 5% to 14% for adult patients hospitalized with this illness.[4]

Because of the associated adverse outcomes and related costs, CAP has been a focus for quality improvement efforts for the past two decades. From 10% to 21% of adult patients hospitalized with CAP are readmitted within 30 days of discharge.[5, 6] Short-term readmission following CAP-related hospitalization poses significant problems for the patient and hospital. First, unplanned readmission is an undesirable outcome which matters for patients and families and negatively alters patient quality of life. Second, readmission exposes patient to unnecessary risk for hospital-acquired infections and venous thromboembolism. Third, readmission is associated with increased costs and resource utilization.

Readmission rates can be easily computed and tracked from computerized hospital discharge data. As part of the Hospital Readmission Reduction Program (HRRP) effective in fiscal year 2013, United States hospitals with higher than expected 30-day readmission rates after pneumonia hospitalization have been subject to financial penalties from the Center for Medicare and Medicaid Services (CMS).[7, 8] The underlying logic of the HRRP is based upon the notion that short-term readmission is often a preventable adverse outcome, reflecting suboptimal quality of care during index hospitalization. Yet, published evidence suggests that less than one in four all-cause readmissions are deemed avoidable.[9, 10] Because only avoidable readmissions can be influenced by interventions designed to decrease readmission rates, avoidable readmission is a more relevant metric than all-cause readmission for tracking quality of hospital care for pneumonia.

The suboptimal quality of care may relate to the management of pneumonia, the management of comorbid conditions present at the time of the index hospitalization, the continuity of care after the discharge, or ambulatory care after discharge. Causes and factors that contribute to avoidable readmission can be classified into 4 categories, including social context, patient health status, care organization and patient behavior.[11] Socioeconomic features include lower education level, lower income, the lack of occupational activity,[12-15] and health insurance status.[16] Markers of the patient's health status include age greater than 65 years,[17-19] multiple hospitalizations within the previous year,[20] frailty, sensory deficiencies, and the presence of comorbidities with higher Charlson index.[12, 17, 21] Care organization-related factors include early discharge,[22, 23] clinical instability on discharge,[24, 25] and poor discharge processes (e.g., lack of medication reconciliation, patient education regarding continuity of care, and follow-up processes).[17, 22, 24-28] Patient behavioral risk factors for readmission are poor adherence to treatment, alcoholism, drug addiction,[29, 30] psychosocial problems (e.g., housing instability, homeless), psychiatric disorders and depressive states.[17, 24, 26, 29, 31]

Although numerous risk prediction models of hospital readmission for CAP patients have been developed,[15, 32-35] only few focused on potentially avoidable readmission. A systematic review of 11 models found moderate predictive accuracy in terms of discrimination (*C* statistic ranging from 0.59 to 0.77).[34] More recently published models included various risk factors for readmission including comorbidities, pneumonia severity, clinical instability on discharge, number of previous hospitalizations, index length of stay and various clinical and biological data.[15, 20, 24, 32, 35]

The broad objective of this study is to develop an administrative claims-based risk prediction model for identifying readmissions that are potentially avoidable within 30 days of index hospitalization for patients with CAP. The specific aims of this project are:

- to assess the positive predictive value of ICD-10 discharge diagnosis codes for CAP using a retrospective structured chart review as the reference method.
- to estimate the rate of all-cause readmissions in the same hospital within 30 days and one year of discharge for patients.
- to estimate the percentage of unplanned readmissions for patients hospitalized with CAP using a retrospective structured chart review.
- to describe pneumonia-related and –unrelated reasons for readmissions for patients hospitalized with CAP using a retrospective structured chart review.
- to quantify the probability that an unplanned readmission is avoidable using latent class analysis based on independent chart reviews performed by four medical panelists.
- to identify the characteristics abstracted from medical record that are independently associated with potentially avoidable readmission.
- to derive and internally validate a medical record-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP.
- to identify variables from administrative claims data that are independently associated with potentially avoidable readmission.
- to derive and internally validate an administrative claims-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP.
- to compare the overall accuracy, discrimination, and calibration for the administrative claims data-based versus medical record data-based risk prediction model for identifying potentially avoidable 30-day readmission of patients hospitalized with CAP.

Methods

I. Study design

This risk prediction model development study will be conducted according to current guidelines.[36-38] The present protocol describes the inclusion criteria, explains how data collection is undertaken, data will be analyzed and findings will be interpreted.

II. Participating study centers and setting

The study will be conducted in a university-affiliated hospital and a general hospital in France. With a capacity of 1,362 acute care beds, Grenoble university hospital (GUH) serves a predominantly urban population of 675,000 inhabitants and reported 135,999 stays in 2014. Annecy Genevois general hospital (AGH) has a capacity of 896 acute care beds and reported 70,651 stays in 2014.

III. Patients

The study population consists of consecutive patients admitted from the community or nursing home setting with pneumonia. To qualify for inclusion, patients must have a primary discharge diagnosis code of pneumonia or a secondary discharge diagnosis code of pneumonia with a primary diagnosis code of respiratory failure, sepsis, or pneumonia related-symptoms. The specific ICD-10 codes used to define the study cohort are listed in Table 1.

Although nursing home-acquired pneumonia has been termed “healthcare-associated pneumonia”,[39] it remains controversial whether nursing home-acquired pneumonia more closely resembles hospital-acquired pneumonia than CAP. Because nursing home-acquired pneumonia accounts for a limited proportion of CAP-related hospitalizations,[40] it will not be an exclusion criterion for this study. In contrast, patients with hospital-acquired or ventilator-associated pneumonia will be excluded. Hospital-acquired pneumonia is defined as pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission. Ventilator-associated pneumonia is defined as pneumonia occurring more than 48 hours after endotracheal intubation.

Patients will be excluded if they are admitted from another acute care facility, subsequently transferred to another acute care facility, or admitted in a day care unit. Death during index hospitalization will be collected and analyzed, but these patients will not be eligible for readmission analysis.

Consistent with Lindenauer et al.,[33] additional pneumonia admissions within 1 year of discharge from an index pneumonia hospitalization will be considered as readmissions and excluded as index admissions: a single admission cannot be counted both as an index admission and as a readmission for another index admission.

Patient and Public Involvement

Patients are not involved in the design or conduct of the study.

IV. Data sources

Data sources include routinely collected hospital administrative claims data and retrospective structured chart reviews.

Administrative claims data. As part of the French diagnosis-related group (DRG)-based prospective payment system, computerized hospital discharge data include patient and hospital stay identifiers, admission and discharge dates, age, gender, length of stay, discharge location, primary and secondary ICD-10 discharge diagnosis codes for both index admission and readmission. ICD-10 coding complies with national guidelines and is done by trained technicians or physicians, depending on the hospital. Coders usually abstract diagnoses from physician notes, admission notes, daily progress notes, consultation reports, diagnostic imaging, and treatments that are routinely recorded in the medical chart. Discharge diagnosis data are externally audited by reabstracting a random sample of hospital stays every year.

Structured chart review. Two clinical research assistants will perform structured retrospective chart review using a computerized data collection instrument. The following variables are recorded for index hospitalizations: patient and hospital stay identifiers; baseline patient characteristics, including

demographics, preexisting comorbid condition, pneumonia severity index (PSI) risk class, physical examination and laboratory findings on admission, X-ray or CT-scan findings within 48 hours of admission, initial microbiological work-up; in hospital antibiotic therapy and associated treatments, index hospital admission course, intensive care unit (ICU) admission, pneumonia-related and -unrelated complications, physical examination and laboratory findings at discharge; discharge plan and treatments.

The following variables are recorded for the first hospital readmission within one year of discharge: patient and hospital stay identifiers, time from discharge to readmission, length of stay, physical examination and laboratory findings on readmission, X-ray or CT-scan findings within 48 hours of readmission, hospital readmission course (ICU admission, pneumonia-related and -unrelated complications, in-hospital mortality), and primary and secondary reasons for readmissions.

To account for competing risk of death,[41] out-of-hospital mortality will be recorded. Patient vital status will be retrieved using online obituaries.[42]

ED visits that do not result in hospital readmission within 30 days after discharge will be recorded. Similar to hospital readmission measure, only the first post-discharge ED visit will be counted in patients with multiple ED visits.[43]

Data management. To ensure optimal quality, all data collected retrospectively by chart review will be entered electronically by clinical research assistants using a personal identification code and a password-protected web-based data collection system. The clinical research assistants received formal training in the methods of data abstraction and recording. An operation manual that includes definitions and acceptable data sources for all variables have been distributed. Reliability of data abstraction will be assessed by randomly selecting cases for independent collection by a practicising physician.

V. Positive predictive value of ICD-10 discharge diagnosis codes for CAP

The discharge diagnosis codes used in claims databases do not distinguish between community and hospital-acquired pneumonia, two distinct clinical entities.[44] Consistent with previous studies, the positive predictive value of ICD-10 discharge diagnosis codes will be assessed using three reference methods:

1. Medical record and/or discharge letter notation of CAP diagnosis
2. Medical record notation of ≥ 1 respiratory symptom (cough, sputum production, dyspnea, tachypnea, or pleuritic pain), and ≥ 1 auscultation finding (rales or crepitations), and ≥ 1 sign of infection (temperature >38°c, shivering, or white blood cell count >10,000/µL or <4,000/µL), and a new infiltrate on chest radiography or CT-scan performed within 48 hours of admission.
3. A composite of #1 and/or #2

Positive predictive value point estimate along with 95% confidence interval (CI) will be reported for the three reference methods, separately.

VI. Physician review

A convenience sample of nine board-certified physicians with clinical experience in managing CAP was recruited, including three infectious disease specialists, three pulmonologists and three clinical epidemiology specialists. All readmission cases will be reviewed by four panelists, including at least one infectious disease specialist, one pulmonologist, and one clinical epidemiologist (i.e., the fourth panelist will be either an infectious disease specialist, a pulmonologist, or an epidemiologist). The panelists will independently review medical records for both index hospitalization and readmission.

Consistent with Jasti et al.,[12] each panelist will use predefined criteria to categorize the primary reason for rehospitalization as:

1. pneumonia-related worsening of signs or symptoms
2. new or worsening comorbid condition(s) independent of pneumonia
3. any combination of pneumonia-related and comorbidity-related reasons.

The panelists will assign the primary reason for readmission, using 11 mutually exclusive categories [45]: 1) unforeseen readmission for a new affection, 2) complication of surgical care, 3) complication of nonsurgical care, 4) drug-related adverse event, 5) premature discharge, 6) discharge with a missing or erroneous diagnosis or therapy, 7) other inadequate discharge, 8) failure of post-discharge follow-up care, 9) inadequate patient behavior, 10) relapse or aggravation of a previously known condition, 11) social readmission.

Consistent with van Walraven et al.,[46] the panelists will use a 6-point ordinal scale to rate whether the readmission is an adverse event and whether the readmission could be avoided. A readmission with a rating above three in both domains will be classified as potentially avoidable by that panelist. The panelists will indicate the factors contributing to the readmission among 7 non-exclusive categories: medication-related readmission, procedure-related readmission, nosocomial infection, diagnostic error, management error, system error, surgical complication.

VII. Outcome measure

The primary outcome measure is potentially avoidable readmission within 30 days of discharge from index hospitalization. The likelihood that a readmission is potentially avoidable will be quantified using latent class analysis based on the independent reviews by four panelists. A readmission will be considered potentially avoidable if the Bayes' posterior probability exceeds 0.50.[46]

VIII. Statistical analysis

Baseline characteristics. Descriptive summary statistics will be used for reporting continuous (mean and standard deviation or median and 25^{th}-75^{th} percentiles) and categorical (numbers and percentages) variables. Patient stay characteristics will be compared between study subgroups using the χ^2 test or Fisher exact test where appropriate for categorical variables and the Student *t*-test or non-parametric Wilcoxon test for continuous variables.

Latent class analysis. We will perform latent class analysis to quantify the probability that a readmission is avoidable, based on the independent classification by four panelists. This is the same approach as previously used by others.[46] Briefly, latent class analysis is a statistical approach that assigns individuals in two or more latent classes based on a set of observed categorical variables. The latent variable cannot be observed directly; instead it is measured indirectly by using multiple observed variables. We will specify a 2-class model, reflecting the dichotomy of avoidable versus unavoidable readmission. The independent classification of readmission by each of the four panelists will be entered as observed categorical variables.[46] We will derive from the latent class model the Bayes' posterior probability of avoidability for each individual case of readmission. Finally, we will report the model-based sensitivity and specificity of each panelist in classifying readmission as avoidable.

Model development overview. The model development sample will consist of eligible patients who have been readmitted within 30 days of discharge. A flow-chart will present graphically patient flow throughout the study. We will use a two-stage approach to develop an administrative claims-based model intended to identify potentially avoidable readmissions. The first stage implies deriving a medical record-based model with the use of data collected through retrospective chart review only. In the second stage, the predictors included in the resulting medical record-based model will be translated into ICD-10 discharge diagnosis codes in order to obtain an administrative claims-based model.

Medical record-based model development. Derivation and internal validation will be conducted according to current standards.[38] The medical record-based model will be derived using multivariable logistic regression for binary dependent variable. Candidate predictors will be identified among both hospital index admission and readmission variables based on the findings from a systematic review and significant relationship with avoidability. We will assess the log-linearity assumption for continuous variables using fractional polynomial regression. Missing values will be replaced by multiple imputation. In internal validation, the potential for statistical over-fitting will be quantified using bootstrapping. All 30-day readmission cases from the study sample will be used for both derivation and internal validation of the prediction model.

The resulting medical record-based model predictive performance will be evaluated using overall, calibration, and discrimination measures.[36] Overall model performance will be quantified using pseudo-R^2 and Brier score. Discrimination, which refers to the ability of the model to distinguish individuals with and without potentially avoidable readmission, will be quantified by the concordance *C* statistic. Calibration, which refers to the agreement between avoidability likelihood predicted by the model and observed avoidability frequency, will be assessed by calibration slope.

Administrative claims-based model development. Two physicians with expertise in discharge diagnosis coding will independently translate relevant predictors comprising the resulting medical record-based model into ICD-10 diagnosis codes. A single model will be obtained after a reconciliation meeting of the two physicians. The candidate variables include age, sex, diagnosis codes, Charlson's comorbidity index, length of stay, ED readmission, and time from discharge to readmission. The resulting administrative claims-based model predictive performance will be evaluated using overall, calibration, and discrimination measures.

Competing prediction models. External validation of competing prediction models will consist in applying their inherent predictors and parameter coefficients on our study dataset. The predictive performance of the models will be evaluated in terms of both calibration and discrimination.

All statistical analyses will be performed using Stata Special Edition version 16 or higher (Stata Corporation, College Station, TX, USA). Additional software may be used for the production of graphics and for statistical methodology not provided by this software package.

IX. Ethics and dissemination

The protocol for this study was approved by the Comité de Protection des Personnes Sud-Est V, Grenoble, France (IRB#6705). The consent for data collection through chart review and the use of corresponding administrative claims data is sought under a regime of "non-opposition" (opt-out): after appropriate written information is delivered by regular mail, data are collected unless the

patient opposes. Computerized study data will be processed at Grenoble Alpes University Hospital, in compliance with French data protection regulations.

Efforts will be made to reduce the interval between the completion of data collection and the release of the primary study results. It is expected that 6 months will be necessary for the writing committee to compile the primary study results before manuscript submission to an appropriate journal. No later than 3 years after final acceptance of the primary study paper, de-identified data will be available upon request from the corresponding author for sharing purpose.

Study sample

From 1 January 2014 to 31 December 2014, 1,523 hospital stays with a ICD 10 diagnosis code of pneumonia were identified (Figure 1). After excluding 186 hospital stays because of the discovery of an exclusion criterion and 187 hospital stays with a diagnosis other than CAP, our analytical sample consists of 1150 index hospital stays. Overall, 98 (8.5%) patients died in hospital and 184 were readmitted within 30 days of discharge, representing an early readmission rate of 17.5% (i.e., 184/1052, 95% CI, 15.2% to 19.9%). The medical records for both index hospitalizations and readmissions of these 184 CAP patients will be independently reviewed by the panelists for assigning the primary reason for readmission and rating the avoidability of readmission. The median age for all patients was 78 years, 56% were of male gender, and 15% were nursing home residents (Table 2). All patients had clinical or biological signs of infection. Median C-reactive protein was 114mg/L. Hypoxemia was common and more than one-third of patients (41%) required oxygen supplementation. Overall, 63.5% of patients were in PSI risk classes IV-V.

Most patients had pre-existing comorbidities, including arterial hypertension (49.8%), neurological conditions (36.9%), underlying respiratory disease (24.5%), cardiac arrhythmia (23.3%), diabetes mellitus (22.5%), coronary artery disease (20.1%), and kidney failure (15.8%) (Table 3). Fifteen percents of patients had one or more causes of immune depression. Charlson's comorbidity index ranged from 0 to 12 with a median of 2 (25^{th}-75^{th} percentile, 1 to 3). The median duration of the index stay was 8 days. A total of 168 (14.6%) patients were admitted to the ICU, 42 (3.6%) underwent invasive mechanical ventilation and 50 (4.3%) received inotropic or vasopressor support.

Blood was obtained for culturing from 817 patients (71.0%), and an urine sample for urinary antigen detection from 583 patients (50.7%). A pathogen was detected in 311 patients, including one or more viruses in 57 (5.0%) patients, one or more bacteria in 252 (21.9%), both bacterial and viral pathogens in 15 (1.3%), and fungi or mycobacteria in 22 (1.9%). The most common bacteria detected were *S. Pneumoniae* (6.9%), *Haemophilus influenzae* (2.8%) and *Legionella pneumophila (2.3%).*

Discussion

In this study, the 30-day readmission rate is 17.5% for patients hospitalized with CAP. This result is consistent with previous estimates, ranging from 7.3% to 25% across studies. Thus, the rate of readmission varied from 13.6% to 25% in the studies of Makam et al.[35] and of Hatipoglu et al.[32], from 7.3% to 20.1% in the study of Prescott et al.[6] and from 11.8% to 20.8% with a median of 17.3% for Weinreich et al.[34]

Compared with previous reports, the patients enrolled in our study are older (median age, 78 years), more likely to present with severe pneumonia (prevalence of PSI risk classes IV-V, 63.5%) and have more comorbidities (prevalence of Charlson's comorbidity index ≥2, 53%). The 24% rate of patients with identified pathogens is lower than previously reported.[2] The potential explanations for such a low micro-organism detection rate include the lack of testing for known pathogens, antibiotic use before specimen collection, and non-infectious causes. Of notice, our study was observational in design and therefore microbiological diagnostic test ordering was left at the discretion of admitting physicians. Polymerase chain reaction (PCR) assay was rarely performed for the detection of respiratory viruses, which could have led to underestimating the prevalence of viral etiologies. Consistent with previous reports, the most commonly detected bacteria was *Streptococcus pneumoniae*. With the exception of viruses, the distribution of other micro-organisms was the same as reported in the literature.[1, 47, 48]

Various approaches have been used for assessing whether a readmission is potentially avoidable, including implicit assessment, explicit assessment, and latent class analysis. Implicit assessment based on unstructured chart review is the most common approach although its validity and reliability are questioned.[49] The lack of standardization in criteria might explain variations in percentages of potentially avoidable readmissions across primary studies.[49] Yet, implicit assessment may be improved by the use of two independent reviewers, resolution of disagreement by discussion between the two reviewers or by a third reviewer, and by interviews with the physicians in charge of the patient and with the patient.[50, 51]

Explicit assessment based on structured chart review by one or more reviewers has been used in various contexts. Halfon et al.[45] categorized readmissions as planned, unplanned for a new condition, and unplanned for a condition known at index hospitalization. Then, reviewers are asked to assign a root cause for readmission using 11 exclusive categories. This approach has been implemented throughout the «Striving for Quality Level and Analysing of Patient Expense» (SQLape) algorithm for use with administrative claims data.[52]

Van Walraven et al. have refined the explicit assessment approach by quantifying the likelihood that a readmission is potentially avoidable using a latent class analysis based on independent reviews by multiple panelists. We are planning to use the same approach, which is a strength of the present study.

The limitations of our study deserve mention. First, our study tracks index hospital readmissions only. Indeed, previous studies reported that one in five 30-day readmissions may occur at non-index hospitals.[53] Second, the effective sample size for model development is relatively limited with the potential for overfitting. As a rule of thumb, there will be a minimum of five potentially avoidable readmission cases per candidate predictor considered for inclusion in our multivariable logistic regression model. Third, our study is conducted in two hospitals in France and our findings may not apply to other settings or regions.

To conclude, we will develop an administrative claims-based model for identifying potentially avoidable 30-day readmissions of CAP patients, using latent class analysis of explicit assessment by independent panelists as the reference method. Our study will also provide the unique opportunity to estimate the accuracy of competing models in predicting potentially avoidable readmission in an external validation sample.

Author Contributions:

All authors reviewed the manuscript and contributed to its improvement.

All authors were involved in study population development.

Anne-Laure Mounayar: literature review and manuscript writing.

Patrice François: study conceptualization, protocol development, literature review and manuscript writing.

Magali Bouisse: statistical analysis.

Xavier Courtois : sampling and data collection.

José Labarère: statistical expertise, critical revision of the manuscript.

Arnaud Seigneurin: protocol development, statistical analysis.

Patricia Pavese, Elodie Sellier, Jacques Gaillat, Boubou Camara, Bruno Degano, Mylène Maillet: structured medical chart review for avoidability assessment.

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Figure 1: Flow-chart of study population

Abbreviations: CAP = community-acquired pneumonia, GUH = Grenoble University Hospital, AGH = Annecy Genevois general hospital

Table 1. ICD-10 codes that define pneumonia.

ICD-10	Description
Primary diagnosis code of pneumonia	
B01.2	Varicella pneumonia
B20.6	HIV disease resulting in Pneumocystis jirovecii pneumonia
B25.0	Cytomegaloviral pneumonitis
B59	Pneumocystosis
J10.0	Influenza with pneumonia, seasonal influenza virus identified
J11.0	Influenza with pneumonia, virus not identified
J12.x	Viral pneumonia, not elsewhere classified
J13	Pneumonia due to Streptococcus pneumoniae
J14	Pneumonia due to Haemophilus influenzae
J15.x	Bacterial pneumonia, not elsewhere classified
J16.x	Pneumonia due to other infectious organisms, not elsewhere classified
J17.x	Pneumonia in diseases classified elsewhere
J18.x	Pneumonia, organism unspecified
J69.0	Pneumonitis due to inhalation of food and vomit
Primary diagnosis code of sepsis, respiratory failure, or compatible symptoms with a secondary diagnosis code of pneumonia	
A40.x	Streptococcal sepsis
A41.x	Other sepsis
D65	Disseminated intravascular coagulation (defibrination syndrome)
E86.x	Volume depletion
E87.x	Other disorders of fluid, electrolyte and acid-base balance
J80	Adult respiratory distress syndrome
J81	Pulmonary edema
J85.1	Abscess of lung with pneumonia
J90	Pleural effusion, not elsewhere classified
J91	Pleural effusion in conditions classified elsewhere
J96.x	Respiratory failure, not elsewhere classified
O99.5	Diseases of the respiratory system complicating pregnancy, childbirth and the puerperium
R04.2	Haemoptysis
R06.0	Abnormalities of breathing
R07.1	Chest pain on breathing
R07.2	Precordial pain
R07.3	Other chest pain
R07.4	Chest pain, unspecified
R41.0	Disorientation, unspecified
R50.9	Fever, unspecified
R57.1	Hypovolaemic shock
R57.2	Septic shock
R57.9	Shock, unspecified
R91	Abnormal findings on diagnostic imaging of lung

Table 2. Baseline Patient Characteristics (n=1150)

Characteristics*		
Demographics		
Male gender, *n (%)*	651	(56.6)
Age, median (IQR), *y*	77.8	(62.7-86.4)
Nursing home resident, *n (%)*	169	(14.7)
Index hospital stay		
Length of stay, median (IQR), *d*	8	(4-13)
Admission via emergency department, *n (%)*	1001	(87.0)
Physical examination findings		
Altered mental status, *n (%)*	230	(20.0)
Systolic blood pressure, median (IQR), *mmHg*	117	(102-132)
Pulse rate, median (IQR), *per min*	98	(85-113)
Respiratory rate, median (IQR), *per min*	26	(21-31)
Temperature, median (IQR), °C	37.8	(37.0-38.5)
Abnormal auscultation findings, *n (%)†*	931	(81.0)
Laboratory findings		
Arterial hypoxemia, *n (%)‡*	261	(22.7)
Hematocrit, median (IQR), %	38	(35-42)
Blood urea nitrogen, median (IQR), *mmol/L*	8.1	(5.5-11.6)
Serum sodium, median (IQR), *mEq/L*	137	(135-140)
Glucose, median (IQR), *mmol/L*	6.6	(5.6-8.5)
C-reactive protein, median (IQR), *mg/L*	114.0	(49.0-202.3)
White blood cell count, median (IQR), Giga/L	11.4	(8.4-15.5)
Pneumonia severity index, *n (%)*		
Class I	73	6.4
Class II	135	11.7
Class III	212	18.4
Class IV	457	39.7
Class V	273	23.7

Abbreviations: IQR = interquartile range (i.e., 25-75th percentiles)

* Values were missing for systolic blood pressure (n = 8), pulse rate (n = 8), respiratory rate (n = 627), temperature (n=8), arterial hypoxemia (n=29), hematocrit (n = 21), blood urea nitrogen (n

= 30), serum sodium (n = 19), glucose (n = 207), C-reactive protein (n = 18), white blood cell count (n = 13),

† Abnormal auscultation findings included rales and crepitations.

‡ Arterial hypoxemia was defined by O_2 saturation <90% or arterial PO_2<60 mm Hg using pulse oximetry or arterial blood gas.

Table 3. Pre-existing comorbid conditions (n=1150)

Preexisting comorbid conditions	**n**	**(%)**
Cardiovascular disease	754	(65.6)
Arterial hypertension	*573*	*(49.8)*
Congestive heart failure	*150*	*(13.0)*
Peripheral vascular disease	*127*	*(11.0)*
Coronary artery disease	*231*	*(20.1)*
Heart dysrhythmia	*268*	*(23.3)*
Respiratory disease	282	(24.5)
Chronic obstructive pulmonary disease	*204*	*(17.7)*
Other	*109*	*(9.5)*
Active cancer	93	(8.1)
Liver disease (moderate or severe)	32	(2.8)
Renal disease	182	(15.8)
Neurologic and psychiatric disease	424	(36.9)
Cerebrovascular disease	*164*	*(14.3)*
Dementia or Alzheimer's disease	*133*	*(11.6)*
Psychiatric illness	*143*	*(12.4)*
Others	*211*	*(18.3)*
Diabetes mellitus	259	(22.5)
Charlson Index		
0	274	(23.8)
1	263	(22.9)
2	204	(17.7)
>2	409	(35.6)