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**Médecine et
maladies infectieuses**

Médecine et maladies infectieuses xxx (2017) xxx–xxx

Original article

Incidence of all-cause adult community-acquired pneumonia in primary care settings in France^{☆,☆☆}

Incidence des pneumonies aiguës communautaires prises en charge en médecine générale en France

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Received 26 May 2017; received in revised form 18 October 2017; accepted 27 February 2018

Abstract

Objectives. – To estimate the incidence of all-cause outpatient community-acquired pneumonia (CAP) in adults in France from a national prospective observational study of CAP management in general practice (CAPA).

Methods. – Patients aged over 18 years presenting with signs or symptoms indicative of CAP associated with recent onset of unilateral crackles on auscultation and/or a new opacity on chest X-ray were included in the CAPA study. An ancillary survey (AIMSIS) aiming at identifying family physicians' difficulties in including patients and at collecting their opinion on the use of an electronic case report form, determined the number of non-included eligible patients. A three-step analysis was then performed, including computation of the total number of eligible patients, adjustment for seasonality, and extrapolation to the French FP population using indirect standardization to adjust for differences in characteristics between CAPA FPs and French FPs.

Results. – Between September 2011 and July 2012, 267 (63%) CAPA investigators included 886 CAP patients. Most patients presented with mild CAP. The rates of hospitalization and one-month case fatality were 7% and 0.3%, respectively. Data from 336 (79%) AIMSIS investigators identified 641 additional patients and estimated at 234,023 the number of CAP patients per year (incidence of 4.7 per 1000 persons per year).

Conclusions. – Using a pragmatic case definition of CAP patients, this study estimated an incidence of 4.7 per 1000 persons per year that is in the lower half of the range of estimated incidences reported in primary care settings in industrialized countries.

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Keywords: Community-acquired pneumonia; General practice

Résumé

Objectifs. – Estimer l'incidence des pneumonies aiguës communautaires (PAC) chez les adultes pris en charge en médecine générale en France à partir des données prospectives observationnelles de l'étude CAPA.

Méthode. – Ont été inclus dans l'étude CAPA, tous les patients de plus de 18 ans avec symptômes ou signes suggestifs de PAC, associés à un foyer unilatéral de râles crépitants et/ou une opacité radiologique récente. Une étude ancillaire sur l'avis des investigateurs à propos des inclusions et de la saisie informatique (AIMSIS) a déterminé le nombre de cas éligibles non-inclus. Une analyse en trois temps a été réalisée : calcul du nombre total de patients éligibles, ajustement selon la saisonnalité puis extrapolation à la population générale en ajustant sur les différences de caractéristiques entre les investigateurs de CAPA et les médecins généralistes français.

[☆] The AIMSIS study was presented as a poster at the International Meeting on Emerging Diseases and Surveillance: IMED Vienna, in October 2014.

^{☆☆} The CAPA study was presented as a poster at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in April 2013 in Berlin, Germany. It was published in *npj Primary Care Respiratory Medicine* in March 2015 (Reference 9).

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Résultats. – De septembre 2011 à juillet 2012, 267 (63 %) investigateurs de CAPA ont inclus 886 patients, la plupart ayant une forme peu grave de PAC. Les taux d'hospitalisation et la létalité à un mois étaient respectivement de 7 % et de 0,3 %. Les données issues des 336 (79 %) investigateurs d'AIMSIS ont identifié 641 cas éligibles non-inclus et estimé à 234 023 le nombre total annuel de PAC (incidence de 4,7 pour 1000 adultes par an).

Conclusions. – Avec une définition pragmatique de PAC, cette étude montre une incidence annuelle de 4,7 pour 1000 adultes, qui se situe dans la moitié inférieure de l'intervalle des incidences des pays industrialisés.

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Mots clés : Pneumonie communautaire ; Médecine générale

1. Introduction

Community-acquired pneumonia (CAP) is a major infectious disease in adults with a substantial burden in terms of hospitalization, death, and cost in industrialized countries. In the United States CAP patients aged ≥ 50 years accounted for 34.6% of patients hospitalized for infectious diseases in 2005. The mean length of stay for pneumonia was 5 days and the 30-day case fatality was highest (23%) among patients hospitalized for infectious diseases [1]. The highest incidence rates of CAP in adults are reported in patients aged ≥ 65 years, a population at high-risk of death due to pneumonia [1–3]. These rates might increase with population ageing leading to increased healthcare costs [1,2,4]. However, assessing the incidence rate of CAP in ambulatory settings remains difficult due to the very low frequency of consultations for suspected CAP in family physician (FP) practices (less than seven CAP per year per FP in France) [5]. Recent data on CAP outpatients from prospective cohort studies is lacking. Epidemiological data reported in the European primary care guideline for the management of CAP in adults is based on old studies [6]. In France, the latest ambulatory data is derived from Cegedim Strategic Data (CSD) [7], a French company specializing in healthcare market analysis [8].

To characterize CAP burden in the French adult population, a national prospective observational study of CAP management in general practice (CAPA study) [9] and an ancillary survey (AIMSIS) of the opinions and practices of participating FPs [10] were conducted from 2011 to 2012. The aim of this study was to estimate the incidence of all-cause outpatient CAP in adults in France, based on a post-hoc analysis of our two previous studies.

2. Method

2.1. Study periods and setting

The CAPA study was a prospective cohort study conducted between September 21, 2011 and July 2, 2012, in FP practices in France. Data was recorded in an electronic case report form (eCRF) until September 2, 2012 [9].

The AIMSIS survey was an ancillary survey among FPs participating in the CAPA study conducted between July 2, 2012 and August 10, 2012, and the data was recorded in a specific eCRF that allowed collecting FP motivation to participate, their

difficulties in including patients, and their opinions and practices regarding the CAPA study [10].

2.2. FP sampling scheme

Four hundred and twenty-five FPs were asked to include all consecutive outpatients presenting with CAP older than 18 years. All investigators were part of a national FP network involved in clinical research and/or had a part-time FP teaching activity. They were recruited through a website linked to an eCRF. A stratified random sampling based on a multistage geographical cluster design at a departmental level was used to obtain a representative FP sample.

2.3. Definition of CAP and inclusion criteria

Inclusion criteria were being aged 18 years or over, having a recent onset of one or more signs suggestive of acute pneumonia such as fever > 38.5 °C, cough, chest pain, tachycardia > 100 beats/min, polypnea > 25 breaths/min, clinical evaluation of severity associated with at least one recent onset of unilateral crackles on auscultation and/or a new opacity on chest X-ray. Immuno-compromised patients and nursing home patients could be included. Patients hospitalized in the previous month were not included.

2.4. Data collection

The collected data included visit date, age, gender, lifestyle, history and clinical findings, investigations and their results, treatments, reasons for new consultation, duration of main symptoms, sick leave and its duration, hospitalization, and death. Patient data was anonymized. Patients were followed as part of their current management.

A positive chest radiography (X-ray) was defined by the presence of a focal alveolar opacity or multiple, mottled, peribronchial opacities or localized or diffuse interstitial opacities. A negative X-ray was defined by normal or non-specific radiographic findings and/or the presence of isolated pleural effusion.

Two clinical research associates ensured data quality throughout the study. They focused on record completeness and data collection from additional investigations. The monitoring team ensured that inclusion criteria were met, especially in patients without X-ray or with negative X-ray to rule out bronchitis or

crackles due to other causes. A periodical online newsletter was sent to the investigators to prevent any loss to follow-up.

2.5. Assessment of FP exhaustiveness in including CAP patients

The AIMSIS survey determined the number of patients eligible for inclusion among FPs' patients. In addition, the number of eligible CAP patients who were not screened for inclusion was recorded.

2.6. Analysis

The annual number of CAP cases in French adults aged ≥ 18 years consulting in FP practices was estimated based on the number of included CAP case patients using a three-step analysis.

First, the number of CAP case patients was adjusted for inclusion completeness, assessed from the results of the AIMSIS survey. FP participating in the CAPA study and AIMSIS survey were classified as active if they included at least one CAP patient and as inactive otherwise. The accurate numbers of CAP patients who were eligible but not included were collected by FPs participating in the AIMSIS survey who were able to report this data. Then, the mean number of eligible CAP patients who were not assessed for inclusion by FPs was calculated for active and inactive FPs to obtain the overall number of eligible but not included patients in the CAPA study (Table 1).

The number of CAP patients included was then inflated to take into account CAP cases that occurred during the 10 summer weeks with adjustment for inclusion seasonality [11,12]. We used a quadratic function of the weekly number of CAP cases fitted to the observed number of inclusions per week (Fig. 1).

The number of CAP cases included by the 425 participating FPs was extrapolated to the French FP population using an indirect standardization to adjust for differences in characteristics between CAPA FPs and French FPs, according to the French national board of physicians database used as a reference [13].

3. Results

3.1. Investigators

From the network of CAPA investigators, 267 (63%) FPs included ≥ 1 patient(s). These active investigators more often worked in a group practice than inactive investigators (71.5% vs. 19.6%, $P < 0.001$), but their other characteristics did not differ from those of inactive investigators. Compared with the national medical demography, the proportions of men (70% vs. 58.8%), medical trainers (89.1% vs. 9.5%), rural location (30% vs. 12%), and group exercise (71.5% vs. 45.3%) were higher in active investigators [13,14].

Among CAPA investigators, 336 (79%) FPs participated in the AIMSIS survey. Compared with non-participants ($n = 89$), the rate of FPs having a group exercise was significantly higher in participants of the AIMSIS survey (55% vs. 42%, $P = 0.03$).

Table 1
Estimate of the number of CAP patients not included in the CAPA study.
Estimation du nombre de cas de PAC non-inclus dans l'étude CAPA.

	Number of FPs (1)	Number of CAP patients not assessed for inclusion (2)	Ratio of CAP patients not included per FP ^a	Ratio of patients with inclusion criteria but not included per FP ^b
<i>FPs participating in the AIMSIS survey</i>				
Active FPs who did not fail to include patients	117	0		
Active FPs who failed to include patients	100	293	2.93	
Active FPs who failed to include patients, but the number is unknown	18	52.7 ^c		
Inactive FPs who did not fail to include patients	51	0		
Inactive FPs who failed to include patients	32	130	4.06	
Inactive FPs who failed to include patients, but the number is unknown	18	73.1 ^d		
All active FPs in the AIMSIS survey	235	345.7	1.47	1.33 (3)
All inactive FPs in the AIMSIS survey	101	203.1	2.01	1.81 (4)
<i>FPs participating in the CAPA study</i>				
All active FPs in the CAPA study	267	354 ^e		
All inactive FPs in the CAPA study	158	287 ^f		
All participating FPs in the CAPA study	425	641		

CAPA: community-acquired pneumonia in an ambulatory setting; CAP: community-acquired pneumonia; FPs: family physicians; active FPs: who included at least one CAP patient.

^a (2)/(1).

^b $a \times (886/982)$.

^c 18×2.9 .

^d 18×4.1 .

^e $(1) \times (3)$.

^f $(1) \times (4)$.

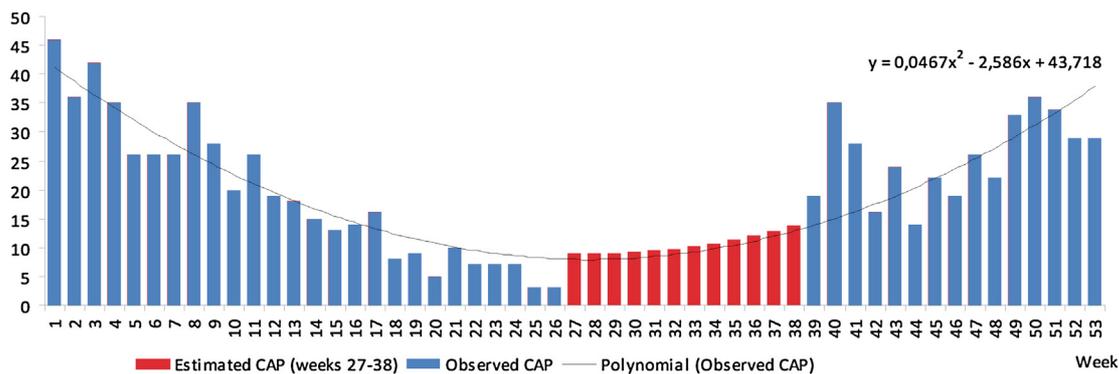


Fig. 1. CAPA study: number of inclusions per week over the September 2011–June 2012 period, and estimated number of inclusions per week over the summer period (weeks 27 to 38). CAPA: community-acquired pneumonia in an ambulatory setting; CAP: community-acquired pneumonia.

Étude CAPA : nombre d'inclusions par semaine de septembre 2011 à juin 2012 et estimation du nombre d'inclusions par semaine durant la période d'été (semaine 27 à 38).

No difference was observed between both groups for the other studied characteristics.

3.2. Number of included patients presenting with CAP

During the study period, 982 patients were assessed for inclusion and 886 (90%) were included. Of the 886 CAP patients, 563 (64%) had a positive chest X-ray and 172 (19%) were managed without chest X-ray.

3.3. Summary of patient characteristics

The median age of patients was 55 (18–102) years. A total of 278 (31%) patients were older than 65 years and 314 (35%) were retired, 467 (53%) were women, 366 (41%) lived in a rural location, 118 (13%) had chronic obstructive pulmonary disease (COPD), and 124 (14%) had experienced a previous episode of CAP. Forty-eight (5%) nursing home patients were included.

Despite a mild disease presentation (62% of patients had a CRB-65 score of 0), the rate of hospitalizations was 7% and the one-month case fatality was 0.3%. Patients at increased risk of invasive pneumococcal disease and patients with CRB-65 score ≥ 1 were more frequently hospitalized than others (respectively, 10% vs. 5%, $P = 0.002$, and 13% vs. 3%, $P < 0.001$) (data not shown).

3.4. Adjusted number of inclusions for completeness over a one-year period

Among FPs participating in the AIMSIS survey, 300 (89%) failed to assess for inclusion 423 eligible patients. The number of patients not included by the 425 CAPA investigators was estimated to be 641 after extrapolation of the results of the AIMSIS investigators resulting in an estimate of 1527 (886 + 641) CAP patients over the survey period (Table 2).

An additional 198 CAP patients could have been included during the 10 summer weeks according to a fitted quadratic regression of the number of inclusions per week (Fig. 1). Finally, a total of 1725 (1527 + 198) CAP patients could have been included in one year assuming a 100% inclusion completeness.

3.5. Estimate of the incidence of CAP patients in FP practices in France

Extrapolating this finding to the 60,925 French FPs, standardized for the proportion of group practices in CAPA investigators and in the French FP population, allowed estimating the number of CAP patients in one year to 234,023 (Table 2) and deducting a yearly incidence of 4.7 CAP cases per 1000 persons aged 18 years or over.

3.6. Estimate of CAP patients aged over 65 years

The number of CAP patients in the French population aged 65 years or over managed in FP practices in one year was calculated to be 73,423 (i.e., 31% of 234,023), under the assumption of a non-differential inclusion by age, resulting in a yearly incidence of 6.7 CAP cases per 1000 persons aged 65 years or over.

4. Discussion

4.1. Main results

This study provided for the first time an estimated incidence of CAP in FP practices in France, on the basis of a prospective cohort study based on a network of 425 FPs proportionally distributed according to the departmental FP demography. The estimated incidence rate of CAP was 4.7/1000 inhabitants aged 18 years or over and 6.7/1000 inhabitants aged 65 years or over.

4.2. Comparison with other results

4.2.1. Comparison with CSD patients (CEGEDIM)

Our estimated incidence is slightly higher than that of CAP adult patients from the French CSD panel (4/1000 inhabitants/year) [8]. The CSD panel consists of 1200 FPs representative of the French practicing FP population in terms of age, gender, activity level, and geographic location. Patients from the CAPA cohort shared the same characteristics in terms of age, sex ratio, and main history as CSD patients. However, the frequency of COPD was higher in CSD patients than in patients

Table 2

Yearly number of CAP patients suspected by French FPs, standardized on group practice.

Nombre annuel de cas de PAC pris en charge par les médecins généralistes français, standardisé sur l'exercice en groupe.

	FPs in group practice	FPs not in group practice	All
Number of FPs participating in the CAPA study	222	203	425
Number of FPs who were active in the CAPA study	191	76	267
Number of FPs who were inactive in the CAPA study	31	127	158
Ratio of patients presenting with CAP included by active FPs			6.5
Number of CAP patients who could have been included in one year	1,234	491	1,725
Ratio of CAP patients by FPs participating in the CAPA study in one year	5.6	2.4	4.1
Number of French FPs	27,609	33,316	60,925
Number of CAP patients in France	153,448	80,575	234,023

CAPA: community-acquired pneumonia in an ambulatory setting; CAP: community-acquired pneumonia; FPs: family physicians; Active FPs: who included at least one CAP patient.

from the CAPA cohort [8,9]. Based on the incidence rate in the CSD panel, the cost of the disease per ambulatory episode was modest in the CAPA study, but substantially increased in case of hospitalizations which were more frequent in COPD patients and in the elderly [8].

4.2.2. Comparison with results of studies conducted in other countries

Our estimate is higher than the estimate of a prospective study conducted in Northern Spain both in 150 FP practices and in a regional emergency department. With a restrictive definition of CAP that had to be confirmed by X-ray (non-representative of the daily practice of FPs), the overall estimated incidence rate of CAP was 3.1 cases per 1000 inhabitants/year and 9.9 per 1000 in patients aged 74 years and over [15]. However, 51% of included patients in this study initially consulted at the emergency department and the high rate of hospitalization (43.5%) suggests a selection of CAP patients with more severe disease.

In a large UK cohort study using electronic health records to determine whether the incidence of pneumonia and other life-threatening infectious diseases was higher when FPs prescribed fewer antibiotics, the authors reported an annual age and gender-standardized incidence rate of pneumonia per 1000 inhabitants ranging between 1.19 and 1.57 depending on the amount of antibiotics prescribed from 2005 to 2014 (high and low amounts, respectively) [16]. These low rates can be explained by the design of the study using the “Read code classification” and taking into account the first episodes experienced by each participant only.

In a large survey of CAP patients visiting the emergency departments of Edmonton, Alberta (Canada), where there is no family physician, Eurich DT et al. reported 3186 patients treated on an outpatient basis whose characteristics were similar to those of the CAPA study patients: mean age of 51 years (55 years in the CAPA study), 29% were aged over 65 years (31% in the CAPA study), 88% had mild pneumonia (73% in the CAPA study), 8% were hospitalized and 1% died (6.9% and 0.33%, respectively in the CAPA study). Patients with abnormal chest X-ray were similar to those with normal chest X-ray but their disease was slightly more severe. No incidence data was reported [17]. However, based on the epidemiological data obtained from the same “pneumonia pathway” (care pathway dedicated to

patients presenting with pneumonia in seven emergency departments using the same inclusion criteria) in Edmonton, Marrie TJ et al. reported two consecutive estimates of the incidence rate of ambulatory pneumonia, i.e. 2.89 and 3.15 cases per 1000 inhabitants/year [12].

In Australia, Li A et al. reported a high estimated incidence rate of consultations for pneumonia (8.61 per 1000 inhabitants/year) based on the data on pneumonia management by a random sample of FPs [18]. Similarly, a high incidence rates of outpatient CAP (8.7 per 1000 persons/year) was reported in a US retrospective cohort study based on data from two databases of the firm Health Analytics, using medical claims [19]. However, in the last two studies, a sampling bias cannot be excluded.

Recently a population-based study based on data of a large German statutory health insurance reported an outpatient incidence of 5.2 cases per 1000 inhabitants, comparable to our result [18].

Finally, our result of the estimated incidence rate is within the range of incidence rates observed in the other similar cohort studies discussed above (from 1.19 to 8.7). The variation in incidence rates could be explained by differences in CAP case definitions and in patient recruitment conditions due to the specific organization of primary care in each region or country. Moreover, vaccination policies could have an impact on the incidence rates of CAP such as in the United States where the herd immunity after routine pneumococcal conjugate vaccine in children may have reduced the incidence rate of invasive pneumococcal disease and pneumonia in adults [20].

4.3. Study limitations

First, this estimate did not take into account patients presenting with CAP who had been assessed in an emergency department and discharged the same day during the CAPA study period. Moreover, mandatory collection of data in an eCRF may have prevented investigators from including nursing home patients (only 5% included). These could have led to underestimating the CAP episodes in outpatients. Conversely, the even distribution of CAPA investigators across the metropolitan country (30% in rural practice) allowed covering primary care management for most patients who experienced a non-life-threatening episode of CAP.

Second, despite our efforts to reach a 100% rate of inclusion completeness, a recall bias cannot be excluded as the missed inclusions were identified from retrospective and self-reported data provided by AIMSIS investigators.

Finally, our CAP case definition including patients without X-ray or with negative X-ray is questionable. However, under the usual conditions of general practice, patients with suspected CAP may be managed as CAP patients without X-ray as recommended by the British Thoracic Society guidelines [6]. Furthermore, the sensitivity of the X-ray in diagnosing CAP compared with chest CT scan (as possible “gold standard”) has been recently questioned by Claessens YE et al. [21]. In the CAPA cohort, two-thirds of patients had a positive chest X-ray. However, in patients with chest X-ray and in those without X-ray, the rates of hospital admission and the 30-day case fatality were similar [9] and also similar to those reported in previous studies [15,17]. Finally, the WHO case definition of CAP that includes all cases of pneumonia confirmed by the presence of an alveolar consolidation on x-ray was called into question by the authors as it underestimated the burden of pneumonia [22].

4.4. Perspectives

This incidence data relates to patients presenting with CAP and pragmatically managed in general practice regardless of the etiology of their disease. Other prospective cohort studies focusing on documented pneumococcal CAP are required to assess the burden of the disease and the impact of the pneumococcal vaccination program on pneumococcal CAP incidence in French primary care settings.

5. Conclusion

This study reports for the first time an estimated incidence of suspected CAP in France in subjects aged 18 years or over, based on a prospective cohort study conducted in primary care settings. Obtained through a large network of FPs evenly distributed across the country, our estimate of 4.7 cases per 1000 persons/year is in the lower range of the rates reported in outpatients and primary care settings in industrialized countries. It is slightly higher than the incidence rate derived from the French CSD panel; a more accurate assessment of the disease burden is therefore possible.

Ethical approval

The CAPA study received the agreement of the institutional review board of Paris North Hospitals, Paris 7 University, AP-HP (n°IRB00006477): reference protocol number 11-030.

Funding

The CAPA study was made possible by a grant from Pfizer. The CAPA observational study was funded by Pfizer (investigator-initiated research). The AIMSIS ancillary study was performed without any additional funding.

Disclosure of interest

HP, CBdV, and SG participated in the CAPA study for which they report having received grant support through the French National College of Teaching Physicians (French acronym CNGE) from Pfizer.

The remaining authors declare that they have no competing interest.

Acknowledgement

The authors would like to thank the investigators of the research network of the National College of Teaching Physicians who took part in the CAPA study, as well as those who participated in the AIMSIS study.

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