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New evidence of risk factors for community-acquired pneumonia: a population-based study

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ABSTRACT: The aim of the present study was to identify risk factors for community-acquired pneumonia (CAP), with special emphasis on modifiable risk factors and those applicable to the general population.

A population-based, case–control study was conducted, with a target population of 859,033 inhabitants aged >14 yrs. A total of 1,336 patients with confirmed CAP were matched to control subjects by age, sex and primary centre over 1 yr.

In the univariate analysis, outstanding risk factors were passive smoking in never-smokers aged >65 yrs, heavy alcohol intake, contact with pets, households with >10 people, contact with children, interventions on the upper airways and poor dental health. Risky treatments included amiodarone, *N*-acetylcysteine and oral steroids. Influenza and pneumococcal vaccine, and visiting the dentist were protective factors. Multivariable analysis confirmed cigarette smoking, usual contact with children, sudden changes of temperature at work, inhalation therapy (particularly containing steroids and using plastic pear-spacers), oxygen therapy, asthma and chronic bronchitis as independent risk factors.

Interventions for reducing community-acquired pneumonia should integrate health habits and lifestyle factors related to household, work and community, together with individual clinical conditions, comorbidities and oral or inhaled regular treatments. Prevention would include vaccination, dental hygiene and avoidance of upper respiratory colonisation.

KEYWORDS: Community-acquired pneumonia, population-based study, risk factors

Community-acquired pneumonia (CAP) remains an important cause of morbidity and mortality. Preventive strategies identifying and acting on modifiable risk factors are of paramount importance in reducing CAP-related death. Population-based studies of risk factors for CAP are scarce. In a Finnish study of subjects aged ⩾60 yrs, alcoholism, heart disease, lung disease and immunosuppressive therapy, among others, were independent risk factors for pneumonia [1]. Similar results were obtained in a study carried out in the UK, in which the importance of cigarette smoking was added [2]. In a study carried out in Spain, other risk factors identified included low body mass index, previous respiratory infection and previous pneumonia [3]. Some studies in USA population-based cohorts confirmed these findings and emphasised the influence of excessive weight gain, asthma and diabetes [4]. Other risk factors for CAP suggested in these studies have been inconsistently observed or statistical confirmation was not possible. A systematic review of 10 studies analysing risk factors for CAP concluded that there is insufficient evidence for other factors, such as medication, dangerous substances, alcohol consumption or sociodemographic factors [5].

With the aim of providing further evidence on known and new risk factors for pneumonia, a large population-based study on CAP in adults was performed with special emphasis on the identification of modifiable risk factors and those applicable to the general population.

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STATEMENT OF INTEREST
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PATIENTS AND METHODS

Study population

A population-based, case–control study was conducted in an extensive area of the eastern coast of Spain, in which ~95% of the population belongs to the National Health Care System, with public primary care centres and regional hospitals in each county. This is a mixed residential–industrial urban area with Mediterranean climatic conditions. The target population included 859,033 inhabitants aged >14 yrs assigned to any of the 64 primary care centres participating in the study. A total of 345 general practitioners were involved; the recruitment of the practitioners was made according to willingness to take part in the study. In order to demonstrate association with an odds ratio (OR) of 1.5 for risk factors for CAP with a prevalence of exposure in the control group of 5%, with 80% statistical power and significance level of 0.05, a sample of 1,500 cases and 1,500 controls was required.

Identification of cases

All patients with clinically suspected CAP presenting from November 1, 1999 to November 30, 2000 were prospectively registered. An active surveillance system was established to ensure the identification of all cases. This register involved all physicians working in public and private healthcare facilities in the study area and reference hospitals both inside and outside the county area of each primary care centre. In order to maintain the system of reporting cases, the coordinator in each of the study areas established periodic contact with responsible persons of all participating centres. Periodic meetings with all professionals involved in the study were also held.

Predefined criteria for case registration were based on acute lower respiratory tract infection for which antibiotics had been prescribed, in association with the appearance of previously unrecorded focal signs on physical examination of the chest and new radiological findings suggestive of pneumonia infiltrate [3]. Criteria for clinical suspicion of acute lower respiratory tract infection included the presence of three or more of the following manifestations: cough with or without sputum production; dyspnoea and/or wheezing; pleuritic chest pain or abdominal pain; fever; headache; pneumonic consolidation on auscultation of the chest; sweating; arthromyalgias; dysphagia; and coryza. For clinically atypical CAP, one or more of the following criteria were considered: sweating; arthromyalgias; dysphagia; and coryza that required antibiotic prescription or persisted $\geqslant$5 days without antibiotics. In elderly patients, the possibility of pneumonia was also considered in the presence of prostration and/or anorexia and/or confusion or disorientation. In all cases in which criteria for clinical suspicion were met, a chest radiograph was ordered. Patients with initial doubtful radiographical images of CAP were tentatively included in the study and then excluded or definitively included according to clinical evolution and subsequent radiographical findings. All cases of CAP were re-evaluated by chest radiographs on the fifth day of illness and at monthly intervals until complete recovery.

Patients with aspiration pneumonia (witnessed aspiration with respiratory symptoms or oral content of aspiration) or active pulmonary tuberculosis, and patients who came from nursing homes or were discharged from hospital within 7 days of the onset of symptoms were excluded.

Selection of controls

Cases and controls were matched by sex, age ($\pm$5 yrs) and primary care centre. Frequency matching was performed. Cases were matched to controls in a 1:1 proportion. Controls were randomly selected from the list of subjects assigned to each primary care centre, and were recruited every 3 months. Controls who could not be contacted by telephone or home visits after three attempts were replaced following the same selection and matching criteria.

Data collection

A questionnaire on CAP risk factors was composed from the current literature and the opinion of international experts, the reliability of which has been demonstrated in previous studies [3, 6]. It was administered directly to participants by trained physicians or nurses at home. The questionnaire included standardised information related to the following three aspects: 1) health habits and lifestyle, 2) clinical conditions and comorbidity, and 3) regular treatments during the last year. Items are briefly described in the Appendix. The complete questionnaire is available from the present authors upon request.

The study protocol was approved by the Ethics Committee of the Consorci Sanitari del Maresme (Barcelona, Spain) and all participants gave written informed consent before enrolment.

Statistical analysis

As a measure of association between risk factors and the occurrence of CAP, estimations of the relative risk through ORs and 95% confidence intervals (CI) were used. These were calculated using unconditional logistic regression. The Chi-squared test was used to assess differences between cases and controls in the frequency of variables related to health habits and lifestyle, clinical conditions and comorbidity, and regular treatments during the last year. All variables that were statistically significant in the univariate analysis with a p-value <0.10 were entered in a multivariable model with a stepwise approach. Moreover, it was considered appropriate to complement the multivariable analysis strategy by adjusting the effect of some drug treatments or vaccines for the underlying illness which were the reason for prescription. This focused on treatments for heart failure, respiratory diseases and the influenza and pneumococcal vaccines. In all cases, if multicollinearity among different variables was detected, the most generic variable was selected. No interaction assessment was systematically performed, due to the broad number of risk factors considered.

RESULTS

During the period of field work, 1,833 cases of clinical suspicion of CAP were identified, the diagnosis of which was not confirmed in 394 (21.5%). There were 1,439 patients with CAP, with an annual incidence rate of 1.54 cases per 1,000 inhabitants aged >14 yrs. A total of 2,107 control subjects were selected. The final study population included 1,336 patients with CAP and 1,326 controls. The distribution of cases and controls, and reasons for exclusion are shown in figure 1. In the group of patients with CAP, 52.9% were males with a mean$\pm$SD age of 58.6$\pm$19.8 yrs and 47.1% were females aged 54.6$\pm$20.7 yrs. In the control group, 52.6% were males aged 58.9$\pm$19.6 yrs and 47.4% were females aged 54.6$\pm$20.6 yrs.

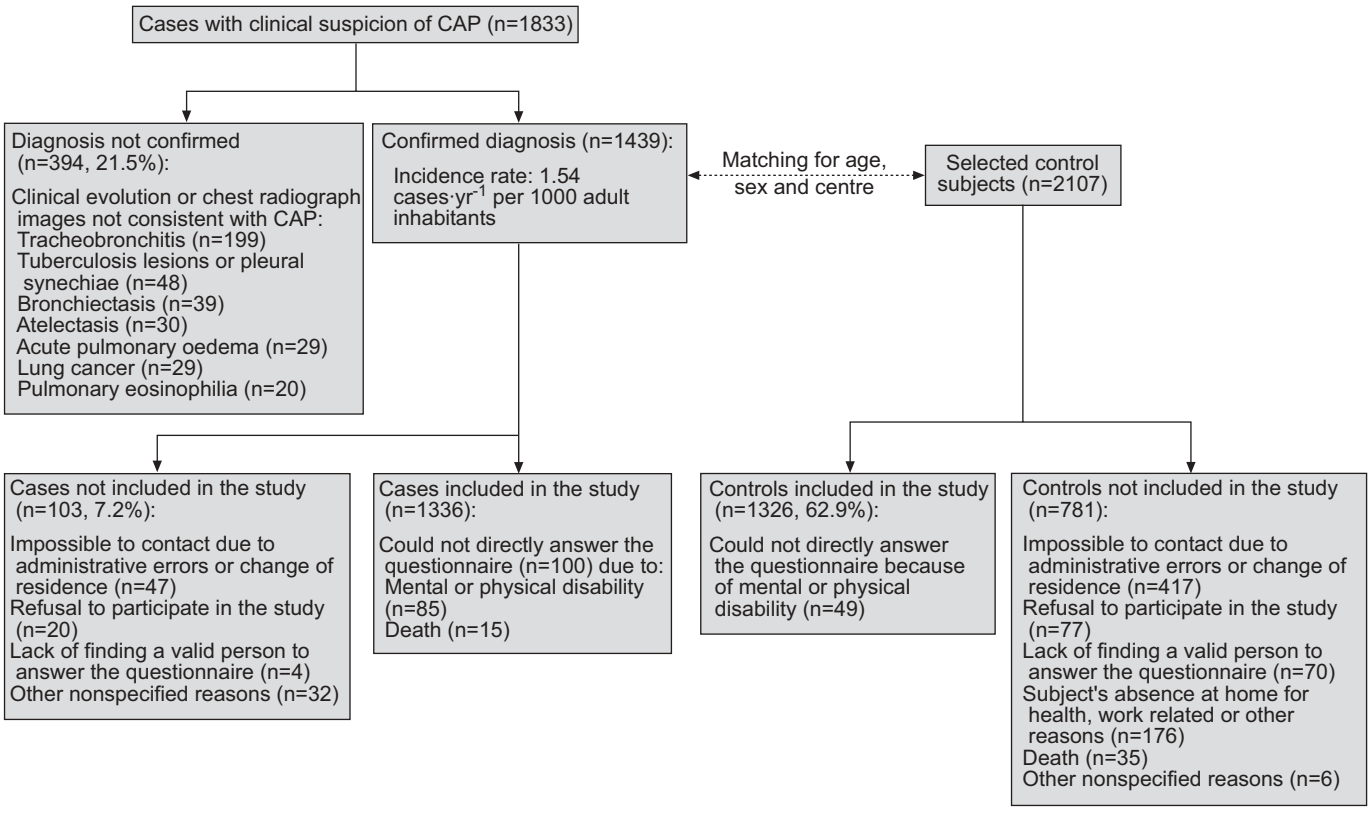

FIGURE 1. Distribution of cases and controls. CAP: community-acquired pneumonia.

Of the CAP patients, 61% were treated at home and the remainder were admitted to hospital.

Univariate results

A comparison of health habits and lifestyle factors between cases and controls is shown in table 1. Risk factors for CAP were as follows: underweight; different measures related to cigarette smoking; alcohol intake in males; contact with animals, excrements or visceras; sudden temperature changes in the workplace; living with >10 persons at home; usual contact with children; and contact with pets. Compared with never-smokers, both current smokers (OR 1.34) and ex-smokers (OR 1.37) showed a higher risk for CAP. Ex-smokers who had ceased smoking for >4 yrs showed a statistically significant reduced risk compared with ex-smokers of <1 yr (OR 0.39, 95% CI (0.17–0.89)). In the never-smokers aged >65 yrs, exposure to passive smoking was associated with a statistically significant increased risk for CAP (1.59 (1.02–2.48)). In males a statistically significant effect of the intensity of alcohol intake was observed above 40 $g \cdot day^{-1}$ (1.62 (1.10–2.39)). With regards to employment, building workers showed a higher risk for CAP (1.62 (1.15–2.28)) as did painters and carpenters (1.48 (1.10–2.0)). The greater the number of pets, the greater the risk for CAP (1.19 (1.097–1.30) for each additional animal).

Risk factors for CAP related to clinical conditions and comorbidities are shown in table 2. Previous hospital admission, previous CAP, history of upper respiratory tract infection, interventions on the upper respiratory tract (bronchoscopy, nasogastric tube), diabetes, heart disease, chronic bronchitis, asthma, nonactive pulmonary tuberculosis, epilepsy, chronic renal failure, cancer, HIV, dental dysaesthesia and dental prosthesis were risk factors for CAP. Visiting the dentist in the last month was a protective factor.

The bivariate effect of regular treatments is summarised in table 3. Treatment with digoxin, amiodarone, diuretics, *N*-acetylcysteine, xanthines, oral steroids, inhaled steroids, inhaled β-agonists and inhaled anticholinergic drugs were risk factors for CAP. Moreover, the use of inhalers was a risk factor for CAP, particularly when medication was delivered through plastic pear-spacers or when medication contained steroids. Influenza and pneumococcal vaccines were protective factors.

Multivariable results

Variables selected in the multivariable model (table 4) included cigarette smoking, sudden temperature changes at work, contact with children, civil status, previous hospitalisation, history of upper respiratory tract infection, chronic bronchitis, asthma, epilepsy, oxygen therapy and use of inhalers with or without plastic pear-spacers. Visits to the dentist in the last month had a protective effect. In the multivariable strategy designed to adjust the effect of some drug treatments or vaccines for the underlying illness (table 4), amiodarone and heart failure were statistically significant variables in the model of treatments for heart diseases, whereas *N*-acetylcysteine, inhalation therapy, oxygen therapy, chronic bronchitis and asthma were statistically significant factors in the model of treatments for respiratory diseases.

TABLE 1 Association between health habits and lifestyle factors and community-acquired pneumonia (CAP)

Variable	CAP	Controls	OR (95% CI)	p-value
Subjects n	1336	1326		
Body mass index				
Normal	769 (64.0)	780 (64.5)	1	
Underweight	115 (9.6)	53 (4.4)	2.20 (1.57–3.09)	<0.001
Overweight	214 (17.8)	245 (20.2)	0.89 (0.72–1.09)	
Obese	103 (8.6)	132 (10.9)	0.79 (0.60–1.04)	
Smoking status				
Never-smoker	548 (41.0)	643 (48.5)	1	
Ex-smoker	423 (31.7)	363 (27.4)	1.37 (1.14–1.64)	0.001
Current smoker	365 (27.3)	320 (24.1)	1.34 (1.11–1.62)	
Passive smoker[#]	143 (30.4)	140 (26.3)	1.22 (0.93–1.61)	0.155
Pack-yrs				
0	548 (43.4)	643 (51.8)	1	
1–150	354 (28.0)	358 (28.8)	1.16 (0.96–1.40)	<0.001
151–300	233 (18.4)	169 (13.6)	1.62 (1.29–2.03)	
>300	129 (10.2)	71 (5.7)	2.13 (1.56–2.91)	
Male frequency of alcohol intake				
Never	205 (31.2)	210 (31.5)	1	
Occasionally	178 (27.1)	156 (23.4)	1.17 (0.88–1.56)	0.269
Usually	274 (41.7)	300 (45.0)	0.94 (0.73–1.21)	
Female frequency of alcohol intake				
Never	353 (59.2)	365 (60.2)	1	
Occasionally	160 (26.8)	163 (26.9)	1.02 (0.78–1.32)	0.860
Usually	83 (13.9)	78 (12.9)	1.1 (0.78–1.55)	
Male alcohol intake g·day^{-1}				
0	239 (33.8)	237 (34.1)	1	
0.1–20	292 (41.3)	304 (43.7)	0.95 (0.75–1.21)	
21–40	91 (12.9)	103 (14.8)	0.88 (0.63–1.22)	
41–80	59 (8.3)	41 (5.9)	1.42 (0.92–2.21)	0.037
>80	26 (3.7)	11 (1.6)	2.34 (1.13–4.85)	
Female alcohol intake g·day^{-1}				
0	396 (63.0)	394 (34.1)	1	
0.1–20	218 (34.7)	221 (43.7)	0.98 (0.78–1.24)	
21–40	11 (1.7)	10 (14.8)	1.09 (0.46–2.61)	0.980
>40	4 (0.6)	5 (0.75)	0.80 (0.21–2.99)	
Work-related contact with				
Smoke	185 (14.2)	163 (12.7)	1.14 (0.97–1.43)	0.243
Petrol	103 (7.9)	102 (8.0)	1.00 (0.75–1.33)	0.989
Dust	257 (19.8)	219 (17.0)	1.20 (0.99–1.47)	0.068
Organic fibres	82 (6.3)	80 (6.2)	1.02 (0.74–1.40)	0.919
Inorganic fibres	87 (6.7)	70 (5.4)	1.25 (0.90–1.72)	0.182
Ionised radiation	22 (1.7)	14 (1.1)	1.56 (0.80–3.10)	0.190
Nonionised radiation	8 (0.6)	12 (0.9)	0.66 (0.27–1.62)	0.357
Animals, excrements, visceras	149 (11.5)	115 (9.0)	1.78 (1.00–3.19)	0.036
Sudden work temperature changes last 3 months[¶]	113 (8.7)	36 (2.8)	3.28 (2.24–4.82)	<0.001
>10 persons at home	35 (2.6)	16 (1.2)	2.20 (1.21–4.00)	0.009
Usual contact with children aged <15 yrs at home or work	472 (35.4)	356 (27.0)	1.48 (1.26–1.75)	<0.001
Contact with pets				
Any	673 (50.6)	565 (42.8)	1.37 (1.18–1.60)	<0.001
Birds	320 (24.0)	254 (19.2)	1.33 (1.10–1.60)	0.003
Cats	189 (14.1)	143 (10.8)	1.36 (1.08–1.72)	0.009
Dogs	380 (28.4)	314 (23.7)	1.28 (1.08–1.52)	0.005
Educational level				
Low	501 (37.7)	441 (33.4)	1	
Middle	540 (40.6)	557 (42.2)	0.86 (0.72–1.01)	0.048
High	288 (21.7)	323 (24.5)	0.78 (0.64–0.96)	
Civil status				
Married or living with partner	886 (66.7)	924 (70)	1	
Single, widowed or divorced	443 (33.3)	396 (30)	1.17 (0.99–1.37)	0.065

Data are presented as n (%), unless otherwise stated. Data are from univariate analysis. OR: odds ratio; CI: confidence interval. [#]: only never-smokers were considered, and compared with those without passive exposure to tobacco smoke. [¶]: sudden work temperature change when coming in or out of a refrigerator, furnace or kitchen.

TABLE 2 Association between clinical conditions and comorbidities and community-acquired pneumonia (CAP)

Variable	CAP	Controls	OR (95% CI)	p-value
Subjects n	1336	1326		
Hospital admission in last 5 yrs	621 (46.5)	452 (34.1)	1.68 (1.44–1.96)	<0.001
Interventions on upper respiratory tract in last year				
Nasal or pharyngeal examination	42 (3.1)	36 (2.7)	1.16 (0.74–1.83)	0.512
Bronchoscopy	27 (2.0)	13 (1.0)	2.09 (1.07–4.06)	0.027
Gastroscopy	36 (2.7)	29 (2.2)	1.24 (0.76–2.04)	0.393
Nasogastric tube	16 (1.2)	5 (0.4)	3.21 (1.17–8.77)	0.026
General anaesthesia	40 (3.0)	30 (2.3)	1.33 (0.83–2.16)	0.237
Upper respiratory tract infections				
More than one during last year	592 (44.4)	447 (33.7)	1.57 (1.35–1.84)	<0.001
Any during last month	424 (31.8)	183 (13.8)	2.91 (2.40–3.53)	<0.001
Previous CAP confirmed by radiograph during life				
None	1104 (82.6)	1219 (91.9)	1	
Any	232 (17.4)	107 (8.1)	2.39 (1.88–3.05)	<0.001
1 CAP	179 (13.4)	94 (7.1)	2.10 (1.62–2.73)	<0.001
2 CAP	36 (2.7)	10 (0.8)	3.98 (1.96–8.05)	
>2 CAP	17 (1.3)	3 (0.2)	6 .25 (1.83–21.40)	
Time since last CAP yrs				
<1	18 (6.4)	1 (0.7)	11.12 (1.46–84.40)	
1–2	40 (14.2)	11 (8.0)	2.25 (1.11–4.56)	0.001
2–3	40 (14.2)	12 (8.8)	2.06 (1.04–4.09)	
⩾3	183 (65.1)	113 (82.5)	1	
Treated diabetes mellitus	135 (10.1)	95 (7.2)	1.43 (1.11–1.92)	0.007
Heart failure	114 (8.6)	65 (4.9)	1.81 (1.33–2.49)	<0.001
Heart valve disease	59 (4.4)	35 (2.6)	1.70 (1.11–2.61)	0.014
Coronary artery disease	80 (6.0)	76 (5.7)	1.05 (0.76–1.45)	0.782
Chronic bronchitis	216 (16.2)	81 (6.1)	2.96 (2.26–3.87)	<0.001
Asthma	375 (28.1)	190 (14.3)	2.33 (1.92–2.84)	<0.001
Nonactive pulmonary tuberculosis	50 (3.8)	28 (2.1)	1.81 (1.13–2.89)	0.013
Epilepsy	17 (1.3)	6 (0.5)	2.83 (1.11–7.21)	0.029
Parkinson's disease	10 (0.79)	15 (1.1)	0.66 (0.30–1.47)	0.309
Stroke	33 (2.5)	37 (2.8)	0.88 (0.55–1.42)	0.601
Dementia	17 (1.3)	8 (0.6)	2.12 (0.91–4.94)	0.074
Psychiatric disorders excluding dementia	178 (13.3)	209 (15.8)	0.82 (0.66–1.02)	0.070
Gastro-oesophageal reflux	352 (26.4)	356 (26.8)	0.98 (0.82–1.16)	0.797
Chronic liver disease	38 (2.9)	23 (1.7)	1.67 (0.99–2.82)	0.550
Chronic renal failure	20 (1.5)	21 (1.6)	0.98 (0.51–1.75)	0.860
Cancer	106 (7.9)	76 (5.7)	1.42 (1.04–1.92)	0.025
HIV	15 (1.1)	2 (0.2)	7.49 (1.71–32.81)	0.008
Dental dysaesthesia	245 (23.3)	210 (19.7)	1.24 (1.01–1.53)	0.043
Dental prosthesis	567 (45.6)	512 (40.8)	1.22 (1.04–1.42)	0.016
Visit to dentist in last month	116 (8.7)	156 (11.8)	0.71 (0.55–0.92)	0.008

Data are presented as n (%), unless otherwise stated. Data are from univariate analysis. OR: odds ratio; CI: confidence interval.

Influenza vaccine was an independent protective variable for CAP but a statistically significant increased risk was observed in association with heart failure, chronic bronchitis, HIV infection and use of oral steroids. In relation to pneumococcal vaccine, pneumococcal vaccine was also an independent protective factor, although a statistically significant increased risk in association with heart failure, chronic bronchitis, asthma, HIV infection, oral steroids and radiation therapy or chemotherapy was found.

DISCUSSION

The present population-based study has provided an optimal framework to assess risk factors for CAP, in particular modifiable risk factors and those insufficiently proven in previous studies.

Being underweight was a risk factor for CAP, probably due to possible nutritional deficiency or associated diseases that may affect the immune system [7]. In contrast to the study of

TABLE 3 Association between treatments and vaccinations and community-acquired pneumonia (CAP)

Variable	CAP	Controls	OR (95% CI)	p-value
Subjects n	1336	1326		
Regular treatments during last year				
Acetylsalicylic acid	98 (7.3)	94 (7.1)	1.04 (0.77–1.39)	0.806
Digoxin	32 (2.4)	13 (1.0)	2.48 (1.30–4.74)	0.005
Amiodarone	24 (1.8)	6 (0.5)	4.02 (1.64–9.88)	0.001
Calcium antagonists	71 (5.3)	84 (6.3)	0.83 (0.60–1.15)	0.261
Diuretics	182 (13.6)	128 (9.7)	1.48 (1.16–1.88)	0.001
Benzodiacepines	109 (8.2)	127 (9.6)	0.94 (0.64–1.10)	0.198
Gastric acid-suppressive drugs				
Any	123 (9.2)	107 (8.1)	1.16 (0.88–1.52)	0.296
Proton pump inhibitors	44 (3.3)	32 (2.4)	1.38 (0.87–2.18)	0.173
Histamine H_2 receptor antagonists	42 (3.1)	38 (2.9)	1.10 (0.70–1.72)	0.675
Antacids	44 (3.3)	43 (3.2)	1.02 (0.66–1.56)	0.942
N-acetylcysteine	30 (2.2)	8 (0.6)	3.78 (1.73–8.29)	<0.001
Xanthines	22 (1.6)	5 (0.4)	4.42 (1.67–11.72)	0.001
Oral corticosteroids	43 (3.2)	12 (0.9)	3.64 (1.91–6.94)	<0.001
Inhaled steroids	117 (8.8)	40 (3.0)	3.09 (2.14–4.46)	0.001
Inhaled β-agonists	103 (7.7)	59 (3.9)	2.05 (1.45–2.88)	<0.001
Inhaled anticholinergic drugs	93 (7.0)	27 (2.0)	3.60 (2.33–5.56)	<0.001
Oxygen therapy	45 (3.6)	18 (1.4)	2.58 (1.49–4.49)	<0.001
Inhalers				
Without spacer device	144 (11.5)	65 (5.2)	2.39 (1.76–3.23)	<0.001
With spacer device	79 (6.3)	25 (2.0)	3.30 (2.09–5.22)	<0.001
Antibiotic treatment during last 3 months#				
Penicillins	30 (2.3)	33 (2.5)	0.90 (0.55–1.49)	0.691
Cefalosporins	15 (1.1)	6 (0.5)	2.50 (0.97–6.46)	0.051
Macrolides	22 (1.6)	11 (0.8)	2.00 (0.97–4.14)	0.057
Aminoglycosides	1 (0.1)	0 (0.0)		
Quinolones	9 (0.7)	4 (0.3)	2.24 (0.69–7.30)	0.266
Vaccinations				
Influenza in last year	469 (35.2)	477 (36.0)	0.96 (0.82–1.13)	0.650
Pneumococcal	50 (3.9)	64 (5.0)	0.78 (0.53–1.13)	0.190
Haemophilus influenzae type b, ever	4 (0.3)	1 (0.1)	4.03 (0.45–36.12)	0.217

Data are presented as n (%), unless otherwise stated. Data are from univariate analysis. OR: odds ratio; CI: confidence interval. #: cases and controls treated with antibiotics in the last 7 days were excluded from the analysis.

BAIK *et al.* [8], neither being overweight nor obese were associated with an increased risk of pneumonia. In the present study, as in others [6, 8], cigarette smoking was a risk factor for CAP. The present authors also found a statistically significant decrease in CAP risk in the second year following smoking cessation [8], which has been attributed to normalisation of immune and inflammatory function of lung tissue. Although other respiratory diseases in adults associated with exposure to environmental tobacco smoke have been reported [9], this is the first study showing a direct relationship between passive smoking and CAP in subjects aged >65 yrs.

High alcohol intake was an important risk factor for CAP [1]; in males, alcohol consumption >40 g·day^{-1} had a statistically significant effect. Alcohol consumption was not a risk factor for CAP in females, maybe due to a lower prevalence of alcohol use or higher under-reporting. Heavy alcohol use causes alterations of the immune system, increasing host susceptibility to infectious diseases especially bacterial pneumonia [10]. In other studies, however, a statistically significant effect of alcohol use has not been found, probably due to the lack of statistical power [3] or the inclusion of populations with low alcohol intake [8].

Exposure to certain environmental factors predisposes workers to occupational respiratory diseases [11]. Contact with dust in the previous month, and some interrelated jobs (builders, carpenters, painters), were more frequent in cases than in controls, but in the multivariable analysis sudden changes of temperature in the workplace was the only independent environmental factor for CAP. It has been shown that inhalation of cold air causes cooling of the nasal epithelium, and that this reduction in nasal temperature is sufficient to inhibit respiratory defences against infection, such as muco-ciliary clearance and the phagocytic activity of leukocytes [12].

TABLE 4 Risk factors for community-acquired pneumonia (CAP)

Variables[#]	OR (95% CI)	p-value[¶]
Smoking pack-yrs		0.006
0	1	
⩽150	1.01 (0.81–1.26)	
>150	1.46 (1.14–1.86)	
Sudden temperature changes at work last 3 months	2.64 (1.67–4.15)	<0.001
Usual contact with children aged <15 yrs at home or work	1.48 (1.20–1.82)	<0.001
Civil status		0.021
Married or living with partner	1	
Single, widowed or divorced	1.28 (1.04–1.59)	
Hospital admission in last 5 yrs	1.39 (1.14–1.70)	0.001
Upper respiratory tract infections in last month	2.28 (1.81–2.89)	<0.001
Number of previous CAP confirmed by chest radiography	1.48 (1.17–1.87)	0.001
Chronic bronchitis	1.81 (1.19–2.75)	0.006
Asthma	1.67 (1.28–2.19)	<0.001
Epilepsy	5.95 (1.62–21.74)	0.007
Visit to dentist in last month	0.69 (0.50–0.95)	0.022
Oxygen therapy in last year	2.42 (1.16–5.05)	0.018
Use of inhalers with or without plastic pear-spacers	1.57 (1.04–2.38)	0.031
Treatment for heart failure[+]		
Amiodarone	3.27 (1.31–8.13)	0.011
Heart failure	1.68 (1.22–2.32)	0.001
Treatment for respiratory diseases[§]		
N-acetylcysteine	2.59 (1.15–5.83)	0.021
Use of inhalers with or without plastic pear-spacers	1.44 (1.02–2.04)	0.038
Oxygen therapy	2.08 (1.16–3.73)	0.014
Asthma	1.85 (1.49–2.29)	<0.001
Chronic bronchitis	1.84 (1.32–2.59)	<0.001
Influenza vaccine[f]		
Heart failure	1.48 (1.05–2.07)	0.024
Chronic bronchitis	3.14 (2.55–4.18)	<0.001
Asthma	2.05 (1.64–2.56)	<0.001
HIV infection	7.96 (1.81–35.1)	0.006
Oral steroids	2.22 (1.12–4.37)	0.022
Influenza vaccine	0.81 (0.68–0.96)	0.014
Pneumococcal vaccine[##]		
Heart failure	1.43 (1.01–2.03)	0.046
Chronic bronchitis	3.16 (2.36–4.24)	<0.001
Asthma	2.20 (1.75–2.77)	<0.001
HIV infection	8.99 (1.98–40.8)	0.004
Oral steroids	2.20 (1.07–4.50)	0.031
Radiation therapy or chemotherapy	2.73 (0.97–7.65)	0.05
Pneumococcal vaccine	0.54 (0.36–0.81)	0.003

Data are from multivariate analysis. OR: odds ratio; CI: confidence interval. [#]: variables with p<0.10 detailed in tables 1, 2 and 3 were included; [¶]: the Wald Chi-squared test was used; [+]: variables included in the model: digoxin, amiodarone, diuretics and heart failure; [§]: variables included in the model: *N*-acetylcysteine, oral steroids, use of inhalers with or without plastic pear-spacers, xanthines, oxygen therapy, asthma and chronic bronchitis; [f]: variables included in the model: heart failure, chronic bronchitis, asthma, diabetes, renal failure, chronic liver disease, HIV infection, oral steroids, radiation therapy or chemotherapy and influenza vaccine; [##]: variables included in the model: heart failure, chronic bronchitis, asthma, diabetes, renal failure, chronic liver disease, HIV infection, oral steroids, radiation therapy or chemotherapy and pneumococcal vaccine.

Living with >10 persons at home was associated with an increased risk for CAP. Contact with children was an independent risk factor in the multivariable analysis. Other studies have shown a higher incidence of CAP in adults with preschool children in the family, probably due to a higher carriage rate of *Streptococcus pneumoniae* [13]. Contact with pets was also associated with an increased risk for CAP, which tended to be higher as the number of pets increased. This effect has only been previously observed in cases of psittacosis or zoonotic pulmonary infections [14]. In relation to civil status,

being single, widowed or divorced was independently associated with a higher risk for CAP than being married or living with a partner but the reasons for this finding are unknown.

Previous admission to hospital was associated with CAP independently of the patient's comorbidity and other risk factors. This finding has been corroborated in other studies [15]. Insertion of a nasogastric tube and the performance of a bronchoscopy can also be risk factors for CAP. A nasogastric tube favours bacterial growth and does not prevent oropharyngeal aspiration, and bronchoscopy may facilitate passage of oropharyngeal organisms to the bronchial tree [16]. A very high risk of CAP associated with upper respiratory tract infections was observed [17], either presented in the previous month or repeated in the last year. Previous infection by respiratory viruses has long been regarded as a risk factor causing predisposition to pneumonia. A previous diagnosis of pneumonia, confirmed by radiographical findings, is also an independent risk factor for subsequent CAP. The risk increases with the number of previous CAP and recentness of infection. According to previous studies, an increased risk of CAP is maintained for at least 2 yrs following diagnosis [18].

With regard to underlying chronic diseases, patients with treated diabetes, heart disease, and nonactive pulmonary tuberculosis showed an increased risk. Heart failure and treatment with amiodarone were risk factors for CAP in the multivariable analysis. Treatment with amiodarone is associated with pulmonary toxicity, which may favour bacterial superinfection [19]. Chronic bronchitis and asthma showed a strong relationship with CAP, which was independent of the remaining clinical factors and drug therapy.

In relation to regular treatments, *N*-acetylcysteine appeared as a statistically significant risk factor for CAP. In other studies, treatment with *N*-acetylcysteine was not effective for the prevention of acute exacerbations in patients with chronic obstructive pulmonary disease (COPD) [20]. Oxygen therapy in the last year was selected as an independent risk factor in the multivariable analysis. Oxygen therapy may cause nasal and oropharyngeal dryness with difficulties in swallowing and favouring aspiration [21].

The use of oral and especially inhaled steroids was associated with CAP in the bivariate analysis. Other studies have shown an increased risk of pneumonia in patients treated with oral steroids [22] but evidence of the impact of inhaled steroids has not been previously documented, except as an unexpected finding in the Towards a Revolution in COPD Health (TORCH) study [23]. The use of inhalers was also an independent risk factor for CAP. Poor hygienic measures and contamination of inhalers, particularly of plastic pear-spacers, is a recognised mechanism of infection [24]. In addition, deep inhalation from pressurised aerosols may favour penetration of organisms from the oropharyngeal cavity to the bronchial tree. One of the most striking findings of the present study is that the risk of acquiring CAP was increased in patients using inhalers, especially with a chamber-spacer. When different medications were investigated, patients using inhaled steroids showed a higher risk compared with β-adrenergics and anticholinergics. These results fit well with the information provided by the TORCH study [23], in which patients treated with inhaled steroids (plus β-adrenergics) presented with a statistically significant higher risk of pneumonia when compared with those only treated with β-adrenergics. The present results highlight a predisposition to acquire pneumonia when using long-term inhaled steroids. Further research is definitely needed in this field.

A visit to a dentist in the last month was an independent protective factor for CAP. This finding may be related to better oral hygiene. Several studies provide evidence that the oral cavity may influence the initiation and/or progression of respiratory infections [25]. In contrast, symptoms of dental dysaesthesia suggestive of dental caries and the use of dental prosthesis were associated with CAP in the bivariate analysis. In other studies, dental caries and periodontal disease were also associated with a higher probability of aspiration pneumonia by aspiration of contaminated saliva [12]. Other factors facilitating aspiration and organisms reaching the lower respiratory tract are gastric acid-suppressive drugs. In a recent study, the use of proton pump inhibitors, especially when recently initiated, was associated with an increased risk of CAP [26]. However, the present authors did not find a relationship between acid-suppressive therapy and CAP. Although bronchial aspiration was an exclusion criterion, it cannot be ruled out that some cases of silent undiagnosed aspiration as a cause of pneumonia could have been included. This may be the reason for the finding of epilepsy as a risk factor for CAP in the multivariable analysis. Conversely, dementia did not reach statistical significance, probably due to the lack of statistical power.

The effectiveness of the influenza vaccine in preventing CAP found in previous observational studies [27] was also confirmed by the present data. Regarding the pneumococcal vaccine, it should be noted that after adjusting for risk factors, which in turn were the reason for vaccination, the pneumococcal vaccine accounted for a 46% reduction in the risk of CAP. This finding is consistent with a previous study [28], although in another study the effect of pneumococcal vaccine in preventing CAP was not observed [29].

Finally, it has been suggested that inappropriate antibiotic treatment could be a risk factor for CAP, especially pneumonia caused by *Legionella pneumophila* or *Chlamydia pneumoniae* [30]. In some patients who are smokers or who have chronic bronchitis, the use of antibiotics in the previous 3 months may determine a selection of respiratory flora, causing predisposition to opportunistic infection with colonisation of more aggressive organisms, which could be causative pathogens of CAP. The present study seems to support this hypothesis for cephalosporins and macrolides, a group of antimicrobials that is frequently used more indiscriminately.

The present results should be interpreted and take into account the influence of possible confounding factors and the presence of correlation between some of the analysed factors.

The current study provides useful clinical information to establish preventive interventions for community-acquired pneumonia in adults especially directed towards modifiable risk factors. Not only new risk factors, such as passive smoking, usual contact with young children, contact with pets or use of inhalers, have been identified, but also the statistically significant effect of other controversial factors in the literature, including pneumococcal vaccine, alcohol consumption and

oxygen therapy, has been recognised. Timely medical care and preventive strategies directed towards the general population or those patients at risk are relevant measures for reducing the incidence of community-acquired pneumonia.

APPENDIX: ITEMS INCLUDED IN THE QUESTIONNAIRE

Identification and sociodemographic data

Identification number

Birth date

Sex

City

Date of the interview

Reason for not responding

Person who answered the questionnaire

Medical history

Hospital admission in the previous 5 yrs, number of admissions, date of the last admission

Diagnostic studies in the previous year: nose, pharynx, bronchoscopy, gastroscopy, nasogastric tube, general anaesthesia

Upper respiratory tract infection in the previous year, number of episodes, purulent tonsillitis

Upper respiratory tract infection in the previous month, number of episodes, purulent tonsillitis

Any previously radiographically confirmed pneumonia

Pathologic conditions

Diabetes, any diagnosis and treatment

Heart failure, any diagnosis

Valve heart disease, any diagnosis

Coronary heart disease, any diagnosis

Chronic bronchitis, any diagnosis; type of chronic obstructive pulmonary disease according to spirometry

Asthma, any diagnosis

Other chronic respiratory diseases (emphysema, bronchiectasis, *etc*.)

Nonactive pulmonary tuberculosis, any diagnosis

Epilepsy, any diagnosis

Parkinson's disease, any diagnosis

Debilitating neuromuscular disorder (amyotrophic lateral sclerosis, multiple sclerosis, *etc*.), any diagnosis

Conditions involving the cranial nerves, any diagnosis

Dementia or Alzheimer's disease, any diagnosis

Stroke, any diagnosis

Gastro-oesophageal reflux, any diagnosis; hiatal hernia, peptic ulcer

Chronic liver disease, any diagnosis

Hepatitis B or C virus infection, any diagnosis

Chronic renal failure, any diagnosis

Mental disorder or depression, any diagnosis

Tonsillectomy or adenoidectomy, any surgical removal

Cancer, type, any diagnosis, treatments in the previous year

HIV infection

Drug treatment

Regular treatments in the previous year: *N*-acetylcysteine, digoxin, amiodarone, diuretics, aminophylline, benzodiazepines, oxygen, inhalers with holding chamber (type and active drug), inhalers without holding chamber (type and active drug), antimicrobials (active compound)

Anthropometric and present conditions

Height and weight

Visit to the dentist in the previous month

Abscess

Edentulous

Caries

Dental prosthesis

Vaccinations

Influenzae in the previous year

Antipneumoccocal, year of administration

Toxic habits

History of tobacco use, to calculate pack-yrs

Passive smoking at work or home

Frequency of consumption of alcoholic beverages

Registration of consumption of alcoholic beverages, to calculate daily ingestion of pure alcohol (g)

Lifestyle and working conditions

Civil status

Living with >10 persons at home

Living or working with children aged <15 yrs

Pets, number and classes

Education level

Occupation (job)

Work-related contact with smoke, vapours, petrol or hydrocarbons, dust, organic fibres, inorganic fibres, ionised radiation, nonionised radiation, animals, excrements or visceras

Sudden changes of temperature in the work place in the previous 3 months

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