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IR-C, MC-L, JP-S and FM-T contributed equally.

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## Correspondence to

Dr Federico Martinón-Torres; federico.martinon.torres@ sergas.es

# Lifestyle and comorbid conditions as risk factors for community-acquired pneumonia in outpatient adults (NEUMO-ES-RISK project) 

Irene Rivero-Calle, ${ }^{1,2}$ Miriam Cebey-López, ${ }^{2}$ Jacobo Pardo-Seco, ${ }^{2}$ José Yuste, ${ }^{3}$ Esther Redondo, ${ }^{4}$ Diego A Vargas, ${ }^{5}$ Enrique Mascarós, ${ }^{6}$ Jose Luis Díaz-Maroto, ${ }^{7}$ Manuel Linares-Rufo, ${ }^{8}$ Isabel Jimeno, ${ }^{9}$ Angel Gil, ${ }^{10}$ Jesus Molina, ${ }^{11}$ Daniel Ocaña, ${ }^{12}$ Federico Martinón-Torres, ${ }^{1,2}$ on behalf of NEUMOEXPERTOS group


#### Abstract

Introduction Information about community-acquired pneumonia (CAP) risk in primary care is limited. We assess different lifestyle and comorbid conditions as risk factors (RF) for CAP in adults in primary care. Methods A retrospective-observational-controlled study was designed. Adult CAP cases diagnosed at primary care in Spain between 2009 and 2013 were retrieved using the National Surveillance System of Primary Care Data (BiFAP). Age-matched and sex-matched controls were selected by incidence density sampling (ratio 2:1). Associations are presented as percentages and OR. Binomial regression models were constructed to avoid bias effects. Results 51139 patients and 102372 controls were compared. Mean age (SD) was 61.4 (19.9) years. RF more significantly linked to CAP were: HIV (OR [ $95 \%$ CI]: 5.21 [4.35 to 6.27]), chronic obstructive pulmonary disease (COPD) ( 2.97 [2.84 to 3.12]), asthma (2.16 [2.07,2.26]), smoking ( 1.96 [1.91 to 2.02]) and poor dental hygiene (1.45 [1.41 to 1.49]). Average prevalence of any RF was 82.2\% in cases and 69.2\% in controls (2.05 [2.00 to 2.10]). CAP rate increased with the accumulation of $R F$ and age: risk associated with 1 RF was 1.42 ( 1.37 to 1.47) in 18-60-year-old individuals vs 1.57 ( 1.49 to 1.66) in $>60$ years of age, with 2RF 1.88 ( 1.80 to 1.97) vs 2.35 ( 2.23 , $2.48)$ and with $\geq 3$ RF $3.11(2.95,3.30)$ vs 4.34 ( 4.13 to 4.57).

Discussion Prevalence of RF in adult CAP in primary care is high. Main RFs associated are HIV, COPD, asthma, smoking and poor dental hygiene. Our risk stacking results could help clinicians identify patients at higher risk of pneumonia.


## INTRODUCTION

Community-acquired pneumonia (CAP) remains a common cause of morbidity and mortality in adults and one of the main public health problems due to its medical and economic burden. ${ }^{1}$ CAP leads to high rates of hospitalisation, particularly in the elderly, and it constitutes one of the principal causes of death globally. ${ }^{2}$

## Key messages

- Information about community-acquired pneumonia (CAP) risk in primary care is scarce despite recognising and managing risk factors (RF) for CAP could be the way to prevent the disease and reduce complications.
- Prevalence of RF in adult CAP in primary care is high and increases with age, mainly associated to HIV, chronic obstructive pulmonary disease, asthma, smoking and poor dental hygiene.
- This is the largest population-based case-control study designed to describe the association of different lifestyle and chronic medical conditions as RF in patients that were diagnosed with the first episode of CAP as adults in a primary care setting and our risk stacking results could help clinicians identify patients at higher risk of pneumonia.

Recognising and managing risk factors (RF) for CAP could be the way to prevent the disease and reduce complications, especially since mortality from CAP has not improved during the last decades despite the best clinical standards available. ${ }^{3}$

Several lifestyle factors and comorbidities have been described as potential RF for pneumonia ${ }^{3-5}$ including smoking, alcohol abuse, being underweight and poor dental hygiene or comorbidities such as chronic respiratory and cardiovascular diseases, neurological diseases or immunocompromised patients.

Although data are available from coun-try-specific reports and a number of national databases, it is difficult to determine the clinical impact of CAP in European adults given that most patients are treated on an outpatient basis and a substantial proportion of studies are based on hospitalised patients; therefore, the burden of CAP may be underestimated.

This study aims to identify the association of different lifestyle and chronic medical conditions as RF in patients that were diagnosed with the first episode of CAP in a primary care setting. This information could potentially be used to guide treatment decisions in clinical practice.

## METHODS

## Study design, population and data sources

A large-scale observational, controlled and retrospective study was designed to describe the prevalence and distribution of RF and comorbidities associated to CAP in adults in primary care in Spain. Data collection was available through a Computerized Database for Pharmacoepidemiological Studies in Primary Care in BiFAP, which aggregates information provided by 2692 general practitioners and paediatricians working in the Spanish National Health Service from 9 of the 17 administrative regions of Spain and includes clinical and prescription data for around 4.8 million patients.

Eligible study participants were Spanish national healthcare users, 18 years of age or older, diagnosed with the first episode of CAP between January 2009 and December 2013, and were attended in primary care consultations by at least 1 year before index date (admission date for each case). Patients with previous diagnoses of pneumonia or nosocomial pneumonia were excluded. A comparison group was selected by frequency density sampling and matched by age, sex and date in a $2: 1$ ratio with the case cohort.

RF studied were those that had been previously described to predispose to CAP including comorbid conditions, poor functional and nutritional status, consumption of alcohol and smoking. ${ }^{6}$ In particular, lifestyle RF analysed include: smoking, poor dental hygiene, low weight, low socioeconomical status (includes homelessness, unemployment and other unspecified economical problems) and alcoholism. In terms of chronic medical conditions, we studied comorbidities such as respiratory diseases (chronic obstructive pulmonary disease [COPD] and asthma), neurological diseases (dementia, epilepsy, Parkinson's disease and multiple sclerosis), dysphagia, heart disease, depression, osteoarthritis, arthritis, chronic renal disease, diabetes and hepatitis. Additionally, we studied morbidities where patients are immune-suppressed (HIV, Guillain-Barré syndrome).

Comorbidities in the BiFAP database are codified according to the Spanish version of the International Classification of Diseases, 9th Revision, Clinical Modification (Modificación Clínica Clasificación Internacional de Enfermedades; CIE-9-MC) and/or the Spanish version of the International Classification of Primary Care (CIAP-2/ICPC-2 PLUS).

## Ethics approval and consent to participate

The information contained in BiFAP is completely anonymous and includes no data that could identify patients, doctors or centres, ensuring full confidentiality. The

Data Protection Agency considers that BiFAP meets the requirements of Law 14/2007 (adopted on July 3) on Biomedical Research regarding the protection of personal data and privacy. The Galician Research Ethics Committee granted permission for the study (Registration number 2014/623).

## Statistical analysis

Data were presented as percentages and ORs. Binomial regression models were constructed for each risk variable, including sex and age, to avoid bias effects. A multiple binomial regression model was considered for those variables that surpassed the Bonferroni threshold of significance, and these were also selected with Akaike's information criterion. $\chi^{2}$ test was used to study the possible association between the case-control status and the number of RF. Significance level was set to 0.05 . The software R V.3.4.2 was employed to analyse the data, using the package stats.

## RESULTS

A total of 4830132 patients were included in the study cohort, of whom 51186 , with a median age of 60 years (IQR: 42-76) had a first episode of CAP during the study period and met inclusion criteria. A total of 102 372 subjects were included in the age-matched and sex-matched comparison control group.

## Lifestyle factors and risk of cap

The potential association between lifestyle factors and the risk of CAP is summarised in tables 1 and 2.

Smoking was associated with an increased risk of CAP. This risk is increased in smokers (current or past smokers) (OR [95\% CI]: 1.96 [1.91 to 2.02]) and passive smokers (OR [95\% CI]: 1.69 [1.64 to 1.74]) (table 3). In patients with higher alcohol consumption or with a history of alcohol abuse/alcoholism, the risk of CAP was increased (OR [95\% CI]: 1.60 [1.49 to 1.72]). Being underweight (OR [95\% CI]: 2.086 [1.899 to 2.292]), having poor dental hygiene (OR [95\% CI]: 1.45 [1.41 to 1.49]) and suffering a social disadvantaged situation (OR [ $95 \% \mathrm{CI}$ ]: 2.49 [1.97 to 3.17]) were also found to be RF for developing CAP (table 1A and B).

## Chronic medical conditions and risk of CAP

All chronic medical conditions studied increased the risk of suffering from CAP (tables 1 and 2). Those with HIV ( $\mathrm{n}=418,0.8 \%$ of the cohort) had the highest risk of CAP (OR [95\% CI]: 5.21 [4.35 to 6.27]), followed by COPD (OR [95\% CI]: 2.97 [2.84 to 3.12]) and asthma (OR [95\% CI]: 2.16 [ 2.07 to 2.26]). Other comorbid clinical conditions with increased risk for CAP were depression, with OR ( $95 \% \mathrm{CI}$ ): 1.47 ( 1.42 to 1.52 ) and diabetes (OR [95\% CI]: 1.37 [1.32 to 1.42]).

Table 1 Prevalence of cases and controls with diagnoses for diseases or lifestyle factors in the studied risk groups prior to the date of diagnosis of cap in cases and to the equivalent index date in controls

| Risk factors | Total cohort (\%) (frequency) | Controls (\%) (frequency) | Cases (\%) (frequency) |
| :---: | :---: | :---: | :---: |
| Comorbid conditions |  |  |  |
| Arthritis | 0.8 (1207/153 417) | 0.6 (662/102 278) | 1.1 (545/51 139) |
| Osteoarthritis | 7.6 (11 716/153 415) | 7.3 (7502/102 278) | 8.2 (4214/51 137) |
| Hepatitis | 2.6 (4030/153 415) | 2.1 (2140/102 278) | 3.7 (1890/51 137) |
| Cardiopathy | 9.1 (14005/153 416) | 7.4 (7583/102 278) | 12.6 (6422/51 138) |
| Stroke | 3.6 (5463/153 417) | 2.9 (2920/102 278) | 5 (2543/51139) |
| Depression | 13.5 (20 685/153 416) | 12 (12289/102 278) | 16.4 (8396/51 138) |
| Diabetes | 13.4 (20 550/153 416) | 12.3 (12543/102 278) | 15.7 (8007/51 138) |
| Anaemia | 10.3 (15 754/153 417) | 8.7 (8906/102 278) | 13.4 (6848/51 139) |
| Chronic renal disease | 2.8 (4279/153 414) | 2.2 (2209/102 277) | 4 (2070/51 137) |
| Dysphagia | 0.8 (1205/153 415) | 0.6 (581/102 278) | $1.2(624 / 51$ 137) |
| Multiple sclerosis | 0.1 (192/153 415) | 0.1 (101/102 278) | 0.2 (91/51 137) |
| Epilepsy | 1.4 (2115/153 415) | 1.1 (1106/102 278) | 2 (1009/51 137) |
| Parkinson | 1.3 (1938/153 415) | 1 (1061/102 278) | 1.7 (877/51 137) |
| Dementia | 3.8 (5880/153 416) | 3.1 (3159/102 278) | 5.3 (2721/51 138) |
| COPD | 6.8 (10 453/153 415) | 4.5 (4647/102 278) | 11.4 (5806/51 137) |
| Asthma | 5.8 (8944/153 417) | 4.4 (4468/102 278) | 8.8\% (4476/51 139) |
| Guillain-Barré | 0 (37/153 415) | 0 (17/102 278) | 0 (20/51 137) |
| HIV | 0.4 (584/153 414) | 0.2 (166/102 277) | 0.8 (418/51 137) |
| Lifestyle factors |  |  |  |
| Alcoholism | 2.3 (3571/153 417) | 2 (2008/102 278) | 3.1 (1563/51 139) |
| Tobacco |  |  |  |
| Passive smoker | 26.8 (38 889/145 059) | 25.9 (24296/93 920) | 28.5 (14593/51 139) |
| Smoker/ex-smoker | 21.4 (31 054/145 059) | 18.1 (16976/93 920) | 27.5 (14078/51 139) |
| Poor dental hygiene | 18.4 (28 262/153 416) | 16.5 (16896/102 278) | 22.2 (11366/51 138) |
| Low weight | 1.1 (1763/153 414) | 0.8 (867/102 277) | 1.8 (896/51 137) |
| Low social status | 0.2 (285/153 414) | 0.1 (128/102 277) | 0.3 (157/51 137) |

COPD, chronic obstructive pulmonary disease.

Risk factors associated to CAP: distribution according to age and gender
The average prevalence of comorbidities was $82.2 \%$ in cases and $69.2 \%$ in controls (OR [95\% CI]: 2.05 [2.00 to 2.10]). For patients $18-60$ years of age, the risk (OR ( $95 \%$ CI)) associated with 1 RF was 1.42 ( 1.37 to 1.47 ), with 2 RF it was 1.88 ( $95 \%$ CI 1.80 to 1.97 ) and with $\geq 3 \mathrm{RF}$ it was 3.11 (2.95 to 3.30). The OR for people $>60$ years of age is higher than for the 18-60 years age group: with 1 RF, the OR was 1.57 ( 1.49 to 1.66 ), with 2 RF it was 2.35 (2.23 to 2.48 ) and with $\geq 3$ RF it was 4.34 (4.13, 4.57) (figures 1 and 2, tables 1 and 2). Regarding sex, the distribution of cases and controls in the number of lifestyle factors are similar for males and females (tables 3 and 4).

Major RF differences between cases and controls, stratified by sex, were: HIV (5.00 [3.61 to 7.03]), COPD (2.81 [2.57 to 3.07] and asthma (2.25 [2.13 to 2.38]) for female, and HIV (5.11 [4.13 to 6.35]), multiple sclerosis (3.28 [2.01 to 5.47]) and low social status (2.78 [1.93 to 4.03]) for males (figure 3, table 3). Regarding age, the main RF
associated with CAP were: in 18-60 years: HIV (5.53 [4.58 to 6.71]), COPD (3.72 [3.29 to 4.22]) and dementia (3.39 [2.1 to 5.57]); in $>60$ years, low social status (2.8 [1.96 to 4.05]), smoking (smoker/ex-smoker) (2.29 [2.19 to 2.38]) and diysfagia (2.25 [1.97 to 2.57]) (figures 2 and 3, table 3).

## DISCUSSION

This is the largest population-based case-control study designed to describe the association of different lifestyle and chronic medical conditions as RF in patients that were diagnosed with the first episode of CAP as adults in a primary care setting. Overall, the study has shown that there are comorbidities and lifestyle factors which increase the risk of developing CAP, and that controlling these RF could be the best way to decrease the prevalence of CAP.

## Age and sex importance in CAP

Previous studies ${ }^{3}{ }^{5-8}$ have shown that the incidence of CAP in Europe varies by country, age and sex, but the real

Table 2 Prevalence of comorbid conditions or lifestyle factors prior to the date of diagnosis of CAP in cases, expressed as OR (95\% CI)

| Risk factors | Simple regression* OR ( $95 \% \mathrm{Cl}$ ) | P value | Multiple regression* OR (95\% CI) | P value |
| :---: | :---: | :---: | :---: | :---: |
| Comorbid conditions |  |  |  |  |
| Arthritis | 1.68 (1.49 to 1.90) | $2.96 \times 10^{-17} \dagger$ | 1.55 (1.37 to 1.75) | $1.29 \times 10^{-12}$ |
| Osteoarthritis | 1.14 (1.09 to 1.19) | $3.82 \times 10^{-09} \dagger$ | 1.04 (0.99 to 1.08) | $1.19 \times 10^{-01}$ |
| Hepatitis | 1.83 (1.71 to 1.96) | $1.59 \times 10^{-72} \dagger$ | 1.47 (1.37 to 1.57) | $7.64 \times 10^{-29}$ |
| Cardiopathy | 1.89 (1.81 to 1.97) | $2.11 \times 10^{-200} \dagger$ | 1.60 (1.54 to 1.67) | $6.84 \times 10^{-114}$ |
| Stroke | 1.84 (1.73 to 1.96) | $6.01 \times 10^{-81} \dagger$ | 1.55 (1.46 to 1.65) | $2.01 \times 10^{-44}$ |
| Depression | 1.47 (1.42 to 1.52) | $7.01 \times 10^{-121} \dagger$ | 1.21 (1.18 to 1.25) | $6.51 \times 10^{-32}$ |
| Diabetes | 1.37 (1.32 to 1.42) | $5.19 \times 10^{-73} \dagger$ | 1.14 (1.10 to 1.18) | $1.69 \times 10^{-14}$ |
| Anaemia | 1.63 (1.57 to 1.69) | $2.19 \times 10^{-151} \dagger$ | 1.42 (1.37 to 1.47) | $1.17 \times 10^{-79}$ |
| Chronic renal disease | 1.99 (1.86 to 2.14) | $6.12 \times 10^{-81} \dagger$ | 1.54 (1.44 to 1.66) | $3.63 \times 10^{-34}$ |
| Dysphagia | 2.21 (1.96 to 2.50) | $6.34 \times 10^{-37} \dagger$ | 1.76 (1.56 to 1.99) | $2.86 \times 10^{-19}$ |
| Multiple sclerosis | 1.82 (1.36 to 2.42) | $4.51 \times 10^{-05} \dagger$ | 1.76 (1.31 to 2.35) | $1.56 \times 10^{-04}$ |
| Epilepsy | 1.86 (1.70 to 2.04) | $1.06 \times 10^{-40} \dagger$ | 1.59 (1.45 to 1.74) | $1.04 \times 10^{-22}$ |
| Parkinson | 1.69 (1.52 to 1.87) | $4.53 \times 10^{-23} \dagger$ | 1.55 (1.40 to 1.72) | $2.41 \times 10^{-17}$ |
| Dementia | 1.86 (1.75 to 1.98) | $4.11 \times 10^{-86} \dagger$ | 1.92 (1.81 to 2.04) | $2.76 \times 10^{-100}$ |
| COPD | 2.97 (2.84 to 3.12) | $0 \dagger$ | 2.48 (2.37 to 2.60) | 0 |
| Asthma | 2.16 (2.07 to 2.26) | $1.18 \times 10^{-252} \dagger$ | 1.87 (1.79 to 1.96) | $1.48 \times 10^{-162}$ |
| Guillain-Barré | 3.09 (1.47 to 6.80) | $3.54 \times 10^{-03}$ |  |  |
| HIV | 5.21 (4.35 to 6.27) | $1.11 \times 10^{-70} \dagger$ | 4.67 (3.89 to 5.64) | $1.99 \times 10^{-59}$ |
| Lifestyle factors |  |  |  |  |
| Alcoholism | 1.60 (1.49 to 1.72) | $2.16 \times 10^{-39} \dagger$ |  |  |
| Tobacco |  |  |  |  |
| Passive smoker | 1.33 (1.30 to 1.37) | $2.06 \times 10^{-93} \dagger$ | 1.26 (1.23 to 1.30) | $1.20 \times 10^{-63}$ |
| Smoker/ex-smoker | 1.96 (1.91 to 2.02) | $0 \dagger$ | 1.69 (1.64 to 1.74) | $2.60 \times 10^{-283}$ |
| Poor dental hygiene | 1.45 (1.41 to 1.49) | $1.20 \times 10^{-151} \dagger$ | 1.27 (1.23 to 1.31) | $5.28 \times 10^{-62}$ |
| Low weight | 2.02 (1.84 to 2.23) | $3.39 \times 10^{-45} \dagger$ | 1.67 (1.51 to 1.84) | $2.71 \times 10^{-24}$ |
| Low social status | 2.49 (1.97 to 3.17) | $4.91 \times 10^{-14} \dagger$ | 1.64 (1.28 to 2.11) | $9.09 \times 10^{-05}$ |

*Including age and sex as covariables. $\dagger P$ values surpassing Bonferroni correction. COPD, chronic obstructive pulmonary disease.
clinical burden of disease, and information on the distribution of the RF relevant for CAP, remained scarce. Our study shows how the incidence increased sharply with age and was appreciably higher in men than in women, in agreement with the literature. ${ }^{3-69}$ Furthermore and considering the projected $20 \%$ increase in people aged $\geq 65$ years in developed regions of the world by 2025, ${ }^{10}$ the burden of CAP will increase in years to come.

## Identifying 'at risk' patients

In addition to positively diagnosing and identifying current cases of CAP, there is a need to identify those people in the community who may be at increased risk of infection. Our study shows that host as well as environmental factors other than age influence the risk of CAP, and many conditions may increase susceptibility.

Nevertheless, comorbidities are more common among the elderly. Consequently, the clinical outcome of pneumonia in elderly individuals with multiple comorbidities can be significantly worse. In addition, a critical consideration to bear in mind in assessing the RF for an individual patient is that multiple underlying conditions have a cumulative effect, with the risk for a person with two conditions being similar to someone officially classified as 'high risk', and for those with three or more conditions being much greater. ${ }^{11}$ Therefore, it is imperative that we make preventive interventions.

## Chronic conditions associated with CAP

CAP represents a heavy disease burden in particular groups, with higher infection and case fatality rates seen in high-risk and immunocompromised patients. ${ }^{12}$ Patients with HIV have particularly highly increased

Table 3 Distribution of cases and controls by sex and age, according to the number of risk lifestyle factors associated

Number of RF

|  | 0 RF | 1 RF | 2 RF | 3 RF | 4 RF | $\begin{aligned} & 5 \\ & \text { RF } \end{aligned}$ | $\begin{aligned} & 6 \\ & \text { RF } \end{aligned}$ | $\begin{aligned} & >6 \\ & \text { RF } \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Control cohort | 30.8 | 33.2 | 20.5 | 9.7 | 3.9 | 1.4 | 0.4 | 0.2 |
| 18-60 | 40.6 | 36 | 16.4 | 5.3 | 1.3 | 0.3 | 0.1 | 0 |
| >60 | 21 | 30.4 | 24.6 | 14.1 | 6.4 | 2.4 | 0.8 | 0.3 |
| Female | 28.8 | 33.5 | 21.5 | 10.2 | 4.1 | 1.4 | 0.4 | 0.1 |
| Male | 32.7 | 32.9 | 19.5 | 9.2 | 3.6 | 1.4 | 0.4 | 0.2 |
| Case cohort | 17.8 | 27.4 | 23.4 | 15.7 | 8.9 | 4.2 | 1.7 | 0.9 |
| 18-60 | 28.1 | 35.4 | 21.4 | 9.8 | 3.7 | 1 | 0.4 | 0.2 |
| >60 | 9.1 | 20.7 | 25.1 | 20.6 | 13.4 | 6.9 | 2.8 | 1.5 |
| Female | 17 | 28.5 | 24.2 | 15.6 | 8.4 | 3.8 | 1.6 | 0.8 |
| Male | 18.5 | 26.4 | 22.6 | 15.8 | 9.5 | 4.5 | 1.8 | 0.9 |

The results are expressed in \%.
RF, risk factors.
risk of CAP; we found a fivefold increase in risk, which is higher than reported in other studies. ${ }^{9}$ Furthermore, the magnitude of this risk exceeds that observed for the other risk groups in our study. The availability of new drugs for HIV, namely highly active antiretroviral therapy (HAART), has been associated with a reduction of both morbidity and mortality in HIV-infected patients. ${ }^{13}$ However, as we could observe in our study, patients with HIV-infection still represent a high-risk group for developing CAP and a focus on further preventive measures should be analysed.

log ODDS RATIO
Figure 1 Coefficients for the risk factors studied. Sex and age were covariables included in both analysis as confounder variables.

As previously described, the risk of CAP may be increased in patients with swallowing problems with aspiration or the use of sedative medications. ${ }^{314}$ We found that patients with neurological disorders (dementia, epilepsy, Parkinson's disease and multiple sclerosis) had an increased risk of CAP between 1.69 and 1.86 compared with controls. Specifically, when we studied dysphagia as a RF alone, a substantially increased risk was associated with CAP (OR: 2.21).

Other common underlying medical conditions with an increased risk of CAP are COPD and asthma. ${ }^{3}$ These conditions have been found to increase the risk of CAP many times over-particularly in patients with COPD, with increases of between 1.3 and 13.5 for CAP. ${ }^{1114-18} \mathrm{We}$ found an OR of 2.97 for COPD and of 2.16 for asthma, linked to the first episode of CAP.

Preexisting chronic cardiovascular conditions have been previously described to increase the risk of CAP up to three times. ${ }^{3}$ We found this condition to be present in more than half of the elderly patients and with a 1.89 association with the first episode of CAP.

## Lifestyle contribution to CAP

In addition to the comorbidities, we also studied lifestyle factors that could increase the risk of CAP. Lifestyle factors such as smoking, high alcohol intake, being underweight, social disadvantaged situation or poor dental hygiene were previously associated with an increased risk of CAP, ${ }^{351819}$ which is consistent with our findings. Many of these factors, such as being underweight, are linked to nutritional deficiencies and influence the efficiency of the immune system. ${ }^{5} 1819$

Lifestyle choices such as being a current or past smoker or frequent alcohol user also confer a significantly increased risk in all adult age groups. ${ }^{311}$ Even a passive exposure to tobacco smoke can increase a person's risk of developing CAP. ${ }^{18}$ We also found that passive smoking was a RF. In this regard, patients should be advised on the risks and offered smoking cessation programmes.

These lifestyle RF are frequently associated or converge in the same population, therefore it is often difficult to determine the specific weight each one of them has in the development of CAP. To clarify this situation, we applied a multiple regression in our study; this showed that each RF, when studied alone, appears to show a higher risk of CAP. The only exception we found was regarding alcohol intake, probably due to a wide variation in the spectrum from acute alcohol intoxication to chronic alcoholism.

## Strengths and limitations

One of the strengths of this study is the database used—BiFAP—one of the largest primary care databases available. The study population and setting, that is, outpatients and primary care, respectively, constitute the main setting for diagnosis, treatment and burden of CAP-and this is precisely the context where fewer studies had been carried out to establish RF for CAP.


Figure 2 Distribution of different risk factors and comorbidities, stratified by age, in cases and controls.

Thus, this research establishes the true baseline risk for pneumonia acquired in the community if specific preventive strategies are to be implemented.

One potential limitation of the study is the wide variation included in some of the RF studied, such as alcohol intake, the lack of information available for some relevant RF (eg, use of immunosuppressive therapy, oral
steroids and treatment with proton pump inhibitors or H 2 antagonists) or the missing values that may exist for some variables such as smoking. Researchers cannot control exposure or outcome assessment, and instead must rely on others for accurate recordkeeping. Furthermore, despite the wide geographical distribution of the clinical network, the BiFAP database

Table 4 Lifestyles factors stratified by age and sex, expressed as OR ( $95 \% \mathrm{Cl}$ )

|  | Female | Male | 18-60 years | >60 years |
| :---: | :---: | :---: | :---: | :---: |
| Stroke | 1.76 (1.62 to 1.92) | 1.80 (1.67 to 1.93) | 2.12 (1.71 to 2.62) | 1.79 (1.69 to 1.89) |
| Alcoholism | 1.37 (1.15 to 1.64) | 1.62 (1.51 to 1.74) | 1.70 (1.54 to 1.88) | 1.47 (1.34 to 1.61) |
| Anaemia | 1.50 (1.44 to 1.56) | 1.88 (1.78 to 1.99) | 1.31 (1.24 to 1.39) | 1.83 (1.76 to 1.91) |
| Arthritis | 1.66 (1.44 to 1.92) | 1.64 (1.35 to 1.98) | 1.54 (1.22 to 1.93) | 1.70 (1.49 to 1.93) |
| Asthma | 2.25 (2.13 to 2.38) | 1.90 (1.78 to 2.04) | 2.03 (1.91 to 2.16) | 2.17 (2.04 to 2.30) |
| Cardiopathy | 1.89 (1.78 to 2.00) | 1.75 (1.67 to 1.83) | 1.72 (1.51 to 1.95) | 1.88 (1.81 to 1.96) |
| Dementia | 1.61 (1.50 to 1.72) | 2.00 (1.85 to 2.17) | 3.39 (2.10 to 5.57) | 1.78 (1.69 to 1.88) |
| Poor dental hygiene | 1.40 (1.35 to 1.46) | 1.48 (1.43 to 1.54) | 1.48 (1.43 to 1.54) | 1.41 (1.36 to 1.46) |
| Depression | 1.45 (1.40 to 1.51) | 1.45 (1.38 to 1.53) | 1.46 (1.39 to 1.53) | 1.43 (1.38 to 1.49) |
| Diabetes | 1.30 (1.24 to 1.36) | 1.35 (1.30 to 1.41) | 1.45 (1.34 to 1.56) | 1.34 (1.29 to 1.38) |
| Dysphagia | 2.03 (1.73 to 2.39) | 2.29 (1.96 to 2.68) | 1.96 (1.58 to 2.43) | 2.25 (1.97 to 2.57) |
| Multiple sclerosis | 1.32 (0.92 to 1.88) | 3.28 (2.01 to 5.47) | 1.72 (1.23 to 2.38) | 2.08 (1.19 to 3.67) |
| Epilepsy | 1.82 (1.60 to 2.08) | 1.85 (1.66 to 2.08) | 2.16 (1.88 to 2.48) | 1.66 (1.48 to 1.85) |
| COPD | 2.81 (2.57 to 3.07) | 2.75 (2.63 to 2.88) | 3.72 (3.29 to 4.22) | 2.71 (2.59 to 2.83) |
| Guillain-Barré | 3.00 (0.86 to 11.74) | 2.15 (1.01 to 4.64) | 5.33 (1.54 to 24.36) | 1.71 (0.78 to 3.71) |
| Hepatitis | 1.82 (1.64 to 2.01) | 1.78 (1.64 to 1.93) | 2.00 (1.80 to 2.21) | 1.69 (1.56 to 1.83) |
| Osteoarthritis | 1.14 (1.08 to 1.20) | 1.13 (1.06 to 1.20) | 1.14 (1.00 to 1.30) | 1.14 (1.09 to 1.19) |
| Parkinson | 1.54 (1.34 to 1.76) | 1.77 (1.57 to 1.99) | 0.92 (0.45 to 1.79) | 1.69 (1.54 to 1.86) |
| Low weight | 2.04 (1.83 to 2.28) | 2.22 (1.86 to 2.65) | 2.04 (1.80 to 2.32) | 2.14 (1.86 to 2.47) |
| Chronic renal disease | 2.04 (1.85 to 2.26) | 1.83 (1.70 to 1.98) | 3.37 (2.55 to 4.48) | 1.88 (1.77 to 2.00) |
| Low social status | 2.26 (1.67 to 3.06) | 2.78 (1.93 to 4.03) | 2.24 (1.65 to 3.04) | 2.80 (1.96 to 4.05) |
| HIV | 5.00 (3.61 to 7.03) | 5.11 (4.13 to 6.35) | 5.53 (4.58 to 6.71) | 2.00 (1.07 to 3.74) |
| Passive smoker | 1.43 (1.38 to 1.48) | 1.38 (1.33 to 1.44) | 1.18 (1.13 to 1.23) | 1.50 (1.45 to 1.55) |
| Smoker/ex-smoker | 1.87 (1.79 to 1.95) | 1.97 (1.90 to 2.04) | 1.73 (1.67 to 1.80) | 2.29 (2.19 to 2.38) |

COPD, chronic obstructive pulmonary disease.

## 18-60 years


$>60$ years


Female


Figure 3 Risk factors studied stratified by age and sex, and expressed as log OR.
only includes information from nine of the seventeen administrative regions of Spain. However, our cohort is very representative of Spain and correlates well with the national registries in terms of age and RF distribution, as well as to access to healthcare. Thus, we have no concerns regarding generalisability or selection bias.

## CONCLUSION

Prevalence of RF in adult CAP in primary care in Spain is high. The main RF associated with CAP are: HIV, COPD, asthma, smoking and low social status. This risk increases with age and, considering the ageing of
the population, the actual burden of adult CAP will probably increase in the short and mid term unless specific measures are taken. Ensuring that patients make appropriate lifestyle changes and the need for adequate management of chronic diseases such as asthma, diabetes or COPD are imperative to prevent unnecessary morbidity and mortality, as well as to reduce healthcare expenditure.

The present results provide robust current evidence of the importance of age, smoking, high alcohol consumption or a history of alcohol abuse, underweight, poor dental hygiene, social disadvantage
situation, HIV, COPD, asthma, depression, diabetes, multiple sclerosis, dementia and dysphagia as definitive RF for CAP in line with recent systematic reviews. ${ }^{3}$

The ability to identify 'at risk' patients in clinical practice may have a huge impact on prevention strategies. Currently, recommendations vary widely depending on whether they are based on age or risk, and how schemes are funded and implemented. Our risk stacking results could help clinicians identify patients at higher risk of pneumonia and may also provide additional recommendations for vaccination strategies against pneumonia.

## Author affiliations

${ }^{1}$ Translational Pediatrics and Infectious Diseases Section, Pediatrics Department, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, Spain
${ }^{2}$ Vaccines, Infections and Pediatrics Research Group (GENVIP), Healthcare Research Institute of Santiago de Compostela, Santiago de Compostela, Spain
${ }^{3}$ Preumococcal Unit of the Laboratory of Reference and Research in Bacterial Diseases Preventable by Vaccines, National Center of Microbiology and CIBER of Respiratory Diseases (CIBERES). Carlos III Health Institute, Madrid, Spain
${ }^{4}$ Preventive and Public Health Activities Group SEMERGEN, International Heath Center, Madrid, Spain
${ }^{5}$ Versatile Hospitalization Unit, Hospital de Alta Resolución El Toyo, Agencia Pública Sanitaria, Hospital de Poniente, Almería, Spain
${ }^{6}$ Health Department, Hospital Dr Peset, Primary Care Center Fuente de San Luís, Valencia, Spain
${ }^{7}$ Primary Care Health Center Guadalajara, Infectious Diseases Group SEMERGEN, Guadalajara, Spain
${ }^{8}$ Specialist in Primary Care and Clinical Microbiology, Infectious Diseases Group SEMERGEN, Fundación io, Madrid, Spain
${ }^{9}$ Primary Care Health Center Isla de Oza, Vaccine Responsible of SEMG, Madrid, Spain
${ }^{10}$ Preventive and Public Health, Rey Juan Carlos University, Madrid, Spain
${ }^{11}$ Primary Care, Health Care Center Francia, Fuenlabrada, Madrid, Spain
${ }^{12}$ Primary Care, Health Care Center Algeciras, Algeciras, Spain
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