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Burden of community-acquired pneumonia in Italian general practice

To the Editor:

Community-acquired pneumonia (CAP) is a major respiratory health disease with high prevalence in the general population, clinical heterogeneity and different degrees of severity. In both the USA and Europe, CAP is the most frequent cause of infection-related death. Its incidence varies from country to country and from study to study, and it is higher in very young children and elderly persons [1]. A recent UK study documented an increase of 34% in hospital admissions due to CAP over the past decade [2].

Despite the importance of its social impact, actual incidence of CAP in different settings is still under scrutiny. Thus, we aimed to explore the epidemiology of CAP in Italian general practice.

We collected data from the Health Search - CSD Patient Database (HSD), an electronic general practice database, representative of the Italian general population, which was set up in 1998 by the Italian College of General Practitioners (Florence, Italy). The HSD contains data from approximately 1.2 million inhabitants under the care of 800 general practitioners (GPs), homogenously distributed across Italy. All clinical diagnoses are coded according to the International Classification of Diseases 9th Revision (ICD-9). Drugs are coded according to the Anatomical Therapeutic and Chemical classification system. The HSD has been extensively used for pharmaco-epidemiologic research [3].

Patients recruited between January 1, 2005 and December 31, 2009 were eligible if aged $\geqslant$15 years with clinical records in the database spanning a minimum duration of 2 years and an ICD-9-based incident diagnosis of CAP. The first date of CAP diagnosis was defined as the index date.

Each calendar year patients were considered as incident if the date of diagnosis fell within that observation year, irrespective of the occurrence of CAP in previous years. The number of persons registered on participating GPs lists by June 30th of each calendar year was used as a denominator.

CAP-related hospitalisation, all-cause mortality and CAP recurrence rates were evaluated by calculating the proportion of pneumonia patients admitted to specific hospital wards (geriatrics, infectious disease, general medicine and respiratory disease), death or a new diagnosis of CAP within 60 days after the index date. Hospitalisation, recurrence and mortality rates were reported for the whole cohort and by patients' characteristics.

This population-based, nationwide study provides estimates of the burden of CAP in Italy. A total of 12 704 consecutive patients with CAP (mean age 61.0±19.6 years) were identified. Incidence remained stable during the study period, ranging from 2.93 cases (95% CI 2.92–2.94) per 1000 inhabitants in 2005 to 3.06 cases (95% CI 3.04–3.07) per 1000 inhabitants in 2009.

Only less than 10% of CAP cases were hospitalised within 60 days from the diagnosis in our study. CAP-related recurrence, hospitalisation and mortality rates increased with age (table 1).

Regarding CAP incidence, our estimates are slightly higher than those reported in adults from previous prospective studies conducted in southern Europe (1.6–1.7 per 1000 adults) [4, 5]. Such a difference might be explained by different definitions of CAP. In the study by ALMIRALL *et al.* [4], CAP diagnoses were confirmed by a pneumologist. Our estimates are significantly lower than those reported in northern European countries such as Germany (8.7 per 1000 adults) [6] and Finland (11.6 per 1000 adults) [7]. This substantial difference may be explained by the exclusion of patients aged <15 years, who accounted for a very high rate in the Finnish study, and a much lower mean temperature in northern European countries compared to Italy. The strong relationship between climate and pneumonia risk is also supported in our study by the seasonal trend, with one-third of cases occurring during winter. CAP rates were slightly higher in males than females and much higher in elderly patients. In line with previous publications, incidence of CAP increases with age, with five-to-six fold higher rates reported in patients aged >85 years compared to patients aged <50 years [4, 5, 7], due to a higher burden of chronic diseases [8]. Around 60% of CAP patients in our study were affected by comorbidities, in particular chronic obstructive pulmonary disease (COPD) and asthma (13%) and diabetes mellitus (12%).

The presence of comorbidities and advanced age seems to influence early CAP recurrence and all-cause mortality rates. Therefore, the deterioration of clinical status rather than severity of CAP itself may be a strong risk factor of CAP-related negative outcomes.

We found a much lower hospitalisation rate as compared to other prospective studies [3, 6], ranging from 22% in UK [9] to 61% in Spain [4].

In a prospective survey in the Italian general practice, a higher hospitalisation rate due to pneumonia was reported in comparison to our estimate (31.8% *versus* 7.0%) [5]. However, in that study a much lower hospitalisation rate (11.5%) was reported for GP diagnosed CAP. Similarly, VIEGI *et al.* [5] reported higher mortality rates than our study (6.0% *versus* 2.7%), but this rate was substantially lower for cases diagnosed directly by GPs (4.4%) than cases diagnosed by specialists in hospital (10.7%).

These findings suggest that we may have underestimated hospitalisation and mortality rates, as the most severe CAP cases may have been directly hospitalised from emergency departments thus bypassing general practitioners. Nevertheless, the aim of this study was to specifically evaluate the burden of CAP in a general practice setting.

Interestingly, we observed high hospitalisation rates (17%) and all-cause mortality rates (7%) in patients who were previously exposed to an anti-pneumococcal vaccine.

Patients who receive vaccinations are generally the frailest patients (*e.g.* elderly persons and those with chronic diseases, *e.g.* diabetes and COPD), thus having a high risk of hospitalisation and mortality at baseline. Moreover, most of the CAP cases occurring in these patients could have been caused by pathogens other than *Streptococcus pneumoniae*, which are not targets of usual empirical pharmacological treatments [10]. The use of proton-pump inhibitors (PPIs), which has been previously described as a CAP risk [11], in our study was associated with higher hospitalisation and mortality rates. Some authors hypothesised that PPIs could allow bacterial colonisation and overgrowth in the oropharynx, promoting infections in the most susceptible patients [11].

We also evaluated the impact of CAP in terms of healthcare service use and related costs. A significant increase of healthcare resource use was observed in the 6 months after CAP diagnosis, with overall extra costs of €170.14 per patient, mainly due to hospitalisations (€126.30). Some study limitations have to be acknowledged. CAP cases were identified in electronic medical records using specific coding algorithms, but

TABLE 1 Community-acquired pneumonia (CAP) patients' characteristics and CAP-related recurrence, hospitalisation and mortality rates within 60 days from diagnosis, stratified by patients' characteristics

	CAP patients	Recurrence		Hospitalisation		Mortality	
	N (%)	Rate %	95% CI	Rate %	95% CI	Rate %	95% CI
Total	12 704 (100)	1.52	1.31–1.73	6.95	6.51–7.39	2.66	2.38–2.94
Age years							
15–35	1562 (12.3)	1.54	0.93–2.15	2.62	1.83–3.42	0.26	0.01–0.51
36–50	2426 (19.1)	0.95	0.56–1.33	3.38	2.66–4.10	0.21	0.03–0.39
51–65	2760 (21.7)	1.30	0.88–1.73	5.62	4.76–6.47	0.83	0.49–1.17
66–75	2354 (18.5)	1.49	1.00–1.98	8.58	7.45–9.71	1.78	1.25–2.32
76–84	2445 (19.3)	1.96	1.41–2.51	10.55	9.33–11.77	5.07	4.20–5.94
⩾85	1157 (9.1)	2.33	1.46–3.20	12.53	10.62–14.44	12.10	10.22–13.98
Sex							
Males	6428 (50.6)	1.70	1.38–2.01	7.72	7.06–8.37	2.54	2.15–2.92
Females	6276 (49.4)	1.34	1.05–1.62	6.17	5.57–6.76	2.79	2.38–3.20
Trimester of diagnosis							
First	4229 (33.3)	0.92	0.63–1.21	6.08	5.36–6.80	2.39	1.93–2.85
Second	3097 (24.4)	1.94	1.45–2.42	6.59	5.71–7.46	2.55	2.00–3.11
Third	2374 (18.7)	1.81	1.27–2.35	7.83	6.75–8.92	3.20	2.49–3.91
Fourth	3004 (23.7)	1.70	1.24–2.16	7.86	6.89–8.82	2.73	2.15–3.31
Number of comorbidities							
0	5079 (40.0)	1.32	1.01–1.63	4.33	3.77–4.89	0.75	0.51–0.99
1	3949 (31.1)	1.52	1.14–1.90	6.41	5.64–7.17	2.20	1.75–2.66
2	2039 (16.1)	1.72	1.15–2.28	8.34	7.14–9.54	4.71	3.79–5.63
⩾3	1637 (12.9)	1.89	1.23–2.55	14.66	12.95–16.37	7.15	5.90–8.40
Concurrent therapies							
Corticosteroids[#]	2375 (18.7)	1.77	1.24–2.30	8.08	6.99–9.18	4.00	3.21–4.79
PPI[#]	3043 (24.0)	1.97	1.48–2.47	10.35	9.27–11.43	5.09	4.31–5.87
Influenza vaccination[¶]	4181 (32.9)	1.53	1.16–1.90	10.55	9.62–11.48	4.74	4.09–5.38
Pneumococcal vaccination[¶]	785 (6.2)	1.15	0.40–1.89	16.82	14.2–19.43	7.13	5.33–8.93

PPI: proton-pump inhibitors. [#]: 6 months prior to index date; [¶]: >1 year prior to index date.

were not manually validated; thus, we may have partly overestimated the incidence of CAP due to misclassification. However, the high proportion of CAP patients receiving a chest radiograph 2 months before or after the index date (45% and 58%, respectively) supports the reliability of the diagnoses.

Finally, as this study was conducted in an outpatient setting, we did not report all the most severe cases leading directly to hospitalisation and death, thus potentially underestimating the hospitalisation and mortality rates. Nevertheless, this study aimed to describe the burden of CAP patients, the majority of whom are under the care of a GP, rather than to provide a global picture on CAP in the Italian general population.

This study shows the high burden of CAP in Italian general practice. Elderly patients and those with several comorbidities are more frequently affected by CAP with a negative prognosis in terms of both hospitalisation and mortality. Prevention strategies in the frailest patients, as well as early diagnosis and appropriate treatments, are key factors for the reduction of the clinical and economic burden of CAP in the general practice.

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Prevention strategies in elderly patients are key factors in reducing the clinical and economic CAP burden in this setting http://ow.ly/p7NxT

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