Burden of Pneumococcal Community-Acquired Pneumonia in Adults Across Europe: A Literature Review

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Abstract

Background: The burden of community-acquired pneumonia (CAP) caused by *Streptococcus pneumoniae* (pneumococcus) among adults in Europe is poorly defined.

Methods: Structured searches of PubMed were conducted to identify the incidence of pneumococcal CAP among adults across Europe.

Results: The overall incidence rates for CAP was 68–7000 per 100,000 and the incidence in hospitalized CAP cases of all causes was 16–3581 per 100,000. In general the incidence of CAP increased consistently with age. Available data indicated higher burdens of pneumococcal CAP caused in groups with more comorbidities. Most cases of pneumococcal CAP (30% to 78%) were caused by serotypes covered by PCV13 vaccine; the incidence of PCV13-related pneumonia decreased after the introduction of childhood vaccination.

Conclusions: We observed a high burden adult pneumococcal CAP in Europe despite use of the 23-valent pneumococcal polysaccharide vaccine, particularly in elderly patients with comorbidities. CAP surveillance presented wide variations across Europe. Pneumococcal CAP has to be monitored very carefully due to the possible effect of current vaccination strategies.

Introduction

Pneumonia is an important infectious disease associated with high morbidity, mortality and health costs worldwide (1,2). In 2015, data from the Global Burden of Disease study reported that lower respiratory tract infections, including pneumonia, were the third most common cause of death globally, exceeded only by ischaemic heart disease and cerebrovascular disease (3). Community-acquired pneumonia (CAP) remains the main cause of death from infectious disease globally, and is associated with considerable impact on morbidity and mortality, especially in older groups in which studies have linked the risk of death to increasing age (1,4,5).

In general, and despite improved microbiological diagnostic technologies, the causative pathogen cannot be identified in approximately 50% of CAP cases (6,7). Nevertheless, the most frequently identified pathogen in CAP, regardless of setting, age or comorbidity, is still *Streptococcus pneumoniae* (pneumococcus) (4,6). This bacterium has more than 90 serotypes, of which some are associated with severe disease, high invasiveness, high case fatality and antimicrobial resistance. These characteristics have led to challenges in vaccine design, because their impact on preventing pneumococcal infection depends on the coverage of serotypes associated with invasive or resistant disease.

Pneumonia, especially pneumococcal CAP, causes significant morbidity and economic burden in adults (8). However, its incidence is decreasingly reported in the United States, where recent published studies have indicated that 5%–15% of pneumonia cases were caused by pneumococcus(9). The major factors influencing this decrease are the universal introduction of the conjugate pneumococcal vaccination in children and adults (10) coupled with the decreased rate of smoking (11,12). By contrast,

pneumococcus remains the most frequent CAP pathogen in Europe, accounting for 19% (range: 0%–67%) of cases in meta-analyses (6,8,13,14). The model of universal vaccination is important because adults, especially those with chronic diseases, are at increased risk of pneumococcal CAP and disproportionally affected by increased mortality and decreased quality of life (1,15).

The introduction in 1983 of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) led to an overall reduction in invasive pneumococcal disease (IPD) in most adult, excluding those with immunocompromised patients(16). Furthermore, the effectiveness of PPSV23 appears to decrease with age and time since vaccination, its use has no significant effect on *S. pneumoniae* carriage, and its efficacy against non-invasive pneumococcal CAP is contentious (17–19). The 13-valent pneumococcal conjugate vaccine (PCV13); comprising serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F, has been licensed in Europe since 2011 for adults aged ≥50 years, based on serologic noninferiority data (20). Recently, a proof-of-concept study in adults aged ≥65 years demonstrated that the PCV13 vaccine had efficacy values of 45% to 46% for confirmed vaccine-type CAP and non-bacteraemic non-invasive CAP, but a vaccine efficacy of 75% for vaccine-type IPD (not including meningitis) (21). In the United Kingdom, 8 years of vaccination with the 7-/13-valent pneumococcal conjugate vaccines (PCV7/PCV13) in children has seen a >50% overall reduction in the incidence of IPD for all ages (22). For adults, recommendations across the European Union now favour the use of PCV13 (with or without additional dose[s] of PPSV23) (23); PCV13 has recently been recommended for use alongside PPSV23 for pneumococcal disease prevention in US adults ≥65 years (24).

It is important to know the true incidence of pneumococcal CAP in Europe to inform effective management and prevention strategies. Our objective in this review was to summarise the available data regarding the incidence of pneumococcal CAP in European adults. We included cases in both non-hospitalised and hospitalised patients, as well as those caused by *S. pneumoniae*. A secondary objective was to assess the rate of pneumococcal CAP caused by serotypes covered by PCV13 vaccine.

Methods

The PubMed database was searched using the following search string: “Pneumonia” AND English AND ("Pneumococcal" OR "Community-acquired" OR "Streptococcus" OR "Community acquired" OR "CAP" OR "Hospitalised" OR "Hospitalised") AND (“Adults” OR “Adult” OR “Elderly” OR “Middle Aged” OR “Older”). Search results were restricted to clinical trials, letters, meta-analyses, observational studies and systematic reviews performed in European countries, as summarised in Table 1. We also include relevant citations that described studies conducted in Europe to obtain data about the incidence of pneumonia and/or coverage of PCV13 in individuals aged ≥18 years.

Titles and abstracts were initially screened to identify relevant citations, which were then reviewed in full by two authors. We included all publications presenting data on pneumonia, regardless of definition, and reviewed the study setting, methodology, and characteristics of the study population. The definition of pneumococcal pneumonia varied between publications, 35 studies used the World Health Organization International Classification of Diseases (ICD) codes, microbiological findings without radiographic diagnosis was used in 12 studies, and 3 used medical records only, other 3 studies did not specify the definition. Invasive pneumococcal

disease (IPD) was defined when isolation of *Streptococcus pneumoniae* from the blood or another normally sterile body site was reported. All authors confirmed the inclusion of the identified publications. Publications reporting data in only paediatric populations were excluded; as were those focusing solely on hospital- or healthcare-acquired pneumonia (the incidence of such pneumonia is highly dependent on healthcare systems and medical practices). Relevant data from all identified sources were inserted into summary tables, including the study country, the study type, the microbiology and serotyping methodologies, the definition of pneumonia, the ages of participants and the year of study.

The principal summary measure was the annual incidence of pneumonia per 100,000 populations in each of the study countries. The following annual incidences were of interest: all-cause pneumonia, pneumococcal pneumonia, non-hospitalised pneumonia, hospitalised pneumonia and hospitalised pneumococcal pneumonia. Additional summary measures were 1) the percentage of cases of pneumococcal CAP caused by serotypes covered by PCV13 vaccine and 2) the pneumococcal vaccination uptake.

Results

Studies included

We identified 2717 articles and included 73 publications covering 16 European countries after screening, (Figure 1) (5, 16, 20, 24–94). These publications are summarised in online supplementary Table S1. Of the included publications, 31 were prospective or surveillance (5,21,25,28,30,33,38,40,41,46,49,50,58,62,63,65–72,78–83) and 42 were retrospective analyses (26,27,29,31,32,34–37,39,42–45,47,48,51–57,59–61,64,73–77,84–93).

National population-based epidemiologic surveillance data for pneumonia were available from Norway (54), Portugal (58) and Spain (59,75,77). As observed by Tichopad and colleagues (29), epidemiologic data in Central and Eastern Europe were predominantly collected from hospital settings, and there was a lack of data on outpatient CAP, with the authors instead using inpatient-to-outpatient ratios from a retrospective chart review to estimate outpatient incidence in the Czech Republic, Hungary, Poland and Slovakia. Three studies specified the number of patients with prior pneumonia before the index case(31,85,90).

The countries with the most data sources were Spain (23 studies plus an additional study combining Italian and Spanish data) (5,25,28,49,59–78) and the United Kingdom (14 studies)(80–88) followed by Italy (7 plus the additional study combining Italian and Spanish data) (42–49), the Netherlands (6 studies)(21,27,50–53), Germany (26,37–40) and France (34–36,94,95) (5 studies each), Denmark (30–32) and Poland (29,55,56) (3 studies each), and Portugal (2 studies)(57,58). Single studies were identified reporting data from the Czech Republic (29), Finland (33), Greece (41), Hungary (29), Norway

(54), Slovakia (29), and Sweden (79). Data from other European countries were not found.

The definition of pneumonia varied between publications, with some authors using a combination of methods. Specifically, 25 of the 73 publications used radiographic diagnosis in all or most cases (5,20,27,29,30,32,35,36,40,45,48,49,60,64,66,67,70,71, 77,79–82,93,94), 35 used the World Health Organization International Classification of Diseases (ICD) codes (5,25–27,29,31,32,34,37,39,42,43,45,47,48,53–57,59,60,63,69,70,75–77,79,86,89–93), 12 used clinical signs and/or microbiological findings without radiographic diagnosis (35,40,51,52,62,64,66,73,74,81–83), 3 used medical records only (84,87,88), and 3 did not specify the definition (29,58,85).

Burden of Disease

Data on the incidence of pneumonia are presented in online supplementary Table S2. The incidence of all-cause pneumonia in Europe was 68–7000 per 100,000 population, but this varied by country, age group, study and time period (Table 2) (5,25,28,29,35–37,39–41,46,49,51,53,55,64,69,72,84,88,89,91,93). The lowest incidence of all-cause pneumonia was reported in Spain between 1999 and 2001 in patients aged 15–44 years (72), and the highest incidence was reported in France between 2011 and 2012 in patients aged >65 years (35).

Spain reported the highest incidence rates for pneumococcal CAP (166 per 100,000) (25) and IPD (or invasive pneumococcal CAP; 60 per 100,000)(69) in patients aged ≥60 and ≥65 years, respectively.

Data from national population based epidemiological surveillance for pneumonia were reported by Spain, Portugal and Norway. The Norway surveillance (54) reported the

incidence of pneumonia of two years (2208- 2009). They observed a relative stable incidence of all cause pneumonia, in 2008 the incidence was 5.28 cases per 100,000 and in 2009 were 5.35 cases per 100,000. However, they observed a decrease in the incidence of pneumococcal pneumonia from 13.66 cases per 100, 000 in 2008 to 10.52 cases per 100,000 in 2009. Data from Portugal surveillance (57) in the a study period between 2000 to 2009, reported that the average annual rate of hospital admissions for adults with CAP was 3.61 per 1000 total population, this rate increased in those aged ≥65 years to 13.4 per 1000 . The authors reported that between 2000-2004 and 2005-2009 the average annual rate of hospital admission for CAP per 1000 population increased by 28.2%.

Data from Spain surveillance was reported in 3 studies: The first study (77) include data from the year's 1995 y 1996. The incidence of hospitalizations for pneumonia was 162 per 100,000 population in the year 1995 and 189 cases per 100,000 population in 1996. Adults ≥ 65 years accounted for 49.5% of cases. The second study (75) covered the period 1995 to 1998. The annual incidence of pneumonia was 177 cases per 100,000 population. The incidence was higher in children <5 years of age and in adults ≥ 65 years compared with other age groups. The third study (59) covered the period 2003 to 2007. The annual hospitalisation rate for all cause pneumonia was 6.27 cases per 1000 and the incidence of pneumococcal pneumonia was 1.09 cases per 1000.

The highest incidence of non-hospitalised CAP (3575 per 100,000) was reported in Hungary in patients aged ≥65 years (29). The incidence of hospitalisation due to CAP was 16 to 3581 per 100,000 population and varied by country, age group, study, and time period (Table 2) (26,29,31,33,34,42,44,49,53,54,56,57,59,67,70,75,79,80,92,93).

The lowest incidence of hospitalised CAP was reported in the United Kingdom between 2008 and 2010 in patients aged 16 to 24 years (80), and the highest incidence was reported in Germany in 2005 to 2006 in patients aged ≥90 years (26) (Table 2).

For hospitalised pneumococcal CAP, the highest incidence (421 per 100,000 population) was reported in Spain in patients aged ≥85 years (96) (Table 2). Data on hospitalised IPD or invasive pneumococcal CAP were only available from Spain, however, with the incidence ranging from 7 per 100,000 population in patients of all ages (74) to 45 per 100,000 population in patients aged >64 years (70) (Table 2).

The incidence rates for all-cause pneumonia, pneumococcal CAP, non-hospitalised CAP, hospitalised CAP and hospitalised pneumococcal CAP all increased with age (Supplemental Table S2) (5,26–29,31,34–36,39,40,44,46,51,53–57,60,64,67,70–72,74–77,80,88,89,91–93,96).

We observed temporal trends between countries. An increase in the incidence of pneumonia over time was observed in the Netherlands (53) and there was a decrease over time in Poland (55). An increase incidence in hospitalised pneumococcal CAP was reported in Spain over time (73). Similarly, there were increases in the incidence of IPD over time in France(36) and the United Kingdom(91), though there was a decrease in pneumococcal CAP in the Netherlands(51). Increases in the incidence rates of hospitalised CAP were also reported over time in Denmark (31), Germany (26), the Netherlands (53), Portugal (57), and the United Kingdom (91,92). However, there was only minimal or variable change in France (34) and Italy (43,47,48), and a minimal change or decrease in Norway that was dependent on age (54). There was an increase in hospitalised pneumococcal CAP in Spain (67), a minimal change in France (34), and a

225 decrease in Norway (54) and the United Kingdom (83).

226 Associations between the incidence of pneumonia and comorbidities were reported in
227 11 publications, including solid organ and allogeneic haematopoietic stem cell
228 transplantation (49,68), systemic lupus erythematosus (52), chronic medical conditions
229 that that require pneumococcal vaccination (39), HIV infection (73,94,95), pernicious
230 anaemia (85), diabetes (86,87), and chronic obstructive pulmonary disease (90) (Online
231 supplementary Table S3). Patients with chronic diseases presented the highest
232 pneumonia incidence rates, with the highest all-cause incidence reported for
233 allogeneic haematopoietic stem cell transplantation recipients in Spain (aged >14
234 years, 52,200 per 100,000) (68) and the highest hospitalised incidence reported in
235 older male patients with type 2 diabetes in the United Kingdom (aged ≥65 years, 1070
236 per 100,000) (87).

237 **Pneumococcal Serotypes Covered by the PCV13 Vaccine**

238 Data on pneumococcal infection caused by serotypes covered by PCV13 vaccine in
239 European countries are show in Online Supplementary Table S4. Twenty-three
240 publications reported data on pneumococcal serotypes and outcomes
241 (21,30,33,36,38,40,50,51,54,58,61,62,65–67,69,70,73,80–83,91), but the method for
242 serotyping varied between studies, including urinary antigen testing (3 studies)
243 (21,38,50), agglutination testing (7 studies) (30,36,61,80–83), the Quellung reaction (7
244 studies) (30,40,50,51,65,67,69), polymerase chain reaction (PCR; 3 studies)(65,66,70),
245 and the capsular reaction test (1 study) (58) (Online Supplementary Table S1).

246 Studies from Finland (33) and the United Kingdom(83) reported the highest
247 percentages of CAP caused by pneumococcal serotypes covered by the PCV13 vaccine

(78% per study). In a Spanish study of patients with cancer who developed pneumococcal bacteraemia, pneumonia was the most frequent source in 84% of cases, and 54% of cases were caused by serotypes covered by the PCV13 vaccine (65). Researchers from the United Kingdom investigated the impact of PCV13 on pneumococcal serotypes implicated in a predominantly non-bacteraemic cohort of pneumococcal CAP adults. In that study, it was reported that the incidence of pneumonia caused by serotypes included in PCV13 vaccine declined from 10.6 to 6.3 per 100,000 population over the 5-year period after the PCV13 was introduced as part of the childhood vaccination schedule, suggesting that herd protection from infant PCV13 affected the incidence of adult non-bacteraemic pneumococcal CAP (83).

Data on the efficacy of PCV13 vaccine was specifically reported in one study. A randomised, double-blind, placebo-controlled trial (the Community-Acquired Pneumonia Immunization Trial in Adults [CAPiTA]) was conducted in the Netherlands. This involved 84,496 adults aged 65 years and over during the period from 2008 to 2013, reported an efficacy of 45.5% (95.2% confidence interval [CI], 21.8–62.5; $p < 0.001$) for PCV13 against all vaccine-type pneumococcal CAP, a 45% efficacy (95.2% CI, 14.2–65.3; $p < 0.001$) against vaccine-type non-bacteraemic pneumococcal CAP and a 75% efficacy (95.2% CI, 41.4–90.8; $p < 0.001$) against vaccine-type IPD among adults aged ≥65 years (21).

Data on vaccination uptake are shown in online supplementary Table S5. However, detailed stratification for the incidence of pneumonia relative to PCV13 uptake in these studies is beyond the scope of this review. Of note, based on the limited data identified in our review, there has been large variation in the reported uptake of the

pneumococcal vaccination (45,49,60,79–83).

Discussion

This review showed a notable burden of pneumococcal CAP in European adults, particularly among the elderly. Data on comorbidities were limited, but suggested a high incidence of pneumonia in patients with chronic diseases. Older patients are especially vulnerable to pneumonia because of both age-related changes in the immune system and a greater prevalence of chronic diseases. For this reason, it is difficult to determine the precise cause of increased risk in these patients. However, the disproportionate burden of pneumococcal disease in older patients should remind us that the incidence of pneumonia and risk of death remain linked to increasing age (4,5,28,34). These data support the importance of adequate prevention against pneumococcal CAP, especially in the elderly population.

The incidence of adult all-cause CAP decreased in the United Kingdom (where infant PCV uptake is >90%) from 91 to 65 cases per 100,000 between 2008 and 2012 (83) after the introduction of the paediatric PCV13 vaccine. However, despite this, there remains a substantial burden of pneumococcal CAP caused by serotypes covered by PCV13 vaccine (i.e., 30%–78%) (42,43,45), even after the introduction of the PCV to infant vaccination schedules in 2005 (42,97). The level of paediatric vaccination uptake required to produce herd immunity in other age groups is currently unknown, although data from the UK and US indicate substantial reductions in IPD associated with universal childhood PCV vaccination (22,98). A study from US that evaluated the direct and indirect effects of PCV13 reported that the introduction of PCV13 substantially reduced the numbers of patients with IPD, non-invasive CAP and all-cause

CAP in both vaccinated children and unvaccinated adults. Nevertheless, because the study considered only the first 2 years after the introduction of PCV13, a period in which approximately 50% of children in the US received the vaccine, the true effect of PCV13 on pneumococcal diseases was not fully measured (99). Notably, there are a lack of data on the overall incidence and prevalence of pneumococcal CAP caused by serotypes covered by PCV13, including the incidence in patients with comorbidities.

Our review identified variability in the reporting of pneumococcal incidence across European countries, including a lack of studies from several countries, with differences in the reported methodologies used and outcomes measured. The resulting absence of comprehensive and reliable data on pneumococcal CAP is of concern. For instance, the lack of such data may lead to decisions regarding vaccination programmes being reliant on IPD data, thereby underestimating the true burden of pneumococcal disease. In the United Kingdom, for example, data from 2013 to 2014 showed that the incidence of IPD caused by PCV13 serotypes was 4.3 per 100,000 in patients aged ≥65 years (22), and that in the same period, the incidence rates for hospitalised adults were 20.6 per 100,000 for those with pneumococcal CAP (including non- invasive disease) and 8.6 per 100,000 for those with pneumococcal CAP caused by PCV13 serotypes (100). Underestimation of non-bacteraemic pneumococcal CAP may also result from a lack of appropriate diagnostic tools. If 10% to 20% of patients with pneumococcal CAP have bacteraemia, preventing 5% of all cases may have more of an impact than preventing 75% of patients with IPD.

In this review, the reported incidence of pneumonia varied widely between countries and across regions within countries, with socioeconomic effects likely to be

317 contributory (88). Only Norway (54) Portugal (57) and Spain (59, 75,77) reported data
318 from population based studies. The differences in the incidence and CAP and PCAP
319 between these countries are difficult to interpret and might be due to differences in
320 the populations studied. In addition some factors that contribute to these differences
321 include the impact of lifestyle factors such as smoking, high alcohol intake, being
322 underweight, living in a large household or having regular contact with children (101).
323 Also, the national immunization practices that in some regions widespread the use of
324 pneumococcal polysaccharide vaccine in adults and the use of conjugate
325 pneumococcal vaccine in children could influence the reported incidence of
326 pneumococcal CAP(102). Similarly, the use of influenza vaccination in adults could
327 influence variations in the incidence of pneumonia(103). Also, much of the variation is
328 likely to have been due to differences in medical systems and practices, rather than
329 differences in underlying epidemiology. Indeed, research highlights the difficulties in
330 estimating the incidence of pneumonia in the community. In Germany, for example,
331 four estimation approaches yielded different annual incidence rates for pneumonia in
332 adults, ranging from 370 to 1230 per 100,000 inhabitants in an urban area(37). In that
333 study, the incidence based on cases reported in general practice was thought to give
334 an underestimate because of underreporting and inaccurate estimation of the
335 population size (lack of patient registration in medical practices). In addition, the
336 incidence of hospitalised CAP depends on the structure of the primary and secondary
337 healthcare systems (60). Countries with uniformly organised healthcare systems (e.g.,
338 Denmark) are able to collect data for hospitalisation (31), which facilitates the
339 development of population-based designs. Furthermore, although every attempt was
340 made to exclude studies from our review that included patients with hospital-acquired

pneumonia, we cannot exclude the possibility that at least some of the cohorts included patients who did not have CAP.

Classification schemes varied between the publications included in our review. Many studies used ICD-9 or -10 codes, which offer different coding for pneumococcal pneumonia. ICD-9 codes for pneumococcal pneumonia have been associated with low sensitivity (104), and consequently, the hospitalised pneumonia incidence may have been underestimated. However, the ICD-10 coding for pneumonia does not necessarily imply microbiological confirmation (54). Accuracy depends on initial coding, and studies have demonstrated the potential for inaccuracies in administrative data (105,106).

A wide range of microbiological methods were used to diagnose pneumococcal CAP and identify serotypes in the studies in this review. These methods included standard culture and PCR-based methods for bacterial identification, as well as agglutination techniques and the Quellung reaction for serotyping. More recently, urinary antigen tests have become available, which facilitate identification of pneumococcal infections and may increase the accuracy in determining the burden of pneumococcal CAP.

In conclusion, this review of the incidence of pneumococcal CAP in European adults highlights the considerable variation in the types of studies and methodologies used between and within European countries, including the lack of surveillance programmes. Nevertheless, the available data demonstrate the significant burden of pneumococcal CAP, especially in the elderly. Given that pneumococcal CAP in the elderly increases the risk of mortality three-fold compared with non-pneumococcal CAP, underestimating the incidence of pneumococcal disease could have a major impact on healthcare outcomes. Pneumococcal CAP has to be monitored very carefully due to the possible effect of current vaccination strategies.

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Table 1. Search Terms and Limits

Search terms: “Pneumonia” AND ("Pneumococcal" OR "Community-acquired" OR "Streptococcus" OR "Community acquired" OR "CAP" OR "Hospitalized" OR "Hospitalised") AND (“Adults” OR “Adult” OR “Elderly” OR “Middle Aged” OR “Older”) AND (“Albania” OR “Andorra” OR “Armenia” OR “Austria” OR “Azerbaijan” OR “Belarus” OR “Belgium” OR “Bosnia and Herzegovina” OR “Bulgaria” OR “Croatia” OR “Cyprus” OR “Czech Republic” OR “Denmark” OR “England” OR “Estonia” OR “Europe” OR “European Union” OR “Finland” OR “France” OR “Georgia” OR “Germany” OR “Great Britain” OR “Greece” OR “Hungary” OR “Iceland” OR “Ireland” OR “Italy” OR “Kazakhstan” OR “Kosovo” OR “Latvia” OR “Liechtenstein” OR “Lithuania” OR “Luxembourg” OR “Macedonia” OR “Malta” OR “Moldova” OR “Monaco” OR “Montenegro” OR “Netherlands” OR “Northern Ireland” OR “Norway” OR “Poland” OR “Portugal” OR “Romania” OR “Russia” OR “San Marino” OR “Scotland” OR “Serbia” OR “Slovakia” OR “Slovenia” OR “Spain” OR “Sweden” OR “Switzerland” OR “Turkey” OR “Ukraine” OR “United Kingdom” OR “UK” OR “Vatican City” OR “Wales”)

748 **Search limits:** Humans; Published from 1 January 2000 to 31 October 2016

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Table 2. Incidence of pneumonia in European countries per 100,000 per year

Country	Non-hospitalized	Hospitalized	Pneumococcal CAP	All cause pneumonia
CZ: Czech Republic	≥ 50 years: 300 ≥65 years: 370	≥ 50 years: 472 ≥65 years: 833	-	-
DK: Denmark	-	15-39 years: 2800 ≥80 years: 2003	-	≥65 years: 1270
DE: Germany	-	≥60 years: 765	≥65 years: 16.2 (IPD)	18-49 years:441 50-59 years: 684 ≥60 years:1439
FR: France	Adults: 400	-	Adults: 7.4 (IPD) Adults: 17.41	-
FI: Finland	-	-	≥65 years: 95	≥65 years : 550
GR: Greece	-	-	-	≥ 50 years: 274

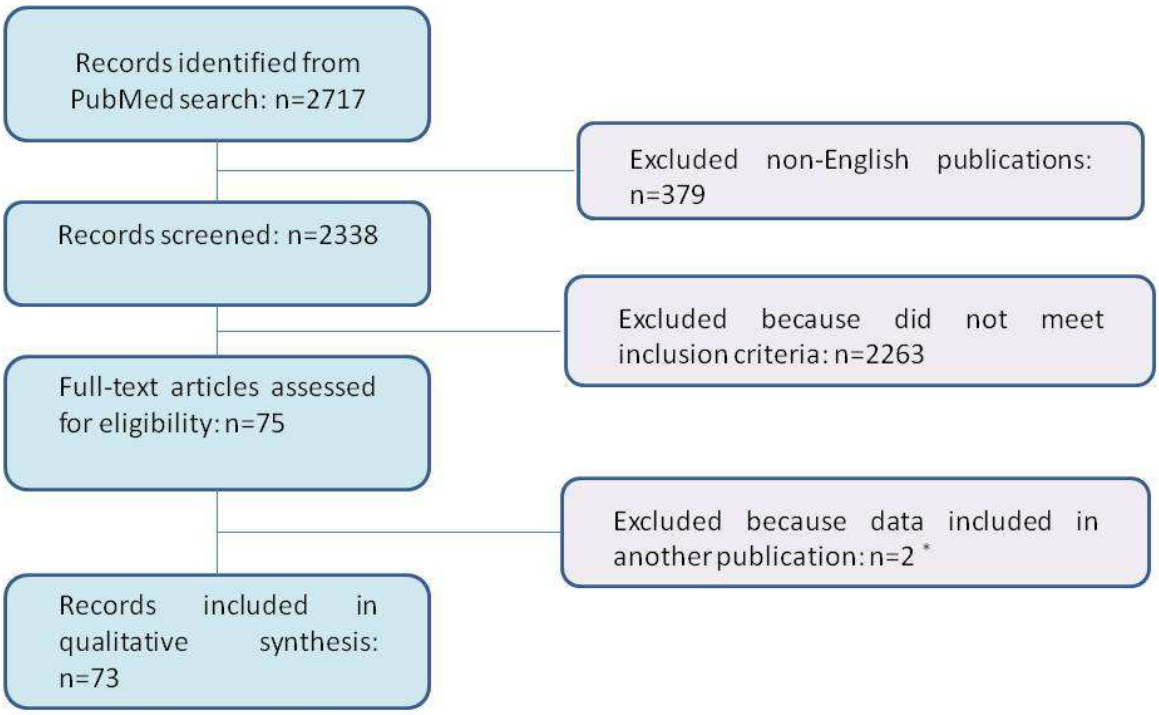
HU: Hungary	≥ 50 years: 3.346 ≥65 years: 3.575	≥ 50 years: 832 ≥65 years: 1.414	-	-
IT: Italy	-	-	13.4	Adults: 320.1
NL: Netherlands	Adults: 109	Adults: 176	≥65 years: 47.11 (2004-2006) ≥65 years: 36.66 (2008-2012)	Adults: 295 ≥65 years: 881
NO: Norway	-	Adults: 531	Adults: 12.09	-
SK: Slovakia	≥ 50 years: 587 ≥65 years: 771	≥ 50 years: 518 ≥65 years: 938	-	-
PL: Poland	≥ 50 years: 316 ≥65 years: 442	≥ 50 years: 366 ≥65 years: 706	-	-
PT: Portugal	-	Adults: 361	-	-

		≥65 years: 1340		
SE: Sweden	-	65-79 years: 107.6 ≥80 years: 510.6	-	-
ES: Spain	2002-2005 Adults: 350	1995- 1996 ≥65 years: 523 1995-1998 ≥80 years: 998 1999- 2001 Adults: 123 ≥75 years: 526 2002-2005 Adults: 1050 2003 – 2007 Adults: 627	1999- 2001 Adults: 20.7 ≥75 years: 10.0 2009 Adults >64 years: 44.7 (IPD) 2003 – 2007 Adults: 109	2002-2005 Adults:140 65-74 years: 99 ≥85 years:294

GB: United Kingdom	-	Adults: 79.9	Adults: 23.4 Adults IPD: 14.1 16-44 years: 12.1 ≥85 years: 274.1	Adults: 799

Note: values ate the mean reported in the identified publications for each respective country. Does not include patients with comorbidities or the combined study from Italy and Spain [48], and values are irrespective of sex. Refer to Supplemental Table S1 and Suplemental Table S2 for additional details regarding each publication. IPD: invasive pneumococcal disease.

Figure 1. Summary of the study selection procedure.



*Reported identical pneumonia incidence data

Highlights

- The data available demonstrate the significant burden of pneumococcal CAP in European adults, especially in the elderly.
- Pneumococcal CAP in the elderly increases the risk of mortality three-fold compared with non-pneumococcal CAP.
- Pneumococcal CAP has to be monitored very carefully, due to the possible effects of current vaccination strategies.