Hospitalization costs for community-acquired pneumonia in Dutch elderly: an observational study

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Abstract

Background: Community-acquired pneumonia (CAP) is one of the most common infections, especially in the elderly (≥65 years). The aim of this study was to quantify hospitalization costs for CAP in different age groups and in patients with different CAP risk profiles. Secondary objectives were to assess disease severity differences between placebo and vaccine receiving participants and identify cost driving factors of CAP in hospitalized elderly in the Netherlands.

Methods: This prospective cohort study of hospitalized CAP patients was executed in parallel to the Community Acquired Pneumonia Immunization Trial in Adults (CAPiTA). Within the CAPiTA, a cohort of 84,496 subjects aged ≥65, all suspected CAP-episodes presenting in one of the 58 participating hospitals between September 2008 and August 2013 were included. CAP was diagnosed on clinical and radiographical criteria. Invasive pneumococcal disease (IPD) and non-IPD-CAP episodes, regardless of the causing pathogen, were evaluated separately. Costs were calculated by multiplying recorded healthcare resources with Dutch unit cost prices for the year 2012. Multivariate regression analysis was performed to identify cost drivers.

Results: In the sentinel hospitals 3225 suspected CAP and IPD episodes were included, of which 1933 were radiographically confirmed by chest X-ray. Analyses were conducted on confirmed CAP episodes only. Overall mean length of hospital stay was 12.1 days, the in-hospital mortality rate was 11.26 %, and mean costs were €8301 (95 % CI: €7760–€8999). When stratified in age-categories 65–74, 75–84 and ≥85, mean hospitalization costs were €8674, €8770 and €6197, respectively (p = 0.649). IPD-CAP and non-IPD-CAP mean hospitalization costs were €13,611 and €8081, respectively. Higher CURB-65 score and individuals at medium risk for developing pneumococcal disease were significantly associated with higher costs. Being male, lower age, previous admissions, lower risk, lower urbanity and higher socio-economic status were associated with lower costs.

Conclusions: Mean hospitalization costs of a CAP subject were €8301 and higher for IPD-CAP compared to non-IPD-CAP cases. Medium risk patients and higher CURB-65 scores were identified as cost driving factors.

Keywords: Community-acquired pneumonia, Costing study, Elderly, Hospitalization, Invasive pneumococcal disease, Risk-groups

Abbreviations: CAP, Community-acquired pneumonia; Etio-CAP, Etiology and prognosis of community-acquired pneumonia study; GP, General practice; ICD, International Classification of Diseases; ICU, Intensive care unit; IPD, Invasive pneumococcal disease; IPD-CAP, Community-acquired pneumonia; CI, Confidence interval; DBC, Diagnosis Related Groups (in Dutch: Diagnose Behandel Combinatie); CAPiTA, Community Acquired Pneumonia Immunization Trial in Adults; DPC, Diagnosis Related Groups (in Dutch: Diagnose Behandel Combinatie)
Background
Community-acquired pneumonia (CAP) is one of the most common infectious diseases in the world [1–4]. In Europe, the incidence of all-cause CAP (hospitalized and outpatient) in the elderly population (≥65 years) is estimated at 14 per 1000 person years [5, 6]. Approximately 56% (equal to €5.7 billion) of CAPs economic burden in Europe is ascribed to hospitalization expenses [7]. The other costs can be attributed to outpatient care, loss of workdays and drug expenses. Increasing CAP incidence due to growth of the elderly population in the upcoming years [8–11], more severe episodes due to increasing comorbidity within the aging population [12], and limited economic resources demand for new preventive measures [13]. In Western countries like the Netherlands, new healthcare interventions will be evaluated for their costs and effects and detailed cost estimates are indispensable in this process. However, most larger studies describing CAP costs were conducted retrospectively and based on insurance claims with limited clinical information [4, 14–19]. The few prospective studies on CAP hospitalization costs covered relative small cohorts only [20–22].

The Community Acquired Pneumonia Immunization Trial in Adults trial (CAPiTA), a nation-wide study assessing the efficacy of the 13-valent pneumococcal vaccine (PCV13) in the elderly, created a unique opportunity to analyze disease severity differences between PCV13 and placebo cohorts and to identify cost drivers in hospitalized CAP cases.

Methods
Study subjects
The etiology and prognosis of community-acquired pneumonia (Etio-CAP) study is a prospective cohort study conducted in parallel to CAPiTA [23, 24]. A parallel study was designed to estimate costs for hospitalized CAP patients, including patients with and without invasive pneumococcal disease (IPD), stratified by age- and risk-groups for developing pneumococcal infections and by outcome (i.e. mortality). Secondary objectives were to analyze disease severity differences between PCV13 and placebo cohorts and to identify cost drivers in hospitalized CAP cases.
hospital admissions 1 year prior to index CAP hospitalization episode, diagnostic and therapeutic interventions for both pneumonia and its complications, additional “waiting days” in the hospital (i.e. before home care could be organized), and location of discharge (own home or nursing home). Pneumonia severity was assessed using the Pneumonia severity index (PSI), as described by Fine et al. [25], and CURB-65 [26]. PSI score was categorized into low (score 1 and 2), medium (score 3 and 4) and high (score 5). Based on postal codes, information on socioeconomic status (continues variable from low to high, scores ranging from -5.5 to 3, with lower scores reflecting lower socio-economic status) and urbanity of neighborhood (from high to low; score 1, 2, 3, 4 and 5) was obtained from Statistics Netherlands and referred to the situation in 2010 [27].

Costs
Hospitalization costs were calculated by multiplying recorded units of healthcare resources used with corresponding unit prices (see Additional file 1: Table S2) [28]. Unit costs were either taken from the Dutch manual for healthcare costing research [28, 29] or were calculated from a unit price medium of different hospital price lists available. All costs were expressed for the year 2012, and if necessary, updated using Dutch consumer price indices [30].

Statistical Analysis
Data were analyzed using IBM SPSS Statistics for Windows, Version 20.0. The one-way ANOVA test, Mann-Whitney U-test and the Kruskal-Wallis test were used to compare quantitative variables and the Chi-square test was used for categorical variables. Intubation days at the ICU were recorded in a dichotome (yes or no) and a quantitative way (e.g. number of days of intubation). There were no missing data with the exception of number of intubated ICU days (0.6 %) and number of previous admissions (0.2 %). Missing data were imputed using multiple imputation. A stepwise multiple regression model was used to identify cost drivers with log-transformed hospitalization costs as a dependent variable. Explanatory variables were gender, age, previous admission (categorized as: none, one, two, three or more admissions), smoking status (non-smoker, previous smoker, current smoker), risk-level, socioeconomic status and urbanity, and CURB-65. The latter was used instead of PSI scoring, because of overlapping definitions between PSI and risk levels as both are estimated using comorbidity information. The 95 % confidence interval (CI) was determined using bootstrapping with 1000 iterations. A p-value of <0.05 was considered significant.

Results
Study participants
There were 3225 registered suspected CAP episodes, of which 138 were not hospitalized. Of these suspected and hospitalized CAPs 1154 cases were not confirmed as CAP (i.e. no positive chest X-rays and/or <2 clinical signs of pneumonia) and consequently excluded from the analysis (Fig. 1). Of the remaining 1933 confirmed CAP admissions, 148 were readmissions, yielding 1785 episodes for analysis. Of these, 74 had IPD-CAP and 1714 had non-IPD-CAP) (Fig. 1).

![Flowchart of the study](image)

**Fig. 1** Flowchart of the study. Legend: *Including 3 readmissions; **Including 145 readmissions. Abbreviations: CAP: community-acquired pneumonia; IPD-CAP: invasive pneumococcal disease
The majority (73%) of CAP patients were male, and the mean length of hospitalization was 12.1 days (95% CI: 2–42 days) consisting of 92% ward days and 8% ICU days (Table 1). The 30-day mortality rate of low, medium and high risk-groups was 4, 10.4 and 29.1%, respectively. Compared to non-IPD-CAP cases, IPD-CAP cases had a longer average duration of stay in hospital ($p = 0.028$) and in ICU ($p = 0.022$) (Table 1).

 Costs
The mean hospitalization cost for all CAP subjects was €8301 (Median: €4809, 95% CI: €7760–€8999) (Table 2 and Additional file 1: Table S3). General ward nursing costs accounted for 63% of total hospitalization costs and ICU nursing for 29%. When stratified by age groups 65–74, 75–84 and ≥85 years, mean hospitalization costs were €8674, €8770 and €6197, respectively ($p = 0.649$). The mean hospitalization costs per IPD-CAP case were significantly higher than for non-IPD-CAP cases (€13,611 versus €8081, $p = 0.025$).

The mean hospitalization cost for survivors and non-survivors in the total CAP cohort was €7638 and €13,526, respectively ($p = 0.30$) (Figs. 2 and 3). ICU costs of survivors were lower ($p < 0.001$) and ward costs were higher ($p < 0.001$) compared to non-survivors.

 Comparison between subjects who received PCV13 ($n = 861$) and placebo ($n = 924$) revealed no differences in LOS (12.03 versus 12.17 days, $p = 0.919$), PSI category (2.13 versus 2.09, $p = 0.368$) and mean hospitalization costs per subject.

### Table 1 Baseline characteristics of study population

|                                | Total CAP          | IPD-CAP   | non-IPD-CAP | p-value |
|--------------------------------|--------------------|-----------|-------------|---------|
| Admission*, n                   | 1785               | 71        | 1714        |         |
| Age in years, mean (SD)         | 77.4 (6.6)         | 76 (5.5)  | 77.5 (6.7)  | *       |
| Male, n (%)                     | 1307 (73.2)        | 43 (60.6) | 1264 (73.7) | *       |
| ReceivedPCV13, n (%)            | 861 (48.2)         | 24 (33.8) | 837 (48.8)  | *       |
| Risk group for developing pneumococcal disease, n (%) | | | | |
| Low                             | 248 (13.9)         | 18 (25.4) | 230 (13.4)  |         |
| Medium                          | 1207 (67.6)        | 47 (66.2) | 1160 (67.7) |         |
| High                            | 330 (18.5)         | 6 (8.5)   | 324 (18.9)  |         |
| Length of stay in days, mean (95% CI) | 12.1 (11.6–12.6)  | 15.3 (12.3–18.9) | 12.0 (11.5–12.4) | *       |
| Ward days, mean (95% CI)        | 11.1 (10.7–11.6)   | 13.0 (10.3–15.8) | 11.1 (10.6–11.5) |         |
| ICU days, mean (95% CI)         | 1.0 (0.8–1.2)      | 2.4 (0.9–4.2) | 0.9 (0.7–1.1) | *       |
| Intubation days, mean (95% CI)  | 0.4 (0.3–0.6)      | 1.1 (0.3–2.2) | 0.4 (0.3–0.6) | *       |
| Illness duration in days, mean (95% CI) | 16.9 (16.3–17.5)$^e$ | 19.8 (16.1–24.1) | 16.7 (16.1–17.4)$^e$ |         |
| Days between onset and hospital admission, mean (95% CI) | 4.9 (4.6–5.2)$^f$ | 4.3 (2.7–6.8) | 4.9 (4.6–5.3)$^f$ |         |
| Pneumococcal severity index (PSI), n (%) | | | | |
| I-II                            | 126 (7.1)          | 5 (7.0)   | 121 (7.1)   |         |
| III-IV                          | 1327 (74.3)        | 48 (67.6) | 1279 (74.6) |         |
| V                               | 332 (18.6)         | 18 (25.4) | 314 (18.3)  |         |
| In-hospital mortality, n (%)    | 201 (11.3)         | 11 (15.5) | 190 (11.1)  |         |
| 30-day mortality, n (%)         | 235 (13.2)$^a$     | 11 (15.5) | 224 (13.1)$^a$ |         |
| 60-day mortality, n (%)         | 300 (16.8)$^a$     | 12 (16.9) | 288 (16.8)$^a$ |         |
| 6-months mortality, n (%)       | 444 (24.9)$^a$     | 18 (25.4) | 426 (24.9)$^a$ |         |
| Location of discharge, n (%)    | 1584 (88.7)        | 60 (84.5) | 1524 (88.9) |         |
| Home                            | 1371 (86.6)        | 51 (85.0) | 1320 (86.6) |         |
| Nursing home                    | 160 (10.1)         | 8 (13.3)  | 152 (10)    |         |
| Others                          | 53 (3.3)           | 1 (1.7)   | 52 (3.4)    |         |

*Statistically significant difference between non-IPD-CAP and IPD-CAP

$^a$Admissions within 30 days post-discharge of a suspected CAP hospitalization episode were labeled as a readmission and analyzed as a continuation of the previous admission

$^b$Number of days from onset to hospital discharge

$^c$11 with missing data

$^d$9 with missing data

$^e$2 with missing data
Costs for a hospitalized CAP episode with IPD were €13,611, or 168 % of the mean costs for a non-IPD-CAP episode (i.e. €8081). A high clinical severity of disease at the time of hospitalization and having medium risk profile for pneumococcal disease were identified as independent drivers of high costs, whereas male gender, increasing age, previous admission(s) in the past year, low risk profile for pneumococcal CAP, lower urbanity and higher socio-economic status were associated with lower overall costs. Vaccination status was not associated with clinical severity of CAP or costs of hospitalization.

Quantification of costs associated with CAP are usually based on retrospective studies using national insurance claims databases. In a previous retrospective study in Netherlands by Spoorenberg et al. [20], median costs based on ICD recordings were estimated at €3899. In the current study median costs were €4809, and the difference could be explained by the younger cohort in the Spoorenberg et al. study (mean age 63.4 versus 77.4) potentially leading to a shorter LOS (8.5 versus 12 days) and a lower case-fatality rate (30-day mortality: 5.1 versus 13.1 %). Furthermore, in the current study, non-survivor costs were €13,526 and appeared to be 177 % of the hospitalization costs of survivors (i.e. €7638). Also, Spoorenberg et al. did not consider the additional costs of readmissions and included patients of only two general hospitals in the Netherlands, as compared to 58 hospitals, of which seven are tertiary care centers, were included in the current study. Indeed, the proportion of patients needing ICU admission was 21.2 % in tertiary care (24/113) and 12.1 % in general hospitals (202/1672).

Another nationwide ICD-based cost analysis by Rozenbaum et al. [19] reported medium costs of CAP of €6060 and €5937 in those 65–74 and 75–84 years of age, respectively, which is also lower than the medium costs for these age cohorts in the current study (€8674 and €8770, respectively). The study by Rozenbaum et al. was based on reimbursement of hospital expenses, as regulated by Diagnosis Related Groups (in Dutch: Diagnose BehandelCombinatie or DBC). By selecting solely DBCs related to pneumonia, other costs (e.g. treatment of complications) were not considered, possibly explaining the lower costs. Also readmissions were not taken into account, resulting in shorter length of stay in the 65–74 and 75–84 age cohorts (7.7 versus 12.4 and 8.1 versus 12.3, respectively). Furthermore, the use of ICD-coding in both Dutch studies [19, 20] may have caused important misclassification. In another Dutch study across seven Dutch hospitals, the sensitivity of ICD-coding was estimated at 79.5 % [31]. The current prospective study with 1933 patients with confirmed CAP based on standardized diagnostic criteria may, therefore, be more precise and generalizable than previous studies [16, 19–22].

### Discussion

Among those who participated in the CAPiTA-study, the mean costs of hospitalization for CAP were €8301.

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**Table 2** Hospitalization costs of CAP and IPD-CAP subjects stratified by age- and risk-groups in 2012 €

| Population | Age group (years) | Risk level | N | Mean | 95 % Confidence Interval Lower | Upper |
|------------|------------------|------------|---|------|------------------------------|-------|
| Total CAP  | All              |            | 1,785 | 8,301 | 7,760 | 8,999 |
|            | 65–74            | All        | 678  | 8,674 | 7,841 | 9,641 |
|            |                  | Low        | 87   | 8,418 | 5,870 | 11,696 |
|            |                  | Medium     | 445  | 9,118 | 7,921 | 10,407 |
|            |                  | High       | 146  | 7,472 | 6,163 | 9,248 |
|            | 75–84            | All        | 807  | 8,770 | 7,748 | 9,847 |
|            |                  | Low        | 73   | 10,387| 7,222 | 14,516 |
|            |                  | Medium     | 574  | 8,270 | 7,187 | 9,550 |
|            |                  | High       | 160  | 9,828 | 7,345 | 12,811 |
|            | ≥85              | All        | 300  | 6,197 | 5,677 | 6,764 |
|            |                  | Low        | 42   | 6,042 | 4,978 | 7,188 |
|            |                  | Medium     | 227  | 6,198 | 5,606 | 6,832 |
|            |                  | High       | 31   | 6,401 | 5,039 | 8,238 |
| IPD-CAP All| 65–74            | All        | 31   | 11,635| 6,996 | 17,982 |
|            |                  | Low        | 8    | 16,185| 5,336 | 34,137 |
|            |                  | Medium     | 20   | 10,615| 5,831 | 17,142 |
|            |                  | High       | 3    | 6,299 | 3,815 | 9,690 |
|            | ≥85              | All        | 34   | 16,496| 7,650 | 30,360 |
|            |                  | Low        | 6    | 18,837| 3,880 | 41,063 |
|            |                  | Medium     | 25   | 16,903| 6,182 | 35,483 |
|            |                  | High       | 3    | 8,416 | 2,946 | 21,971 |
|            | 75–84            | All        | 34   | 16,496| 7,650 | 30,360 |
|            |                  | Low        | 6    | 18,837| 3,880 | 41,063 |
|            |                  | Medium     | 25   | 16,903| 6,182 | 35,483 |
|            |                  | High       | 3    | 8,416 | 2,946 | 21,971 |
|            | ≥85              | All        | 6    | 7,478 | 3,456 | 12,416 |
|            |                  | Low        | 2    | 7,440 | 3,860 | 11,020 |
|            |                  | Medium     | 4    | 7,497 | 2,238 | 16,577 |
|            |                  | High       | 0    | -     | -     | -     |

Due to minimal differences between total CAP and non-IPD-CAP cohorts costs, the latter are presented in Additional file 1: Table S3

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Cost drivers

A high CURB-65 score and medium risk profile for pneumococcal CAP were associated with higher hospitalization cost (Table 3). Male gender, increasing age, one or more previous admissions in the past year, low risk profile for pneumococcal CAP, lower urbanity and higher socio-economic status were associated with lower costs.

Costs (€8115 versus €8475, p = 0.835). Furthermore, LOS, PSI category and costs were similar for subjects with IPD-CAP and non-IPD-CAP.

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Different settings and healthcare systems makes a comparison between countries nearly impossible at the level of cost estimates [32]. Length of Stay (LOS) has been identified as a major contributor to healthcare resource utilization. We found a mean of 12 days which is within the range of other European studies, [21, 22, 33–40], ranging from 8 up to 13.2 days.

There are also limitations of this study that need to be addressed. An exclusion criterion for the CAPITA-trial was the presence of immunodeficiency (i.e. individuals at high risk for developing pneumococcal infections), except for patients with asplenia. However, there were 330 (18.5 %) patients with CAP that had developed immune deficiencies after enrollment in the CAPITA-trial. Hospital costs might be slightly underestimated as we did not have exact information on the percentage of patients that received in-hospital rehabilitation services, or because some diagnostic or therapeutic procedures, such as incidental pleural punctures, may not have been reported. Additionally, in the current cohort 10.1 % of the survivors were discharged to a nursing home or rehabilitation center. As information on the total length of stay in nursing home or rehabilitation center was lacking, we could not add these costs to our cost estimates.

**Conclusion**

The current study showed variability in hospitalization cost between different ages, disease severities and survival status. The eldest group experienced high mortality and shorter ICU admission. Mean hospitalization
Table 3 Cost driving factors in the CAPcohort

| Multiple regression | \( \beta \) | SE | p-value |
|---------------------|----------|----|---------|
| Constant            | 9.23     | 0.06| <0.001  |
| Male                | −0.06    | 0.01| <0.001  |
| Age                 | −0.01    | 0.00| <0.001  |
| Previous admission  | −0.03    | 0.00| <0.001  |
| CURB-65             | 0.12     | 0.01| <0.001  |
| Low risk            | −0.09    | 0.02| <0.001  |
| Medium risk         | 0.03     | 0.01| 0.049   |
| Urbanity            | −0.03    | 0.00| <0.001  |
| Socioeconomic status| −0.01    | 0.00| 0.02    |

Cost for a CAP subject was €8301. Costs are significantly higher for IPD-CAP than for non-IPD-CAP cases. With an aging population and a rising life expectancy the disease and economic burden may further increase in the near future.

Additional files

Additional file 1: Table S1. Comorbidities considered at increased risk for developing pneumococcal infections; Table S2. Unit cost prices; Table S3. Hospitalization costs of non-IPD-CAP subject stratified by age- and risk-category in 2012 €.

Funding

The Eto-CAP study and the CAPiTA-trial are made possible by an unrestricted grant from Wyeth Pharmaceuticals (now Pfizer Inc.) to the University Medical Center of Utrecht (UMCU). Pfizer Inc. (the sponsor) had no role in the design, analysis, interpretation of the data, or the writing of the manuscript. Pfizer Inc. did review a penultimate version of the manuscript.

Availability of data and material

The data used in this paper were obtained from a third party and are therefore only available on request. These data from the CAPiTA-trial and from the Eto-CAP study may be requested by contacting Marie-Josée Mangen (m.j.mangen@umcutrecht.nl) or Susanne Huijts (s.m.huijts@umcutrecht.nl).

Authors’ contributions

SMH, MJMB and MJJM contributed to conception and design of the study. SMH and MJMB drafted the approved study protocol. CEV, MJJM and SMH conducted the data analysis. CEV drafted the current manuscript. GAdW, MJMB, MJJM and SMH critically revised the current manuscript. All authors read and approved the final manuscript.

Competing interests

MJMB reports receipt of research funding from Pfizer, and service on the CAPiTA European Expert Meeting. SMH’s research funding is partially supported by grants provided to UMCU (University Medical Center Utrecht) by Pfizer. MJMM’s research funding is partially supported by grants provided to UMCU by Pfizer. GAdW reports receipt of an unrestricted research grant from Pfizer. SMH, MJMB, GAdW and MJJM are employed by UMCU. CEV was a Master student doing an internship at UMCU when performing this study. The authors declare that they have no other competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the Central Committee on Research Involving Human Subjects (CCMO11.0810/TV/NL23.004) as a sub-study of the CAPiTA-trial. Therefore no separate informed consent was required for the Eto-CAP study.

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Received: 9 September 2015 Accepted: 16 August 2016
Published online: 02 September 2016

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