University of Louisville
Journal of Respiratory Infections

REVIEW ARTICLE

One-Year Mortality in Patients with Community-Acquired Pneumonia

*Paula Peyrani and Julio A. Ramirez

Abstract

Pneumonia remains a common cause of morbidity and mortality in the US. Although, communityacquired pneumonia (CAP) has traditionally been considered an acute process, more recently, data have emerged showing that patients surviving an episode of CAP are at increased risk of death long after hospital discharged. In this descriptive review, we examine the current knowledge of long-term mortality and propose a hypothesis explaining the pathogenesis of long-term mortality in patients with CAP.

DOI: 10.18297/jri/vol1/iss4/10
Received Date: July 21, 2017
Accepted Date: August 30, 2017
Website: https://ir.library.louisville.edu/jri
Affiliations:
Department of Medicine-Division of Infectious Diseases,University of Louisville, Louisville, KY

Introduction

Pneumonia remains a common cause of morbidity and mortality in the US. Published data from the Centers for Disease Control and Prevention ranks pneumonia as the first leading cause of death from infectious diseases and eight from all diseases [1]. A total of 53,282 individuals died of pneumonia in 2013 [2]. Based on the most recent report from the Agency for Healthcare Research and Quality, pneumonia was the second most common reason for hospital admissions after liveborn (newborn) in 2011 with over 1.1 million hospitalizations [3]. Another study reported 3.9 million hospitalizations due to pneumonia between 2007 and 2011 [4]. CAP has traditionally been considered an acute process that, once resolved, has no further impact on patients' survival. Studies evaluating clinical outcomes have focused on early mortality; either during hospitalization or within 30 days after the initial episode. Early mortality rates range from 4 - 30% depending on the studied population, treatment setting, and severity of disease [5–8]. Considering this short-term impact on patients' outcomes, CAP research has been traditionally focused on improving short-term outcomes such as time to clinical stability, clinical failure, length of stay, in-hospital mortality, and 30-day mortality. Different immunomodulatory strategies including corticosteroids, antiplatelets, and specific antibiotics have been considered as interventions, sometimes in a particular setting or type of patient [9–12].

More recently, data have emerged showing that patients surviving an episode of CAP are at increased risk of death long after hospital discharge [13–26]. In this descriptive review, we examine the current knowledge of long-term mortality and propose a hypothesis explaining the pathogenesis of long-term mortality in patients with CAP. A search was performed using MEDLINE/PubMed through April 2017 with the following keywords: community-acquired pneumonia, mortality, long-term, outcomes.

In an attempt to standardize the follow-up period, we only included in this review original studies that either reported mortality at 1 year or had enough data to estimate this information.

Current Literature

A total of 21 articles reporting long-term mortality data after hospitalizations for CAP were identified, with rates up to 10 or more years ranging between 17 and 50%, and up to 2-3 times higher than patients without a hospitalization for CAP [13–33]. After the initial review, we identified 15 articles reporting 1-year mortality rates. In **Table 1** we summarized studies describing 1-year mortality in patients with CAP [13–19]. In **Table 2** we summarized studies comparing 1-year mortality in patients with CAP to control groups [20–27]. Figure 1 represents the reported 1-year mortality for hospitalized patients with CAP for each study. These studies suggest that for all hospitalized patients with CAP, the 1-year mortality is approximately 30 to 35%. For hospitalized patients without CAP, the 1-year mortality is approximately 20 to 25%, whereas for those patients not hospitalized and not developing CAP the 1-year mortality was even lower, ranging between 1 and 5%. In hospitalized patients with CAP, there is a 10% increased risk for 1-year mortality in relation to hospitalized patients with other medical conditions. Follow-up periods vary among the different published studies evaluating long-term mortality. This, along with differences in the studied population, makes comparisons difficult. We believed that different exclusion criteria among the studies is the likely explanation for the wide range mortality reported in the studies.

*Correspondence To: Paula Peyrani
Work: Address: 501 East Broadway, Suite 120 Louisville, KY 40202
Work Email: popeyr01@louisville.edu

Table 1 Studies evaluating 1-year mortality after hospitalization due to CAP without a control group

Author	Study criteria	Study subjects	1-year mortality
Waterer (2004)[19]	• Prospective • Subjects: age ≥ 18 years old hospitalized with CAP (Healthcare organization hospitals - Memphis, TN) • *Pneumonia definition*: acute illness (< 14 days of symptoms) with a positive chest image plus one criterion of Group A or two of Group B: Group A ✓ Fever > 37.8°C or Hypothermia < 36°C ✓ Cough or sputum production Group B ✓ Dyspnea ✓ Pleuritic chest pain ✓ Physical findings of lung consolidation ✓ Leukocyte count > 12 x 10/L or < 4.5 x 10/L • *Exclusion criteria*: AIDS, chemotherapy in the past 60 days, treatment with immunosuppressive medication, non-ambulatory nursing home patients, hospitalization within the prior 30 days.	N= 366	Not provided Estimated by age group 18-40: 4% 41-60: 8% 61-80: 20% ≥81: 30%
El Solh (2006)[15]	• Prospective, observational • Subjects: age ≥ 65 years old hospitalized with CAP (single center - Buffalo, NY) • *Pneumonia definition*: positive chest image plus at least 2 of the following: ✓ Cough ✓ Dyspnea ✓ Chest pain ✓ Change in mental status and at least 1 of the following: ✓ Temperature ≥ 38°C or ≤ 36°C ✓ Leukocytosis (>11.0 x 10^9/L) or leukopenia (<3.5.0 x 10^9/L) and absence of evidence of a cause other than pneumonia • *Exclusion criteria*: nursing home residents, hospitalization in the prior 90 days, aspiration, severe immunosuppression (solid organ transplantation, HIV/AIDS, steroid therapy > 10 mg/d for > 2 weeks), underlying active malignancy, or do-nor resuscitate order	N= 301	10%
Johnstone (2008)[17]	• Secondary analysis of prospective (implementation of a critical pathway for the management of CAP) • Subjects: age ≥ 18 years old hospitalized with CAP (all 6 hospitals - Alberta, Canada) • *Pneumonia definition*: positive chest image plus at least 2 of the following: ✓ Temperature > 38°C ✓ Chest pain ✓ Productive cough ✓ Crackles on auscultation ✓ Shortness of breath • *Exclusion criteria*: immune deficiency (HIV, use of > 10 mg/d of prednisone or other immunosuppressive agents, active treatment for cancer, history of organ transplantation, active TB, cystic fibrosis), shock, intubation or direct ICU admission, pregnant or breastfeeding women, alcohol addiction, chronic renal failure	N= 3,284	28%
Cecere 2010[14]	• Prospective, observational • Subjects: age ≥ 18 years old hospitalized with CAP (1 hospital - Washington, SA) • *Pneumonia definition*: positive chest image plus either: ≥1 major criterion ✓ Cough ✓ Sputum production ✓ Fever (>37.9°C) or hypothermia (<35.0°C) ✓ Crackles on auscultation ≥2 minor criteria ✓ Pleuritic chest pain ✓ Dyspnea ✓ Altered mental status ✓ Abnormal chest examination findings ✓ Leukocytosis (white blood cell count >12,000 cells/mL), or left shift (>10% band forms) • *Exclusion criteria*: transferred from another hospital, were hospitalized within 7 days before the index admission, were admitted for terminal care, or refused to give consent	N= 457	15% Estimated from survival analysis
Koskela 2014[18]	• Prospective, observational • Subjects: age ≥ 18 years old hospitalized with CAP (1 hospital – Kuopio, Finland) • *Pneumonia definition*: acute febrile illness with a new radiographic shadowing (referencing BTS guidelines 2009) • *Exclusion criteria*: severe pneumonia requiring ICU, refused to give consent, antibiotic treatment started in another institution	N= 153	5% Estimated from survival analysis
Adamuz 2014[13]	• Prospective, observational • Subjects: age ≥ 18 years old hospitalized with CAP (1 hospital - Barcelona, Spain) • *Pneumonia definition*: not listed • *Exclusion criteria*: neutropenia, immunoglobulin deficiencies, HIV infection, transplantation or splenectomy, receiving immunosuppressant and/or corticosteroid therapy (>20 mg/day of prednisone or its equivalent)	N= 1,284	7.2%
Holter 2016[16]	• Subjects: age ≥ 18 years old hospitalized with CAP (South-Eastern Norway) • *Pneumonia definition*: positive chest image plus: ✓ Rectal temperature >38.0°C ✓ At least one of the following symptoms or signs: ✓ Cough (productive or non-productive) ✓ Dyspnea ✓ Chest pain ✓ Crackles or reduced respiratory sounds • *Exclusion criteria*: non-infectious causes (pulmonary infarction, tumor or bronchiectasis) or if the patient had been hospitalized within the past 2 weeks.	N= 259	9%

Table 2 Studies evaluating 1-year mortality after hospitalization due to CAP with a control group

Author	CAP cases	Controls	1-year mortality
Koivula 1999[25]	N= 122 • Subjects: age ≥ 60 years old enrolled in a randomized, pneumococcal vaccination trial in Finland • *Pneumonia definition*: positive chest image plus one of the following: ✓ Temperature over 38.7°C and new or worsening cough PLUS one of the following: moist rales, dyspnea, tachypnea, cyanosis, pain in the chest or abdomen at respiration, purulent or blood stained sputum, acute deterioration of the general condition ✓ ≥2 of the following: temperature over 38.7°C, new/worsening cough plus moist rales, dyspnea, tachypnea, or cyanosis, pain in the chest or abdomen at respiration, purulent or blood stained sputum ✓ New or worsening cough and temperature over 38°C for more than 5 days. • *Exclusion criteria*: none	N= 4,045 • Subjects enrolled in same randomized, pneumococcal vaccination trial in Finland who did not develop pneumonia	CAP: 19% Controls: 4%
Kaplan 2003[24]	N= 158,960 • Subjects: age ≥ 65 years old from the 1997 Medicare hospital discharge database • *CAP definition*: ICD-9 codes 481, 482, 485, or 486 listed both at admission and discharge plus a pulmonary complaint on admission (ICD-9 518.81, 496, 786.09, 491.21, 507.0, 466.0, 786.3, 493.90, 786.3, 518.82) • *Exclusion criteria*: transferred from other hospitals	N= 794,333 • Five age, sex, and race matched from the same database who did not meet ICD-9 criteria	CAP: 34% Controls: 25%
Carriere 2004[22]	N= 43,642 • Subjects: age ≥ 18 years old from 2 Canadian (Alberta Province) administrative health service databases • *CAP definition*: ICD-9 codes 480.0 - 487.8 (pneumonia) or 507.0 – 507.8 (aspiration pneumonia) • *Exclusion criteria*: ICD-9 codes 484.1 – 484.7, non-Alberta residents, not treated in an Alberta acute care facility, previous hospitalization within 10 days	N= 1,950,997 • Alberta general population not hospitalized with pneumonia in 1994/1995	CAP: 26 % Controls: 5% Percentages estimated from data in manuscript
Bordon 2010[20]	N= 624 • Subjects: age ≥ 18 years old admitted to VA hospital • *CAP definition*: positive chest image plus ≥1 of the following: ✓ New or increased cough ✓ Abnormal temperature ✓ Abnormal serum leukocyte count • *Exclusion criteria*: none	N= 6,347 • Hospitalized patients during same period due to medical conditions other than CAP	CAP: 32% Controls: 20% Percentages estimated from data in manuscript
Bruns 2010[21]	N= 356 • Subjects: age ≥ 18 years old prospective cohort derived from two randomized clinical trials • *CAP definition*: positive chest image plus ≥2 of the following: ✓ Cough ✓ Sputum production ✓ Rectal temperature> 38°C or < 36.1°C ✓ Auscultatory findings consistent with pneumonia ✓ Leukocytosis (>10^9 white blood cells/litre or > 15% bands) ✓ Positive culture of blood or pleural fluid ✓ C reactive protein more than three times the upper limit of normal • *Exclusion criteria:* mechanical ventilation in an intensive care unit, cystic fibrosis; a history of colonization with Gram-negative bacteria due to structural damage to the respiratory tract; malfunction of the digestive tract; life expectancy of less than one month because of underlying disease, infections other than pneumonia that needed antibiotic treatment, severe immunosuppression	N= 356 • Age and sex matched general population cohort	CAP: 17% Controls: 4%
Sandvall 2014[26]	N= 392 • Subjects: age ≥ 18 years old admitted to VA hospital with Streptococcal pneumonia • *CAP definition*: positive chest image plus ≥1 of the following: ✓ Subjective fever ✓ Cough ✓ Sputum production ✓ Pleuritic chest pain • *Exclusion criteria:* none	N= not documented • Expected 1-year survival of an average 63-year-old American male from the Human mortality database	CAP: 15% Controls: 1% Percentages estimated from data in manuscript
Eurich 2015[23]	N= 6,078 • Subjects: Age: ≥ 18 years old enrolled in a clinical registry • *CAP definition*: positive chest image plus ≥2 of the following: ✓ Cough ✓ Pleuritic chest pain ✓ Shortness of air ✓ Temperature >38°C ✓ Crackles on auscultation • *Exclusion criteria:* immune deficiency, shock, mechanical ventilation on admission, pregnancy, breastfeeding, alcoholism, chronic renal disease.	N= 29,402 • Age and sex matched • Alive at time of CAP case • Presenting to the hospital within the same month/year with a non-pneumonia diagnosis • No history of CAP in the prior year	CAP: 13% Controls: 5% Percentages estimated from data in manuscript
Mangen 2017[27]	N= 562 • Subjects: age ≥ 65 years old enrolled in a pneumococcal vaccine study • *CAP definition*: positive chest image plus a positive PCV 13 vaccine-type–specific urinary antigen test or isolation of vaccine-type *S. pneumoniae* from blood or another sterile site, plus the presence of ≥2 of the following: ✓ Cough ✓ Production of purulent sputum or a change in the character of sputum ✓ Temperature >38.0°C or <36.1°C ✓ Auscultatory findings consistent with pneumonia including rales and/or evidence of pulmonary consolidation ✓ Leukocytosis (>10^9 white blood cells/liter or >15% bands) ✓ C-reactive protein >3 times the upper limit of normal ✓ Hypoxemia with a partial oxygen pressure (PO2) <60 mm Hg while the patient is breathing room air • *Exclusion criteria:* previous vaccination with any pneumococcal vaccine, residence in long-term care facility, contraindication for 13vPnC, contraindication for influenza vaccines, use of investigational products in 30 days prior to study vaccine administration, history of severe adverse reaction associated with any vaccine component, immunodeficiency or immune suppression.	N= 1,123 • Age and sex matched subjects enrolled in the same vaccination trial without pneumonia	CAP: 8% Controls: 1%

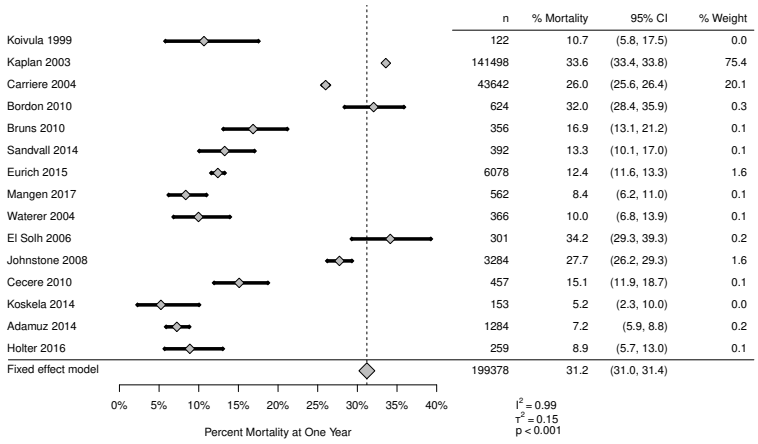

Fig. 1 Forest plot display of studies evaluating 1-year mortality after hospitalization for CAP

A hypothesis to explain long-term mortality

Chronic inflammation has been associated with aging and early death; a process described as "inflammaging" [34]. Persistent elevated levels of inflammatory cytokines have been documented in patients with CAP at time of hospital discharge. The increased long-term mortality after CAP may be mediated by an inflammatory response that persists after hospital discharge, adds to the inflammaging process, and accelerates the progression of medical comorbidities and early death [35, 36]. Months after hospital discharge, the primary cause of death may be cardiovascular disease or other underlying comorbidities. The prior episode of CAP would influence death by worsening the underlying comorbidity. **Figure 2** is a schematic representation indicating the projectedlife expectancy of a 50-year old patient who is hospitalized due to CAP (**Figure 2**: point 1). After the patient is discharged from the hospital, the projected life expectancy changes to line B and is considerably decreased (**Figure 2**: point 2).

Mortality rates for patients with CAP have not significantly decreased since the 1950s [37]. Adjunctive therapies such as macrolides, statins, corticosteroids, and antiplatelet agents have been studied in an attempt to improve short-term outcomes [38]. Despite the knowledge of higher mortality rates long after hospitalization for CAP, no studies evaluating the impact of adjunctive therapies on longterm outcomes have been conducted. It can be speculated that medications able to decrease chronic inflammation may reduce long term mortality in hospitalized patients with CAP.

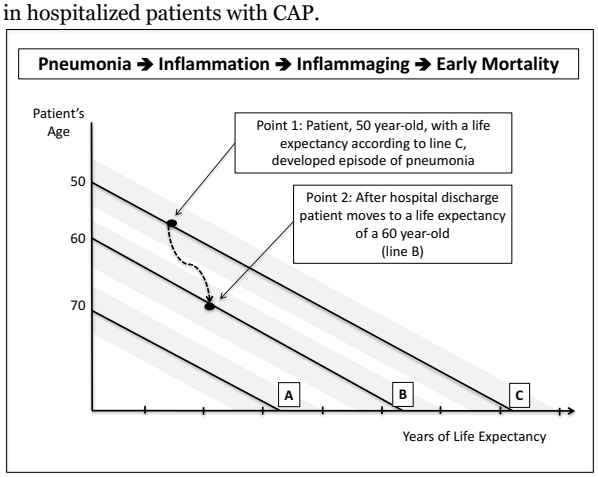

Fig. 2 Schematic representation of the change in life expectancy for a patient hospitalized with CAP

Conclusions

Improving the clinical outcomes of hospitalized patients with CAP is of paramount importance for patients, as well as clinical investigators. The recent recognition of long-term mortality associated with CAP is opening a new frontier for clinical research in the field. We need studies to better define the underlying pathophysiology explaining the association of CAP with long-term mortality. Intervention to improve clinical outcomes in patients with CAP have frequently been tested in short term 30-day studies, since CAP was considered an acute problem without chronic implications. We need a new paradigm to design clinical trials to test interventions that may reduce long-term mortality.

References

1. Kochanek KD, Murphy SL, Xu J, Tejada-Vera B. Deaths: final data for 2014. National vital statistics reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics. National Vital Statistics System. 2016 Jun;65(4):1–22.
2. Trends in Pneumonia and Influenza Morbidity and Mortality. American Lung Association, Epidemiology and Statistics Unit, Research and Health Education Division 2015 [Available from: http://www.lung.org/assets/documents/research/pi-trend-report.pdf. Accessed February 15, 2017
3. Pfuntner A, Wier LM, Stocks C. Most Frequent Conditions in U.S. Hospitals, 2011: Statistical Brief #162. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville (MD). US: Agency for Healthcare Research and Quality; 2013.[[cited 2017 Feb 15]], https://www.ncbi.nlm.nih.gov/books/NBK169248/pdf/Bookshelf_NBK169248.pdf
4. Park H, Adeyemi AO, Rascati KL. Direct Medical Costs and Utilization of Health Care Services to Treat Pneumonia in the United States: An Analysis of the 2007-2011 Medical Expenditure Panel Survey. Clinical therapeutics. 2015;37(7):1466-76 e1.
5. Blasi F, Garau J, Medina J, Ávila M, McBride K, Ostermann H; REACH study group. Current management of patients hospitalized with community-acquired pneumonia across Europe: outcomes from REACH. Respir Res. 2013 Apr;14(1):44.
6. Daniel P, Woodhead M, Welham S, Mckeever TM, Lim

WS; British Thoracic Society. Mortality reduction in adult community-acquired pneumonia in the UK (2009-2014): results from the British Thoracic Society audit programme. Thorax. 2016 Nov;71(11):1061–3.
7. Kolditz M, Tesch F, Mocke L, Höffken G, Ewig S, Schmitt J. Burden and risk factors of ambulatory or hospitalized CAP: A population based cohort study. Respir Med. 2016 Dec;121:32–8.
8. Liapikou A, Polverino E, Cilloniz C, Peyrani P, Ramirez J, Menendez R et al.; Community-Acquired Pneumonia Organization (CAPO) Investigators. A worldwide perspective of nursing home-acquired pneumonia compared with community-acquired pneumonia. Respir Care. 2014 Jul;59(7):1078–85.
9. Confalonieri M, Urbino R, Potena A, Piattella M, Parigi P, Puccio G et al. Hydrocortisone infusion for severe community-acquired pneumonia: a preliminary randomized study. Am J Respir Crit Care Med. 2005 Feb;171(3):242–8.
10. Emmet O'Brien M, Restrepo MI, Martin-Loeches I. Update on the combination effect of macrolide antibiotics in community-acquired pneumonia. Respir Investig. 2015 Sep;53(5):201–9.
11. Meijvis SC, Hardeman H, Remmelts HH, Heijligenberg R, Rijkers GT, van Velzen-Blad H et al. Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial. Lancet. 2011 Jun;377(9782):2023–30.
12. Gross AK, Dunn SP, Feola DJ, Martin CA, Charnigo R, Li Z et al. Clopidogrel treatment and the incidence and severity of community acquired pneumonia in a cohort study and meta-analysis of antiplatelet therapy in pneumonia and critical illness. J Thromb Thrombolysis. 2013 Feb;35(2):147–54.
13. Adamuz J, Viasus D, Jiménez-Martínez E, Isla P, Garcia-Vidal C, Dorca J et al. Incidence, timing and risk factors associated with 1-year mortality after hospitalization for community-acquired pneumonia. J Infect. 2014 Jun;68(6):534–41.
14. Cecere LM, Rubenfeld GD, Park DR, Root RK, Goss CH. Long-term survival after hospitalization for community-acquired and healthcare-associated pneumonia. Respiration; international review of thoracic diseases. 2010;79(2):128-36. https://doi.org/https://doi.org/10.1159/000255764..
15. El Solh A, Pineda L, Bouquin P, Mankowski C. Determinants of short and long term functional recovery after hospitalization for community-acquired pneumonia in the elderly: role of inflammatory markers. BMC Geriatr. 2006 Aug;6(1):12.
16. Holter JC, Ueland T, Jenum PA, Müller F, Brunborg C, Frøland SS et al. Risk Factors for Long-Term Mortality after Hospitalization for Community-Acquired Pneumonia: A 5-Year Prospective Follow-Up Study. PLoS One. 2016 Feb;11(2):e0148741.
17. Johnstone J, Eurich DT, Majumdar SR, Jin Y, Marrie TJ. Long-term morbidity and mortality after hospitalization with community-acquired pneumonia: a population-based cohort study. Medicine (Baltimore). 2008 Nov;87(6):329–34.
18. Koskela HO, Salonen PH, Romppanen J, Niskanen L. Long-term mortality after community-acquired pneumonia—impacts of diabetes and newly discovered hyperglycaemia: a prospective, observational cohort study. BMJ Open. 2014 Aug;4(8):e005715.
19. Waterer GW, Kessler LA, Wunderink RG. Medium-term survival after hospitalization with community-acquired pneumonia. Am J Respir Crit Care Med. 2004 Apr;169(8):910–4.
20. Bordon J, Wiemken T, Peyrani P, Paz ML, Gnoni M, Cabral P et al.; CAPO Study Group. Decrease in long-term survival for hospitalized patients with community-acquired pneumonia. Chest. 2010 Aug;138(2):279–83.
21. Bruns AH, Oosterheert JJ, Cucciolillo MC, El Moussaoui R, Groenwold RH, Prins JM et al. Cause-specific long-term mortality rates in patients recovered from community-acquired pneumonia as compared with the general Dutch population. Clin Microbiol Infect. 2011 May;17(5):763–8.
22. Carriere KC, Jin Y, Marrie TJ, Predy G, Johnson DH. Outcomes and costs among seniors requiring hospitalization for community-acquired pneumonia in Alberta. J Am Geriatr Soc. 2004 Jan;52(1):31–8.
23. Eurich DT, Marrie TJ, Minhas-Sandhu JK, Majumdar SR. Ten-Year Mortality after Community-acquired Pneumonia. A Prospective Cohort. Am J Respir Crit Care Med. 2015 Sep;192(5):597–604.
24. Kaplan V, Clermont G, Griffin MF, Kasal J, Watson RS, Linde-Zwirble WT et al. Pneumonia: still the old man's friend? Arch Intern Med. 2003 Feb;163(3):317–23.
25. Koivula I, Stén M, Mäkelä PH. Prognosis after community-acquired pneumonia in the elderly: a population-based 12-year follow-up study. Arch Intern Med. 1999 Jul;159(14):1550–5.
26. Sandvall B, Rueda AM, Musher DM. Long-term survival following pneumococcal pneumonia. Clin Infect Dis. 2013 Apr;56(8):1145–6.
27. Mangen MJ, Huijts SM, Bonten MJ, de Wit GA. The impact of community-acquired pneumonia on the health-related quality-of-life in elderly. BMC Infect Dis. 2017 Mar;17(1):208.
28. Yende S, Alvarez K, Loehr L, Folsom AR, Newman AB, Weissfeld LA et al.; Atherosclerosis Risk in Communities Study, the Cardiovascular Health Study, and the Health, Aging, and Body Composition Study. Epidemiology and long-term clinical and biologic risk factors for pneumonia in community-dwelling older Americans: analysis of three cohorts. Chest. 2013 Sep;144(3):1008–17.
29. Yende S, Angus DC, Ali IS, Somes G, Newman AB, Bauer D et al. Influence of comorbid conditions on long-term mortality after pneumonia in older people. J Am Geriatr Soc. 2007 Apr;55(4):518–25.
30. Hedlund JU, Ortqvist AB, Kalin ME, Granath F. Factors of importance for the long term prognosis after hospital treated pneumonia. Thorax. 1993 Aug;48(8):785–9.
31. Ajayi OO, Norton NB, Gress TW, Stanek RJ, Mufson MA. Three Decades of Follow-up of Adults After Recovery From Invasive Pneumococcal Pneumonia. Am J Med Sci. 2017 May;353(5):445–51.
32. Honselmann KC, Buthut F, Heuwer B, Karadag S, Sayk F, Kurowski V et al. Long-term mortality and quality of life in intensive care patients treated for pneumonia and/or sepsis: predictors of mortality and quality of life in patients with sepsis/pneumonia. J Crit Care. 2015 Aug;30(4):721–6.
33. Lenz H, Norby GO, Dahl V, Ranheim TE, Haagensen RE. Five-year mortality in patients treated for severe

community-acquired pneumonia - a retrospective study. Acta Anaesthesiol Scand. 2017 Apr;61(4):418–26.
34. Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. J Gerontol A Biol Sci Med Sci. 2014 Jun;69 Suppl 1:S4–9.
35. Guertler C, Wirz B, Christ-Crain M, Zimmerli W, Mueller B, Schuetz P. Inflammatory responses predict long-term mortality risk in community-acquired pneumonia. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2011;37(6):1439-46. https://doi.org/10.1183/09031936.00121510.
36. Yende S, D'Angelo G, Kellum JA, Weissfeld L, Fine J, Welch RD et al.; GenIMS Investigators. Inflammatory markers at hospital discharge predict subsequent mortality after pneumonia and sepsis. Am J Respir Crit Care Med. 2008 Jun;177(11):1242–7.
37. Austrian R, Gold J. Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia. Ann Intern Med. 1964 May;60(5):759–76.
38. Feldman C, Anderson R. Community-Acquired Pneumonia: Pathogenesis of Acute Cardiac Events and Potential Adjunctive Therapies. Chest. 2015 Aug;148(2):523–32.