# The adherence of Greek chest physicians to CAP Guidelines:

## The role of patient-related factors

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**SUMMARY.** OBJECTIVE: Multiple international studies have shown that the adherence of chest physicians to guidelines is variable. In Greece there is lack of information on this subject. An epidemiological study was conducted to evaluate the temporal trends of the adherence to guidelines of Greek chest physicians. Retrospective assessment was made of their degree of adherence to international guidelines for the management of patients hospitalized for community acquired pneumonia (CAP) and the patient-related factors that influence this. METHODS: The medical records were studied of 80 randomly selected patients admitted to the Chest Diseases Hospital of Athens in the first 6 months of 2000 with a presumptive diagnosis of CAP. Epidemiological and clinical data and information on admission criteria, diagnostic procedures and antibiotic treatment were collected from those fulfilling the diagnostic criteria for CAP. The appropriateness of the recorded procedures and treatment was evaluated in comparison to the CAP guidelines that were in use during the study period. Odds ratios (OR) for associated factors were calculated (the lower the OR value the lower the degree of adherence). RESULTS: During the study period 67 eligible patients, with a mean age of 58.8 years, were identified. The rate of diagnostic procedures ranged from 100% for chest X-ray to 12% for blood culture. About 71% of patients had received appropriate antibiotic treatment on admission. An age of above than 70 years, altered mental status, aspiration, respiratory failure and multilobar pneumonia were found to be significant predictors of inappropriate therapy with ORs of 0.2 (95% CI: 0.1-0.6, p=0.004), 0.04 (95% CI: 0-0.4, p=0.004), 0.04 (95% CI: 0-0.3, p=0.002), 0.3 (95% CI: 0-0.87, p=0.02), and 0.1 (95% CI:0.04-0.50, p=0.001) respectively. Aspiration was the most important factor for non-adherence on multivariate analysis adjusted for age (OR:0.05, 95% CI: 0.005-0.45, p=0.008). CONCLUSIONS: The adherence to CAP management guidelines was not grossly unsatisfactory but room for improvement was revealed. *Pneumon 2011, 24(4):361-367.*

## INTRODUCTION

Community acquired pneumonia (CAP) constitutes a serious health problem because of its high incidence, which in the USA and Europe reaches $160 \times 10^5$ cases per year, with considerable morbidity and mortality[1,2]. In Spain it has been estimated that the financial burden of patients hospitalized with CAP approximates €115 million per year[2]. Since the early 1990s various relevant scientific societies have developed clinical guidelines on patients with CAP in an effort to optimize their management. These documents include a large amount of evidence-based information on diagnostic recommendations, discussion about which patients should be admitted to the hospital and which to the intensive care unit (ICU), summaries of the most likely pathogens and their susceptibility profiles to antimicrobial agents, preventive strategies for patients at risk for CAP and, most important, algorithms for the ideal implementation of initial empirical treatment[1,3-9]. Although several studies have shown that the administration of antibiotic therapy in accordance with the current recommendations can improve pneumonia-related morbidity and mortality, and also reduce the duration of hospital stay and health care costs, the adherence of chest physicians to these recommendations presents considerable heterogeneity[2,10-19]. Furthermore, it is not known whether adherence is influenced by professional and hospital factors only, or also by patient characteristics, such as comorbid conditions and the initial severity of disease. A retrospective epidemiological study was designed to evaluate the temporal trends of the adherence of Greek chest physicians to the current recommendations for the management of CAP, preliminary to applying a prospective protocol for improving their adherence to CAP guidelines. The aims of this study were to evaluate the adherence of chest physicians to specific guidelines for the diagnosis and empirical treatment of patients hospitalized with CAP and to identify patient-related factors among the admission criteria that may influence the adherence to treatment guidelines.

## MATERIAL AND METHODS

Random selection was made of the medical records of 80 patients admitted to the Pulmonary Departments of the "SOTIRIA" Hospital for Chest Diseases in Athens, Greece in the first six months of the year 2000 with an admission diagnosis of CAP. For the purposes of the study, CAP was defined as new infiltrate(s) on the chest X-ray of a patient who had not been hospitalized for any reason during the previous two weeks, and with at least one of the following symptoms of lower respiratory tract infection: fever >37.8° and/or cough, and/or sputum and/or dyspnoea, and/or pleuritic pain, and/or leukocytosis, and/or mental confusion[18]. Patients not fulfilling the above definition, and those with severe immunosuppression [Human Immunodeficiency Virus (HIV) positive status, malignancy] and/or a definitive diagnosis other than CAP, were excluded from the study. Information on age, gender, smoking history, comorbidities [chronic obstructive pulmonary disease (COPD), congestive heart failure, and diabetes mellitus (DM)], risk for aspiration (alcohol or drug abuse, cerebrovascular disease) and previous use of corticosteroids was retrieved from the medical records. The criteria for hospital admission, such as failure of previous antibiotic treatment, age over 70 years, comorbidities, mental confusion, respiratory failure, history of aspiration, tachypnoea (>30 breaths/min), haemodynamic instability, anaemia, acute renal failure, severe leucopenia (<4,000/mm$^3$) or severe leukocytosis (>20,000/mm$^3$), and the presence on chest X-ray of pleural effusion or cavitation or multiple infiltrates on both lung fields, were also recorded and evaluated[4,9]. Concerning the diagnostic procedures, the following parameters were studied: sputum Gram stain and culture, blood culture, serology testing for viruses and atypical agents, fiberoptic bronchoscopy and cultures of bronchial secretions or bronchoalveolar lavage (BAL), chest X-ray and computed tomography (CT) of the chest. The urine antigen test for Legionella and *Streptococcus pneumoniae* was not available at the time of the study. The type and duration of antibiotic therapy and the proportion of patients who were treated according to clinical practice guidelines were examined. The appropriateness of the treatment was derived by comparing the therapeutic options found in the patients' records with those developed in the CAP Guidelines of the American Thoracic Society (ATS)[4] and the European Respiratory Society (ERS)[9] that were in use during the study period. Treatment was considered appropriate if it adhered to these Guidelines. All other regimes were considered non-adherent to guidelines.

### Statistical Analysis

Statistical analyses were performed using the Intercooled Stata 7 software programme. Therapy and age were treated as binary variables (0: not according to guidelines, 1: in accordance with guidelines, and greater or less than 70 years, respectively). The $\chi^2$ test was used in

univariate analysis to assess the relationship of appropriate therapy on admission with each of the admission criteria, following which multivariate logistic regression was applied. The stepwise method was used the selection of the best model describing the study data, and ORs were calculated (the lower the OR value the lower the degree of adherence).

A p-value <0.05 was deemed significant.

## RESULTS

### Descriptive data

In total 67 (84%) patients fulfilled the selection criteria and were included in the study. As shown in Table 1, 58.2% of the patients were men and 41.8% were women, with a mean age of 58.8±18.1years, whilst most of them were smokers (only 27.9% had never smoked). The mean duration of hospitalization was 10.8±5.7 days and the fatality rate was 4.5%.

Table 2 summarizes the frequencies in the study population of the admission criteria proposed by the CAP Guidelines in use during the study period[4,9].

### Adherence to management guidelines

As shown in Table 1, all patients underwent chest X-ray on admission, but only 46% of them had a sputum Gram stain and culture examination. Blood cultures were obtained in 12% of patients. Fiberoptic bronchoscopy and CT of the chest were performed in 18% and 41% of patients respectively.

Type of antibiotic treatment administered is summarized in Table 3. Various antimicrobial agents were used in the study population, either as monotherapy (38%) or as combination therapy (62%) during their whole hospital stay. The most frequently prescribed antibiotic regime (33%) consisted of a beta lactam as monotherapy followed by the combination of a cephalosporin and penicillin (17%) or a beta lactam and a macrolide (16%). Overall 71.6% of the patients received appropriate treatment on the first day of hospitalization. More than 85% of the patients who initially received appropriate treatment continued to receive appropriate treatment the third day of hospitalization. Appropriate treatment on first day of hospitalization showed statistically significant positive association with appropriate treatment on the third day of hospitalization (p<0.001) (data not shown).

Table 4 presents patient-related parameters associated with the adherence of chest physicians to treatment

**TABLE 1.** Characteristics of patients with community acquired pneumonia (CAP) admitted to the hospital (n=67)

| Subjects (n=67) | |
| --- | --- |
| **Mean age (years)** | 58.8 ±18.1 |
| **Gender** | |
| Male | 39 (58.2 %) |
| Female | 28 (41.8 %) |
| **Smoking history (n=61)** | |
| Current smokers | 38 (62.3%) |
| Ex smokers | 6 (9.8%) |
| Non smokers | 17 (27.9%) |
| **Duration of hospitalization (days (n=67)** | 10.8 ± 5.7 |
| **Diagnostic assessment (n=67)** | |
| Chest X-ray | 67 (100%) |
| Sputum Gram stain and culture | 31 (46.3%) |
| Computed tomography of the chest | 27 (41.0%) |
| Fiberoptic bronchoscopy | 12 (18.0%) |
| Blood culture | 8 (12.0%) |
| Serology testing for viruses | 7 (8.0%) |
| **Fatality (n=67)** | 3 (4.5%) |

**TABLE 2.** Frequencies of hospital admission criteria in study patients with community acquired pneumonia (CAP) (n=67)

| | |
| --- | --- |
| Age over 70 years | 20 (30.8%) |
| Coexistence of a chronic debilitating disease* | 30 (46.2%) |
| No response after 3 days of prior antibiotic treatment | 19 (29.7%) |
| Confusion or decreased level of consciousness | 7 (11.7%) |
| Aspiration | 9 (14.5%) |
| Respiratory failure | 25 (39.1%) |
| Pleural effusion | 17 (27.4%) |
| Multilobar pneumonia | 18 (28.1%) |

*Chronic obstructive pulmonary disease, congestive heart failure, chronic liver disease, chronic renal disease, diabetes mellitus

guidelines on the day of admission. Among these, age above 70 years, a history of altered mental status, aspiration, respiratory failure and multilobar pneumonia were found to be significant independent factors for inappropriate therapy on the day of admission with ORs of 0.2 (95% CI: 0.1-0.6, p=0.004), 0.04 (95% CI: 0-0.4, p=0.004), 0.04 (95% CI: 0-0.3, p=0.002), 0.3 (95% CI: 0-0.87, p=0.02), and 0.1 (95% CI:0.04-0.50, p=0.001) respectively. In multivariate analysis adjusted for age, aspiration was

**TABLE 3.** Use of antibiotic therapy during hospitalization of patients with community acquired pneumonia (CAP) (n=67)

| Antibiotic agent(s) | Frequency (%) |
|---|---|
| β-lactam | 33 |
| Macrolide | 5 |
| Macrolide plus β-lactam | 16 |
| Cephalosporin 2nd or 3rd GCS plus penicillin | 17 |
| β-lactam plus clindamycin | 8 |
| β-lactam plus aminoglycoside | 16 |
| Cephalosporin 2nd GCS plus aminoglycoside plus clindamycin | 2.5 |
| Cephalosporin 2nd GCS plus aminoglycoside plus macrolide | 2.5 |

found to be the most significant independent risk factor for non-adherence to treatment guidelines (OR: 0.05, 95% CI: 0.005-0.450, p=0.008). Specifically, patients with aspiration were about 95% less likely to receive appropriate treatment for CAP than those without aspiration, adjusted for age. No information was available on the records either on prior immunization against influenza virus and *S. pneumoniae*, or on the use of antibiotics prior to admission.

## DISCUSSION

The aims of this study were to assess the adherence of chest physicians to specific guidelines for the management of CAP in hospitalized patients, and to identify patient-related factors influencing optimal application of treatment guidelines. No such study had been previously conducted on the practices of Greek chest physicians. In this study population about 70% of the patients were treated according to the recommendations of international CAP Guidelines on admission. Even higher adherence rates were found for admission risk factors and specific diagnostic procedures, with the exception of blood and sputum cultures. No information was available in the hospital records on immunization and use of antibiotics prior to admission. Among patient-related parameters, age above 70 years, a history of altered mental status, aspiration, respiratory failure and multilobal pneumonia were found to be significant independent risk factors for inappropriate therapy, with aspiration being the most significant.

The rate of adherence to guidelines for the management of hospitalized patients with CAP reported in other countries ranges from 47.9% to 100%[21-27]. The rate of adherence to treatment guidelines of 71.6% found in the present study is fairly high by these standards, although

**TABLE 4.** Factors influencing adherence to treatment guidelines on the day of admission of patients hospitalized with community acquired pneumonia (CAP) (n=67)

| | | N | Recommended treatment (%) | OR (95%CI)* | p-value |
|---|---|---|---|---|---|
| Age over 70 years | YES | 20 | 9 (45.0) | 0.20 (0.10-0.60) | 0.004** |
| | NO | 45 | 37 (82.2) | | |
| Comorbidities | YES | 30 | 21 (70.0) | 0.80 (0.30-2.40) | 0.701 |
| | NO | 35 | 26 (74.3) | | |
| Prior antimicrobial treatment | YES | 19 | 14 (73.7) | 1.00 (0.30-3.40) | 0.977 |
| | NO | 45 | 33 (73.3) | | |
| Mental confusion | YES | 7 | 1 (14.3) | 0.04 (0.00-0.40) | 0.004** |
| | NO | 53 | 43 (81.1) | | |
| Aspiration | YES | 9 | 1 (11.1) | 0.04 (0.00-0.30) | 0.002** |
| | NO | 53 | 42 (79.3) | | |
| Respiratory failure | YES | 25 | 14 (56.0) | 0.30 (0.10-0.87) | 0.027** |
| | NO | 39 | 32 (82.1) | | |
| Pleural effusion | YES | 17 | 14 (82.4) | 2.30 (0.60-9.40) | 0.233 |
| | NO | 45 | 30 (66.7) | | |
| Multilobar pneumonia | YES | 18 | 7 (38.9) | 0.10 (0.04-0.50) | 0.001** |
| | NO | 46 | 38 (82.6) | | |

* 95% CI = 95% confidence interval, OR=odds ratio, ** p<0.05 was considered statistically significant

it leaves ample room for improvement. It parallels those in recent reports from other European Countries, such as Spain where adherence reaches 80%[2,10,19]. In the American continent greater heterogeneity is encountered, with rates varying from 48% to 90%[19,20]; In Canada, adherence is around 80%, whereas in Chile it is 46%[16,27]. This variation is mostly explained by physician-related factors, such as differences in awareness of the presence of guidelines, the different practices between large teaching/university hospitals and others, the lead provided by the senior doctors, and the amount of experience in treating CAP in inpatients[17,22]. There is evidence that trained and trainee pneumonologists show a higher rate of adherence to guidelines than other specialists treating CAP[19]. The major argument given for not following treatment Guidelines is that they do not provide answers to problems not fitting the strict patterns of the algorithms[24,25]. The international CAP Guidelines, however, have managed to organize a huge amount of information, which has led to improvement of CAP-related outcomes andlowering of costs in comparison to alternative treatment regimes, without implying replacement of clinical judgment[8].

In the literature, 30% of reported inappropriate treatment is associated with monotherapy with advanced-generation macrolides[28]. In the patients of the present study, the rate of such treatment was found to be very low. This could reflect current knowledge of the epidemiological data on resistance profiles of *S.pneumoniae* to macrolides in Greece, showing resistance rates as high as 30.3%[29-31]. On the other hand, aminoglycosides were used in combination therapy with other antibiotics in a significant number of patients in this study, probably as a relic of the tradition of the pre-guidelines era, when 30-40% of inpatients were reported to be given aminoglycoside therapy for CAP[23].

Concerning the investigational parameters of the CAP Guidelines, adherence rates to recommendations were higher compared to the treatment section, reflecting how well they represent empirical clinical knowledge. The exception was for blood and sputum cultures; in this study only a minority a patients underwent these diagnostic procedures, which could be attributed to the awareness of physicians of the low yield of blood and sputum cultures in CAP[1,32]. Studies from other countries report much higher rates of adherence for blood cultures (ranging from 57% to 83%), although it is noted that respiratory physicians perform fewer blood cultures than the other specialists[33,34]. The findings of this study suggest that greater use of blood and sputum culture may be warranted, that could provide reliable identification of

CAP pathogens, in an era of emergence of multi-drug resistant bacteria[35].

There is sparse documentation of patient-related parameters that may possibly influence the adherence to guidelines for the treatment of CAP. The study results show that patient age over 70 years, a history of altered mental status, aspiration, respiratory failure and multilobar pneumonia were significant predictors of low adherence to treatment guidelines. In the international literature it is reported that comorbidity (mainly DM, COPD and central nervous system and renal disorders) almost doubles the lack of adherence to guidelines without any other obvious aetiological explanation. Rates of adherence are even lower when patients have a history of recent use of antibiotics[18,28]. The findings of the present study are in agreement with others and reflect the fact that older patients with CAP due to aspiration have more concomitant disease and usually present with a more serious clinical picture[36,37]. This may increase the insecurity of the treating physicians, leading to the use of a broader spectrum antibiotic treatment than that recommended by CAP Guidelines.

In most studies mortality rates for hospitalized patients with CAP range from 8.9% to 14%[10,15,18]. The mortality is reported to be significantly lower in the group of patients for whom adherence to guidelines was higher[18]. The low fatality rate in the patients of this study could be attributed to the high adherence rate to CAP guidelines, but also to the fact that the condition of no study patient necessitated ICU admission. Although neither the PORT nor the PSI index[38,39] was calculated on admission, almost 80% of the study population fulfilled at least one of the CAP Guidelines admission criteria[9]. The possibility cannot be excluded that some of the study patients were admitted despite not fulfilling the criteria of the guidelines for hospitalization, and thus had a lower mortality risk, which may have influenced the final fatality rate.

The review of the patients' hospital records revealed very little information on prior immunization and use of antibiotics before admission. In an era of increasing emerging resistance of pathogens to antibiotics, the newer guidelines recommend that patients with CAP who have been treated with antibiotics within the previous 90 days do not receive the same class of antibiotics as initial treatment for CAP[1]. The present study confirms the necessity of this addition, since most Greek chest physicians until recently did not include this information in their treatment decision making.

The limitations of the present study are its retrospective

design and the limited number of patients studied. The findings, however, demonstrate the positive attitude of Greek chest physicians towards the Guidelines in general, but considerable heterogeneity in their adherence to various aspects. This study highlights the issue that non-adherence to treatment Guidelines is influenced not only by physician-related factors, but also by patient-related parameters, age and history of aspiration being the most important. This new evidence could lead to further improvement in clinical practices in Greece, and it provides justification for educational intervention directed at better adherence to the diagnostic, therapeutic and preventive strategies for hospitalized patients with CAP recommended in the guidelines.

## REFERENCES

1. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. CID 2007; 44 (Suppl 2): S27-S72.

2. Menéndez R, Reyes S, Martínez R, de la Cuadra P, Manuel Vallés J, Vallterra J. Economic evaluation of adherence to treatment guidelines in nonintensive care pneumonia. Eur Respir J 2007; 29: 751-756.

3. Mandell LA, Bartlett JG, Dowell SF, et al. Update of Practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. CID 2003; 37: 1405-1433.

4. Niederman MS, Bass JB, Campbell GD, et al. Guidelines for the initial management of adults with community-acquired pneumonia: diagnosis, assessment of severity, and initial antimicrobial therapy. Am Rev Respir Dis 1993; 148: 1418-1426.

5. Barlett JG, Breiman RF, Mandell LA, File TM Jr. Community-acquired pneumonia in adults: guidelines for management. Clin Infect Dis 1998; 26: 811-838.

6. Bernstein JM. Treatment of Community-Acquired Pneumonia-IDSA Guidelines. Chest 1999; 115: 9S-13S.

7. The British Thoracic Society. Guidelines for the management of community-acquired pneumonia in adults admitted to the hospital. BJHM 1993; 49: 346-350.

8. Niederman MS. Guidelines for the management of community-acquired pneumonia. Current Recommendations and antibiotic selection issues. Med Clin North Am 2001; 85: 1493-1509.

9. ERS Task force. Guidelines for management of adult community-acquired lower respiratory tract infections. Eur Resp J 1998;11:986-991

10. Menéndez R, Ferrando D, Vallés JM, Vallterra J. Influence of deviation from guidelines on the outcome of community-acquired pneumonia. Chest 2002; 122: 612-617.

11. Dean NC, Silver MP, Bateman KA, James B, Hadlock CJ, Hale D. Decreased mortality after implementation of a treatment guideline for community-acquired pneumonia. Am J Med 2001; 110: 451-457.

12. Blasi F, Iori I, Bulfoni A, Corrao S, Constantino S, Legnani D. Can CAP guideline adherence improve patient outcome in internal medicine departments? Eur Respir J 2008; 32: 902-910.

13. Gleason PP, Kapoor WN, Stone RA, et al. Medical outcomes and antimicrobial costs with the use of the American Thoracic Society guidelines for outpatients with Community-acquired pneumonia. JAMA 1997; 278: 32-39.

14. Gleason PP, Meehan TP, Fine JM, Galusha DH, Fine MJ. Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. Arch Intern Med 1999; 159: 2562-2572.

15. Feagan B, Marrie T, Lau C, Wheeler SL, Wong CJ, Vandervoort MK. Treatment and outcomes of community-acquired pneumonia at Canadian hospitals. CMAJ 2000; 162: 1415-20.

16. Marras TK, Chan CK. Use of guidelines in treating community acquired pneumonia. Chest 1998; 113: 1689-94.

17. Ali MH, Kalima P, Maxwell SRJ. Failure to implement hospital antimicrobial prescribing guidelines: a comparison of two UK academic centers. JAC 2006; 57: 959-962.

18. Menéndez R, Torres A, Zalacaín R, et al. Guidelines for the treatment of community-acquired pneumonia. Predictors of adherence and outcome. Am J Respir Crit Care Med 2005; 172: 757-762.

19. Dambrava PG, Torres A, Vallès X, et al. Adherence to guidelines' empirical antibiotic recommendations and community-acquired pneumonia outcome. Eur Respir J 2008; 32: 892-901.

20. Ruiz M, Ewig S, Marcos MA, et al. Etiology of community acquired pneumonia: Impact of age, comorbidity and severity. Am J Respir Crit Care Med 1999; 397-405.

21. Jencks SF, Curedon T, Burwen DR, et al. Quality of medical care delivered to Medicare beneficiaries: A profile at State and National Levels. JAMA 2000; 284: 1670-1676.

22. Switzer G, Halm E, Chang CC, Mihman BS, Walsh MB, Fine MJ. Physician awareness and self reported use of local and national guidelines for community acquired pneumonia. J Gen Intern Med 2003; 18: 816-823.

23. Tunis SR, Hayward R, Wilson M, et al. Internists' Attitudes about Clinical Practice Guidelines. Annals Int Med 1994; 120: 956-963.

24. Keeley D. Guidelines for managing community-acquired pneumonia in adults. BMJ 2002; 324: 436-437.

25. Robinson T. Compliance is limited by opposing recommendations. (Letter) BMJ 2002; 324: 1159.

26. Gilbert K, Gleason PP, Singer DE, et al. Variations in antimicrobial use and cost in more than 2000 patients with community acquired pneumonia. Am J Med 1998; 104: 17-27.

27. Diaz A, Kuzmanic G, Platzer L, Sanfuentes F, Espinosa MA, Saldías F. Medical outcomes and antimicrobial compliance according to the Chilean Society of Respiratory Diseases guidelines for hospitalized patients with community acquired pneumonia. Rev Med Chil 2003; 131: 847-56.

28. Wu JH, Howard DH, McGowan JE Jr, Turpin RS, Henry Hu X. Adherence to Infectious Diseases Society of America Guidelines for Empiric therapy for patients with community-acquired pneumonia in commercially insured cohort. Clin Ther 2006; 28: 1451-1461.

29. Kanavaki S, Karabela S, Makarona M, Moraiti H, Koumantakis P, Refanis A. Current tnimicrobial resistance of pneumococcus. Pneumon 2005; 18:263-274.

30. Poulakou G, Katsarolis I, Mattaiopoulou I, et al. Nationwide surveillance of *Streptococcus pneumoniae* in Greece: patterns of resistance and serotype epidemiology. Int J Antimicrob Agents 2007; 30: 87-92.

31. Souli M, Volonakis K, Kapaskelis A, et al. Characterisation of macrolide non-susceptible *S. pneumoniae* colonizing children in attending day-care centers in Athens, Greece during 2000 and 2003. Clin Microbiol Infect 2007; 13: 70-77.

32. Corbo J, Friedman B, Bijur P, et al. Limited usefulness of initial blood cultures in community-acquired pneumonia. Emerg Med J 2004; 21: 446-8.

33. Flanders SA, Halm EA. Guidelines for community-acquired pneumonia: are they reflected in practice? Treat Respir Med 2004; 3: 67-77.

34. Schouten JA, Hulscher ME, Kullberg BJ, et al. Understanding variation in quality of antibiotic use for community-acquired pneumonia: effect of patient, professional and hospital factors. J Antimicrob Chem 2005; 56: 575-582.

35. Heffelfinger JD, Dowell SF, Jorgensen JH, et al. Management of community-acquired pneumonia in the era of pneumococcal resistance: a report from the drug-resistant Streptococcus pneumoniae Therapeutic Working Group. Arch Intern Med 2000; 160: 1399-1408.

36. Genné D, Sommer R, Kaiser L, et al. Analysis of factors that contribute to treatment failure in patients with community-acquired pneumonia. Eur J Clin Microbiol Infect Dis 2006; 25: 159-166.

37. Menéndez R, Torres A, Zalacain R, et al. Risk factors of treatment failure in community-acquired pneumonia: implication for disease outcome. Thorax 2004; 59: 960-965.

38. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997; 336: 243-250.

39. Anevlavis S, Bouros D. Scoring systems in community acquired pneumonia. Pneumon 2009; 22:286-289.