Guidelines for the Treatment of Community-acquired Pneumonia

Predictors of Adherence and Outcome

Rosario Menéndez, Antoni Torres, Rafael Zalacaín, Javier Aspa, Juan J. Martín-Villasclaras, Luis Borderías, José M. Benítez-Moya, Juan Ruiz-Manzano, Felipe Rodríguez de Castro, José Blanquer, Diego Pérez, Carmen Puzo, Fernando Sánchez-Gascón, José Gallardo, Carlos Álvarez, and Luis Molinos, on behalf of the NEUMOFAIL Group

Servicio de Neumología, Hospital Universitario La Fe; Cuidados Intensivos, and Servicio de Neumología, Hospital Clínico, Valencia; Instituto de Neumología y Alergia, Hospital Clinic (Red Gira FIS-ISCIII-03/063); Servicio de Neumología, Hospital San Pablo, Barcelona; Servicio de Neumología, Hospital de Cruces, Bilbao; Servicio de Neumología, Hospital de la Princesa; Servicio de Neumología, Hospital 12 de Octubre, Madrid; Servicio de Neumología, Hospital Carlos Haya, Malaga; Servicio de Neumología, Hospital San Jorge, Huesca; Servicio de Neumología, Hospital Virgen de la Macarena, Sevilla; Servicio de Neumología, Hospital Germans Trias i Pujol, Badalona; Servicio de Neumología, Hospital Dr. Negrín, Las Palmas de Gran Canaria; Servicio de Neumología, Hospital General Universitario, Murcia; Servicio de Neumología, Hospital General, Guadalajara; and Servicio de Neumología, Hospital Ntra. Sra. de Covadonga, Oviedo, Spain

Rationale: **Some studies highlight the association of better clinical responses with adherence to guidelines for empiric treatment of community-acquired pneumonia (CAP), but little is known about factors that influence this adherence.** *Objectives:* **Our objectives were to identify factors influencing adherence to the guidelines for empiric treatment of CAP, and to evaluate the impact of adherence on outcome.** *Methods*: **We studied 1,288 patients with CAP admitted to 13 Spanish hospitals. Collected variables included the patients' clinical and demographic data, initial severity of the disease, antibiotic treatment, and specialty and training status of the prescribing physician.** *Measurements and Main Results:* **Adherence to guidelines was high (79.7%), with significant differences between hospitals (range, 47–97%) and physicians (pneumologists, 81%; pneumology residents, 84%; nonpneumology residents, 82%; other specialists, 67%). The independent factors related to higher adherence were hospital, physician characteristics, and initial high-risk class of Fine, whereas admission to intensive care unit decreased adherence. Seventy-four patients died (6.1%), and treatment failure was found in 175 patients (14.2%). After adjusting for Fine risk class, adherence to the guidelines was found protective for mortality (odds ratio [OR], 0.55; 95% confidence interval [CI], 0.3–0.9) and for treatment failure (OR, 0.65; 95% CI, 0.5–0.9). Treatment prescribed by pneumologists and residents was associated with lower treatment failure (OR, 0.6; 95% CI, 0.4–0.9).** *Conclusions:* **Adherence to guidelines mainly depends on the hospital and the specialty and training status of prescribing physicians. Nonadherence was higher in nonpneumology specialists, and is an independent risk factor for treatment failure and mortality.**

Keywords: antibiotic; compliance; mortality; pneumologist; resident

Community-acquired pneumonia (CAP) has an incidence of 3 to 5 cases per 1,000 persons, and a mortality of 5 to 15% in hospitalized patients (1). Initial antibiotic treatment is key for the resolution of infection and for prognosis, with higher mortality if the treatment is inappropriate. The difficulty in selecting the appropriate antibiotics arises because CAP can be caused by multiple organisms, which cannot be identified on clinical and radiographic findings, and the conventional microbiological methods have limited sensitivity and specificity (2).

It has been shown that the shorter the time between diagnosis and initiation of treatment, the better the impact on prognosis (3, 4), and this is more effective than to be adequate to results from microbiological tests if this delays treatment (5, 6). Thus, usually the antibiotic treatment is chosen empirically at the time of diagnosis. Evidence-based guidelines have been developed by scientific societies to assist physicians in the selection of antibiotics (7–9) and to reduce variability in clinical care (10).

Some studies have shown that adherence to guidelines results in reduced need for hospitalization, shorter stays, and lower mortality. Nevertheless, adherence is variable among clinicians (11) and may be due to individual disposition (12, 13). Halm and coworkers (14) identified factors associated with nonadherence to guidelines in the decision of hospitalizing patients with CAP, but there is little information regarding factors that influence adherence to guidelines for the selection of treatment of CAP (13).

The differences in adherence to guidelines between specialists in pneumology and other physicians have not been studied enough, and it is not known if adherence is also influenced by patient characteristics such as comorbid condition or initial severity. This is an important issue because some processes of care for CAP, with an impact on outcome, could be improved (15–17), and the choice of antibiotic treatment is one of the processes associated with differences in the outcome of hospitalized CAP (18–20). Efforts should be directed to identify factors that influence the adherence to guidelines to prepare strategies to improve it.

The primary objective of this study was to evaluate adherence to the Spanish guidelines for the empiric antibiotic treatment of CAP, and to identify factors related to compliance with these guidelines. This study analyzed factors associated with the

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Investigators in the NEUMOFAIL Research Study Group: Rosalía Domenech, Hospital Universitario La Fe, Valencia; Malina Ioanas, Hospital Clinic, Barcelona; Ainhoa Gómez Bonilla, Hospital de Cruces, Bilbao; Olga Rajas, Hospital de la Princesa, Madrid; Marta Arzola, Hospital Carlos Haya, Málaga; Agustín Valido, Hospital Virgen Macarena de Sevilla; Felipe Andreo, Hospital Germans Trias i Pujol, Badalona; Alicia López, Hospital Dr. Negrín, Las Palmas de Gran Canaria; Manuel Brufal, Hospital San Pablo, Barcelona; and Damian Malia, Hospital General de Murcia.

Correspondence and requests for reprints should be addressed to Rosario Menéndez, M.D., Servicio de Neumología, Hospital Universitario La Fe, Avda. de Campanar 21, 46009 Valencia, Spain. E-mail: rmenend@separ.es

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characteristics of the patients, the initial severity of the infection, and the specialty and training status of the prescribing physician. Furthermore, we aimed to study the impact of adherence on treatment failure and mortality. A part of this work has been published as an abstract (21).

METHODS

Design and Study Population

Between October 2000 and April 2001, a multicenter observational prospective study was carried out in 15 Spanish hospitals (22). All hospitals are part of the Spanish National Health System and have a pneumology service. The study cohort comprised nonimmunosupressed adult patients hospitalized because of CAP. (Additional details are provided in the online supplement.)

The attending physician prescribed the initial empiric antibiotic therapy. Compliance with the latest consensus Spanish guidelines from the Sociedad Espanõla de Quimioterapia-Sociedad Espanõla de Neumologia y Cirugia Torácica (SEQ-SEPAR) (23) was evaluated. Data on the prescribing physician were collected and categorized as follows: pneumologist (4 years' training), other internal medicine specialist, resident in pneumology (undergoing training), or resident in another specialty. Initial empiric treatment was considered to adhere to guidelines when antibiotics were prescribed as follows: in hospitalized patients with CAP, either third-generation cephalosporin (cefotaxime or ceftriaxone), or amoxycillin-clavulanate combined or not combined with a macrolide, or fluoroquinolone (third or fourth generation) in monotherapy; in patients admitted to the intensive care unit (ICU), third- or fourth-generation cephalosporin combined with intravenous macrolide or with intravenous fluoroquinolone (levofloxacin; *see* Table E1 in the online supplement). All other antibiotic regimens were considered as being nonadherent to guidelines. Outcome variables were treatment failure (22) and mortality. (Additional details are available in the online supplement.)

Data Collection

Demographic and clinical characteristics and analytic data have been described elsewhere (22). For the present study, data for age, sex, prior antibiotic treatment, adherence to guidelines, comorbidity, signs of initial severity, and pneumonia severity index (PSI) or the risk class of Fine and colleagues (24) were analyzed.

Statistical Study

Univariate analysis. Statistical analyses were performed using the SAS 8.2 software program (SAS, Inc., Cary, NC). Qualitative variables were compared using the χ^2 test. Differences in quantitative variables were assessed with analysis of variance or with a Kruskal-Wallis test when appropriate. Values of $p \leq 0.05$ were considered significant. Variables dichotomized for univariate analysis were tachycardia ($\geq$ 100 beats/minute), tachypnea ($\geq$ 30 breaths/minute), hypotension (systolic blood pressure $\leq$ 90), and hypoxemia ($Pa_{O_2} \leq$ 60 mm Hg).

Multivariate analysis. A logistic regression analysis to predict adherence to guidelines was performed using as independent variables those found significant in univariate analyses (unemployed status, previous antibiotic treatment, confusion, hypotension, admission to ICU, PSI, hospital, and prescribing physician). The PSI was dichotomized as risk class I or greater than I, based on the found overall adherence (70.5% for risk class I and 77–82% for the rest). Four dummy variables for each prescribing physician were introduced into the model so as to analyze the independent effect of each physician category. Interactions between hospital, physicians, comorbid conditions, and PSI were assessed.

Two logistic regression analyses were performed to assess the impact of adherence and prescribing physician on mortality and treatment failure. The independent variables were as follows: adherence, prescribing physician, and PSI dichotomized as low (Fine risk classes I–III) and high (risk classes IV–V).

The logistic regression analyses were performed with a likelihood ratio–based stepwise method. Variables that reached a p value of 0.05 or less were considered significant and their odds ratios (OR) with 95% confidence intervals (CI) were calculated. The Hosmer and Lemeshow (25) goodness-of-fit test was used to evaluate the adequacy of the models. The areas under the receiver operating characteristic curves were also calculated.

RESULTS

The original study comprised 1,424 patients from 15 Spanish hospitals. Data on the prescribing physician were available for 1,228 patients (additional details provided in the online supplement) who were included in the study. Eighty-six (7%) were admitted to ICU, 74 died (6.1%), and 175 had treatment failure (14.2%). The main demographic characteristics, comorbidities, and PSI scores have been published elsewhere (22).

The initial empiric therapy prescribed on admission was adherent to the SEQ-SEPAR guidelines in 979 patients (79.7%); of those, adherence was 80% in patients hospitalized in the ward (921/1,142), and 67.4% in those admitted to ICU (58/86; $p < 0.05$). (Additional details on antibiotic regimes are provided in the online supplement). Adherence to guidelines differed between hospitals, with a range of 47 to 97% (*see* Table E2).

The initial treatment was prescribed as follows: 786 patients (64%) were treated by residents (239 [19%] by a resident in pneumology and 547 [45%] by a resident in other specialties), 244 (20%) by a trained specialist in pneumology, and 198 (16%) by other specialists in internal medicine. In patients hospitalized in ward, adherence to the guidelines with respect to physician was as follows: pneumologists, 187 of 230 patients (81%); pneumology residents, 196 of 231 patients (85%); residents of other specialties, 427 of 524 patients (82%); and other specialists, 111 of 157 patients (71%) adhered to the guidelines ($p < 0.05$). In patients admitted to ICU, patient adherence was as follows: pneumologists, 10 of 14 patients (71%); pneumology residents, 5 of 8 patients (63%); residents of other specialties, 21 of 23 patients (91%); and other specialists, 22 of 41 patients (54%) adhered to the guidelines ($p < 0.05$).

Table 1 shows the adherence to guidelines in the whole group stratified according to the characteristics and comorbidities of the patients. We did not find significant differences with regard to age, sex, or tobacco and alcohol intake. Adherence was lower in patients who were unemployed, with confusion, and with hypotension. Table 2 shows the results of adherence stratified by characteristics of the patients as well as the prescribing physician. The presence of comorbidity decreased adherence to guidelines when the treatment was prescribed by a nonpneumology specialist. Adherence with respect to initial severity also showed differences between prescribing physicians: the pneumology specialists and residents had increased adherence to the guidelines in patients with severe CAP (risk class V), whereas in the nonpneumology specialists, this was significantly ($p < 0.05$) decreased.

Multivariate adherence predictors. A stepwise regression logistic analysis of 1,134 patients was performed to predict adherence. The independent variables included were unemployed status, previous antibiotic treatment, confusion, hypotension (systolic blood pressure $\leq$ 90), admission to ICU, Fine risk class, hospital, and prescribing physician. Interactions between hospital, physicians, comorbid conditions, and initial severity were assessed and not found. The χ^2 goodness-of-fit analysis demonstrated the adequacy of the model ($p = 0.2$). The independent factors related to higher adherence were hospital, physician characteristics, and initial Fine high-risk class, whereas admission to the ICU decreased adherence (Table 3).

Adherence and Outcome: Treatment Failure and Mortality

Univariate statistical analyses. Seventy-four patients died (6.1%), and treatment failure was found in 175 patients (14.2%). The

TABLE 1. ADHERENCE TO GUIDELINES, ACCORDING TO RISK FACTORS AND COMORBIDITY

	Risk Factor Present, Adherence/Total (%)			
	Yes	No	OR	p
Host factors				
Unemployed	21/36 (58.3)	958/1,192 (80.4)	0.3 (0.2–0.7)	0.001
PabT	300/363 (82.6)	677/863 (78.5)	1.3 (1–2)	0.095
Comorbidity				
COPD	287/354 (81.0)	666/846 (78.7)	1.1 (0.8–1.6)	0.402
Asthma	66/89 (74.2)	893/1,115 (80.1)	0.7 (0.4–1.1)	0.181
Cardiac	298/359 (83.0)	676/861 (78.5)	1.4 (1–2)	0.07
CNS	140/186 (75.3)	836/1,039 (80.5)	0.7 (0.5–1.1)	0.105
Diabetes	161/209 (77.0)	816/1,014 (80.5)	0.8 (0.5–1.1)	0.26
Renal	87/114 (76.3)	894/1,108 (80.7)	0.7 (0.5–1.4)	0.3
Related symptoms				
Confusion	94/134 (70.2)	879/1,088 (80.8)	0.6 (0.4–0.8)	0.004
Tachypnea ⩾ 30	218/281 (77.6)	761/947 (80.4)	0.8 (0.6–1.1)	0.309
BPs ⩽ 90	18/35 (51.4)	962/1,193 (80.6)	0.3 (0.1–0.5)	0.001

Definition of abbreviations: BPs = systolic blood pressure; CNS = central nervous system; COPD = chronic obstructive pulmonary disease; OR = odds ratio; PabT = previous antibiotic treatment.

overall treatment failure (19.7 vs. 13%) and mortality (8.9 vs. 5.4%) were significantly greater in the group of patients treated with schedules nonadherent to the guidelines (Table 4). Adherence reduced treatment failure (unadjusted OR, 0.66; 95% CI, 0.43–0.87) and mortality (OR, 0.58; 95% CI, 0.35–0.97). For patients admitted to the ward, treatment failure in the adherent group was 10.9 versus 13.1% in the nonadherent group ($p = 0.36$), and mortality was 3.9 versus 6.4%, respectively ($p = 0.09$). In ICU patients who received adherent treatment, treatment failure was 44.8 versus 71.4% ($p = 0.02$), and mortality was 29.3 versus 29.6%, respectively ($p = 0.6$; *see* Table E3 for patients stratified by ICU and non-ICU).

Comparing the prescribing physicians, we found that patients treated by nonpneumology specialists with schemes not adherent to the guidelines showed a greater percentage of treatment failure and death (albeit the latter did not reach statistical significance).

Multivariate analysis. After adjustment for initial severity, adherence to the guidelines (OR, 0.65; 95% CI, 0.5–0.9) and treatment prescribed by the pneumologist or the residents were protective against treatment failure, whereas only adherence was protective against mortality (OR, 0.55; 95% CI, 0.3–0.9; Table 5). The χ^2 goodness-of-fit analysis demonstrated the adequacy of the model ($p = 0.22$).

DISCUSSION

The most relevant findings of our study are as follows: (*1*) adherence to guidelines greatly differs between hospitals and is significantly lower in nonpneumology specialists, (*2*) patients with confusion and hypotension are treated more often with regimens that do not comply with guidelines, (*3*) nonpneumology specialists have a lower adherence to the guidelines when treating patients

TABLE 2. ADHERENCE TO GUIDELINES ACCORDING TO PATIENT AND PRESCRIBING PHYSICIAN CHARACTERISTICS

	Specialists		Residents	
Characteristics	Non-Pneu (%)	Pneu (%)	Non-Pneu (%)	Pneu (%)
Host factors				
Unemployed	4/11 (36.7)	6/10 (60.0)	6/8 (75.0)	5/7 (71.4)
PabT	34/45 (75.6)	71/86 (82.6)	142/161 (88.2)	53/71 (74.7)
Comorbidity				
COPD	46/66 (69.7)	63/72 (87.5)	118/149 (79.2)	60/67 (89.5)
Asthma	10/17 (58.8)	19/21 (90.5)	24/33 (72.7)	13/18 (72.2)
Cardiac	44/65 (67.7)	53/59 (89.8)	138/166 (83.1)	63/69 (91.3)
CNS	14/27 (51.9)	21/23 (91.3)	76/101 (75.6)	29/35 (82.9)
Diabetes	20/34 (58.8)	33/36 (91.7)	82/107 (76.6)	26/32 (81.2)
Renal	19/33 (57.6)	9/10 (90)	44/55 (80)	15/16 (93.7)
Related symptoms				
Confusion*	15/37 (40.5)	16/18 (88.9)	47/59 (79.7)	16/20 (80.0)
Tachypnea ⩾ 30	38/60 (63.3)	37/46 (80.4)	100/117 (85.5)	43/58 (74.1)
BPs ⩽ 90*	3/7 (42.9)	5/5 (100.0)	7/17 (41.2)	3/6 (50.0)
Fine risk class*				
I	17/21 (85)	24/36 (66.6)	30/41 (73.2)	15/24 (62.5)
II	21/29 (72.6)	41/54 (75.9)	87/103 (84.4)	48/55 (87.3)
III	28/43 (65.1)	59/65 (90.7)	121/154 (78.5)	55/61 (90.1)
IV	43/63 (68.2)	61/75 (81.3)	140/168 (83.3)	68/81 (77.2)
V	24/42 (57.1)	13/14 (92.8)	55/65 (84.6)	15/18 (83.3)

Definition of abbreviations: BPs = systolic blood pressure; CNS = central nervous system; COPD = chronic obstructive pulmonary disease; PabT = previous antibiotic treatment; Pneu = pneumologist.

* $p < 0.05$.

TABLE 3. PREDICTORS OF ADHERENCE TO GUIDELINES: MULTIVARIATE ANALYSIS

Independent Variables	OR (*95% CI*)
Hospital 10 vs. 13	0.02 (0.003–0.07)
Hospital 6 vs. 13	0.026 (0.004–0.094)
Hospital 2 vs. 13	0.04 (0.007–0.162)
Hospital 7 vs. 13	0.058 (0.009–0.22)
Hospital 4 vs. 13	0.092 (0.014–0.359)
Hospital 9 vs. 13	0.154 (0.24–0.574)
Hospital 3 vs. 13	0.215 (0.033–0.789)
Hospital 12 vs. 13	0.224 (0.024–2.092)
Hospital 1 vs. 13	0.327 (0.046–1.514)
Hospital 5 vs. 13	0.341 (0.048–1.602)
Hospital 11 vs. 13	0.347 (0.043–2.234)
Hospital 8 vs. 13	0.530 (0.078–2.226)
Admission to ICU	0.43 (0.24–0.78)
Pneumologist vs. others	5.24 (2.74–10.21)
Pneumology resident vs. others	3.72 (2.04–6.87)
Nonpneumology resident vs. others	1.41 (0.86–2.28)
Fine classification: II–V vs. I	2.35 (1.37–3.97)

Definition of abbreviations: CI = confidence interval; ICU = intensive care unit; OR = odds ratio.

Area under receiver operating characteristic curve: 0.8. OR between two hospitals is calculated as follows: for example, OR Hospital 10 vs. Hospital 6 = OR Hospital 10 vs. 13 × 1/OR Hospital 6 vs. 13: 0.02 × 1/0.026 = 0.769.

with severe CAP and greater risk for treatment failure, and (*4*) adherence to the guidelines is an independent protective factor for treatment failure and death.

In our study, 84% of the patients received the initial treatment from a pneumologist or a resident, with a high global adherence to guidelines, although with great differences among hospitals. We have confirmed the large variability in compliance with guidelines between hospitals even in the same country (26). Differences between hospitals prove the heterogeneity in treating CAP and possibly are due to different reasons, such as local epidemiologic peculiarities and, mainly, a shared collective attitude. In the three hospitals where the adherence of pneumologists/pneumology residents was the lowest (Hospitals 6, 9, and 12), the global adherence was also low. This might reflect the effect of nonadherence of pneumologists on the behavior of others physicians. In general, our findings reveal that trained and trainee pneumologists showed a high degree and similar pattern of compliance.

This higher grade of adherence by the pneumologists is probably due to the better access these clinicians have to recommended guidelines, the rapid dissemination of current guidelines, and the capacity for prompt decision by the specialist. Clinicians in the course of their training are also very receptive to the information made available by the scientific societies, and sensitive to the opinions of the experts (14). Clinicians in nonrelated fields use treatment schemes that often do not adhere to the specialist guidelines and, as such, our findings sound the alert regarding lack of adherence when the treatment is provided by clinicians who are not specialists in the patient's specific condition (27).

In some countries, many patients with CAP are treated by general practitioners or other specialists, so there is a need to disseminate and implement guidelines among those physicians. Switzer and colleagues (28) found different and low levels of awareness of guidelines between generalists and even pneumologists. They found that a positive attitude toward guidelines correlated with a higher awareness and adherence more than specialty itself did. Other reasons for nonadherence could include the difficulty in the application of the guidelines in some individual patients.

When analyzing patient characteristics associated with adherence to the guidelines, we found a pattern of behavior, which was similar between the residents and pneumologists, with respect to patient comorbidity and signs of severity of CAP. The presence of concomitant diseases almost doubled the lack of adherence in other specialists, especially in patients with diabetes, or central nervous system and renal disorders, without an evident explanation. These data are important because comorbidity is frequent among hospitalized patients with CAP (29), and is the cause of poor prognosis (30, 31).

Compliance with guidelines was lower in the two extremes of severity of CAP: in the most severe—that is, those admitted to ICU—and in the least severe cases (Fine risk class I). Furthermore, the behavior of physicians was opposite in pneumologists and other specialists in these circumstances: although in severe CAP (Fine risk class V), adherence was higher for pneumology specialists and residents and lower for nonpneumology specialists, the opposite happened in risk class I. This is of considerable note because the former are at very high risk of death, and mortality increases if the prescribed treatment does not adhere to the guidelines. Signs of severity of CAP, such as hypotension and confusion, were associated with lower adherence, especially in nonpneumology specialists. These signs of severity are widely known by pneumologists, and well documented on the severity scales that are commonly used in the management of CAP (24, 32). Our results highlight an area warranting improvement in the management of CAP (33). In countries where patients are treated by nonpneumology specialists, it would be important to confirm our findings to increase the awareness of signs of severity of CAP.

The initial antibiotic treatment is among the processes and outcome measures used to assess the quality of hospital care (34, 35). Several studies have found lower mortality when the antibiotic treatment adheres to guidelines (19, 36–38). Our results confirm the independent protective effect of adherence to guidelines on mortality and treatment failure. In a prior publication, we found that treatment failure was lower when treatment was adherent, and it was independently associated with fluorquinolone, but the independent effect of the prescribing physician was not analyzed (22). In addition to adherence, when the treat-

TABLE 4. TREATMENT FAILURE AND OVERALL MORTALITY ACCORDING TO ADHERENCE AND PRESCRIBING PHYSICIAN

Prescribing Physician	Treatment Failure			Mortality		
	n	%	p	n	%	P
Pneumology resident						
Adherent	16/201	8.0	0.04	8/200	4.0	0.29
Nonadherent	7/38	18.4		3/38	7.9	
Nonpneumology resident						
Adherent	57/445	12.8	0.40	25/436	5.7	0.23
Nonadherent	16/100	16		9/99	9.1	
Pneumologist						
Adherent	29/195	15.4	0.98	9/196	4.6	0.55
Nonadherent	7/46	15.2		3/45	6.6	
Other specialists						
Adherent	24/133	18	0.07	10/128	7.8	0.43
Nonadherent	19/65	29.2		7/63	11.1	
Total*						
Adherent	126/974	12.9	0.03	52/960	5.4	0.008
Nonadherent	49/249	19.7		22/245	8.9	

*Adherence reduces treatment failure (odds ratio, 0.66; 95% confidence interval, 0.43–0.87) and mortality (odds ratio, 0.58; 95% confidence interval, 0.35–0.97).

TABLE 5. PREDICTORS OF TREATMENT FAILURE AND MORTALITY: RESULTS OF REGRESSION LOGISTIC ANALYSES

	Treatment Failure		Mortality	
Independent Variables	OR (*95% CI*)	p	OR (*95% CI*)	P
Adherence	0.65 (0.5–0.9)	< 0.05	0.55 (0.3– 0.9)	< 0.03
Residents and pneumologists vs. others	0.6 (0.4–0.9)	< 0.05		
Fine IV–V vs. I–III			10.8 (5.3–21.8)	< 0.001

Definition of abbreviations: CI = confidence interval; OR = odds ratio.
Area under receiver operating characteristic curve for treatment failure and death: 0.6 and 0.77, respectively.

ment was prescribed by the pneumologist or residents, the treatment failure was lower. Marrie and coworkers (39) found that clinicians who treat a higher volume of patients with pneumonia achieve better outcomes, which could explain our findings.

The independent effect of adherence on mortality was demonstrated after adjusting by Fine risk class. However, because our study was observational and nonrandomized, possible limitations are that factors not assessed by the Fine risk class, or confounding variables that were not measured, could have influenced the outcome. These could include differences in the characteristics of the hospitals, differences in the management of CAP between hospitals (39), or factors arising during hospitalization. Another limitation is that we don't have a code for the actual medical provider and therefore we cannot perform clustered or hierarchic analyses.

In summary, we found that adherence to guidelines for the empiric treatment of CAP differs considerably between hospitals and prescribing physicians. The pattern of adherence in the residents was similar to that in pneumologists, in relation to comorbidity and severity of CAP. Adherence to guidelines was an independent protective factor for treatment failure and mortality. Our findings identify factors associated with nonadherence, and highlight inefficiencies and heterogeneity in clinical practice. Strategies for achieving better adherence need to be implemented to improve our medical practice.

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References

1. Kaplan V, Angus DC, Griffin MF, Clermont G, Scott Watson R, Linde-Zwirble WT. Hospitalized community-acquired pneumonia in the elderly: age- and sex-related patterns of care and outcome in the United States. *Am J Respir Crit Care Med* 2002;165:766–772.
2. San Pedro GS, Campbell GD Jr. Limitations of diagnostic testing in the initial management of patients with community-acquired pneumonia. *Semin Respir Infect* 1997;12:300–307.
3. Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for medicare patients hospitalized with community-acquired pneumonia. *Arch Intern Med* 2004;164:637–644.
4. Meehan TP, Fine MJ, Krumholz HM, Scinto JD, Galusha DH, Mockalis JT, Weber GF, Petrillo MK, Houck PM, Fine JM. Quality of care, process, and outcomes in elderly patients with pneumonia. *JAMA* 1997;278:2080–2084.
5. El-Solh AA, Aquilina AT, Dhillon RS, Ramadan F, Nowak P, Davies J. Impact of invasive strategy on management of antimicrobial treatment failure in institutionalized older people with severe pneumonia. *Am J Respir Crit Care Med* 2002;166:1038–1043.
6. Sanyal S, Smith PR, Saha AC, Gupta S, Berkowitz L, Homel P. Initial microbiologic studies did not affect outcome in adults hospitalized with community-acquired pneumonia. *Am J Respir Crit Care Med* 1999;160:346–348.
7. Niederman MS, Mandell LA, Anzueto A, Bass JB, Broughton WA, Campbell GD, Dean N, File T, Fine MJ, Gross PA, *et al.* Guidelines for the management of adults with community-acquired pneumonia: diagnosis, assessment of severity, antimicrobial therapy, and prevention. *Am J Respir Crit Care Med* 2001;163:1730–1754.
8. Bartlett JG, Dowell SF, Mandell LA, File TM Jr, Musher DM, Fine MJ. Practice guidelines for the management of community-acquired pneumonia in adults. Infectious Diseases Society of America. *Clin Infect Dis* 2000;31:347–382.
9. Macfarlane J, Boswell T, Douglas G, Finch R, Holmes W, Honeybourne D, Lim WS, Marriott R, Nathwani D, Sane P, *et al.* BTS guidelines for the management of community acquired pneumonia in adults. *Thorax* 2001;56(IV):1–64.
10. Fine JM, Fine MJ, Galusha D, Petrillo M, Meehan TP. Patient and hospital characteristics associated with recommended processes of care for elderly patients hospitalized with pneumonia: results from the Medicare Quality Indicator System Pneumonia Module. *Arch Intern Med* 2002;162:827–833.
11. Feagan BG, Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Vandervoort MK. Treatment and outcomes of community-acquired pneumonia at Canadian hospitals. *CMAJ* 2000;162:1415–1420.
12. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, Rubin HR. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999;282:1458–1465.
13. Marras TK, Chan CK. Use of guidelines in treating community-acquired pneumonia. *Chest* 1998;113:1689–1694.
14. Halm EA, Atlas SJ, Borowsky LH, Benzer TI, Metlay JP, Chang YC, Singer DE. Understanding physician adherence with a pneumonia practice guideline: effects of patient, system, and physician factors. *Arch Intern Med* 2000;160:98–104.
15. Battleman DS, Callahan M, Thaler HT. Rapid antibiotic delivery and appropriate antibiotic selection reduce length of hospital stay of patients with community-acquired pneumonia: link between quality of care and resource utilization. *Arch Intern Med* 2002;162:682–688.
16. Englert J, Davis KM, Koch KE. Using clinical practice analysis to improve care. *Jt Comm J Qual Improv* 2001;27:291–301.
17. Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Vandervoort MK, Feagan BG. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. CAPITAL Study Investigators. Community-Acquired Pneumonia Intervention Trial Assessing Levofloxacin. *JAMA* 2000;283:749–755.
18. File TM. Community-acquired pneumonia. *Lancet* 2003;362:1991–2001.
19. 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.
20. 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.
21. Menendez R, Torres A. Neumofail Group. Adherence to guidelines for treatment of community-acquired pneumonia: related factors [abstract]. *Proc Am Thorac Soc* 2005;2:A797.
22. Menendez R, Torres A, Zalacain R, Aspa J, Martin Villasclaras JJ, Borderias L, Benitez Moya JM, Ruiz-Manzano J, Rodriguez de Castro F, Blanquer J, *et al.* Risk factors of treatment failure in community acquired pneumonia: implications for disease outcome. *Thorax* 2004; 59:960–965.
23. Frias J, Gomis M, Prieto J, Mensa J, Bouza E, Garcia-Rodriguez JA, Torres A, Dorca J, Zalacain R, Garcia de Lomas J. Initial empirical antibiotic treatment of community-acquired pneumonia [in Spanish]. *Rev Esp Quimioter* 1998;11:255–261.
24. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, Coley CM, Marrie TJ, Kapoor WN. A prediction rule to identify low-

risk patients with community-acquired pneumonia. *N Engl J Med* 1997; 336:243–250.
25. Hosmer D, Lemeshow S. Applied logistic regression. New York: John Wiley & Sons; 1989.
26. Campbell SG. The use of clinical practice guidelines for community-acquired pneumonia in hospitals in Atlantic Canada. *Can Respir J* 2004;11:301–303.
27. Dean NC, Silver MP, Bateman KA. Frequency of subspecialty physician care for elderly patients with community-acquired pneumonia. *Chest* 2000;117:393–397.
28. Switzer GE, Halm EA, Chang CC, Mittman 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.
29. Fine MJ, Stone RA, Singer DE, Coley CM, Marrie TJ, Lave JR, Hough LJ, Obrosky DS, Schulz R, Ricci EM, *et al.* Processes and outcomes of care for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team (PORT) cohort study. *Arch Intern Med* 1999;159:970–980.
30. Mortensen EM, Coley CM, Singer DE, Marrie TJ, Obrosky DS, Kapoor WN, Fine MJ. Causes of death for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team cohort study. *Arch Intern Med* 2002;162:1059–1064.
31. Greenfield S, Aronow HU, Elashoff RM, Watanabe D. Flaws in mortality data: the hazards of ignoring comorbid disease. *JAMA* 1988;260:2253–2255.
32. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, Lewis SA, Macfarlane JT. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377–382.
33. Meehan TP, Weingarten SR, Holmboe ES, Mathur D, Wang Y, Petrillo MK, Tu GS, Fine JM. A statewide initiative to improve the care of hospitalized pneumonia patients: the Connecticut Pneumonia Pathway Project. *Am J Med* 2001;111:203–210.
34. Nathwani D, Rubinstein E, Barlow G, Davey P. Do guidelines for community-acquired pneumonia improve the cost-effectiveness of hospital care? *Clin Infect Dis* 2001;32:728–741.
35. Barlow GD, Lamping DL, Davey PG, Nathwani D. Evaluation of outcomes in community-acquired pneumonia: a guide for patients, physicians, and policy-makers. *Lancet Infect Dis* 2003;3:476–488.
36. Dudas V, Hopefl A, Jacobs R, Guglielmo BJ. Antimicrobial selection for hospitalized patients with presumed community-acquired pneumonia: a survey of nonteaching US community hospitals. *Ann Pharmacother* 2000;34:446–452.
37. Menendez R, Ferrando D, Valles JM, Vallterra J. Influence of deviation from guidelines on the outcome of community-acquired pneumonia. *Chest* 2002;122:612–617.
38. Mortensen EM, Restrepo M, Anzueto A, Pugh J. Effects of guideline-concordant antimicrobial therapy on mortality among patients with community-acquired pneumonia. *Am J Med* 2004;117:726–731.
39. Marrie TJ, Carriere KC, Jin Y, Johnson DH. Mortality during hospitalisation for pneumonia in Alberta, Canada, is associated with physician volume. *Eur Respir J* 2003;22:148–155.