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Development of a prognostic index for 90-day mortality among patients discharged after hospitalization for community-acquired pneumonia

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ABSTRACT

Background: Although patients hospitalized for community-acquired pneumonia (CAP) experience substantial short-term mortality following hospital discharge, few studies have focused on identifying factors that predict post-hospitalization mortality in this population. Our objective was to develop and validate a prognostic index for 90-day mortality after hospital discharge among patients with CAP.

Methods: The prognostic index was derived in 1117 adult patients discharged between 2003 and 2007 from a general hospital following hospitalization for CAP. It was validated among 646 consecutive patients with CAP discharged from three other hospitals between November 1, 2005, and July 31, 2006. Risk factors evaluated included host-related factors, severity upon admission, in-hospital management, and bacteriology.

Results: In the derivation cohort, 3 factors were independently associated with 90-day mortality: pre-illness functional status, Charlson index (composite measure of co-morbid illnesses), and severity upon admission**.** Mortality at 90 days was 0.7% in the low-risk group, 3.5% in the intermediate-risk group, and 17.2% in the high-risk group. In the validation cohort, 90-day mortality was 0.6%, 3.9%, and 19.6% respectively. Compared with the low-risk group, the odds ratio for mortality was 43.5 for the high-risk group. The risk categories showed an area under the receiver operating characteristic curve of 0.79 in the derivation cohort and 0.82 in the validation cohort.

Conclusions: The prognostic index accurately stratifies patients hospitalized for CAP into low-, intermediate-, and high-risk groups for 90-day mortality upon discharge. The use of this index could help clinicians improve outcomes in this vulnerable population by targeting specific interventions to each group.

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Abbreviation: CAP, community-acquired pneumonia; CURB, **C**onfusion, **U**rea nitrogen, **R**espiratory rate, **B**lood pressure; PSI, pneumonia severity index

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INTRODUCTION

With more than 5 million cases occurring annually in the United States alone, community-acquired pneumonia (CAP) is a leading cause of hospital admissions, not to mention morbidity and mortality. Numerous investigations have yielded important information about factors that influence the evolution and treatment of CAP during hospitalization (1-5). The period after discharge from the hospital, though a promising step in the resolution of CAP, should not be considered an all-clear signal. On the contrary, patients who survive hospitalization for CAP are prone to readmission and are at high risk of dying (6-9). The 1-year mortality is considerably higher than that of the general population or a control population hospitalized for reasons other than CAP (8). To date, only a few trials have examined risk factors for short-term mortality focusing on post-discharge period for a CAP-related hospitalization (6, 7).

A study conducted in North America identified clinical factors that were useful in deciding whether a patient with CAP was sufficiently stable to be discharged from the hospital (6). The presence of two or more features of clinical instability predicted a significant chance of readmission or mortality. This assessment is now recommended as part of discharge planning (10). However, a patient's trajectory after discharge is influenced by numerous other factors, including host factors, bacteriologic factors, the severity of CAP upon admission, the evolution of the disease during hospitalization, and the therapy received (11).

The aim of this study was to design and validate an accurate, easy-to-use index, the CAP-90, capable of classifying adults with CAP as low, intermediate, or high risk for 90-day mortality after hospital discharge.

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METHODS

Selection criteria

Community-acquired pneumonia was defined as pulmonary infiltrate on chest radiograph not known to be old and symptoms consistent with pneumonia, including cough, dyspnea, fever, and/or pleuritic chest pain not acquired in a hospital or a nursing home residence. Patients with pneumonia were excluded if they were known to be positive for human immunodeficiency virus, chronically immunosuppresed (defined as immunosuppression for solid organ transplantation, postsplenectomy, receiving ≥10 mg/day of prednisone or the equivalent for more than 30 days, treatment with other immunosuppressive agents, or neutropenia, i.e., $<1.0 \times 10^9$/L neutrophils), or who had been hospitalized for the previous 14 days. The study sample was restricted to patients who survived the index hospitalization.

Derivation and validation cohort

The prognostic index was derived in a cohort from Galdakao Hospital, a 400-bed general teaching hospital in the Basque Country (northern Spain) serving a population of 300,000 inhabitants. A total of 1189 consecutive patients 18 years or older hospitalized for CAP between July 15, 2003, and June 30, 2007, in Galdakao Hospital were prospectively enrolled in an observational cohort study. Of these, 1117 survived the index hospitalization and satisfied all criteria for inclusion in the study. An external validation cohort was formed with 671 consecutive adult patients hospitalized for CAP between November 1, 2005, and July 31, 2006, in three nearby large teaching hospitals: Cruces Hospital in Vizcaya, Clinic Hospital in Barcelona, and La Fe Hospital in Valencia. Of these, 646 survived the index hospitalization and satisfied all criteria for inclusion in the analysis.

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The local ethics committees approved the project.

Predictors of mortality

Variables that may predict short-term mortality among patients discharged following hospitalization for CAP were selected and defined after an exhaustive literature review. To promote clinical utility, we arranged these into host-related factors (functional status measured by Katz index (12), age, gender, comorbid illness measured by Charlson index (13)), severity of illness upon admission (CURB (**C**onfusion, **U**rea nitrogen, **R**espiratory rate, **B**lood pressure) score (14), bilateral or multilobe radiographic involvement), factors related to in-hospital evolution (treatment failure, septic shock), stability upon hospital discharge, therapy-related factors (appropriate antibiotic according to local practice guidelines that are similar to ATS guidelines (15), administration of antibiotics within 8 hours of admission, antibiotics taken prior to admission, and use of mechanical ventilation), length of stay, and bacteriology-related factors.

Additional details are provided in the on line data supplement.

Outcomes

The primary outcome was all-cause mortality within 90 days of the index hospital discharge date. Vital status was initially determined by telephone interview 90 days after discharge. Reported deaths and dates of deaths were confirmed by review of medical records, public death registries, or both. Mortality data were available for the entire cohort within 90 days, except for two cases in the validation sample for whom the exact dates of death were unknown.

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Statistical analysis

Descriptive statistics included frequency tables and mean and standard deviation. Chi-square and Fisher's exact tests were performed for categorical variables, and the Student *t* test and nonparametric Wilcoxon tests were performed for continuous variables. Mortality within 90 days of hospital discharge was also compared between patients in the derivation and validation cohorts by means of a logistic regression model.

Univariate logistic regression models were first used to identify risk factors associated with 90-day mortality; we determined the odds ratio (OR) and 95% confidence interval (95% CI). Multivariate logistic regression models were then performed to identify the statistical significance and weight of each risk factor. The dependent variable was mortality within 90 days of discharge; the independent variables were factors identified as having $P<0.15$ in the univariate analysis. Two multivariate models were considered: one included baseline functional status, as measured by the Katz index; the other did not. The predictive accuracy of the prognostic models was determined by calculating the area under the receiver operating characteristic (ROC) curve (discrimination) (16) and by comparing predicted and observed mortality by means of the Hosmer and Lemeshow test (calibration) (17). Area under the curve (AUC) values were compared using the non-parametric method described by Hanley and NcNeil (18). Points were assigned to each predictive variable from the β parameter obtained in the 90-day mortality multivariate model. To create the CAP-90 index, we added the points assigned to each of the selected variables, with a higher score corresponding to a higher likelihood of 90-day mortality. Once the index was developed, we created three categories (low, intermediate, and high risk) in relation to the predicted mortality.

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After developing the CAP-90 index, we attempted to validate it in a separate cohort. First, the predictive accuracy of the point-based CAP-90 index was determined by calculating the AUC values in each cohort. Second, logistic regression models were performed in each cohort considering the low-risk group as the reference category. Finally, Kaplan-Meier curves were constructed for each of the three risk groups, and comparisons were performed by the log-rank test. For the comparison of survival curves between derivation and validation cohorts, a Cox proportional hazard regression model was created, considering the risk group, the cohort, and the interaction between risk group and cohort as independent variables.

All effects were considered significant at $P<0.05$. All statistical analyses were performed using SAS for Windows statistical software, version 8.0 (SAS Institute, Inc., Carey, NC) and S-Plus 2000 (MathSoft Inc., 1999).

RESULTS

Patients in the derivation and validation cohorts differed significantly in several key characteristics (Table 1). In the derivation cohort, 36.8% of patients were discharged with 1 or more instability criteria, compared with 4.1% in the validation cohort. However, the rate of 90-day mortality after discharge was 4.9% (55/1117) in the derivation cohort and 3.3% (21/646) in the validation cohort, a non-significant difference that remained non-significant after adjustment. The introduced interaction terms were not statistically significant. The comorbidities of patients in the derivation and validation cohorts are described in Table E1 (in the online supplement).

Additional details are provided in the on line data supplement (Table E2, E3, E4).

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Table 1. Characteristics of patients hospitalized with community-acquired pneumonia who survived to hospital discharge in the derivation and validation cohorts.

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Characteristics	Derivation cohort (N=1117)	Validation cohort (N=646)	*P* value
Host related			
Baseline functional status*, mean (SD)	22.9 (11.0)	19.8 (9)	<0.001
Baseline functional status*			<0.001
15	440 (42.5)	391 (63.1)	
16-30	372 (35.9)	160 (25.8)	
>30	224 (21.6)	69 (11.1)	
Age, years, mean (SD)	69.4 (16.6)	66.9 (16.8)	0.003
Age >75 years	488 (43.7)	244 (37.8)	0.02
Women	388 (34.7)	222 (34.4)	0.88
Charlson index			0.008
0	389 (34.9)	237 (36.8)	
1	367 (32.9)	178 (27.6)	
2	214 (19.2)	113 (17.6)	
≥3	144 (12.9)	116 (18)	
Severity of illness in admission			
PSI risk class†			0.07
I-III	574 (51.4)	359 (55.8)	
IV-V	543 (48.6)	284 (44.2)	
CURB score‡			0.11
0	403 (36.1)	214 (33.1)	
1	460 (41.2)	257 (39.8)	
>1	254 (22.7)	175 (27.1)	
Bilateral or multilobe radiographic involvement	264 (23.6)	144 (22.4)	0.54
Process-of-care			
Appropriate antibiotic	1040 (93.2)	527 (86.5)	<0.001
Antibiotics within 8 hours from ED arrival	955 (87.7)	538 (86.1)	0.34
Prior antibiotics to admission	247 (22.1)	151 (23.7)	0.43
Mechanical ventilation	16 (1.4)	15 (2.3)	0.16
Length of stay (days)			
Mean (sd)	4.2 (3.8)	9.1 (8.1)	<0.001
>3	510 (45.7)	591 (91.6)	<0.001
In-hospital evolution			
Treatment failure	116 (10.4)	56 (8.7)	0.25
Septic shock	35 (3.1)	24 (3.7)-	0.51-
Number of instability criteria on discharge			<0.001
0	684 (63.2)	615 (95.9)	
≥1	399 (36.8)	26 (4.1)	
Causal microorganism			<0.001
Streptococcus pneumoniae	250 (22.4)	124 (19.2)	
Atypical bacterial pathogens	114 (10.2)	14 (2.2)	
Mixed infections	100 (9.0)	9 (1.4)	
Legionella pneumophila	38 (3.4)	22 (3.4)	
Atypical virus pathogens	13 (1.2)	3 (0.5)	
Others	37 (3.3)	40 (6.2)	
Unknown	565 (50.9)	434 (67.2)	

SD, standard deviation; ED, Emergency Department.

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Data are presented as numbers (percentage) unless otherwise stated. Percentages exclude patients with missing data. Treatment failure and instability criteria on discharge are defined in text.

* Baseline functional status was measured by Katz index (nº of patients = 1036 in derivation cohort and 620 in validation cohort); functional status range, 15 to 52 (excellent functional status, 15).

† Severity of illness on admission assessed with PSI (Pneumonia Severity Index).

‡ Severity of illness on admission assessed with CURB score (Confusion, Urea nitrogen, Respiratory rate, Blood pressure).

Derivation of the prognostic index

In univariate analyses, several host-related factors, severity of illness upon admission, and clinical instability at the time of discharge were associated with the likelihood of 90-day mortality (Table 2).

Table 2. Factors significantly associated in univariate analyses with mortality within 90 days of hospital discharge in the derivation cohort (N=1117).

Factors	OR (95% CI)	*P* value
Host related		
Baseline functional status (continuous)*	1.09 (1.07 to 1.11)	<0.001
Baseline functional status*		
16-30 vs. 15	4.86 (1.36 to 17.34)	0.02
>30 vs. 15	22.53 (6.79 to 74.70)	<0.001
Age, years	1.06 (1.04 to 1.09)	<0.001
Age >75 years	3.33 (1.84 to 6.03)	<0.001
Male vs. female	1.96 (1.02 to 3.77)	0.04
Charlson index		
1 vs. 0	3.05 (1.09 to 8.54)	0.03
2 vs. 0	6.21 (2.24 to 17.19)	<0.001
≥3 vs. 0	12.39 (4.55 to 33.69)	<0.001
Severity of illness in admission		
CURB score†		
1 vs. 0	1.97 (0.92 to 4.22)	0.08
>1 vs. 0	3.91 (1.83 to 8.37)	<0.001
Bilateral or multilobe radiographic involvement	1.61 (0.90 to 2.89)	0.11
Process-of-care		
Appropriate antibiotic	0.93 (0.33 to 2.64)	0.89
Antibiotics within 8 hours	0.82 (0.38 to 1.77)	0.60
Prior antibiotics to admission	1.22 (0.65 to 2.27)	0.54
Mechanical ventilation‡	---	---
Length of stay (days)		
Length of stay, days	1.05 (1.00 to 1.10)	0.06
>3 vs. ≤3	1.70 (0.98 to 2.94)	0.06
In-hospital evolution		

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Treatment failure	2 (0.98 to 4.09)	0.06
Septic shock	0.56 (0.08 to 4.17)	0.57
Number of instability criteria on discharge		
≥1 vs. 0	1.70 (0.99 to 2.93)	0.06
Causal microorganism[§]		
Streptococcus pneumoniae	Ref	
Atypical bacterial or virus pathogens	0.48 (0.13 to 1.73)	0.26
Mixed infections	0.20 (0.03 to 1.56)	0.13
Others	1.75 (0.47 to 6.52)	0.40
Unknown	1.35 (0.69 to 2.64)	0.38

OR, Odds ratio; 95% CI, 95% confidence interval.
Treatment failure and instability criteria on discharge are defined in text. Each factor was examined individually. [*] Baseline functional status was measured by Katz index (nº of patients = 1036); functional status range, 15 to 52 (excellent functional status, 15). Baseline functional status was analyzed as continuous and categorical variable separately.
[†] Severity of illness on admission was assessed with CURB score (Confusion, Urea nitrogen, Respiratory rate, Blood pressure).
[‡] No deaths within 90 days of discharge were recorded for patients with mechanical ventilation during hospitalization.
[§]In the univariate analyses for causal microorganism, streptococcus pneumoniae category was considered as the reference group.

In multivariate analyses that included the Katz index (model 1), three factors were found to be independently associated with 90-day mortality: the Katz index, Charlson index, and CURB score at emergency department admission (Table 3). When the analyses were repeated without the Katz index (model 2), the Charlson index, and CURB score remained independently associated with 90-day mortality (Table E5, available on line). In addition, age emerged as a significant predictor. Both logistic models showed excellent discrimination, with AUC values of 0.81 in model 1 and 0.74 in model 2, but these were significantly different ($P = 0.01$). Both models were also well calibrated, with Hosmer-Lemeshow P values of 0.910 in model 1 and 0.919 in model 2. In case of model 1, if we performed the analyses using the CURB-65 or the CRB-65 instead of CURB score as a marker for the severity of acute illness, the results are very similar (Table E6, E7, available on line). In case of model 2, if we use as risk factor the CURB-65 score or CRB-65 score instead of the CURB score and age, the discrimination of this new model is similar to model 2 (Table E8, available on line).

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Table 3. Risk factors significantly associated in multivariate analyses with mortality within 90 days of hospital discharge in the derivation cohort (N=1117).

Risk factors	β parameter	OR (95% CI)	*P* value	Points
Intercept	-5.33			
Baseline functional status*				
16-30 vs. 15	1.26	3.51 (0.96 to 12.79)	0.06	3
>30 vs. 15	2.61	13.62 (3.96 to 46.85)	<0.001	6
Charlson index				
>1 vs. 0+1	0.87	2.38 (1.24 to 4.59)	0.009	2
CURB score†				
>1 vs. 0+1	0.79	2.20 (1.16 to 4.15)	0.01	2
AUC		0.81		
Hosmer-Lemeshow *P* value‡		0.910		

OR, Odds ratio; 95% CI, 95% confidence interval; β parameter, estimated β coefficient; AUC, area under the receiver operating characteristic curve.
All risk factors were examined jointly.
N = 1033 (Deaths = 45, Survive = 988). No answers to Katz index: 84 cases (10 deaths).
* Baseline functional status was measured by Katz index (nº of patients = 1036); functional status range, 15 to 52 (excellent functional status, 15).
† Severity of illness on admission was assessed with CURB score (Confusion, Urea nitrogen, Respiratory rate, Blood pressure).
‡ A significant value for Hosmer-Lemeshow statistic indicates a significant deviation between predicted and observed outcomes.

Validation of the prognostic index

Based on the results of model 1, patients were divided into 3 groups from low to high risk (Table 4). In the validation cohort, the mortality risk ranged from 0.6% in those with 0 to 2 points on the CAP-90 index to 19.6% in those with >7 points (trend test, $P<0.001$), with a 43-fold increase in the ORs between the referent low-risk group and the high-risk group. The risk categories showed excellent discrimination, with AUC values of 0.82 in the validation cohort. Kaplan-Meier survival curves of the three risk groups in the derivation and validation cohorts demonstrate markedly different survival trajectories with persistent differences in 90-day mortality (Figure 1). No significant differences were observed in the survival curves between derivation and validation cohorts in any of the risk groups. Data based on the result of model 2 are available in the online supplement (Table E9, Figure E1).

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Table 4. Validation of the CAP-90 index: 90-day mortality in the derivation and validation cohorts by index score categories.

Risk group, (points)	Derivation Cohort (N=1117)		Validation Cohort (N=646)		*P* value†
	No. who died/No. at risk (%)*	OR (95% CI)	No. who died/No. at risk (%)*	OR (95% CI)	
Low risk (0-2)	3/428 (0.7)	1	2/358 (0.6)	1	0.80
Intermediate risk (3-7)	16/454 (3.5)	5.18 (1.50 to 17.89)	8/205 (3.9)	7.23 (1.52 to 34.36)	0.81
High risk (>7)	26/151 (17.2)	29.47 (8.77 to 98.97)	11/56 (19.6)	43.50 (9.34 to 202.54)	0.66
AUC		0.79		0.82	

AUC, area under the receiver operating characteristic curve; OR, odds ratio; 95% CI, 95% confidence interval.
The low-risk group was considered as the reference group.
* $P<0.001$ for the Cochran-Armitage test for trend.
† Chi-square or Fisher's exact tests for comparison of mortality proportion between the derivation and validation cohorts.

DISCUSSION

This study confirmed the substantial rates of short-term mortality among patients hospitalized with community-acquired pneumonia following discharge seen in previous studies (6-8). Equally important, we identified a simple, easy-to-apply prognostic index composed of three variables—functional status prior to hospitalization, the Charlson index, and the severity of CAP at the time of presentation to the hospital—that can categorize patients in this population into low, intermediate, and high risk for 90-day mortality. The model we developed shows excellent discrimination and calibration.

To our knowledge, this is the first study that identifies predictors of short-term mortality following hospital discharge for CAP and combines them into a single score. In addition to evaluating information that is nearly always readily available at the time of admission, such as the severity of CAP, host status, and parameters of clinical stability in the 24 hours prior to

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discharge, we also examined the evolution of the disease during the index hospitalization, the pathogen responsible for pneumonia, process-of-care variables, and the length of stay.

A new finding in our study is that health status prior to the acute illness, as measured by the Katz index, is a strong predictor of short-term mortality in patients with CAP who survive to hospital discharge. The Katz index is not routinely used to assess functional status and can be seen as a complicated tool for use in daily practice. However, the survey takes only a few minutes, and can be used to satisfy the Centers for Medicare and Medicaid Services requirements for collecting functional status data (19). As an alternative, the Katz index can be replaced by variables included in a second model (age, Charlson index, and the CURB score at admission) which retains a high discriminatory power. Those parameters are easily obtained in daily clinical practice.

The inclusion of functional status may provide the CAP-90 with good discriminatory power. A study conducted among older patients with CAP found an association between pre-illness functional status and mortality risk (20), a finding previously documented only among residents of long-term care facilities (21). Pneumonia-specific scoring systems such as the PSI (3) or CURB-65 scale (5) have proven to offer valuable prognostic information for adults with CAP. However, they do not provide an assessment of patients' functional status which, among the elderly, appears to be a vital contributor to outcomes such as disability and survival (22, 23).

Numerous studies have highlighted the importance of comorbid disease in determining patient outcomes after a critical illness (24, 25), including CAP (7, 8). Our results show that comorbid illness measured by the Charlson is a major independent predictor of 90-day mortality.

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Comorbid illness scales have proven useful in identifying subgroups of patients who are more likely to benefit from high-quality care (26). Our findings emphasize the importance of optimal management of comorbidities, given evidence that changes to the organization and delivery of care – including improving patients' self-management education; instituting programmes using education, feedback, or reminders for healthcare providers; and ensuring continuity of care – can improve the quality of care and certain outcomes (27, 28).

Previous studies have reported an association between CAP severity upon admission and 30-day mortality (3, 5, 14). Our data show that this association persists for at least 90 days after discharge. This raises an interesting question: Why is the extent of illness and physiologic compromise upon admission associated with mortality 90 days after discharge? A recent study showed that persistent inflammation at hospital discharge after CAP is associated with higher mortality over the subsequent 3 months. The authors speculate that the high inflammatory concentrations observed at hospital discharge in more than half of their patients could be due to an interaction between poor chronic health and acute illness (29). Among patients admitted with severe CAP, systemic inflammation may resolve slowly and persist long after discharge. Indeed, the levels of inflammatory cytokines induced during an episode of CAP have been correlated with the severity of pulmonary infection (30).

The significant differences observed in the characteristics and management of patients in the derivation and validation cohorts are almost certainly related to the implementation of practice guidelines for CAP in Galdakao Hospital, which provided the derivation cohort, in 2000 (31). The use of these guidelines may have led to higher admission rates among older patients and those with poorer functional status upon admission, as well as shorter lengths of stay (32). The substantially higher rate of patients with any instability criteria on discharge in the derivation

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cohort (36.8%) than in the validation cohort (4.1%) is associated with the shorter length of stay and the conservative threshold for temperature used to defined instability (≥37.2 ºC) (6). Despite the large difference in clinical instability between the cohorts, the rate of 90-day mortality after discharge was similar. Neither length of stay nor the presence of instability criteria, which were presented differently among both cohorts, were statistically significant when studied as interaction terms in relation to mortality.

Our study has several strengths: detailed clinical prospective data collection, large sample size, use of a standardized tool for assessing pre-illness status, and validation in an independent sample whose characteristics differed substantially at baseline from the derivation cohort.

Limitations of the study must also be discussed. We did not identify the actual cause of death in our subjects because many patients died at home without autopsies. Although these data are potentially available from death certificates, the deficiencies in this approach are well documented (33). In addition, the validity of using a clinical review committee to determine cause of death for patients with CAP has not been previously established (7). We determined patients' pre-illness functional status from their responses to a questionnaire at the time of diagnosis. This could bias the results in either direction: acutely ill patients could overestimate the presence of symptoms and functional limitations prior to the onset of illness or underestimate these symptoms and limitations. However, previous studies have demonstrated the validity of retrospective reports for assessing functional status prior to hospitalization in acutely ill patients (34, 35). Finally, one needs to be appropriately cautious in the interpretation of our study findings because of the relatively small number of post-discharge deaths.

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In summary, we developed a prognostic index (CAP-90) that uses information from just 3 readily available factors to estimate short-term mortality following discharge for patients hospitalized with CAP. This index could improve the management of CAP in several ways. By identifying low-, intermediate-, and high-risk patients, it could help clinicians target specific interventions to each group. For example, a low-risk patient (an index score of 0-2) could be safely discharged. Optimal management of intermediate- and high-risk patients remains to be determined. Interventions such as immunizations for influenza and pneumococcus when indicated, review of signs or symptoms that suggest a worsening of the underlying condition, an appropriate outpatient follow-up with a physician, and non-specific measures like regular physical activity and better social support, may improve post-discharge outcomes.

Physicians treating patients with CAP should be aware that discharge of patients with risk factors is common and increases the risk of poor post-hospital outcome. Although it is possible that the natural course of some of the disease processes may not be alterable, earlier recognition of high-risk patients maximizes the potential for interventions to minimize subsequent morbidity and mortality.

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REFERENCES

1- **España PP**, Capelastegui A, Gorordo I, et al. Development and validation of a clinical prediction rule for severe community-acquired pneumonia. *Am J Respir Crit Care Med* 2006;174:1249-56.

2- **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;165:766-72.

3- **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;336:243–50.

4- **Ewig S**, Ruiz M, Mensa J, et al. Severe community-acquired pneunonia: assessment of severity criteria. *Am J Respir Crit Care Med* 1998;158:1102-8.

5- **Lim WS**, Van der Eerden MM, Laing R, et al. Defining community-acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377-82.

6- **Halm EA**, Fine MJ, Kapoor WN, Singer DE, Marrie TJ, Siu AL. Instability on hospital discharge and the risk of adverse outcomes in patients with pneumonia. *Arch Intern Med* 2002;162:1278-84.

7- **Mortensen EM**, Coley CM, Singer DE, et al. Causes of death for patients with community-acquired pneumonia. Results from the pneumonia patients outcomes research team cohort study. *Arch Intern Med* 2002;162:1059-64.

8- **Kaplan V**, Clermont G, Griffin MF, et al. Pneumonia. Still the old man`s friend? *Arch Intern Med* 2003;163:317-23.

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9- **Waterer GW**, Kessler LA, Wunderink RG. Medium-term survival after hospitalization with community-acquired pneumopnia. *Am J Respir Crit Care Med* 2004;169:910-4.

10- **Macfarlene JT**, Boldy D. 2004 update of BTS pneumonia guidelines: what`s new?. *Thorax* 2004;59:364-6.

11- **Niederman MS**. Understanding the natural history of community-acquired pneumonia resolution: vital information for duration of therapy. *Clin Infect Dis* 2004;39:1791-3.

12- **Katz S**, Downs TD Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970;10:20-30.

13- **Charlson M**, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994;47:1245-51.

14- **Lim WS**, Macfarlane JT, Boswell TC, et al. Study of community acquired pneumonia aetiology (SCAPA) in adults admitted to hospital: implications for management guidelines. *Thorax* 2001;56:296-301.

15- **Niederman MS**, Mandell LA, Anzueto A, 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;163:1730-54.

16- **Hanley JA**, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;143:29-36.

17- **Hosmer DW**, Lemeshow S. Applied logistic regression. New York, John Wiley and Sons, Inc., 1989 pp. 140-145.

18- **Hanley JA**, McNeil BJ. A method of comparing areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983;148:839–43.

19- **Inouye SK**, Bogardus ST, Vitagliano G, et al. Burden of illness score for elderly persons. Risk adjustment incorporating the cumulative impact of diseases, physiologic abnormalities, and functional impairments. *Med Care* 2003;41:70-83.

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20- **Torres OH**, Muñoz J, Ruiz D, et al. Outcome predictors of pneumonia in elderly patients: importance of functional assessment. *J Am Geriatr Soc* 2004;52:1603-9.

21- **Muder RR**, Brennen C, Swenson DL, Wagener M. Pneumonia in a long-term care facility: a prospective study of outcome. *Arch Intern Med* 1996;156:2365-70.

22- **Inouye SK**, Peduzzi PN, Robison JT, Hughes JS, Horwitz RI, Concato J. Importance of functional measures in predicting mortality among older hospitalized patients. *JAMA* 1998;279:1187-93.

23- **Metlay JP**, Fine MJ, Schulz R, et al. Measuring symptomatic and functional recovery in patients with community-acquired pneumonia. *J Gen Intern Med* 1997;12:423-30.

24- **Poses RM**, McClish DK, Smith WR, et al. Prediction of survival of critically ill patients by admission comorbidity. *J Clin Epidemiol* 1996;49:743-7.

25- **de Groot V,** Beckerman H, Lankhorst GJ, et al. How to measure comorbidity. A critical review of available methods. *J Clin Epidemiol* 2003;56:221-9.

26- **Meng L,** Maskarinec G, Lee J, Kolonel LN. Lifestyle factors and chronic diseases: application of a composite risk index. *Prev Med* 1999;29:296-304.

27- **Bodenheimer T,** Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA* 2002;288:2469-75.

28- **Weingarten SR,** Henning JM, Badamgarav E, Knight K, Hasselblad V, Gano A, Ofman JJ. Interventions used in disease management programmes for patients with chronic illness-which ones work? Meta-analysis of published reports. *BMJ* 2002;325:925-8

29- **Yende S,** D`Angelo G, Kellum JA, et al. Inflammatory markers at hospital discharge predict subsequent mortality after pneumonia and sepsis. *Am J Respir Crit Care Med* 2008;177:1242-7.

30- **Glynn P**, Coakley R, Kilgallen I, Murphy N, O´Neill S. Circulating interleukin 6 and interleukin 10 in community acquired pneumonia. *Thorax* 1999;54:51-5.

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31- **Capelastegui A**, España PP, Quintana JM, et al. Improvement of process-of-care and outcomes after implementing a guideline for management of community-acquired pneumonia: a controlled before-and-after study. *Clin Infect Dis* 2004;39:955-63.

32- **Marrie TJ**, Lau CY, Wheeler SI, Wong CJ, Vandervoort MK, Feagan BG. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. *JAMA* 2000;283:749-55.

33- **Sington JD**, Cottrell BJ. Analysis of the sensitivity of death certificates in 440 hospital deaths: a comparison with necropsy findings. *J Clin Pathol* 2002;55:499-502.

34- **Covinsky KE**, Palmer RM, Counsell SR, Pine ZM, Walter LC, Chren MM. Functional status before hospitalization in acutely ill older adults: validity and clinical importance of retrospective reports. *J Am Geriatr Soc* 2000;48:164-9.

35- **Sager MA**, Franke T, Inouye SK, et al. Functional outcomes of acute medical illness and hospitalization in older persons. *Arch Intern Med* 1996;156:645-52.

Development of a prognostic index for 90-day mortality among patients discharged after hospitalization for community-acquired pneumonia

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ON LINE DATA SUPPLEMENT

Addition details of the methods used and results are included in this section.

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METHODS

Predictors of mortality: definitions

Informed consent was obtained, and trained clinicians carried out structured interviews with patients and family members within 72 hours of admission. We assessed patients' functional status 2 weeks before admission by asking about the performance of 15 daily activities (walking, getting out of bed, feeding, bathing, dressing, grooming, going to the bathroom, sphincter control, ability to make telephone calls, preparing meals, housekeeping, shopping, self-administering medications, handling finances, and driving or riding public transport). These activities are an expanded version of the activities-of-daily-living index published by Katz et al. (1). The activities were graded according to a 4-point system in which performance of the activity "without help" was scored 1, performance "with a little help" 2, performance "with a lot of help" 3, and the response "do not do activity" (which was not included for some activities) was assigned 4 points. A summary score was obtained by adding the scores across all 15 activities (range, 15 to 52, with 15 being autonomous function in all recorded activities) (2).

We measured comorbid illness by Charlson index (3). The Charlson co-morbidity index predicts the 1 year mortality for a patient who may have a range of co-morbid conditions. Each comorbid condition is assigned with a weight of 1, 2, 3 or 6 depending on the risk of dying associated with this condition. Conditions with a weight of 1 included: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease and diabetes. Conditions with a weight of 2 included: hemiplegia, moderate or severe renal disease, diabetes with end organ damage and any malignancy. Moderate or severe liver disease (e.g., cirrhosis with ascites) was given a weight of 3 and metastatic solid tumor or

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AIDS received a weight of 6. Then the Charlson co-morbidity index was calculated for each patient as the total of the patient's comorbid conditions which have been weighted. A higher Charlson co-morbidity score indicates an increased severity of conditions. Therefore, the Charlson index provides a simple, readily applicable and valid method of estimating risk of death from comorbid disease.

To measure the severity of CAP upon admission to the emergency department, we used CURB (4) scores because risk classes defined by the Pneumonia Severity Index (5) can be influenced by the presence of comorbid illness as well as by severe acute illness.

A patient was classified as having treatment failure if during the hospital stay he or she developed clinical deterioration with hemodynamic instability, demonstrated respiratory failure or the appearance of it, required mechanical ventilation, demonstrated radiographic progression of pneumonia or the appearance of a new infectious foci, or had persistent fever or the reappearance of fever if change in treatment was needed.

A patient's stability on discharge was assessed by the measurement of temperature, heart rate, respiratory rate, systolic blood pressure, and oxygenation in the 24 hours before discharge. A patient was considered stable with a temperature <37.2 ºC, a heart rate <120/min, a respiratory rate <24/min, and a systolic blood pressure >90 mm Hg. Oxygenation was considered stable if the oxygen saturation rate was ≥90% or the partial pressure of oxygen was ≥60 mm Hg and the patient was not receiving mechanical ventilation or supplemental oxygen by face mask or nasal prongs. Patients receiving supplemental oxygen were considered to be in stable condition if they had an oxygen saturation rate ≥95%. Patients who had been using

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supplemental oxygen at home before admission were not considered to have unstable oxygenation on discharge. All patients at discharge were able to eat (or resume long-term tube feeding) and to receive oral medication.

Patients were treated empirically with antibiotics according to local practice guidelines: betalactam with macrolide, levofloxacin or betalactamic. Medical care following discharge was determined by patient's health-care providers; no interventions were instigated as part of this study. Patients at discharge were not explicitly classified as "permit natural dying" or "do not resuscitate" orders.

Bacteriologic studies

The strategy for bacteriologic diagnosis included two blood cultures, sputum for culture, a urinary antigen during the acute phase of the infection, and serological tests for atypical bacteria during the acute and remittance phases.

A representative lower respiratory tract sample was defined as containing >25 leukocytes and <10 epithelial cells per low-power field. All bacterial species isolated were identified by standard techniques. In the first few days after hospital admission and 4 to 6 weeks thereafter, sera were collected, and tested for the presence of IgG and IgM to *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Chlamydophila psittaci, Coxiella burnetii,* and *Legionella pneumophila*. Antibodies to *M. pneumoniae, C. Burnetti,* and *L. pneumophila* were tested by immunofluorescent antibody assay and to *Chlamydophila spp* by microimmunofluorescence assay. Tests to detect influenza virus types A and B, parainfluenza virus types 1 to 3, adenovirus, and respiratory syncytial virus were performed with monoclonal antibodies for direct immunofluorescence assay. The collected urine samples were stored at –70°C or –20°C

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until testing. The detection of *L. pneumophila* by means of an enzyme immunoassay system and *Streptococcus pneumoniae* by means of an immunochromatographic membrane assay (Binax Inc; Scarborough, ME) in a nonconcentrated urine sample was performed.

An etiologic diagnosis was considered to be definitive if one of the following criteria were met: (1) isolation of respiratory pathogen in a sterile specimen (blood and pleural fluid); (2): four-fold rise in IgG titers for *M. pneumoniae*, *C. pneumoniae*, *C. psittaci*, *C. burnetii,* and *L. pneumophila*; (3) a single increased IgM titer for *M. pneumoniae* (≥1:16) or *C. pneumoniae* (≥ 1:10) or *C. psittaci* (≥1:32) or *C. burnetii* (≥1:64); (4) positive urinary antigen for *L. pneumophila* type 1 or *S. pneumoniae*; and (5) a positive result for one respiratory virus. An etiologic diagnosis was considered to be presumptive if a validated sputum sample yielded one or more bacterial strains or a single increased IgG titer for *M. pneumoniae* (≥1:180), for *C. pneumoniae* (≥1:512), for *C. psittaci* (≥1:128), for *C. burnetii* (≥1:512), for *L.pneumophila* (≥ 1:256).

RESULTS

Additional results and tables are included in this section

The rate of 90-day mortality after discharge was 4.9% (55/1117) in the derivation cohort, with 24 of the deaths (43.6%) occurring in the hospital after readmission. In the validation cohort, the rate of 90-day mortality after discharge was 3.3% (21/646), with 10 of the deaths (47.6%) occurring in the hospital after readmission. In the derivation cohort, 49 (4.4%) patients were admitted to the intensive care unit (ICU), compared with 49 (7.6%) in the validation cohort. Among those admitted to the ICU, the 90-day mortality rate after discharge was 2% (1/49) in

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both cohorts. The comorbidities of patients in the derivation and validation cohorts are described in Table E1.

Table E1. Comorbid conditions of patients hospitalized with community-acquired pneumonia who survived to hospital discharge in the derivation and validation cohorts.

Comorbidities	Derivation cohort (N=1117)	Validation cohort (N=646)	*P* value
Chronic pulmonary disease	401 (36)	188 (29.1)	0.003
Congestive heart failure	117 (10.5)	75 (11.6)	0.47
Myocardial infarction	54 (4.9)	51 (7.9)	0.009
Peripheral vascular disease	41 (3.7)	43 (6.7)	0.005
Diabetes	196 (17.6)	106 (16.4)	0.52
Diabetes with chronic complications	11 (1)	27 (4.2)	<0.0001
Cerebrovascular disease	86 (7.7)	75 (11.6)	0.006
Dementia	73 (6.5)	22 (3.4)	0.005
Hemiplegia or paraplegia	10 (0.9)	23 (3.6)	<0.0001
Peptic ulcer disease	82 (7.4)	43 (6.7)	0.58
Malignancy	48 (4.3)	34 (5.3)	0.36
Metastatic solid tumor	2 (0.2)	3 (0.5)	0.28
Mild liver disease	20 (1.8)	12 (1.9)	0.92
Moderate liver disease	9 (0.8)	5 (0.8)	0.94
Severe liver disease	3 (0.3)	1 (0.2)	0.63
Rheumatologic disease	12 (1.1)	12 (1.9)	0.17
Moderate renal disease	10 (0.9)	7 (1.1)	0.70
Severe renal disease	3 (0.3)	8 (1.2)	0.01
Others	2 (0.2)	3 (0.5)	0.28
Charlson index			0.008
0	389 (34.9)	237 (36.8)	
1	367 (32.9)	178 (27.6)	
2	214 (19.2)	113 (17.6)	
≥3	144 (12.9)	116 (18)	

Data are presented as numbers (percentage) unless otherwise stated. Percentages exclude patients with missing data.

In the derivation cohort, there were no statistically significant differences between patients who completed the Katz index and those who did not. In the validation cohort, men were more likely to have completed the Katz index than women.

Characteristics of antibiotic treatment according age and comorbidities are available in Table E2, E3. The findings showed that in more comorbid elderlies patients antibiotic treatment is

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not worse in comparison to other - younger, more healthy – patients. Other characteristics of antibiotic treatment according 90-days vital status are showed in Table E4.

Table E2. Characteristics of antibiotic treatment: comparison according age.

Antibiotic treatment	Age ≤75 years (N=629)	Age>75 years (N=488)	*P* value
Appropriate antibiotic	566 (90.1)	474 (97.1)	<0.001
Antibiotics within 8 hours from ED arrival	525 (85.5)	430 (90.5)	0.01
Duration total (days), mean (SD)	10.3 (3.9)	9.8 (2.7)	0.16
Duration of intravenous treatment (days), mean (SD)	2.9 (3.7)	2.7 (2.2)	0.71
Mono therapy antibiotic	564 (89.8)	458 (93.9)	0.02
Broad spectrum antibiotics	559 (89)	454 (93)	0.02

ED, Emergency Department; SD, standard deviation.
Data are presented as numbers (percentage) unless otherwise stated. Percentages exclude patients with missing data**.**

Table E3. Characteristics of antibiotic treatment: comparison according Charlson index.

Antibiotic treatment	Charlson index 0 (N=389)	Charlson index 1 (N=367)	Charlson index 2 (N=214)	Charlson index ≥3 (N=144)	*P* value
Appropriate antibiotic	357 (92)	346 (94.3)	199 (93)	135 (93.8)	0.66
Antibiotics within 8 hours from ED arrival	331 (86.7)	320 (89.6)	181 (85.4)	122 (90.4)	0.31
Duration total (days), mean (SD)	10 (2.9)	10 (2.7)	9.9 (2.8)	10.6 (5.4)	0.73
Duration of intravenous treatment (days), mean (SD)	2.7 (2.8)	2.7 (2.8)	2.8 (2.3)	3.5 (4.5)	0.18
Mono therapy antibiotic	353 (91)	338 (92.1)	197 (92.1)	131 (91)	0.93
Broad spectrum antibiotics	344 (88.7)	338 (92.1)	196 (91.6)	133 (92.4)	0.33

ED, Emergency Department; SD, standard deviation.
Data are presented as numbers (percentage) unless otherwise stated. Percentages exclude patients with missing data.

Table E4. Characteristics of antibiotic treatment according 90-days vital status in the derivation cohort.

Characteristic of antibiotic treatment	90-days vital status		P value
	Alive (N=1062)	Dead (N=55)	
Mono vs. combination therapy			0.80
Mono therapy	972 (91.6)	50 (90.9)	
Combination therapy	89 (8.4)	5 (9.1)	
Small vs. broad spectrum			0.09
Small spectrum	94 (8.9)	9 (6.4)	
Broad spectrum	967 (91.1)	46 (83.6)	
Duration of treatment (days), mean (SD)			
Duration intravenous	2.8 (3)	3.6 (2.3)	<0.001
Duration total	10 (3.2)	10.7 (4.1)	0.28

SD, standard deviation.

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Data are presented as numbers (percentage) unless otherwise stated. Percentages exclude patients with missing data.

Derivation of the prognostic index

In multivariate analyses that included model 2, three factors were found to be independently associated with 90-day mortality: the Charlson index, age>75 years, and CURB score at emergency department admission (Table E5). The logistic model shows good discrimination, with AUC values of 0.74 in model 2, and excellent calibration, with a Hosmer-Lemeshow *P* value of 0.919.

Table E5. Risk factors significantly associated in multivariate analyses with mortality within 90 days of hospital discharge in the derivation cohort to model 2 (N=1117).

Risk factors	β parameter	OR (95% CI)	*P* value	Points
Intercept	-4.24			
Age >75	0.84	2.33 (1.26 to 4.31)	0.007	2
Charlson index				
>1 vs. 0+1	1.23	3.41 (1.90 to 6.12)	<0.001	3
CURB score*				
>1 vs. 0+1	0.69	1.99 (1.12 to 3.53)	0.018	2
AUC		0.74		
Hosmer-Lemeshow *P* value†		0.919		

OR, Odds ratio; 95% CI, 95% confidence interval; β parameter, estimated β coefficient; AUC, area under the receiver operating characteristic curve.
All risk factors were examined jointly.
N = 1114 (Deaths = 55, Survive = 1059).
*Severity of illness on admission was assessed with CURB score (Confusion, Urea nitrogen, Respiratory rate, Blood pressure).
†A significant value for Hosmer-Lemeshow statistic indicates a significant deviation between predicted and observed outcomes.

In case of model 1, we repeated the analyses using the CURB-65 and the CRB-65 instead of CURB score. The results are very similar to our prognostic index (CAP-90) that uses the CURB score as a marker for the severity of acute illness (Table E6, E7).

Table E6. Severity of illness on admission assessed with CURB-65 and CRB-65 scores: association in univariate analyses with mortality within 90 days of hospital discharge in the derivation cohort (N=1117).

Factors	N (%)	OR (95% CI)	*P* value
Severity of illness in admission			

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CURB-65 score			
0	210 (18.8)	Ref.	
1	296 (26.5)	2.9 (0.6 to 13.7)	0.18
2	409 (36.6)	6.2 (1.4 to 26.5)	0.01
>2	202 (18.1)	12.7 (2.9 to 54.8)	<0.001
CRB-65 score			
0	264 (23.6)	Ref.	
1	593 (53.1)	5.77 (1.36 to 24.52)	0.02
2	231 (20.7)	14.49 (3.38 to 62.15)	<0.001
>2	29 (2.6)	27.29 (5.02 to 148.24)	<0.001

OR, odds ratio; 95% CI, 95% confidence interval; CURB-65, Confusion, Urea nitrogen, Respiratory rate, Blood pressure, Age; CRB-65, Confusion, Respiratory rate, Blood pressure, Age).
Ref.: Reference category.

Table E7. Risk factors significantly associated in multivariate analyses with mortality within 90 days of hospital discharge in the derivation cohort to new model 1 using the CURB-65 and the CRB-65 instead of CURB score (N=1117).

Risk factors	**β parameter**	**OR (95% CI)**	***P* value**	**Points**
Model with CURB-65 score				
Intercept	-5.30			
Baseline functional status*				
16-30 vs. 15	1.23	3.41 (0.93 to 12.43)	0.06	3
>30 vs. 15	2.55	12.76 (3.69 to 44.11)	<0.001	6
Charlson index				
>1 vs. 0+1	0.86	2.37 (1.23 to 4.80)	0.01	2
CURB-65 score†				
>2 vs. ≤2	0.93	2.52 (1.33 to 4.80)	0.005	2
AUC		0.818		
Hosmer-Lemeshow *P* value‡		0.902		
Model with CRB-65 score				
Intercept	-5.35			
Baseline functional status*				
16-30 vs. 15	1.24	3.44 (0.94 to 12.54)	0.06	3
>30 vs. 15	2.52	12.42 (3.59 to 43.06)	<0.001	6
Charlson index				
>1 vs. 0+1	0.84	2.31 (1.20 to 4.47)	0.01	2
CRB-65 score§				
>2 vs. ≤2	0.93	2.54 (1.33 to 4.82)	0.005	2
AUC		0.822		
Hosmer-Lemeshow *P* value‡		0.945		

OR, Odds ratio; 95% CI, 95% confidence interval; β parameter, estimated β coefficient; AUC, area under the receiver operating characteristic curve.
All risk factors were examined jointly.
N = 1033 (Deaths = 45, Survive = 988). No answers to Katz index: 84 cases (10 deaths).
* Baseline functional status was measured by Katz index (nº of patients = 1036); functional status range, 15 to 52 (excellent functional status, 15).
† Severity of illness on admission was assessed with CURB-65 score (Confusion, Urea nitrogen, Respiratory rate, Blood pressure, Age).
‡ A significant value for Hosmer-Lemeshow statistic indicates a significant deviation between predicted and observed outcomes.
§ Severity of illness on admission was assessed with CRB-65 score (Confusion, Respiratory rate, Blood pressure, Age).

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In case of model 2, if we use as risk factor the Charlson index and the CURB-65 score (or CRB-65 score) instead of the CURB score and age >75 years, the discrimination of this new model is similar to model 2 and is also well calibrated (Table E8).

Table E8. Risk factors significantly associated in multivariate analyses with mortality within 90 days of hospital discharge in the derivation cohort to new model 2 using the CURB-65 and the CRB-65 instead of CURB score (N=1117).

Risk factors (using CURB-65 score)	**β parameter**	**OR (95% CI)**	***P* value**	**Points**
Intercept	-4.29			
Charlson index				
>1 vs. 0+1	1.23	3.43 (1.91 to 6.16)	<0.001	3
CURB-65 score*				
2 vs. 0+1	0.81	2.45 (1.04 to 4.85)	0.04	2
>2 vs. 0+1	1.50	4.50 (2.05 to 9.86)	<0.001	4
AUC		0.75		
Hosmer-Lemeshow *P* value†		0.996		
Risk factors (using CRB-65 score)				
Intercept	-3.98			
Charlson index				
>1 vs. 0+1	1.31	3.72 (2.08 to 6.64)	<0.001	3
CRB-65 score‡				
>2 vs. ≤2	1.12	3.08 (1.76 to 5.39)	<0.001	2
AUC		0.73		
Hosmer-Lemeshow *P* value†		0.990		

OR, Odds ratio; 95% CI, 95% confidence interval; β parameter, estimated β coefficient; AUC, area under the receiver operating characteristic curve.
All risk factors were examined jointly.
* Severity of illness on admission was assessed with CURB-65 score (Confusion, Urea nitrogen, Respiratory rate, Blood pressure, Age).
† A significant value for Hosmer-Lemeshow statistic indicates a significant deviation between predicted and observed outcomes.
‡ Severity of illness on admission was assessed with CRB-65 score (Confusion, Respiratory rate, Blood pressure, Age).

Validation of the prognostic index

Based on the results of model 2, patients were divided into 3 groups from low to high risk (Table E9). In the validation cohort, the mortality risk ranged from 0.8% in those with 0 to 2 points on the CAP-90 index to 12.1% in those with >5 points (trend test, $P<0.001$), with a 17-fold increase in the ORs between the referent low-risk group and the high-risk group. The risk

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categories also showed good discrimination, with AUC values of 0.76 in the validation cohort. Kaplan-Meier survival curves of the three risk groups in the derivation and validation cohorts demonstrate different survival trajectories with persistent differences in mortality over 90 days of follow-up (Figure E1). No significant differences were found in the survival curves between derivation and validation cohorts in any of the risk groups.

Table E9. Validation of model 2 of the CAP-90 index: 90-day mortality in the derivation and validation cohorts by index score categories.

Risk group, (points)	Derivation Cohort (N=1117)		Validation Cohort (N=646)		*P* value[†]
	No. who died/No. at risk (%)[*]	OR (95% CI)	No. who died/No. at risk (%)[*]	OR (95% CI)	
Low risk (0-2)	13/678 (1.9)	1	3/379 (0.8)	1	0.15
Intermediate risk (3-5)	28/365 (7.7)	4.25 (2.17 to 8.31)	11/207 (5.3)	7.03 (1.94 to 25.51)	0.28
High risk (>5)	14/71 (19.7)	12.56 (5.64 to 28.02)	7/58 (12.1)	17.20 (4.31 to 68.64)	0.24
AUC		0.72		0.76	

AUC, area under the receiver operating characteristic curve; OR, odds ratio; 95% CI, 95% confidence interval.

The low-risk group was considered as the reference group.

[*] $P<0.001$ for the Cochran-Armitage test for trend.

[†] Chi-square or Fisher's exact tests for comparison of mortality proportion between the derivation and validation cohorts.

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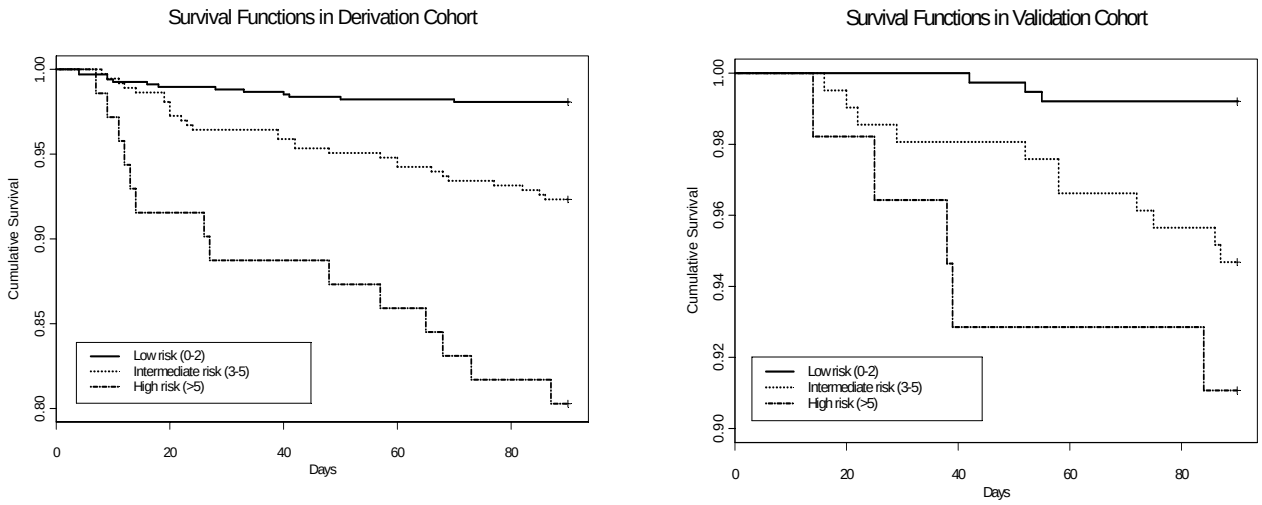
Figure E1. Kaplan-Meier survival curves for the 3 risk groups in the derivation and validation cohorts (model 2).



Kaplan-Meier survival curves for each of the 3 risk groups in the derivation and validation cohorts according to the model 2 prognostic index CAP-90: 2 points for age >75 years; 3 points for Charlson index >1; 2 points for CURB score >1. The log-rank test detected statistically significant differences between all curves (P<0.01) except between intermediate and high risk in the validation cohort (P=0.30).

REFERENCES

1. **Katz S**, Downs TD Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970;10:20-30.
2. **Clermont G**, Angus DC, Linde-Zwirble WT, Griffin MF, Fine MJ, Pinsky MR. Does acute organ dysfunction predict patient-centered outcomes? *Chest* 2002;121:1963-71.
3. **Charlson M**, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994;47:1245-51.
4. **Lim WS**, Macfarlane JT, Boswell TC, et al. Study of community acquired pneumonia aetiology (SCAPA) in adults admitted to hospital: implications for management guidelines. *Thorax* 2001;56:296-301.
5. **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;336:243–50.

Figure 1. Kaplan-Meier survival curves for the 3 risk groups in the derivation and validation cohorts.

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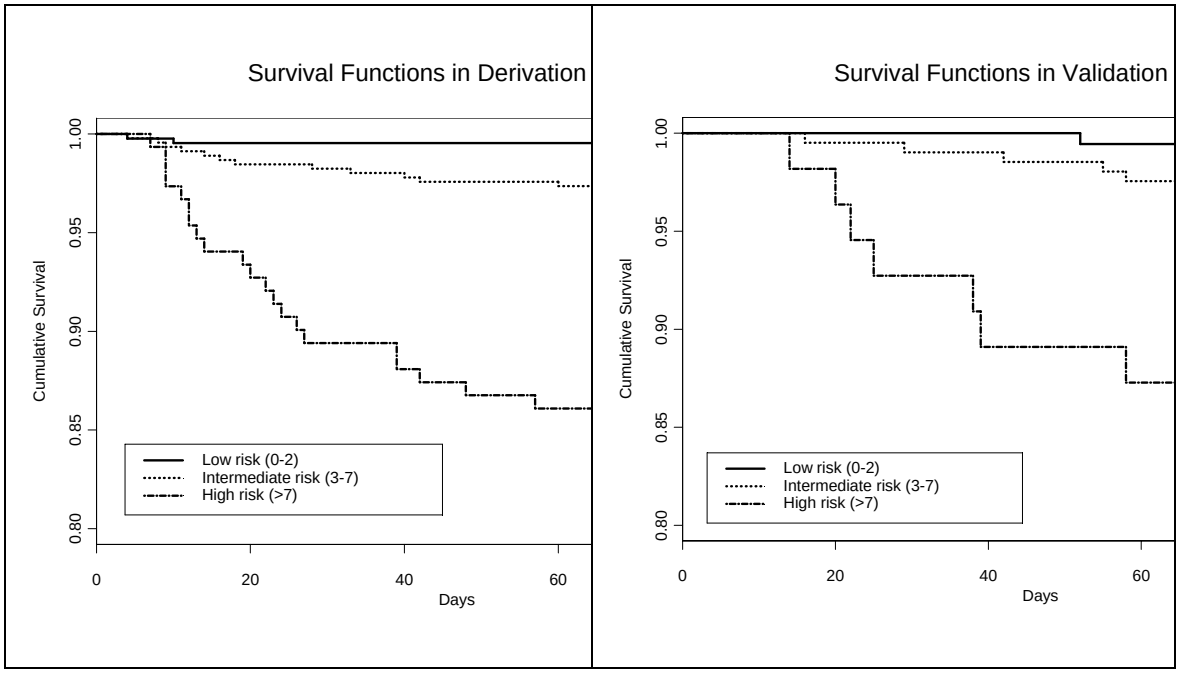

Kaplan-Meier survival curves for each of the 3 risk groups in the derivation and validation cohorts according to the CAP-90 prognostic index: baseline functional status: 6 points for >30 and 3 points for 16 to 30, measured by Katz index; 2 points for Charlson index >1; 2 points for CURB score >1. The log-rank test detected statistically significant differences between all curves (P<0.01) in both cohorts.

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