Severity scores are helpful in predicting mortality in patients presenting with community-acquired pneumonia (CAP). They enable physicians to decide their management strategies and site of care according to the expected mortality risk. In Europe, most cases of lower respiratory tract infections (LRTIs) and CAP are managed in primary care settings by general practitioners (GPs). However, most severity scores have been derived and validated in a hospital setting.

The best accepted tools to discriminate patients with CAP into high or low risk are the CURB-65 score (confusion, serum urea nitrogen level ≥19.6 mg/dL [to convert to millimoles per liter, multiply by 0.357], respiratory rate ≥30/min, low blood pressure, and age ≥65 years) and the Pneumonia Severity Index (PSI).1,2 The CURB-65 score consists of 5 easily accessible data, while the PSI includes many tests that are not accessible in primary care. This latter score is therefore not useful for the GP. Recently, several studies evaluated the CURB-65 score and confirmed its validity, but validation was not yet done in an unselected primary care population.3-9

A modification of the CURB-65 score, the CRB-65 score, is recommended by GPs in the communities where serum urea nitrogen measurements are often unavailable. It is expected to support GP judgment in stratifying patients into different management groups, ranging from home treatment to urgent hospital admission (Figure).1 This management model seems unlikely to be practical in a primary care population because it recommends hospital referral for a score of 1 or higher and thus for all patients older than 65 years (Figure). We therefore conducted a study to evaluate the validity of the CRB-65 score in primary care.

Methods. Study Population. Between November 2005 and May 2006, Dutch GPs prospectively included patients with CAP who were 65 years or older. Community-acquired pneumonia was diagnosed on the basis of the presence of 1 or more features, including new localizing signs present during chest examination, new infiltrates on a chest radiograph, or when the GP had a strong suspicion of the patient having CAP because of severe dyspnea in a very ill patient, even in the absence of chest signs. This third criterion for CAP was chosen because it equates to usual practice in daily primary care, thus ensuring the generalizability of study results.

Patients were not included in the study if they were known to have lung cancer, a hematologic malignant neoplasm, or an infection with the human immunodeficiency virus; used immunosuppressive medication (except prednisone); had been hospitalized during the 2 weeks preceding the diagnosis; or were nursing home residents.

Data, including all CRB items and age, were collected prospectively at the same time as the index consultation, when diagnosis and management was decided. The CRB-65 rule is scored on the presence of the following: confusion, respiratory rate 30/min or higher, low blood pressure (systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg), and age 65 years or older. The main outcome measure was 30-day mortality.

Statistical Analysis. Descriptive statistics included frequencies, percentages, and means. We examined the accuracy of the CRB-65 rule in episodes of CAP using SPSS version 12.1 for Windows (SPSS Inc, Chicago, Illinois), with 30-day mortality as the outcome. Positive predictive value, negative predictive value, sensitivity, specificity, and the area under the receiver operating curve (ROC curve) were calculated.
operating characteristic curve with corresponding 93% confidence intervals (CIs) were calculated and compared with the original study of Lim et al. Next, the mortality for different CRB-65 scores was determined. We also calculated the correlation between the individual CRB-65 scores and referral patterns.

Results. Patients’ Characteristics. The study population comprised 315 elderly patients (mean age, 77.3 years) who lived at home and were diagnosed as having CAP. Of these, the diagnosis for 17 patients was only on the basis of a strong suspicion of having pneumonia (third diagnostic criterion). In 119 patients, a chest radiograph was present, with 50 showing infiltrates. One patient was lost to follow-up. The study recorded only heart failure.

In our study cohort, only 23 patients (7.3%) with pneumonia were referred to the hospital. Of the 230 patients with a score of 1, only 9 were referred to the hospital and 1466 patients.

### Table 1. Demographics, Comorbidities, and Clinical Features of the Derivation Cohort (Lim et al) and the Validation Cohort of Primary Care Patients With CAP (Present Study)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Derivation Cohort, Primary Care Setting (n=821)</th>
<th>Validation Cohort, Primary Care Setting (n=314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, No. (%)</td>
<td>550 (51)</td>
<td>145 (46)</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>64.1</td>
<td>77.3</td>
</tr>
<tr>
<td>≥65, No. (%)</td>
<td>475 (58)</td>
<td>314 (100)</td>
</tr>
<tr>
<td>≥75, No. (%)</td>
<td>296 (36)</td>
<td>187 (60)</td>
</tr>
<tr>
<td>Comorbid illnesses, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>375 (35)</td>
<td>123 (39)</td>
</tr>
<tr>
<td>IHD/heart failure</td>
<td>197 (18)</td>
<td>65 (21)</td>
</tr>
<tr>
<td>CVD</td>
<td>91 (9)</td>
<td>27 (9)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>107 (10)</td>
<td>61 (19)</td>
</tr>
<tr>
<td>Signs and symptoms, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>NR</td>
<td>221 (70)</td>
</tr>
<tr>
<td>Cough</td>
<td>NR</td>
<td>300 (96)</td>
</tr>
<tr>
<td>Sputum</td>
<td>NR</td>
<td>233 (48)</td>
</tr>
<tr>
<td>Painful breathing</td>
<td>NR</td>
<td>75 (24)</td>
</tr>
<tr>
<td>Confusion</td>
<td>125 (13)</td>
<td>10 (3)</td>
</tr>
<tr>
<td>Respiratory rate ≥30/min</td>
<td>217 (24)</td>
<td>50 (16)</td>
</tr>
<tr>
<td>Pulse rate ≥125/min</td>
<td>87 (11)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>BP ≤90 mm Hg systolic</td>
<td>199 (24)</td>
<td>41 (13)</td>
</tr>
<tr>
<td>or ≤60 mm Hg diastolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auscultatory abnormalities</td>
<td>NR</td>
<td>290 (92)</td>
</tr>
<tr>
<td>Radiography-confirmed CAP</td>
<td>821 (100)</td>
<td>50 (16)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-Day mortality</td>
<td>89 (9.5)</td>
<td>11 (3.5)</td>
</tr>
<tr>
<td>30-Day hospitalization</td>
<td>NR</td>
<td>47 (15.0)</td>
</tr>
</tbody>
</table>

Abbreviations: BP, blood pressure; CAP, community-acquired pneumonia; CVD, cerebrovascular disease; IHD, ischemic heart disease; NR, not reported.

### Table 2. Association Between Number of Prognostic Features of the CRB-65 Score and Risk of 30-Day Mortality Between the Original Study by Lim et al and the Present Study

<table>
<thead>
<tr>
<th>CRB-65 Score</th>
<th>Original Data Set by Lim et al, No. (%) (n=314)</th>
<th>Present Study, No. (%) (n=314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>212 (22.7)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>1</td>
<td>344 (36.9)</td>
<td>18 (5.2)</td>
</tr>
<tr>
<td>2</td>
<td>251 (26.9)</td>
<td>30 (11.8)</td>
</tr>
<tr>
<td>3</td>
<td>111 (11.9)</td>
<td>36 (12.4)</td>
</tr>
<tr>
<td>4</td>
<td>14 (1.5)</td>
<td>3 (21.4)</td>
</tr>
</tbody>
</table>

Abbreviation: CRB-65, confusion, respiratory rate 30/min or higher, low blood pressure (<90 mm Hg systolic or ≤60 mm Hg diastolic), age 65 years or older.

### Table 3. Comparison of the Test Characteristics of CRB-65 Score of 2 or Higher Between the Original Data Set of Lim et al and the Present Study, With 30-Day Mortality as the End Point

<table>
<thead>
<tr>
<th>Test Characteristic</th>
<th>Original Data Set by Lim et al, Derivation Set (n=718)</th>
<th>Present Study, Validation Set (n=314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>76.8</td>
<td>82.2</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>64.3</td>
<td>75.2</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>18.6</td>
<td>10.7</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>96.3</td>
<td>99.1</td>
</tr>
</tbody>
</table>

Abbreviations: CRB-65, confusion, respiratory rate 30/min or higher, low blood pressure (<90 mm Hg systolic or ≤60 mm Hg diastolic), age 65 years or older; NPV, negative predictive value; PPV, positive predictive value.

Accuracy of the CRB-65 Score. By comparison with the original study by Lim et al, a similar trend was found in the association between the CRB-65 score and 30-day mortality, although none of our patients had a score of 0 (since they were all 65 years or older) or a high score of 4 (Table 2). The test characteristics of the CRB-65 score in our study, taking a cutoff score of 2 or higher, were very much similar to that of the original cohort (Table 3). Also, the discriminative value was good (area under receive operating characteristic curve, 0.79; 95% CI, 0.65-0.92).

Management of CAP. Patients with a score of 1 (73%) had a low mortality rate of 0.9%, suggesting that they may be suitable for usual home management. A score of 2 or higher was associated with a much higher mortality rate (11%), suggesting patients required either close monitoring at home or hospital referral (Table 2). This is not in agreement with the site of care decision recommended in the British Thoracic Society guidelines and the study by Lim et al (Figure).
the remainder were treated at home. Two patients (0.9%) died, both in the home-managed group. Only 7 patients with a CRB-65 score of 3 were referred to the hospital, and of the other 16 patients treated at home, 2 (13%) died (Table 4).

Comment. When using a score of 2 or higher to indicate high risk, our study showed that the CRB-65 score has similar accuracy in predicting 30-day mortality in elderly primary care patients compared with the original study of Lim et al1 including patients of all ages in a hospital setting. Thus, our study shows that in an elderly primary care population, the cutoff for considering hospital referral can be increased to a score of 2 or higher. This does not imply that all such patients should be referred to a hospital. Referral also depends on other adverse prognostic features, social circumstances, and wishes of the patient, as well as the availability of close health monitoring at home. Whether referral to a hospital will decrease mortality rates in high-risk patients with CAP is even not entirely clear. In our study, most patients with an elevated risk were not referred. Whether the mortality rate would be lower if they would have been sent to a hospital is unknown.

The results from this study differ somewhat from other validation studies. In particular, the a priori probability of 30-day mortality was lower than in previous validation studies (3.5% vs 4.3% to 14%).1,3–6,8,12 In these earlier studies, however, mixed groups of referred and non-referred patients with probably a higher risk for complications were studied. Another possible explanation for the low mortality could be that bacterial resistance rates are low in the Netherlands. However, overall Dutch mortality rates for CAP are not lower compared with those in countries with higher resistance rates.13

Discrimination between different kinds of LRTI is difficult in primary care because pulmonary radiography and laboratory tests are not routinely carried out. We chose to include CAP without radiographic evidence to follow daily GP practice more accurately. Although it seems that differentiation between CAP and acute bronchitis is more difficult without radiography, the prognosis of these 2 forms of LRTI was very different in our whole study, with a mortality rate of 3.5% in patients with CAP and 0.2% for those with acute bronchitis. Because death in acute bronchitis was very infrequent, using the CRB-65 score as a predictor of 30-day mortality in acute bronchitis was not useful. New studies should focus on predicting other unfavorable outcomes, apart from death, in a broader range of LRTIs.

In conclusion, the simple CRB-65 severity assessment tool accurately identifies low-risk patients in an elderly primary care population and suggests that age alone is not a sufficient reason to classify patients as high risk. Patients with a score of 2 or higher have an increased risk and should be intensively monitored, for example, by reconsultation within 24 to 48 hours or should be referred to secondary care. Because mortality rates are low in primary care, new studies should focus on less severe outcomes.

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Author Contributions: Dr Bont had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Bont, Hak, Hoes, and Verheij. Acquisition of data: Bont and Verheij. Analysis and interpretation of data: Bont, Hak, Hoes, Macfarlane, and Verheij. Drafting of the manuscript: Bont, Hak, and Verheij. Critical revision of the manuscript for important intellectual content: Hoes, Macfarlane, and Verheij. Statistical analysis: Bont, Hak, and Hoes. Obtained funding: Hoes and Verheij. Administrative, technical, and material support: Bont, Verheij. Study supervision: Hak, Hoes, and Verheij.

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5. Buising KL, Thursky KA, Black JF, et al. A prospective comparison of se-

Table 4. General Practitioner Referral Pattern of 314 Elderly Patients With Pneumonia in Relation to the CRB-65 Score

<table>
<thead>
<tr>
<th>Referral Pattern</th>
<th>Low Risk, CRB-65 Score=1 (n=230 [73.2%])</th>
<th>Medium Risk, CRB-65 Score=2 (n=61 [19.4%])</th>
<th>High Risk, CRB-65 Score=3 (n=23 [7.3%])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients directly referred to a hospital</td>
<td>9 (4)</td>
<td>7 (11)</td>
<td>7 (30)</td>
</tr>
<tr>
<td>30-Day mortality</td>
<td>0</td>
<td>2 (29)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Patients not directly referred to a hospital</td>
<td>221 (96)</td>
<td>54 (87)</td>
<td>16 (70)</td>
</tr>
<tr>
<td>30-Day mortality</td>
<td>2 (0.9)</td>
<td>3 (6)</td>
<td>2 (13)</td>
</tr>
</tbody>
</table>

Abbreviations: CRB-65, confusion, respiratory rate 30/min or higher, low blood pressure (<90 mm Hg systolic or ≤60 mm Hg diastolic), age 65 years or older.

aData are given as number (percentage) of patients.
COMMENTs AND oPINIONS

OCCUPATIONAL EXPOSURE AND RAPID HIV TEST

We read with interest the report by Giulieri et al1 on professional exposures to patients with acute primary human immunodeficiency virus (HIV) infection (PHI) with high viral load and a positive P24 antigen test result but no detectable antibodies. The authors warned about the limits of the rapid HIV test, which does not include p24 antigen detection. We recently experienced these limits.

According to European and Swiss recommendations,2,3 24-hour rapid HIV testing (Determine HIV-1/2 Ac; Abbott Diagnostics, Abbott Park, Illinois) was available in emergency departments in hospitals of our network through routine onsite laboratories. A fourth-generation test, including antibodies and p24 antigen testing (AxSYM HIV, Ag/Ab Combo; Abbott Diagnostics), was then performed within 24 hours or, at the latest, on the following working day by a specialized central laboratory closed at night and during weekends.

On a Friday at 9:00 AM, a nurse reported a needle stick injury while drawing blood samples from a 29-year-old man admitted the day before for acute abdominal pain, fever, and lymphadenopathy. Given the absence of recognized risk factors in this patient and the negative result of the rapid HIV test obtained within 1 hour, no post-exposure prophylaxis (PEP) was administered first. At 4:30 PM, the laboratory issued a positive result of the fourth-generation HIV test. Postexposure prophylaxis was started at 5:00 PM, 8 hours after the exposure. Had the accident occurred late in the afternoon, this result would not have been known before the next Monday. Subsequently, the confirmatory antibody immunoblot assay (Inno-LIA HIV I/II Score; Innogenetics, Ghent, Belgium) gave a negative result for the source patient, but his HIV-1 RNA viral load measurement was above 100,000 copies/mL (Cobas Amplicor; Roche Diagnostics, Rotkreuz, Switzerland). Three months after the end of PEP, the nurse tested negative for HIV.

Studies have shown that the use of rapid HIV tests for the management of occupational exposures can avoid unnecessary PEP while waiting for the results of conventional tests, reduce psychological stress in exposed health care workers, and save money.4,5 However, as demonstrated by our present report and the study by Giulieri et al,1 rapid HIV tests can miss primary HIV infection in source patients with high viral loads and contribute to delays in the initiation of PEP in high-risk situations. This prompted us to introduce around-the-clock fourth-generation HIV testing (Vidas HIV DUO; bioMérieux, Lyon, France) in onsite routine laboratories for occupational exposures occurring in our hospitals.

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Mortality in Humans With Pneumonia and Sepsis Is Related to an Uncompensated Anti-inflammatory Response to Infection

In the interesting article by Kellum et al1 on the systemic cytokine response to pneumonia in a cohort study of 1886 subjects hospitalized for community-acquired pneumonia (CAP), the authors report that the highest risk of death was with combined high levels of the proinflammatory cytokine interleukin (IL)-6 and the anti-inflammatory cytokine IL-10. They conclude that mortality is highest when both anti-inflammatory and pro-inflammatory cytokine levels are high.