Safety and efficacy of CURB65-guided antibiotic therapy in community-acquired pneumonia

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Objectives: To determine whether the introduction of a community-acquired pneumonia (CAP) severity assessment tool to guide antibiotic selection could reduce broad-spectrum antibiotic prescribing without compromising patient safety.

Methods: A prospective before and after evaluation study. Empirical antibiotic prescribing was studied for 18 months from June 2006 to January 2008 (pre-intervention) and then for 18 months following the implementation of a CURB65-guided antibiotic therapy guideline in June 2008. The primary outcome was the use of broad-spectrum antibiotics (cephalosporin, amoxicillin plus clavulanic acid and macrolides) in patients with CAP. Safety outcomes were 30 day mortality, requirement for mechanical ventilation and/or vasopressor support (MV/VS), development of complicated pneumonia, time to clinical stability (TCS) and length of hospital stay.

Results: The introduction of CURB65-guided therapy resulted in an overall reduction in the prescription of cephalosporins (from 27.1% of patients receiving this agent in the overall pre-intervention cohort to 8.0% in the post-intervention cohort, \( P < 0.0001 \)) and macrolides (72.8% to 58.7%, \( P < 0.0001 \)), particularly among low-risk patients. There was a corresponding increase in the prescription of the narrower-spectrum agent amoxicillin (29.7% to 41.7%, \( P < 0.0001 \)) and an increase in the use of amoxicillin monotherapy (10.4% to 29.9%, \( P < 0.0001 \)). Co-amoxiclav use increased slightly as this agent replaced cephalosporins as first-line treatment for severe CAP. The guideline had no impact on 30 day mortality, MV/VS, complicated pneumonia, TCS or length of stay. Following the intervention, adherence to national guidelines increased from 25.4% of prescriptions to 61.9%, suggesting the potential for further improvements.

Conclusions: CURB65-guided antibiotic therapy was associated with a significant decrease in broad-spectrum antibiotic use. The intervention was safe with no impact on mortality, treatment failure or clinical response.

Keywords: pneumonia, antibiotic resistance, Clostridium difficile, severity of illness scores

Introduction

Community-acquired pneumonia (CAP) is the leading cause of death from infectious disease in western countries and a leading indication for antibiotic prescribing in emergency departments. Improving antibiotic prescribing for respiratory tract infections is a priority internationally to prevent the spread of antibiotic-resistant pathogens.

Severity assessment tools have been developed to guide initial treatment for patients with CAP. The pneumonia severity index (PSI) is the most widely used severity assessment tool, and is composed of 20 patient variables including demographics, co-morbidities, clinical, laboratory and radiological variables. Guidelines incorporating the PSI have been shown to increase the proportion of patients treated in the community.

CURB65 is an alternative severity score proposed by the British Thoracic Society (BTS). It is significantly more simple to calculate, being composed of only five variables. It has been shown to perform similarly to the PSI in predicting 30 day mortality. There are, however, no studies of the impact of CURB65-based guidelines in clinical practice.

There is evidence that antibiotic prescribing for CAP is suboptimal. Inadequate antibiotic therapy can lead to treatment...
failure and increased mortality.\textsuperscript{15} While excessive, broad-spectrum antibiotic therapy for some patients may contribute to antibiotic resistance and healthcare-associated infections such as \textit{Clostridium difficile}.\textsuperscript{16–18}

CURB65-guided antibiotic therapy is recommended by the BTS guidelines.\textsuperscript{1} By providing an objective measure of severity, CURB65 may improve targeting of broad-spectrum therapy to high-severity patients and reduce excessive prescribing to less severely ill patients. The effectiveness and safety of this approach in secondary care has not previously been reported.

CURB65-guided antibiotic therapy was introduced as part of a practice guideline in NHS Lothian Hospitals in June 2008. This study describes the impact of severity-guided antibiotic prescribing on antibiotic use and outcomes in patients with CAP.

Methods

The authors performed a prospective before and after evaluation study between June 2006 and December 2009. The study was conducted in NHS Lothian University Hospitals Division, Edinburgh, UK.

The study consisted of an 18 month (pre-intervention) observation followed by the introduction in June 2008 of a clinical guideline incorporating CURB65-guided antibiotic prescribing. Post-intervention data collection was conducted from July 2008 to December 2009.

The study was approved by the Lothian Research Ethics Committee.

Inclusion and exclusion criteria

Patients were included in the study if they presented with a new infiltrate on a chest radiograph and had three or more symptoms or signs consistent with pneumonia (incorporating new or increased shortness of breath, cough, sputum production, sputum purulence, haemoptysis, chest pain, fever/ rigors or signs consistent with pneumonia on chest auscultation). Exclusion criteria were: hospital-acquired pneumonia (development of symptoms 48 h after admission or discharge from an acute care facility <2 weeks prior to admission); healthcare-associated pneumonia; age <18 years; active thoracic malignancy; immunosuppression (including maintenance corticosteroid therapy at any dose); pulmonary embolism; active tuberculosis; and patients in whom active treatment was not considered appropriate at the time of admission (palliative care). In addition to these standard exclusion criteria for CAP studies, the protocol did not recommend CURB65-guided antibiotic therapy for patients with suspected aspiration pneumonia, lung abscess, empyema or patients allergic to the first-line therapy. These patients were excluded from the analysis. Inclusion and exclusion criteria were the same in both pre- and post-intervention cohorts.

Pre-intervention

From June 2006, CURB65-guided antibiotic therapy was not recommended in the study hospitals. Local guidelines recommended a combination of a β-lactam plus a macrolide for all hospitalized patients with CAP. For moderate–severely ill patients, ceftriaxone 2 g/24 h plus clarithromycin 500 mg twice daily was recommended (alternatively co-amoxiclav (amoxicillin/clavulanic acid) 1.2 g/8 h iv plus clarithromycin 500 mg twice daily). Amoxicillin 500 mg three times daily plus clarithromycin 500 mg twice daily was recommended for non-severe patients. Based on the most recent BTS survey,\textsuperscript{19} these are the most frequently recommended regimens for CAP in the UK.

Respiratory fluoroquinolones are not recommended or generally available at the study hospitals. The CURB65 score was not recommended or widely used during the pre-intervention period. The pre-intervention guidelines provided no information on how to assess the severity of CAP.

Post-intervention

A clinical guideline, covering all aspects of antibiotic prescribing in hospitalized patients was implemented in the study hospitals in June 2008. This guideline contained a recommendation to guide antibiotic therapy for CAP based on the CURB65 score and mirrored the recommendations of the BTS guidelines.\textsuperscript{1} The recommended antibiotic therapy is shown in Figure 1.

Implementation of the guideline was supported by providing pocket-book reminders to junior medical staff and by ward pharmacist review and feedback to prescribers. Although compliance with guidelines was encouraged, prescribing decisions were entirely at the discretion of the attending physician.

Data collection

At the study sites, patients present to an Accident and Emergency department or Medical Assessment Unit. Patients are assessed and may be hospitalized or discharged. Patients are assessed within a maximum of 4 h after admission according to national guidelines and initial antibiotic therapy is commenced. Initial clinical observations (oxygen saturation, respiratory rate, blood pressure, pulse rate and blood glucose) are recorded in the emergency department and standard initial blood tests (full blood count, urea and electrolytes, liver function tests and C-reactive protein) are performed in all patients. Study investigators independently calculated the CURB65 score from these data, but the use of CURB65, and the initial antibiotic prescribing decision was left to the discretion of the attending physicians with no interference from the investigators. To determine reasons for compliance/non-compliance with guidelines, data were collected regarding the site of care and specialty of prescribers commencing initial antibiotic therapy.

Duration of antibiotic therapy was determined as the number of whole days of antibiotic treatment received or the prescribed duration of treatment as supplied for patients discharged from hospital before completion of treatment.

Outcomes

The goal of the intervention was to reduce broad-spectrum antibiotic prescribing in CAP patients without compromising safety of care. Therefore, the primary outcome was use of broad-spectrum antibiotics in the post-intervention group compared with the pre-intervention group. Broad-spectrum antibiotics were defined as co-amoxiclav, cephalosporins or macrolides as these agents are the most frequently associated with \textit{C. difficile} and other antibiotic-associated adverse effects.\textsuperscript{1,15,17,18,20} Reducing prescription of these agents is a national priority.\textsuperscript{20}

The safety of the intervention was assessed by 30 day mortality, requirement for mechanical ventilation and/or vasopressor support, complicated pneumonia (defined as the development of a complicated parapneumonic effusion, empyema or lung abscess\textsuperscript{11}) time to clinical stability (defined using the modified Halms criteria as the first 24 h period in which the following criteria were met: temperature <37.2°C; heart rate <100 beats/min; respiratory rate <24 breaths/min; systolic blood pressure >90 mmHg; oxygen saturation >90% on room air; able to maintain oral intake; normal mental status\textsuperscript{22}) and the length of hospital stay.

As in previous studies, for analyses of the impact of antibiotics we used 30 day mortality, requirement for mechanical ventilation/vasopressor support and complicated pneumonia occurring after 48 h of treatment, as it is suggested that antibiotics are unlikely to influence outcome prior to this timepoint.\textsuperscript{23}
Statistical analysis

All data were analysed using Graphpad Prism (Graphpad software, San Diego, CA, USA). Descriptive statistics for demographic and clinical variables are presented as median (IQR) or mean [standard deviation (SD)] as appropriate. The χ² test and Mann–Whitney U test, respectively, were used to assess categorical and numerical data. To assess the relationship between compliant antibiotic therapy and outcomes, a multivariate logistic regression model was constructed by incorporating all demographic, laboratory, clinical and radiographic variables included in the PSI and compliant antibiotic therapy as a dichotomous independent variable. To assess the relationship between compliant antibiotic therapy and time to clinical stability and length of stay, a multiple linear regression analysis was performed including recognized prognostic variables contained in the PSI (as above) and compliant antibiotic therapy as an independent variable. For these analyses, therapy was considered compliant if it matched the recommended treatment for the corresponding CURB65 score of the patient. For subsequent analyses, ‘over-treatment’ was regarded as the use of co-amoxiclav, cephalosporins or β-lactam plus macrolide therapy in CURB65 0–1, the use of cephalosporins in the CURB65 2 group or the use of additional therapy other than co-amoxiclav or cephalosporins plus macrolide in CURB65 3–5 (e.g. meropenem, piperacillin/tazobactam and macrolide). ‘Under-treatment’ was regarded as non-use of macrolide in CURB65 2–5, or non-use of co-amoxiclav or a cephalosporin in CURB65 3–5. Under- or over-treatment was incorporated into each multivariate analysis as a dichotomous variable. For each multivariate analysis, the Hosmer–Lemeshow goodness of fit test was calculated.

A P value of <0.05 was considered statistically significant for each analysis.

Results

Characteristics of included patients

Initially 765 patients were assessed for inclusion in the pre-intervention cohort and 710 patients were evaluated for inclusion in the post-intervention group. One hundred and seventy patients were excluded from the pre-intervention and 161 patients were excluded from the post-intervention group. The details of the patients included in each phase of the study are shown below (Figure 2).

Following exclusions, the pre-intervention observation phase enrolled 595 patients with CAP and 549 patients were enrolled following the intervention. The demographics, clinical characteristics and laboratory test results obtained on admission for these patients are shown in Table 1. No significant differences were observed between the two groups with the exception of a small difference in median respiratory rate, which was higher in the pre-intervention group.

The effect of the intervention on antibiotic use

The intervention resulted in an overall reduction in the prescription of cephalosporins (from 27.1% of patients receiving this agent in the overall pre-intervention cohort to 8.0% in the post-intervention cohort, P<0.0001). Macrolide use was also reduced substantially (72.8% to 58.7%, P<0.0001). There was a corresponding increase in the prescription of the narrower-spectrum
agent amoxicillin (29.7% to 41.7%, $P<0.0001$) and an increase in the use of amoxicillin monotherapy (10.4% to 29.9%, $P<0.0001$). This is shown in Figure 3.

The intervention did not result in a reduction in prescribing of the broad-spectrum agent co-amoxiclav, and overall use of this agent increased (from 38.7% to 46.4%, $P=0.008$). Subanalysis is shown in Figure 4(c) and demonstrates that the majority of this increase resulted from co-amoxiclav replacing cephalosporins as first-line therapy for severe CAP (CURB65 scores 3–5) in accordance with the national guidelines. Prescribing of co-amoxiclav did not increase in low- or intermediate-risk patients.

When antibiotic use was stratified by CURB65 score, substantial changes were observed. Before the change in guidelines, a variety of regimens were used in the low-risk CURB65 groups (0–1), most frequently amoxicillin/macrolide (29.0%), amoxicillin monotherapy (21.2%), co-amoxiclav/macrolide (20.7%), co-amoxiclav alone (11.4%) and cephalosporins with or without macrolide (9.8%). Following the intervention, there was a significant increase in the proportion of patients receiving amoxicillin monotherapy (52.9%, $P<0.0001$). Co-amoxiclav/macrolide was the second most frequent regimen (24.2%, $P=0.4$ compared with pre-intervention). Overall, the use of cephalosporins (9.8% versus 2.1%, $P=0.005$) and macrolides (64.8% versus 40.8%, $P<0.0001$) decreased significantly in the post-intervention group. Overall co-amoxiclav use was unchanged (32.1% versus 27.9%, $P=0.4$).

Among patients with intermediate severity (CURB65 2) CAP, there was an overall reduction in cephalosporin prescribing (18.2% versus 6.5%, $P=0.007$), while the use of co-amoxiclav (54.5% versus 47.1%, $P=0.2$) was unchanged. Interestingly, although the guidelines did not recommend this regimen, the use of amoxicillin monotherapy increased in the CURB65 2 group (4.4% versus 18.8%, $P<0.0001$) and macrolide use was slightly reduced (76.9% versus 62.3%, $P=0.005$).

Finally, in the highest risk CURB65 group, the major change was a shift from ceftriaxone and macrolide as first-line therapy to co-amoxiclav and macrolide. Cephalosporin/macrolide combination use reduced from 47.9% to 14.0%, $P<0.0001$, while co-amoxiclav/macrolide combination use increased from 25.7% to 62.6%, $P<0.0001$. No significant differences were observed in the use of other regimens. Figure 4 shows the changes in antibiotic prescribing across the three CURB65 groups.

**Duration of therapy and additional antibiotic use**

The guideline implementation did not have a significant effect on duration of antibiotic therapy in any of the CURB65 groups. There was no change in mean duration of therapy in the CURB65 0–1 group (mean ± SD 8.95 ± 3.66 days versus 8.56 ± 3.14 days, $P=0.2$). Similarly, there were no changes in duration of therapy in the CURB65 2 group (9.79 ± 4.4 days versus 9.12 ± 3.63 days, $P=0.1$) or the CURB65 3–5 group (10.1 ± 3.12 days versus 9.93 ± 3.0 days, $P=0.6$).

Use of additional broad-spectrum antibiotics after initial therapy was unchanged in the pre- and post-intervention groups (14.1% versus 15.3%, $P=0.6$).

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**Figure 2.** Flow diagram illustrating the conduct of the before and after evaluation study. Abbreviations: HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia.
Safety of the intervention

Table 2 shows the outcomes between groups in the pre-intervention and post-intervention groups. There was no change in overall 30 day mortality, or in mortality stratified by CURB65 group. Patients in the post-intervention group also showed no increase in requirement for mechanical ventilation/vasopressor support or complicated pneumonia. Time to clinical stability and length of hospital stay was also unchanged between the two groups (Table 2). Similarly, when stratified by CURB65 group, no increases in complicated pneumonia, time to clinical stability or length of hospital stay were observed between the pre- and post-intervention groups (data not shown).

Guideline compliance and outcome

Following the intervention, compliance with national guidelines increased from 25.4% of prescriptions to 61.9%.

Across the entire cohort, compliant antibiotic therapy was not associated with a reduction in 30-day mortality [adjusted odds ratio (AOR) 0.91, 95% confidence interval (95% CI) 0.40–2.06, \(P = 0.8\)], requirement for mechanical ventilation/vasopressor support (AOR 0.57, 95% CI 0.25–1.30, \(P = 0.2\)) or development of complicated pneumonia (AOR 1.31, 95% CI 0.54–3.15, \(P = 0.5\)). Compliance with guidelines was also not significantly associated with time to clinical stability or length of hospital stay.

In the CURB65 3–5 group, the association between compliant treatment and reduced 30 day mortality did not reach statistical significance (AOR 0.45, 95% CI 0.15–1.16, \(P = 0.09\)). There was no association with mechanical ventilation/vasopressor support (AOR 1.63, 95% CI 0.66–4.06, \(P = 0.3\)) and no relationship with complicated pneumonia (AOR 1.23, 95% CI 0.37–4.10, \(P = 0.7\)). There was no relationship with length of hospital stay or time to clinical stability and guideline compliance.

Using the definition of under-treatment in the CURB65 3–5 group, under-treatment (primarily failure to use a macrolide) was associated with increased 30 day mortality (AOR 2.17, 95% CI 1.02–4.61, \(P = 0.04\)), but there was no relationship with requirement for mechanical ventilation/vasopressor support (AOR 2.17, 95% CI 0.70–6.73, \(P = 0.2\)) or development of complicated pneumonia (AOR 0.81, 95% CI 0.20–3.22, \(P = 0.8\)). Patients ‘under-treated’ according to the guidelines had a longer time to clinical stability (co-efficient 0.82

Table 1. Clinical characteristics on admission of patients in the pre-intervention and post-intervention cohorts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients recruited</td>
<td>595</td>
<td>549</td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>age (years)</td>
<td>69 (52 – 79)</td>
<td>69 (53 – 79)</td>
<td>0.6</td>
</tr>
<tr>
<td>sex (% male)</td>
<td>50.1</td>
<td>49.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Co-morbidities, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>congestive cardiac failure</td>
<td>19.7</td>
<td>20.2</td>
<td>0.8</td>
</tr>
<tr>
<td>cerebrovascular disease</td>
<td>11.6</td>
<td>11.5</td>
<td>1.00</td>
</tr>
<tr>
<td>liver disease</td>
<td>4.9</td>
<td>5.3</td>
<td>0.8</td>
</tr>
<tr>
<td>chronic renal failure</td>
<td>5.5</td>
<td>6.4</td>
<td>0.6</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>9.1</td>
<td>10.9</td>
<td>0.3</td>
</tr>
<tr>
<td>COPD</td>
<td>21.5</td>
<td>21.9</td>
<td>0.9</td>
</tr>
<tr>
<td>current smokers</td>
<td>34.5</td>
<td>33.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Clinical characteristics on admission, (n) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CURB65 score 0</td>
<td>127 (21.3)</td>
<td>105 (19.1)</td>
<td>0.4</td>
</tr>
<tr>
<td>CURB65 score 1</td>
<td>124 (20.8)</td>
<td>135 (24.6)</td>
<td>0.1</td>
</tr>
<tr>
<td>CURB65 score 2</td>
<td>158 (26.6)</td>
<td>138 (25.1)</td>
<td>0.7</td>
</tr>
<tr>
<td>CURB65 score 3</td>
<td>109 (18.3)</td>
<td>103 (18.8)</td>
<td>0.9</td>
</tr>
<tr>
<td>CURB65 score 4</td>
<td>62 (10.4)</td>
<td>57 (10.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>CURB65 score 5</td>
<td>15 (2.5)</td>
<td>11 (2.0)</td>
<td>0.7</td>
</tr>
<tr>
<td>confusion</td>
<td>70 (11.8)</td>
<td>86 (15.7)</td>
<td>0.06</td>
</tr>
<tr>
<td>respiratory rate (breaths/min)</td>
<td>24 (20 – 32)</td>
<td>24 (18 – 32)</td>
<td>0.03</td>
</tr>
<tr>
<td>systolic blood pressure (mmHg)</td>
<td>115 (100 – 137)</td>
<td>118 (100 – 132)</td>
<td>0.8</td>
</tr>
<tr>
<td>diastolic blood pressure (mmHg)</td>
<td>66 (58 – 75)</td>
<td>67 (58 – 78)</td>
<td>0.7</td>
</tr>
<tr>
<td>temperature (°C)</td>
<td>37.4 (36.9 – 38.2)</td>
<td>37.3 (36.9 – 38.2)</td>
<td>0.8</td>
</tr>
<tr>
<td>pulse rate (beats/min)</td>
<td>100 (90 – 120)</td>
<td>100 (90 – 120)</td>
<td>0.7</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>haematocrit (%)</td>
<td>39.5 (35.7 – 42.8)</td>
<td>38.8 (35.5 – 42.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>white cell count ((x10^9/L))</td>
<td>13.7 (10.1 – 17.5)</td>
<td>14.3 (10.6 – 18.6)</td>
<td>0.2</td>
</tr>
<tr>
<td>platelet count ((x10^9/L))</td>
<td>238 (193 – 316)</td>
<td>247 (194 – 323)</td>
<td>0.7</td>
</tr>
<tr>
<td>urea (mmol/L)</td>
<td>6.5 (4.5 – 9.6)</td>
<td>6.6 (4.7 – 10.5)</td>
<td>0.4</td>
</tr>
<tr>
<td>sodium (mmol/L)</td>
<td>137 (134 – 139)</td>
<td>137 (134 – 139)</td>
<td>0.7</td>
</tr>
<tr>
<td>potassium (mmol/L)</td>
<td>4 (3.7 – 4.4)</td>
<td>4 (3.7 – 4.4)</td>
<td>0.4</td>
</tr>
<tr>
<td>glucose (mmol/L)</td>
<td>6.4 (5.4 – 7.9)</td>
<td>6.6 (5.6 – 7.9)</td>
<td>0.3</td>
</tr>
<tr>
<td>albumin (g/L)</td>
<td>36 (32 – 39)</td>
<td>37 (33 – 40)</td>
<td>0.1</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>163 (58 – 323)</td>
<td>157 (61 – 267)</td>
<td>0.2</td>
</tr>
<tr>
<td>hydrogen ion (mmol/L)(a)</td>
<td>38 (34 – 44.3)</td>
<td>38 (34.1 – 42.7)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease.
\(a\)Measured in arterial blood, all other variables measured in venous blood.

Figure 3. Overall changes in targeted antibiotic use following the introduction of CURB65-guided therapy guidelines.
standard error 0.40, $P=0.04$), but adequacy of treatment did not affect length of hospital stay (co-efficient 1.80 standard error 2.08, $P=0.4$).

The Hosmer–Lemeshow goodness of fit test indicated model adequacy ($P>0.05$) in each of the logistic regression analyses.

The Hosmer–Lemeshow goodness of fit test indicated model adequacy ($P>0.05$) in each of the logistic regression analyses.

**Prescriber information**

In 96.4% of patients the first dose of antibiotics was received in either the emergency department or medical assessment unit, which is staffed by non-respiratory specialists (accident and emergency specialists, or acute medicine specialists and trainees). The remaining patients received initial antibiotic therapy in the respiratory ward. We did not collect information regarding the grade of prescribers (trainee versus consultant staff) or details of prescribers making subsequent changes to therapy.

**Discussion**

This study has found that the introduction of CURB65-guided antibiotic treatment for patients with CAP was associated with a significant reduction in broad-spectrum antibiotic use. The intervention was safe, with no increases in mortality or major morbidity as a result of the intervention. These changes in antibiotic prescribing are likely to reduce antibiotic-associated complications and reduce treatment-related costs without compromising patient care.

As found in other studies, there was no evidence that broad-spectrum therapy in low-risk patients improved 30 day mortality, requirement for mechanical ventilation/vasopressor support, complicated pneumonia, time to clinical stability or length of hospital stay.\(^{24,25}\)

Although the reductions in antibiotic prescribing described in this study are modest (a 19% reduction in cephalosporins, a 14% reduction in macrolides and a 12% increase in the narrow-spectrum agent amoxicillin) the potential benefits are significant if applied nationally. In the most recent BTS survey of antibiotic prescribing in CAP, it was reported that 61% of Trusts still recommended β-lactam/macrolide combination therapy for mild CAP and that 49% still recommended cephalosporins as first line for severe CAP. Only 34% recommended the BTS-

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>595</td>
<td>549</td>
<td>0.7</td>
</tr>
<tr>
<td>30-day mortality, $n$ (%)</td>
<td>49 (8.2)</td>
<td>42 (7.7)</td>
<td>0.7</td>
</tr>
<tr>
<td>requirement for mechanical ventilation/vasopressor support, $n$ (%)</td>
<td>50 (8.4)</td>
<td>43 (7.8)</td>
<td>0.7</td>
</tr>
<tr>
<td>complicated pneumonia, $n$ (%)</td>
<td>31 (5.2)</td>
<td>33 (6.0)</td>
<td>0.6</td>
</tr>
<tr>
<td>time to clinical stability (days)</td>
<td>3 (1–5)</td>
<td>3 (1–5)</td>
<td>0.9</td>
</tr>
<tr>
<td>length of hospital stay (days)</td>
<td>5 (2–11)</td>
<td>5 (3–10)</td>
<td>0.7</td>
</tr>
<tr>
<td>30 day mortality by CURB65 score</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>CURB65 0–1</td>
<td>7 (2.8)</td>
<td>5 (2.1)</td>
<td>0.8</td>
</tr>
<tr>
<td>CURB65 2</td>
<td>12 (7.6)</td>
<td>8 (5.8)</td>
<td>0.6</td>
</tr>
<tr>
<td>CURB65 3–5</td>
<td>30 (16.1)</td>
<td>29 (17.0)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**Figure 4.** Changes in antibiotic prescribing between the pre-intervention and post-intervention phases of the study according to CURB65 score. (a) CURB65 score 0–1. (b) CURB65 score 2. (c) CURB65 score 3–5.
recommended first-line therapy of co-amoxiclav plus a macrolide.\textsuperscript{19} Based on the results of this study, it seems likely that many hospitals could reduce macrolide and cephalosporin use by using CURB65-guided antibiotic therapy without compromising patient safety.

Use of broad-spectrum antibiotics such as cephalosporins and macrolides is primarily to cover the possibility of Gram-negative, antibiotic-resistant or atypical pathogens and \textit{Staphylococcus aureus}.\textsuperscript{13} Evidence from the UK suggest that these pathogens are less common in patients with mild CAP, where \textit{Streptococcus pneumoniae} is by far the most frequent pathogen.\textsuperscript{26} The frequency of \textit{S. aureus}, Gram-negative organisms and \textit{Legionella pneumophila} increases in patients with severe CAP, and particularly those managed in the intensive care unit (ICU).\textsuperscript{26} This evidence supports the BTS recommendations to use narrow-spectrum agents in mild CAP while recommending broader-spectrum agents and dual therapy in severe CAP.

CURB65 has now been validated in >12,000 patients worldwide and has been shown to have moderate to good performance for predicting 30 day mortality.\textsuperscript{8–14} It is equivalent to the other widely used scoring system, the PSI, in terms of mortality prediction and is recommended by a large number of international CAP guidelines.\textsuperscript{1,27} Nevertheless, a major criticism of CURB65 up to now has been that it has never been shown to improve patient care in a clinical study,\textsuperscript{28} in contrast to PSI, which was shown to increase the proportion of patients treated in the community in several studies.\textsuperscript{6,7} This study therefore represents the first ‘impact analysis’ the authors are aware of, demonstrating that CURB65 can improve patient care by improving antibiotic prescribing.

The level of compliance achieved in the post-intervention phase (60%) is similar to those achieved in previous studies of antibiotic guideline implementation such as Yealy et al.\textsuperscript{7} in which 70% adherence was seen in the most intensive intervention group, but only 50% compliance was seen in the low- and moderate-intensity guideline implementation groups. The difficulties in maintaining guideline compliance were illustrated by a recent study by Blasi et al.\textsuperscript{29} in which an intervention resulted in only 44% compliance with national guidelines.

The reasons for non-compliance with guidelines have been investigated previously. Menendez et al.\textsuperscript{31} found in a large Spanish study that adherence to the guidelines was most common among respiratory specialists or respiratory specialists in training, compared with general physicians. Management by a respiratory specialist was associated with improved prescribing and better outcomes in the Menendez study. In the UK, initial care is provided largely by accident and emergency and acute medicine physicians and in this study >95% of initial prescribing was by non-respiratory specialists. The BTS guidelines\textsuperscript{1} and a recent study by Berwick et al.\textsuperscript{30} have discussed the fact that much of acute care in the UK is now delivered by the speciality of acute medicine, and by junior doctors with limited respiratory specialist experience. Barlow et al.\textsuperscript{31} showed that junior doctors in the UK have poor knowledge of the national guidelines and the majority were unable to calculate a CURB65 score when asked. This may explain some of the deviation from guidelines observed in this study. In addition, Menendez found that non-adherence to guidelines was more common in more severely ill patients, particularly in ICUs. This is understandable, as broader-spectrum antimicrobial treatment may be needed in these patients. No previous study has demonstrated 100% guideline compliance and it is likely that guideline recommendations are not appropriate for a proportion of patients.\textsuperscript{23}

This study will give significant reassurance to clinicians about the potential impact of the BTS CAP guidelines. Previously, CAP guidelines were blamed for promoting excessive antibiotic prescribing leading to epidemics of \textit{C. difficile}\textsuperscript{17} and linked to increased rates of meticillin-resistant \textit{S. aureus}.\textsuperscript{18} Oosterheert et al.\textsuperscript{32} predicted that implementation of the 2001 BTS guidelines in the Netherlands would increase the use of broad-spectrum antibiotics by 21%, while Barlow et al.\textsuperscript{33} showed that implementation of the 2001 BTS guidelines led to a significant increase in broad-spectrum antibiotic use in a single-centre study, although the sample size in this study was small and the intervention included other measures that may have impacted the results.

The current study, therefore, represents, to our knowledge, the first positive impact analysis of CURB65 in clinical practice and the first positive impact analysis for the BTS antibiotic guideline recommendations.

This study did not assess whether CURB65 increased the proportion of patients treated in the community and this study should not be used to extrapolate that CURB65 can be used in other contexts, such as to guide ICU admissions, microbiology tests or other investigations. This study only enrolled hospitalized patients and further studies are required to determine whether CURB65 can guide antibiotic use in primary care.

This study has limitations. This was a before and after evaluation rather than a randomized controlled trial and therefore does not have the level of rigour in matching between the two groups that would be expected in a randomized controlled trial.

The study took place over 3 years and it is possible that some of the improvements in antibiotic prescribing were the result of temporal trends in antibiotic prescribing rather than directly due to the guideline. We have observed, however, that annual antibiotic use in CAP from 2004 to 2008 followed broadly the same pattern as reported in the pre-intervention cohort and that the significant change only occurred after the introduction of the guideline in 2008. This study included only patients with confirmed CAP and does not apply to the larger groups of patients with non-pneumonic lower respiratory tract infection and exacerbations of airway disease where CAP guidelines are often erroneously applied. This study provided data for the safety of the intervention up to 30 days but did not consider mortality or recurrent infection after that time. Evidence suggests that mortality after 30 days is less likely to be CAP related and unlikely to be influenced by antibiotic therapy.\textsuperscript{34} This study took place in the UK, where resistance of \textit{S. pneumoniae} to penicillin and macrolides is relatively low. The antibiotic regimens described in this study may not be appropriate for other healthcare systems with higher rates of antimicrobial resistance.

\textbf{Conclusions}

CURB65-guided antibiotic therapy was associated with a significant reduction in broad-spectrum antibiotic use. The intervention was safe, with no increase in 30 day mortality or major morbidity.
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References
15 Wilcox MH. Respiratory antibiotic use and Clostridium difficile infection: is it the drugs or is it the doctors? Thorax 2000; 55: 633–4.