Severity assessment in community-acquired pneumonia: a review

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Summary

Severity assessment is an important early step in the management of patients presenting with community-acquired pneumonia. Various pneumonia-specific scores, generic sepsis scores and predictive biomarkers have been proposed as tools to aid clinicians in key management decisions. However, there is no uniform agreement about the optimum severity assessment tool to use. This review provides a summary of current evidence surrounding severity assessment in adult patients presenting with community-acquired pneumonia.

Introduction

Community-acquired pneumonia (CAP) is the leading cause of death from infectious diseases in the developed world and is a major burden on healthcare resources. Current guidelines agree that severity assessment is a pivotal early step in the management of patients presenting with CAP. There is, however, no uniform agreement on the optimum severity assessment tool or an agreed definition of the term ‘severe pneumonia’.

The aim of this review is to:

- Discuss the advantages and limitations of the currently available clinical prediction rules for community-acquired pneumonia
- Explore the definition of ‘severe’ community-acquired pneumonia
- Discuss the present and future role of biomarkers in CAP
- Discuss limitations of severity assessment rules and the implications for clinical practice.

Search criteria

The current review was based on a search of Pubmed for articles on major MeSH terms ‘Severity of Illness Index’ and ‘Pneumonia’ between 1981 and 2008. We also performed separate Pubmed searches for terms ‘CURB65’, ‘pneumonia severity index’ and a combination of major MeSH terms ‘C-reactive protein’ and ‘Procalcitonin’ with ‘Pneumonia’. Only articles in English or English translation were reviewed. The articles were selected on the basis of originality and relevance.

What is severity assessment?

Severity assessment is critical for both primary and secondary care physicians to aid in clinical decisions such as need for hospital admission, requirement for intravenous therapy and level of monitoring if admitted. Routine clinical judgement alone has been shown to be a poor predictor of disease severity and evidence suggests that, in many cases, clinicians tend to both overestimate and underestimate the potential severity of CAP. This has led to the development of prognostic scoring systems aimed at assisting in risk stratification of patients presenting with CAP. Important factors to consider in any potential assessment tool...
include its accuracy to predict a specific outcome, its applicability to different healthcare settings and its simplicity for use in everyday clinical practice. Existing severity tools incorporate various combinations of co-morbidities, clinical and laboratory variables that are felt to be important in determining the clinical course of CAP.

The area under the receiver operating characteristic curve (AUC) is a measure of the accuracy of a test to correctly classify patients with and without a particular outcome and is used frequently in studies of severity assessment in CAP. A test with no value, such as a coin toss, would give an AUC of 0.5. With increasing levels, there is increasing discriminatory value, up to a ‘perfect test’ score of 1 (Figure 1).

Pneumonia-specific severity scores

The Pneumonia severity index (PSI) was introduced in 1997 following a study in over 50,000 patients and has now been validated in large, independent populations. It is based on 20 demographic, co-morbid and clinical variables (Table 1) and stratifies patients into five risk classes, three with a low risk of 30-day mortality (class I = 0.1–0.4%; class II = 0.6–0.7% and class III = 0.9–2.8%), a fourth with an increased risk (4–10%) and a fifth with a high risk (27%).

Although, it has been shown to perform consistently well as a predictor of mortality in CAP with AUC values for mortality ranging from 0.74 to 0.83 and is recommended by the current American thoracic society (ATS)/Infectious diseases society of America (IDSA) guidelines, PSI is complex to calculate and therefore difficult to implement in routine clinical practice.

The British Thoracic Society (BTS) proposes use of the CURB65 rule, a 5-point scoring system with three risk categories: 0–1 (low risk of mortality; class 0 = 0.7%; class 1 = 3.2%), 2 (intermediate risk of mortality – 13%) and > 3 (high risk of mortality; class 3 = 17%; class 4 = 41.5%; class 5 = 57%). The individual components involved are shown in Table 2. This severity score, introduced in 2003, has now been extensively validated in over 12,000 patients from several different countries. Studies assessing CURB65 have shown it to be a robust tool with moderate to good discriminatory value (AUC values ranging from 0.73 to 0.83) for prediction of 30-day mortality.

Several studies have prospectively compared the operating characteristics of these two assessment tools and most have found no significant difference in predictive accuracy, except for one study that found a small but significant difference in favour of PSI. However, given CURB-65 is easier to remember and calculate, it is perhaps more likely to gain general acceptance. The ATS recognize the complexity of the PSI for clinical practice and have thus taken the step of recommending use of CURB65 in their latest international CAP guideline.

Table 1 Variables used to calculate the pneumonia severity index

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Physical examination</th>
<th>Laboratory findings</th>
<th>Radiographic findings</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>Altered mental status</td>
<td>pH &lt; 7.35</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>Male sex</td>
<td>Respiratory rate &gt; 30/min</td>
<td>Blood urea &gt; 10.7 mmol/l</td>
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<tr>
<td>Nursing home residency</td>
<td>Systolic blood pressure &lt; 90 mmHg</td>
<td>Sodium &lt; 130 mEq/l</td>
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<tr>
<td>Co-morbid illnesses</td>
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<tr>
<td>Neoplastic disease</td>
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<tr>
<td>Cerebrovascular disease</td>
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<tr>
<td>Congestive cardiac failure</td>
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<tr>
<td>Chronic renal disease</td>
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<td></td>
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<tr>
<td>Chronic liver disease</td>
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<tr>
<td>Temperature &lt; 35°C or &gt; 40°C</td>
<td>PULSE &gt; 125/min</td>
<td>Haematocrit &lt; 30%</td>
<td></td>
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<tr>
<td>Systolic blood pressure &lt; 90 mmHg</td>
<td></td>
<td>PaO₂ &lt; 60 mmHg</td>
<td></td>
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<tr>
<td>Glucose &gt; 13.9 mmol/l</td>
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</table>
One disadvantage of both PSI and CURB65 is their reliance on laboratory investigations for calculation which limits their use by health care professionals in the community. This has led to development of the CRB65 score (CURB65 without the blood nitrogen urea component), a modified version of CURB65 that does not rely on the results of any laboratory tests and is thus better suited to use in the community. This modified tool appears to perform equally well compared with both CURB65 and PSI with AUC values ranging from 0.69 to 0.78. However, despite being proposed as a score for use by general practitioners, most studies have assessed CRB65 solely in a hospital setting. Only one study to date has examined the performance of CRB65 specifically in a community setting and further validation of this score in primary-care based populations is therefore warranted. Another important advantage of CRB65 is increased simplicity, as it relies on fewer components, and a recent study has shown it can be simplified even further without compromising predictive accuracy by omitting the diastolic blood pressure and using only systolic blood pressure <90 mmHg as a criterion of hypotension.

Other proposed assessment tools include ADROP, CORB and the SCAP prediction rule (see Appendix 1 and Table 7). These derived scores are relatively simple to calculate and differ from CURB-65 by giving greater weight to markers of deranged physiology such as assessment of oxygenation. At present, their use is supported by either a single study or small number of preliminary studies and further external validation is thus required.

**Alternative definitions of ‘Severe’ pneumonia**

It is recognized that the majority of mortality in CAP occurs in the elderly and many patients that die are treated palliatively. In addition, the mortality will include both pneumonia related and pneumonia unrelated deaths and up to 50% of deaths from CAP are unrelated to initial severity. Therefore, 30-day mortality may not be the ideal measure to identify patients requiring the most intensive management. Other endpoints have been sought to predict severe pneumonia such as ICU admission and the need for ventilatory or vasopressor support. The American Thoracic Society states that ‘severe community-acquired pneumonia is an entity described in the literature in reference to patients with CAP admitted to the intensive care unit (ICU)’.

Some studies have thus investigated the predictive value of the commonly used severity scores PSI and CURB-65 for the outcome of need for admission to ICU. When considering these outcomes, PSI and CURB-65 tend to perform less effectively with studies showing AUC values as low as 0.69 and 0.66, respectively.

In comparative studies, the modified American Thoracic society (mATS) rule has been shown to be the existing score with the best accuracy in predicting need for ICU admission with AUC values as high as 0.90 in one study and it is also recommended by the current ATS guidelines. This score was designed specifically to guide clinical decisions for transfer to ICU, indicated by the presence on admission of, either a single major criterion or three minor criteria (Table 3). A major problem with advocating the mATS rule to guide clinical decisions is that it uses two outcome measures (development of septic shock and need for mechanical ventilation) as its ‘major criteria’ variables. Therefore, any patient that fulfils a modified ATS major criteria will, by definition, need ICU care (as this is the site where patients are transferred to for mechanical ventilation and/or vasopressors support). Therefore, it is perhaps unsurprising that this score performs so well for the outcome of need for ICU admission and raises questions over its use clinically as it is not truly predictive of outcome.

There are also significant concerns about the use of ICU admission as a reliable marker of severity in CAP as the decision to admit a patient to ICU differs according to local policies and availability of ICU resources. Therefore, ICU rates may vary significantly between departments, nationally and internationally and this raises questions over its use as a standardized definition of severity in CAP. Existing studies have shown widely varying ICU admission rates from as low as 4% in some cohorts to as high as 17% in others.

Other studies have evaluated PSI and CURB65 for their predictive accuracy for the major ATS criteria of need for mechanical ventilation, or presence of septic shock with need for vasopressors. These outcomes appear to be more robust measures.
of CAP severity compared with need for ICU admission, as they are less subjective to interpretive variability between centres. Studies have shown that AUC values for PSI and CURB65 range from 0.69 to 0.79 and 0.59 to 0.77 respectively, for prediction of these outcomes.\(^10,12,26\)

Table 4 shows AUC values for 30-day mortality and need for mechanical ventilation and/or inotropic support in some of the existing pneumonia-specific scores. The SMART-COP is an 8-point scoring system that has been shown to outperform PSI and CURB65 for predicting need for intensive respiratory or vasopressor support in preliminary analyses (see Appendix 1 and Table 7).\(^26\)

Patients with community-acquired pneumonia may develop infective complications such as pulmonary abscess, complicated parapneumonic effusion and empyema. These complications require admission to hospital and often require prolonged antibiotic treatment and/or percutaneous drainage procedures. Such outcomes are not included in any recognized definition of severe pneumonia but most physicians would recognize them as indicative of ‘severe’ CAP. One study has evaluated the accuracy of CURB65 and PSI to predict development of complicated pneumonia and/or empyema and showed they have poor predictive accuracy (AUC 0.54 and 0.60 respectively).\(^10\) Admission C-reactive protein (CRP) levels, however, had a better predictive accuracy for this outcome (AUC 0.76). In addition, a CRP level that failed to fall by 50% or more in 4 days following hospital admission was associated with increased risk of development of complicated effusion or empyema.\(^10\)

Other variables that have been shown to be predictive of development of complicated pneumonia or empyema include hypoalbuminaemia\(^27,28\) and prior alcohol abuse.\(^29,30\)

Other studies have looked at alternative measures of severity including need for hospital admission and length of hospital stay.\(^8,31\) However, these outcomes are likely to be influenced by social factors and may not solely reflect disease severity. Therefore, they may be less preferable to more robust measures such as 30-day mortality and need for mechanical ventilation and/or inotropic support.

### Generic sepsis scores as assessment tools in CAP

More recently, it has been suggested that pneumonia-specific severity scores, such as PSI and CURB65, should be replaced by generic severity scores as these have been shown to perform well in populations with sepsis, many of whom have pneumonia.\(^32–38\) This is driven by evidence that pneumonia specific rules are underutilized in clinical practice. One study found that only 7% of junior doctors were able to name the CURB criteria correctly\(^39\) while another found that only a small proportion (13%) of patients with CAP received severity assessment, of any kind, on admission.\(^40\) An abundance of severity scores for different conditions may cause confusion and there is an argument that
pneumonia-specific tools should be supplanted by a generic ‘one size fits all’ illness scoring tool. It has been proposed that a generic predictive tool applicable to all forms of sepsis including pneumonia may be easier to remember and thus more useful in clinical practice. Scoring systems such as SIRS (systemic inflammatory response syndrome) criteria and SEWS (standardized early warning score) have been extensively studied in acutely unwell patients and are relatively simple to calculate. The results of one study comparing CURB65/CRB65 against the generic sepsis scores SIRS and SEWS, suggested that pneumonia-specific scores should not be supplanted by generic scores for severity assessment in CAP with AUC values of 0.68 and 0.64 for SIRS/SEWS compared with 0.78 for CURB65. However, notable limitations of this study included inconsistencies in the definition of CAP with only 52% having radiographically confirmed disease. Other studies have shown that SIRS performs less favourably than PSI for prediction of progression to sepsis in severe CAP. However, one potential advantage of generic scores such as SEWS is that it can be measured daily and allows monitoring over time, unlike most other prediction rules which have been designed solely for use on admission.

Studies have compared the more complicated generic sepsis score APACHE II (Acute physiology and chronic health evaluation II) with pneumonia-specific scores. APACHE is a severity score calculated from 12 physiological measurements, designed for use in ICU admitted patients. It has been shown to outperform CURB65/CRB65 as a predictor of outcome in patients specifically with Methicillin Resistant Staphylococcus Aureus (MRSA) pneumonia and showed equal performance to CURB65 and PSI in pneumococcal pneumonia. However, it remains to be seen if this holds true for all forms of CAP, regardless of microbiological cause.

Overall, the limited numbers of studies to date do not support use of generic sepsis scores over pneumonia-specific scores in CAP (summarized in Table 5). The absence of methodologically sound research in this area means this issue is largely unresolved and further comparison in independent populations is therefore warranted.

### Predictive biomarkers in severity assessment

As existing scoring systems may be too complicated for use in everyday practice, it would be appealing to have a single blood test that would provide rapid prognostic information equivalent to these scores. This has led to increasing interest in the use of serum biomarkers as potential predictors of outcome in CAP. Several biomarkers have been evaluated to date, such as C-reactive protein (CRP), procalcitonin, proadrenomedullin, pro-atrial natriuretic peptide, pro-vasopressin and copeptin.

CRP is an acute phase protein synthesized by the liver in response to tissue damage. Initial small studies suggested that it did not appear to correlate with severity in CAP and, on the basis of this evidence, CRP was not recommended as a reliable admission severity marker in national guidelines. However, a more recent larger study demonstrated that a low CRP (<100 mg/l) has similar negative predictive values to CURB 65 and PSI for predicting 30-day mortality and need for mechanical ventilation and/or inotropic support in CAP. The authors concluded that CRP may be a useful adjunct to clinical judgement in identifying low-risk patients. Furthermore, failure of CRP to fall by 50% or more on repeat measurement at Day 4, independent of admission CRP level, was shown to be associated with increased 30-day mortality and need for mechanical ventilation and/or inotropic support and complicated pneumonia. These findings
were supported by a large Spanish study that found a high CRP on admission and at Day 3 to be predictive of treatment failure in CAP. Another biomarker gaining interest is procalcitonin (PCT), a precursor of the hormone calcitonin produced by the C cells of the thyroid gland. Blood levels of procalcitonin rise in response to systemic inflammation associated with infection and several studies have shown that serum PCT levels correlate with pneumonia severity. A recent large study showed that a low PCT (<0.228 ng/ml) has a high negative predictive value for mortality from CAP and similar receiver operating characteristics for survival when compared with the CRB65 score. Other studies however, have shown little advantage for the use of procalcitonin over the cheaper and more widely available alternative biomarker CRP.

If simplicity is the key to acceptance and integration of a severity assessment tool into clinical practice, there may be an argument for advocating the use of these serum biomarkers as potential predictors of outcome in CAP. However, they have not been extensively studied and further validation studies are required to investigate the safety of using a single blood test to guide placement and management of patients with CAP. The incorporation of biomarkers into existing scores may further improve their accuracy and also warrants investigation. Other markers including pro-adrenomedullin, pro-atrial natriuretic peptide, pro-vasopression and copeptin have been investigated with remarkably high AUC values for mortality in pilot studies. Larger confirmatory studies will be required before any of these tests can be recommended for routine use.

One major advantage that biomarkers offer is that serial measurements can be taken as a marker of treatment response. Measurement of CRP on Day 3 or of admission has been shown to be a reliable marker of treatment failure in patients with CAP. There is no reason why severity assessment should end at the hospital ‘front door’ and this is a genuine advantage that biomarkers offer over traditional severity scores such as PSI and CURB65, which are designed only for use on admission. This potential use is acknowledged by national guidelines.

Limitations to severity assessment

Although severity assessment scores are a useful aid to clinical decision making for patients with CAP, they have important limitations to their use. Table 6

<table>
<thead>
<tr>
<th>Assessment tool</th>
<th>Strengths</th>
<th>Weaknesses</th>
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<tbody>
<tr>
<td>PSI</td>
<td>Well validated and shown to improve outcome</td>
<td>Complex to calculate</td>
</tr>
<tr>
<td></td>
<td>Useful research tool</td>
<td>Performs less well for need for ICU/ventilatory or vasopressor support</td>
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<tr>
<td></td>
<td></td>
<td>Underestimates severity in young patients</td>
</tr>
<tr>
<td>CURB65</td>
<td>Well validated and simple to calculate</td>
<td>Performs less well for need for ICU/ventilatory or vasopressor support</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Underestimates severity in young patients</td>
</tr>
<tr>
<td>CRB65</td>
<td>Well validated, simple and suitable for use in community</td>
<td>As for CURB65</td>
</tr>
<tr>
<td>SMART-COP</td>
<td>Superior accuracy for prediction of need for ventilatory/vasopressor support</td>
<td>Complex to calculate with multiple points for different variables and age-adjusted cut-offs</td>
</tr>
<tr>
<td>Modified ATS</td>
<td>Performs well for predicting ICU admission</td>
<td>Need for ICU is a less accurate measure of severity due to inter-center variability</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Questionable clinical use</td>
</tr>
<tr>
<td>C-Reactive protein</td>
<td>Cheap, simple and widely available</td>
<td>Not extensively validated</td>
</tr>
<tr>
<td></td>
<td>Serial measurements can detect treatment failure</td>
<td>May be affected by factors other than pneumonia severity</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>Simple</td>
<td>Not routinely available</td>
</tr>
<tr>
<td></td>
<td>Serial measurements can detect treatment failure</td>
<td>Relatively expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not extensively validated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May be affected by factors other than pneumonia severity</td>
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</tbody>
</table>
Severity criteria have been used to guide clinicians about need for hospital admission and to determine site of care. Low admission severity scores (CRB65 0, CURB65 0 or 1 or PSI 1-3) are regarded as low risk and can potentially be managed at home. However, PSI or CURB65 cannot be used solely by the clinician to define site of care as they do not consider social factors that often dictate need for hospitalization. Studies have revealed that a large proportion of patients with low risk pneumonia according to severity scoring still require hospitalization for concomitant social factors such as acute alcohol intoxication, lack of a stable home environment or other factors such as intolerance of oral therapy or occurrence of medical conditions other than CAP.

Studies have also shown that both PSI and CURB65 can also underestimate the potential severity of CAP in young patients, who may be at risk of death or serious complications such as need for mechanical ventilation and/or inotropic support, despite being classified in a ‘low risk’ category. A recent study has shown that CURB65 and PSI have sensitivities as low as 54% for prediction of need for mechanical ventilation and/or inotropic support in patients under the age of 50 years and this reinforces the fact that severity scores should only be used in conjunction with clinical judgement.

The United Kingdom department of health has recognized this limitation by specifically advising that CURB65 may underestimate severity of pneumonia in young adults.

Conclusion

Severity assessment is a crucial component of the management of patients presenting with CAP to guide physicians in clinical decisions. There are large numbers of pneumonia-specific severity and generic sepsis scores available for this purpose. The pneumonia severity index is regarded as the ‘gold standard test’ but complexity limits its use in routine clinical practice. Given that simplicity is critical to acceptance for general use, CRB65 is the most useful clinical score currently available. Severity assessment tools are evolving, but at present have major limitations and should be used with caution and only in conjunction with clinical judgment.

References


Appendix 1: Alternative pneumonia specific severity scores

**SMART-COP**

SMART-COP is a recently described tool designed to predict patients admitted with community-acquired pneumonia likely to require intensive respiratory or vasopressor support (IRVS). The score was retrospectively calculated from prospectively collected data. Factors involved are shown in Table 7.

The authors recommend the following interpretation:

- 0–2 points Low risk of needing IRVS
- 3–4 points Moderate risk (one in eight) of needing IRVS

### Table 7: Alternative pneumonia-specific severity scores

<table>
<thead>
<tr>
<th>SMART-COP</th>
<th>A-DROP</th>
<th>CORB</th>
<th>SCAP rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP &lt;90 mmHg (2 points)</td>
<td>Age (male &gt;70 years, female &gt;75 years)</td>
<td>Confusion</td>
<td>Arterial pH &lt;7.30</td>
</tr>
<tr>
<td>Multilobar Chest X-ray involvement (1 point)</td>
<td>Dehydration (blood urea nitrogen &gt;210 mg/l)</td>
<td>Oxygen saturations &lt;90%</td>
<td>Systolic blood pressure &lt;90 mmHg</td>
</tr>
<tr>
<td>Albumin &lt;35 g/l (1 point)</td>
<td>Respiratory failure (SaO2 ≤90% or PaO2 ≤60 mmHg)</td>
<td>Respiratory rate ≥30/min</td>
<td>Respiratory rate &gt;30/min</td>
</tr>
<tr>
<td>Respiratory rate (age-adjusted cut-offs)</td>
<td>Orientation disturbance (confusion)</td>
<td>Blood pressure (systolic ≤90 mmHg)</td>
<td>Altered mental status</td>
</tr>
<tr>
<td>Age ≤50 years; ≥25 br/min (1 point)</td>
<td>Blood pressure (Systolic ≤90 mmHg)</td>
<td></td>
<td>Blood urea nitrogen &gt;30 mg/dl</td>
</tr>
<tr>
<td>Age &gt;50 years; ≥30 br/min (1 point)</td>
<td>Tachycardia ≥125 b.p.m. (1 point)</td>
<td>Oxygen arterial pressure &lt;54 mmHg</td>
<td>Oxygen arterial pressure &lt;54 mmHg or ratio of arterial oxygen tension to fraction of inspired oxygen &lt;250 mmHg</td>
</tr>
<tr>
<td>Confusion of new onset (1 point)</td>
<td>Oxygenation (Age-adjusted cut-offs)</td>
<td>Age ≥80 years</td>
<td>Multilobar/bilateral lung affection</td>
</tr>
<tr>
<td>Age ≤50 years: &lt;70 mmHg or O2 sat ≤93% (2 points)</td>
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</table>
5–6 points  High risk (one in three) of needing IRVS
>7 points  Very high risk (two in three) of needing IRVS

**A-DROP**
A recently described modified version of CURB-65, showing similar predictive accuracy in a retrospective observational study of 329 patients.\textsuperscript{18} It comprises of five separate variables (Table 7).

**CORB**
A modified version of CURB-65 which showed similar accuracy to existing tools for prediction of mortality and need for ventilatory/inotropic support in derivation and validation cohorts.\textsuperscript{19} Table 7 illustrates the parameters involved.

**SCAP prediction rule**
A clinical prediction rule consisting of eight variables (Table 7) identified on multivariate analysis of data collected in 1057 patients with CAP.\textsuperscript{20} The rule showed superior predictive accuracy to CURB65, PSI and modified ATS scores for a combined endpoint of in hospital death, mechanical ventilation and septic shock.