Severity assessment scores to guide empirical use of antibiotics in community acquired pneumonia

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Severity assessment scores were first developed to predict the 30 day mortality in community acquired pneumonia; however, several guidelines have extended their use to guide empirical antibiotic prescription decisions. This approach has theoretical advantages because a decrease in broad-spectrum antibiotic treatment in low-risk patients might reduce antibiotic-related side-effects, and to give broad-spectrum therapy to patients at higher risk of death is intuitive. However, evidence in support of this approach is not clear. In particular, the British Thoracic Society guidelines suggest withholding a macrolide from patients with low CURB 65 scores, despite evidence that these patients have a higher frequency of atypical pathogens than do those with a higher severity of pneumonia. Severity scores do not perform well in some groups and might overestimate disease severity in elderly people, leading to inappropriate broad-spectrum treatment to those at high risk of complications such as *Clostridium difficile* infection. In this Review, we discuss the evidence for antibiotic prescribing guided by severity score and suggest that more evidence of effect and implementation is needed before this approach can be universally adopted.

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Introduction

Community acquired pneumonia is the largest cause of death from infectious diseases in developed countries and a major indication for antibiotic prescription in primary and secondary care.[1] The prognosis of community acquired pneumonia varies, mortality is less than 1% in patients from outpatient departments and discharged from emergency departments,[2] but can exceed 50% in patients admitted to intensive care units (ICU).[3] Severity of infection is not always obvious at presentation; use of clinical judgment alone might underestimate or overestimate true severity of illness.[4,5] Therefore, severity scores have been developed to help clinicians in a range of decisions. Although severity scores were originally developed for the prediction of 30 day mortality, they are increasingly used in other clinical decisions on the presumption that patients at higher risk of death need intensified care and extensive investigation, whereas patients at lower risk do not.

The microbial causes of community acquired pneumonia are rarely known at diagnosis and so initial antibiotic prescription decisions are empirical and directed at several probable causative pathogens. Various factors can affect a clinician's choice of antimicrobial drug, including patient's age and underlying comorbidities, place of residence, geographical location and local resistance patterns, previous sputum microbiology samples, and patient-specific factors such as antibiotic intolerance or allergies. Most international guidelines recommend broad-spectrum empirical treatment based on site of care. Narrower-spectrum antibiotics are recommended for those seen in outpatient settings where drug-resistant pathogens or Gram-negative bacteria are fairly uncommon. By contrast, broader-spectrum antibiotics are recommended in inpatients settings, with the most intensive treatment for patients in the ICU, including coverage of drug-resistant or Gram-negative bacteria.[6–10]

The British Thoracic Society guidelines[11] recommend the CURB 65 score (presence of confusion, urea >7·0 mmol/L, systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg, respiratory rate ≥30 breaths per min, age ≥65 years). Other international guidelines[12,13] recommend similar approaches.

Antibiotic prescription is suboptimal in community acquired pneumonia, and an incorrect choice of antibiotics might lead to treatment failure and increased mortality.[14] By contrast, for some patients, excessive treatment with broad-spectrum antibiotics might increase the risk of antibiotic resistance and healthcare-associated infections such as with *Clostridium difficile*.[15,16] This risk has led to recommendations for decisions to be based on severity score, targeting broad-spectrum therapy at high-severity patients, and reducing excessive treatment of less severely ill patients. Most acute care in the UK is now done by acute medicine specialists and by junior doctors with little specialist respiratory experience.[17] More than 95% of initial prescription is done by non-respiratory specialists.[18] Therefore, clear guidance is needed, and approaches based on severity score might provide a simple algorithm to help those with a small amount of specialist experience to make appropriate antibiotic choices in community acquired pneumonia. However,

Key messages

- Initial empirical antibiotic choice is a key early decision in the management of patients presenting with community acquired pneumonia.
- An increasing number of international guidelines, including those of the British Thoracic Society, recommend antibiotic prescribing guided by admission severity score.
- Analysis of the evidence suggests that severity scores do not accurately predict microbial aetiology, with little evidence that they modify antibiotic response and scarce data on the effect of these strategies in clinical practice.
- Although severity scores might provide a simple strategy for antibiotic prescribing, further evidence for effect and implementation is needed before these approaches can be universally adopted.

because severity scores were not originally designed to guide antibiotic prescription, whether their use in clinical practice is a rational and effective approach is not known.

In this Review, we discuss the evidence for severity scores to guide antibiotic choices in patients presenting with community acquired pneumonia.

Microorganisms that cause community acquired pneumonia

Knowledge of the most common causes of community acquired pneumonia is important to allow clinicians to make informed choices about initial empirical antibiotic prescription. A range of pathogens can cause community acquired pneumonia, and *Streptococcus pneumoniae* is the most commonly identi ed. Other common pathogens are *Haemophilus in uenzae, Staphylococcus aureus, Moraxella catarrhalis, Coxiella burnetii,* Gram‑neg ative enteric bacilli, some atypical bacteria (*Mycoplasma pneumoniae*, *Chlamydophila pneumoniae* and *Legionella* spp), and some respiratory viruses. Although clinical features cannot accurately distinguish between causative pathogens in community acquired pneumonia, some microorganisms have recognised risk factors (table 1).

Some studies, particularly those from the USA, show an increasing prevalence of antibiotic‑resistant pathogens in community acquired pneumonia. Several studies have de ned risk factors for meticillin‑resistant *S aureus*, *Pseudomonas aeruginosa*, and Gram‑negative Entero‑bacteriaceae. These risk factors are: hospital admission for 2 days or more in the preceding 90 days, residence in a nursing home, chronic kidney dialysis, home wound care, home intravenous infusion therapy, or a family member with multidrug‑resistant pathogens.[31,34,35] In 2005, the Infectious Diseases Society of America and American Thoracic Society guidelines de ned these patients as those with healthcare‑associated pneumonia, and recommend different empirical antibiotic treatment to community acquired pneumonia. These recommendations are controversial, and the ndings of high incidence of drug‑resistant pathogens reported in studies from the USA and Asia[34,36,37] have not been replicated in European studies of health‑care‑associated pneumonia.[35,38,39]

In a cohort from the USA, Shorr and colleagues[34] showed that the criteria for health‑care‑associated pneumonia has poor speci city for the identi cation of patients with drug‑resistant organisms. The investigators proposed an alternative scoring system based on the presence or absence of factors such as recent admission into hospital, the patient living in a long‑term care facility, haemodialysis, or admission to an ICU in the 24 h before presentation. In Europe, Aliberti and colleagues[35] reported that both admission into hospital in the previous 90 days and living in a nursing home were independent predictors of drug‑resistant pathogens. The researchers also proposed a scoring system with weighted risk for comorbidities such as diabetes, chronic obstructive pulmonary disease, and cerebrovascular disease, residence in a nursing home, previous admission to hospital, and chronic renal failure. A multivariate analysis found no link between the severity score, pneumonia severity index, and the presence of drug‑resistant pathogens. This result suggests that background and demographic factors, rather than severity scores, might be the most important considerations when identifying patients at risk of resistant pathogens. Very few of the factors associated with drug‑resistant pathogens are included in pneumonia severity scores (table 1).

Although risk factors have been established for several microorganisms that can cause community acquired pneumonia, no studies have identi ed a predictive severity score for speci c disease patterns (table 1). Because none of the risk factors are likely to be sufficiently robust to determine cause on admission, broad‑spectrum empirical antibiotic treatment is recommended in all guidelines.

	Risk factor	Prognostic scores that contain risk factor
Streptococcus pneumoniae	Older age (>75 years),[19] intubation,[20,21] overcrowding,[22] smoking[23]	CURB 65, PSI, SMART‑COP (age), ATS criteria (intubation)
Haemophilus in uenzae	Elderly patient,[24] chronic lung disease,[24] smoking[24]	CURB 65, SMART‑COP, PSI (age)
Mycoplasma pneumoniae	Younger age, previous antibiotic use,[25] extrapulmonary manifestations (thrombocytosis, haemolysis, etc)[26]	None
Staphylococcus aureus	Concomitant or preceding in uenza infection,[27] haemoptysis, cavitating lung lesions[28]	None
Legionella pneumophila	Intubation,[21] geography,[29] water storage systems,[29] smoking, immunosuppression,[26] liver enzyme disorders,[26] hyponatraemia[26]	ATS criteria (intubation) PSI (hyponatraemia)
Chlamydophila pneumoniae	Older age (>75 years),[19] resident in a nursing home[30]	CURB 65, PSI, SMART‑COP (age), PSI (resident in a nursing home)
Enterobactericeae	Residence in a nursing home,[31] aspiration,[32] chronic lung disease[32]	PSI (living in a nursing home)
Pseudomonas aeruginosa	Aspiration, chronic lung disease,[32,33] previous antibiotic use[33]	None
Drug‑resistant pathogens combined	Previous admittance into hospital,[34,35] living in a nursing home,[34,35] chronic renal failure and haemodialysis,[34,35] previous antibiotic use[35]	PSI (living in a nursing home, chronic renal failure)

CURB 65=confusion, urea, respiratory rate, blood pressure, age 65 years. PSI=pneumonia severity index. ATS=American Thoracic Society.

Table 1: **Risk factors for speci c pathogens in patients with community acquired pneumonia**

Comparison of guidelines for empirical antibiotic prescription

Site of care versus severity score approaches

Various local, national, and international guidelines exist for the management of community acquired pneumonia, and the recommendations for empirical antibiotic treatment differ substantially. Most guidelines recommend empirical therapy to be based on site of care, with speci c recommendations to those managed as outpatients, as

inpatients, and in ICUs.[7,8,40,41] A few guidelines, including those from Britain, Australia, and Japan, recommend antibiotic prescription based on severity assessment.[11–13]

Although not a formal severity score prescription strategy, site of care approaches are made on the premise that disease severity is probably lower in outpatients or inpatients without complications than in patients in ICUs. Whether severity scores or site of care approaches are more accurate predictors of prognosis or for determining microbial cause has not been studied. However, microbial cause varies significantly with site of care.[42] Notably, site of care approaches might be less applicable in the UK, where fewer patients with community acquired pneumonia are managed in ICUs than for those in the USA, which has seven times more ICU beds per capita.[43] Furthermore, patients might not be admitted to an ICU directly on admission, with the decision to move occurring later.[3] Studies have suggested that severity scores are poorly predictive of the need for ICU admission,[43,44] with one study[44] reporting that only 20% of patients in pneumonia severity index class 5 were admitted to the ICU. Therefore, site of care decisions might lead to different antibiotic choices compared to strategies based on severity score (figure 1). For example, in a recent UK-based prospective study of 1079 patients, 41·0% were classified as low risk with CURB 65, 26·5% as intermediate risk, and 32·5% as high risk, with 9·5% admitted to an ICU.[47] If managed according to the British Thoracic Society severity score, 32·5% of patients would be given a broad-spectrum antibiotic and 59% would be given a macrolide. However, if patients were managed with a site of care approach, only 9·5% would get broad-spectrum treatment and 100% would get a macrolide (table 2).[7]

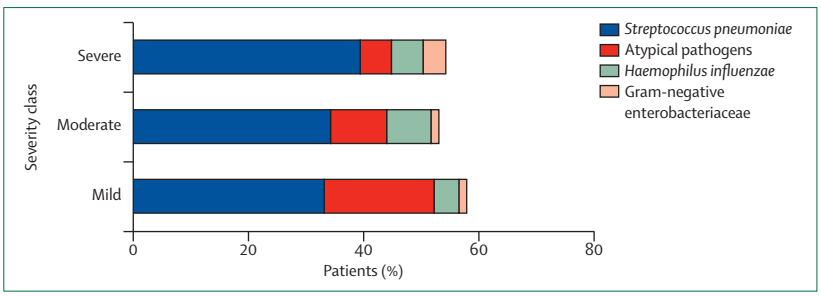

Figure 1: **Microbial aetiology of community acquired pneumonia according to severity score**
Frequency of selected pathogens, stratified according to severity class by PSI,[42,45] CURB 65,[42] and CRB 65[46] in studies of patients with community acquired pneumonia. ICU=intensive care unit. PSI=pneumonia severity index. CURB 65=confusion, urea, respiratory rate, blood pressure, age 65. CRB 65=confusion, respiratory rate, blood pressure, age 65 years. AUC=area under the receiver operator characteristic curve.

British Thoracic Society guidelines

The British Thoracic Society guidelines[1] recommend initial severity assessment with the admission CURB 65 score, and for this score to guide empirical antibiotic choices (figure 2). The society recommend that patients with low-severity community acquired pneumonia (CURB 65=0–1) are given oral amoxicillin, unless oral therapy is contraindicated. Those with moderate-severity disease (CURB 65=2) should be treated with oral combination therapy of amoxicillin plus a macrolide, unless oral therapy is contraindicated or the patient has not responded to amoxicillin before admission—a macrolide monotherapy is recommended in such cases. The guidelines recommend that patients with high-severity disease (CURB 65=3–5) are given intravenous antibiotics that consist of a broad-spectrum β-lactamase drug such as co-amoxiclav (amoxicillin and clavulanate acid) with a macrolide such as clarithromycin. Alternative regimens are suggested for all severity groups if a patient has previous history of antibiotic allergy. The guidelines also recommend that clinical judgment should always be used with CURB 65 scoring and, therefore, suggest that deviations from the recommended strategy are acceptable if clinically justified, although the circumstances in which this is appropriate are not clearly stated.

The European Respiratory Society

The European Respiratory Society guidelines[6] recommend empirical treatment based on site of care. Patients that have been admitted to hospital but who do not need ICU therapy are recommended to receive one of the following: an aminopenicillin with or without a macrolide; a non-antipseudomonal cephalosporin; or fluoroquinolone (levofloxacin or moxifloxacin). Patients admitted to an ICU or are given intermediate-level care with no risk factors for *P aeruginosa,* are recommended to receive a third-generation cephalosporin, plus either a macrolide or a fluoroquinolone. If *P aeruginosa* is suspected or confirmed, the patient should be given a combination of the following antibiotics: an antipseudomonal cephalosporin or a carbopenem; or either ciprofloxacin or a macrolide, plus an aminoglycoside.

American Thoracic Society and Infectious Diseases Society of America

The American Thoracic Society and the Infectious Diseases Society of America guidelines[7] also recommend prescription based on site of care, with patients stratified into outpatient, inpatient non-ICU, and inpatient ICU groups. The guidelines recommend outpatients are given a macrolide or doxycycline, unless major comorbidities are present, in which situation a fluoroquinolone or β-lactam, plus a macrolide, is suggested. Inpatients that do not require ICU admission are recommended to receive a β-lactam, plus a macrolide or a fluoroquinolone. Patients admitted to ICUs are recommended a β-lactam, plus either azithromycin or a fluoroquinolone, with specific guidance given for *Pseudomonas* spp or community acquired meticillin-resistant *S aureus* infections.

Other international guidelines

Antibiotic treatment guided by severity score is also recommended by other international guidelines.

	Method of prescription guidance	Recommendation
Infectious Diseases Society of America and American Thoracic Society[7]	Site of care, risk factors for speci c pathogens, risk factors for antimicrobial resistance	Previously healthy outpatients with no risk factors for resistant pathogens: macrolide or doxycycline; outpatients with risk factors for speci c pathogens or antimicrobial resistance*: respiratory uoroquinolone, β lactam, and a macrolide; inpatients not in an ICU: respiratory uoroquinolone, β lactam, plus a macrolide; inpatients in an ICU: β lactam (cefotaxime, ceftriaxone, or ampicillin sulbactam), and either azithromycin or a respiratory uoroquinolone
European Respiratory Society and the European Society of Intensive Care Medicine[6]	Site of care, risk factors for *Pseudomonas aeruginosa*	Outpatients: amoxicillin or doxycycline; inpatients not in an ICU: β lactam, with or without a macrolide and a respiratory uoroquinolone; inpatients in an ICU: cephalosporin and a macrolide, plus a respiratory uoroquinolone with or without cephalosporin
British Thoracic Society[1]	CURB 65	See gure 2
Japanese Respiratory Society[13]	A DROP, pathogen directed	Mild to moderate pneumonia (A DROP 0 3): typical amoxicillin, atypical macrolide or tetracycline; severe pneumonia (A DROP 4 5) young age (men <70 years, women <75 years), intravenous uoroquinolone; severe pneumonia (A DROP 4 5) elderly patient (men >70 years, women >75 years) or comorbidity: third generation cephalosporin and tetracycline or macrolide
Australia[12]	SMART COP, CORB	Non severe pneumonia (CORB <2 or SMART COP <5): intravenous benzylpenicillin plus oral doxycycline or roxithromycin; severe pneumonia (CORB >2 or SMART COP >5): intravenous benzylpenicillin plus intravenous gentamicin or intravenous ceftriaxone or intravenous cefotaxime, plus intravenous azithromycin
Canadian Infectious Disease Society and Canadian Thoracic Society[9]	Site of care, risk factors for speci c pathogens and comorbidities	Outpatients: a macrolide; outpatient with chronic obstructive pulmonary disease: a newer macrolide; Outpatient with recent antibiotic or corticosteroid use: respiratory uoroquinolone; nursing home resident: uoroquinolone, or β lactam plus macrolide, inpatient: a respiratory uoroquinolone; patient in ICU: β lactam plus a respiratory uoroquinolone; risk factors for *P aeruginosa:* antipseudomonal cephalosporin plus a uoroquinolone
Brazilian Thoracic Association[10]	Site of care, risk factors for *P aeruginosa*	Outpatients: previously healthy macrolide monotherapy, comorbidities or recent antibiotics respiratory quinolone; inpatients: a respiratory quinolone or beta lactam plus a macrolide; patient in ICU: β lactam, plus quinolone or a macrolide; risk factors for *P aeruginosa*: β lactam, plus quinolone
Spanish Society of Chest Diseases and Thoracic Surgery[8]	Site of care, risk factors for *P aeruginosa*	Outpatients: a respiratory uoroquinolone; inpatients: β lactam plus a macrolide; patient in ICU: β lactam plus a macrolide; risk factors for *P aeruginosa*: carbopenem, or piperacillin or tazobactam, plus levo oxacin

CORB=confusion, oxygen saturations >90%, respiratory rate ≥30 breaths per min and systolic blood pressure <90 mm Hg or diastolic <60 mm Hg. *Risk factors for resistance listed are: the presence of comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressant disorders or use of immunosuppressing drugs; or use of antimicrobials in the previous 3 months. β lactams include penicillins, aminopenicillins, aminopenicillins and beta lactamase inhibitors, and cephalosporins. Japanese Respiratory Society guidelines recommend different empirical treatment if typical or atypical infections are suspected. ICU=intensive care unit. A DROP=age, dehydration, respiratory failure, orientation disturbance, blood pressure.

***Table 2*: Antibiotic prescription recommendations from international and national guidelines**

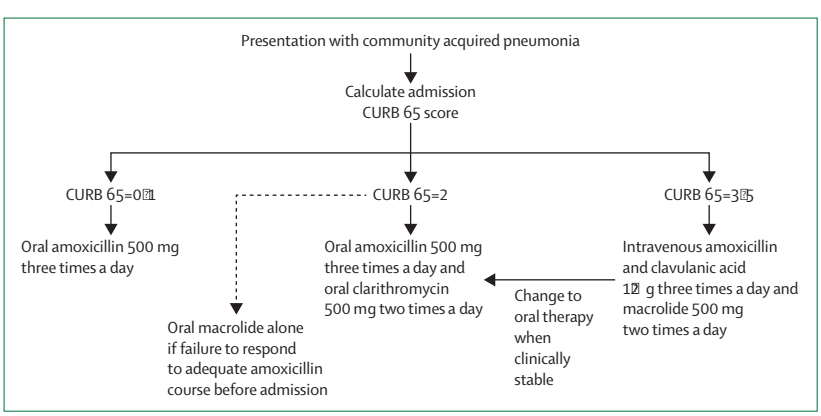

***Figure 2*: CURB 65 guided antibiotic treatment as recommended by the British Thoracic Society[1]**

The Japanese guidelines[13] recommend severity assess ment based on physical examination and chest radio graph, and recommend empirical antibiotic choices based on severity at admission. The Australian guidelines[12] recommend antibiotic choice based on severity assessment according to two less validated scores, the CORB score (presence of confusion, oxygen saturation ≤90%, respiratory rate ≥30 breaths per min, and systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg and SMART C OP, a more complex method that predicts the need for mechanical ventilation or vasopressor support.

Identi cation of causative microorganism by severity scores

Severity score based antibiotic treatment guidelines such as those from the British Thoracic Society[1] assume that severity community acquired pneumonia can be safely treated with oral amoxicillin monotherapy, with the requirement for broader spectrum drugs (including coverage of atypical bacteria) rising as severity increases. The British Thoracic Society recommendations are designed to cover Gram negative organisms (excluding *P aeruginosa*) and atypical pathogens in patients with

severe community acquired pneumonia, with no coverage of these organisms in patients with low-severity disease.

A few studies have investigated the identity of causative microorganisms relative to different severity classes with CURB 65 score and the pneumonia severity index (figure 1). Cilloniz and colleagues[42] assessed the microbiological cause of community acquired pneumonia in a Spanish hospital, with patients assessed with both the pneumonia severity index and CURB 65 score. The investigators reported that *S pneumoniae* is frequent in all severity classes, irrespective of the system used. This result is reflected in most guidelines, which recommend penicillin-based drugs as first-line therapy in all patients with community acquired pneumonia, irrespective of severity class. However, atypical pathogens (*Legionella pneumoniae*, *M pneumoniae*, *C pneumonia*, and *C burnetii*) were more frequently identified in lower-severity classes of pneumonia, whether stratified according to the pneumonia severity index or CURB 65 score. Such data argue against the use of amoxicillin monotherapy in low-severity community acquired pneumonia since 25% of all low-severity cases assessed with the CURB 65 or by the pneumonia severity index were caused by atypical bacteria, which would not be adequately treated with amoxicillin alone.

Cilloniz and colleagues[42] identified Gram-negative enteric bacteria and *P aeruginosa* as more frequent in higher-risk groups than in low-risk groups, strengthening the argument that coverage of Gram-negative organisms is needed for these patients. Most guidelines recommend at least dual antibiotic treatment in patients with severe disease (defined according to severity scores or site of care). Mixed infections become more common as severity increases,[42] but even in those with confirmed pneumococcal pneumonia, use of a macrolide might give additional survival benefit, which is presumed to be because of non-antibiotic, anti-inflammatory effects.[45]

Stralin and colleagues[46] assessed bacterial cause in 235 patients admitted to hospital with community acquired pneumonia. The investigators scored patients according to CRB 65 (a simplified version of CURB 65, which contains the same parameters apart from urea >7·0 mmol/L, and is promoted for use in general practice). They also reported that *S pneumoniae* was common in all severity classes, and that atypical bacteria was more frequent in patients with a low-severity score than for patients with a high-severity score. Roson and colleagues[48] evaluated 533 patients admitted to hospital with community acquired pneumonia. *S pneumoniae* was common in all pneumonia severity index classes, although more frequent in higher severity classes. Atypical pathogens were again most frequent in the mild severity class.

Most studies of the causes of community acquired pneumonia have focused on patients in hospital, with only a small amount having done detailed microbiological investigation in ambulatory patients with community acquired pneumonia.[42,49–51] Patients managed in the community setting would be expected to have a lower disease severity than those needing admittance to hospital. Studies that have directly compared the cause of community acquired pneumonia in outpatients to those in hospital have found that atypical pathogens are more common in outpatients,[42,51] reinforcing the findings from patients admitted to hospital that those with lower-severity classes of pneumonia have an increased frequency of atypical pathogens.

In summary, only a few researchers have assessed the frequency of pathogens across severity class and all are limited by the low yield of positive microbiological tests. All studies found *S pneumoniae* to be common across severity classes and atypical pathogens to be more common

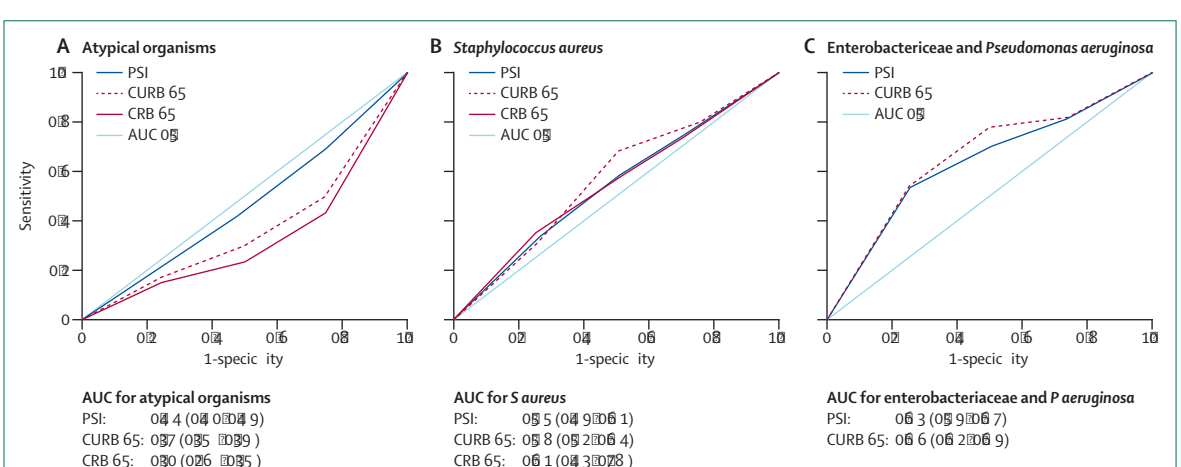

Figure 3: **Receiver operator characteristic curves showing predictive value of severity scores for determining pathogens**[42,46,47]
PSI=pneumonia severity index. CURB 65=confusion, urea, respiratory rate, blood pressure, age 65 years. CRB 65=confusion, respiratory rate, blood pressure, age 65 years. AUC=area under the receiver operator characteristic curve.

in low-severity classes than in high-severity classes. Torres and Rello[52] raised concerns about the poor coverage of atypical microorganisms for patients with low-severity disease in the British Thoracic Society guidelines. The counter argument, however, is that inadequate coverage of atypical bacteria in patients with a low CURB 65 score might not be harmful and a change in treatment might be all that is needed. A small risk of treatment failure in these patients might be acceptable if the antibiotics used have low potential to cause resistance or lead to adverse effects such as *C difficile*-associated diarrhoea.

We performed a pooled meta-analysis of the previously discussed studies to assess accuracy of the CURB 65 and CRB 65 scores, and the pneumonia severity index, in the prediction of important pneumonia-causing micro-organisms with the inclusion of atypical pathogens, *S aureus*, and Gram-negative Enterobacteriaceae and *P aeruginosa* (figure 3). All scores had poor accuracy for predicting causative pathogens, with the area under the receiver operator characteristic curve lower than previously described for prediction of 30 day mortality,[53] and importantly, lower than 0·7, which is the threshold above which scores are typically described as clinically useful.[54]

Treatment guided by severity score

Despite the British Thoracic Society guidelines advocating antibiotic therapy guided by severity score, there are very few analyses of the effect of this approach. Use of the pneumonia severity index can increase the proportion of patients treated in the community,[55] but there are no trial data on how the index affects antibiotic prescribing. There has been only one analysis of the effect of CURB 65 on clinical practice;[18] the study assessed the safety and efficacy of a CURB-65-guided prescription strategy, and compared antibiotic prescription before and after implementation. The investigators reported a reduction in broad-spectrum antibiotic use in the group after implementation of CURB-65-guided prescription, with no significant change in clinical outcomes with the intervention. These results suggest CURB-65-guided antibiotic therapy is achievable in a secondary care setting and does not compromise patients' safety.

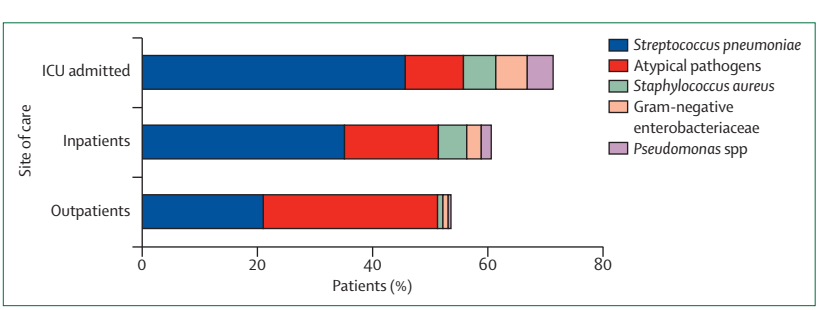

***Figure 4*: Microbial aetiology of community acquired pneumonia with respect to site of care**
Shows frequency of pathogens in patients with community acquired pneumonia managed as outpatients,[42,51,67,68] inpatients,[42,51,67,68,70] and the ICU.[20,42,71] ICU=intensive care unit.

However, the study had a before and after design and so does not have the same amount of rigour as would a randomised controlled trial. Additionally, macrolide use remained high in the low-risk groups even after implementation of CURB-65-guided therapy (40·8%), as did prescription of broad-spectrum drugs such as co-amoxiclav (27·9%) and even cephalosporins (2·1%). Further studies are needed to assess the safety and efficacy of strategies based on severity score.

Despite specific guidance in the British Thoracic Society guidelines, a recent national audit of pneumonia management in the UK[56] reported poor compliance in severity guided antibiotic treatment, particularly in low severity classes, with 51% of patients with CURB 65=0–1 receiving broad-spectrum therapy of a combination macrolide and β-lactam. Whether this prescription was because of inappropriate overuse of broad-spectrum antibiotics, intolerance of oral therapy, or if other severity markers prompted the use of broad-spectrum antibiotics in patients with low-severity disease with CURB 65 was not noted in the audit. Importantly, some recognised features of severity such as multilobar radiographical changes and hypoxaemia,[57,58] are not included in the CURB 65 score,[14] and a previous study[59] showed that 39·3% of patients classified as low severity with CURB 65 have additional markers of severity. Presence of these features can cause hospital admission in patients with a so-called "falsely low" CURB 65 score[59] and might also cause the use of broad-spectrum intravenous antibiotics. Additionally, CURB 65 might underestimate severe disease in some groups, such as young[60] and elderly[61] patients, and this discrepancy might argue against a one-size-fits-all approach for severity guided antibiotic treatment.

Additionally, the British Thoracic Society guidelines recommend treatment of different duration based on CURB 65 score at admission. The guidelines advise an antibiotic course of 7 days for patients with mild (CURB 65=0–1) or moderate (CURB 65=2) community acquired pneumonia, and of 7–10 days for patients with severe (CURB 65=3–5) disease.[11] Some data support duration of antibiotic treatment guided by severity score. In mild-to-moderate community acquired pneumonia, a randomised controlled trial suggested short courses of treatment are equivalent to longer regimens in terms of clinical success at day 10 and day 28.[62] An observational study[63] suggested that even for severe community acquired pneumonia, short antibiotic courses (≤7 days) are as effective as longer courses (>7 days) if the patient has responded adequately to treatment in the first week. In a large observational cohort,[64] duration of treatment did not significantly correlate with severity of community acquired pneumonia at admission when assessed with the use of either CURB 65 score or the pneumonia severity index. Therefore, few data exist to suggest that patients with high severity scores need prolonged treatment.

Treatment response (de ned with the use of Halm3 criteria or reduction in C reactive protein <50% of admission value) might be a better guide to antibiotic duration,[47] but more studies are needed.

Limitations to treatment based on site of care

Most international guidelines recommend antibiotic prescribing on the basis of site of care rather than severity scoring (table 1). Evidence exists of differences in the microbial cause of community acquired pneumonia with site of care (gure 4). In outpatients, *S pneumoniae* is common, with a high frequency of *M pneumoniae*, *H in uenzae*, other atypical bacteria, and respiratory viruses reported.[49,65–68] Data from inpatient populations show a higher frequency of *S aureus*, enteric Gram negative organisms, and *P aeruginosa* than for outpatients.[42,68–70] Similarly, studies of ICU admitted patients report an increase in *S aureus*, enteric Gram negative bacteria, and *P aeruginosa*.[20,42,71] Site of care, therefore, seems to be a poor predictor for the microbiological cause of com munity acquired pneumonia. Particularly, *L pneumophila* is equally frequent in patients with community acquired pneumonia managed in the community and those that have been admitted to hospital. Therefore, inadequate therapy with antibiotics that do not cover *L pneumophila* in outpatients might lead to treatment failure and subsequent adverse outcomes. von Baum and colleagues[72] analysed 2503 patients with community acquired pneumonia, and found that 94 had con rmed *L pneumophila*. 12 patients died within 6 months and, of these, 16·7% were given discordant antimicrobial treatment that did not cover *L pneumophila* after they presented with mild pneumonia before they deteriorated. Most guidelines that recommend treatment based on site of care recommend coverage of atypical microbials with a macrolide in outpatients, although some guidelines[6] do include amoxicillin monotherapy.

Cilloniz and colleagues[42] are the only investigators to have compared microbial cause across outpatients, ward admitted, hospital inpatients, and patients admitted to the ICU. Their ndings were similar to that for severity score, showing a higher frequency of atypical organisms in outpatients (36%) giving an area under the receiver operator characteristic curve of 0·43 (95% CI 0·40–0·44). *S aureus* was not strongly associated with the site of care, 0·56 (0·50–0·62). Results for Enterobacteriaceae and *P aeruginosa* were both 0·55 (0·51–0·58). Site of care approaches have other shortcomings; the approach assumes that all patients are admitted because of their severity of illness, although many would be treated as outpatients if other social factors or other non medical issues did not exist.[59,73] Additionally, site of care approaches recommend broad spectrum antibiotic treatment to all inpatients, with scarce evidence that this will improve clinical outcomes, and the risk that this will increase antibiotic related side effects.

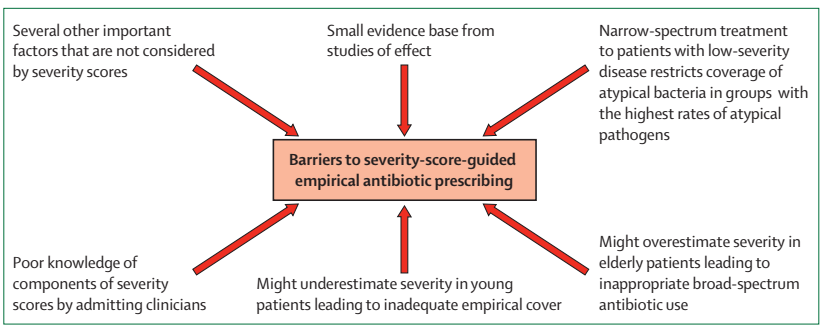

Figure 5: **Barriers to severity score guided empirical antibiotic prescription**

Panel: Advantages and limitations of the approaches to antibiotic treatments

Treatment guided by severity score

Advantages

- Reduction of broad spectrum antibiotic use
- Objective decision making
- Can discriminate patients with Gram negative bacteria from those without

Disadvantages

- Scores might be misleading and result in undertreatment
- Does not discriminate patients with *Staphylococcus aureus* or atypical organisms from those without
- Some scores weighted by age or comorbidities might lead to overuse of antibiotics in elderly patients and underuse in young patients
- Insufficient data available on implementation

Treatment based on site of care

Advantages

- Simple, easy to implement
- Agrees with clinical judgment
- Ensures broad spectrum coverage for all hospital inpatients and intensive care unit patients

Disadvantages

- Will probably increase broad spectrum antibiotic use in inpatients
- Poor discrimination of patients with *S aureus* from those without, and poor discrimination of patients with atypical organisms from those without

Limitations to treatment guided by severity score

Although antibiotic prescription guided by severity score has potential advantages, some limitations to their use exist (gure 5; panel). First, junior doctors have poor knowledge of national guidelines, with only 4% able to correctly name the parts of the CURB 65 score,[74] and a similar proportion with knowledge of the pneumonia severity index.[75] This knowledge base provides a major barrier to the use of severity score approaches because their use relies on the admitting clinician's familiarity. Second, as mentioned above, severity scores such as CURB 65 might underestimate or overestimate severity of illness in some groups of patients and clinical judgment should always be used. Since severity score guided antibiotic treatment is designed to simplify empirical antibiotic decisions, this restricts their

Search strategy and selection criteria

We searched PubMed for papers published from Jan 1, 1981, to Jan 1, 2013, with the terms: "community acquired pneumonia", "pneumonia", "aetiology", "antibacterial agent", "antiinfective agent", "bacteria", "microbiology", "severity of illness", "CURB 65", "CRB 65", and "pneumonia severity index". We did not apply any language criteria. We selected the articles on the basis of originality and relevance. We supplemented the search strategy by reviewing reference lists, bibliographies, and our files.

usefulness in clinical practice. In particular, inexperienced junior doctors might have little experience in recognising a severely unwell patient who is misclassified as having mild disease with a severity score. Third, the initial antibiotic choice is a complex decision and several other factors other than severity of community acquired pneumonia might be important. The European Respiratory Society guidelines[6] list ten criteria that should be considered when deciding upon empirical antibiotics, of which severity of disease is only one. Others, such as comorbidity, risk factors for immunosuppression, place of residence, aspiration, regional patterns of resistance, and tolerability and toxic effects of drugs in individual patients, are not accurately distinguished by severity scores and, therefore, antibiotic guidance based only on severity might be an oversimplification. Finally, as discussed, despite being recommended in the British Thoracic Society guidelines, the use of severity scores such as CURB 65 to guide antibiotic prescription has a small evidence base and further studies are needed.

Conclusions

Severity guided antibiotic treatment of community acquired pneumonia provides a simple strategy to guide clinicians towards making empirical choices when patients are admitted to hospital. However, the limitations of severity scores and other important factors that might influence decisions suggest such strategies should be used with caution and always in conjunction with clinical judgment. Strategies based on severity score might allow for earlier identification of patients with more severe disease and could allow earlier commencement of appropriate antibiotics. However, a one-size-fits-all approach to the prescription of antibiotics is challenging to devise and implement. Empirical antibiotic recommendations vary widely between guidelines from different countries, and even within one country. More evidence and a more multidisciplinary and collaborative approach to prescription guideline development is needed to resolve these issues and to determine the best empirical strategy for community acquired pneumonia.

Further studies are needed to directly evaluate severity score and site-of-care approaches in a clinical setting, along with the development of new scores designed specifically to predict disease cause. Implementation of advanced strategies such as point-of-care molecular-based tests might also help future improvements in prescription of antibiotics for patients presenting with community acquired pneumonia.

Contributors

Both authors participated equally in the preparation of the paper.

Conflicts of interest

We declare that we have no conflicts of interest.

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