BTS GUIDELINES FOR THE MANAGEMENT OF COMMUNITY ACQUIRED PNEUMONIA IN ADULTS - 2004 UPDATE

Prepared by the BTS Pneumonia Guidelines Committee
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INTRODUCTION AND METHODS

The BTS guidelines for the management of Community Acquired Pneumonia (CAP) in Adults were published in December 2001 (1) and are available on the BTS website (www.brit-thoracic.org/guidelines). They superseded guidelines published in 1993.
The 2001 Guidelines assessed relevant evidence published up to September 2000.

This update summarises our further assessment of published or available evidence from September 2000 up to end of December 2002 and a further search for articles related to relevant antibiotics up to the end of August 2003.

An identical search strategy, assessment of relevance and appraisal of articles, and grading system was used. In total 280 abstracts were screened and 130 articles were obtained and assessed.

Note was also made of any feedback received following the publication of the 2001 Guidelines, specifically corrections to typographical or factual errors have been included in this update. This applies only to one drug dose in section 8 and table 11.

Whilst the BTS committee were compiling this update, the Infectious Diseases Society of America published their update of their practice guidelines for the management of community acquired pneumonia in immunocompetent adults, in December 2003 as a follow up of their 2000 guidelines (2). Their update quotes 235 references and will act as a useful extra source of information.

Separate guidelines on the management of SARS are available on the BTS website (www.brit-thoracic.org.uk) with links to other relevant web site sources.

PRESENTATION OF RESULTS OF THE UPDATE

This update should be read in conjunction with the 2001 guidelines document available on the BTS website (www.brit-thoracic.org/guidelines). It is recommended that a copy of this update be kept with the 2001 guidelines document. Relevant sections in the 2001 document on the website have been flagged to indicate where updates have been made.

We make statements only where we judge it is appropriate to alter or add (a) important statements of fact or (b) recommendations.

For each section where changes are suggested, such statements are listed under:

- What section and subject is this relevant to?
- What is the new evidence?
- What is our interpretation of this evidence?
- What changes are needed to the 2001 guidelines recommendations, if any?

Reference is made to the section/subsection relevant to the 2001 guidelines to allow easy cross reference (e.g. Section: 5.6 General investigations).

Articles referred to are listed at the end of the update and the grade of evidence is indicated in the text next to the reference suffix, as was done with the 2001 guidelines.

SUMMARY OF WHERE CHANGES ARE SUGGESTED

No changes were considered necessary in sections:

Section 1	Introduction and Methods
Section 2	Incidence, Mortality and Economic Consequences
Section 4	Clinical Features
Section 9	Complications and Failure to Improve

Changes or comments were made in the following sections

Section 3	Aetiology and Epidemiology
Section 5	Radiological, General and Microbiological Investigations
Section 6	Severity Assessment
Section 7	General Management in the Community and in Hospital
Section 8	Antibiotic Management
Section 10	Prevention and Vaccination Strategies

SECTION 3: AETIOLOGY AND EPIDEMIOLOGY

What section and subject is this relevant to?

Section 3.5 Is the aetiology different in specific population groups?
This relates to the aetiology of nursing home acquired pneumonia

What is the new evidence?

The first UK prospective cohort study comparing 40 patients with nursing home acquired pneumonia with 236 adults age ≥ 65 years with community-acquired pneumonia (3) [Ib].

What is our interpretation of this evidence?

There is no evidence that the distribution of causative pathogens is different to that in other older adults with CAP.

What changes are needed to the 2001 guidelines recommendations, if any?

None. Patients in nursing homes should be treated according to the general antibiotic recommendations in these guidelines and no specific antibiotic recommendation for nursing home acquired pneumonia is required.

SECTION 5: RADIOLOGICAL, GENERAL AND MICROBIOLOGICAL TESTS

i) What section and subject is this relevant to?

5.6 General investigations.
This relates to the measurement of CRP

What is the new evidence?

A prospective study performed in Spain of consecutive patients investigated in the emergency ward of one hospital with CAP (208 patients) and 27 patients with a variety of other diagnoses not ultimately requiring antibiotics, reported a highly significant difference in CRP between the groups with a 96% specificity for CAP using a cut-off of CRP of > 100mg/l and 100% specificity using a cut-off > 125 mg/l.. CRP had a higher level of significant difference between the 2 groups than ESR, leucocyte count or temperature (4) [II]. Criticisms of this study are the small number of patients in one group and the fact that patients with infective exacerbations of COPD were excluded. Surprisingly the mean CRP in the non infective control group was as high as 88 mg/l.

Another study found no association between CRP and severity or aetiology in 96 consecutive admissions for CAP (5) [II].

However in a sub analysis of 258 patients out of a prospective cohort study of 1222 where a single aetiological agent had been identified, admission CRP levels were not significantly related to severity, but were significantly higher in legionella infection compared to other identified infective aetiologies (6) [II].

What is our interpretation of this evidence?

We think that there is no clear consensus in the literature about value of CRP in differentiating between infective causes. There is no value of CRP in severity assessment.

What changes are needed to the 2001 guidelines recommendations, if any?

No change to our recommendation that CRP is measured on admission, when locally available [B-]

ii) What section and subject is this relevant to?

Section 5.8-9: Microbiological investigations.
This relates to the value of blood and sputum cultures and the use of urinary antigen

What is the new evidence?

Several recent studies (7,8,9,10) [all II] have examined the positivity rate of routine microbiological investigations (blood cultures and sputum cultures) for patients with CAP. These studies provide further evidence that the overall sensitivity of such tests in CAP is low, particularly for patients with non-severe CAP and no co-morbid disease, and for those who have received antibiotic therapy prior to admission. One study (9) demonstrated a direct correlation between the severity of pneumonia (using the Fine Pneumonia Severity Index) and blood culture positivity rate, and questioned the value of routine blood cultures for CAP patients in PSI Risk Classes I – III (i.e. not severe).

Two studies (11) [II], (12) [III] have evaluated the performance of a new commercially available urine antigen test for *Streptococcus pneumoniae* (BINAX NOW) in the diagnosis of pneumococcal pneumonia. The studies have shown the potential usefulness of this assay in determining the aetiology of CAP, with significantly greater sensitivity rates than routine blood or sputum cultures.

One study looked at the value of rapid legionella urine antigen testing in a large outbreak of Legionnaires' disease in Holland (13) [III]. This showed a higher test positivity rate for patients with severe legionella infection. The authors also demonstrated that the antibiotic management of patients could be guided by the results of rapid testing, resulting in an improved outcome as shown by reducing both mortality and need for intensive care. Patients who had a negative test on admission and hence did not receive anti-legionella antibiotics immediately but who were subsequently shown to have legionella infection did not have a worse clinical outcome.

In another prospective study of sporadic CAP in adults, the early detection of urine legionella antigen positively influenced the management of 7 of 9 patients in whom it was detected (14) [Ib].

What is our interpretation of this evidence?

For patients with non-severe CAP routine microbiological tests may not always be needed, particularly for patients with no co-morbid illness. The healthcare setting, severity indicators, patient age, co-morbid illness and prior antibiotic therapy should guide the routine performance of blood cultures and sputum cultures.

A full range of microbiological investigations should be performed for patients with severe CAP.

The addition of *S pneumoniae* urine antigen testing should now be considered for these patients, along with legionella urine antigen tests. Routine legionella and pneumococcal antigen testing in patients at low risk of death is probably not cost-effective.

What changes are needed to the 2001 guidelines recommendations, if any?

We suggest the following changes to sections 5.7 and 5.9

5.7 Why are microbiological tests performed?

Recommendation

A full range of microbiological tests should be performed on patients with severe CAP. For patients with non-severe CAP the extent of microbiological investigations should be guided by clinical factors (age, co-morbid illness, severity indicators), epidemiological factors, and prior antibiotic therapy. [A-]

5.9 What microbiological tests should be performed in hospitalised patients?

BLOOD CULTURES

Recommendation

- Blood cultures are recommended for all patients with severe CAP and most other patients admitted with CAP, preferably before antibiotic therapy is commenced. However, if a diagnosis of CAP has been definitely confirmed, and a patient has no severity indicators or co-morbid disease, then blood cultures may be omitted [A-]

SPUTUM CULTURES

Recommendation

Both recommendations remain the same but are now graded as [A-], rather than [D]

- Sputum samples should be sent for culture and sensitivity tests from patients with non-severe CAP who are able to expectorate purulent samples *and* have not received prior antibiotic therapy. Specimens should be transported rapidly to the laboratory [A-].
- Sputum cultures should also be performed for patients with severe CAP, or those who fail to improve [A-].

PNEUMOCOCCAL ANTIGEN DETECTION

Recommendation

- Pneumococcal urine antigen tests should be performed for patients with severe CAP [B+].

TESTS FOR LEGIONNAIRES' DISEASE

Recommendation

- Legionella urine antigen tests should be performed for patients with severe CAP [B+].
- A rapid testing and reporting service for legionella urine antigen should be available to all hospitals admitting patients with CAP [B+].

SECTION 6: SEVERITY ASSESSMENT

What section and subject is this relevant to?

> **Section 6.2. What clinical features and investigations are associated with a poor prognosis?**
> **This related to clinical features associated with a poor prognosis**

What is the new evidence?

In a retrospective study of elderly patient with CAP the importance of bilateral radiographic infiltrates, raised blood urea, absence of fever, raised respiratory rate, confusion and shock as poor prognostic features was further underlined. (15) [II])

In patients with legionella pneumonia, a positive urine antigen test result has been found for the first time to be related to ICU admission. (16) [II])

What is our interpretation of this evidence?

This provides further evidence for the use of specific core adverse prognostic features in assessing severity. Legionella urine antigen test is useful not only for early diagnosis but also for assessing severity of legionella infection

What changes are needed to the 2001 guidelines recommendations, if any?

None

What section and subject is this relevant to?

> **Section 6.3 What predictive models for assessing severity have been tested?**
> **This relates to predictive models for assessing severity on admission and the need for hospital admission**

What is the new evidence?

A recently published paper by Lim et al (17) [Ib] sets out a severity assessment model which allows patients to be stratified into different mortality groups suitable for different management pathways. This large study included a dataset of over 1000 prospectively studied patients with CAP from 3 countries – UK, New Zealand and the Netherlands, divided into derivation and validation cohorts. A 6-point score, one point for each of **C**onfusion, **U**rea >7 mmol/l, **R**espiratory rate >= 30/min, low systolic (<90mmHg) or diastolic (<= 60 mmHg) **B**lood pressure, age >= **65** years (CURB-65 score) based on information available at initial hospital assessment, enabled patients to be stratified according to increasing risk of mortality or need for intensive care admission (Score 0, 0.7%; Score 1, 3.2%; Score 2, 13%; Score 3, 17%; Score 4, 41.5% and Score 5, 57%). A similar pattern of increasing disease severity was reported when only clinical parameters were considered (CRB-65) giving a 5–point score (risk of mortality for each score: Score 0, 1.2%; Score 1, 5.3%; Score 2, 12.2%; Score 3, 32.9%; Score 4, 18.2%).

There have also been a number of studies to indicate that patients classified as having a low-risk of mortality based on a severity prediction model may still require hospital-based treatment. Angus *et al* reported that ICU admission occurred in 27% of patients assigned to Pneumonia Severity Index (PSI) risk classes I – III (ie. low risk) (18) [II]). This high ICU admission rate is surprising and may reflect different entry criteria and use of ITUs in different health care services. Roson *et al* reported in their series that 40% of patients with CAP who were hospitalised were assigned to low risk classes based on the PSI (19) [II].
These reports reflect the importance of clinical judgment in assessing disease severity.

What is our interpretation of this evidence?

Overall the pneumonia subcommittee were in favour of adopting a revision to the recommended BTS severity assessment model based on CURB-65, but because two committee members were authors on one of the studies being assessed (17), the evidence was passed to the BTS Standards of Care Committee for an independent view. Following review of the available evidence, they unanimously agreed to the adoption of the CURB-65 prediction model described by Lim *et al* in place of the existing BTS severity assessment strategy in view of the following advantages: a) more robust evidence for the CURB-65 model, b) 1-step compared to the current 2-step model and c) simple to remember.

What changes are needed to the 2001 guidelines recommendations, if any?
The following changes are made:

Section 6.5 Identifying those patients seen out of hospital, who can usually be safely treated at home or who require hospital referral (Revised figure 7 from 2001 guidelines).

Recommendations

- Patients who have a CRB-65 score of 0 are at low risk of death and do not normally require hospitalisation for clinical reasons [B].
- Patients who have a CRB-65 score of 1 or 2 are at increased risk of death and hospital referral and assessment should be considered, particularly with Score 2 [B].
- Patients who have a CRB-65 score of 3 or more are at high risk of death and require urgent hospital admission [B].

Section 6.6 Identifying those with severe CAP from those with non-severe CAP after initial hospital assessment (Revised figue 8 from the 2001 guidelines).

Recommendations

- Patients who have a CURB-65 score of 3 or more are at high risk of death and should be managed as having severe pneumonia according to the recommendations outlined in sections 7.3-7.4 and 8.11, of the 2001 guidelines [B].
- Patients who have a CURB-65 score of 2 are at increased risk of death. They should be considered for short stay inpatient treatment or hospital supervised outpatient treatment. This decision is a matter of clinical judgement [B].
- Patients who have a CURB-65 score of 0 or 1 are at low risk of death. They can be treated as having non-severe pneumonia and may be suitable for home treatment [B].

SECTION 7: GENERAL MANAGEMENT

What section and subject is this relevant to?

7.1 Management in the community.
This relates to the use of oximetry for ambulatory patients with CAP

What is the new evidence?

Pulse oximetry is now widely available in North America. A survey of 944 outpatients and 1,332 inpatients with evidence of CAP enrolled from 5 sites in the United States and Canada reported increasing assessment of arterial oxygen saturation with pulse oximetry in up to 58% of outpatients and 85% of inpatients (20) [II].

What is our interpretation of this evidence?

This provides support to the idea that it is practical to use oximeters for assessing ambulatory patients with CAP

What changes are needed to the 2001 guidelines recommendations, if any?

A strengthening of this recommendation from [D] to [C].

- Pulse oximetry, with appropriate training, should become increasingly available to general practitioners and others responsible for the assessment of patients in the out of hours setting, for assessment of severity and oxygen requirement for patients with CAP and other acute respiratory illnesses [C].

What section and subject is this relevant to?

7.3 General management in hospital.
This relates to the use of non-invasive ventilation (NIV) for CAP

What is the new evidence for the use of non-invasive ventilation (NIV) for CAP?

Several studies reported that provision of NIV in patients with severe CAP can lead to initial improvement in SaO2 and fall in pulse. However over 50% of these patients later deteriorated requiring intubation. Arterial blood gas tension measurements prior to starting NIV were not predictive of outcome and there were a higher failure rate of those with an initial respiratory rate of greater than 38 per minute and those aged over 40 years (21,22,23) [II].

What is our interpretation of this evidence?

NIV may have a place in the initial management of patients with CAP, but very close observation is needed to detect deterioration and need for intubation.

What changes are needed to the 2001 guidelines recommendations, if any?

Readers are referred to the BTS guidelines on non-invasive ventilation in acute respiratory failure (24), which reviews the evidence and states:

- Many patients with acute pneumonia and hypoxaemia resistant to high flow oxygen will require intubation. In this context trials of NIV or CPAP (Continuous Positive Airways Pressure) should only occur in HDU and ITU settings [D].

What section and subject is this relevant to?

7.3 What general management strategy should be offered to patients in hospital? This relates to the use of discharge planning for CAP

What is the new evidence regarding discharge planning?

In a recent US prospective, multi-centre, observational cohort study of 680 patients admitted to hospital with CAP it was reported that almost 20% left hospital with 1 or more unstable factors in the 24 hours prior to discharge. These included temperature > 37.8^{o}C, heart rate > 100/minute, respiratory rate > 24/minute, systolic blood pressure of < 90mmHg, oxygen saturation of < 90%, inability to take oral medication or abnormal mental status. Forty six per cent of those discharged home with 2 of these "instabilities" died or were readmitted within 30 days. In contrast only 11% of those with no "instabilities" died or were readmitted within 30 days (25) [II].

What is our interpretation of this evidence?

There is often pressure to discharge patients home early. However instability on discharge is associated with adverse clinical outcomes. This study was performed in a different health care system to the UK, and had a surprisingly high readmission rate, but provides some guidance regarding simple parameters to review when considering hospital discharge and persuaded us to add a recommendation to section 7.3 of the guidelines.

What changes are needed to the 2001 guidelines recommendations, if any?

New recommendation for section 7.3:

- Patients should be reviewed within 24 hours of planned discharge home and those suitable for discharge should not have more than one of the following characteristics present (unless they represent the usual baseline status for that patient). These clinical "instabilities" include temperature > 37.8^{o}C, heart rate > 100/min, respiratory rate > 24/min, systolic blood pressure <90mmHg, oxygen saturation < 90%, inability to maintain oral intake and abnormal mental status [B+]

SECTION 8: ANTIBIOTIC MANAGEMENT

What section and subject is this relevant to?

Section 8.10. What are the principles and practice of empirical choice for adults with non-severe pneumonia?
This relates to the use of new antibiotics

What is the evidence?

Since our 2001 Guidelines were published, moxifloxacin has been licensed in the UK for the treatment of non-severe CAP. It is not licensed at this time for severe CAP, nor is an IV preparation available, in the UK; hence we have not assessed studies which have used IV moxifloxacin.

There are reported microbiological, pharmacokinetic and pharmacodynamic advantages for moxifloxacin compared to levofloxacin (26,27)[II].

Clinical studies have generally shown equivalence with other oral antibiotics used for CAP (28) [Ib]; (29) [Ib]; (30) [Ib]. One showed similar outcomes but fewer side effects when compared with oral amoxycillin (One gram tds) and/or clarithromycin (31) [Ib].

In a recent meta-analysis of mostly non-severe CAP, the newer oral fluoroquinolones showed modest therapeutic benefit compared with other studied antibiotics in CAP (32) [1b], but the authors questioned whether this warranted the use of a fluoroquinolone for an illness with a generally favourable outcome regardless of antibiotic selection and at a time when fluoroquinolone resistance may be increasing.

What is our interpretation of this evidence?

For hospital treated non-severe CAP we conclude that (a) either fluoroquinolone, levofloxacin or moxifloxacin, could be used as the alternative regimen to the preferred choice of oral amoxicillin and macrolide, where oral therapy is appropriate and (b) that moxifloxacin has theoretical microbiological, pharmacokinetic and pharmacodynamic advantages over levofloxacin.

Moxifloxacin is not licensed either for IV therapy or for severe CAP.

We still judge that oral fluoroquinolones are not recommended for home therapy given the low level of penicillin resistant pneumococci in the UK and the evidence of rising fluoroquinolone resistance among pneumococci and other pathogens in countries where fluoroquinolones are more widely used in the community (33,34).

What changes are needed to the 2001 guidelines recommendations, if any?

We suggest the following changes to the recommendations in section 8.10 (and similar changes to table 8 of the 2001 guidelines):

- New fluoroquinolones are not recommended as first line agents or for community use for pneumonia, but may provide a useful alternative in selected hospitalised patients with CAP [B].
- A fluoroquinolone active against *S pneumoniae* is an alternative regimen for those intolerant of penicillins or macrolides or where there are local concerns whether the use of broad-spectrum beta lactam antibiotics may be linked to *C difficile* associated diarrhoea. [B] Currently levofloxacin and moxifloxacin are the only recommended agents licensed in the UK. Moxifloxacin is not licensed for use for severe pneumonia in the UK, nor available in a parenteral formulation.

Correction

Correction to table 11, page 46 'Recommended therapy of microbiologically documented pneumonia' – typographical error.
The dose of ceftriaxone should be 2gm given once daily, not twice daily.
A corrected version of the table is included in this update.

SECTION 10: PREVENTION AND VACCINATION STRATEGIES

What section and subject is this relevant to?

Section 10.2: Influenza virus and vaccination

What is the new evidence?

A recent Cochrane review of 20 trials including 30,429 healthy adults aged 14-60 years showed that vaccination reduced serologically confirmed cases of influenza A but was less effective in reducing "clinical influenza" [1A] (35).

What is our interpretation of this evidence?

This provides further evidence that influenza vaccine provides some benefit for low risk groups and supports the Departments of Health advice for health care workers to be vaccinated.

What changes are needed to the 2001 guidelines recommendations, if any?

None

What section and subject is this relevant to?

Section 10.3: Pneumococcal vaccination

What is the new evidence?

A recent meta-analysis of 14 randomised controlled trials involving 48,837 patients showed that pneumococcal polysaccharide vaccine prevented definite pneumococcal pneumonia by 71%, presumptive pneumococcal pneumonia by 40% and mortality due to pneumonia by 32%. However there was no apparent benefit in a smaller subgroup of 7,907 patients aged over 55 years (36) [Ia].

A new conjugate pneumococcal vaccine will soon become available in the UK. In small studies there is evidence of effect with production of an IgG response without significant adverse effects (37) [II].

What is our interpretation of this evidence?

The area remains confusing with some evidence of overall efficacy for pneumococcal vaccination, but not for the "at risk" individuals, such as older patients. It is hoped that new conjugate vaccines may be the way forward for at risk adults in the future.

What changes are needed to the 2001 guidelines recommendations, if any?

None

SECTION 11. ACKNOWLEDGEMENTS AND DECLARATIONS OF INTEREST

We are grateful for the comments from the BTS Standards of Care Committee (Chairman Dr David Boldy).
The following Declarations of Interest were made by committee members during the development of this update:

TB has received research funding from Eisai Ltd., lecture fees from Aventis and Gilead, and support for attending conferences from Wyeth. GD has received research funding from Chiron, Sky Pharma and Boehringer, lecture fees from GSK, AstraZeneca and Boehringer and support for attending conferences from GSK and AstraZeneca. DH has received consultancy fees from Bayer and Abbott, research funding from Hoechst Marion Roussel, SmithKlineBeecham, Pharmacia/Upjohn, Grunenthal and Abbott, lecturing fees from Key Med, Bayer and AstraZeneca, and support for attending conferences and meetings from Bayer, Abbott and Pharmacia. RGF has received consultancy fees from British Biotech, Parke Davies, Pan Therix, Glaxo Wellcome and SmithKlineBeecham, research funding from Glaxo Wellcome and Pharmacia and support for attending conferences from Glaxo Wellcome, Aventis, Wyeth and Pfizer. DH holds shares in GlaxoSmithKline. WFH is medical director of Nestor Healthcare, one of whose companies is Primecare, which provides out of hours care. WFH has no income or association with pharmaceutical companies. WSL – none declared. JTM has received consultancy fees from GlaxoSmithKline and lecture fees from AstraZeneca and SmithKlineBeecham. PM – none declared. DN has received consultancy fees from Pharmacia/Upjohn and Bayer and research funding from Hoechst Marion Roussel and Pharmacia/Upjohn. MAW has received lecture fees from Pfizer and support to attend conferences from Pfizer. JW – none declared.

AUDIT TOOL

A web based audit tool with autoanalysis and intercentre comparison facilities is being piloted by the audit subcommittee of the BTS Standards of Care Committee, and is expected to be available on the BTS website during 2004.

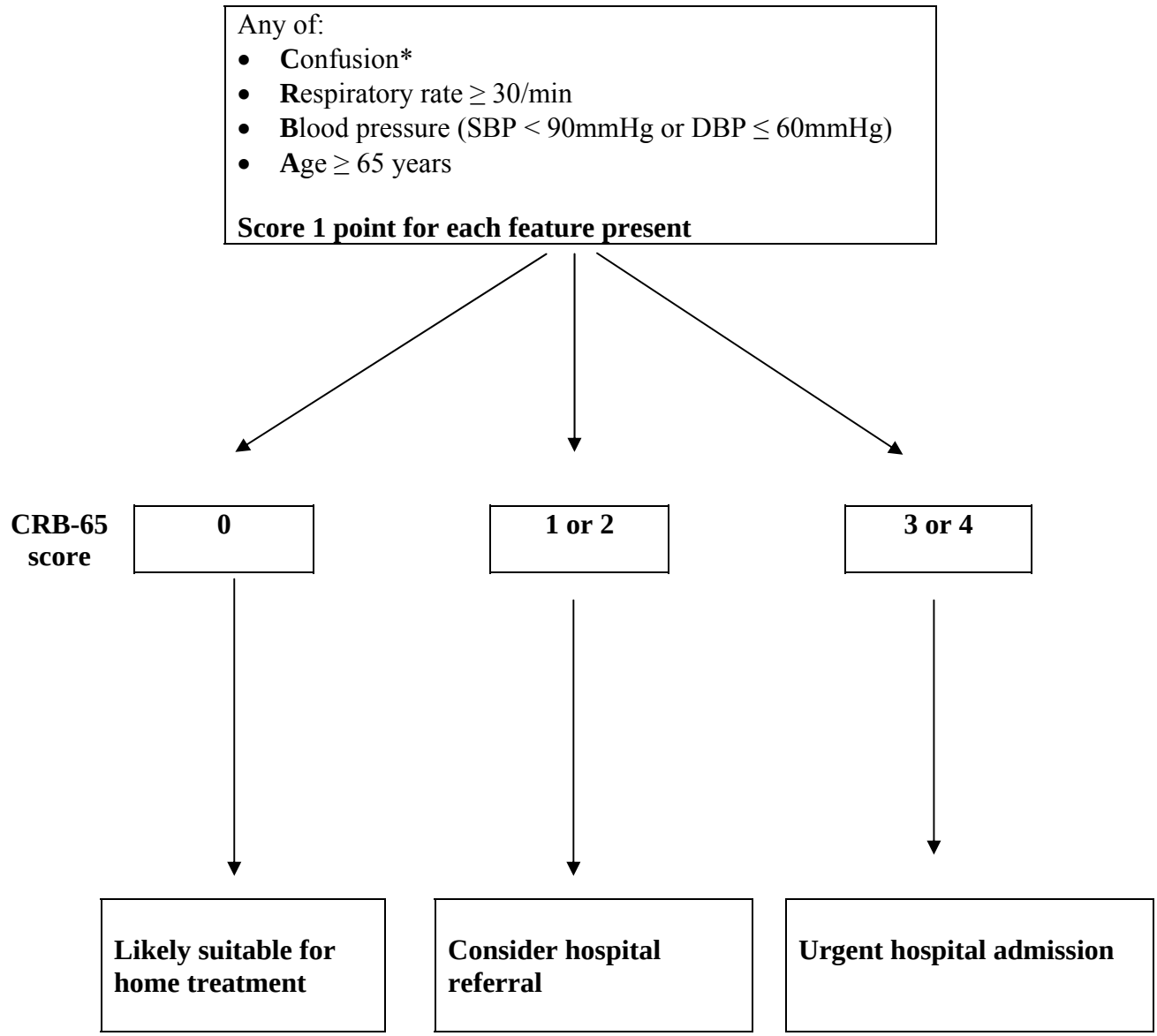
REFERENCES

At the end of this document.

REVISED FIGURES

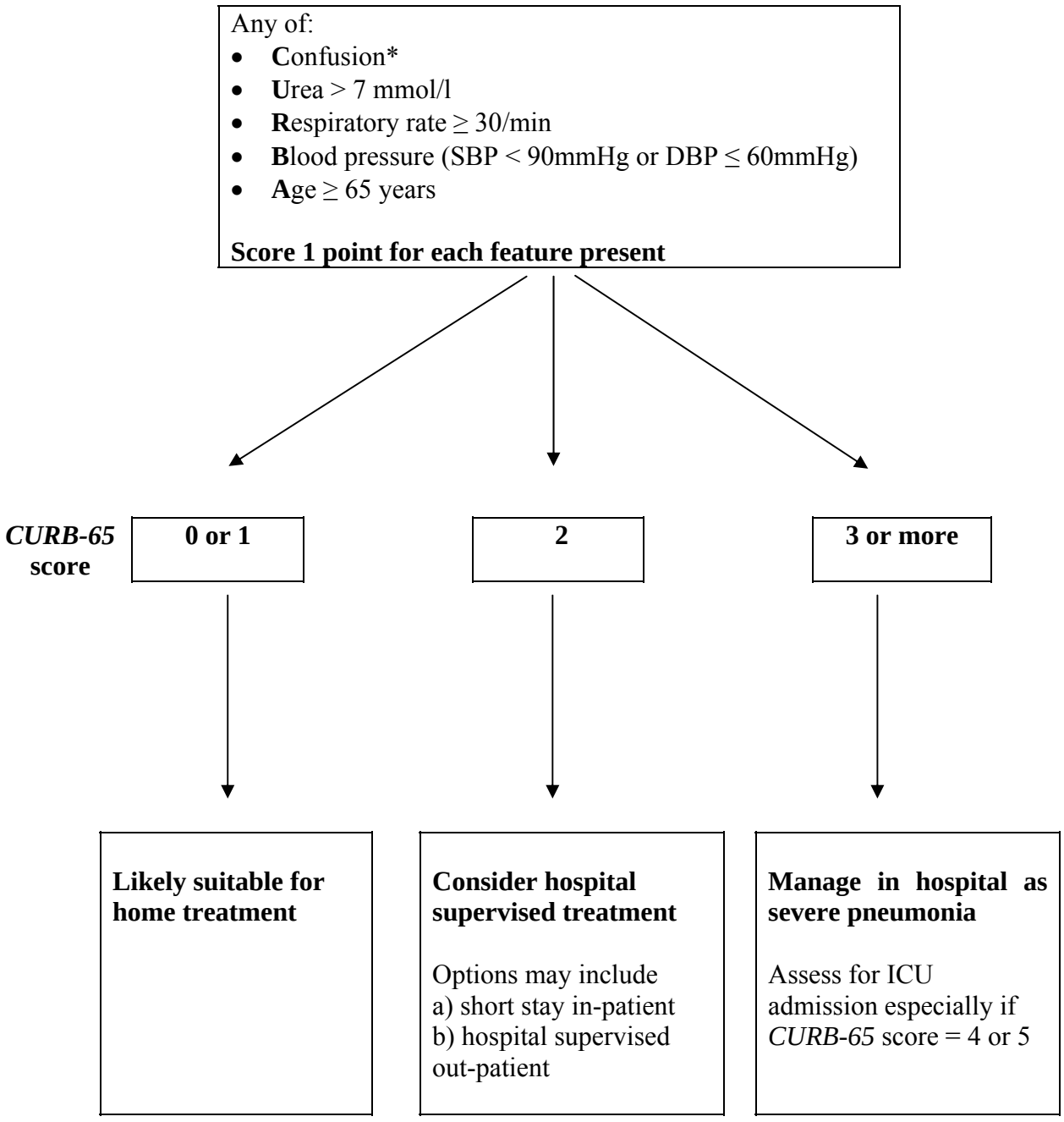
These are shown on the following pages. We use the numbering from the 2001 guidelines document. They include:
Figure 7
Figure 8
Table 8
Table 11

Figure 7: Severity assessment used to determine the management of CAP in patients **in the community (CRB-65 score) UPDATED 2004.**



* Defined as a Mental Test Score of 8 or less, or new disorientation in person, place or time.

Figure 8: Severity assessment used to determine the management of CAP in patients **admitted to hospital (CURB-65 score) UPDATED 2004.**



* Defined as a Mental Test Score of 8 or less, or new disorientation in person, place or time.

Table 8: Preferred and alternative initial empirical treatment regimens and parenteral to oral switch regimens for community acquired pneumonia UPDATED 2004

	PREFERRED	ALTERNATIVE [a]
[1] Home-treated, not severe	amoxicillin 500 mg - 1.0 g tds po	erythromycin 500 mg qds po *or* clarithromycin 500 mg bd [b] po
[2i] Hospital-treated, not severe [Admitted for non-clinical reasons or previously untreated in the community]	As under Home-treated, not severe	
[2ii] Hospital-treated, not severe		
Either oral	amoxicillin 500 mg – 1.0 g tds po *plus* erythromycin 500 mg qds po or clarithromycin 500 mg bd [b] po	***Fluoroquinolone with enhanced pneumococcal activity*** e.g. levofloxacin 500 mg od po OR moxifloxacin 400mg od po[c] *(the only such licensed agents in the UK at time of writing)*
or if IV needed	ampicillin 500 mg qds iv *or* benzylpenicillin 1.2g qds iv *plus* erythromycin 500 mg qds iv *or* clarithromycin 500 mg bd iv	levofloxacin 500 mg od iv [c]
[3] Hospital-treated, severe	co-amoxiclav 1.2 g tds iv *or* cefuroxime 1.5 g tds iv *or* cefotaxime 1gm tds iv *or* ceftriaxone 2 gm od iv *plus* erythromycin 500 mg qds iv *or* clarithromycin 500 mg bd iv (*with or without* rifampicin 600 mg od or bd iv)	***Fluoroquinolone with enhanced pneumococcal activity*** e.g. levofloxacin 500 mg bd iv or po [c] ***plus*** benzylpenicillin 1.2g qds iv

a) An alternative regimen is provided for those intolerant of or hypersensitive to preferred regimen, or where there are local concerns over *C difficile* associated diarrhoea related to beta- lactam use.

b) Clarithromycin may be substituted for those with gastrointestinal intolerance to oral erythromycin and also has the benefit of twice daily dosage. Clarithromycin modified release 500mg or 1gm od is licensed for once daily dosing.

c) Levofloxacin and moxifloxacin are the only currently UK licensed fluoroquinolones with enhanced activity against *S pneumoniae.* Levofloxacin comes in an oral and parenteral formulation and is licensed for severe pneumonia. Moxifloxacin comes in an oral formulation only in the UK and is not licensed for severe pneumonia. In the future other fluoroquinolones such as gemafloxacin and gatifloxacin are likely to extend this choice, when licensed in the UK.

d) Concurrent administration of rifampicin reduces the serum level of macrolides; the clinical significance of this is not known.

Switch from parenteral drug to the equivalent oral preparation should be made as soon as clinically appropriate, in the absence of microbiologically confirmed infection. In the case of the parenteral cephalosporins, the oral switch to co-amoxiclav 625 mg tds is recommended rather than to oral cephalosporins; for those treated with benzylpenicillin plus levofloxacin, oral levofloxacin with or without oral amoxicillin 500 mg – 1.0 g tds is recommended.

Abbreviations: od = once daily; bd = twice; tds = 3 times; qds = 4 times: iv = intravenous; po = oral

Table 11: Recommended therapy of microbiologically documented pneumonia. Local specialist advice should also be sought. Results can be modified once sensitivities tests are available UPDATED 2004

PATHOGEN	PREFERRED	ALTERNATIVE
S pneumoniae	amoxicillin 500 mg – 1.0 g[a] tds po *or* benzylpenicillin 1.2 g qds iv	erythromycin 500 mg qds po *or* clarithromycin 500 mg bd po *or* cefuroxime 0.75-1.5 g tds iv *or* cefotaxime 1-2 g tds iv *or* ceftriaxone 2g od iv
M pneumoniae *C pneumoniae*	erythromycin 500 mg qds po *or* iv *or* clarithromycin 500 mg bd po *or* iv	tetracycline 250 – 500 mg qds po *or* fluoroquinolone[b] po *or* iv
C psittaci *C burnetii*	tetracycline 250 mg – 500 mg qds po *or* 500 mg bd iv	erythromycin 500 mg qds po *or* clarithromycin 500 mg bd iv
Legionella spp.	clarithromycin 500 mg bd po *or* iv ± rifampicin [c] 600 mg od *or* bd, po/ iv	fluoroquinolone po *or* iv [b]

H influenzae	*Non-β-lactamase-producing:* amoxicillin 500 mg tds po *or* ampicillin 500 mg qds iv	cefuroxime 750 mg -1.5 g tds iv *or*
	β-lactamase-producing: co-amoxiclav 625 mg tds po *or* 1.2 g tds iv	cefotaxime 1-2 g tds iv *or* ceftriaxone 2 g od iv *or* fluoroquinolone[b] po *or* iv
Gram negative enteric bacilli	cefuroxime 1.5 g tds *or*	fluoroquinolone[b] iv *or*
	cefotaxime 1-2 g tds iv *or*	imipenem 500 mg qds iv *or*
	ceftriaxone 2 g <u>od</u> iv *(Comment: the table in the 2001 version incorrectly stated bd)*	meropenem 0.5-1.0 g tds iv
P aeruginosa	ceftazidime 2 g tds iv *plus* gentamicin *or*	ciprofloxacin 400 mg bd iv *or*
	tobramycin (dose monitoring)	piperacillin 4 g tds iv *plus* gentamicin *or* tobramycin (dose monitoring)
S aureus	Non-MRSA: flucloxacillin 1-2 g qds iv ± rifampicin 600 mg od *or* bd, po/iv	teicoplanin 400 mg bd iv ± rifampicin 600 mg od *or* bd po/iv
	MRSA: vancomycin 1 g bd iv (dose monitoring)	linezolid 600mg bd iv or po is a recently available alternative

a) a higher dose of 1.0 g tds is recommended for infections documented to be caused by less susceptible strains (MIC> 1.0mg/L)

b) currently UK licenced and available, suitable fluoroquinolones include ciprofloxacin, ofloxacin, moxifloxacin and levofloxacin

c) concurrent administration of rifampicin reduces the serum level of macrolides; the clinical relevance of this is not known

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