Synopsis

Scope of these guidelines (sections 1.1–1.7)

- These guidelines refer to the management of adults with community acquired pneumonia (CAP) of all ages in the community or in hospital. They have been developed to apply to the UK healthcare system and population, but they should equally be applicable to any other countries which operate similar healthcare services.
- They are not aimed at patients with known predisposing conditions such as cancer or immunosuppression admitted with pneumonia to specialist units such as oncology, haematology, palliative care, infectious diseases units, or AIDS units.
- They do NOT apply to the much larger group of adults with non-pneumonic lower respiratory tract infection, including illnesses labelled as acute bronchitis, acute exacerbations of chronic obstructive pulmonary disease (COPD), or "chest infections".
- Details of methods, the level of evidence, and grading of recommendations are given in the text (sections 1.8–1.15) and appendices and are summarised briefly for easy reference in table 1.

Synopsis of main summary points

AETIOLOGY AND EPIDEMIOLOGY (SECTION 3)

- Only a small range of pathogens causes CAP, with *Streptococcus pneumoniae* being the most frequent (tables 2–6, fig 3) [**Ib**].
- The frequency of pathogens can vary in specific patient groups. Mycoplasma and legionella infections are less frequent in the elderly (box 1, fig 5) [**Ib**].
- The low frequency of legionella, staphylococcal, *Chlamydia psittaci* and *Coxiella burnetii* infection in patients with CAP, together with the likely high frequency of the relevant epidemiological risk factors in the general population (for example, recent travel or contact with someone with an influenza type disease) suggests that routine enquiry about such factors is likely to be misleading [**IV**].
- Only in those with severe illness, where the frequency of legionella and staphylococcal infection is higher, may enquiry about foreign travel and influenza symptoms be of predictive value [**IV**].
- Knowledge of increased mycoplasma activity in the community during an epidemic period may help guide the clinician to the increased likelihood of mycoplasma infection (fig 4) [**IV**].

CLINICAL AND RADIOLOGICAL FEATURES (SECTIONS 4, 5.1–5.3)

- The likely aetiological agent causing CAP cannot be accurately predicted from clinical or radiological features [**II**].
- The term "atypical" pneumonia should be abandoned as it incorrectly implies that there is a characteristic clinical presentation for patients with infection caused by "atypical" pathogens [**II**].
- Elderly patients with CAP more frequently present with non-specific symptoms and are less likely to have a fever than younger patients [**II**].
- Radiological resolution often lags behind clinical improvement from CAP, particularly following legionella and bacteraemic pneumococcal infection [**III**].
- Radiographic changes caused by atypical pathogens clear more quickly than those associated with pneumonia caused by bacterial infection [**III**].
- Radiological resolution is slower in the elderly and in cases where there is multilobe involvement [**Ib**].

MANAGEMENT

- Figure 1 provides an algorithm for the management of adult patients with CAP in the community, and fig 2 provides an algorithm for the management of adult patients with CAP in hospital (see over).

Table 1 Brief description of the generic levels of evidence and guideline statement grades used*

Evidence level	Definition	Guideline statement grade
Ia	A good recent systematic review of studies designed to answer the question of interest	**A+**
Ib	One or more rigorous studies designed to answer the question, but not formally combined	**A−**
II	One or more prospective clinical studies which illuminate, but do not rigorously answer, the question	**B+**
III	One or more retrospective clinical studies which illuminate, but do not rigorously answer, the question	**B−**
IVa	Formal combination of expert views	**C**
IVb	Other information	**D**

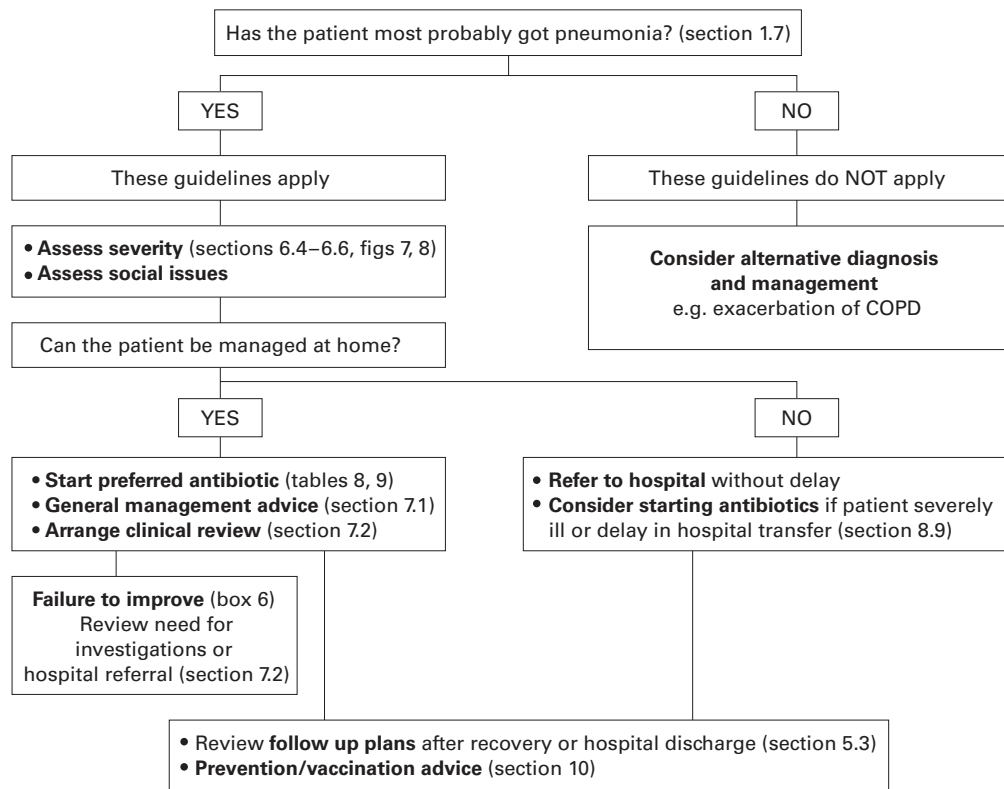*A fuller description is given in section 1 and in appendices 1–4.

Has the patient most probably got pneumonia? (section 1.7)

YES

These guidelines apply

- **Assess severity** (sections 6.4–6.6, figs 7, 8)
- **Assess social issues**

Can the patient be managed at home?

YES

- **Start preferred antibiotic** (tables 8, 9)
- **General management advice** (section 7.1)
- **Arrange clinical review** (section 7.2)

Failure to improve (box 6)
Review need for investigations or hospital referral (section 7.2)

NO

These guidelines do NOT apply

Consider alternative diagnosis and management
e.g. exacerbation of COPD

NO

- **Refer to hospital** without delay
- **Consider starting antibiotics** if patient severely ill or delay in hospital transfer (section 8.9)

- Review **follow up plans** after recovery or hospital discharge (section 5.3)
- **Prevention/vaccination advice** (section 10)

Figure 1   Synopsis of the management of adult patients seen in the community with suspected CAP.

Has the patient got pneumonia? (section 1.7)

YES

These guidelines apply

Assess severity (sections 6.4–6.6, figs 7, 8)

Mild non-severe pneumonia
?Suitable for outpatient management

Non-severe pneumonia
Manage in hospital

NO

These guidelines do NOT apply

Consider alternative diagnosis and management e.g. exacerbation of COPD

Severe pneumonia
Manage in hospital
?Needs high dependency bed

- **Antibiotic management**. Initial empirical choice (tables 8, 9)
- **General management** (section 7)
- **Investigations** (section 5, table 7, fig 6)
- **Monitoring and medical review plan** (sections 6.7, 7.3)

Specific pathogen identified
Review antibiotic choice (table 11)

Improvement
Review antibiotic duration and route (boxes 4, 5, table 10)

Failure to improve (box 6)
Complications (table 12)

- **Discharge and follow up planning** (section 5.3)
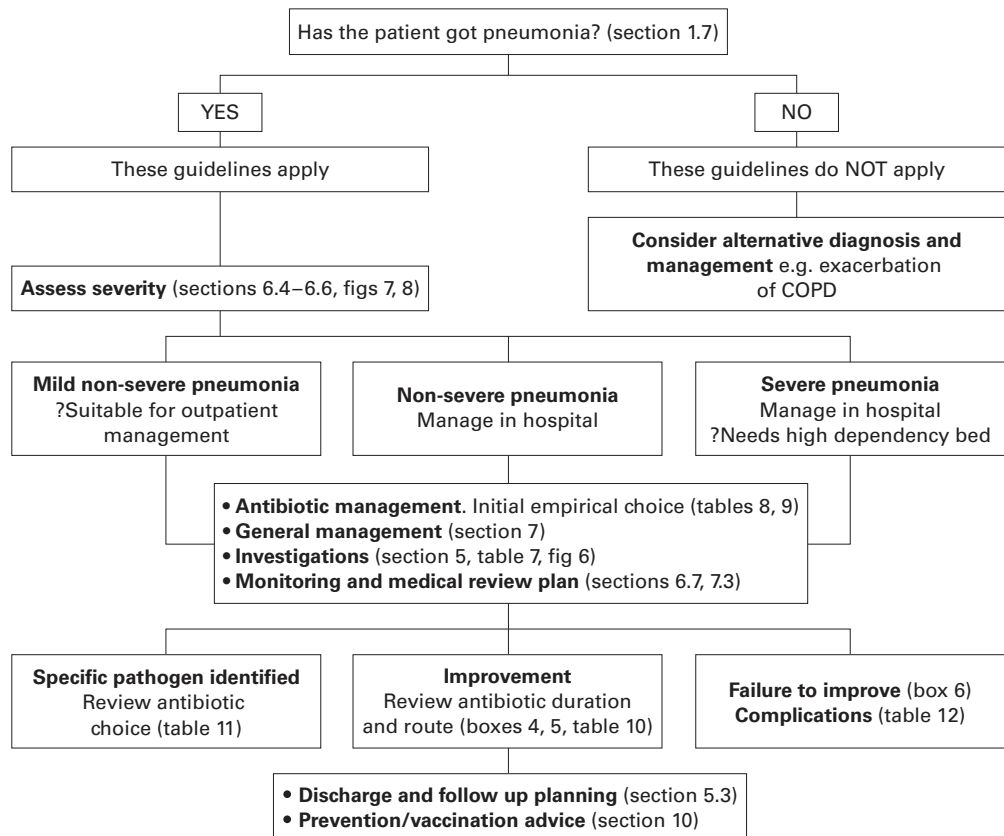- **Prevention/vaccination advice** (section 10)

Figure 2   Synopsis of the management of adult patients seen in hospital with suspected CAP.

Synopsis of main recommendations

Investigations (section 5)

GENERAL INVESTIGATIONS FOR PATIENTS MANAGED IN THE COMMUNITY (SECTION 5.5)

- General investigations, including a chest radiograph, are not necessary for the majority of patients with suspected community acquired pneumonia (CAP) who are managed in the community [**C**].
- Out of hours and emergency general practitioner assessment centres should consider using pulse oximeters to allow for simple assessment of oxygenation [**D**].

MICROBIOLOGICAL INVESTIGATIONS FOR PATIENTS MANAGED IN THE COMMUNITY (SECTION 5.8)

- Microbiological investigations are not recommended routinely [**D**].
- Examination of sputum should be considered for patients who do not respond to empirical antibiotic therapy [**D**].
- Examination of sputum for *Mycobacterium tuberculosis* should be considered for patients with a persistent productive cough, especially if malaise, weight loss or night sweats, or risk factors for tuberculosis (e.g. ethnic origin, social deprivation, the elderly) are present [**D**].
- Serological investigations may be considered during outbreaks (e.g. Legionnaires' disease) or epidemic mycoplasma years, or when there is a particular clinical or epidemiological reason [**D**].

GENERAL INVESTIGATIONS FOR PATIENTS ADMITTED TO HOSPITAL (SECTION 5.6)

> **Sect. 5.6 Refer to 2004 updated document**

- All patients should have the following investigations performed on admission: chest radiograph [**C**]; full blood count [**B–**]; urea, electrolytes and liver function tests [**C**]; C reactive protein (CRP) when locally available [**B–**]; oxygenation assessment [**C**].

MICROBIOLOGICAL INVESTIGATIONS FOR PATIENTS ADMITTED TO HOSPITAL (SECTIONS 5.7–5.9)

> **Sect. 5.7-5.9 Refer to 2004 updated document**

- It is not necessary or appropriate to perform a full range of microbiological investigations on every patient with CAP. The investigations performed should be guided by the severity of pneumonia, epidemiological risk factors, and the response to treatment (table 7) [**D**].
- Blood culture is recommended for all patients, preferably before antibiotic treatment is commenced [**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 treatment. Specimens should be transported rapidly to the laboratory [**D**].

- Sputum cultures should also be performed for patients with severe CAP or those who fail to improve [**D**].
- Laboratories should offer a reliable Gram stain for patients with severe CAP or complications, as on occasions this can give immediate indication of likely pathogens. Routine performance or reporting of sputum Gram stain on all patients is unnecessary but can aid the laboratory interpretations of culture results [**D**].
- Laboratories performing sputum Gram stains should adhere to strict and locally agreed criteria for interpretation and reporting of results [**B+**].
- Paired serological tests should be performed for all patients with severe CAP, those who are unresponsive to β-lactam antibiotics, and for selected patients with particular epidemiological risk factors or in whom a specific microbiological diagnosis is important for public health measures (fig 6) [**D**].
- Serological tests should be extended to all patients admitted to hospital with CAP during outbreaks and when needed for the purposes of surveillance. The criteria for performing serological tests in these circumstances should be agreed locally between clinicians, laboratories, and public health officers [**D**].
- Pneumococcal antigen tests should be used for patients with severe CAP, if available locally [**D**].
- Investigations for legionella infection are recommended for all patients with severe CAP, for other patients with specific risk factors, and for all patients with CAP during outbreaks [**D**].
- Rapid testing and reporting for legionella urine antigen should be available in at least one laboratory per region [**D**].
- Legionella culture should be specifically requested by clinicians on laboratory request forms from patients with severe CAP, or where legionella infection is suspected on epidemiological grounds [**D**].
- Legionella cultures should be routinely performed on invasive respiratory samples (e.g. obtained by bronchoscopy) from patients with CAP [**D**].
- Serological assays with complement fixation tests (CFTs) are widely available and should remain the mainstay of diagnosis for atypical and common respiratory viral pathogens [**C**].
- Chlamydial antigen detection tests should be available for invasive respiratory samples from patients with severe CAP or where there is a strong suspicion of psittacosis [**D**].

- The CFT remains the most suitable and practical serological assay for routine diagnosis of respiratory mycoplasmal and chlamydial infections [**B–**]. There is no currently available serological test that can reliably detect infections due to *Chlamydia pneumoniae*.

Severity assessment (section 6)

GENERAL RECOMMENDATIONS

- Severity assessment is recommended as the key to planning appropriate management both in the community and in hospital [**D**].
- Certain adverse prognostic features (detailed below) have been associated with an increased risk of death and should be assessed in all patients [**A–**].
- None of the available predictive models or the algorithms provided in these guidelines allow the unequivocal categorisation of patients into definite risk groups and they should be regarded as an aid to clinical judgement, which is essential in assessing appropriate management [**D**]
- Regular reassessment of severity during the course of the illness is mandatory if management is to be adjusted appropriately [**D**].

ADVERSE PROGNOSTIC FEATURES

"Pre-existing" adverse prognostic features

- Age 50 years and over [**Ib**].
- Presence of coexisting disease [**Ib**].

*"Core" clinical adverse prognostic features (***CURB***)*

- **C**onfusion: new mental confusion (defined as an Abbreviated Mental Test score of 8 or less, see box 2) [**Ib**].
- **U**rea: raised >7 mmol/l (for patients being seen in hospital) [**Ib**].
- **R**espiratory rate: raised ⩾30/min [**Ib**].
- **B**lood pressure: low blood pressure (systolic blood pressure <90 mm Hg *and/or* diastolic blood pressure ⩽60 mm Hg) [**Ib**].

"Additional" clinical adverse prognostic features

- Hypoxaemia (SaO_2 <92% or PaO_2 <8 kPa) regardless of FiO_2 [**Ib**]. Oxygen saturation measurements may be available to some general practitioners in the community who have oximeters.
- Bilateral or multilobe involvement on the chest radiograph [**Ib**].

IDENTIFYING THOSE PATIENTS WHO CAN USUALLY BE SAFELY TREATED AT HOME (FIG 7)

- Patients who display no adverse prognostic features are at low risk of death and do not normally require hospitalisation for clinical reasons [**D**].
- Patients who display two or more "core" adverse prognostic features are at high risk of death and should be referred urgently to hospital [**D**].
- For all other patients the decision to treat at home or refer to hospital is a matter of clinical judgement [**D**].

- When deciding on home treatment, the patient's social circumstances and wishes must be taken into account in all instances [**D**].

IDENTIFYING THOSE WITH SEVERE CAP IN HOSPITAL (FIG 8)

- Patients who have two or more "core" adverse prognostic features are at high risk of death and should be managed as having severe pneumonia [**A–**].
- Patients who display one "core" adverse prognostic feature are at increased risk of death. The decision to treat such patients as having severe or non-severe pneumonia is a matter of clinical judgement, preferably from an experienced clinician. This decision can be assisted by considering "pre-existing" and "additional" adverse prognostic features [**D**].
- Patients who display no adverse prognostic features can be managed as having non-severe pneumonia and may be suitable for outpatient treatment or early hospital discharge [**B+**].

REVIEWING SEVERITY STATUS AFTER INITIAL ASSESSMENT (SECTION 6.7)

- Regular assessment of disease severity is recommended for *all* patients following hospital admission. The "post take" round by a senior doctor and the medical team provides one early opportunity for this review [**D**].
- All patients who display one or more "core" adverse prognostic features on admission should be reviewed *medically* at least 12 hourly until shown to be improving [**D**].

General management of CAP (section 7)

IN THE COMMUNITY (SECTIONS 7.1–7.2)

- The need for hospital referral should be assessed using the recommended severity criteria and clinical judgement [**C**].
- Those with features of severe infection should be admitted urgently to hospital [**C**].
- Patients with suspected CAP should be advised not to smoke, to rest, and to drink plenty of fluids [**D**].
- Pleuritic pain should be relieved using simple analgesia such as paracetamol [**D**].
- Nutritional supplements should be considered in prolonged illness [**C**].
- Pulse oximetry, with appropriate training, should become increasingly available to general practitioners for assessment of severity and oxygen requirement for patients with CAP and other acute respiratory illnesses [**D**].
- Review of patients in the community with CAP is recommended after 48 hours or earlier if clinically indicated. "Core" and "additional" adverse prognostic features should be assessed as part of the clinical review [**D**].

- Those who fail to improve after 48 hours of treatment should be considered for hospital admission or chest radiography [**D**].

Sect. 7.3 Refer to 2004 update with particular reference to Point 2.

IN HOSPITAL (SECTION 7.3)
- All patients should receive appropriate oxygen therapy with monitoring of oxygen saturations and FIO_2 with the aim to maintain PaO_2 ⩾8 kPa and SaO_2 ⩾92%. High concentrations of oxygen can safely be given in uncomplicated pneumonia [**D**].
- Oxygen therapy in patients with pre-existing chronic obstructive pulmonary disease complicated by ventilatory failure should be guided by repeated arterial blood gas measurements [**C**].
- Patients should be assessed for volume depletion and may require intravenous fluids [**C**].
- Nutritional support should be given in prolonged illness [**C**].
- Temperature, respiratory rate, pulse, blood pressure, mental status, oxygen saturation, and inspired oxygen concentration should be monitored and recorded initially at least twice daily and more frequently in those with severe pneumonia or requiring regular oxygen therapy [**C**].
- The CRP level should be remeasured [**B–**] and the chest radiograph repeated [**C**] in patients who are not progressing satisfactorily.

ON THE INTENSIVE CARE UNIT (SECTION 7.4)
- Detailed recommendations are outside the scope of these guidelines.
- Patients with CAP admitted to an intensive care unit (ICU) should be managed by specialists with appropriate training in intensive care and respiratory medicine [**D**].
- Bronchoscopy can be valuable to remove retained secretions, obtain samples for culture for other microbiological investigations, and to exclude endobronchial abnormality [**C**].

FOLLOW UP PLANNING: WHEN TO REPEAT THE
CHEST RADIOGRAPH AND WHAT ACTION TO TAKE IF THE
RADIOGRAPH HAS NOT RETURNED TO NORMAL
(SECTIONS 5.2, 5.3, 7.5)
- The chest radiograph need not be repeated prior to hospital discharge in those who have made a satisfactory clinical recovery [**D**].
- At discharge or at follow up, patients should be offered access to information about CAP such as a patient information leaflet [**D**].
- Clinical review should be arranged for all patients at around 6 weeks, either with their general practitioner or in a hospital clinic [**D**].
- It is the responsibility of the hospital team to arrange the follow up plan with the patient and the general practitioner [**D**].
- A chest radiograph should be arranged at that time for those patients who have persistent symptoms or physical signs or who are at higher risk of underlying malignancy (especially smokers and those over 50 years) [**C**].

- In a patient who is improving clinically and for whom there are no concerning clinical features, it will usually not be necessary to perform further investigations just because radiological improvement lags behind clinical recovery [**B+**].
- Further investigations which may include bronchoscopy should be considered in patients with persisting signs, symptoms, and radiological abnormalities about 6 weeks after completing treatment [**C**].

Antibiotic management (section 8)
EMPIRICAL ANTIBIOTIC CHOICE IN THE COMMUNITY
(TABLE 8)
- Amoxicillin remains the preferred agent but at a higher dose than previously recommended [**D**].
- A macrolide (erythromycin or clarithromycin) is offered as an alternative choice and for those patients who are hypersensitive to penicillins [**D**].
- For those patients referred to hospital with suspected CAP, general practitioners may consider administering antibiotics immediately where the illness is considered to be life threatening or where there are likely to be delays (over 2 hours) in admission [**D**].

EMPIRICAL ANTIBIOTIC CHOICE FOR ADULTS
HOSPITALISED WITH NON-SEVERE CAP (TABLE 9)
- Most patients can be adequately treated with oral antibiotics [**C**].
- Combined oral therapy with amoxicillin and a macrolide (erythromycin or clarithromycin) is preferred for patients who require hospital admission for clinical reasons [**D**].
- Oral monotherapy should be considered in the following circumstances:
  - Amoxicillin monotherapy: (i) those previously untreated in the community or (ii) those admitted to hospital for non-clinical reasons who would otherwise be treated in the community (e.g. the elderly or socially isolated) [**D**].
  - Monotherapy with a macrolide may be suitable for patients who have failed to respond to an *adequate* course of amoxicillin prior to admission. Deciding on the adequacy of prior therapy is difficult and is a matter of individual clinical judgement. It is therefore recommended that combination antibiotic therapy is the preferred choice in this situation and that the decision to adopt monotherapy is reviewed on the "post take" round within the first 24 hours of admission [**D**].
- When oral treatment is contraindicated, recommended parenteral choices include intravenous ampicillin or benzylpenicillin, together with erythromycin or clarithromycin [**D**].

- 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 [**C**].
- A fluoroquinolone active against *S pneumoniae* is an alternative regimen for those intolerant of penicillins or macrolides or where there are local concerns over *Clostridium difficile* associated diarrhoea. However, experience with such newer fluoroquinolones in the treatment of CAP and their interaction and side effect profile is at present limited and further reported experience is required [**B–**]. Levofloxacin is the only recommended agent currently licensed in the UK.

EMPIRICAL ANTIBIOTIC CHOICE FOR ADULTS HOSPITALISED WITH SEVERE CAP (TABLE 9)
- Patients with severe pneumonia should be treated immediately after diagnosis with parenteral antibiotics [**B–**].
- An intravenous combination of a broad spectrum β-lactamase stable antibiotic such as co-amoxiclav or a second generation (e.g. cefuroxime) or third generation (e.g. cefotaxime or ceftriaxone) cephalosporin together with a macrolide (e.g. clarithromycin or erythromycin) is preferred [**C**].
- For those who are intolerant of β-lactam or macrolide therapy or where there are local concerns over *C difficile* associated diarrhoea, a fluoroquinolone with enhanced activity against *S pneumoniae* together with intravenous benzylpenicillin is offered as an alternative [**D**]. Levofloxacin is currently the only such fluoroquinolone licensed in the UK.

ROUTE OF ANTIBIOTIC ADMINISTRATION (BOXES 4 AND 5)
- The oral route is recommended in those with non-severe pneumonia admitted to hospital provided there are no contraindications to oral therapy [**B+**].
- Patients treated initially with parenteral antibiotics should be transferred to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 hours, providing there is no contraindication to the oral route [**B+**].
- The choice of route of administration should be reviewed initially on the "post take" round and then daily [**D**].
- Ward pharmacists could play an important role in facilitating this review by highlighting prescription charts where parenteral antibiotic treatment continues [**D**].

DURATION OF ANTIBIOTIC ADMINISTRATION (TABLE 10)
- For patients managed in the community and most of those admitted to hospital with non-severe and uncomplicated pneumonia, treatment with appropriate antibiotics for 7 days is recommended [**C**].

- For patients with severe microbiologically undefined pneumonia, 10 days of treatment is proposed. This should be extended to 14–21 days where legionella, staphylococcal, or Gram negative enteric bacilli pneumonia are suspected or confirmed [**C**].

FAILURE TO IMPROVE (TABLE 12, BOX 6)
- For patients who fail to improve as expected, there should be a careful review by an experienced clinician of the clinical history, examination, prescription chart, and results of all available investigation results [**D**].
- Further investigations, including a repeat chest radiograph, CRP and white cell count, and further specimens for microbiological testing should be considered in the light of any new information after the clinical review [**D**].
- When a change in empirical antibiotic treatment is considered necessary, a macrolide could be substituted for or added to the treatment for those with non-severe pneumonia treated with amoxicillin monotherapy in the community or in hospital [**C**].
- For those with non-severe pneumonia in hospital on combination therapy, changing to a fluoroquinolone with effective pneumococcal cover is an option [**C**].
- The addition of rifampicin may be considered for those with severe pneumonia not responding to combination antibiotic treatment [**C**].

ANTIBIOTIC THERAPY WHEN A SPECIFIC PATHOGEN HAS BEEN IDENTIFIED (TABLE 11)
- If a specific pathogen has been identified, the guidelines recommend specific antibiotic options [**C**].

Prevention: vaccination strategies (section 10)

INFLUENZA VACCINATION (SECTION 10.2)
- Influenza vaccination is recommended for those at "high risk" of mortality from influenza or complicating pneumonia [**C**].
- These "high risk" groups include those with chronic lung, heart, renal and liver disease, diabetes mellitus, immunosuppression due to disease or treatment, and those aged over 65 years [**C**].
- Influenza vaccine is contraindicated for those with hypersensitivity to hens' eggs [**C**].

PNEUMOCOCCAL VACCINATION (SECTION 10.3)
- Pneumococcal vaccination is recommended by the Departments of Health for all those aged 2 years or older in whom pneumococcal infection is likely to be more common or serious, although there is no evidence that it is effective in preventing CAP in such "at risk" groups [**A+**].
- Pneumococcal vaccine should not be given during acute infection and is not recommended during pregnancy. Re-immunisation within 3 years is contraindicated [**C**].
- Pneumococcal and influenza vaccines can be given together at different sites [**A–**].

1   Introduction and methods

1.1 Introduction
Community acquired pneumonia (CAP) is common. It is associated with significant morbidity, mortality and utilisation of health service resources (see section 2). Changes over the last decade suggest that it is appropriate to review the UK guidelines for the management of CAP published in 1993.

1.2 Available management guidelines for CAP
Recognising the clinical importance of CAP, numerous countries have developed national guidelines in the last decade, including the UK,[1] USA,[2 3] Canada,[4] France,[5] and Italy,[6] among others. Those from the British Thoracic Society (BTS)[1] and the American Thoracic Society[3] received much publicity and differed with regard to likely aetiology and antibiotic management.

More recently the Infectious Disease Society of America[2] and the Canadian Infectious Diseases Society working with the Canadian Thoracic Society[4] have updated their recommendations for North America, and the Centers for Disease Control and Prevention of the USA have also published their own recommendations, specifically regarding the treatment and control of drug resistant *Streptococcus pneumoniae*.[7] The European Respiratory Society[8] has also provided a review of the management of lower respiratory tract infections, including pneumonia, to cover Europe. (Since finalising the contents of these guidelines, the American Thoracic Society has also published its own revised guidelines for North America.[9])

However, it may be unwise to extrapolate national guidelines from other countries to the UK for a number of reasons:

(1) They should depend on the results of good CAP studies performed within that country. There are substantial differences in study results from different parts of the world (see section 3).[6 10]

(2) Diagnosis and management of CAP will be influenced by the organisation of the health system. In common with some other countries, the UK has a network of National Health Service general practitioners who are the first port of call for most people with an acute illness and without cost to the patient. They will often diagnose and manage a patient without any investigations or secondary care advice. General practitioners usually only refer patients to hospital either just for a chest radiograph or because of clinical concern and the likely need for admission.

(3) By contrast, other health services such as in the USA depend on primary care physicians or specialists, some operating on a fee for service basis and usually operating from well equipped clinics or emergency rooms with easy and immediate access to radiology and other investigations. In such circumstances most patients with suspected pneumonia will be diagnosed by chest radiography and investigated before deciding on optimum management either as an outpatient or by admission to hospital.

(4) There is a difference in antimicrobial agents licensed and available in different countries. For instance, levofloxacin is the only fluoroquinolone with some enhanced pneumococcal activity licensed and available in the UK at the time of preparing these guidelines, whereas other countries also have available newer agents such as moxifloxacin.

1.3 What problems have become apparent with the 1993 BTS CAP guidelines?
Firstly, these were consensus guidelines[1] which relied on UK CAP studies performed in the early 1980s,[11–15] all of which had design limitations which question the application of their results to current UK practice.

Secondly, they have also been criticised for not clearly differentiating between CAP and non-pneumonic lower respiratory tract infections such as acute exacerbations of chronic obstructive pulmonary disease and thus encouraging overtreatment of some patients, particularly the elderly. The severity criteria proposed by the 1993 BTS guidelines resulted in many patients both with and without pneumonia being identified as severely ill. These factors have been blamed for the dramatic increase in the use of intravenous broad spectrum antibiotics, combination antibiotic therapy, antibiotic costs, and side effects, particularly *Clostridium difficile* associated diarrhoea.[16–18]

New guidelines must try to address these areas of misunderstanding. Unfortunately, there have been no comprehensive, prospective hospital studies of CAP published in the UK since the early 1980s, although there have been a number of focused hospital and community studies to address specific areas.[13 19–23] While providing useful information about particular facets of CAP, such studies do not allow a balanced overview of its current aetiology in the UK.

By contrast, CAP continued to be actively studied in other countries during the 1990s.[24–29] These data suggest that the importance of *S pneumoniae* infection is waning as the frequency of newer pathogens such as *Chlamydia pneumoniae* and "non-penicillin responsive" pathogens such as the aerobic Gram negative enteric bacilli increase, including the *Enterobacteriaceae* and *Pseudomonas aeruginosa*.

1.4 What changes have happened in the area of CAP in the last two decades?
Over the last decade there is perceived to have been a change in the pattern of adult CAP in the UK. This has resulted in a pressure to alter the empirical management of CAP to new broader spectrum antibiotics and also combination antibiotic therapy.

These perceived changes include:

(1) Increasing emphasis on new pathogens, particularly *C pneumoniae* and *Legionella* species and on older pathogens such as *Moraxella catarrhalis* and Gram negative enteric bacilli, but the clinical relevance to UK practice needs to be clarified (see section 3).

(2) The increasing age of the population, many with co-morbid illness, and the marked increase in the use of residential and nursing homes over the last few years is perceived to provide an expanding "at risk" population for respiratory pathogens such as Gram negative enteric bacilli[30] who therefore require broad spectrum antibiotic therapy (see section 3).

(3) The admission of patients for non-medical reasons (such as inadequate social support for the elderly) and the common use of antibiotics for minor respiratory illness in the community[31] may encourage the hospital doctor to use broad spectrum antibiotics because of the perceived problem of either failed community therapy or antibiotic resistant bacteria in hospitalised patients who have not responded to initial antibiotics.

(4) A change in delivery of acute medical services in most hospitals, with integration of adult and geriatric medicine and the use of assessment and admissions wards and loss of continuity of care throughout the admission, has encouraged the use of a "belt and braces" management strategy for all types of patients with CAP in order to cover all pathogens and "be safe", with an emphasis on parenteral and combination antibiotic therapy. This occurs especially in the elderly who are perceived to be at increased risk of complicated bacterial infections, but also at risk of antibiotic related morbidity including *C difficile* associated diarrhoea (see sections 3, 6 and 8).

(5) Patients with CAP will usually be assessed and admitted by relatively inexperienced medical trainees which may contribute to overtreatment "to be safe".[32] It is now recommended that the "consultant post take" round within 24 hours of admission is a part of good medical practice[33] [**IVb**] and this valuable resource needs to be integrated into guideline practice for the management of patients hospitalised with pneumonia (section 7).

(6) Reports of increasing antibiotic resistance of common respiratory pathogens have produced recent worries about antibiotic resistance in the UK from Government expert committees.[34 35] Such concerns have already influenced antibiotic prescribing in several European countries and in North America.[36] The issue of penicillin resistant pneumococci is particularly relevant. It is important to review whether such changes in antibiotic resistance are now clinically important in UK practice[37] and in countries with similar characteristics (see section 8).

(7) The marketing of newer antibiotics (particularly macrolides and fluoroquinolones) is exposing doctors to increasing pressure to use them "to cover all likely pathogens" because of concerns about changes in pathogens, antibiotic resistance, and the "at risk" population. Some of these compounds may appear to have attractive properties for the management of CAP, but guidance is needed on the strength of the available comparative data of these newer antibiotics (see section 8). In these guidelines we only consider antibiotics licensed and available in the UK at the time of preparation of the document.

(8) Newer serological, molecular biological, and antigen detection techniques are now available for the diagnosis of viral, atypical, and bacterial pathogens—for example, urine antigen detection which has improved diagnosis of legionella infections—and guidance is needed on when to request such tests (see section 5).

(9) There has been a dramatic increase in the use of both influenza vaccine (1.3 million doses in 1980/81 and 7 million in 1997/8) and pneumococcal vaccine (5000 doses in 1989 and 750 000 in 1997) in the community which may have influenced the aetiology of community acquired pneumonia (data provided by Dr Jane Leese, Department of Health). Advice is needed on the value of preventative strategies (see section 9 on guidelines on vaccination).

Summary
- Up to date guidelines are needed to review the current data and to assess the impact, if any, of these changes on new management guidelines of CAP in the UK.

1.5 What is the target end user audience?
We want these guidelines to be of value to:
- hospital based medical and other staff involved with managing adult patients with community acquired pneumonia;
- general practitioners;
- those teaching the subject at both under-graduate and postgraduate level.

The guidelines have been developed to apply to the UK healthcare system and population, but they should also be of value to other countries which operate similar healthcare services with appropriate modification to take into account differences in licensing and availability of antimicrobial agents.[38]

1.6 What patient populations are included and excluded?
Our guidelines address the management of unselected adults with CAP who are managed by their general practitioner or admitted to hospital as an emergency.

They are *not* aimed at the much larger group of adults with non-pneumonic lower respiratory tract infection, including illnesses labelled as acute bronchitis, acute exacerbations of chronic obstructive pulmonary disease (COPD), or "chest infections".

Although there are similarities in the principles of management between pneumonic lower respiratory tract infection (CAP) and non-pneumonic lower respiratory tract infection, there are differences in the aetiology, severity assessment, management, and outcome. Recommendations for the antibiotic management of acute exacerbations of COPD are included

in the published BTS guidelines on the management of chronic obstructive pulmonary disease.[39]

We do not consider the management of pneumonia in:

(1) Patients where the pneumonia is an expected terminal event or who are known to have lung cancer, pulmonary tuberculosis, cystic fibrosis, primary immune deficiency or secondary immune deficiency related to HIV infection, or drug or systemic disease induced immunosuppression. We do include patients receiving oral corticosteroid therapy as this is a not uncommon situation for patients admitted on medical "take".

(2) Patients who have been in hospital within the previous 10 days and may have hospital acquired pneumonia. Patients admitted from healthcare facilities such as nursing homes and residential homes will be commented on separately.

(3) Children with CAP. Such guidelines are being published by the BTS guidelines committee on pneumonia in children.

Summary
- The guidelines are aimed to aid the management of unselected adults with CAP seen by a general practitioner or admitted to hospital as an emergency, on general medical "take", in the UK or in other countries with similar care systems.
- They are not aimed at patients with known predisposing conditions admitted with pneumonia to specialist units such as oncology, haematology, palliative care, infectious diseases or AIDS units.

1.7 Definitions
DEFINITION OF CAP

The diagnosis in hospital will be made with the benefit of a chest radiograph. In the community the recognition and definition of CAP by general practitioners in the UK, without the benefit of investigations or radiology, poses greater problems and the diagnosis will be invariably based only on clinical features.

DEFINITION OF CAP IN A COMMUNITY SETTING

The clinical definition of CAP that has been used in community studies has varied widely but has generally included a complex of symptoms and signs both from the respiratory tract and regarding the general health of the patients. Features such as fever (>38°C), pleural pain, dyspnoea, and tachypnoea and signs on physical examination of the chest (particularly when new and localising) seem most useful when compared with the gold standard of radiological diagnosis of CAP[38] [**II**].

Woodhead *et al*[40] found that 39% of adults treated with antibiotics for an acute lower respiratory tract infection associated with new focal signs on chest examination had evidence of CAP on chest radiograph compared with 2% of patients who did not have new focal chest signs [**II**]. By contrast, Melbye *et al*[41] found that respiratory symptoms and signs were of only minor value in differentiating patients with radiographic pneumonia in a study of 71

patients suspected by their general practitioners of having CAP [**II**]. The clinical findings reported by the general practitioners to be most suggestive to them of CAP (typical history of cough, fever, dyspnoea, chest pains, and lung crackles on examination) had low predictive values; only a short duration of symptoms (less than 24 hours) was of significant predictive value.

Various prediction rules have been published for the diagnosis of CAP [**II**] but have generally shown the need for confirmatory radiographic evidence. Statistical modelling was used by Diehr *et al*[42] to predict the presence of CAP in 1819 adults presenting as hospital outpatients with acute cough, 2.6% of whom had CAP on chest radiographic examination [**II**]. The presence of fever (>37.8°C), raised respiratory rate (>25 breaths/min), sputum production throughout the day, myalgia and night sweats, and absence of sore throat and rhinorrhoea were the only clinical features that predicted CAP when included in a diagnostic rule which had a sensitivity of 91% and a specificity of 40%.

For the purposes of these guidelines CAP in the community has been defined as:
- symptoms of an acute lower respiratory tract illness (cough and at least one other lower respiratory tract symptom);
- new focal chest signs on examination;
- at least one systemic feature (either a symptom complex of sweating, fevers, shivers, aches and pains and/or temperature of 38°C or more);
- no other explanation for the illness, which is treated as CAP with antibiotics.

DEFINITION OF CAP IN PATIENTS ADMITTED TO HOSPITAL (WHEN CHEST RADIOGRAPHY IS AVAILABLE)

Studies of CAP from different countries have used very different definitions and inclusion criteria[10 38 43]; most have required a combination of symptoms, signs, and radiological features. The BTS study of CAP used a definition which included an acute illness with radiographic shadowing which was at least segmental or present in more than one lobe and was not known to be previously present or due to other causes.[14] Like most studies, cases were excluded if pneumonia occurred distal to a known carcinoma or foreign body.

For the purposes of these guidelines CAP in hospital has been defined as:
- symptoms and signs consistent with an acute lower respiratory tract infection associated with new radiographic shadowing for which there is no other explanation (e.g. not pulmonary oedema or infarction);
- the illness is the primary reason for hospital admission and is managed as pneumonia.

DEFINITION OF THE TERMS "ATYPICAL PNEUMONIA" AND "ATYPICAL PATHOGENS"

Another issue relevant to the aetiology, diagnosis, management, and prognosis of CAP is the use of the descriptive term "atypical" when describing pneumonia or groups of pathogens. The term "atypical pneumonia" has outgrown

its historical usefulness and we do not recommend its continued use as it implies, incorrectly, a distinctive clinical pattern (see section 4.2).

We do, however, use the term "atypical pathogens" which, for the purposes of these guidelines, are defined as infections caused by *Mycoplasma pneumoniae*, *C pneumoniae*, *C psittaci*, and *Coxiella burnetii*. These pathogens are characterised by being difficult to diagnose early in the illness and are sensitive to antibiotics other than beta-lactams such as macrolides, tetracyclines, or fluoroquinolones. They are concentrated intracellularly which is the usual site of replication of these pathogens. We conclude that the term "atypical pathogens" is still useful to clinicians in guiding discussion about aetiology and management of CAP.

Legionella species, although sharing some of these characteristics, are not considered to be an "atypical pathogen" for the purpose of this document as there are different species and these can be acquired both in the community and hospital environment.

DEFINITION OF THE TERM "ELDERLY"
There is no agreed age cut off to define the term "elderly" and published guidelines have used very different definitions.[2] [3] [5–7] When referring to published research, wherever possible we define the age limits that are used in studies of CAP in older patients. When making recommendations we arbitrarily use the term "elderly" to include those adults aged 75 years and over.

1.8 Guidelines committee membership
As recommended by guideline developers,[44] [45] a representative group of clinical specialists, a methodologist, and an information specialist were selected to join the committee. These included:

- four practising general physicians with a special interest in respiratory medicine and active research interest in respiratory infection (DH, GD, JTM, MAW)
- two general practitioners (PS, WFH)
- one clinical microbiologist (TB)
- two physicians with an interest in infectious diseases (DN, RGF)
- a specialist registrar trainee in general and respiratory medicine (WSL)
- a clinical epidemiologist/health services researcher (JW)
- a medical librarian/information scientist (RM)

1.9 Involvement with other groups
PS and WFH also acted as mandated representatives for the Royal College of General Practitioners, RGF for the British Infection Society, DN for the British Society for Antimicrobial Chemotherapy, and GD and JTM for the Standards of Care Committee of the British Thoracic Society.

Designated representatives of the following professional groups later provided formal review, comments on, and endorsement of the draft guidelines synopsis: Royal College of Physicians of London (including the Clinical Effectiveness and Evaluation Unit and the Advisory Committees on General Internal Medicine, Respiratory Medicine and Geriatrics), the Public Health Laboratory Service (including the Committee on Respiratory and Systemic Infections and the Primary Care Coordinating Committee), the British Geriatrics Society (including the BGS Executive Committee, the Policy Committee and the Special Interest Group in Respiratory Medicine), and the British Lung Foundation. The Lower Respiratory Tract Infection Guidelines Committee of the Scottish Intercollegiate Guidelines Network (SIGN) provided formal review and comments on the draft as part of the peer review process.

As CAP is usually an acute self-limiting disease we did not feel that patient involvement on the committee was appropriate. However, we did involve a group of 200 patients who had recently recovered from CAP in validating and revising a British Lung Foundation patient information leaflet on pneumonia[46] [**III**]. The leaflet, revised during 2001, is available on request from the British Lung Foundation headquarters (78 Hatton Gardens, London EC1N 8LD, UK) and regional offices.

1.10 Scope of the task and question setting
The broad remit of the group was determined by the BTS Standards of Care Committee and included producing updated and evidence based guidelines for the management of CAP in adults over 16 years for the UK. The group refined this remit by considering documented problems in the current management of CAP both in primary care and in hospital practice and issues arising from previously published guidelines for CAP, such as the 1993 BTS guidelines.[1]

A postal questionnaire was sent to one consultant respiratory physician at each of the 263 UK hospitals listed in the BTS Directory of Respiratory Services enquiring about local written guidelines for the empirical management of CAP and their views about the 1993 BTS CAP guidelines. There were 215 responses (82%) which were reviewed and discussed by the committee when assessing question setting and guideline development.[47] From these sources the nine broad clinical areas listed below were identified. Each issue was expanded into specific clinical questions which were structured to facilitate easy literature searches.[48]

1.11 Literature search, assessment strategy, and critical appraisal
LITERATURE SEARCH
Search strings developed by North Thames Regional Library service and published on the website (www.nthames-health.tpmde.ac.uk/evidence_strategies.htm) were adapted to our purpose by combining them with free text and key word terms for CAP to produce 16 search strategies. These were applied to locate all English language studies relevant to the aetiology, diagnosis, severity staging, investigation, prognosis, complications, or treatment of

> Sect. 1.8 Refer to 2004 update for details of Guidelines Committee membership update.

CAP in adults over 16 years. Initial searches were conducted on Medline (1966 onwards), Embase (1980 onwards), and the Cochrane Library in February 1998. These searches were repeated in May 1999 and again in January and September 2000 (on the latter occasions supplemented by a search of the National Library of Medicine PreMedline database featuring articles not yet fully indexed). A low yield of relevant references in sections on antibiotic management, non-antibiotic management, and complications led to a series of additional searches being conducted for these sections.

ASSESSMENT OF RELEVANCE
One individual (WSL) read the title and abstract of each article retrieved by the literature searches and decided whether the paper was definitely relevant, possibly relevant, or not relevant to the project. For each paper in the first and second categories the full paper was ordered and allocated to the relevant section(s). During the 2 year period of the project a total of 578 papers were judged to be relevant and circulated for critical appraisal.

CRITICAL APPRAISAL
At least two clinical experts were identified for each of the main clinical topic areas:
- Incidence and mortality (JTM, WSL)
- Aetiology and epidemiology (MAW, GD)
- Clinical and radiological features (DH, TB)
- General and microbiological investigations (DH, TB)
- Severity assessment (WSL, JTM)
- General management in hospital (GD, WSL, MAW)
- Antibiotic therapy (RGF, DH, DN)
- Complications and failure to improve (GD, WSL)
- Prevention including vaccination (GD, WFH)

Each expert independently judged the clinical relevance and scientific rigour of each paper assigned to them using generic study appraisal checklists (see appendices 1 and 2) adapted from published checklists.[45] [49–51] With the wide range of study designs relevant to the questions,[52] no single set of pass/fail criteria could be applied across all topic areas. Subject area experts determined the relevance of studies to CAP in the UK by examining the patient groups studied, the healthcare setting (primary care, etc), and the healthcare system where this might influence patient case mix at presentation.

Experts sorted studies into those relevant to their own topic area, those relevant to other areas (which were copied on to experts in other relevant sections), or those not relevant. The approximate agreement rates between assessors for this process was between 70% and 90% for different sections. They also added relevant studies from their own knowledge and personal research reference lists.

Experts individually assessed the literature selected and wrote a short document describing study findings and answering specific pre-identified questions. These documents were discussed by the whole committee to identify areas of overlap and gaps. Given the heterogeneous nature of the patient groups, outcomes, interventions, and tests studied, no formal meta-analysis was carried out.

The reliability of the evidence in each study was graded from Ia to IVb using a new generic list of evidence levels (see appendix 3) developed from existing insights and checklists.[44] [53] Disagreements were resolved by discussion. Where relevant, individual references used in this document are followed by an indication of the evidence level in square brackets.

1.12 Grading of recommendations and drafting of guidelines

GRADING OF RECOMMENDATIONS
Recommendations were graded from A+ to D as indicated by the strength of the evidence as listed in the table in appendix 4.

DRAFTING OF GUIDELINES
Once the outline guideline sections were complete and summarised, they were circulated to representatives of the professional bodies given above for comments.

A detailed guideline synopsis was circulated to the membership of the BTS prior to its winter 1999 conference. The guidelines were discussed in a plenary session at the conference and, in addition, 213 structured feedback forms from BTS members were analysed.

Revisions were made, which also included an updated literature search performed in February and September 2000, and the document content was finalised by the end of 2000. Thus, antibiotics which were not licensed for use in the UK by the end of 2000 could not be included in our recommendations. Similarly relevant products that are not licensed in the UK but are available in other countries are not reviewed. Updates to include any new relevant information or products are planned for the future.

1.13 Plans for updating these guidelines

Following the BTS protocol for guidelines revisions, the committee will meet on an annual basis and review new published evidence obtained from a structured literature search, comment on any newly licensed and relevant antibiotics, and issue guideline updates or revisions as necessary. Important changes will be posted on the BTS website (www.brit-thoracic.org.uk). The membership of the guideline committee will change over time on a rolling programme, dictated by the BTS Standards of Care Committee policy for guideline committee membership.

Sect. 1.13 Refer to 2004 update "Intro and methods"

1.14 Auditing management of CAP
The management of CAP is a sufficiently common and important issue to warrant the development of audit measures of the process of care and outcome to evaluate the quality of care for CAP using guidelines as a standard of management. There is evidence from Hiriani and Macfarlane[22] [**III**], Gleason *et al*[54] [**II**], and

Gilbert *et al*[55] [**II**] that guidelines do guide and standardise management, but with less measurable effect on outcome.

The issue of choosing quality indicators and audit tools for CAP has recently been extensively reviewed [56][**III**]. With guidance from this review, an audit tool has been developed by the committee, refined by the BTS Audit Committee, and tested in pilot hospitals. This will be made available through the BTS website (www.brit-thoracic.org.uk).

1.15 Implementation of the guidelines

We expect that these guidelines will act as a framework for local development or modification of protocols after discussion with local clinicians and management. The subsequent dissemination, implementation, and evaluation of these guidelines should be undertaken by the hospital Quality and Clinical Effectiveness group in conjunction with relevant committees such as those responsible for therapeutics, antibiotic prescribing, or protocol development. Countries with similar health service systems will also find the framework of value, adapting the guidelines to take into account any relevant national differences in disease presentation and the availability of investigations and antimicrobial agents.

For maximal long term impact, the guidelines should be the subject of continuing education and quality improvement activities. Production of summary statements, algorithms, pocket sized reminders, wall charts, and material specific to primary care will be helpful for both individual doctors and departments working with patients with CAP.

2   Incidence, mortality and economic consequences

2.1 How common is adult CAP in the community and in hospital?

Prospective population studies from the UK[40] [**II**], Finland [57] [**Ib**], and North America[58] [**Ib**] have reported an annual incidence of CAP diagnosed in the community of between 5 and 11 per 1000 adult population. Pneumonia, diagnosed clinically by general practitioners, accounts for only 5%[40] [**Ib**] to 12%[59] [**Ib**] of all cases of adult lower respiratory tract infection treated with antibiotics by general practitioners in the community in the UK.

The incidence varies markedly with age, being much higher in the very young and the elderly. In the Finnish study the annual incidence in the 16–59 age group was 6 per 1000 population, 20 for those aged 60 years and over, and 34 per 1000 population for those aged 75 and over[57] [**Ib**]. A similar pattern was reported from Seattle, USA[58] [**Ib**].

Population based studies of the incidence of CAP requiring hospitalisation have reported overall incidences of 1.1 per 1000 adult population per annum in Canada[60] [**Ib**], 2.6 per 1000 in Spain[25] [**II**], 2.7 per 1000 population in Ohio, USA[61] [**Ib**], and 4 per 1000 population in Pennsylvanian hospitals, USA[62] [**III**].

The proportion of adults with CAP who require hospital admission in the UK has been reported as being between 22%[40] [**Ib**] and 42%[63] [**III**]. This figure varies in other countries, probably depending on the structure of the primary and secondary healthcare systems. In a Finnish prospective longitudinal population study 42% were admitted to hospital[57] [**Ib**]. A 50% admission rate was reported in one study from Spain but this only included patients referred by their general practitioner to the hospital emergency service for confirmation of the diagnosis of CAP[25] [**II**].

In Seattle, USA 15% were hospitalised[64] [**Ib**]. In the Pneumonia Patient Outcomes research multicentre, prospective cohort study of CAP in America, 41% of adults studied were managed initially as outpatients and the remainder were admitted to hospital. Of those initially treated as outpatients, only 7.5% were subsequently admitted, 56% because of the CAP and the rest because of worsening of a comorbid illness[65] [**Ib**].

The proportion of adults admitted to hospital with CAP who require management on an ICU varies from 5% in the BTS multicentre study[66] [**II**] to 10% in a Spanish study [**II**].[67] Between 8%[25] [**II**] and 10%[21] [**III**] of medical admissions to an ICU are for severe CAP.

Summary
- The annual incidence in the community is 5–11 per 1000 adult population [**Ib**].
- CAP accounts for 5–12% of all cases of adult lower respiratory tract infection managed by general practitioners in the community [**Ib**].

- The incidence varies markedly with age, being much higher in the very young and the elderly [**Ib**].
- The incidence of CAP requiring admission to hospital varies between 1.1 and 4 per 1000 population [**Ib**].
- Between 22% and 42% of adults with CAP are admitted to hospital [**Ib**].
- Between 5% and 10% of adults admitted to hospital with CAP are managed on an ICU [**II**].

2.2 What is the mortality of CAP?

The reported mortality of adults with CAP managed in the community is low at less than 1%[25] [**II**], [40] [**Ib**], [65] [**Ib**]. Deaths in the community due to CAP are rare in the UK. In one study only seven cases were identified by coroners' post mortem examinations over 1 year in Nottingham, a large urban city of three quarters of a million, giving an incidence of 1 per 100 000 [68] [**III**].

The reported mortality of adults admitted to hospital with CAP has varied widely. The BTS multicentre study reported a mortality of 5.7%[14] [**II**] but did not study patients over the age of 74 years. Other UK studies have reported mortalities of 8%[12] [**II**], 12%[11] [**Ib**], and 14%[69] [**Ib**]. Countries with similar healthcare systems have reported hospital mortality rates of 4%[57] [**Ib**], 7%[70] [**II**], 8%[71] [**Ib**], and 10%[72] [**Ib**]. Mortality figures from North American hospital studies have tended to be higher, probably because more patients with CAP are provided with ambulatory care as outpatients and only those with more severe pneumonia or co-morbid disease are admitted to hospital.

The mortality of patients with severe CAP requiring admission to an intensive care unit (ICU) is high. This is likely to be particularly evident in health services such as the National Health Service where ICU beds are at a premium such that only critically ill patients in need of assisted ventilation can be admitted. ICU based studies in the UK report mortality rates of over 50%[21] [**III**], [22] [**III**], [66] [**III**], [73] [**III**]. Nearly all of the patients required assisted ventilation. By contrast, the mortality rate in a large multicentre study of severe CAP in four French ICUs reported a mortality rate of 35% with a ventilation rate of only 52%[74] [**Ib**]. Similar figures were reported from another ICU based study in France[75] [**II**]. In a specialist ICU in Spain a mortality rate of 22% was reported, rising to 36% in the 61% of patients who required assisted ventilation[67] [**II**].

Summary
- The reported mortality rate of adults with CAP managed in the community in the UK is very low at less than 1% [**Ib**].

- The reported mortality rate of adults admitted to hospital with CAP in the UK has varied between 5.7% and 12% [**Ib**].
- The mortality rate of patients with severe CAP requiring admission to an ICU in the UK is high at over 50% [**III**].

2.3 What are the economic consequences of CAP?

A prevalence based burden of illness study estimated that CAP in the UK incurred a direct healthcare cost of £441 million annually at 1992–3 prices. The average cost for managing pneumonia in the community was estimated at £100 per episode compared with £1700–5100 for hospitalised patients. Hospitalisation accounted for 87% of the total annual cost[63] [**III**].

A similar exercise for the USA calculated that annual CAP costs amounted to $8.4 billion, 52% of the costs being for the inpatient care of 1.1 million patients and the remaining costs for the 4.4 million outpatient consultations. The average length of stay in hospital varied between 5.8 days for those under 65 years of age and 7.8 days for older patients[76] [**III**]. A prospective study of costs and outcome of CAP from five hospitals in North America concluded that the costs of antibiotic treatment varied widely but had no effect on outcome or mortality. Patients treated in hospitals with the lowest costs did not demonstrate worse medical outcomes[55] [**Ib**].

Summary

- The direct costs associated with CAP are high and mostly associated with inpatient care costs [**III**].
- Substantial cost savings could probably be made by strategies to prevent CAP, reduce the requirement for hospital admission, and shorten the length of hospital stay for patients with non-severe CAP [**III**].

2.4 What comments can be made about cost effectiveness of different treatments?

We are not able to provide any structured guidance on this subject. Modern guidelines should attempt to provide information not only on clinical management, but also on the assessment of robust published data on the cost effectiveness of therapies. However, it was noted that there is a clear deficiency of good quality comparative clinical data which would allow meaningful comparisons of management and antibiotic strategies for CAP, whether assessing for clinical or cost effectiveness outcomes.

Summary

- We have not attempted a systematic appraisal of current pharmacoeconomic evidence for CAP and do not give a structured view on cost effectiveness.
- Cost effectiveness data pertinent to UK practice do not exist at the time of writing and are an area for further research.

3   Aetiology and epidemiology

3.1 Introduction

No two studies of the aetiology of CAP are the same. Apparent differences in the observed frequency of pathogens, while possibly real, may also be due to a number of other factors including health care delivery (distribution of management between primary and secondary care; hospital and ICU admission practices); population factors such as age mix, the frequency of alcoholism, comorbid diseases, immunosuppression, and malignancy; and study factors such as the type and number of samples collected, investigations performed, and interpretation of results. Frequently such details are not explicitly stated in the study methodology and, although we have not included studies which do not comply with certain standards, apparently similar studies may hide very different methodologies. With the exception of the elderly, few adequately powered studies using the same methodology have been used to compare different population groups. Conclusions about observed differences in the following data must therefore be treated with caution.

Many of the statements in the following text arise from a comparison of studies rather than data from individual studies. For this reason evidence grades follow statements to justify the conclusions, as well as individual references.

3.2 What are the causes of adult CAP in the UK?

These are set out in table 2, together with details of the relevant references (and grading of evidence from those individual references), grouped together according to whether patients have been managed in the community, in hospital, or on an ICU. For all these groups a common range of pathogens is regularly identified as causing CAP [**Ib**]. Although a single pathogen is identified in 85% of patients where an aetiology is found, the true frequency of polymicrobial CAP is not known and

observed figures are dependent on the intensity of the investigation. *S pneumoniae* is the most frequently identified pathogen [**Ib**]. The relative frequency of pathogens in patients managed in the community and in hospital is probably similar, but the absence of more than one study in the community makes further conclusions uncertain. *Legionella* species and *S aureus* are identified more frequently in patients managed on the ICU [**Ib**]. The apparent difference in the frequency of *M pneumoniae* may depend on whether or not a study is performed in an epidemic year [**II**]. Gram negative enteric bacilli, *C psittaci*, and *C burnetii* are uncommon causes of CAP [**Ib**].

3.3 What are the causes of adult CAP in similar populations elswhere in the world?

The results and references of relevant studies from the remainder of Europe, Australia and New Zealand, and North America are compared in tables 3, 4, and 5. For patients managed in the community and in hospital, the frequency of pathogens is broadly similar to that in the UK [**II**]. This suggests that aspects of these guidelines will be applicable to other countries as well as the UK. The absence of studies using sensitive methods for pneumococcal polysaccharide capsular antigen detection for the identification of *S pneumoniae* may be the explanation for the lower frequency outside the UK (fig 3). The apparent differences in *M pneumoniae* may relate to the presence or absence of epidemics at the time of the study (fig 4). *C pneumoniae* is identified regularly in Europe and North America as well as in a recent UK study [**II**].

There are no North American studies of patients managed in an ICU. Antibiotic resistant *S pneumoniae* appears to be no more frequent in severely ill patients admitted to the ICU than in those managed on an ordinary hospital ward in a country where such resistance is common[77] [**Ib**]. Studies of patients with severe CAP from Europe suggest a lower frequency of legionella and a higher frequency of Gram negative enteric bacilli infections than in the UK. These differences may be real or methodological [**IVa**].

3.4 How does the aetiology differ in certain geographical areas?

Specific studies suggest a higher frequency of certain pathogens in the geographical areas shown in table 6 [**II**].

3.5 Is the aetiology different in specific population groups?

THE ELDERLY

Three UK studies (two using a definition of elderly of over 65 years of age but excluding those aged over 79[13] [**Ib**] and one using a definition of over 75 years[69] [**Ib**]) have reported

Table 2   CAP studies conducted in the UK in different settings

	Community (1 study*, n=236)		In hospital (5 studies†, n=1137)		Intensive care unit (4 studies‡ n=185)	
	Mean (%)	95% CI	Mean (%)	95% CI	Mean (%)	95% CI
S pneumoniae	36.0	29.9 to 42.1	39	36.1 to 41.8	21.6	15.9 to 28.3
H influenzae	10.2	6.3 to 14.0	5.2	4.0 to 6.6	3.8	1.5 to 7.6
Legionella spp	0.4	0.01 to 2.3	3.6	2.6 to 4.9	17.8	12.6 to 24.1
S aureus	0.8	0.1 to 3.0	1.9	1.2 to 2.9	8.7	5.0 to 13.7
M catarrhalis	?		1.9	0.6 to 4.3	?	
Gram negative enteric bacilli	1.3	0.3 to 3.7	1.0	0.5 to 1.7	1.6	0.3 to 4.7
M pneumoniae	1.3	0.3 to 3.7	10.8	9.0 to 12.6	2.7	0.9 to 6.2
C pneumoniae	?	?	13.1	9.1 to 17.2	?	?
C psittaci	1.3	0.3 to 3.7	2.6	1.7 to 3.6	2.2	0.6 to 5.4
C burnetii	0	0 to 1.6	1.2	0.7 to 2.1	0	0 to 2.0
All viruses	13.1	8.8 to 17.4	12.8	10.8 to 14.7	9.7	5.9 to 14.9
Influenza A & B	8.1	4.9 to 12.3	10.7	8.9 to 12.5	5.4	2.6 to 9.7
Mixed	11.0	7.0 to 15.0	14.2	12.2 to 16.3	6.0	3.0 to 10.4
Other	1.7	0.5 to 4.3	2	1.3 to 3	4.9	2.3 to 9.0
None	45.3	39.0 to 51.7	30.8	28.1 to 33.5	32.4	25.7 to 39.7

*Reference 40 [**Ib**].
†References 11 [**Ib**], 12 [**Ib**], 14 [**Ib**], 15 [**Ib**], 69 [**Ib**].
‡References 21 [**Ib**], 22 [**Ib**], 66 [**Ib**], 73 [**II**].

Table 3 Studies of CAP conducted in the community

	UK (1 study*, n=236)		Rest of Europe (6 studies†, n=654)		North America (1 study‡, n=149)	
	Mean (%)	95% CI	Mean (%)	95% CI	Mean (%)	95% CI
S pneumoniae	36.0	29.9 to 42.1	8.4	6.4 to 10.8	?	?
H influenzae	10.2	6.3 to 14.0	1.1	0.4 to 2.2	?	?
Legionella spp	0.4	0.01 to 2.3	2.8	1.6 to 4.3	0.7	0.01 to 3.7
S aureus	0.8	0.1 to 3.0	0	0.0 to 0.7	?	?
M catarrhalis	?		0	0.0 to 0.6	?	
Gram negative enteric bacilli	1.3	0.3 to 3.7	0.2	0.0 to 1.0	?	?
M pneumoniae	1.3	0.3 to 3.7	13.3	10.7 to 15.9	26.2	19.3 to 34.0
C pneumoniae	?	?	8.7	6.5 to 11.3	14.8	9.5 to 21.5
C psittaci	?	?	2.0	1.1 to 3.4	14.8	9.5 to 21.5
C burnetii	0	0 to 1.6	0.8	0.3 to 1.9	2.7	0.7 to 6.7
All viruses	13.1	8.8 to 17.4	12.4	9.9 to 14.9	8.1	4.2 to 13.6
Influenza A & B	8.1	4.9 to 12.3	6.3	4.5 to 8.4	6.0	2.8 to 11.2
Mixed	11.0	7.0 to 15.0	4.7	2.8 to 7.3	4.7	1.9 to 9.4
Other	1.7	0.5 to 4.3	2.0	1.1 to 3.4	0	0 to 2.5
None	45.3	39.0 to 51.7	53.7	49.8 to 57.5	50.3	42.0 to 58.6

*Reference 40 [Ib].
†References 25 [Ib], 370 [II], 371 [Ib], 372 [Ib], 373 [Ib], 374 [Ib].
‡Reference 29 [II].

data on the comparative frequency of pathogens in the elderly compared with that in a younger population. The results are combined in fig 5. For most pathogens their frequency is the same in the young and in the elderly, but *M pneumoniae* and legionella infection are less frequent in the elderly [Ib]. *M pneumoniae* and other atypical pathogens were found to occur more frequently in patients aged <60 years in one other study[78] [Ib]. *H influenzae* may also be more commonly identified in the elderly [II]. Gram negative enteric bacilli were no more common in elderly patients [III], although this has been reported in at least one other study[79] [II]. No difference in the frequency of pathogens according to age was found in one study of patients with severe CAP[80] [III].

PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

There are no relevant UK studies. *H influenzae* and *M catarrhalis* may be more frequent. One Danish study directly compared those with and without COPD and found no difference in pathogen frequency, but numbers were small so real differences may have been missed[81] [II]. A Spanish study of patients with COPD but with no control group found a pathogen distribution similar to that described in studies of CAP in the general population[82] [II]. A further Spanish study found *S pneumoniae*, *Enterobacteriaceae*, *P aeruginosa*, and mixed infections to occur more frequently in those with chronic lung disease[77] [Ib]. COPD was found more frequently in patients with bacteraemic pneumococcal pneumonia than in those with other community acquired pneumonias in one study[83] [Ib].

PATIENTS WITH DIABETES

Diabetes was found to be more frequent in patients with bacteraemic pneumococcal pneumonia than in those with either non-bacteraemic pneumococcal pneumonia or all community acquired pneumonias in one study[83] [Ib].

NURSING HOME RESIDENTS

There are no UK studies. Aspiration[43] [II], [84] [II], Gram negative enteric bacilli[85] [III], and anaerobes [IVb] may occur more frequently than in matched elderly patients. North American studies, which suggest these differences, may not be relevant to the UK population and healthcare system. Legionella infections and atypical pathogens are uncommon[43] [II], [86] [III].

New evidence - Refer to 2004 update, Sect. 3.5

ALCOHOLIC PATIENTS

There are no UK studies. Aspiration[87] [II], pneumococcal infection overall[77] [Ib], bacteraemic pneumococcal infection[77] [Ib], [83] [II], Gram negative enteric bacilli[79] [II], Legionella[88] [III], atypical pathogens[77] [Ib], *C pneumoniae*[77] [Ib], anaerobes [IVb], and mixed infections[77] [Ib] may be more frequent.

PATIENTS ON ORAL STEROIDS

There are no UK studies. Infection with *Legionella* species may be more frequent[89] [III].

ASPIRATION PNEUMONIA

There are no UK studies. Most studies of CAP exclude such patients. Anaerobic bacteria and Gram negative enteric bacilli may be more common[87] [III], [90] [III].

Table 4 Studies of CAP conducted in hospital

	UK (5 studies*, n=1137)		Rest of Europe (23 studies†, n=6026)		Australia & New Zealand (3 studies‡, n=453)		North America (4 studies§, n=1306)	
	Mean (%)	95% CI	Mean (%)	95% CI	Mean (%)	95% CI	Mean (%)	95% CI
S pneumoniae	39	36.1 to 41.8	19.4	18.4 to 20.4	38.4	33.9 to 42.9	11.3	9.5 to 13.0
H influenzae	5.2	4.0 to 6.6	3.9	3.4 to 4.4	9.5	7 to 12.6	6.3	5.0 to 7.7
Legionella spp	3.6	2.6 to 4.9	5.1	4.6 to 5.7	7.5	5.3 to 10.3	4.8	3.7 to 6.0
M catarrhalis	1.9	0.6 to 4.3	1.2	1.0 to 1.5	3.1	1.4 to 6.1	1.2	0.5 to 2.5
S aureus	1.9	1.2 to 2.9	0.8	0.5 to 1.1	2.9	1.5 to 4.9	3.8	2.9 to 5.0
Gram negative enteric bacilli	1	0.5 to 1.7	3.3	2.8 to 3.7	4.6	2.9 to 7	5.3	4.1 to 6.6
M pneumoniae	10.8	9.0 to 12.6	6	5.4 to 6.6	14.6	11.3 to 17.8	4.1	3.1 to 5.3
C pneumoniae	13.1	9.1 to 17.2	6.3	5.5 to 7.3	3.1	1.4 to 6.1	5.9	4.3 to 7.8
C psittaci	2.6	1.7 to 3.6	1.4	1.1 to 1.8	1.4	0.5 to 3.2	0.1	0 to 0.7
C burnetii	1.2	0.7 to 2.1	0.9	0.6 to 1.1	0	0 to 3.4	2.3	1.5 to 3.7
All viruses	12.8	10.8 to 14.7	9.5	8.6 to 10.3	10.6	7.8 to 13.4	8.9	7.4 to 10.6
Influenza A & B	10.7	8.9 to 12.5	5.3	4.6 to 6.1	6.4	4.3 to 9.1	5.9	4.5 to 7.6
Mixed	14.2	12.2 to 16.3	6.3	5.5 to 7.1	19.6	16 to 23.3	8.5	7.0 to 10.3
Other	2	1.3 to 3	2	1.7 to 2.4	4	2.4 to 6.2	8.0	6.6 to 9.7
None	30.8	28.1 to 33.5	50.7	49.5 to 52.0	31.6	27.3 to 35.8	40.7	38.1 to 43.4

*References 11 [Ib], 12 [Ib], 14 [Ib], 15 [Ib], 69 [Ib].
†References 24 [Ib], 77 [Ib], 78 [Ib], 79 [Ib], 81 [Ib], 122 [Ib], 156 [Ib], 190 [Ib], 193 [Ib], 372 [Ib], 373 [Ib], 375 [Ib], 376 [Ib], 377 [Ib], 378 [II], 379 [Ib], 380 [Ib], 381 [Ib], 382 [Ib], 383 [Ib], 384 [Ib], 385 [Ib]
‡References 70 [Ib], 71 [Ib], 72 [Ib].
§References 43 [Ib], 113 [Ib], 386 [Ib], 387 [Ib].

Table 5   *Studies of CAP conducted in the intensive care unit*

	UK (4 studies*, n=185)		Rest of Europe (10 studies†, n=1148)	
	Mean (%)	95% CI	Mean (%)	95% CI
S pneumoniae	21.6	15.9 to 28.3	21.8	19.4 to 24.2
H influenzae	3.8	1.5 to 7.6	5.3	4.1 to 6.8
Legionella spp	17.8	12.6 to 24.1	5.5	4.2 to 7.2
S aureus	8.7	5.0 to 13.7	7.0	5.6 to 8.6
M catarrhalis	?	?	3.8	2.4 to 5.9
Gram negative enteric bacilli	1.6	0.3 to 4.7	8.6	7.1 to 10.4
M pneumoniae	2.7	0.9 to 6.2	2.0	1.3 to 3.0
C pneumoniae	?	?	6.6	2.5 to 13.8
C psittaci	2.2	0.6 to 5.4	0.9	0.4 to 1.9
C burnetii	0	0 to 2.0	0.7	0.3 to 1.4
Viruses	9.7	5.9 to 14.9	4.0	2.7 to 5.6
Influenza A & B	5.4	2.6 to 9.7	2.3	1.1 to 4.2
Mixed	6.0	3.0 to 10.4	5.0	2.4 to 9.1
Other	4.9	2.3 to 9.0	8.4	6.8 to 10.1
None	32.4	25.7 to 39.7	43.3	40.4 to 46.2

*References 21 [**Ib**], 22 [**Ib**], 66 [**Ib**], 73 [**II**].
†References 67 [**Ib**], 75 [**Ib**], 77 [**Ib**], 187 [**Ib**], 188 [**Ib**], 388 [**Ib**], 389 [**Ib**], 390 [**Ib**], 391 [**Ib**], 392 [**II**].

Table 6   *Pathogens which are more common as a cause of CAP in certain geographical regions*

| Pathogen	Geographical area	References
Legionella spp	Countries bordering the Mediterranean	28 [**II**], 382 [**II**]
C burnetii	North West Spain	393 [**II**]
C burnetii	Canada	394 [**II**]
Klebsiella pneumoniae	South Africa	395 [**II**], 396 [**II**]
Burkholderia pseudomallei	South East Asia and Northern Australia	94 [**II**], 397 [**II**], 398 [**II**], 399 [**II**]
Gram negative enteric bacilli	Italy	383 [**II**]
Mycobacterium tuberculosis	Non-industrialised countries	94 [**II**], 95 [**II**]
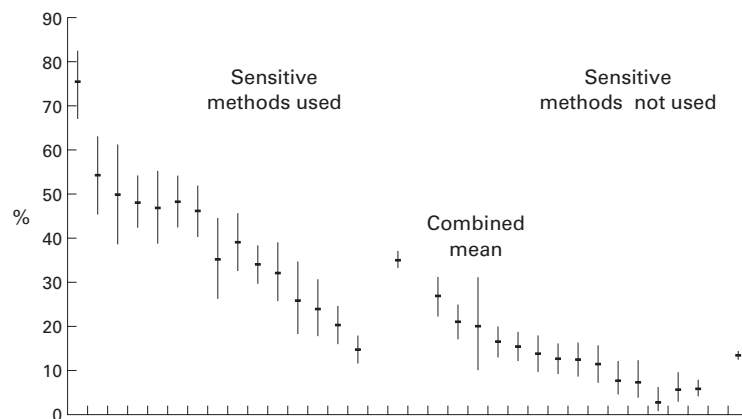
Figure 3   *Frequency of identification of pneumococcal infection in studies of adults admitted to hospital in Europe in relation to the use of sensitive detection methods for S pneumoniae (with 95% CI).*
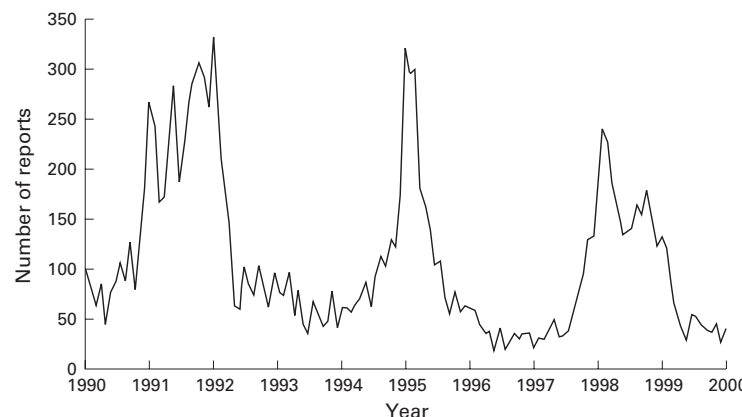

Figure 4   *Laboratory reports of mycoplasma infections to the Communicable Disease Surveillance Centre, England and Wales, 1990–2000 (4 weekly)*[101] [**II**].

3.6 What are the epidemiological patterns of pathogens causing CAP and is this information useful to the clinician?

Streptococcus pneumoniae
S pneumoniae occurs most commonly in the winter[91] [**II**]. Outside the UK epidemics have occurred in overcrowded settings such as mens' shelters and prisons[92] [**II**], [93] [**II**].

Legionella species
Legionella infection is most common in September and October in the UK (www.phls.co.uk/facts) [**II**]; 52% (95% CI 49 to 54) of UK cases are related to travel, 91% (95% CI 87 to 94)[94 95] of these relating to travel abroad[96] [**II**], [97] [**II**], [98] [**II**], [99] [**II**], [100] [**II**]. Clusters of cases are linked to Mediterranean resorts, especially Turkey and Spain, but only 23% (95% CI 19 to 26)[97 99] of cases occur in clusters[96] [**II**], [97] [**II**], [98] [**II**], [99] [**II**], [100] [**II**]. Epidemics occur related to water containing systems in buildings[96] [**II**].

Mycoplasma pneumoniae
Epidemics spanning three winters occur every 4 years in the UK[101] [**II**] as shown in fig 4.

Chlamydia pneumoniae
Epidemics occur in the community and in closed communities[102] [**II**], [103] [**II**], [104] [**II**]. Its direct pathogenic role as a cause of—as opposed to being associated with—CAP is not clear. Evidence that antibiotic treatment directed against this organism alters the course of the illness is lacking. When identified, other bacterial pathogens such as *S pneumoniae* are often identified in the same host[26] [**II**], [28] [**II**], [105] [**II**]. Patients may recover when antibiotics to which *C pneumoniae* is not sensitive are given[105] [**II**].

Chlamydia psittaci
Infection is acquired from birds and animals but human to human spread may occur [**II**]. Epidemics are reported in relation to infected sources at work—for example, poultry or duck workers [**II**]. Only 20% of UK cases have a history of bird contact[106] [**II**].

Coxiella burnetii
Cases are most common in April to June, possibly related to the lambing and calving season [**II**]. Epidemics occur in relation to animal sources (usually sheep), but a history of occupational exposure is only present in 7.7% (95% CI 6.2 to 9.4) of cases[107] [**II**].

Staphylococcus aureus
It is more common in the winter months. Coincident influenza type symptoms are reported in 39% (95% CI 27 to 53)[11 12 14 15] [**II**]. Evidence of coincident influenza virus infection is found in 39% (95% CI 17 to 64) of those admitted to hospital[11 12 14 15] [**II**], and 50% (95% CI 25 to 75) of those admitted to an ICU[21 22 66 73] [**II**].

Influenza virus
Annual epidemics of varying size are seen during the winter months[108] [**II**]. Pneumonia complicates 2.9% (95% CI 1.4 to 5.4) of cases in
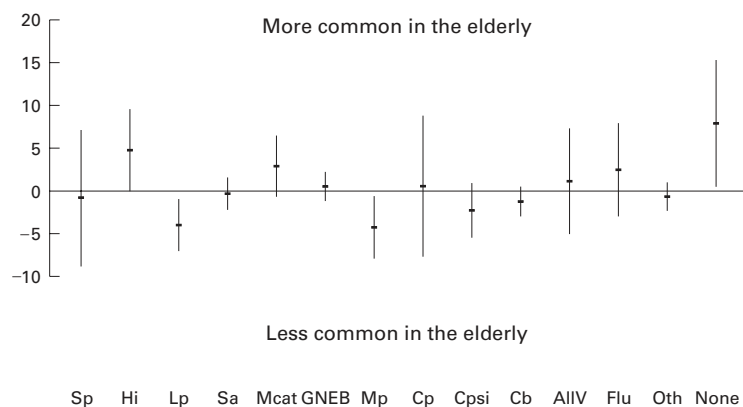
*Figure 5 Difference in causative pathogens between young and elderly patients. Vertical axis shows the percentage difference in frequency between young and the elderly groups for pooled data from three UK studies (with 95% confidence intervals) [**Ib**].[13 69] Sp = Streptococcus pneumoniae, Hi = Haemophilus influenzae, Lp = Legionella spp, Sa = Staphylococcus aureus, Mcat = Moraxella catarrhalis, GNEB = Gram negative enteric bacilli, Mp = Mycoplasma pneumonia, Cp = Chlamydia pneumoniae, Cpsi = Chlamydia psittaci, Cb = Coxiella burnetti, AllV = viruses, Flu = influenza viruses, Oth = other organisms, None = no pathogen identified.*

the community[109] [**Ib**]. The frequency of staphylococcal pneumonia in patients with influenza symptoms is not known. Of adults with CAP admitted to UK hospitals in whom influenza infection is confirmed, 10% (95% CI 4.1 to 19.5) have coincident *S aureus* infection [**II**]. Of those admitted to an ICU, the corresponding figure is 67% (95% CI 35 to 90)[21 22 66 73] [**II**].

Summary

- The low frequency of legionella, staphylococcal, *C psittaci*, and *C burnetii* infection in patients with CAP in both the community and in hospital, together with the likely high frequency of the relevant risk factors (outlined above) in the general population suggests that routine enquiry about such factors is likely to be misleading [**IV**].
- Only in those with severe illness where the frequency of legionella and staphylococcal infection is higher, may enquiry about foreign travel and influenza symptoms be of predictive value [**IV**].
- Knowledge of increased mycoplasma activity in the community during an epidemic period may help guide the clinician to the increased likelihood of mycoplasma infection [**IV**].

4   Clinical features

4.1 Can CAP be reliably differentiated from other respiratory conditions by clinical features alone?

Diagnosing pneumonia clinically without a chest radiograph is inaccurate[110] [**Ia**], but the presence of normal vital signs on chest examination makes an underlying diagnosis of pneumonia unlikely[110] [**Ia**]. A review of published studies reported that there were no individual clinical findings that reliably diagnosed CAP[110] [**Ia**]. The problem is compounded by poor interobserver reliability in eliciting respiratory signs[111] [**II**]. Although most patients with CAP can be managed successfully in the community by their general practitioner without investigations, distinguishing CAP from other causes of respiratory symptoms and signs can be difficult, particularly where the presence of comorbidity such as left ventricular failure, chronic lung disease, or COPD complicate the clinical picture. The elderly can present a particularly difficult diagnostic challenge because they more frequently present with non-specific or absent symptoms and signs[112] [**II**].

Summary
- The diagnosis of CAP on the basis of history and physical findings is inaccurate without a chest radiograph [**Ia**].

4.2 Can the aetiology of CAP be predicted from clinical features?

There have been a large number of publications looking at the possibility of predicting the aetiological agent from clinical features.

Fang *et al*[113] [**II**] found no overall distinctive clinical features at presentation that enabled prediction of the aetiological agent and suggested that the term "atypical" pneumonia should be abandoned (see sections 1 and 8). Similarly Farr *et al*[114] [**II**] reported that aetiology could not be predicted reliably using five clinical variables. For patients with severe CAP admitted to the ICU, clinical features had little value in predicting the aetiological agent[75] [**II**] with the exception of those patients with fever (>39°C) or chest pain who were statistically more likely to have pneumococcal pneumonia. Similarly, pleuritic chest pain was found to be less likely in those patients with "atypical" pathogens[115] [**II**]. The term "atypical pathogen" is defined in section 1.

Summary
- The likely aetiological agent causing CAP cannot be accurately predicted from clinical features [**II**].
- The term "atypical" pneumonia should be abandoned as it incorrectly implies that there is a characteristic clinical presentation for patients with infection caused by "atypical" pathogens [**II**].

4.3 Specific clinical features of particular respiratory pathogens

CLINICAL FEATURES

The clinical features associated with specific pathogens are described below and summarised in box 1.

Streptococcus pneumoniae
- Increasing age, comorbidity, acute onset, high fever and pleuritic chest pain

Bacteraemic *Streptococcus pneumoniae*
- Female sex, excess alcohol, diabetes mellitus, chronic obstructive pulmonary disease, dry cough

Legionella pneumophila
- Younger patients, smokers, absence of comorbidity, diarrhoea, neurological symptoms, more severe infection, evidence of multisystem involvement (e.g. abnormal liver function tests, elevated serum creatine kinase)

Mycoplasma pneumoniae
- Younger patients, prior antibiotics, less multisystem involvement

Chlamydia pneumoniae
- Longer duration of symptoms before hospital admission, headache

Coxiella burnetii
- Male sex, dry cough, high fever

Box 1   Some clinical features reported to be more common with specific pathogens (references are given in the text).

Streptococcus pneumoniae

One study using discriminant function analysis found pneumococcal aetiology to be more likely in the presence of cardiovascular comorbidity, an acute onset, and pleuritic chest pain, and less likely if patients had a cough or flu-like symptoms or had received an antibiotic before admission[116] [**III**].

Bacteraemic pneumococcal pneumonia was found to be more likely in those patients who had at least one of the following features: female sex, history of no cough or a non-productive cough, history of excess alcohol, diabetes mellitus, or COPD[83] [**II**].

Mycoplasma pneumoniae

One study compared CAP due to *M pneumoniae* to patients with pneumococcal or legionella pneumonia[40] [**III**] and reported that patients with mycoplasma pneumonia were younger and less likely to have multisystem involvement and were more likely to have received an antibiotic before admission. By contrast, another report[117] [**II**] found no distinctive clinical features in patients with *M pneumoniae*.

Legionella pneumophila

Numerous studies have reported a variety of clinical features to be more common with legionella pneumonia. In a study comparing

clinical features of different CAP pathogens, patients with *L pneumophila* were more likely to have encephalopathy, elevated levels of liver enzymes, haematuria and, less commonly, to have upper respiratory tract symptoms[118] [**III**]. A subsequent study by the same group, however, found no significant clinical differences[119] [**III**]. A study in Israel reported patients with *L pneumonia* to have no differentiating clinical features apart from being younger with a low incidence of comorbidity[120] [**II**].

Two studies have compared cases of legionella and pneumococcal pneumonia. One reported that patients with legionella infection were less likely to be smokers, have pleural symptoms and arthromyalgia and were more likely to be older or to be dyspnoeic than those with pneumococcal pneumonia[121] [**II**], while the other found that patients with legionella were more likely to be alcoholics, smokers, to have already received an antibiotic, and to have gastrointestinal or neurological symptoms but were less likely to have purulent sputum or pleuritic chest pain[122] [**II**]. A recent prospective study also showed that patients with legionella pneumonia have a low incidence of comorbidity and an increased frequency of diarrhoea and raised serum creatinine kinase[88] [**II**].

Chlamydia pneumoniae
A comparative study of patients with *C pneumoniae* and *S pneumoniae* pneumonia found the former more likely to present with headaches and a longer duration of symptoms before hospital admission[105] [**II**]. A study from Israel reported no distinguishing clinical features for chlamydial pneumonia, except that it affected older patients when compared with pneumococcal and mycoplasma infections[123] [**II**]. A recent study reported that, in cases where *C pneumoniae* was the only pathogen identified, the illness was generally mild with non-specific symptoms[124] [**II**].

Coxiella burnetii
CAP due to *C burnetii* (Q fever) causes non-specific clinical features[125] [**II**], [126] [**II**]. Two reviews of Q fever have reported that infection was more common in younger men and that dry cough and high fever were common[127] [**III**], [128] [**III**]. Epidemiological features are discussed in section 3.

Klebsiella pneumoniae
The clinical features of bacteraemic pneumonia due to *S pneumoniae* and *K pneumoniae* have been compared[129] [**III**]. In the latter group men were more commonly affected and presented with a lower platelet count and leucopenia. Alcoholics were at particular risk of bacteraemic and fatal *Klebsiella* pneumonia.

Some rarer community respiratory pathogens
Community acquired acinetobacter pneumonia is seen more often in older patients with a history of alcoholism and has a high rate of mortality[130] [**III**]. CAP due to *Streptococcus milleri* may indicate a dental or abdominal source of infection[131] [**III**], while CAP caused by viridans streptococci is associated with aspiration[132] [**III**].

4.4 CAP in the elderly: are risk factors and clinical features different?
The classic symptoms and signs of pneumonia are less likely in the elderly while non-specific features, especially confusion, are more likely[112] [**II**], [115] [**II**], [133] [**II**]. Comorbid illness is more common in older patients with CAP and two studies have found absence of fever is more likely than in younger patients[113] [**II**], [134] [**II**].

Case controlled studies of pneumonia acquired in nursing homes have shown that both aspiration and comorbidity were more common in nursing home acquired pneumonia than in others with CAP[84] [**II**]. The inpatient mortality rate for nursing home acquired pneumonia was higher than for age matched non-nursing home acquired pneumonia patients[135] [**II**].

The relationship between the aetiology of CAP and the age of the patient is discussed in section 3.

Summary
- Elderly patients with CAP more frequently present with non-specific symptoms and have comorbid disease and a higher mortality rate, and are less likely to have a fever than younger patients [**II**].
- Aspiration is a risk factor for CAP in elderly patients, particularly nursing home residents [**II**].

5 Radiological, general and microbiological investigations

5.1 Are there characteristic features that enable the clinician to predict the likely pathogen from the chest radiograph?

In a comparative study of cases of legionella pneumonia, pneumococcal pneumonia, mycoplasma pneumonia and psittacosis no unique radiological pattern was found although some differences were reported[136] [**III**]. The lower lobes were affected most commonly, regardless of aetiology.

Homogenous shadowing was less common in mycoplasma pneumonia than in the other types. Multilobe involvement at presentation was more likely in bacteraemic pneumococcal pneumonia than in non-bacteraemic pneumococcal pneumonia or legionella pneumonia. Pleural effusions were more common in bacteraemic pneumococcal disease. Lymphadenopathy was noted in some cases of mycoplasma infections but not in the other types of infection.

The frequency of radiographic deterioration after hospital admission and the rates of resolution of radiographic shadowing differed according to the underlying aetiology (see below). In one study of 149 patients, pneumococcal infections were found to be associated with multilobe involvement more often than pneumonia caused by atypical pathogens[29] [**II**], a finding not reported in another comparative study[137] [**II**]. Other studies have found no difference between *C pneumoniae* and *S pneumoniae* pneumonia[138] [**II**], between *C pneumoniae* and a variety of other causes of CAP[123] [**II**], or between cases of Q fever pneumonia and those due to other pathogens[139] [**II**].

CAP caused by *S aureus* appears to be more likely to present with multilobar shadowing, cavitation, pneumatoceles, or spontaneous pneumothorax[140] [**III**].

K pneumoniae has been reported to produce chest radiograph changes with a predilection for upper lobes (especially the right), a bulging interlobar fissure, and abscess formation with cavitation. However, a prospective study of 15 proven cases of klebsiella pneumonia, mostly hospital acquired, found that although the right upper lobe was most likely to be involved, no case had a bulging interlobar fissure or cavitation[141] [**II**]. A bulging interlobar fissure is probably just a reflection of an intense inflammatory reaction that can occur in any severe infection such as pneumonia due to *S aureus*[140] [**III**].

There are few data on the role of high resolution CT lung scans in CAP. One study has reported a difference in CT appearances in 18 patients with CAP due to bacterial infections compared with 14 patients with atypical pathogens[142] [**III**]. A smaller study has reported that high resolution CT scans may improve the accuracy of diagnosing CAP compared with chest radiography alone[143] [**II**]. Similarly, CT lung scans have better sensitivity than standard chest radiographs in patients with mycoplasma pneumonia[144] [**II**]. CT lung scans may be useful in subjects where the diagnosis is in doubt[145] [**III**], but in general there seems little role for CT scanning in the usual investigation of CAP.

Summary

- There are no characteristic features of the chest radiograph in CAP that allow a confident prediction of the likely pathogen [**II**].

5.2 How quickly do chest radiographs improve after CAP?

Radiographic changes resolve relatively slowly after CAP, and lag behind clinical recovery. Complete resolution of chest radiographic changes occurred at 2 weeks after initial presentation in 51% of cases, by 4 weeks in 64%, and at 6 weeks in 73% in one study of CAP[146] [**II**]. Clearance rates were slower in the elderly, those with more than one lobe involved at presentation, in smokers, and inpatients rather than outpatients. Multivariate analysis showed that only age and multilobe involvement were independently related to the rate of clearance. Age was also a major factor influencing the rate of radiographic recovery in the BTS multicentre CAP study[14] [**Ib**]. When chest radiographs of patients with bacteraemic pneumococcal pneumonia were followed, only 13% had cleared at 2 weeks and 41% at 4 weeks[147] [**III**]. Pneumonias caused by atypical pathogens clear more quickly. The clearance rate has been reported to be faster for mycoplasma pneumonia than for legionella or pneumococcal pneumonia which may take 12 weeks or more[136] [**III**]. In a series of patients with *C burnetii* pneumonia, 81% of the chest radiographs had returned to normal within 4 weeks[127] [**III**].

Legionella pneumonia seemed to be particularly slow to resolve[136] [**III**]. In this study radiographic deterioration after admission to hospital was more common with legionella (65% of cases) and bacteraemic pneumococcal pneumonia (52%) than with non-bacteraemic pneumococcal (26%) or mycoplasma pneumonia (25%). Residual pulmonary shadowing was found in over 25% of cases of legionella and bacteraemic pneumococcal pneumonia. Deterioration after admission has also been reported in more than 50% of cases of *S aureus* pneumonia[140] [**III**]. Radiographic deterioration after hospital admission appears to be more common in older patients (aged 65 years or over)[134] [**II**].

Summary

- Radiological resolution often lags behind clinical improvement from CAP, particularly following legionella and bacteraemic pneumococcal infection [**III**].

- Pneumonia caused by atypical pathogens clears more quickly than pneumonia caused by bacterial infection [**III**].
- Radiological resolution is slower in the elderly and where there is multilobe involvement [**Ib**].

Recommendation

- **In a patient who is improving clinically and for whom there are no concerning clinical features, it will usually not be necessary to perform further investigations just because radiological improvement lags behind clinical recovery [B+].**

5.3 When should the chest radiograph be repeated during recovery and what action should be taken if the radiograph has not returned to normal?

Repeat chest radiographs are probably often ordered unnecessarily following CAP[148] [**IVa**]. Although it is usual practice to repeat the chest radiograph on discharge from hospital and again at "routine" hospital clinic follow up about 6 weeks later, there is no evidence on which to base a recommendation regarding the value of this practice in patients who have otherwise recovered satisfactorily. It is also not known whether there is any value in arranging clinical follow up in a hospital clinic rather than with the patient's general practitioner.

The main concern is whether the CAP was a complication of an underlying condition such as lung cancer. This concern will depend on a variety of factors such as age, smoking status, pre-existing conditions such as COPD, and the clinical condition of the patient. In a study of 236 adults presenting to their general practitioner with a clinical diagnosis of CAP, 10 were found to have underlying lung cancer on investigation. There was a high frequency of lung cancer in older smokers (six of 36 (17%) smokers aged over 60 years), suggesting that a chest radiograph is particularly indicated in this group of patients with CAP in the community[40] [**II**].

Studies of CAP in hospital often exclude patients found to have lung cancer, making it difficult to assess how frequently lung cancer presents acutely with CAP. In one study of 162 adults hospitalised with suspected CAP the diagnosis was accepted in only 127, 10 (6%) of whom were found to have cancer[11] [**II**]. Another study found only 13 (1.3%) of 1011 patients hospitalised with CAP to have an underlying lung cancer on investigation[149] [**III**]. Eight of these were detected on the admission chest radiograph and the others were detected because of unsatisfactory clinical recovery. They concluded that a convalescent radiograph was useful in detecting occult lung cancer only if signs or symptoms persisted after a month or so. The practice of performing a bronchoscopy before discharge from hospital on patients admitted with CAP has been investigated[150] [**III**]. In patients aged over 50 or those who were current or ex-smokers, 14%

were found to have an abnormality at bronchoscopy (bronchial carcinoma was diagnosed in 11%).

Recommendations

- **The chest radiograph need not be repeated before hospital discharge in those who have made a satisfactory clinical recovery from CAP [D].**
- **A chest radiograph should be arranged after about 6 weeks for all those patients who have persistent symptoms or physical signs or who are at higher risk of underlying malignancy (especially smokers and those over 50 years), whether or not they have been admitted to hospital [C].**
- **Further investigations which may include bronchoscopy should be considered in patients with persisting signs, symptoms, and radiological abnormalities at around 6 weeks after completing treatment [C].**
- **It is the responsibility of the hospital team to arrange the follow up plan with the patient and the general practitioner for those patients admitted to hospital [D] (see section 7.5).**

5.4 Why are non-microbiological investigations performed in CAP?

General investigations are performed to assess severity (see section 6), to assess the impact on or detect the presence of any co-morbid disease, to provide some pointer to the particular aetiological agent or group of pathogens, to identify complications, and to monitor progress (see section 9).

5.5 What general investigations should be done in a patient with suspected CAP in the community?

Recommendations

- **General investigations, including a chest radiograph, are not necessary for the majority of patients with CAP who are managed in the community [C].**
- **Out of hours and emergency general practitioner assessment centres should consider obtaining pulse oximeters to allow for simple assessment of oxygenation [D] (see section 7).**

5.6 What general tests should be done on all patients admitted to hospital?

It is normal practice to perform a routine biochemical and haematological profile on admission. A white cell count of $>15 \times 10^9$/l strongly suggests a bacterial (particularly pneumococcal) aetiology[151] [**III**], although lower counts do not exclude a bacterial cause. A white cell count of $>20 \times 10^9$/l or $<4 \times 10^9$/l is an indicator of severity (see section 6). Urea, electrolytes, and liver function tests are performed to assess severity (see section 6) and for the identification of underlying or associated renal or hepatic disease.

Sect. 5.6
Refer to 2004
update

There is some recent evidence that measurement of C reactive protein (CRP) may have a useful role in the management of hospitalised adult patients with CAP. Raised levels of CRP on admission are a relatively more sensitive marker of pneumonia than an increased temperature or raised white cell count[152] [**II**]. One study found that only 5% of patients admitted with CAP had CRP levels of <50 mg/l[153] [**III**], while another reported that all patients with CAP had levels above 50 mg/l and 75% of patients had levels above 100 mg/l[152] [**II**]. CRP levels are generally higher in patients who have not received antibiotics before admission[152] [**II**], [154] [**III**]. Higher CRP levels have been reported in patients with pneumococcal pneumonia (especially if complicated by bacteraemia) than in those with mycoplasma or viral pneumonias[154] [**III**]. One study has also reported that measurement of CRP can help to distinguish pneumonia from exacerbations of COPD using an arbitrary cut off of 100 mg/l[152] [**III**].

Serial measurements of CRP may be especially useful for monitoring the response of patients to treatment. One study found that the median time for a 50% reduction in the CRP level was 3.3 days[153] [**III**]. A CRP level that does not fall by 50% within 4 days suggests failure of treatment or the development of complications such as empyema or antibiotic associated diarrhoea.

Further prospective studies are required to define the role of CRP measurements in the management of patients with CAP. The specificity of CRP measurement in this patient population requires further evaluation as a number of other respiratory conditions— for example, neoplasia and pulmonary infarction—and other non-respiratory bacterial infections can cause an increase in levels of CRP.

Summary
- The published evidence to date suggests that measurement of CRP on admission may be helpful in distinguishing pneumonia from other acute respiratory illnesses and may also allow useful comparison with a repeat measurement in patients who subsequently fail to improve [**III**].

Recommendations
- **All patients should have the following tests performed on admission:**
  - **Chest radiograph [C].**
  - **Full blood count [B–].**
  - **Urea, electrolytes and liver function tests [C].**
  - **CRP when locally available [B–].**
  - **Oxygenation assessment. Oxygen saturation should be measured on admission. Those with Sao$_2$ <92% or with features of severe pneumonia should have an arterial blood gas measurement. It is essential to record the inspired oxygen concentration when measuring oxygen saturation and blood gases to allow correct interpretation of the results (see section 7.3) [C].**

5.7 Why are microbiological investigations performed in patients with CAP?

Establishing the microbial cause of CAP is useful for several reasons:

(1) Identification of pathogens and antibiotic sensitivity patterns permits selection of optimal antibiotic regimens.

(2) Targeted and narrow spectrum antibiotic therapy limits drug costs, the threat of antibiotic resistance, and adverse drug reactions such as *C difficile* associated diarrhoea.

(3) Specific pathogens have public health or infection control significance, including legionella, psittacosis, Q fever, influenza A, and penicillin resistant pneumococci. Patients with these infections should be identified quickly so that appropriate treatment and control measures can be implemented.

(4) Microbiological investigations allow monitoring of the spectrum of pathogens causing CAP over time. This allows trends regarding aetiology and antibiotic sensitivity to be tracked for public health needs.

Unfortunately, microbiological investigations are insensitive and often do not contribute to initial patient management[155] [**III**]. In detailed prospective aetiology studies the microbial cause is not found in 25–60% of patients[40] [**II**], [156] [**II**], and the yield is even lower in routine hospital practice[157] [**III**], [158] [**III**].

Recommendations
- **It is not necessary or appropriate to perform a full range of microbiological investigations on every patient with CAP. The investigations performed should be guided by the severity of pneumonia, epidemiological risk factors, and the response to treatment [D].**

5.8 Which microbiological investigations should be performed in patients with suspected CAP in the community?

Comments about the pros and cons of different microbiological investigations are given below in section 5.9. Many of these investigations will not be appropriate for patients with CAP managed in the community. Such patients are not usually severely ill, are at low risk of death, and delays in transport of specimens to the laboratory reduce the yield of bacterial pathogens especially *S pneumoniae* from sputum cultures. The results are often received too late by the general practitioner to be of much practical value in initial management.

Recommendations
- **For patients managed in the community, microbiological investigations are not recommended routinely [D].**
- **Examination of sputum should be considered for patients who do not respond to empirical antibiotic treatment [D].**
- **Examination of sputum for *Mycobacterium tuberculosis* should be considered for patients with a persistent productive cough, especially if malaise, weight loss,**

Table 7 Recommendations for the microbiological investigation of patients admitted to hospital with community acquired pneumonia (CAP)

Routine investigations in hospital for all patients with non-severe CAP	Routine investigations in hospital for all patients with severe CAP
• Blood cultures (minimum 20 ml) • Sputum for routine culture and sensitivity tests for those who have *not* received prior antibiotics (± Gram stain*) • Clotted (acute) serum sample for store‡ • Pleural fluid, if present, for microscopy, culture and sensitivity	• Blood cultures (minimum 20 ml) • Sputum or other respiratory sample† for Gram stain, routine culture and sensitivity tests • Pleural fluid, if present, for microscopy, culture and sensitivity • Pneumococcal antigen tests (if available): urine, sputum or blood
For selected patients only • Investigations for legionella pneumonia:§ (a) urine for legionella antigen; (b) sputum or other respiratory sample for legionella culture and direct immunofluorescence (if available); (c) initial and follow up legionella serology • Follow up viral and atypical pathogen serology (to be run in parallel with initial serum sample)¶	• Investigations for legionella pneumonia: (a) urine for legionella antigen; (b) sputum or other respiratory sample for legionella culture and direct immunofluorescence (if available); (c) initial and follow up legionella serology • Investigations for atypical and viral pathogens: (a) if available, sputum or other respiratory sample for direct immunofluorescence (or other antigen detection test) to *Chlamydia* spp, influenza A & B, parainfluenza 1–3, adenovirus, respiratory syncytial virus, *Pneumocystis carinii* (if at risk); (b) initial and follow up viral and "atypical pathogen" serology

*The routine use of sputum Gram stain is discussed in the text.
†Consider obtaining lower respiratory tract samples by more invasive techniques such as bronchoscopy (usually after intubation) or percutanous fine needle aspiration for those who are skilled in this technique.
‡The date of onset should be clearly indicated on the laboratory request form.
§Patients with clinical or epidemiological risk factors (travel, occupation, co-morbid disease). Investigations should be considered for all patients with CAP during outbreaks.
¶For patients unresponsive to β-lactam antibiotics or those with a strong suspicion of an "atypical" pathogen on clinical, radiographic, or epidemiological grounds.

> **Sect. 5.8-9: Microbiological investigations.**
> See changes to this section in the 2004 update.

night sweats or risk factors for tuberculosis (e.g. ethnic origin, social deprivation, the elderly) are present [D]. Serological investigations may be considered during outbreaks (e.g. Legionnaires' disease) or epidemic mycoplasma years, or when there is a particular clinical or epidemiological reason [D].

5.9 What microbiological investigations should be performed in patients admitted to hospital with CAP?

The investigations that are recommended for patients admitted to hospital are summarised in table 7. More extensive microbiological investigations are recommended only for patients with severe CAP unless there are particular clinical or epidemiological features that warrant further microbiological studies. Comments and recommendations regarding specific investigations are given below.

BLOOD CULTURES
Microbial causes of CAP that can be associated with bacteraemia include *S pneumoniae*, *H influenzae*, *S aureus*, and *K pneumoniae*. Isolation of these bacteria from blood cultures in patients with CAP is highly specific in determining the microbial aetiology. Bacteraemia is also a marker of illness severity. However, many patients with CAP do not have an associated bacteraemia. Even in pneumococcal pneumonia the sensitivity of blood cultures is at most only 25%[47] [**II**], [103] [**II**], and is even lower for patients given antibiotic treatment before admission[14] [**II**].

Recommendation
- **Blood culture is recommended for all patients admitted with CAP, preferably before antibiotic treatment is commenced [D].**

SPUTUM CULTURES
Sputum cultures may identify the causative agent in CAP including unexpected or antibiotic resistant pathogens such as *S aureus* or penicillin resistant pneumococci. Routine sputum cultures are, however, neither very sensitive nor specific[2] [**Ia**], and often do not contribute to initial patient management[159] [**II**].

Problems include:
(1) The inability of patients to produce good specimens.
(2) Prior exposure to antibiotics.
(3) Delays in transport and processing.
(4) Difficulty in interpretation due to contamination of the sample by upper respiratory tract flora which may include potential pathogens such as *S pneumoniae* and coliforms (especially in patients already given antibiotics).

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

SPUTUM GRAM STAIN
The value of performing a Gram stain on expectorated sputum has been widely debated. A meta-analytical review concluded that the sensitivity and specificity of Gram stains of sputum in patients with CAP varied substantially in different settings[160] [**Ia**]. The presence of large numbers of Gram positive diplococci in purulent samples from patients with CAP can indicate pneumococcal pneumonia[161] [**II**]. There are many factors that determine the reliability and usefulness of Gram stain results, which are summarised below.

Advantages
- Quick and inexpensive.
- Can assess quality of samples (cytological content) with rejection of poor quality samples.
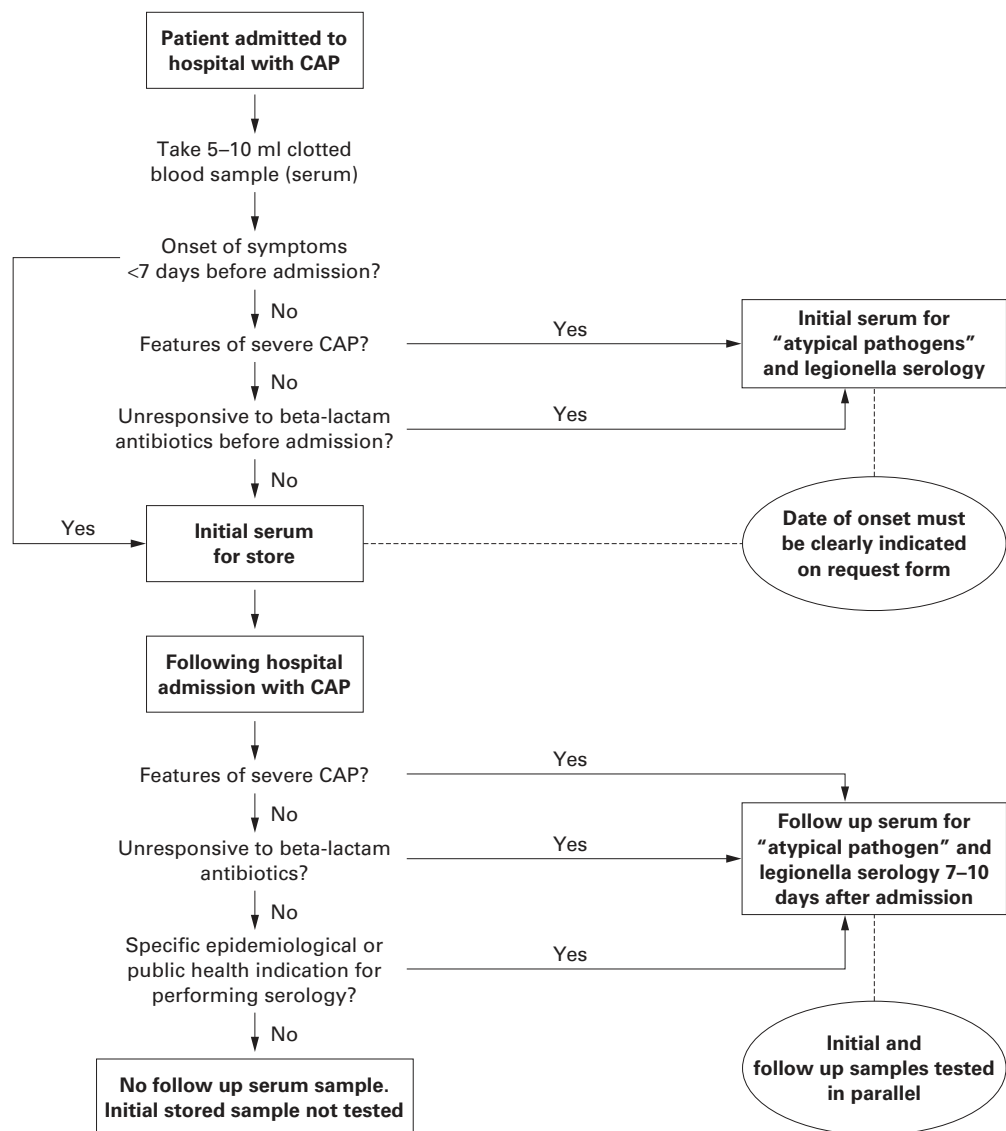
Figure 6   Suggested algorithm for serological testing in patients with CAP.

- Can aid the interpretation of culture results and occasionally give an early indication of possible aetiology.

Disadvantages
- Strict criteria for interpretation require appropriate operator training.
- Validity of results is directly related to the experience of the interpreter[162] [**II**].
- Sputum Gram stain correlates poorly with culture results in conditions other than CAP[163] [**II**]. This poses practical difficulties for laboratories that frequently have to interpret results with little or no clinical information.

Recommendations
- **Laboratories should be able to offer a reliable Gram stain for patients with severe CAP or complications as, on occasions, this can give an immediate indicator of the likely pathogen. Routine performance or reporting of sputum**

Gram stain on all patients is unnecessary but can aid the laboratory interpretations of culture results [**D**].
- **Laboratories performing sputum Gram stains should adhere to strict and locally agreed criteria for interpretation and reporting of results [B+].**

SEROLOGY FOR RESPIRATORY PATHOGENS
Respiratory serological tests usually comprise antibody tests for the atypical pathogens (*M pneumoniae*, *Chlamydia* spp, *C burnetii*), influenza A virus, influenza B virus, adenovirus, respiratory syncytial virus, and *L pneumophila*. Many laboratories still rely on complement fixation tests (CFTs) which are time consuming and inconvenient to perform and have poor sensitivity and specificity. Other tests are becoming increasingly available, but for some of the "atypical" pathogens there are no alternative assays.

There is little value in testing single serum samples taken within 7 days of the onset of

CAP. Such samples can be stored until the follow up (convalescent) sample is taken 7–10 days later and the paired samples can be tested in parallel.

However, raised antibody titres, particularly to *L pneumophila* or *M pneumoniae*, may be found in some patients on or soon after admission to hospital, particularly if the onset of symptoms is more than 7 days before admission. It is thus important that the date of onset of symptoms is clearly indicated on serological request forms so that serum samples taken more than 1 week into the illness can be tested immediately.

A suggested algorithm for performing serological investigations is shown in fig 6.

Recommendations
- **Paired serological tests should be performed for all patients with severe CAP, those who are unresponsive to β-lactam antibiotics, and for selected patients with particular epidemiological risk factors or in whom a specific microbiological diagnosis is important for public health measures [D].**
- **Serological tests should be extended to all patients admitted to hospital with CAP during outbreaks and when needed for the purposes of surveillance. The criteria for performing serological tests in these circumstances should be agreed locally between clinicians, laboratories, and public health officers [D].**

NON-CULTURAL TESTS FOR *S PNEUMONIAE*
Pneumococcal antigen detection
Pneumococcal antigens can be detected in various body fluids during active pneumococcal infection including sputum, pleural fluid, serum, and urine. Antigen detection is less affected by prior antibiotic treatment and the detection of antigenaemia is correlated with clinical severity[164] [**IVb**].

Various techniques have been used to detect pneumococcal polysaccharide antigens or C-polysaccharide[165] [**IVb**]. Counterimmunoelectrophoresis is the least sensitive technique but has been studied the most. Latex agglutination has improved sensitivity but produces poor results with urine samples. Enzyme immunoassays (EIAs) are promising in terms of improved sensitivity and specificity but have not been rigorously evaluated, and a commercial immunochromatographic test for detection of antigen in urine has recently been introduced.

The detection of pneumococcal antigen in serum or urine is reasonably specific but less sensitive. Higher sensitivity is found with sputum, but specificity is compromised by cross reactions with "viridans" streptococci and false positive results due to oropharyngeal carriage of *S pneumoniae*.

Pneumococcal antigen detection has not been widely adopted in the UK due to cost, lack of sensitivity, and lack of "robustness" in a routine diagnostic setting[165] [**IVb**]. However, the development of a well validated technique

with good sensitivity and specificity for detection of pneumococcal antigen in urine would complement the now established legionella urine antigen test (see below) for patients with severe CAP, and further work in this area is awaited.

Pneumococcal serology
The detection of antibodies to the pneumococcal toxin pneumolysin has been reported to be both sensitive (80–90%) and specific in the diagnosis of pneumococcal infection[166] [**II**]. The antibody response is usually delayed and, to date, this technique has been reserved for epidemiological studies.

Pneumococcal polymerase chain reaction
Polymerase chain reaction (PCR) based methods for detection of pneumococcal DNA in clinical samples are still under development for routine diagnosis.

Recommendations
- **There is currently insufficient evidence to recommend widespread use of pneumococcal antigen tests or serological tests in CAP [D].**
- **Antigen tests should be used for patients with severe CAP, if available locally [D].**

TESTS FOR LEGIONNAIRES' DISEASE
Legionella pneumonia can be severe and carries a significant mortality. Prompt diagnosis is important both for patient management and for public health investigations. Risk factors for legionella infection include recent travel (within 10 days of onset), certain occupations, recent repair to domestic plumbing systems, and immunosuppression.

Urine antigen detection
Detection of *L pneumophila* urinary antigen by EIA is now established as a highly specific (>95%) and sensitive (~80%) test[167] [**III**]. Rapid results can be obtained at an early stage of the illness, and this is a valuable method for the early diagnosis of legionella infection[99] [**III**].

Several commercial assays are available including a rapid immunochromatographic test. These assays principally detect infection with *L pneumophila* serogroup 1 and do not detect antigen from other *Legionella* species.

Legionella direct immunofluorescence (DIF) tests
L pneumophila can be detected by DIF on invasive respiratory samples such as bronchial aspirates. *L pneumophila* specific reagents should be used and not hyperimmune rabbit antisera which are poorly specific. The value of performing DIF on expectorated sputum samples is less well established.

Culture
Every effort should be made to diagnose by culture of *Legionella* species from clinical samples (principally respiratory samples). Culture is 100% specific and is the only method of detecting infection with *Legionella* species other

than *L pneumophila*. Culture is also valuable for epidemiological investigations, allowing phenotypic and genotypic comparison of clinical and environmental legionella strains.

Problems with culture include the inability of many patients with legionella pneumonia to produce sputum samples; prior antibiotic treatment; laboratory time and cost in processing samples; and lack of rapid results (cultures need to be incubated for up to 10 days). Many laboratories do not set up legionella cultures on respiratory samples unless specifically requested to do so.

Serology
The diagnosis by determination of antibody levels is well established and has been the mainstay of diagnosis in the past. Serological assays previously employed in the UK were highly specific, although false positive results due to a serological cross reaction may occur in patients with recent campylobacter infection[168] [**II**]. Serological reagents for diagnosis of legionella infection are no longer available from the Public Health Laboratory Service, compromising the use of this diagnostic method in the UK, although commercial assays are currently under evaluation.

PCR
Detection of legionella DNA by PCR from respiratory samples, blood, and urine is still only available as a research tool.

Recommendations
- **Investigations for legionella pneumonia are recommended for all patients with severe CAP, for other patients with specific risk factors, and for all patients with CAP during outbreaks [D].**
- **Rapid testing and reporting for legionella urine antigen should be available in at least one laboratory per region [D].**
- **Legionella culture should be specifically requested by clinicians on laboratory request forms from patients with severe CAP, or where Legionnaires' disease is suspected on epidemiological grounds.**
- **Legionella cultures should be routinely performed on invasive respiratory samples (e.g. obtained by bronchoscopy) from patients with CAP [D].**

TESTS FOR *M PNEUMONIAE*
The mainstay of diagnosis at the present time is by serological testing. Culture of *M pneumoniae* is generally not available in diagnostic laboratories.

The most common serological assay used is the CFT but various alternative assays such as microparticle agglutination and EIAs are also available. The CFT is still regarded as the "gold standard" to which other assays have been compared, although it does lack some sensitivity and specificity. A comparison of various mycoplasma antibody assays (including IgM and CFTs) concluded that no single assay has significantly better sensitivity and specificity than the others[169] [**III**].

Raised CFT titres are usually detected no earlier than 10–14 days after the onset of mycoplasma infection, but the insidious onset and slow progression of symptoms means that many patients admitted to hospital with mycoplasma CAP have raised titres on or shortly after admission.

Genomic detection of *M pneumoniae* in respiratory specimens by amplification techniques such as PCR is currently under development.

Recommendation
- **Serological assay with CFTs is widely available and should remain the mainstay of diagnosis [C].**

TESTS FOR *CHLAMYDIA* SPECIES
Culture
It is not appropriate for routine diagnostic laboratories to attempt culture of *Chlamydia* species from respiratory samples from patients with CAP as special laboratory precautions are required. *C psittaci* is a "category 3 pathogen" indicating a high risk pathogen that may put laboratory staff at risk of serious illness if infected occupationally. *C pneumoniae* is very difficult to grow in the laboratory; culture is slow, time consuming, expensive, and insensitive.

Antigen detection
Chlamydial antigen can be detected in respiratory samples using direct immunofluorescence (DIF) with species and genus specific monoclonal antibodies[170] [**II**]. Genus specific reagents are not available for *C psittaci* which is antigenically highly diverse. DIF requires expertise in slide preparation and reading and is not available in all diagnostic laboratories. *C pneumoniae* can also be detected by DIF on throat swabs with a comparable sensitivity to sputum.[171] However, antigen may be detected for several months after "acute" infection, making interpretation difficult.

Chlamydial antigen can also be detected in respiratory samples by EIA with a comparable sensitivity to PCR,[172] but this approach requires further study.

Serology
Various serological assays are used in the diagnosis of respiratory chlamydial infections. The CFT is available in most diagnostic serology laboratories. Microimmunofluorescence (MIF) and whole cell immunofluorescence (WHIF) are specialised reference tests. Several EIAs have been described and at least one is commercially available in the UK. Each of these assays has advantages and disadvantages, and there are particular problems in the serological diagnosis of *C pneumoniae* infections.

The CFT uses a genus specific antigen and is relatively sensitive and specific for diagnosing psittacosis. However, in adults, most infections with *C pneumoniae* are re-infections and these generate only a weak or absent CFT response. The MIF and WHIF tests require considerable experience to read and interpret. They can

detect a species specific response, although this may be delayed for 4–6 weeks, especially with *C pneumoniae* re-infections. They may also miss *C psittaci* infections, depending on the particular serovars included in the test, and there are conflicting reports regarding the accuracy of these tests in reliably distinguishing chlamydial species[173] [**IVb**].

A commercial EIA has been used with success[174] [**III**] but has not been shown to be significantly superior to the CFT.

Molecular techniques
Amplification of chlamydial DNA by PCR using genus or species specific primers has been reported from a variety of respiratory samples, but these molecular techniques are still confined to research/reference laboratories at the present time.

Recommendations
- **Chlamydial antigen detection tests should be available for invasive respiratory samples from patients with severe CAP or where there is a strong suspicion of psittacosis [D].**
- **The CFT remains the most suitable and practical serological assay for routine diagnosis of respiratory chlamydial infections [B–]. There is no currently available serological test that can reliably detect infections due to *C pneumoniae*.**

6   Severity assessment

6.1 Why is severity assessment important?

CAP presents to physicians both in primary and secondary care as a wide spectrum of illness from mild and self-limiting to a life threatening and occasionally fatal disease. This breadth of illness severity is reflected in the variable mortality rates reported by studies of CAP in different clinical settings.

The decision regarding the most appropriate site of care, including whether admission to hospital is warranted, is the first and single most important decision in the overall management of CAP. It has consequences both for the level of treatment received by the patient as well as the overall costs of treatment[63] [**III**]. This decision is best informed by an accurate assessment of the severity of illness at presentation and the likely prognosis. Recognition of patients at low risk of complications and therefore suitable for outpatient treatment has the potential for reducing inappropriate hospitalisation and consequent inherent morbidity and costs.

When hospital admission is required, further management is also influenced by illness severity. This includes the extent of microbiological investigation, the choice of initial empirical antimicrobial agents, route of administration, duration of treatment, and level of nursing and medical care. Early identification of patients at high risk of death allows initiation of appropriate antibiotic treatment and admission to an ICU where assisted ventilation can be readily initiated if necessary.

6.2 What clinical factors and investigations are associated with a poor prognosis on univariate and multivariate analysis?

A large number of studies conducted in hospital and ICUs have employed univariate analysis to identify risk factors associated with a poor prognosis. In hospital mortality has been the most common outcome measure. Some studies have used admission to the ICU as the main outcome measure[175] [**Ib**]. However, differences in ICU admission criteria make it difficult to compare results from these studies. This is reflected in the widely varying rates of admission of patients with CAP to ICU, ranging from 1–3% in New Zealand, 5% in the UK, 12–18% in the USA, to 35% in Germany[14] [**Ib**], [43] [**Ib**], [71] [**Ib**], [176] [**II**], [177] [**III**], [178] [**III**]. In these guidelines we have concentrated only on studies that have used mortality as the main outcome measure.

Univariate studies have suggested that over 40 different parameters are associated with mortality. However, an independent association of only a few of these risk factors with mortality have been demonstrated by studies employing multivariate analysis.

AGE

Age has consistently been shown to be significantly associated with mortality in studies from a variety of countries[14] [**Ib**], [43] [**Ib**], [71] [**Ib**], [179] [**Ia**], [180] [**Ib**], [181] [**Ib**], [182] [**III**]. However, recent studies of CAP in the elderly (>65 years) have suggested that, within this population, age by itself is not of prognostic importance[183] [**Ib**], [184] [**Ib**], [185] [**II**]. Importantly, the *lack* of pyrexia, which is easily overlooked in clinical practice, has been identified by some as an important prognostic factor[13] [**II**], [184] [**Ib**]. Being previously bedridden and having been admitted from a nursing home are other poor prognostic factors that may be interrelated and warrant attention[43] [**Ib**], [135] [**II**], [184] [**Ib**]. Admission criteria to nursing homes may differ in the UK from the countries where these studies were conducted, so validation of these findings is desirable.

Based on current evidence, there is no firm reason to support the use of a different set of clinical features in assessing disease severity in this group of patients.

PRESENCE OF COEXISTING ILLNESSES

Concomitant congestive cardiac failure[181] [**Ib**], [186] [**III**], coronary artery disease[186][**III**], stroke[43] [**Ib**], [179] [**III**], [186] [**III**], diabetes mellitus[179] [**Ia**], [187] [**II**], chronic lung disease[11] [**II**], [187] [**II**], cancer[43] [**Ib**] and other coexisting illnesses have been shown to predict death in patients with CAP[180] [**Ib**], [188] [**III**], [189] [**III**]. However, the magnitude of the contribution of these coexisting illnesses to disease severity is difficult to ascertain due to variations in disease definition and problems in determining the severity of these conditions themselves. This may partly explain the low predictive power of the presence of coexisting illnesses as a risk factor for death on multivariate analysis, despite the large number of studies that have demonstrated significance on univariate analysis.

RESPIRATORY RATE

A raised respiratory rate has emerged as one of the most reliable indicators of disease severity in both univariate and multivariate analysis across all age groups[14] [**Ib**], [43] [**Ib**], [71] [**Ib**], [177] [**III**], [179] [**Ia**], [184] [**Ib**], [189] [**Ib**], [190] [**Ib**]. Although a linear correlation of respiratory rate with mortality has been reported[191] [**III**], in clinical practice a respiratory rate of 30 breaths/min or more is accepted as indicating severe disease[14] [**Ib**], [71] [**Ib**], [189] [**Ib**]. Increased awareness and better documentation of this valuable clinical sign is strongly recommended.

MENTAL STATUS

An altered mental state has been identified as an independent risk factor for mortality in at least two large studies[14] [**Ib**], [180] [**III**]. It also appears to be useful in the elderly, although differences in definition make integration of results difficult[182] [**III**], [184] [**Ib**]. The more

widespread use of the Abbreviated Mental Test score[192] **[II]** (summarised in box 2) as a measure of acute confusion will help future validation of the importance of this clinical sign as part of a severity prediction rule[71] **[Ib]**.

The Abbreviated Mental Test (each question scores 1 mark, total 10 marks)
- Age
- Date of birth
- Time (to nearest hour)
- Year
- Hospital name
- Recognition of two persons (e.g. doctor, nurse)
- Recall address (e.g. 42 West Street)
- Date of First World War
- Name of monarch
- Count backwards 20 → 1

Box 2 Summary of questions asked of a patient to assess the degree of mental confusion as part of the severity assessment. A score of 8 or less has been used to define mental confusion in the modified BTS severity rule.

BLOOD PRESSURE

A low systolic (<90 mm Hg) or diastolic (≤60 mm Hg) blood pressure or the presence of septic shock on admission to hospital are recognised poor prognostic factors[13] **[II]**, [14] **[Ib]**, [71] **[Ib]**, [114] **[III]**, [179] **[Ia]**, [182] **[III]**, [184] **[Ib]**, [187] **[II]**, [189] **[III]**, [193] **[II]**. In the intensive care setting septic shock, defined as (a) a sustained decrease (for at least 1 hour) in systolic blood pressure of at least 40 mm Hg from baseline or (b) a resultant systolic blood pressure of <90 mm Hg after adequate volume replacement in the absence of antihypertensive drugs occurring more than 12 hours after admission to the ICU is an additional adverse sign[74] **[II]**, [185] **[II]**.

OXYGENATION

Hypoxaemia is an important adverse finding across all ages and the need to apply positive end expiratory pressure (PEEP) or an inspired oxygen concentration of over 60% to maintain adequate oxygenation are both poor prognostic indicators[67] **[II]**, [71] **[Ib]**. Respiratory failure and the need for mechanical ventilation, whether upon admission to the ICU or subsequently, is a predictor of mortality in itself[43] **[Ib]**, [67] **[II]**, [74] **[Ib]**, [75] **[II]**.

WHITE CELL COUNT

Both leucopenia (white cell count <4 × 10^9) and leucocytosis (>20 × 10^9) on admission have been associated with mortality on univariate analysis[177] **[III]**, [182] **[III]**, [188] **[III]**, [194] **[III]**. Results from multivariate analyses have been variable and suggest that leucopenia may be the more important variable[14] **[Ib]**, [179] **[Ia]**.

RADIOGRAPHIC CHANGES

Bilateral involvement or the involvement of more than two lobes on the chest radiograph are poor prognostic factors[43] **[Ib]**, [74] **[III, Ib]**, [179] **[Ia]**, [184] **[Ib]**, [188] **[III]**, [193] **[II]**. The presence of bilateral parapneumonic effusions has also been associated with an increased risk of death in one large study[195] **[Ib]**.

In patients admitted to an ICU, progression of chest radiographic changes is associated with mortality[67] **[II]**. However, outside an ICU repeated radiological investigations are not routinely recommended as a means of severity assessment unless otherwise indicated.

MICROBIOLOGY

A positive blood culture, regardless of the pathogen isolated, is associated with a poor outcome[43] **[Ib]**, [67] **[II]**, [74] **[Ib]**, [75] **[II]**, [179] **[Ia]**, [188] **[III]**, [194] **[III]**. In bacteraemic patients, pathogens particularly associated with severe disease include *S pneumoniae*, Gram negative enteric bacilli, *S aureus*, and *P aeruginosa*[11] **[II]**, [43] **[Ib]**, [67] **[II]**, [75] **[II]**. Although *Legionella* species have not been shown to be specifically associated with increased mortality in studies employing multivariate analysis of risk factors, it is the second most common pathogen isolated in patients with CAP admitted to ICUs in the UK (see section 6). It should therefore always be considered in patients with severe pneumonia. However, as clinical features at presentation are generally unhelpful in accurately differentiating between causative pathogens in CAP, patients should be managed according to other more readily available predictors of severity in the first instance.

6.3 What predictive models for assessing severity on or shortly after hospital admission have been tested?

Clinical assessment of disease severity is dependent on the experience of the attending clinician, but such clinical judgement has been shown to result in apparent underestimation of severity[71] **[Ib]**. No single prognostic factor of mortality is adequately specific and sensitive. Various severity scoring systems and predictive models have therefore been developed in an attempt to help the clinician identify patients with pneumonia and a poor prognosis at an early stage.

None of the predictive models developed thus far allow the unequivocal categorisation of patients into definite risk groups and it is unrealistic to expect this[196] **[IVb]**. Until recently, the few studies that have examined the impact of severity based practice guidelines on clinical outcomes have not demonstrated significant beneficial effects[22] **[III]**, [54] **[II]**, [197] **[II]**. However, new data are emerging to suggest that such practice guidelines may be useful in identifying patients with CAP who are suitable for ambulatory outpatient care and who therefore do not require hospital admission[198] **[II]**. A study of a clinical practice guideline embracing a strict antibiotic policy together with criteria for hospital admission and for regular review and the switch from intravenous to oral antibiotics resulted in reductions in hospital admission, use of intravenous antibiotics, and length of hospital stay[199] **[Ib]**. These encouraging results are preliminary and will need confirmation in a wider setting such as the UK.

Sect. 6.3 Refer to 2004 update for changes in this section.

CONCLUSIONS REGARDING PREDICTIVE MODELS
- None of the available predictive models allows the unequivocal categorisation of patients into definite risk groups.
- Predictive models based on severity are best viewed as useful adjuncts to clinical assessment.
- Regular reassessment of severity during the course of hospital stay is mandatory if treatment is to be adjusted appropriately, avoiding the morbidity of overtreatment as well as the complications of undertreatment.

FURTHER DETAILS OF TWO PREDICTIVE MODELS

Predictive models have been developed to address two main areas in the management of CAP.

Approach A: Predicting patients at low risk of death

Based on work carried out in the USA, a Pneumonia Severity Index (PSI) for stratifying patients into five risk classes according to the risk of mortality has been published[189] [**Ib**]. Patients identified as being in risk class I are at low risk of death and adverse outcomes, with a mortality risk of 0.1–0.4%. In an observational study of those patients in risk class I judged to be suitable for outpatient treatment, the rate of subsequent hospitalisation within 30 days was 5.5%[65] [**II**].

This index relies on the identification of two "pre-existing" patient features (age over 50 years and the presence of certain coexisting chronic illnesses) and five adverse clinical features (mental state, respiratory rate, systolic blood pressure, pulse rate, and temperature—with twice as much risk weighting being placed on the first three features) for the categorisation of patients into risk class I. Its use in the primary care setting to identify patients at low risk of death is therefore feasible although at present there are no UK validation studies. The omission of chronic lung disease (CLD) as an adverse chronic illness in the PSI is notable and is based on the absence of an independent association of chronic lung disease with mortality in the studies from which this rule was derived. This may be because the contribution of underlying chronic lung disease to clinical outcome is partly accounted for by measures of respiratory rate and oxygenation status. In a clinical intervention trial conducted in Canada in which about 30% of patients had chronic lung disease, no harm was demonstrated from using the PSI to stratify patients into groups suitable for home or hospital management[199] [**Ib**].

Approach B: Predicting patients at high risk of death

In 1987 the BTS derived a rule for predicting mortality based on three easily measured clinical parameters[14] [**Ib**]. Patients were found to have a 21-fold increased risk of death if they had two or more of the following "core" adverse prognostic features: (a) admission respiratory rate ≥30/min, (b) admission diastolic blood pressure ≤60 mm Hg, and (c) blood urea >7 mmol/l during admission. The sensitivity of the rule is 88%, specificity 79%, false negative rate 12%, false positive rate 21%, positive predictive value (PPV) 19%, and negative predictive value (NPV) 99%.

This rule has been validated by groups in the USA and New Zealand and appears to remain useful when all three parameters are measured at the time of admission. From these studies the BTS rule has an overall sensitivity and specificity of approximately 80%[71] [**Ib**], [177] [**III**]. However, there are some recent data to suggest that the BTS rule is less sensitive at predicting mortality in older patients (65 years and above)[182] [**III**].

A modification of this rule to add mental confusion on hospital admission as a fourth "core" adverse prognostic feature was first evaluated in 1991[70] [**II**]. Since then, incorporation of confusion measured as a score of 8 or less on a 10 point Abbreviated Mental Test Score (box 2)[192] [**II**] has been shown to increase the sensitivity of the rule at the expense of specificity[69] [**II**], [71] [**Ib**]. This modified BTS rule has recently been prospectively validated in the UK in adults of all ages[69] [**Ib**]. Combining results from the derivation and validation studies yields a sensitivity of 83%, specificity 70%, negative predictive value 97%, and positive predictive value 26%. The number of "core" adverse prognostic features present correlated well with mortality, with a mortality of 2.4% in the presence of no "core" features, 8% with one "core" feature, 23% with two, 33% with three, and 83% with all four "core" features present[69] [**Ib**]. It has been proposed that these four "core" adverse prognostic features could be remembered as the **CURB** severity score (**C**onfusion, **U**rea, **R**espiratory rate, **B**lood pressure)[69] [**Ib**].

The use of the APACHE II scoring system as well as other specialised ICU scoring systems for organ system failure in CAP has been described to predict outcome[74] [**IIb**], [154] [**Ib**], [185] [**IIb**]. However, general use of these scoring systems outside the intensive care setting is difficult, time consuming, and likely to be impractical.

6.4 What severity assessment strategy do we recommend for CAP?

We have been keen to recommend one severity assessment strategy that is simple to remember and practical to implement both in the community and in hospital and that is adapted from the results of studies previously discussed.

This strategy places patients into three groups including those with:

(a) low risk of death (0.1–0.4%): they may be suitable for either treatment at home, as an outpatient or for early discharge from the medical assessment unit or medical ward;

(b) high risk of death (22–30%): they should be managed using the recommendations for severe pneumonia;

(c) some increased risk compared with the low risk group because they demonstrate some individual adverse prognostic features independently associated with death, but for which a risk ratio cannot be calculated from a compilation of the data in the available literature. Clinical
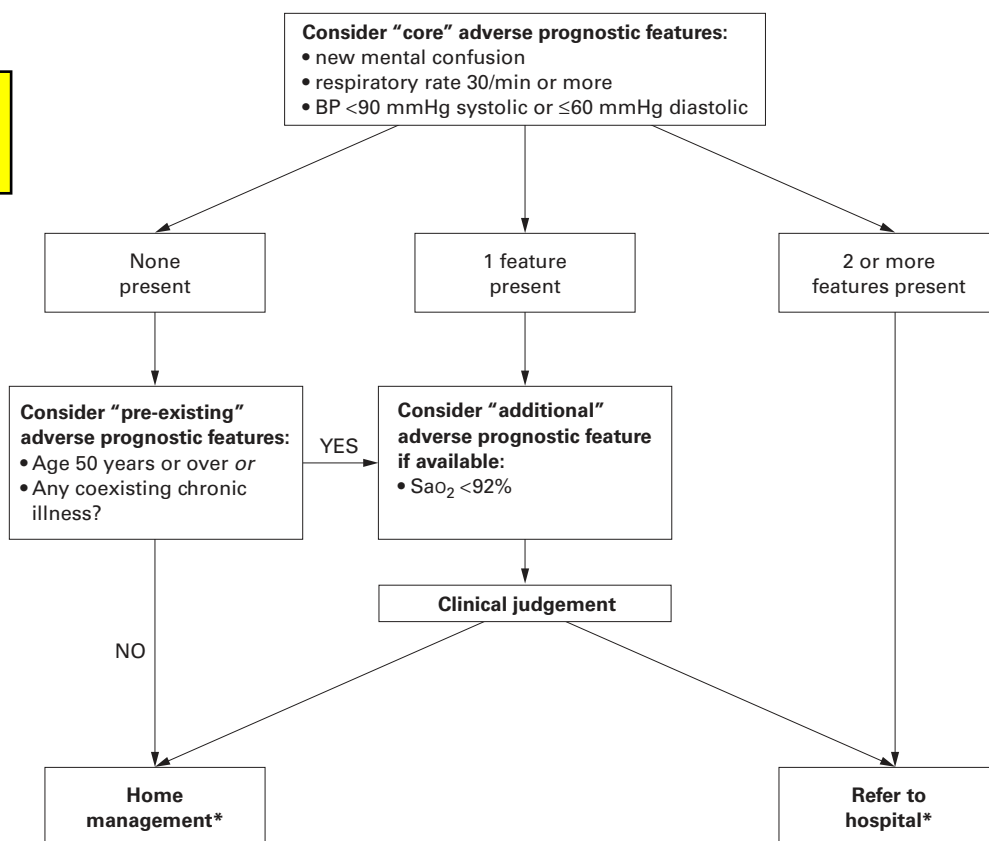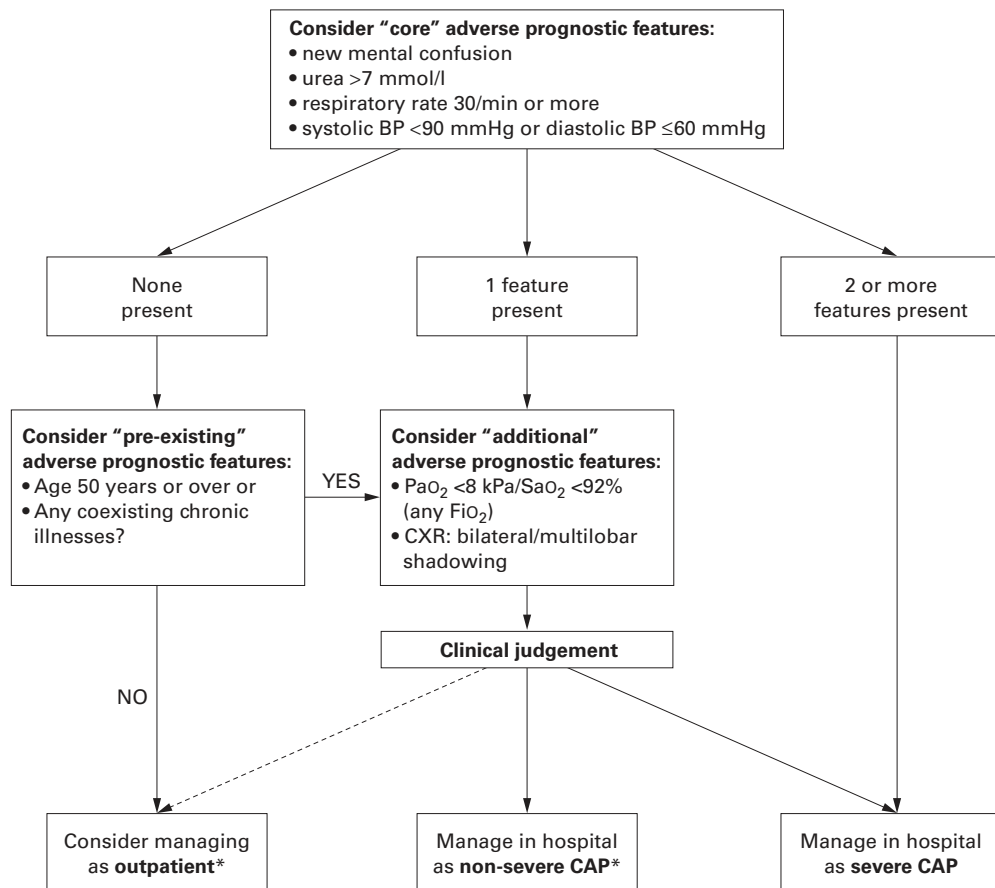
Figure 7   Severity assessment used to determine the management of CAP in patients in the community.
*The social circumstances and wishes of the patient should also be considered.

judgement is essential when deciding on the management of all patients with CAP, and will be particularly important for this group.

We emphasise the importance of assessing and recording the presence of "core" adverse prognostic features for all patients, whether in the community or in hospital, the presence of any of which has been associated with an increased risk of death in studies. Patients who have two or more "core" adverse prognostic features and who therefore fulfil the modified BTS severity prediction rule are at high risk of death. Where the risk assessment using the modified BTS severity prediction rule is unclear, clinical judgement can also be helped by assessing "additional" adverse prognostic features that have been independently associated with outcome. Three of the "core" adverse prognostic features are derived from simple clinical observations and therefore will be readily available to doctors when assessing patients in the community. Age less than 50 years and the absence of coexisting disease are also useful "pre-existing" features for identifying those with a very good prognosis who may be suitable for home treatment.

We also recommend how and when to review severity status after initial assessment.

SUMMARY OF THE FOUR "CORE" ADVERSE PROGNOSTIC FEATURES (**CURB** SCORE)[69]
These should be assessed for all patients:
- **C**onfusion: new mental confusion defined as an Abbreviated Mental Test score of 8 or less [**Ib**]
- **U**rea: raised >7 mmol/l (for patients being seen in hospital) [**Ib**]
- **R**espiratory rate: raised $\geqslant$30/min [**Ib**]
- **B**lood pressure: low blood pressure (systolic <90 mm Hg *and/or* diastolic $\leqslant$60 mm Hg) [**Ib**]

SUMMARY OF "ADDITIONAL" ADVERSE PROGNOSTIC FEATURES
These can aid clinical judgement as they are readily available for patients in hospital. Oxygen saturation measurements may be available to some general practitioners in the community who have oximeters.
- Hypoxaemia (Sao_2 <92% or Pao_2 <8 kPa), regardless of inspired oxygen concentration [**Ib**]
- Bilateral or multilobe involvement on the chest radiograph [**Ib**]

SUMMARY OF "PRE-EXISTING" ADVERSE PROGNOSTIC FEATURES
Absence of these features, which are easily identified in all patients, can be useful in identifying those at low risk of death:
- Age 50 years and over [**Ib**]
- Presence of coexisting disease [**Ib**]

6.5 Identifying those patients who can usually be safely treated at home (also summarised in fig 7)

Summary
Patients are at low risk of death if they fulfil the following three criteria and hence do not display any adverse prognostic features:

Figure 8
This figure has been changed
- refer to the 2004 update.

Consider "core" adverse prognostic features:
• new mental confusion
• urea >7 mmol/l
• respiratory rate 30/min or more
• systolic BP <90 mmHg or diastolic BP ≤60 mmHg

| None present | 1 feature present | 2 or more features present |

Consider "pre-existing" adverse prognostic features:
• Age 50 years or over or
• Any coexisting chronic illnesses?

YES

Consider "additional" adverse prognostic features:
• PaO$_2$ <8 kPa/SaO$_2$ <92% (any FiO$_2$)
• CXR: bilateral/multilobar shadowing

Clinical judgement

NO

Consider managing as **outpatient***

Manage in hospital as **non-severe CAP***

Manage in hospital as **severe CAP**

Figure 8   Severity assessment used to determine the management of CAP in patients admitted to hospital.
*The social circumstances and the wishes of the patient and general practitioner should also be considered.

● Age less than 50 years [**Ib**]
● No coexisting disease—that is, they do not have any one of congestive cardiac failure, cerebrovascular disease, chronic renal disease, chronic liver disease, or neoplastic disease [**Ib**]
● No "core" adverse prognostic features [**Ib**]. In practice, the general practitioner will not usually have the result of blood urea measurements and will rely on assessing the three simple "core" clinical features of confusion, respiratory rate, and blood pressure.

Recommendations
● **Patients who display no adverse prognostic features are at low risk of death and do not normally require hospitalisation for clinical reasons [D].**
● **Patients who display two or more "core" adverse prognostic features are at high risk of death and should be referred urgently to hospital [D].**
● **For all other patients the decision to treat at home or refer to hospital is a matter of clinical judgement [D].**
● **When deciding on home treatment, the patient's social circumstances and wishes must be taken into account in all instances [D].**

6.6 Identifying those with severe CAP from those with non-severe CAP in hospital (also summarised in fig 8)

Sect. 6.6
Refer to the 2004 update

Summary
● The key to identifying those with severe pneumonia remains assessing the four "core" adverse prognostic features [**Ib**].
● "Pre-existing" and "additional" adverse prognostic features also relate to outcome [**Ib**] and their assessment can be helpful to clinical judgement.

Recommendations
● **Patients who have two or more "core" adverse prognostic features (fig 7) are at high risk of death and should be managed as having severe pneumonia according to the recommendations outlined in sections 7 and 8 [A–].**
● **Patients who display one "core" adverse prognostic feature are at increased risk of death. The decision to treat such patients as having severe or non-severe pneumonia is a matter of clinical judgement, preferably from an experienced clinician. This decision can be assisted by considering "pre-existing" prognostic features (including age and the presence of pre-existing chronic illness) and "additional" adverse prognostic features (including hypoxaemia and the extent of radiographic shadowing) [D].**

- **Patients who display no adverse prognostic features can be managed as having non-severe pneumonia and may be suitable for outpatient treatment or early hospital discharge [B+].**

6.7 Reviewing severity status after initial assessment

Summary
- Regular and structured clinical review and reassessment of disease severity facilitates the stepping down and stepping up of antibiotic management [**Ib**].

Recommendations
- **Regular assessment of disease severity is recommended for ALL patients following hospital admission. The "post take" round by a senior doctor and the medical team provides one early opportunity for this review [D].**
- **All patients who display one or more "core" adverse prognostic features on admission should be reviewed *medically* at least 12 hourly until shown to be improving [D].**

7 General management

7.1 What general management strategy should be offered to patients treated in the community?

Patients with CAP may present with fever, cough, sputum production or pleuritic pain and usually have localised signs on chest examination. They should be advised to rest and avoid smoking[200] [**IIb**] and, especially when febrile, be encouraged to drink plenty of fluids. It is important to relieve pleuritic pain using simple analgesia such as paracetamol or non-steroidal anti-inflammatory drugs. Physiotherapy is of no proven benefit in acute pneumonia[201] [**III**]. Nutritional status appears important both to the outcome and the risk of acquiring pneumonia and nutritional supplements may be helpful in prolonged illness. Patients with pneumonia are often catabolic and those over 55 years who are malnourished appear to be at greater risk of developing pneumonia[115] [**III**], [202] [**III**].

Patients with pneumonia often become hypoxic because pulmonary blood flow takes place through unventilated lung tissue. The clinical signs of hypoxia are non-specific and often difficult to recognise in the early stages. They include altered mental state, dyspnoea, and tachypnoea. Respiratory rate should therefore always be assessed. Central cyanosis is unreliable both as a clinical sign and also as an indicator of tissue hypoxia. In contrast, pulse oximetry which measures arterial oxygen saturation (Sao_2) is in most situations a simple and reliable method of assessing oxygenation. However, poor peripheral perfusion, jaundice, and pigmented skin can produce a falsely low saturation, and carboxyhaemoglobin can result in a falsely high saturation. It is recommended that pulse oximetry, with appropriate training, should become more widely available in general practice for use in the assessment of patients who may have pneumonia and other acute respiratory illnesses. Sao_2 below 92% in a patient with CAP is an "additional" adverse prognostic feature (see section 6.4) and also an indication for oxygen therapy[203] [**IVb**] which will usually require urgent referral to hospital.

Patients who fall outside the low risk severity criteria for CAP should be assessed for the need for hospital referral (section 6). Social factors will also play an important part in the decision to refer a patient to hospital. Patients with severe pneumonia should be admitted to hospital and managed, where possible, with input from a physician with an interest in respiratory medicine.

Recommendations
- **Patients with suspected CAP should be advised not to smoke, to rest, and to drink plenty of fluids [D].**
- **Pleuritic pain should be relieved using simple analgesia such as paracetamol [D].**
- **Nutritional supplements should be considered in prolonged illness [C].**
- **The need for hospital referral should be assessed using the criteria recommended in section 6 [C].**
- **Pulse oximetry, with appropriate training, should become increasingly available to general practitioners for assessment of severity and oxygen requirement for patients with CAP and other acute respiratory illnesses [D].**

7.2 What review policy should be adopted in patients managed in the community?

When to review a patient with CAP in the community will be determined by the initial severity assessment and other factors such as reliable help in the home. Patients assessed as being at low risk should improve on appropriate treatment within 48 hours, at which time severity reassessment is recommended. Those who fail to improve within 48 hours should be considered for hospital admission. Patients who do not fulfil the criteria for low risk severity and are being managed at home will require more frequent review.

Recommendations
- **Review of patients in the community with CAP is recommended after 48 hours or earlier if clinically indicated. "Core" and "additional" adverse prognostic features should be assessed as part of the clinical review [D].**
- **Those who fail to improve after 48 hours treatment should be considered for hospital admission or chest radiography [D].**

7.3 What general management strategy should be offered to patients in hospital?

INITIAL MANAGEMENT

There is some evidence that use of a critical care pathway for patients referred to hospital can reduce the hospital admission of "low risk" patients and can also rationalise inpatient management[199] [**Ib**].

All patients referred to hospital with CAP should have a chest radiograph (if not already performed in the community) and should have oxygenation assessed by pulse oximetry, preferably while breathing air. Those with Sao_2 <92% should have arterial blood gas measurements, as should all patients with features of severe pneumonia. Knowledge of the inspired oxygen concentration is essential to the interpretation of blood gas measurements and should be clearly recorded with the blood gas result.

Continuous oxygen therapy is indicated for those patients with Pao_2 <8 kPa, hypotension with systolic blood pressure <100 mm Hg, metabolic acidosis with bicarbonate <18 mmol/l, or respiratory distress with a respiratory rate of >24 breaths/min[203] [**IVb**]. The aim of oxygen therapy should be to maintain Pao_2 at ⩾8 kPa or Sao_2 ⩾92%. In nearly all

cases of CAP, unless complicated by severe chronic obstructive pulmonary disease with ventilatory failure, high concentrations of oxygen of 35% or more are indicated and can be safely used.

High concentration oxygen therapy given to patients with pre-existing chronic obstructive pulmonary disease who may have carbon dioxide retention can reduce hypoxic drive and increase ventilation-perfusion mismatching. In such patients initial treatment with low oxygen concentrations (24–28%) should be progressively increased on the basis of repeated arterial blood gas measurements, the aim being to keep Pao_2 >6.65 kPa without causing a fall in arterial pH below 7.26[204] [**IVb**], in line with the management strategy recommended in the BTS guidelines on the management of COPD.[39] In severe cases non-invasive ventilation or respiratory stimulants may be of value and transfer to a high dependency unit or ICU should be considered.

Patients admitted with pneumonia should be assessed for volume depletion and may require intravenous fluids. While physiotherapy is of no proven value in acute pneumonia[205] [**III**], a single randomised trial has suggested that "bottle-blowing" into an underwater seal bottle on 10 occasions daily can shorten the time in hospital[206] [**II**]. There is also evidence that, in selected patients, particularly those with concurrent COPD, continuous positive airways pressure (CPAP) treatment can occasionally be of additional value[207] [**II**]. In cases of severe pneumonia requiring prolonged hospital admission, increased nutritional support—whether enteral, parenteral, or via a nasogastric tube—should be arranged.

Recommendations
- **All patients should receive appropriate oxygen therapy with monitoring of oxygen saturations and inspired oxygen concentration (see section 5.3) with the aim of maintaining Pao_2 at ≥8 kPa and Sao_2 at ≥92%. High concentrations of oxygen can safely be given in uncomplicated pneumonia [D].**
- **Oxygen therapy in patients with pre-existing COPD complicated by ventilatory failure should be guided by repeated arterial blood gas measurements [C].**
- **Patients should be assessed for volume depletion and may require intravenous fluids [C].**
- **Nutritional support should be given in prolonged illness [C].**

MONITORING IN HOSPITAL
Pulse, blood pressure, respiratory rate, temperature, oxygen saturation (with a recording of the inspired oxygen concentration at the same time), and mental status should be measured initially at least twice daily. Those with severe pneumonia who require continuous oxygen or cardiovascular support should be monitored more frequently.

The acute phase reactant CRP is a sensitive marker of progress in pneumonia[153] [**III**],

[154] [**III**]. A fall in CRP of 50% over 4 days is consistent with a good clinical response. A fall in the level of CRP of less than 50% or a persistently high or rising white cell count suggests failure of antibiotic treatment or development of an infective complication such as an empyema (see sections 5.6 and 9).

Failure to improve over 4 days is an indication to repeat the chest radiograph.

Recommendations
- **Temperature, respiratory rate, pulse, blood pressure, mental status, oxygen saturation, and inspired oxygen concentration should be monitored and recorded initially at least twice daily and more frequently in those with severe pneumonia or requiring regular oxygen therapy [C].**
- **The CRP level should be remeasured [B–] and the chest radiograph repeated [C] in patients who are not progressing satisfactorily.**

7.4 What advice should be given regarding ICU management of CAP?
Severity assessment is an important part of hospital management as it can identify those patients at increased risk of death (section 6). Patients who fulfil the severity criteria for severe CAP on admission and who do not respond rapidly should be considered for transfer to a high dependency unit or an ICU (see section 6). Persisting hypoxia with Pao_2 <8 kPa despite maximal oxygen administration, progressive hypercapnia, severe acidosis (pH <7.26), shock, or depressed consciousness are also indications for transfer to the ICU for assisted ventilation and cardiovascular support[208] [**IVb**].

Bronchoscopy after intubation may be valuable to remove retained secretions, to obtain further samples for culture, and to exclude endobronchial abnormalities such as carcinoma. Hydrocortisone given to patients in the ICU with severe pneumonia does not alter levels of circulating inflammatory cytokines such as tumour necrosis factor (TNF)α[209] [**III**], and there is no evidence that systemic corticosteroids are of benefit. Hospital acquired ventilator associated pneumonia can occur in approximately 14% of patients mechanically ventilated for severe CAP and causes increased mortality[80] [**III**]. Other aspects of ICU management are outside the scope of these guidelines.

Recommendations
- **Patients with CAP admitted to ICU should be managed by specialists with appropriate training in intensive care and respiratory medicine [D].**
- **Bronchoscopy can be valuable to remove retained secretions, obtain samples for culture for other microbiological investigations, and to exclude endobronchial abnormality [C].**

> See the 2004 update for recommendations regarding discharge planning

> Sect. 7.4 IVb See the 2004 update for further info on non invasive ventilation

7.5 What arrangements should be made for follow up after hospital discharge and by whom?

It is usual practice to arrange "routine" follow up at a hospital clinic and to repeat the chest radiograph about 6 weeks after discharge. However, there is no evidence on which to base a recommendation regarding the value of this practice in patients who have otherwise recovered satisfactorily. It is also not known whether there is any value in arranging clinical follow up in a hospital clinic rather than with the patient's general practitioner. The main concern is whether the CAP was a complication of an underlying condition such as lung cancer (see section 5.3).

At discharge or at follow up patients should be offered access to information about CAP (see section 1.9). In one study of 200 patients who had recently recovered from CAP a patient information leaflet was judged to be very helpful by the majority of patients[46] [**III**]. An updated leaflet on CAP is available on request from the British Lung Foundation headquarters (78 Hatton Gardens, London EC1N 8LD, UK) and UK regional offices.

Recommendations

- **Clinical review should be arranged for all patients at around 6 weeks, either with their general practitioner or in a hospital clinic [D].**
- **At discharge or at follow up patients should be offered access to information about CAP such as a patient information leaflet [D].**
- **It is the responsibility of the hospital team to arrange the follow up plan with the patient and the general practitioner [D].**
- **Guidelines on whether or not to repeat the chest radiograph or perform further investigations at that time are given in section 5.3:**
  - **A chest radiograph should be arranged at that time for those patients who have persistence of symptoms or physical signs or who are at higher risk of underlying malignancy (especially smokers and those over 50 years) [C].**
- **Further investigations which may include bronchoscopy should be considered in patients with persisting signs, symptoms, and radiological abnormalities about 6 weeks after completing treatment [C].**

8   Antibiotic management

8.1 Introduction

Antimicrobial chemotherapy is essential to the management of CAP. While mild pneumonia may be self-limiting, the timely use of appropriate antibiotics abbreviates illness, reduces the risk of complications, and lowers mortality.

Few pneumonias are defined microbiologically at initial assessment and hence most prescribing is empirical, especially when managed in the community. In hospitalised patients the aetiology may be determined, thereby permitting modification of the initial empirical regimen. However, in practice this applies to the minority of infections[158] [**II**]. Clinical, epidemiological, and radiographic information is rarely predictive of the microbial aetiology.

The pathogens responsible for CAP are diverse and vary in their ability to cause severe disease[179] [**Ib**]. For example, bacteraemic pneumococcal pneumonia caused by serotype 3 is more likely to cause fatal disease than CAP caused by *M pneumoniae*.

Severity assessment and the association of pre-existing co-morbid disease is essential in predicting prognosis and, in turn, determines management, choice of antibiotic therapy, and its method of administration (see section 6).

Age will also have some influence on the likely causative pathogens and consequently the choice of empirical therapy in some circumstances. For the purpose of this discussion on antibiotic management we have arbitrarily chosen the term "elderly" to include those aged 75 years and over.

8.2 The term "atypical" pathogen

The definitions used are described in sections 1.7 and 4.4. In summary, for the purposes of these guidelines infections caused by *M pneumoniae*, *C pneumoniae*, *C psittaci*, and *C burnetii* are captured in the phrase "atypical" pathogens. *Legionella* species, although sharing some similar characteristics, are not considered to be an "atypical" pathogen for the purpose of this document. We do not recommend the use of the term "atypical" pneumonia.

8.3 Local issues affecting the choice of antibiotic regimen

The choice of antibiotic regimen may have consequences beyond the management of the individual patient. Overprescribing of macrolides and β-lactams, especially when administered parenterally in the management of hospitalised patients with CAP, possibly resulted from too loose an interpretation of "severe pneumonia". Furthermore, the application of the earlier pneumonia guidelines to community acquired lower respiratory tract infections other than pneumonia and hospital acquired pneumonia added to this overuse. This has increased the cost of management and, in the case of cefotaxime and other injectable cephalosporins, has been linked to an increase in complicating *C difficile* associated diarrhoea and enteropathy[16]

[**II**], [19] [**Ib**], [210] [**IVa**], [211] [**II**], [212] [**II**], [213] [**Ib**], [214] [**Ia**], [215] [**Ib**]. Alternative agents such as the aminopenicillins, with or without a β-lactamase inhibitor, can also induce *C difficile* associated diarrhoea[216] [**Ia**]. Although the excess and inappropriate use of such antibiotics for treating lower respiratory tract infections has been very important, *C difficile* associated diarrhoea is also linked to hospital hygiene and cross infection practices[217 218] [**IVa**] and is particularly prevalent in elderly patients on medical wards. An important aspect of implementing these guidelines locally and auditing their use will be the emphasis with which they are directed at the management of pneumonia and *not* at non-pneumonic lower respiratory tract infections such as exacerbations of COPD. Hospitals that continue to have a problem with *C difficile* enteropathy in spite of attention to the appropriate use of these guidelines for pneumonia should consider choosing the alternative regimens over the preferred regimen for a period, a strategy that anecdotally has been associated with a reduction in cases of antibiotic associated diarrhoea. With regard to the latter, a fluoroquinolone is suggested although the evidence for a lower risk of *C difficile* enteropathy remains limited[214] [**Ia**], [219] [**IVb**], [220] [**Ib**], [221][**II**].

8.4 Antibiotic resistance of respiratory pathogens

Resistance among respiratory pathogens is increasing and is of concern. Beta-lactamase production among *H influenzae* varies geographically but ranges from 2% to 17% in various parts of the UK [222] [**II**], [223] [**II**]. However, this is an uncommon cause of pneumonia and, unless local data suggest otherwise, there is insufficient justification to include a β-lactamase resistant antibiotic regimen in initial empirical treatment of non-severe CAP. *M catarrhalis* is an even rarer cause of CAP for which the same argument applies.

S aureus is widely resistant to penicillin[224] [**II**] and an increasing number are now methicillin resistant (MRSA). When this occurs in the community it generally reflects hospitalisation within the recent past or residence in a nursing home. Hence, β-lactamase unstable penicillins (penicillin G, aminopenicillins) and, in the case of MRSA, isoxazolyl penicillins (flucloxacillin, cloxacillin) and cephalosporins are inappropriate for such infections.

Antibiotic resistance of *S pneumoniae* is of greater concern because of the dominance of this organism as a cause of CAP and because penicillin and macrolide resistance are frequently linked[223] [**II**], [225] [**II**]. Resistance among pneumococci is the result of alterations in one or more of the penicillin binding proteins which reduces their affinity for penicillin. This, in turn, leads to a requirement for higher drug concentrations to bring about death of the organism. Of the >90 known pneumococcal serotypes, a small number have

been responsible for penicillin resistance worldwide, among which selected clones (such as 23F, 9V, and 6B) have become widely disseminated. However, despite these concerns, the clinical importance of in vitro penicillin resistance among *S pneumoniae* remains uncertain when treating pneumococcal pneumonia[226] [**II**], [227] [**II**], [228] [**IVb**], [229] [**IVa**], [230] [**II**], [231] [**II**]. This is reflected in the continued ability of current doses of penicillins to inhibit strains of intermediate susceptibility (minimum inhibitory concentration (MIC) of penicillin 0.1–1.0 mg/l), as well as many strains exhibiting higher level resistance (defined by an MIC of >1 mg/l). Resistance to erythromycin is the result of genetic mutations that either affect the target site (*erm* gene mutations) or result in elimination of the drug by an efflux pump (*mef* gene mutation). The distribution of such strains differs internationally and probably explains the variation in the clinical impact of such resistance since *erm* gene mutations are linked to high level resistance. Tetracyclines are not widely used in the treatment of CAP and resistance among *S pneumoniae* is relatively low. Likewise, reduced susceptibility of *S pneumoniae* to fluoroquinolones is beginning to be reported [232] [**II**]. The trends in penicillin, erythromycin, and tetracycline resistance in England and Wales are shown in fig 9.

Legionella pneumophila and *Legionella* species in general remain susceptible to rifampicin, macrolides, and the fluoroquinolones, although low level resistance has been found in vitro in some isolates. However, the clinical significance of these observations remains unclear.[233]

Linked to the issue of antibiotic resistance is the problem of use and abuse of antibiotic prescribing. Excessive or inappropriate use of antibiotics has been highlighted in the House of Lords Select Committee Report[234] and by the Department of Health.[34] Proper patient selection for treatment and the correct use of agents are emphasised in this document.
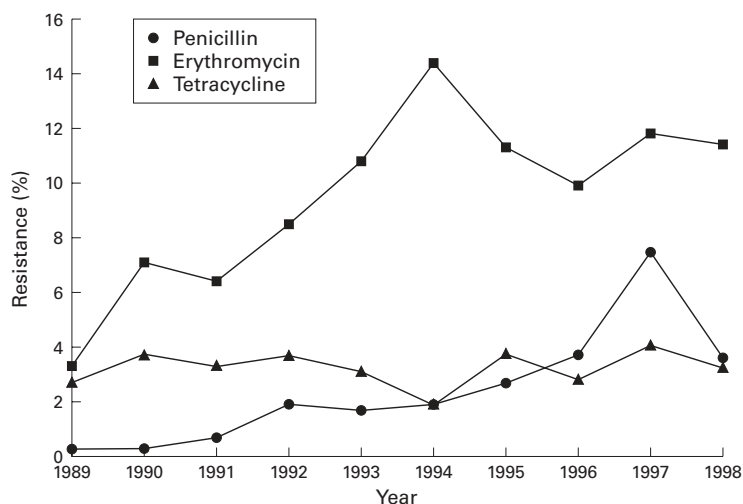

Figure 9   Resistance (%) to penicillin (high and intermediate), erythromycin and tetracycline among selected S pneumoniae isolates (blood and cerebrospinal fluid) from laboratories reporting to the Public Health Laboratory Service.

8.5 Newer antibiotics

Since the first BTS guidelines were published there have been a number of new antibiotics licensed for the treatment of CAP. These include new macrolides (clarithromycin and azithromycin) and several fluoroquinolones with greater in vitro activity against respiratory pathogens and, in particular, *S pneumoniae*, regardless of their susceptibility to penicillin. Their role in the initial empirical and specific antibiotic management of CAP is discussed below. Much has also been learned about antibiotic distribution within the lung, based on studies that detect penetration within bronchial tissue, alveolar macrophages, and epithelial lining fluid obtained at bronchoscopy [235] [**Ia**], [236] [**Ia**]. Furthermore, in the development of these new agents there is substantial evidence that links antimicrobial performance in vivo to the pharmacokinetic profile of an agent and the in vitro susceptibility of target pathogens. Such pharmacodynamic approaches are likely to influence dosage regimens increasingly in the future[237] [**Ia**], [238] [**II**], [239] [**II**], [240] [**Ia**].

8.6 International differences in recommendations and clinical studies of management

In defining the UK choice of empirical and specific treatment for CAP, it is apparent that the international differences in published recommendations cannot be entirely based on geographical variation in the distribution and antibiotic susceptibility of pathogens responsible. There is clearly variation in medical practice with regard to licensing, availability, choice, dose, route of administration, and duration of treatment which is more a reflection of local custom and practice than robust scientific evidence. The literature review for the period 1981–99 provided only 16 acceptable articles relevant to the antibiotic management of CAP[54] [**Ib**], [221] [**II**], [241] [**Ib**], [242] [**Ib**], [243] [**Ib**], [244] [**Ib**], [245] [**Ib**], [246] [**Ib**], [247] [**Ib**], [248] [**Ib**], [249] [**Ib**], [250] [**Ib**], [251] [**Ib**], [252] [**Ib**], [253] [**Ib**], [254] [**Ib**]. The remainder were rejected for the following reasons: inadequately powered studies or a retrospective design,[15 255–272] antibiotic not available in the UK or withdrawn,[27 273–306] study population or management unrepresentative of normal clinical practice in the UK,[253 307–315] or they included mixed lower respiratory tract infections including CAP.[253 286 316 317]

Few of the studies reviewed were conducted within a healthcare system comparable to that of the UK. Others were designed to support the licensing of new therapies. For this reason they are primarily designed to demonstrate equivalence between the new agent and comparator therapy, which may or may not have been selected in accordance with current standard management. This invariably makes it difficult to offer evidence based recommendations since superiority of a particular regimen is rarely identified. Likewise, matters of differential safety for the various regimens is difficult to assess since this information is essentially a byproduct of these licensing studies, is rarely standardised, and has often not been compared with current standard treatment.

8.7 Formulation of these recommendations

For these reasons the recommendations for treatment have been made on the basis of assessing a matrix of laboratory, clinical, pharmacokinetic and safety data, interpreted in an informed manner. While this remains an unsatisfactory basis for making robust evidence based recommendations, it highlights the need for appropriate, prospective, randomised controlled studies designed to address the many key questions that will enable the management of CAP to be placed on a sounder basis. The responsibility for this presents a challenge to medical practitioners, healthcare systems, grant giving bodies, and industry. We have also only considered antibiotics licensed and available in the UK at the time these guidelines were prepared.

As stated by Finch and Woodhead[318] [**IVa**], "it is important to recognise that these are simply guidelines and reflect our interpretation of good practice within an evolving area. Guidelines cannot capture every clinical situation and it therefore remains the responsibility of the physician to balance the history and clinical features, assess the importance of risk factors and interpret local epidemiology and laboratory data in order to make the best judgement for an individual patient".

(A) EMPIRICAL TREATMENT

8.8 What are the principles and practice of empirical antibiotic choice for CAP in the community?

Most patients with pneumonia are treated successfully in the community in the absence of any microbial definition of an infecting microorganism(s). The decision to manage a patient in the community is based on a range of factors which include an assessment that the pneumonia is non-severe, that oral treatment is appropriate and will be complied with, and that the social circumstances and available care for an individual are satisfactory.

Empirical therapy is primarily directed at *S pneumoniae* which remains the leading cause of CAP (section 3)[179] [**Ia**]. Apart from *M pneumoniae*, atypical pathogens, *Legionella* species and β-lactamase producing bacteria are uncommon in the community setting. *M pneumoniae* exhibits epidemic periodicity every 4–5 years and largely affects younger persons. A policy for initial empirical therapy that aimed always to cover this pathogen was considered inappropriate. The possibility of recommending a tetracycline was considered on the basis of lower resistance rates among pneumococci (fig 9) and activity against atypical pathogens. However, this would require a major change in current prescribing practice by general practitioners in the community where the majority of pneumonias are treated, and hence would limit compliance with the recommendations. In addition, there are safety concerns in women of childbearing potential.

For these reasons, as well as the issues of current practice, cost, wide experience and drug tolerance, amoxicillin remains the preferred agent. The alternative agent for those intolerant of amoxicillin is erythromycin[54] [**Ib**], primarily for its activity against *S pneumoniae* although recognising that it is also active against *M pneumoniae*, other atypical pathogens, and *Legionella* species. Gastrointestinal intolerance to erythromycin is the major indication for substituting an alternative macrolide such as clarithromycin or modified formulations of erythromycin. Concern over the rising frequency of in vitro resistance of *S pneumoniae* to macrolides (which is often linked to penicillin resistance) is recognised (fig 9), yet published clinical evidence for clinical failure of macrolides in the treatment of pneumococcal pneumonia remains limited [319] [**III**], [320] and controversial[321] [**IVa**], [322] [**IVa**].

The newer macrolides[323] [**IVa**] and fluoroquinolones[324] [**IVa**] have microbiological strengths in vitro, yet in published studies to date have not been shown to be more efficacious than standard therapy in treating patients with CAP. They are clearly more costly and, in the case of most fluoroquinolones, experience currently remains limited. Concerns also remain with regard to the safety of the new fluoroquinolones, with several compounds having been withdrawn because serious adverse events have become apparent after marketing.[324]

The association of *H influenzae* and, to a much lesser extent *M catarrhalis*, with acute exacerbations of COPD is recognised[325] [**II**]. However, both remain uncommon causes of CAP. When CAP does arise with these pathogens, an even smaller percentage of such patients will be infected with β-lactamase producing strains. To illustrate the clinical significance of such resistance for managing CAP, it is estimated that 5% of cases of CAP may be caused by *H influenzae*, of which 15% may be β-lactamase producing strains in the UK. Thus, of 500 patients with CAP, only four may be infected with such antibiotic resistant strains.

A view that specific pathogens are associated with other comorbid diseases (for example, *H influenzae* and COPD) to increase the risk of CAP is not supported by the literature. For these reasons these guidelines do not offer alternative regimens for patients with or without comorbid illness, while recognising that such diseases can affect the severity of CAP in an individual.

The current concerns over the increasing prevalence of pneumococci with reduced susceptibility to penicillin is recognised. However, the incidence of highly resistant strains (MIC ≥4 mg/l) remains uncommon in the UK. Furthermore, the rarity of documented clinical failures among penicillin resistant pneumococcal pneumonia, if treated with adequate doses of penicillin, is the basis for endorsing oral amoxicillin as first line therapy, but at an increased dosage of 500–1000 mg three times daily.

Table 8: this table has been modified. Refer to update.

Table 8   Preferred and alternative initial empirical treatment regimens for adults with CAP managed in the community

Preferred	Alternative*
Home treated, not severe	
• Amoxicillin 500 mg–1.0 g tds po	• Erythromycin 500 mg qds po *or* clarithromycin 500 mg bd† po

bd = twice daily; tds = 3 times/day; qds = 4 times/day; po = oral.
*An alternative regimen is provided for those intolerant of or hypersensitive to the preferred regimen.
†Clarithromycin may be substituted for those with gastrointestinal intolerance to oral erythromycin and also has the benefit of twice daily dosage.

Table 9   Preferred and alternative initial empirical treatment regimens for adults with CAP seen and managed in hospital

Preferred	Alternative*
Hospital treated, not severe (admitted for non-clinical reasons or previously untreated in the community)	
• Amoxicillin 500 mg–1.0 g tds po	• Erythromycin 500 mg qds po *or* clarithromycin 500 mg bd† po
Hospital treated, not severe	
Oral:	
• Amoxicillin 500 mg–1.0 g tds po *plus* erythromycin 500 mg qds po or clarithromycin 500 mg bd po	• Fluoroquinolone with some enhanced pneumococcal activity, e.g. levofloxacin 500 mg od po‡ (the only such licensed agent in the UK at the time of writing)
If intravenous treatment needed:	
• Ampicillin 500 mg qds iv *or* benzylpenicillin 1.2 g qds iv *plus* erythromycin 500 mg qds iv *or* clarithromycin 500 mg bd iv	• Levofloxacin 500 mg od iv‡
Hospital treated, severe	
• Co-amoxiclav 1.2 g tds *or* cefuroxime 1.5 g tds *or* cefotaxime 1 g tds *or* ceftriaxone 2 g od (all 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 some enhanced pneumococcal activity, e.g. levofloxacin 500 mg bd iv, po‡ *plus* benzylpenicillin 1.2 g qds iv

od = once daily; bd = twice daily; tds = 3 times/day; qds = 4 times/day; iv = intravenous; po = oral.
*An alternative regimen is provided for those intolerant of or hypersensitive to the preferred regimen, or where there are local concerns over *C difficile* associated diarrhoea related to β-lactam use.
†Clarithromycin may be substituted for those with gastrointestinal intolerance to oral erythromycin and also has the benefit of twice daily dosage.
‡Levofloxacin is the only currently UK licensed fluoroquinolone with some enhanced activity against *S pneumoniae* and comes in an oral and parenteral formulation. In the future other fluoroquinolones such as moxifloxacin, gemafloxacin, and gatifloxacin are likely to extend this choice, when licensed in the UK. Oral moxifloxacin is already licensed and is available in some other countries.
§Concurrent administration of rifampicin reduces the serum level of macrolides; the clinical significance of this is not known.
Recommendations for switching from a parenteral drug to the equivalent oral preparation are shown in box 3.

Recommendations (table 8)
- **Amoxicillin remains the preferred agent but at a higher dose than previously recommended [D].**
- **A macrolide (erythromycin or clarithromycin) is offered as an alternative choice and for those patients who are hypersensitive to penicillins [D].**
- **Those with features of severe infection should be admitted urgently to hospital [C].**

8.9 Should general practitioners administer antibiotics before transfer to hospital in patients who need admission?

There is no direct evidence upon which to provide clear guidance on this question. There is, however, some circumstantial evidence to suggest that early antibiotics are of benefit in severe pneumonia.

Delay in prescribing antibiotics for patients in hospital with diagnosed pneumonia is associated with a worse outcome[326] [III] and, in patients dying from CAP, the majority have not received prior antibiotics even though most had visited a general practitioner in the previous few days. In a national confidential enquiry into CAP deaths in young adults in England and Wales, 20 of the 27 fatal cases investigated had seen their general practitioner for the illness and only nine had received antibiotics[327] [II]. In the multicentre BTS study of CAP in 1982, none of the patients who died from pneumococcal pneumonia had received an antibiotic before admission. The authors concluded that some deaths may have been preventable and recommended that an antibiotic active against *S pneumoniae* should be started as soon as pneumonia is recognised[14] [Ib]. In a study of CAP from New Zealand significantly fewer (p=0.05) of those who died had received antibiotics before admission (20%) than those who survived (42%)[60] [Ib]. Currently, less than half of adults admitted to hospital in the UK with severe CAP have already received antibiotics from their general practitioner[22] [III], [66] [III]. Many deaths and requirements for assisted ventilation occur in the first few days of admission for severe CAP[14] [Ib], [69] [Ib], [71] [Ib]. All of these studies provide further support to the suggestion that, in cases of diagnosed pneumonia, antibiotics should be given as early as possible, if necessary before hospital admission.

Delays do occur between general practitioner assessment in the community, arranging admission, confirmation of the diagnosis in hospital, and the start of treatment. These delays are probably inevitable and will be exacerbated by transport distances and ambulance availability and prioritisation, bed availability, and triage in the medical assessment unit or accident and emergency department. Delays between admission and receiving antibiotics of over 6 hours have been reported for younger adults dying in hospital of CAP (mean delay 260 minutes[20] [III]). This study was conducted before acute assessment units were introduced into most UK hospitals, a change which may have speeded up the management of medical admissions. Although it is likely that most patients with low risk CAP which proves to be non-fatal come to no harm in the time that this whole process takes, it appears far from ideal to delay giving antibiotics when the general practitioner is reasonably sure of the diagnosis.

From time to time general practitioners do see patients who are severely ill with what appears to be pneumonia. In such circumstances treatment should commence as soon as possible, providing it does not delay transfer to hospital. When general practitioners feel treatment in such circumstances is needed, it should aim to cover pneumococcal pneumonia, the commonest cause of severe CAP, with parenteral penicillin G or oral amoxycillin 1 g orally (or erythromycin in cases of penicillin sensitivity). General practitioners are likely to carry such antibiotics with them as parenteral penicillin is recommended as the immediate treatment for suspected meningococcal infection. Ambulance services should allocate a high priority for transfer to hospital of patients with pneumonia.

Prescribing antibiotics does have an influence on some microbiological investigations[14] [**Ib**]. However, when general practitioners feel a patient is severely ill or circumstances suggest that delays in transfer will slow assessment and treatment in hospital, concern over the potential effect on subsequent investigations is not a reason to withhold treatment.

It is important to state that, as with the whole of this document, these comments refer to patients with CAP and not to the much larger group of patients with non-pneumonic lower respiratory tract infection or exacerbations of COPD.

Summary
- Delays occur in the process of admitting patients to hospital with CAP and in administration of antibiotics [**III**].
- There is direct and indirect evidence that administering antibiotics early is important in the outcome of CAP, particularly when it is assessed as severe [**Ib**].
- Less than half of patients admitted with severe CAP have received antibiotics before admission, even though they may have seen their general practitioner [**III**].
- Most deaths from CAP occur shortly after admission [**Ib**].
- Antibiotics given before admission can negatively influence the results of subsequent microbiological investigations [**Ib**], but this is not seen as a reason for withholding antibiotics if the general practitioner feels they are indicated.

Recommendations
- **For those patients referred to hospital with suspected CAP, general practitioners may consider administering antibiotics immediately where the illness is considered to be life threatening or where there are likely to be delays (>2 hours) in admission [D].**

Sect. 8.10 Refer to 2004 updated document

8.10 What are the principles and practice of empirical antibiotic choice for adults hospitalised with non-severe CAP?
Approximately 20% of patients with CAP are admitted to hospital in the UK (section 2). The reasons for hospitalisation vary and include severity of the infection, an unsatisfactory response to treatment initiated by the general practitioner, significant co-morbid illness, and non-clinical reasons such as inappropriate home circumstances suitable for community management.

The principles of antibiotic selection for non-severe CAP managed in hospital are similar to those for its management in the community. The predominant pathogen will be *S pneumoniae*. However, overall, atypical pathogens and *Legionella* species account for approximately 20% of defined infections. For these reasons a combined β-lactam/macrolide regimen is recommended (table 9). Oral amoxicillin and erythromycin or clarithromycin is the preferred regimen. When oral therapy is inappropriate, parenteral ampicillin or penicillin G are offered as alternatives to oral

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Switch from parenteral drug to the equivalent oral preparation
- This should be made as soon as clinically appropriate, in the absence of microbiologically confirmed infection.
- Change is straightforward when there is an effective and equivalent oral and parenteral formulation.
- 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 + levofloxacin, oral levofloxacin with or without oral amoxicillin 500 mg–1.0 g tds is recommended.

Box 3 Recommendations for switching from a parenteral drug to the equivalent oral preparation.

amoxicillin. Erythromycin by the intravenous route is given four times daily; thus clarithromycin, given twice a day, is offered as the preferred macrolide for parenteral therapy and an alternative for oral administration.

The new fluoroquinolones may be given as an alternative in hospitalised patients in specific circumstances. While these fluoroquinolones possess in vitro activity against *S pneumoniae*, including strains with reduced susceptibility to penicillin, experience to date in treating such infections remains limited. The role of the new fluoroquinolones is addressed later in section 8.18. At the time of completing these guidelines only levofloxacin is licensed and available in the UK.

Regardless of the regimen selected, it is critical that the antibiotics are administered promptly (within 2 hours of admission) and, in the case of the patient with severe pneumonia, without delay by the admitting doctor in the admissions ward or by the general practitioner if delays are expected in the hospital admission process (see section 8.9). Delays in administration of antibiotics are related adversely to mortality[326] [**Ib**].

In practice, it is recognised that a significant number of patients with non-severe pneumonia are admitted to hospital for non-clinical reasons—for example, advanced age, personal or family preference, inadequate home care, or adverse social circumstances—who might otherwise be adequately managed in the community. Others will be admitted who have not received antibiotic treatment. They cannot be considered to have failed community treatment and initial treatment with a single agent as for the "home treated, not severe" group (table 8) is considered appropriate. Furthermore, *M pneumoniae* is an important contributor to the overall incidence of atypical pathogens but is an infrequent cause of CAP in elderly patients. This provides further justification for monotherapy in the hospitalised non-severe elderly patient. In all such circumstances patient management requires careful clinical judgement and regular reviews.

Following initial assessment and empirical therapy, progress should be monitored carefully. The route and choice of antibiotic treatment will require adjustment, either by stepping up and broadening the spectrum of microbiological activity in the light of clinical deterioration or as a result of positive microbiological information, or stepping down with improvement as discussed below. The review of antibiotic treatment forms an obvious and essential part of the regular clinical review of patients with CAP.

Recommendations (table 9)
- **Most patients can be adequately treated with oral antibiotics [C].**
- **Combined oral treatment with amoxicillin and a macrolide (erythromycin or clarithromycin) is preferred for patients who require hospital admission for clinical reasons [D].**
- **Oral monotherapy should be considered in the following circumstances:**
  - **Amoxicillin monotherapy may be considered for (i) those previously untreated in the community or (ii) those admitted to hospital for non-clinical reasons who would otherwise be treated in the community [D]. The latter factor will often apply to the elderly in whom it is also recognised that infection with atypical pathogens requiring macrolide therapy is uncommon (see section 3).**
  - **Monotherapy with a macrolide may be suitable for patients who have failed to respond to an *adequate* course of amoxicillin prior to admission. Deciding on the adequacy of prior therapy is difficult and is a matter of individual clinical judgement. It is therefore recommended that combination antibiotic therapy is the preferred choice in this situation and that the decision to adopt monotherapy is reviewed on the "post take" round within the first 24 hours of admission (see section 9.1) [D].**
- **When oral treatment is contraindicated, recommended parenteral choices include intravenous ampicillin or benzylpenicillin together with erythromycin or clarithromycin [D].**
- **A fluoroquinolone active against *S pneumoniae* is an alternative regimen for those intolerant of penicillins or macrolides or where there are local concerns over *C difficile* associated diarrhoea. However, experience with such newer fluoroquinolones in the treatment of CAP and their interaction and side effect profile is at present limited and further reported experience is required [B–]. Levofloxacin is currently the only recommended agent licensed in the UK.**

8.11 What are the principles and practice of empirical antibiotic choice for adults hospitalised with severe CAP?
Mortality is greatly increased in those with severe pneumonia (see section 6). The illness may progress before microbiological information is available.

Preferred and alternative initial treatment regimens are summarised in table 9 and mostly include combination therapy with broad spectrum β-lactams and a macrolide. While *S pneumoniae* remains the predominant pathogen, *S aureus* and Gram negative enteric bacilli, although uncommon, carry a high mortality[179] [**Ia**], hence the recommendation for broad spectrum β-lactam regimens in those with severe CAP [**C**]. Parenteral antibiotics are recommended in those with severe CAP, regardless of the patient's ability or otherwise to take oral medication [**C**]. This is to ensure prompt high blood and lung concentrations of antibiotic.

Patients admitted to hospital with CAP caused by *Legionella* species are more likely to have severe pneumonia[179] [**Ia**], so the initial empirical antibiotic regimen should also capture this pathogen within its spectrum of activity.[328] Efficacy data from prospective controlled clinical trials are not available. However, a retrospective study suggests a reduction in mortality for those treated with a third generation cephalosporin plus a macrolide[54] [**III**], although no additional benefit has been noted in another study[329] [**II**]. Currently, a macrolide or a fluoroquinolone is preferred for treating legionella infections. The choice of a macrolide is based on a combination of in vitro pharmacokinetic and animal model data supplemented with limited clinical information[330] [**IVb**] [**C**]. Azithromycin is currently only available for oral administration and is therefore inappropriate for treating severe infection. For life threatening infection where *Legionella* species could be present, the addition of rifampicin is recommended despite the absence of clinical data supporting its benefit [**C**]. The risk of lowering macrolide plasma and tissue concentrations as a result of induction of the P 450 enzyme system is acknowledged,[331 332] but there are no data to indicate that this is of clinical significance when treating CAP.

Fluoroquinolones are offered as an alternative, despite limited data on their use in severe CAP[324] [**IVa**]. Levofloxacin is the only licensed agent available in the UK at the time of writing, and is marketed in parenteral and oral formulations. Since the latter is 98% bioavailable, this indicates that it can be used in severe pneumonia provided there are no contraindications to oral administration. While it has modest activity against pneumococci in vitro, the published evidence for efficacy in severe CAP is reassuring[199] [**Ib**], [247] [**Ib**], [270] [**Ib**], [333] [**Ib**], [334] [**Ib**]. However, until more clinical experience is available, we recommend combining it with another agent active against *S pneumoniae* such as parenteral benzylpenicillin in cases of severe CAP. Future Gram positive fluoroquinolones such as gatifloxacin, gemafloxacin and moxifloxacin, which are currently unlicensed in

the UK, may be found through clinical experience to have greater activity against *S pneumoniae* than levofloxacin and hence may be effective as monotherapy.

Recommendations

- **Patients with severe pneumonia should be treated immediately after diagnosis with parenteral antibiotics [B–].**
- **An intravenous combination of a broad spectrum β-lactamase stable antibiotic such co-amoxiclav or a second generation (e.g. cefuroxime) or third generation (e.g. cefotaxime or ceftriaxone) cephalosporin together with a macrolide (e.g. clarithromycin or erythromycin) is preferred [C].**
- **For those who are intolerant of β-lactam or macrolide therapy or where there are local concerns over *C difficile* associated diarrhoea, a fluoroquinolone with enhanced activity against pneumococci together with benzylpenicillin is offered as an alternative [D]. Levofloxacin is currently the only such fluoroquinolone licensed in the UK.**

8.12 When should the intravenous or the oral route be chosen?

Parenteral administration of antibiotics is widely and often unnecessarily used in managing hospitalised patients including those with CAP[245] [**Ib**], [335] [**IVa**]. Approximately 30–50% of patients admitted to hospital will initially require treatment with parenteral antibiotics[245] [**Ib**]. Apart from the discomfort to the patient of inserting intravenous devices, there are significant complications, notably infection. In addition, the total cost of parenteral regimens greatly exceeds orally administered treatment.

Factors determining the route of administration are summarised in box 4. Parenteral antibiotics are clearly indicated for patients unable to swallow where there is concern about adequate absorption of drug from the gut, and in the presence of severe pneumonia. However, many antibiotics are well absorbed following oral administration and achieve their maximum plasma concentration within 1–2 hours.

Parenteral treatment
- severe pneumonia
- impaired consciousness
- loss of swallowing reflex
- functional or anatomical reasons for malabsorption

Oral treatment
- community managed
- hospital managed, non-severe with no other contraindications

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Box 4 Indications for parenteral and oral antibiotic treatment of adult CAP.

Recommendation

- **The oral route is recommended in those with non-severe pneumonia admitted to hospital provided there are no contraindications to oral treatment [B+].**

8.13 When should the intravenous route be changed to oral?

As stated above, parenteral antibiotic treatment is widely and often unnecessarily used in hospitalised patients with non-severe pneumonia. This in part reflects custom and practice but, in addition, may be driven by too liberal an interpretation of the "criteria" for identifying severe CAP for which parenteral agents are recommended. The current practice of medicine surrounding emergency medical admissions may also be a factor in the choice of parenteral administration where it provides greater confidence to admitting junior medical staff that the patient is receiving the "best" management. Oral treatment was clearly more widely adopted in the past.[335] Published evidence indicating comparable efficacy of parenteral and oral regimens is limited but has been shown for intravenous cefuroxime and oral levofloxacin[247] [**Ib**].

The choice and timing of any change to oral treatment will be affected by several factors. These include the absence of any contraindications to oral administration, the availability of any microbiological information regarding aetiology of the infection, and clear evidence that the patient is responding to initial treatment. Some of the criteria indicating improvement are summarised in box 5.

- Resolution of fever for >24 hours
- Pulse rate <100 beats/min
- Resolution of tachypnoea
- Clinically hydrated and taking oral fluids
- Resolution of hypotension
- Absence of hypoxia
- Improving white cell count
- Non-bacteraemic infection
- No microbiological evidence of legionella, staphylococcal or Gram negative enteric bacilli infection
- No concerns over gastrointestinal absorption

Box 5 Features indicating response to initial empirical parenteral treatment permitting consideration of substitution with oral antibiotics.

There can be no rigid recommendation concerning the timing of transfer to oral treatment and further studies are needed[305] [**II**], [336] [**Ia**], [337] [**II**]. Any decision must be individualised on the basis of assessing all factors. Nonetheless, the recommended guideline is that oral treatment be considered in a patient who has shown clear evidence of improvement and whose temperature has resolved for a period of 24 hours. The features indicating response to parenteral treatment are summarised in box 5. This policy will allow a significant proportion of patients with non-severe pneumonia to be safely transferred to an oral regimen after a period of initial parenteral treatment[198] [**II**], [248] [**Ib**], [266] [**Ia**], [305] [**II**], [336] [**Ia**], [338] [**IVa**].

Recommendations
- **Patients treated initially with parenteral antibiotics should be transferred to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 hours, providing there is no contraindication to the oral route. Pointers to clinical improvement are given in table 9 [B+].**
- **The choice of route of administration should be reviewed initially on the "post take" round and then daily [D].**
- **Ward pharmacists could play an important role in facilitating this review by highlighting prescription charts where parenteral antibiotic treatment continues [D].**

8.14 Which oral antibiotics are recommended on completion of intravenous treatment?

The selection of agents for oral administration following initial intravenous treatment is based on antimicrobial spectrum, efficacy, safety, and cost considerations (summarised in box 3). Although it may appear logical to select the oral formulation of a parenteral agent, this is not essential and such oral agents may not meet the criteria for selection. For macrolides, oral clarithromycin is better tolerated than oral erythromycin[241] [**Ib**], [242] [**Ib**] but is more expensive. A clinical judgement can be made whether to change to oral monotherapy in those who have responded favourably to parenteral combination therapy or where there is microbiological documentation of the nature of the infection, in which case the recommendations in table 10 should be adopted.

Recommendation
- **The choice of antibiotics when switching from the intravenous to the oral route is summarised in box 3 [C].**

8.15 For how long should antibiotics be given?

The precise duration of antibiotic treatment for the management of microbiologically documented and non-documented CAP is not supported by robust evidence. The Summary of Product Characteristics (formerly the Drug Data Sheets) for many agents used in the treatment of CAP mention a range of treatment durations which sometimes differ internationally.

In the case of documented infections there is evidence that pneumonia caused by *Legionella* species may require 14 days of treatment or up to 21 days in severe infections[330] [**IVa**]. Likewise, intracellular pathogens responsible for pneumonia sometimes respond slowly and hence a 2 week treatment regimen has been proposed for atypical pathogens.

The aim of antibiotic treatment is to ensure elimination of the target pathogen in the shortest time. In uncomplicated infections this is likely to occur rapidly (within 3 days) with many common respiratory pathogens such as *S pneumoniae*. The resolution of pneumonia involves not only the elimination of the invading pathogen and its products, but also the subsidence of the host inflammatory response which together are responsible for the many clinical and radiographic features of pneumonia.

Until we have more precise methods to identify microbiological and clinical end points reliably, the duration of treatment will remain subject to clinical judgement and will vary with the individual patient, disease severity, and speed of resolution. Table 10 offers guidance based largely on custom and practice but modified where evidence exists.

Recommendations (table 10)
- **For patients managed in the community and most of those admitted to hospital with non-severe and uncomplicated pneumonia, treatment with appropriate antibiotics for 7 days is recommended [C].**
- **For patients with severe microbiologically undefined pneumonia, 10 days of treatment is proposed. This should be extended to 14–21 days where legionella, staphylococcal, or Gram negative enteric bacilli pneumonia are suspected or confirmed [C].**

8.16 Failure of initial empirical treatment

In those patients who fail to respond to initial empirical treatment, several possibilities need to be considered. The first is whether the correct diagnosis been made. Radiographic review is recommended for both community and hospital managed patients. This may also indicate complications of CAP such as pleural effusion/empyema, lung abscess, or worsening pneumonic shadowing. This aspect is considered in detail in section 9.

The initial empirical antibiotic regimen may need to be reassessed. However, compliance with and adequate absorption of an oral regimen should first be considered.

Microbiological data should be reviewed and further specimens examined with a view to excluding less common pathogens such as *S aureus*, atypical pathogens, *Legionella* species, viruses, and *Mycobacteria* species. It should also be noted that mixed infections can arise in approximately 10% of patients admitted to hospital with CAP. In the absence of any microbiological indicators of infection, the management of those failing initial empirical treatment will vary according to the severity of

Table 10   Duration of antibiotic management by place of care, severity, and microbiological data

Place/severity or pathogen	Duration of treatment (days)
Home treated, not severe (microbiologically undefined)	7
Hospital treated, not severe (microbiologically undefined)	7
Hospital treated, severe (microbiologically undefined)	10
Legionella infection	14–21
"Atypical" pathogen	14
Pneumococcal infection (uncomplicated)	7
Staphylococcal infection	14–21
Gram negative enteric bacilli	14–21

the illness at reassessment. In patients managed in the community with non-severe pneumonia a macrolide could be substituted for amoxicillin. However, when the patient's condition has deteriorated, admission to hospital should be considered.

In the hospital managed, non-severely ill patient the addition of a macrolide is recommended in those patients initially managed with amoxicillin alone. Changing to a new fluoroquinolone such as levofloxacin provides a second alternative.

In the severely ill patient already receiving a β-lactam/clarithromycin regimen it is recommended that rifampicin should be added. In addition, urgent referral to a respiratory physician should be made for clinical assessment including the possible need for bronchoscopic sampling.

Recommendations
- **When a change in empirical antibiotic treatment is considered necessary, a macrolide could be substituted for or added to the treatment for those with non-severe pneumonia treated with amoxicillin monotherapy in the community or in hospital [C].**
- **For those with non-severe pneumonia in hospital on combination therapy, changing to a fluoroquinolone with effective pneumococcal cover is an option [C].**
- **The addition of rifampicin may be considered for those with severe pneumonia not responding to combination antibiotic treatment [C].**

3) SPECIFIC PATHOGEN DIRECTED ANTIBIOTIC TREATMENT

17 What are the optimum antibiotic choices when specific pathogens have been identified?

In routine clinical practice only about one third to one quarter of patients with CAP admitted to hospital will be defined microbiologically. Of these some, such as mycoplasma, chlamydial, and Q fever infection will be diagnosed late in the illness on the basis of seroconversion, reducing the opportunity for early targeted treatment. In patients managed in the community, very few will be microbiologically defined.

When a pathogen has been identified, specific treatment as summarised in table 11 is proposed. In transferring patients from empirical to pathogen targeted treatment, the regimen and route of administration will be determined by the continued need for parenteral treatment and known drug intolerance. Hence, table 11 provides preferred and alternative regimens for intravenous or oral administration. However, it should be remembered that approximately 10% (see section 3) of infections will be of mixed aetiology, although many of such co-pathogens will be viral and hence not influenced by antibiotic choice. These recommendations are again based on a synthesis of information which includes the in vitro activity of the drugs, appropriate pharmacokinetics, and clinical evidence of efficacy gleaned from a variety of studies. The choice of agent may be modified following the availability of sensitivity testing or following consultation with a specialist in microbiology, infectious disease, or respiratory medicine.

S pneumoniae highly resistant to penicillin (MIC ≥4 mg/l) is currently uncommon in the UK. However, it is important that the situation is monitored and in future higher doses of penicillins or alternative regimens may need to be considered.

S aureus is an uncommon cause of CAP in the UK. Most community isolates are sensitive to methicillin, although the recent increase in MRSA in hospitalised patients may result in subsequent readmission with an MRSA infection which may include CAP. Options for methicillin sensitive and resistant infections are

> Table 11 - a typographical error in the title, should read 'Recommended therapy...' and a correction has been made to the highlighted text in the 2004 update - ceftriaxone is given once daily, not bd

Table 11   *Recommended treatment of microbiologically documented pneumonia* (local specialist advice should also be sought)*

Pathogen	Preferred	Alternative
S pneumoniae	Amoxicillin 500 mg–1.0 g† 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 2 g od iv
M pneumoniae and *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‡ po or iv
C psittaci and *C burnetii*	Tetracycline 250–500 mg qds po *or* 500 mg bd iv	Erythromycin 500 mg qds *or* clarithromycin 500 mg bd, both po or iv
Legionella spp	Clarithromycin 500 mg bd po *or* iv ± rifampicin§ 600 mg od or bd po/iv	Fluoroquinolone po or iv‡
H influenzae	*Non-β-lactamase-producing:* amoxicillin 500 mg tds po *or* ampicillin 500 mg qds iv *β-lactamase-producing:* co-amoxiclav 625 mg tds po *or* 1.2 g tds iv	Cefuroxime 750 mg–1.5 g tds iv *or* cefotaxime 1–2 g tds iv *or* ceftriaxone 2 g od iv *or* fluoroquinolone‡ po *or* iv
Gram negative enteric bacilli	Cefuroxime 1.5 g tds *or* cefotaxime 1–2 g tds iv *or* ceftriaxone 1–2 g bd iv	Fluoroquinolone‡ iv *or* imipenem 500 mg qds iv *or* meropenem 0.5–1.0 g tds iv
P aeruginosa	Ceftazidime 2 g tds iv *plus* gentamicin *or* tobramycin (dose monitoring)	Ciprofloxacin 400 mg bd iv *or* 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 or iv *MRSA:* vancomycin 1 g bd iv (dose monitoring)	Teicoplanin 400 mg bd iv ± rifampicin 600 mg od *or* bd po/iv

*Can be modified once the results of sensitivity testing are available.
†A higher dose of 1.0 g tds is recommended for infections documented to be caused by less susceptible strains (MIC >1.0 mg/l).
‡Currently UK licensed and available suitable fluoroquinolones include ciprofloxacin, ofloxacin and levofloxacin.
§Concurrent administration of rifampicin reduces the serum level of macrolides; the clinical relevance of this is not known.

based on parenteral administration in view of the serious nature of staphylococcal pneumonia.

Recommendation
- **If a specific pathogen has been identified, the antibiotic recommendations are summarised in table 11. Local microbiological advice is recommended [C].**

8.18 What is the role of the newer antibiotics such as fluoroquinolones, new macrolides, and oxazolidinone derivatives?

Several new antibiotics have become available since the 1993 BTS guidelines were published. Among these are the fluoroquinolones (with improved activity against *S pneumoniae* compared with ciprofloxacin and ofloxacin), the macrolide clarithromycin, and the azalide azithromycin.

The largest class of agents are the fluoroquinolones. These include levofloxacin which is currently licensed in the UK and gatifloxacin, gemifloxacin, and moxifloxacin which are not licensed in the UK at the time of writing[306] [**Ib**]. CAP is likely to be included among their licensed indications. Many of these new agents are active against respiratory "atypical" pathogens and *Legionella* species.[328] Their activity against *S pneumoniae* may also give them a more important role in the future should penicillin and erythromycin resistance continue to increase and be associated with demonstrable clinical failure. However, caution should remain since pneumococcal resistance to the fluoroquinolones, including levofloxacin, is already recognised and has been associated with clinical failures, although varying qualitatively[232] and geographically.

Resistance to fluoroquinolones is mediated by alterations in the target sites, topoisomerase 2 and 4, which is a consequence of mutations in the *gyrA* and *parC* genes, respectively. Whether future respiratory quinolones will be less subject to such mutational resistance will have to await their availability. By limiting recommendations for the empirical use of fluoroquinolones to alternative agents in selected patients managed in hospital, it is hoped that the potential risks of quinolone resistance among pneumococci can be minimised. Such a strategy of restricting use to prevent the emergence of resistance is also recommended by other recent guidelines.[7]

In considering their role in the management of CAP, it is important to note the limited clinical experience to date. There are relatively few studies that have recruited populations of patients representative of UK community and hospital treated patients with CAP.

Fluoroquinolones have also been associated with unexpected side effects. Three fluoroquinolones (sparfloxacin, trovafloxacin, and grepafloxacin) have had their licensing arrangements altered or withdrawn after launch because of the appearance of side effects. Phototoxicity or interactions with theophylline have complicated the use of some of these agents, while prolongation of the QT_c interval and dysrrhythmias have affected others. Hepatotoxicity and features of hypersensitivity have complicated the use of trovafloxacin.

For these reasons, as well as their likely greater acquisition costs, the new fluoroquinolones are not recommended as first line agents or for community use for pneumonia and should be restricted in their use to specific situations. They may provide a useful alternative in selected hospitalised patients with CAP as indicated in table 9, or when there are concerns about the risk of *C difficile* enteropathy with broad spectrum β-lactams.

Clarithromycin, which is available for oral and parenteral administration, has many features that are an improvement on erythromycin[249] [**Ib**]. It is more active against *H influenzae,* is administered twice daily, and is better absorbed with fewer gastrointestinal side effects. The relatively greater acquisition cost, particularly when administered orally, means it is offered as an alternative rather than a preferred choice to erythromycin.

Azithromycin is licensed for the treatment of CAP including pneumococcal pneumonia[244] [**Ib**], [339] [**Ib**]. It has good activity against *Legionella* species in vitro, but there is currently no parenteral formulation in the UK. Despite the high tissue and lung concentrations, blood levels are very low and published experience in treating bacteraemic infections remains limited with occasional failures being reported.[320] For these reasons, as well as cost, this drug has not been included in the recommendations.

Linezolid is the first member of a new class of antibiotic (the oxazolidinones) and was licensed in the UK around the end of 2000. Its major indications are for the treatment of resistant staphylococcal (notably MRSA) and enterococcal infections. It is also active against penicillin susceptible and resistant pneumococci. Although licensed for the treatment of CAP, its use is limited to hospitalised patients. Its restricted spectrum of activity would also require combined treatment. Although available for intravenous and oral use, experience remains limited and hence it is not recommended for empirical treatment. It may have occasional use in the management of documented MRSA infections in those intolerant or unresponsive to other regimens.

Recommendations
- **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, as indicated in table 9 [C].**
- **Oral and parenteral clarithromycin is offered as an alternative to erythromycin [B+].**

9 Complications and failure to improve

9.1 What factors and action should be considered in patients who fail to improve in hospital?

When a patient in hospital with CAP fails to improve with initial management, they should be carefully reviewed. Failure to improve should lead to consideration of the various possibilities summarised in box 6. Elderly patients often respond less rapidly.

In this situation there should be a careful review by an experienced clinician of the clinical history, examination, prescription chart, and results of initial available investigation results. Further investigations, including a repeat chest radiograph, CRP and white cell count, and further specimens for microbiological testing should be considered in the light of any new information after the clinical review. Consideration should be given to referral to a physician with an interest in respiratory medicine.

Recommendations
- **For patients who fail to improve as expected, there should be a careful review by an experienced clinician of the clinical history, examination, prescription chart, and results of all available investigation results [D].**

(A) Incorrect diagnosis or complicating condition

COMMON REASONS
- Pulmonary embolism/infarction
- Pulmonary oedema
- Bronchial carcinoma
- Bronchiectasis
- Slow response in the elderly patient

UNCOMMON REASONS
- Pulmonary eosinophilia/eosinophilic pneumonia
- Cryptogenic organising pneumonia
- Pulmonary alveolar haemorrhage
- Foreign body
- Congenital pulmonary abnormality e.g. lobar sequestration

(B) Unexpected pathogen or pathogens not covered by antibiotic choice
- Pathogens always resistant to common antibiotics (e.g. an "atypical" pathogen not responding to penicillin)
- Pathogens sometimes resistant to commonly used antibiotics (e.g. ampicillin resistant *H influenzae*, penicillin resistant *S pneumoniae,* mycobacteria)

(C) Antibiotic ineffective or causing allergic reaction
- Poor absorption of oral antibiotic
- Inadequate dose
- Antibiotic hypersensitivity
- Patient not receiving or taking prescribed antibiotic

(D) Impaired local or systemic defences
- Local (e.g. bronchiectasis, endobronchial obstruction, aspiration)
- Systemic immune deficiency (e.g. HIV infection, hypogammaglobulinaemia, myeloma)

(E) Local or distant complications of CAP

PULMONARY
- Parapneumonic effusion
- Empyema
- Lung abscess
- Adult respiratory distress syndrome (ARDS)

EXTRAPULMONARY
- Phlebitis at intravenous cannula site
- Metastatic infection
- Septicaemia
- End organ sequelae of septicaemia (e.g. renal failure)

(F) Overwhelming infection

(G) Improvement expected too soon
- In the elderly, for example

Box 6   Reasons for failure to improve as expected.

- **Further investigations including a repeat chest radiograph, CRP and white cell count, and further specimens for microbiological testing should be considered in the light of any new information after the clinical review [D].**

9.2 What are the common complications of CAP?

A brief description of the common complications of CAP is given below. Complications associated with specific infections are summarised in table 12.

PLEURAL EFFUSION AND EMPYEMA

Parapneumonic effusions develop in 36–57% of patients with bacterial pneumonia admitted to hospital and can be the cause of persisting pyrexia despite adequate antibiotic treatment[340] [**II**]. The presence of bilateral pleural effusions in CAP is associated with increased mortality[195]

Table 12   Some complications associated with specific infections

Pathogen	Complications
S pneumoniae	Septicaemia Pyopneumothorax Pericarditis/endocarditis Meningitis/brain abscess Peritonitis Arthritis Herpes labialis
M pneumoniae	Meningoencephalitis Aseptic meningitis Guillain-Barré syndrome Transverse myelitis Cerebellar ataxia Ascending polyneuropathy Pericarditis Myocarditis Diarrhoea Haemolytic anaemia Skin rashes Polyarthropathy Hepatitis Pancreatitis Splenomegaly Acute glomerulonephritis Haemorrhagic myringitis
Legionella spp	Confusion Encephalomyelitis Guillain-Barré syndrome Cerebellar signs Pericarditis Hyponatraemia Renal failure Rhabdomyolysis and myositis Diarrhoea Polyarthropathy Jaundice/abnormal liver function Pancreatitis Thrombocytopenia
C burnetii	Optic neuritis Hepatitis Haemolytic anaemia Osteomyelitis Endocarditis with chronic infection
S aureus	Pneumatoceles and/or pneumothorax (especially in children) Septicaemia Lung abscess Metastatic infection

[**II**]. Although most effusions will resolve with antibiotic treatment alone, it is recommended that thoracocentesis is performed promptly in patients admitted to hospital with parapneumonic effusion. Those patients found to have an empyema (defined as the detection of cloudy fluid, pus or organisms on Gram's stain or culture[341] [**II**]) or a complicated parapneumonic effusion (defined as clear pleural fluid with a pH of <7.2[342] [**II**]) should then have early and effective pleural space drainage. Pleural fluid for measurement of pH should be collected anaerobically in a heparinised blood gas syringe and measurement should be performed in a blood gas analyser. While empyema has become relatively uncommon, delayed thoracocentesis and chest tube drainage leads to longer and more costly hospitalisation[340] [**III**]. Further details of the management of empyema will be available in the BTS guidelines on the management of patients with pleural disease which are in preparation.

Recommendations
- **Early thoracocentesis is indicated for all patients with parapneumonic effusion [D].**
- **Those found to have an empyema or clear pleural fluid with pH <7.2 should have early and effective pleural fluid drainage [C].**
- **The BTS guidelines on the management of empyema should be followed [D].**

LUNG ABSCESS

Lung abscess is a rare complication of CAP, being seen most commonly in the debilitated or alcoholic patient and following aspiration. Infection with anaerobic bacteria, *S aureus*, Gram negative enteric bacilli, or *S milleri* (in the presence of poor dental hygiene) should be considered. Although most patients respond to appropriate antibiotics, early surgical drainage via pneumonotomy may occasionally be needed. Patients with lung abscess may require a prolonged course of antibiotics.

Recommendations
- **Less usual respiratory pathogens including anaerobes, *S aureus*, Gram negative enteric bacilli, and *S milleri* should be considered in the presence of lung abscess [D].**
- **Prolonged antibiotic treatment and occasionally surgical drainage should be considered [D].**

METASTATIC INFECTION

Patients with septicaemia associated with pneumonia can occasionally develop metastatic infection. Meningitis, peritonitis, endocarditis, and septic arthritis have all been reported. Purulent pericarditis can occur, usually in direct relation to an empyema.

Most such complications can be detected by careful history and examination.

10   Prevention and vaccination strategies

10.1 Introduction
Although considerable progress has been made over recent years in antimicrobial treatment and supportive care for patients with CAP, the issue of prevention remains important especially for those at "high risk". Vaccines against influenza A and against *S pneumoniae* are available currently.

10.2 Influenza virus and vaccination
Influenza is an acute viral infection of the respiratory tract affecting all age groups. It is usually self-limiting with recovery in 2–7 days, but can be complicated by bronchitis, otitis media in children, and secondary bacterial pneumonia notably due to *S aureus*. Primary influenza pneumonia occurs but is rare and carries a high mortality rate. The greatest mortality from influenza is in patients with underlying disease such as severe chronic respiratory, cardiac, or renal disease or diabetes mellitus[343 344] [**Ib**], particularly in those aged over 65 years[343 345] [**III**]. In patients over 65 years death from influenza occurs predominantly due to secondary bacterial pneumonia and cardiac failure and not primary infection[346] [**Ib**].

INFLUENZA VIRUS
Influenza viruses are single stranded, segmented RNA viruses belonging to the family Orthomyxoviridae. Two forms of influenza virus are responsible for most clinical illness—influenza A and influenza B. Influenza C only gives rise to an acute pharyngitis. Outbreaks of influenza A occur most years and can cause epidemics (defined as >300 cases per 100 000 patients at risk). Influenza B can also cause outbreaks but these tend to be less extensive and to be associated with less severe illness. Pandemics result from the emergence of new viruses in which there are major changes in the surface proteins, mainly haemagglutinin (H) and neuraminidase (N). Influenza A viruses are antigenically labile and minor changes in these surface proteins ("antigenic drift") occur progressively from season to season. Major changes ("antigenic shift") due to acquisition of a "new" haemagglutinin results in the emergence of modified viruses against which the population has little or no immunity. Influenza B viruses are also prone to antigenic drift but with less frequent changes. The World Health Organisation monitors influenza viruses throughout the world and makes recommendations each year about the strains to be included in vaccines for the forthcoming winter.

INFLUENZA VACCINE
Influenza vaccine is prepared each year using viruses similar to those considered most likely to be circulating in the forthcoming winter. The viruses are grown in the allantoic cavity of chick embryos and are therefore contraindicated in individuals with egg allergy. They are then chemically inactivated, treated, and purified. Current vaccines are trivalent containing two type A and one type B subtype viruses. Two types of vaccine are available—those prepared by disrupting whole viruses using organic solvents for detergents ("split virus vaccines") and those which contain purified H and N surface antigens ("surface antigen vaccines"). Both vaccines are given as a single 0.5 ml intramuscular injection and are equivalent in efficacy and adverse reactions. Vaccines should be stored at 2–8°C and protected from the light. They must not be frozen. They should be allowed to reach room temperature and shaken well before they are given.

In the UK immunisation is currently recommended for those of all ages with:
- chronic respiratory disease including asthma;
- chronic heart disease;
- chronic renal disease;
- immunosuppression due to disease or treatment;
- diabetes mellitus;
- all those aged 65 years or older;
- those in long stay residential care.

ADVERSE EFFECTS
Uptake of influenza immunisation by those for whom it is recommended is low in many countries[347 348] [**III**]. Patients are often concerned about side effects and both doctors and patients may have doubts about the protective efficacy of the vaccine. Reported side effects include fever, myalgia, and local and systemic allergic reactions but, in a randomised double blind controlled study of 1806 patients aged 60 years or older, only discomfort at the injection site was more common in the vaccinated group[349] [**Ib**].

EVIDENCE OF EFFICACY
Evidence of the efficacy of influenza vaccine in humans has derived from three types of clinical studies: experimental studies in which volunteers are challenged by live viruses under strictly controlled circumstances; field studies which register morbidity and mortality during naturally occurring influenza outbreaks; and immune response studies which measure antibody responses as a surrogate marker for protection against influenza infection. Experimental studies are not applicable in populations at risk of serious complications from influenza infection.

Several large well designed case-control field studies from North America have focused on the efficacy of influenza vaccine in reducing admissions for pneumonia and influenza in those over 65 years of age and in the reduction of mortality[346 350–352] [**Ia**]. They show that influenza vaccination reduces hospital deaths from pneumonia and influenza by about 65% and from all respiratory causes by 45%. Vaccination is also associated with fewer hospital admissions for pneumonia and influenza and fewer

> 10.2 Evidence of Efficacy - Further evidence is available in the 2004 update.

outpatient visits for all respiratory conditions in those aged 65 years and over with chronic lung disease[353] [**III**].

In a further UK case-control study of 315 deaths during the 1989–90 influenza epidemic and 770 matched controls, vaccination reduced mortality by 41%[344] [**Ia**]. In subjects who received the vaccine for the first time in 1989 vaccination reduced mortality by 9%, while in those who had been previously vaccinated mortality was reduced by 75%. Vaccination was also found to be equally effective in reducing mortality in nursing homes as in the community. Such studies may tend to underestimate the protective effect of influenza vaccination as some illnesses considered to be influenza are likely to be caused by other coincidental pathogens.

Possibly the most impressive evidence of the efficacy of vaccination has come from the Netherlands where a randomised double blind controlled trial of influenza vaccine in subjects over 65 years of age reduced the incidence of serologically proven influenza by 50%[354] [**Ib**]. In a meta-analysis of 20 cohort studies of patients aged over 65 the pooled estimates of the efficacy of vaccination were 56% for preventing respiratory illness, 53% for preventing pneumonia, 50% for preventing admission to hospital, and 68% for preventing death[355] [**Ia**].

Immune response studies support these findings and show that the protection rate from influenza vaccine judged by serological testing is over 75% for influenza A and 51–97% for influenza B[356] [**Ib**]. A recent meta-analysis of seven field studies (including 13 trials) and 12 immune response studies (including 53 trials) confirmed that protection does not decrease with annual repeated influenza vaccination[357] [**Ia**].

EFFICACY IN LOW RISK GROUPS
While studies in "high risk" groups including those over 65 years of age have shown benefit from influenza vaccination, it remains unclear whether healthy working adults and, particularly, those in the medical and nursing professions should be offered immunisation. In a randomised, double blind, placebo controlled trial in Los Angeles, 179 hospital employees showed no clear reduction in influenza-like illness, severity of illness or sick absenteeism[358] [**Ib**]. In contrast, a study of 849 subjects in Minneapolis randomly assigned influenza vaccine or placebo showed 25% fewer episodes of upper respiratory illness, 43% fewer days of sick leave, and 44% fewer visits to physicians' offices for upper respiratory tract illness in those receiving active vaccine[346] [**IIa**]. Similarly, influenza vaccination prevented infection by influenza A and B in 264 healthy hospital based healthcare professionals of mean age 28 years and may reduce cumulative days of illness and absence[359] [**Ib**]. Although there is currently insufficient evidence on which to base a clear recommendation about the routine immunisation of healthcare workers, the Department of Health in the UK now advises National Health Service employers to offer influenza vaccination to all staff.

FUTURE DEVELOPMENT
Intranasal vaccination appears to be highly effective and has been shown to reduce the incidence of laboratory confirmed influenza A in nursing home residents when compared with inactivated vaccine alone.[360] New forms of delivery system are also being developed including an oral vaccine using biodegradable microspheres designed to be taken up in the small bowel and reformulations of influenza vaccine with antigen delivery systems which produce significantly greater increases in antibody response.

Recommendations (based on the Departments of Health guidelines)
- **Influenza vaccination is recommended for those at "high risk" of mortality from influenza or pneumonia [C].**
- **These "high risk" groups include those with chronic lung, heart, renal and liver disease, diabetes mellitus, immunosuppression due to disease or treatment, and those aged over 65 years[C].**
- **Influenza vaccine is contraindicated for those with hypersensitivity to hens' eggs [C].**

10.3 Pneumococcal vaccination

S pneumoniae, the most common aetiological cause of CAP, is an encapsulated Gram positive coccus. The capsule is composed of one of 90 serologically distinct polysaccharides and virulence of the organism appears to be determined by the nature of this capsule. Immunity to pneumococci depends largely on production of type specific anticapsular antibodies. Geographical, temporal, and age differences in the distribution of the 90 different serotypes and the ability of *S pneumoniae* to transfer capsular genes from one strain to another[361 362] all have implications for vaccination strategy. The current 23-valent vaccine includes serotypes that cause 88% of the bacteraemic infections in the USA and 96% of those in the UK.[363]

PNEUMOCOCCAL VACCINE
Pneumococcal vaccine is a polyvalent vaccine containing 25 mg purified capsular polysaccharide from each of 23 capsular types of *S pneumoniae*. It is supplied in single dose vials and should be stored at 2–8°C. A single dose of 0.5 ml is given subcutaneously or, preferably, intramuscularly into the deltoid muscle or lateral aspect of the mid thigh. Mild soreness and induration at the site of injection is common and a low grade fever occasionally occurs. Re-immunisation is not normally advised and is contraindicated within 3 years because of the risk of severe reactions. Such reactions appear to relate to high levels of circulating antibodies. Pneumococcal vaccine should not be given during acute infection and is not recommended during pregnancy or lactation. However, in those aged over 65 years it can be given safely at the same time as influenza vaccine at a different site[364] [**Ib**].

In the UK pneumococcal vaccine is recommended by the Department of Health for all those aged 2 years or older in whom pneumococcal infection is likely to be more common or more dangerous. Such groups include those with:

- asplenia;
- severe dysfunction of the spleen including sickle cell disease and coeliac disease;
- chronic renal disease or nephrotic syndrome;
- chronic heart disease;
- chronic lung disease;
- chronic liver disease including cirrhosis;
- diabetes mellitus;
- immunodeficiency or immunosuppression due to disease or treatment including HIV infection.

ANTIBODY RESPONSE

Pneumococcal vaccination given to middle aged and elderly patients (age range 50–85 years) at follow up 8 weeks after treatment in hospital for pneumonia has been shown to produce an antibody response without severe adverse reactions[365] [**Ib**]. A case-control study of adults aged 33–85 years of age showed that antibody levels appeared to wane 6 years after immunisation[366] [**IIa**]. However, the level of pneumococcal antibody required for protection is not currently known. The newer CRM_{197} conjugated pneumococcal oligosaccharide vaccines do not appear to offer any advantages over polysaccharide vaccines in those aged over 60 years[367] [**IIb**].

CLINICAL EFFICACY OF PNEUMOCOCCAL VACCINE

> 10.3 Clinical Efficacy of Pneumococcal vaccine - further evidence is available in the 2004 update.

The results of numerous efficacy studies have found it difficult to reach firm recommendations. A meta-analysis of nine randomised controlled trials with 12 vaccine treated and control study groups comprising 40 431 individuals has shown that pneumococcal vaccination offers protection of around 66% against definitive pneumococcal pneumonia with bacteraemia for normal or "low risk" adults[368] [**Ia**]. Surprisingly, this effect could not be shown for the more heterogeneous group of "high risk" patients who are those for whom vaccination is recommended. It seems likely that some of the trials included lacked sufficient size to show protection in those aged over 65 years and other "high risk" groups.

Furthermore, the vaccine could not be shown to protect against pneumonia (all causes) or mortality due to pneumococcal pneumonia in those aged 60–70 years[368] [**Ia**]. However, a recent 2 year retrospective cohort study of 1898 subjects aged over 65 years with chronic lung disease reported that pneumococcal vaccination was associated with fewer hospital admissions for pneumonia, fewer deaths, and direct medical care cost savings[369] [**III**].

At the present time it seems reasonable to conclude that, at least in immunocompetent patients, the current 23-valent vaccine may be clinically effective for preventing pneumococcal pneumonia with associated bacteraemia. Efficacy in immunocompromised patients or other "high risk" groups is much less certain.

Recommendations (based on the Departments of Health guidelines)

- **While pneumococcal vaccination is recommended by the Departments of Health for all those aged 2 years or older in whom pneumococcal infection is likely to be more common or serious, there is no evidence that it is effective in such "at risk" groups [A+].**
- **Pneumococcal vaccine should not be given during acute infection and is not recommended during pregnancy. Re-immunisation within 3 years is contra-indicated [C].**
- **Pneumococcal and influenza vaccines can be given together at different sites [A–].**

11 Acknowledgements and declaration of interest

11.1 Acknowledgements

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11.2 Declaration of interests of committee members

The committee members fulfilled the requirements of the British Thoracic Society regarding personal declaration of interests. Declaration of Interest forms were updated annually by committee members and contents shared within the committee and with the Secretary of the British Thoracic Society.

A summary of declarations of interests for the life time of the committee is given below:

TB has received research funding from Eisai Ltd, lecture fees from Aventis and support for attending conferences from Wyeth; GD has received research funding from SmithKline Beecham and Astra, lecture fees from Allen and Hanburys and support for attending conferences from Allen and Hanburys and 3M; RGF has received consultancy fees from Glaxo Wellcome, Nexstar, Bristol Myers Squibb, SmithKline Beecham, AstraZeneca, Pharmacia, Parke Davis and Pantherix, research funding from GlaxoWellcome and Pharmacia, and support for attending conferences from Glaxo Wellcome, Aventis, Wyeth, and Biomerieux; WFH has received consultancy fees from GlaxoWellcome, Schering Plough, Boehringer Ingleheim, Hoechst Marion Roussel, Astra, 3M, Zeneca and Rhone Poulenc Rorer, research funding from 3M and Rhone Poulenc Rorer, and support for attending conferences or courses from GlaxoWellcome, Schering Plough, Zeneca and 3M; DH has received consultancy fees from Bayer, GlaxoWellcome, SmithKline Beecham, Pfizer, Abbott and Bristol Myers Squibb, research funding from Hoechst Marion Roussel, SmithKline Beecham, Pharmacia/Upjohn, Grunenthal and Abbott, lecturing fees from Key Med, Hoechst Marion Roussel, GlaxoWellcome, Bayer and Schering Plough, and support for attending conferences and meetings from Bayer, Glaxo Wellcome, Schering Plough, SmithKline Beecham and Abbott; DH holds shares in SmithKline Beecham; WSL has received research funding from Hoechst Marion Roussel and Bayer and support for attending conferences from Bayer; JTM has received consultancy fees from Pfizer, Abbott, Hoechst Marion Roussel, Trinity, GlaxoWellcome, research funding from Hoechst Marion Roussel, Rhone Poulenc Rorer and Bayer, lecture fees from AstraZeneca, Hoechst Marion Roussel and Pfizer, and support for attending conferences from Astra, Pfizer, Allen and Hanburys and 3M; RM—none declared; DN has received consultancy fees from Pharmacia/Upjohn and Bayer and research funding from Hoechst Marion Roussel and Pharmacia/Upjohn; PS—none declared; MAW has received consultancy fees from Bayer, Glaxo, and Pfizer, lecture fees from Abbott, Pasteur Merieux, Bayer, Wyeth and Glaxo, and support to attend conferences from Schering Plough, Pasteur Merieux, Glaxo and Boehringer Ingelheim; JW—none declared.

11.3 Affiliations and addresses of committee members

Pneumonia Guidelines Committee of the British Thoracic Society Standards of Care Committee: Dr J Macfarlane (Chairman and Editor), Consultant Physician, Nottingham City Hospital; Dr T Boswell, Consultant Microbiologist, Nottingham City Hospital; Dr G Douglas, Consultant Physician in Respiratory Medicine and Infection, Aberdeen Royal Infirmary; Professor R Finch, Professor of Infectious Diseases, University of Nottingham, Nottingham City Hospital; Dr W Holmes, General Practitioner, Sherrington Park Medical Practice, Nottingham; Dr D Honeybourne, Consultant Physician, Heartlands Hospital, Birmingham; Dr W S Lim, Specialist Registrar in General and Respiratory Medicine, Nottingham City Hospital; Mr R Marriott, Senior Medical Librarian, Nottingham City Hospital; Dr D Nathwani, Consultant Physician in Infectious Diseases, Kings Cross Hospital, Dundee; Dr P Saul, General Practitioner, Beech Avenue Health Centre, Wrexham; Dr M Woodhead, Consultant Physician, Manchester Royal Infirmary; Dr J Wyatt, Director of Knowledge Management Centre, School of Public Policy, University College, London.

Appendix 1   Check list used by reviewers for appraising studies

Study: .... Reviewer: ....

Please complete section 1 first. If study OK, complete one of sections 2a–d, as appropriate.

1. General: is the study relevant to our question ?

☐ Were the patients studied similar (in age, sex, disease severity...) to target patients?

☐ Were the outcome measures of interest to us and our patients ?

☐ Was the clinical setting (primary care, intensive care...) similar to our setting ?

☐ Was the study carried out in a healthcare system similar to ours ?

☐ Is the study design recognisable and appropriate, with clear methods described ?

☐ Is the study recent enough to take account of any important advances ?

☐ If negative, was this study large enough to provide useful information ?

2a. Studies of cause and effect (randomised trial of treatment)

☐ Was assignment of patients to treatment truly randomised ?

☐ Was the planned treatment concealed from those recruiting patients before enrolment ?

☐ Were all patients who entered the study accounted for ?

☐ Were patients analysed in the groups to which they were initially randomised ?

☐ Were patients and doctors blind to the treatment given ?

☐ Were groups treated the same way, apart from the treatment ?

☐ Were the groups similar at the start of the trial ?

2b. Studies of aetiology (case-control study of a harmful agent)

☐ Were there two groups of cases, similar except for exposure to a harmful agent ?

☐ Was occurrence of the outcome measured in the same way for both groups ?

☐ Were enough patients followed up for long enough for the outcome to develop ?

☐ Did exposure clearly precede the outcome ?

☐ Was there a dose-response gradient ?

☐ Was there a re-challenge, or improvement after the drug stopped?

☐ Does the association make biological sense ?

2c. Studies of diagnosis (evaluation of clinical findings or tests)

☐ Was the finding or result compared with a 24 carat gold standard for diagnosis ?

☐ Was the finding or result determined blind to the gold standard ?

☐ Was the gold standard determined blind to the finding or test result ?

☐ Was the gold standard determined in all cases, not just those with an abnormal result ?

2d. Studies of prognosis, prognostic index (cohort studies)

☐ Was a defined sample of patients assembled at an early stage of the disease ?

☐ Were patients followed up long enough for the outcome to develop ?

☐ Was the outcome clearly defined, objective and assessed blind to exposure in all cases?

☐ Was the performance of any prognostic index tested on a fresh set of cases ?

3. Comments:

Appendix 2   Additional checklist used for appraising studies to inform pneumonia aetiology

Absolute requirements:
- Is this an original report ?
- Were patients with community acquired pneumonia separately identified?
- Was the study designed to assess community acquired pneumonia aetiology?
- Was the patient sample representative (e.g. sufficient numbers, consecutive cases, exclusions clearly defined)?
- Was the study of sufficient duration to exclude seasonal bias?

Data qualification:
- Is the geographical area clear and relevant?
- Is the patient age group defined?
- Are microbial investigations clearly defined?
- Was the investigation biased toward a specific pathogen?
- Is the setting community, hospital, intensive care or a combination?

Appendix 3 Types of study and levels of evidence used to illuminate specific clinical questions

Type of clinical question	Evidence level	Brief definition	Types of study providing this level of evidence
Treatment:	Ia	A good recent systematic review	Systematic review of randomised trials
	Ib	A rigorous study designed to answer the question	A rigorous randomised trial comparing T with best alternative
	II	One or more prospective clinical studies	A cohort study or faulty randomised trial
• Is treatment (T) effective?	III	One or more retrospective clinical studies	A case control study
	IVa	Formal expert consensus	Delphi study of expert practice
	IVb	Other information	Study of pharmacology of T
Aetiology or harm:	Ia	A good recent systematic review	Systematic review of cohort studies
	Ib	A rigorous study designed to answer the question	A large, well designed cohort study
• Does the aetiological agent (A) cause disease?	II	One or more prospective clinical studies	A faulty cohort study
• Does a certain drug (D) cause a specific side effect?	III	One or more retrospective clinical studies	A case control study
	IVa	Formal expert consensus	Delphi study of expert opinion
	IVb	Other information	Study of pathophysiology of D
Diagnosis or prognosis:	Ia	A good recent systematic review	Systematic review of blind comparisons of T with gold standard
• Is the investigation (T) an accurate test for diagnosis of the disease (D)?	Ib	A rigorous study designed to answer the question	Blind prospective comparison of T, F or M with gold standard for D or E (eg. response to specific therapy) with multivariate analysis
• Is finding (F) an accurate predictor of event or outcome (E)?	II	One or more prospective clinical studies	Analysis of prospective test results in patients enrolled in an RCT of therapy for varying stages of D. Prospective validation study with univariate analysis
• Does severity measure accurately predict event or outcome (E)?	III	One or more retrospective clinical studies	Retrospective study of test results or findings in a database of patients with univariate or multivariate analysis
	IVa	Formal expert consensus	Delphi study of expert opinion about T
	IVb	Other information	Study of pathophysiology of D
Public health, health policy:	Ia	Economic and policy analysis based on good recent systematic reviews	Economic and policy analysis with modelling and sensitivity analysis using data from SRs of effectiveness and SRs of cost studies in the same routine clinical settings
• Is policy (P) cost effective in the National Health Service?	Ib	Economic and policy analysis based on a rigorous study designed to answer the question	Economic and policy analysis with modelling and sensitivity analysis using data from an RCT of effectiveness and a cost study in the same routine clinical setting
	II	Economic and policy analysis based on one or more prospective clinical studies	Economic and policy analysis with modelling and sensitivity analysis using other prospective data in various settings
	III	Economic and policy analysis based on one or more retrospective clinical studies	Economic and policy analysis with modelling and sensitivity analysis using retrospective data
	IVa	Formal expert consensus	Delphi study of national expert opinion about P
	IVb	Other information	Local opinion about P

Appendix 4   Generic levels of evidence and guideline statement grades, appropriate across all types of clinical questions

Evidence level	Definition	Example of study providing this level of evidence for a therapy question	Guideline statement grade
Ia	A good recent systematic review of studies designed to answer the question of interest	Cochrane systematic review of randomised controlled trials studying the effectiveness of flu vaccines	**A+**
Ib	One or more rigorous studies designed to answer the question, but not formally combined	Randomised controlled trial of effectiveness of a flu vaccine	**A–**
II*	One or more prospective clinical studies which illuminate, but do not rigorously answer, the question	Prospective cohort study comparing pneumonia rates in patients who are and are not vaccinated against flu; non-randomised controlled trial	**B+**
III†	One or more retrospective clinical studies which illuminate but do not rigorously answer the question	Audit or retrospective case control study, comparing flu vaccination history in patients who did and did not present with pneumonia	**B–**
IVa‡	Formal combination of expert views	Delphi study of UK expert recommendations for flu vaccination	**C**
IVb	Other information	Expert opinion, informal consensus; in vitro or in vivo studies on related topics	**D**

*Hard to differentiate AHCPR's "well designed controlled study without randomisation" (level IIa) from "other type of well designed experimental study" (level IIb).

†Major criterion is retrospective versus prospective data collection since non-experimental designs are better suited than even RCTs for answering certain questions.

‡Distinguish formal consensus from informal consensus methods according to HTA systematic review (1998).

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