# **BMJ** Best Practice

Community-acquired pneumonia in adults (non COVID-19)

Straight to the point of care



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# Summary

Community-acquired pneumonia (CAP) typically presents with symptoms and signs consistent with a lower respiratory tract infection (i.e., cough, dyspnoea, pleuritic chest pain, mucopurulent sputum, myalgia, fever) and no other explanation for the illness. Older people present more frequently with confusion or worsening of pre-existing conditions, and without chest signs or fever.

Confirm diagnosis in all patients presenting to hospital with evidence of consolidation (new shadowing that is not due to any other cause) on chest x-ray. A chest x-ray should not be requested routinely for patients managed in the community.

Use the CURB-65 mortality risk score (hospital setting) or CRB-65 severity score (community setting), together with your clinical judgement, to decide whether to manage the patient in hospital or at home and to determine appropriate therapy.

Initial treatment is with empirical antibiotics, following national/international guidelines and local epidemiology. In hospital, administer antibiotics within 4 hours of presentation.

Send sputum and blood samples for culture in people with moderate- or high-severity CAP, ideally before antibiotics are started, and consider legionella and pneumococcal urine antigen testing.

Give supplemental oxygen to patients with oxygen saturation <94% (or <88% in patients at risk of CO  $_2$  retention).

Consider sepsis whenever an acutely unwell person presents with likely infection, even if their temperature is normal. Follow your local protocol for prompt management of all patients with suspected sepsis, or those at risk.

# Definition

Community-acquired pneumonia (CAP) is defined as pneumonia acquired outside hospital or healthcare facilities. Clinical diagnosis is based on a group of signs and symptoms related to lower respiratory tract infection with presence of fever >38°C (>100°F), cough, mucopurulent sputum, pleuritic chest pain, dyspnoea, and new focal chest signs on examination such as crackles or bronchial breathing. Older patients present more frequently with confusion or worsening of pre-existing conditions, and without chest signs or fever.[1]

This topic focuses on the diagnosis and management of non-COVID-19 CAP in adults. For patients with suspected or confirmed COVID-19 pneumonia, see our topic [Coronavirus disease 2019 (COVID-19)] . Consider all patients with cough, fever, or other suggestive symptoms to have COVID-19 until proven otherwise. Pneumonia due to COVID-19 is not covered in this topic.

In 2019, lower respiratory tract infections affected 489 million people worldwide, and were the cause for approximately 2.5 million deaths. Children <5 years old and adults >70 years old were the populations most affected by pneumonia. Mortality was highest in patients aged >70 years old. Lower respiratory tract infections were the leading cause of infectious disease mortality worldwide in 2019.[4] [5]

A literature review found that the overall annual incidence of CAP in Europe is between 1.07 and 1.2 per 1000 person-years and 1.54 and 1.7 per 1000 people.[6] The incidence of CAP increases with age to 14 per 1000 person-years in adults aged ≥65 years, and the incidence of CAP appears to be significantly higher in men than in women.[6] It is the fifth leading cause of mortality in Europe.[7] Estimates of mortality among patients range from 1% to 5% in outpatients, from 5.7% to 14% in general wards, and from 34% to 50% in the intensive care unit (especially in ventilated patients).[8] [9] Another study reported that mortality rates of CAP in Europe vary widely from country to country, ranging between <1% and 48%.[10] The mortality rate for pneumococcal pneumonia is about 5%, rising to between 6% and 30% in adults with associated bacteraemia.[11] [12]

# **Risk factors**

# Strong

# age >65 years

Incidence increases significantly with age. Very advanced age has been associated with higher mortality from CAP.[34]

# residence in a healthcare setting

Approximately 10% to 18% of all patients hospitalised for pneumonia are nursing home residents. Mortality in these patients may reach 55%. [35] [36] Patients in residential homes who develop pneumonia have traditionally been considered to have healthcare-associated pneumonia (HCAP) and not CAP. However, this definition has been criticised because it is not able to distinguish patients at risk for resistant pathogens, and each patient ought to be evaluated individually.

# COPD

Associated with a 2- to 4-fold increased risk of CAP.[6] Data from one study conducted in patients with CAP compared the outcome of patients with and without COPD and found that the presence of COPD was an independent risk factor for mortality.[37]

# exposure to cigarette smoke

Colonisation with pathogenic bacteria is frequent in smokers and presents an increased risk of lung infections, especially pneumococcal pneumonia.[38] One study of bacterial pneumonia found that HIV-infected smokers had >80% higher risk of developing pneumonia than those who had never smoked.[12] [39] Another study showed that current smokers with pneumococcal CAP often develop sepsis and require hospitalisation at a younger age despite having fewer comorbid conditions than older patients. [40] Current and former smokers are more likely to develop CAP than neversmokers.[41] Passive smoking at home is a risk factor for CAP in people aged 65 years or older.[41] [42]

# alcohol abuse

There is clear evidence that alcohol consumption increases the risk for CAP. A meta-analysis of 14 studies found that people who consumed alcohol at all or in higher amounts had an 83% higher risk of CAP compared to people who consumed no alcohol or lower amounts (relative risk of 1.83).[43] Consumption of 24 g, 60 g, and 120 g of pure alcohol daily has been shown to result in a relative risk for incident CAP of 1.12 (95% CI, 1.02-1.23), 1.33 (95% CI, 1.06-1.67), and 1.76 (95% CI, 1.13-2.77), respectively, relative to non-drinkers.[44]

### poor oral hygiene

Oral and respiratory bacteria in dental plaques are shed into the saliva and can then be aspirated into the lower respiratory tract to cause infection. Aspiration pneumonia is one of the most serious problems in older patients. Low-quality evidence suggests that professional oral health care measures (e.g., brushing, swabbing, denture cleaning, mouth rinses) may reduce mortality due to pneumonia in nursing home residents compared to usual care, however the effect of these measures on preventing pneumonia remains unclear.[45]

### use of acid-reducing drugs

CAP is one of the most common adverse effects associated with use of proton-pump inhibitors.[46] This is thought to be due to a decrease in gastric acid secretion, which allows pathogens to colonise the upper respiratory tract more easily. Outpatient use of these drugs is associated with a 1.5-fold increased risk of CAP.[47] H2 antagonists may also be associated with an increased risk of CAP.[48]

### contact with children

Regular contact with children is associated with an increased risk of CAP.[49] Two studies have reported that having children in the household increases the adjusted odds ratio from 1.00 for households with no children to 3.2, or 3.41 for households with 3 or more children.[50] [51]

# Weak

# diabetes mellitus

Associated with a moderate increase in the risk of CAP. The main reasons are the increased risk of aspiration, hyperglycaemia, decreased immunity and impaired lung function, and coexisting morbidity.

One study found that diabetes (type 1 and type 2) was a risk factor for pneumonia-linked hospitalisation. Another study[52] reported that pre-existing diabetes was associated with a higher risk of death after hospitalisation for CAP compared with patients hospitalised for non-infectious illnesses.[53] The risk of severe pneumococcal bacteraemia is also higher in diabetic patients.[54]

#### chronic renal disease

A significant risk factor for mortality in patients with CAP.[55] [56]

### chronic liver disease

It is known that bacterial infections occur in 32% to 34% of hospitalised patients with cirrhosis, and approximately 15% of these infections are pneumonia (the third most common cause of infection in these patients).[57] One study reported that chronic liver disease is a risk factor for pulmonary complications in patients hospitalised with pneumococcal pneumonia.[58]

Theory

# use of opioids

A case-control study found that prescribed opioids, especially those with immunosuppressive properties or higher doses, are associated with an increased risk of CAP in people with and without HIV infection.[59]

# Aetiology

*Streptococcus pneumoniae* (the pneumococcus) is the most common causative pathogen of CAP across a range of severities and patient ages.[13] [14] [15] [16] [17] However, other studies have found that influenza virus is the most common cause of CAP in adults.[7] [18] In Europe and the US, *S pneumoniae* accounts for about 30% to 35% of cases.[14] [19] Other bacterial causes include *Haemophilus influenzae*, *Staphylococcus aureus* (including MRSA), group A streptococci, and *Legionella* spp. For example, *Legionella pneumophila* (especially serogroup 1) accounts for 2% to 6% of CAP in immunocompetent patients.[20]

Atypical bacteria are also common causes, although they vary in frequency depending on the year and any epidemics.[17] [21] The incidence of atypical pathogens in community-acquired pneumonia is approximately 22% globally, but this varies with location.[22] Commonly reported atypical bacteria include *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Chlamydia psittaci* and *Coxiella burnetii*.[1] These pathogens are difficult to diagnose early in the illness and are sensitive to antibiotics other than beta-lactams (e.g., macrolides, tetracyclines or fluoroquinolones).[1]

*M pneumoniae* accounts for up to 37% of CAP patients treated as outpatients and 10% of patients who are hospitalised.[14] *C pneumoniae* accounts for 5% to 15% of cases of CAP. However, a Dutch study identified *C psittaci* by polymerase chain reaction (PCR) of sputum (when available) as a cause of CAP in 4.8% of cases.[23] One German study identified *C burnetii* by PCR and/or antibody detection as the cause of CAP in 3.5% of patients.[24]

*Pseudomonas aeruginosa* may also be prevalent in patients with pneumonia, depending on the region; however, it is more common in hospital-acquired and ventilator-associated pneumonia compared with CAP. It accounted for 7.7% of all isolates in CAP in a systematic review in China.[25]

Respiratory viruses are reported in about 10% to 30% of immunocompetent adults hospitalised with CAP.[14] [26] [27] [28] Influenza virus A/B, respiratory syncytial virus, adenovirus, rhinovirus, and parainfluenza virus are the most common viral causes of CAP in immunocompetent adults. Newer pathogens reported to cause CAP include metapneumovirus and coronaviruses.[29] Detection of viral causes is increasing because of the use of PCR.

Polymicrobial aetiology in CAP varies from 5.7% to 13%, depending on the population and the microbiological diagnostic test used.[14] [27] [30]

# Pathophysiology

Pneumonia develops subsequent to the invasion and overgrowth of a pathogenic micro-organism in the lung parenchyma, which overwhelms host defences and produces intra-alveolar exudates.[31]

The development and severity of pneumonia is a balance between pathogen factors (virulence, inoculum size) and host factors. The likely microbial causes of CAP differ according to a number of factors, including

differences in local epidemiology, the setting (outpatients, hospitalised, or intensive care unit), severity of disease, and patient characteristics (e.g., sex, age, and comorbidities).[14]

Microbes that are present in the upper airways can enter the lower airways by microaspiration. Nevertheless, the defence mechanisms of the lungs (innate and acquired) keep the lower airways sterile. The development of pneumonia indicates a defect in host defences, exposure to a particularly virulent micro-organism, or a large inoculum size.

Impaired immune response (e.g., caused by HIV infection or advanced age) or dysfunction of defence mechanism (e.g., through current or passive smoking, COPD, or aspiration) leads to greater susceptibility to respiratory infections in patients.[6]

Pathogens can reach the lower respiratory tract by 4 mechanisms:

- Inhalation, a common route of entry for viral and atypical pneumonia in younger healthy patients. Infectious aerosols are inhaled into the respiratory tract of a susceptible person to initiate infection
- Aspiration of oropharyngeal secretions into the trachea, the primary route through which pathogens enter the lower airways
- Haematogenous spread from a localised infected site (e.g., right-sided endocarditis)[32]
- Direct extension from adjacent infected foci (e.g., tuberculosis can spread contiguously from the lymph nodes to the pericardium or the lung, albeit rarely).

There is a new theory that CAP may result from dysbiosis of the normal lung flora, rather than invasion of pathogenic micro-organisms in a sterile environment; however, this model requires further research.[33]

# Case history

# Case history #1

A 54-year-old smoker with multiple comorbidities (diabetes, hypertension, coronary artery disease) presents with a 2-day history of a productive cough with yellow sputum, chest tightness, and fever. Physical examination reveals a temperature of 38.3 °C (101 °F), BP of 150/95 mmHg, heart rate of 85 bpm, and a respiratory rate of 20 breaths per minute. His oxygen saturation is 95% at rest; lung sounds are distant but clear, with crackles at the left base. Chest x-ray reveals a left lower lobe infiltrate.

# Other presentations

Pneumonia can occur at any age, but the incidence increases significantly in old age, and pneumonia is a leading cause of illness and death in older patients. The clinical manifestations of pneumonia in elderly persons are often less intense than those in younger patients.[2] Atypical pathogens such as *Mycoplasma pneumoniae*, *Chlamydophila pneumophila*, and respiratory viruses can present in a subacute fashion with gradual onset of fever, non-productive cough, constitutional symptoms, relatively normal white blood cell count, and absent or diffuse findings on lung examination.[3] Patients with severe pneumococcal or *Legionella pneumophila* pneumonia often progress rapidly to respiratory failure.

Theorv

# Recommendations

# Urgent

Suspect CAP in patients with symptoms and signs of an acute lower respiratory tract infection and, in a hospital setting, with **new radiographic shadowing** (consolidation) for which there is no other explanation.[1] [63] [64] [65]

During the COVID-19 pandemic, consider all patients with cough, fever, or other suggestive symptoms to have COVID-19 until proven otherwise. For patients with suspected or confirmed COVID-19 pneumonia, see our topic [Coronavirus disease 2019 (COVID-19)].

• Pneumonia due to COVID-19 is not covered in this topic.

Think '**Could this be sepsis?**' based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[66] [67]

• Use a systematic approach, alongside your clinical judgement, for assessment; urgently consult a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis.[67] [68] [69] [70]

Refer to local guidelines for the recommended approach at your institution for assessment and management of the patient with suspected sepsis. See Sepsis in adults .

# Urgent: in hospital

Prioritise a chest radiograph for all patients with suspected CAP within 4 hours of presentation to hospital.[1] [63] [65]

Order blood tests including:[1] [65]

- **Oxygen saturations** to guide supportive treatment
- Arterial blood gases in patients with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO <sub>2</sub> retention), and all patients with high-severity CAP (see our *Management recommendations* section for more detail on assessing severity)
- · Urea and electrolytes to inform severity
- Full blood count, liver function tests, and C-reactive protein to aid diagnosis and for baseline measurements.

Assess oxygen requirements. Prescribe oxygen if oxygen saturation <94% and maintain at target range.[1] [65] In patients at risk of CO<sub>2</sub> retention prescribe oxygen if oxygen saturation <88%.[71]

Monitor controlled ox ygen therapy. An upper SpO <sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are not at risk of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO 2 of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

Assess mortality risk using the CURB-65 score and your clinical judgement for all patients with pneumonia confirmed by chest radiography (see our *Management - full recommendations* section for more information). [1] [63] [65]

• Score of 3-5: high-severity.

- Score of 3 or more: **discuss with a senior colleague at the earliest opportunity** and manage as high-severity pneumonia.[1] [63] [65]
- Score of 4 or 5: arrange emergency assessment by a critical care specialist.[1]
- Score of 2: manage as moderate-severity pneumonia.[1] [63] [65]
- Score of 0 or 1: manage as low-severity pneumonia.[1] [63] [65]

Send sputum and blood samples for culture in people with moderate- or high-severity CAP, ideally before starting antibiotics.[1] [65] Consider legionella and pneumococcal urine antigen testing.[63]

**Measure observations** initially at least twice daily, and more frequently (e.g., every hour) in those admitted to a critical care unit (high-dependency unit or intensive care unit).[1] [65]

# Urgent: in the community

Perform a chest radiograph ONLY if you are unsure of the diagnosis and radiography will help you to manage the acute illness. [1] [63] [65]

• For the majority of patients you should make a clinical diagnosis.[1] [63] [65]

**Use pulse oximetry** as part of your assessment of disease severity and to determine oxygen requirement.[71]

Assess mortality risk using the CRB-65 score (see *Management - full recommendations*) and your clinical judgement to inform severity.[1] [63] [65]

- Score of 3 or more (high-severity): admit patient to hospital immediately.[1] [63] [65]
- Score of 1 or 2 (moderate-severity): consider referral to hospital.[1]
- Score of 0 (low-severity): treat most patients at home.[1] [63] [65]

# **Key Recommendations**

# Presentation

Patients with CAP typically present with symptoms and signs consistent with a lower respiratory tract infection (i.e., cough, dyspnoea, pleuritic chest pain, mucopurulent sputum, myalgia, fever) and no other explanation for the illness (e.g., sinusitis or asthma). [63]

Remember to **consider atypical presentations** (without obvious chest signs). For example:

- Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea[73]
- Legionella pneumonia may present as constitutional upset, diarrhoea, and confusion[73]
- Pneumocystis pneumonia in immunosuppressed people may present only as cough, dyspnoea, and marked hypoxia[73]
- Older people frequently present with non-specific symptoms (especially confusion) and worsening of pre-existing conditions, and without chest signs or fever [1] [65]
- Some people present with acute confusional states.[73]

**Do not use clinical features alone** to predict the causative agent or to influence your initial choice of antibiotic.[1] [65] [74]

# **Risk stratification**

Determine whether the patient should be managed in hospital or at home using the **CURB-65 mortality risk score** (hospital setting) or **CRB-65 score** (community setting) (see our *Management - recommendations* section for more detail on risk stratification). [1] [63] [65]

## **Risk stratification in hospital\***

Severity of CAP	CURB-65 score	Management decision
High	4 or 5	Arrange emergency assessment by a critical care specialist [1] [63] [65]
	3	Discuss with senior colleague at the earliest opportunity and manage as high-severity pneumonia[1] [63] [65]
Moderate	2	Consider for short-stay inpatient treatment or hospital supervised outpatient treatment[1] [63] [65]
Low	0 or 1	Consider for outpatient treatment[1] [63] [65]

# Risk stratification in the community

Severity of CAP	CRB-65	Management decision
High	3 or more	Admit to hospital immediately [1] [63] [65]
Moderate	1 or 2	Consider hospital referral for assessment and treatment*[1] [63] [65]
Low	0	Consider for treatment at home*[1] [63] [65]

# Imaging

Confirm the diagnosis by chest radiograph in all patients presenting to hospital with suspected CAP. [1] [63] [65]

• A definitive diagnosis of CAP requires evidence of consolidation on chest x-ray.[75]

In community settings base the diagnosis on signs and symptoms of lower respiratory tract infection, focal chest signs, and illness severity.[1] [63] [65]

# **Further investigations**

### Discuss with a senior colleague any patient who does not improve as expected. [1] [65]

- Consider repeat chest radiograph, C-reactive protein, white cell count, and further specimens for microbiology in patients not progressing satisfactorily after 3 days of treatment.[1] [65]
- Consider referral to a respiratory physician.[1] [65]

In patients with **high-severity CAP who do not respond to beta-lactam antibiotics** or in whom you suspect an **atypical or viral pathogen**, order **polymerase chain reaction** (or other antigen detection test) of sputum or other respiratory tract sample.[1] [65]

• Consider initial and follow-up viral and atypical pathogen serology.[1] [65]

In the community assess oxygenation via pulse oximetry.[71]

- Oxygen saturation <94% is an adverse prognostic factor in CAP and also usually an indication for ox ygen therapy.[76]
- Consider urgent hospital referral in these patients.[1] [65]

General investigations are not necessary in the majority of patients presenting in the community, but you should **consider a point-of-care C-reactive protein test** if you cannot make a diagnosis of CAP from the clinical assessment and you are not sure whether antibiotics are indicated.[1] [63] [65]

During the COVID-19 pandemic, order a nucleic acid amplification test, such as real-time PCR, for SARS-CoV-2 in any patient with suspected infection whenever possible.[77] [78] See our topic [Coronavirus disease 2019 (COVID-19)].

# **Full Recommendations**

# **Clinical presentation**

No constellation of signs and symptoms is predictive of CAP. However, **patients typically present** with:[1] [63] [64] [65]

- · Symptoms and signs consistent with a lower respiratory tract infection:
  - · Cough and at least one other respiratory tract symptom:
    - Shortness of breath usually present[1]
    - Pleuritic chest pain
    - Tachypnoea
    - Mucopurulent sputum associated with bacterial pneumonia (scant or watery sputum is associated with an atypical pathogen)[1]
  - At least one systemic feature:
    - Rigors or night sweats usually present, but less common in older patients[1]
    - Fever (> $38^{\circ}C$  [> $100^{\circ}F$ ]) older patients may be afebrile [1]
    - Non-specific symptoms may include myalgia, lethargy, malaise, anorexia. **Confusion** is often seen in **older patients** [1]
- New focal chest signs on examination such as crackles or bronchial breathing
- No other explanation for the illness.

**Remember to consider atypical presentations of CAP** (i.e., without obvious chest signs). For example:

- Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea[73]
- Legionella pneumonia may present as constitutional upset, diarrhoea, and confusion[73]
- Pneumocystis pneumonia in the immunosuppressed may present only with cough, dyspnoea, and marked hypoxia[73]
- Older people frequently present with non-specific symptoms (e.g., lethargy, malaise, anorexia, confusion) and worsening of pre-existing conditions, and without chest signs or fever[1]
- Some people present with acute confusional states.[73]

#### Consider speed of symptom onset in your differential diagnosis:

• Symptoms developing within minutes may be suggestive of pulmonary embolism, pneumothorax, or a cardiac aetiology.

#### Practical tip

Think '**Could this be sepsis?**' based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[66] [67] [68] See Sepsis in adults .

- The patient may present with non-specific or non-localised symptoms (e.g., acutely unwell with a normal temperature) or there may be severe signs with evidence of multi-organ dysfunction and shock.[66] [67] [68]
- Remember that sepsis represents the severe, life-threatening end of infection.[79]
- Pneumonia is one of the main sources of sepsis.[80]

Use a systematic approach (e.g., National Early Warning Score 2 [NEWS2]), alongside your clinical judgement, to assess the risk of deterioration due to sepsis.[66] [68] [69] [81] Consult local guidelines for the recommended approach at your institution.

Arrange urgent review by a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis:[70]

- Within 30 minutes for a patient who is critically ill (e.g., NEWS2 score of 7 or more, evidence of septic shock, or other significant clinical concerns).
- Within 1 hour for a patient who is severely ill (e.g., NEWS2 score of 5 or 6).

Follow your local protocol for investigation and treatment of all patients with suspected sepsis, or those at risk. Start treatment promptly. Determine urgency of treatment according to likelihood of infection and severity of illness, or according to your local protocol.[70] [81]

In the community: refer for emergency medical care in hospital (usually by blue-light ambulance in the UK) any patient who is acutely ill with a suspected infection and is:[67]

- Deemed to be at high risk of deterioration due to organ dysfunction (as measured by risk stratification)
- At risk of neutropenic sepsis.

#### Some symptoms and signs are more common with specific pathogens. [1]

• Do not, however, use clinical features alone to predict the causative agent or to influence your initial choice of antibiotic.[1] [65] [74]

# Typical pathogens causing CAP in adults in the UK and their most commonly associated features [1]

# Diagnosis

Pathogens	Most commonly associated clinical features	Other features
Streptococcus pneumoniae	Acute onset, high fever, and pleuritic chest pain	Most common overall pathogen
		More likely in the presence of cardiovascular comorbidity, increasing age
		Bacteraemic <i>S pneumoniae</i> is more likely in:
		<ul> <li>Females</li> <li>People with a history of excess alcohol intake</li> <li>People with diabetes mellitus</li> <li>People with COPD</li> </ul>
Haemophilus influenzae	No specific defining features	More likely in older people and those with COPD
Legionella pneumophila	Diarrhoea, encephalopathy and other neurological symptoms, severe infection more likely and evidence of multisystem involvement (e.g., abnormal liver function tests, elevated serum creatine kinase)	More likely in young patients without comorbidities, smokers, immunocompromised people, people exposed to contaminated artificial water systems (e.g., air conditioning units, spas, fountains, repair of domestic plumbing systems) Higher frequency in severe illness (patients in the intensive care unit) Enquire about foreign travel
Staphylococcus aureus	No specific defining features	More likely if preceding or concurrent influenza infection Higher frequency in severe illness (patients in the intensive care unit)
		Enquire about influenza symptoms as they are of predictive value. Influenza virus infection can be

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Pathogens	Most commonly associated clinical features	Other features
		complicated by co-/secondary infection with <i>S aureus</i>

# Atypical pathogens causing CAP in adults in the UK and their most commonly associated features $\left[1\right]$

Pathogens	Most commonly associated clinical features	Other features
Mycoplasma pneumoniae	In young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea[73]	More likely in younger patients Epidemic years occur in roughly 4-yearly cycles
Chlamydophila pneumoniae	No specific defining features	None
Coxiella burnetii	History of dry cough and high fever	More likely in males Exposure to infected animal sources (especially during parturition) is the main epidemiological link[82]
Klebsiella pneumoniae	No specific defining features	<b>People with alcohol</b> <b>dependency</b> are at higher risk of bacteraemic and fatal <i>Klebsiella</i> pneumonia

# History

Your history should cover risk factors to help you assess whether the patient has CAP, a lower respiratory tract infection, or an alternative diagnosis. You should also identify factors that may influence the management plan if CAP is diagnosed.

Be aware that you cannot make a definitive diagnosis of CAP from the history alone.

# **Medical history**

(\*Denotes a strong risk factor for CAP.)

- · Respiratory chronic diseases:
  - **COPD\***, **asthma**, **and bronchitis** are associated with a 2-fold to 4-fold increased risk of CAP[6]
  - COPD is an independent risk factor for mortality in patients with CAP.[37]
- Other chronic comorbidities:
  - Chronic heart disease [6] [37]

• **Diabetes** [6] [37] – the risk of severe pneumococcal bacteraemia is higher in people with diabetes.[54]

### Practical tip

Consider aspiration pneumonitis/pneumonia in patients at high risk of aspiration, such as those with chronic swallowing difficulties, those with organic neurological conditions (e.g., Parkinson's disease, stroke, dementia), or those who cannot protect their airways easily.[1]

# **Social history**

- Age ≥65 years\*
  - Incidence of CAP increases significantly with age. Advanced age is associated with a higher mortality from CAP.[10]
- Residence in a nursing home\*
  - Mortality rates due to pneumonia in nursing home residents have been reported to reach 55%.[83] [84]
  - Nursing home residents also have an increased risk of aspiration pneumonia.[85]

#### Contact with children\*

· Regular contact with children is associated with an increased risk of CAP.[49]

CAP is more severe in males than in females, leading to higher mortality in males overall and especially those of older age.[86]

# Lifestyle history

- Alcohol use/misuse\*
  - People who consume alcohol at all or in higher amounts have an 83% higher risk of CAP compared with people who consume no alcohol or lower amounts (relative risk of 1.83).[43] For every 10 to 20 g higher alcohol intake per day, there is an 8% increase in the risk of CAP.[43]
- Smoking\*
  - · Smoking is an independent risk factor for developing CAP.[41]
  - Passive smoking at home is also a risk factor for CAP in people aged 65 years or older.[42]
     [41]
- Poor oral hygiene
  - Poor oral hygiene (particularly dental dysaesthesia and wearing dental prostheses) may contribute to a higher risk of CAP in adults.[87]

Diagnosis

# **Drug history**

• Proton pump inhibitors, H2 antagonists, and prescribed opioids (particularly immunosuppressive opioids) are associated with CAP.[59]

# **Physical examination**

Carry out a thorough examination, particularly of the **cardio-respiratory system**, to identify features consistent with CAP.

Check for:

- Fever (>38°C [>100°F])
- · Raised respiratory rate
- Tachycardia
- Focal chest signs none, some, or all of these may be present:
  - Crackles
  - · Bronchial breathing
  - · Decreased chest expansion
  - · Dullness to percussion (suggests consolidation and/or pleural effusion)
  - · Decreased entry of air.

Focus in addition on other areas (e.g., throat, legs) if the presentation suggests an alternative diagnosis, such as an **upper respiratory tract infection**, **deep vein thrombosis**, or **pulmonary embolism**.

# Imaging

# In hospital

# All patients on presentation

Send all patients seen in hospital with suspected CAP for a chest radiograph as soon as possible to confirm the diagnosis, and within 4 hours of presentation to hospital. [1] [63] [65]

- New shadowing (consolidation) on chest x-ray confirms the diagnosis of CAP [1] [63] [65]
- Reassess the patient if the chest x-ray shows no consolidation.[1]



Posterior-anterior chest radiograph showing right upper lobe consolidation in a patient with community-acquired pneumonia Durrington HJ, et al. Recent changes in the management of community acquired pneumonia in adults. BMJ 2008;336:1429.

#### **Practical tip**

A high-quality chest radiograph is important to ensure accurate diagnosis and to avoid inappropriate antibiotic prescribing. One study reported that 29% of hospitalised patients treated for CAP did not have radiographic abnormalities.[88]

Bear in mind that it is more difficult to obtain a high-resolution image from a person with class III obesity (body mass index  $\geq$ 40).

### Reserved for specific circumstances

Consider a chest computed tomography (CT) scan if the radiograph is of poor quality or an ill-defined consolidation is present. [1]

Consider a **chest CT scan or other imaging investigations** for 'complicated' pneumonia or atypical changes on a chest radiograph, such as **cavitation**, **multifocal consolidation pattern**, or **pleural effusion**.[89]

# Community-acquired pneumonia in adults (non COVID-19)

# Diagnosis



*Chest radiograph showing left upper lobe cavitating pneumonia From the collection of Dr Jonathan Bennett. Used with permission* 

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# Community-acquired pneumonia in adults (non COVID-19)



Left-sided pleural effusion From the collection of Dr R Light. Used with permission

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Diagnosis

# Community-acquired pneumonia in adults (non COVID-19)



Diagnosis

Increased opacification of the right perihilar region and superior segment of the right lower and upper lobes consistent with worsening aspiration pneumonia From the collection of Dr Roy Hammond. Used with permission

# Diagnosis

X-ray findings	Further imaging	Consider alternative diagnosis
Cavitation	Chest CT scan	<ul> <li>Tuberculosis</li> <li>Lung cancer</li> <li>Pulmonary infarct</li> <li>Septic pulmonary emboli</li> <li>Infected bulla</li> <li>Lung abscess</li> </ul>
<b>Multifocal consolidation</b> (note that it is the multifocal nature, not the consolidation that is the distinguishing feature)	Chest CT scan	<ul> <li>Staphylococcal infection</li> <li>Tuberculosis</li> <li>Aspiration pneumonia</li> <li>Allergic bronchopulmonary aspergillosis</li> <li>Cryptogenic organising pneumonia</li> <li>Drug hypersensitivity reaction</li> </ul>
Pleural effusion	Chest ultrasound +/- guided aspiration +/- chest CT scan	<ul> <li>Parapneumonic effusion</li> <li>Congestive heart failure</li> <li>Tuberculosis</li> <li>Pulmonary embolism</li> <li>Lung cancer</li> <li>Fungal infection</li> </ul>

### **Practical tip**

'Complicated' pneumonia refers to pneumonia that is complicated by the presence of parapneumonic effusion (an exudative pleural effusion associated with pulmonary infection), empyema (pus in the pleural space), abscess, pneumothorax, necrotising pneumonia, or bronchopleural fistula.

Around 40% of people who are hospitalised for pneumonia develop parapneumonic effusion.[90] Empyema is a type of pleural effusion that is difficult to distinguish from a parapneumonic effusion on chest radiograph.

Findings on a CT scan suggestive of a parapneumonic effusion (as opposed to empyema) include:[91]

- · Usually small volume
- · Normal meniscus sign
- Dependent
- No loculation.

Split pleura sign' is not typical and is more specific for empyema.

Consider **CT pulmonary angiography** (CTPA) to rule out pulmonary embolism if symptoms came on quickly (within minutes) or pain and breathlessness preceded infective symptoms.[92]

# In the community

**Do not request a chest radiograph** for patients with suspected CAP seen in the community **unless**:[1] [63] [65]

- There is diagnostic doubt
- The patient is deemed to be **at risk of underlying lung pathology** (e.g., they have risk factors for lung cancer)
- Progress following treatment is not satisfactory at review.

In community settings base the diagnosis on signs and symptoms of lower respiratory tract infection, focal chest signs, and illness severity.[1] [63] [65]

#### Debate: Ultrasound in the diagnosis of CAP

Although a chest radiograph showing new shadowing that cannot be attributed to any other cause is the 'gold-standard' for the diagnosis of pneumonia, it may not always be feasible in a community setting and it involves exposure to radiation.

- Emerging evidence has shown that lung ultrasound is a possible accurate diagnostic test for people with CAP. However, the benefits of its use in practice over chest radiography are still unclear.
- A meta-analysis of 12 studies looking at the diagnostic accuracy of lung ultrasound in people with CAP found a sensitivity and specificity of 0.88 and 0.86, respectively.[93] However, there were limitations, such as the large variability in the findings and the lack of heterogeneity of the studies reviewed.
- Further evidence is required before recommendations can be made.

# Other investigations

# **General investigations**

# In a hospital setting

#### Arrange the following tests for all patients admitted to hospital.

Start with oxygen saturations and urea (and electrolytes) as these will inform supportive treatment and severity, respectively:[1] [65]

- Pulse oximetry (preferably while breathing air) to assess oxygenation saturations.
  - Oxygen saturation <94% is an adverse prognostic factor in patients with CAP and may be an indication for oxygen therapy.[76]
- Arterial blood gas (ABG) measurements in patients receiving ox ygen therapy.[71]
  - Measure ABG in patients with SpO<sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO<sub>2</sub> retention), and all patients with high-severity CAP.[1]
- Urea (and electrolytes) to inform severity of disease.

- Urea >7 mmol/L (>19.6 mg/dL) counts for 1 point in the 6-point CURB-65 score to assess severity.[1]
- Chronic renal failure is a significant risk factor for mortality in patients with CAP.[56]

#### Practical tip

Always record the inspired oxygen concentration clearly as this is essential for interpreting blood gas results.

**Order full blood count, C-reactive protein, and liver function tests** to help identify underlying or associated pathology, and for baseline measurements.[1] [65]

- Full blood count . Leukocytosis is often seen in people with CAP:
  - A white cell count of >15 x 10<sup>9</sup>/L indicates a bacterial (particularly pneumococcal) aetiology.[1]
- C-reactive protein (CRP) to help rule out other acute respiratory illnesses and as a baseline measure:
  - A level >100 mg/L makes pneumonia likely[94]
    - High levels of CRP do not necessarily indicate that pneumonia is bacterial or SARS-CoV-2, but low CRP levels make a secondary bacterial infection less likely.[95]
  - A level <20 mg/L with symptoms for more than 24 hours makes the presence of pneumonia highly unlikely[94]
  - A failure of CRP to fall by 50% or more at day 4 is associated with an increased risk for 30-day mortality, need for mechanical ventilation and/or inotropic support, and complications.[96]
- Liver function tests to assess liver function:
  - Abnormal in patients with underlying liver disease and legionella infection[1]
  - Chronic liver disease is a risk factor for pulmonary complications in patients hospitalised due to pneumococcal pneumonia.[58]

Consider ordering serum procalcitonin. Baseline procalcitonin is increasingly being used in critical care settings and in the emergency department to guide decisions on antibiotic treatment in patients with highly suspected sepsis and in those with suspected bacterial infection.[81] [97] [98] [99] [100]

- Increased values of procalcitonin are correlated with bacterial pneumonia, whereas lower values are correlated with viral and atypical pneumonia. Procalcitonin is especially elevated in cases of pneumococcal pneumonia.[101] [102]
- Procalcitonin is a peptide precursor of calcitonin, which is responsible for calcium homeostasis. It is currently excluded from key guidelines, but increasingly used in practice.

Perform early **thoracocentesis** in all patients **with pleural effusion** as this can reveal an infected pleural space consistent with a parapneumonic effusion or empyema.[1] [65]

• Drain pleural fluid in patients with an empyema or clear pleural fluid with pH <7.2.[1]

# Monitoring

# Measure observations initially at least twice daily, and more frequently (e.g., every hour) in patients admitted to a critical care unit (high-dependency unit or intensive care unit). [1] [65]

- Pulse
- Blood pressure
- Respiratory rate
- Temperature
- Blood pressure
- Oxygen saturation (with a recording of the inspired oxygen saturation at the same time)
- Mental status.

All patients with high-severity CAP (high risk of death) should be reviewed at least every 12 hours until improvement. [1] [65] This should be done by a senior colleague and the medical team. [1] [65]

# In the community

**General investigations are not necessary for the majority of patients** with CAP who are managed in the community.[1] [65] However, you should **consider a point-of-care C-reactive protein** (**CRP**) if you cannot make a diagnosis of CAP from the clinical assessment and it is not clear whether antibiotics should be prescribed.[63]

### Assess oxygenation via pulse oximetry. [71]

Ox ygen saturation <94% is an adverse prognostic factor in CAP and also may be an indication for ox ygen therapy.[76]

Consider urgent hospital referral in these patients. [1] [65]

# Microbiological investigations

Be aware that the extent of microbiological testing in an individual patient is guided by severity, presence of risk factors (e.g., COPD), and disease outbreaks (e.g., legionella pneumonia).[1] [65]

# In hospital

Do not perform microbiological tests routinely in patients with low-severity CAP presenting in hospital. [1] [65] Empirical antibiotic therapy is associated with a good prognosis in these patients.[1]

# Blood cultures

Order blood cultures, ideally before antibiotics are given, in all patients with moderate- or high-severity CAP (as determined by the CURB-65 score – see our *Management recommendations* section).[1] [63] [65]

- Isolation of bacteria can be highly specific in determining the microbial aetiology in people with moderate or severe CAP.[1] [63] [65]
- Bacteraemia is also a marker of illness severity. However, many patients with CAP do not have associated bacteraemia.[1] Microbial causes of CAP that can be associated with bacteraemia include:[1]
  - Streptococcus pneumoniae (identified in around 60% of positive blood cultures)[103]
  - Haemophilus influenzae (identified in 2% to 13% of positive cultures)[103]

• Staphylococcus aureus and Klebsiella pneumoniae.

Do not order blood cultures in patients with confirmed CAP who have low-severity disease and no comorbid conditions. [1] [65]

#### Debate: Blood cultures

There is debate around the practicality of ordering routine blood cultures in patients hospitalised with CAP. This is mainly due to low sensitivity, cost, and the fact that results rarely influence antimicrobial management.

- In a study of 355 patients admitted to hospital for CAP, the proportion of false-positive blood cultures was 10%, and the proportion of true positives was 9% (95% CI, 3.3% to 5.5%).[104]
- Antibiotic therapy was changed on the basis of blood culture results in only 5% of patients (95% CI, 3% to 8%).[104]
- However, despite these limitations, most experts still recommend blood cultures in patients with high-severity CAP.[1]

#### Sputum cultures

#### Send sputum cultures in:

- All patients with moderate- or high-severity CAP (as determined by CURB-65 score).[63] The British Thoracic Society recommends sputum cultures in patients with moderate-severity CAP only if they have not received prior antibiotic therapy [1] [65]
- Patients who do not improve regardless of disease severity (sputum or other respiratory samples).[1] [65]

#### Gram stain of sputum cultures

Order Gram stain of sputum cultures in patients with high-severity CAP or complications if available in your local laboratory.[1] [65]

• Gram stain is an immediate indicator of the likely pathogen and can help with interpreting culture results.[1] [65]

#### Evidence: sputum Gram stain

A prospective study of 1390 patients with bacteraemic CAP found a sensitivity for sputum Gram stain of :[105]

- 82% for pneumococcal pneumonia
- 79% for *H influenzae* pneumonia
- 76% for staphylococcal pneumonia.

Specificities ranged from 93% to 96%.

#### **Practical tip**

Carrying out routine sputum Gram stains for all patients is unnecessary.[1] The test has a low sensitivity and specificity, and often does not contribute to initial management. Problems include:[1]

- · Patients may not be able to produce good specimens
- · Prior exposure to antibiotics
- Delays in transport and processing of samples, which reduces the yield of bacterial pathogens
- Difficulty interpreting the results 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).

#### Urine antigen testing

#### Streptococcus pneumoniae

# Consider pneumococcal urine antigen tests for people with moderate- or high-severity CAP. [63]

• Urine antigen testing is useful for diagnosing pneumococcal pneumonia in adults and is less affected than blood/sputum cultures by prior antibiotic therapy.[1] [65]

#### Evidence: Urine antigen testing for pneumococcal pneumonia

Studies have shown significantly greater sensitivity rates for the pneumococcal urine antigen test than for routine blood or sputum cultures. [106]

 Results remain positive in 80% to 90% of patients for up to 7 days after starting antimicrobial treatment.[106]

#### Debate: Patient groups for pneumococcal testing

# The British Thoracic Society (BTS) and the National Institute for Health and Care Excellence (NICE) guidelines differ in their recommendations regarding who should be tested for pneumococcal pneumonia using urine antigen.

- The BTS recommends testing all patients with high-severity CAP,[1] whereas NICE recommends considering testing in patients with moderate- or high-severity CAP.[63] [65]
- A later comparison by the BTS of the key recommendations in the two guidelines (BTS published in 2009 and NICE in 2014) concluded that there were no major differences between them and, where there were differences, clinicians should follow the NICE guideline instead of the BTS guideline.[107]

#### Legionella

Order legionella urine antigen tests in all patients with specific risk factors and for all patients with CAP during outbreaks. [1] [65] Consider testing also for people with moderate- or high-severity CAP.[63]

- It is important that legionella pneumonia is diagnosed promptly as it is associated with significant mortality and has public health significance.[1] [65]
- Detection of *Legionella pneumophila* urinary antigen by enzyme immunoassay allows for rapid results early in the illness.[1] [65]

• Legionella antigen testing by enzyme immunoassay is highly specific (>95%) and sensitive (80%) for detecting *L pneumophila* serogroup 1, which is the most common cause of sporadic CAP and CAP due to foreign travel in the UK.[108]

#### Debate: Patient groups for legionella testing

The British Thoracic Society (BTS) and the National Institute for Health and Care Excellence (NICE) guidelines differ in their recommendations regarding the patient groups that should be tested for legionella pneumonia using urine antigen.

- The BTS recommends testing only patients with high-severity CAP, patients with risk factors, and all patients with CAP during outbreaks,[1] whereas NICE recommends that clinicians consider testing in people with moderate- or high-severity CAP.[63] [65]
- A later comparison by the BTS of the key recommendations in the two guidelines (BTS published in 2009 and NICE in 2014) concluded that there were no major differences between them and, where there were differences, clinicians should follow the NICE guideline instead of the BTS guideline.[107]
- In the comparison, the BTS also stated that its recommendation to test for legionella in patients with risk factors and all patients with CAP during outbreaks remains valid as this was not examined by NICE.[107]

If the legionella urine antigen test is positive remember to order sputum cultures from respiratory samples (e.g., obtained from bronchoscopy) for *Legionella* species. This is to aid outbreak and source investigation to prevent further cases.[1] [65]

Polymerase chain reaction (PCR) and serological tests

Use **PCR of sputum** or other respiratory tract samples for **respiratory viruses** (influenza A and B, parainfluenza 1-3, adenovirus, respiratory syncytial virus) and **atypical pathogens** (*Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Chlamydophila psittaci*, *Coxiella burnetii*, and *Pneumocystis jirovecii* [if at risk]) in patients with **high-severity CAP**:[1] [65]

- · If unresponsive to beta-lactam antibiotics
- If there is a strong suspicion of an 'atypical' pathogen.

During the COVID-19 pandemic, order a nucleic acid amplification test, such as real-time PCR, for SARS-CoV-2 in any patient with suspected infection whenever possible.[77] [78] See our topic [Coronavirus disease 2019 (COVID-19)]

 Differentiating community-acquired bacterial pneumonia from COVID-19 is not usually possible from signs and symptoms. However, patients with bacterial pneumonia are more likely to have rapid development of symptoms and purulent sputum. They are less likely to have myalgia, anosmia, or pleuritic pain.[109]

# Consider urine antigen, PCR of upper (e.g., nose and throat swabs) or lower (e.g., sputum) respiratory tract samples, or serological investigations in patients with moderate- or low-severity CAP:[1]

- During outbreaks (e.g., Legionnaires' disease)
- · During mycoplasma epidemics, or
- When there is a particular clinical or epidemiological reason
  - If available, PCR is preferred over serological investigations.

# In the community

**Do not order microbiological tests routinely** in patients presenting with CAP in the community as:[1] [63] [65]

- These patients are not usually severely ill and are at low risk of death[1]
- Delays in transport of specimens to laboratory reduces the yield of bacterial pathogens (especially *S pneumoniae*) from sputum cultures, and results are often received too late by the general practitioner to have any impact on initial management.[1]

#### Only consider ordering microbiological tests in the community if:[1] [65]

- The patient's symptoms do not improve with empirical antibiotic therapy
  - · Consider sputum examination
- The patient has a **persistent productive cough**, especially if they also have malaise, weight loss, or night sweats, or risk factors for tuberculosis (e.g., ethnic origin, social deprivation, older patients, previous history of tuberculosis, contact history of tuberculosis)
  - · Consider sputum examination for Mycobacterium tuberculosis
- There is a clinical or epidemiological reason, such as an **outbreak (e.g., Legionnaires' disease)** or during mycoplasma epidemics
  - Consider urine antigen, PCR of upper (e.g., nose and throat swabs) or lower (e.g., sputum) respiratory tract samples or serological investigations. If available, PCR is preferred over serological investigations.[1] [65]

During the COVID-19 pandemic, order a nucleic acid amplification test, such as real-time PCR, for SARS-CoV-2 in any patient with suspected infection whenever possible.[77] [78] See our topic [Coronavirus disease 2019 (COVID-19)]

Summary of the recommendations for microbiological investigations from the British Thoracic Society (BTS) and the National Institute for Health and Care Excellence (NICE) [1] [63] [65]

CAP severity and treatment site	Preferred microbiological tests
High-severity (CURB-65 = 3-5; CRB-65 = 3-4): treat in hospital	<ul> <li>Blood and sputum (or other respiratory sample) cultures (plus Gram stain if available)</li> <li>Legionella and pneumococcal urin antigen if legionella or pneumococcal pneumonia is suspected</li> </ul>
	• If legionella urine antigen is positive: sputum or other respiratory sample for legionella culture
	<ul> <li>If legionella urine antigen is positive: sputum or other respiratory sample for legionella culture</li> <li>PCR of sputum (or other respirator tract sample) for respiratory viruse (influenza A and B, parainfluenza 1-3, adenovirus, respiratory syncytial virus) and atypical pathogens (<i>Mycoplasi</i> <i>pneumoniae</i>, <i>Chlamydophila</i> <i>pneumoniae</i>, <i>Chlamydophila psittaci</i>, <i>Coxiella burnetii</i>, <i>Pneumocystis jirovec</i> if at risk) if unresponsive to beta-lactam antibiotics and/or with a strong suspicio of an 'atypical' pathogen</li> </ul>
Moderate-severity (CURB-65 = 2; CRB-65 = 1-2): treat in hospital	<ul> <li>Blood and sputum cultures (consid Gram stain if available)</li> <li>Legionella and pneumococcal urin antigen if legionella or pneumococcal pneumonia is suspected</li> </ul>
	• If legionella urine antigen is positive: sputum or other respiratory sample for legionella culture
	• During outbreaks (e.g., Legionnaires' disease) or mycoplasma epidemic: consider urir antigen, PCR* of upper (e.g., nose and throat swabs) or lower (e.g., sputum) respiratory tract samples or serological investigations
Low-severity (CURB-65 = 0-1; CRB-65 = 0): treat at home or in hospital	<ul> <li>None routinely</li> <li>During outbreaks (e.g., Legionnaires' disease) or mycoplasma epidemics: consider urine antigen, PCR* of upper (e.g., nose and throat swabs) or lower (e.g., sputur respiratory tract samples or serological investigations</li> </ul>

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CAP severity and treatment site

Preferred microbiological tests

\*If available, PCR is preferred over serological investigations.[1] [65]

#### Practical tip

In routine clinical practice, pathogens are identified only in about one third to one quarter of patients with CAP admitted to hospital.[1] Despite this, identifying the causative organism of CAP and sensitivity patterns is important because it:[1]

- Allows for appropriate selection of antibiotic regimens. Change to targeted and narrow-spectrum antibiotic therapy is recommended once the pathogen is identified unless there are concerns of dual infection
- Detects certain pathogens with public health significance and/or those that cause serious conditions that require different treatment from standard empiric antibiotics. These include:
  - Legionella species
  - Influenza A and B, including avian influenza A H5N1 and avian influenza A H7N9
  - Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV)
  - Community-associated methicillin-resistant S aureus (CA-MRSA)
  - Agents of bioterrorism
  - Other emerging pathogens
- Allows for monitoring of the spectrum of organisms that cause CAP over time. This is important to establish sensitivity patterns.

# Failure to improve

# In hospital

#### Discuss with a senior colleague any patient who does not improve as expected. [1]

Consider repeat chest radiograph, C-reactive protein (CRP), white cell count, and further specimens for microbiology in patients not progressing satisfactorily after 3 days of treatment.[1] [65]

• A failure of CRP to fall by 50% or more at day 4 is associated with an increased risk for 30-day mortality, need for mechanical ventilation and/or inotropic support, and complications.[96]

### Practical tip

#### Pointers to clinical improvement:[1] [65]

- Resolution of fever for >24 hours
- Pulse rate <100 beats/minute
- 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.

#### Consider referral to a respiratory physician.[1] [65]

In patients with high-severity CAP who are not responding to beta-lactam antibiotics or for whom an atypical or viral pathogen is suspected, order PCR (or other antigen detection test) of sputum or other respiratory tract sample.[1] [65]

# In the community

#### Assess oxygenation via pulse oximetry.[71]

- Oxygen saturation <94% is an adverse prognostic factor in CAP and also may be an indication for oxygen therapy.[76]
- Consider referring these patients to hospital urgently. [1] [65]

# **During recovery**

**Do not request a repeat chest radiograph** before discharge from hospital in patients who have recovered satisfactorily from CAP.[1] [65]

Request a repeat chest radiograph during recovery after about 6 weeks for patients (regardless of whether they have been admitted to hospital):[1] [65]

- With persisting symptoms or physical signs
- Who are at **higher risk of underlying malignancy** (especially people who smoke and those aged >50 years).

### Practical tip

Resolution of radiographic changes occurs relatively slowly after CAP and lags behind clinical recovery.[1]

**Consider bronchoscopy** in patients with **persisting signs**, **symptoms**, **and radiological abnormalities** at around 6 weeks after completing treatment.[1] [65]

# History and exam

# Key diagnostic factors

# cough with increasing sputum production (common)

Symptoms of a lower respiratory tract infection such as cough are frequently seen in people with CAP. [1] [63] [65]

- Cough is one of the most common symptoms present in patients with CAP.[1] Cough is usually productive with mucopurulent sputum.
- The presence of **mucopurulent sputum** is associated with **bacterial pneumonia**.[1] **Scant or watery sputum** is associated with an **atypical pathogen**.[1]
- Older patients may not present with cough and are more likely to have non-specific symptoms (e.g., confusion) and may be afebrile.[1]

# dyspnoea (common)

Dyspnoea is frequently seen in people with CAP. [1] [63] [65]

• Dyspnoea is one of the most useful predictive symptoms of CAP in the community (together with fever, tachypnoea, pleuritic chest pain, and new/focalising signs on physical examination of chest) when compared with the gold standard of radiological diagnosis of CAP.[1]

# pleuritic chest pain (common)

Pleuritic chest pain is frequently reported in people with CAP #ccuring in 30% of patients. [1] [63] [65] [110]

• Pleuritic chest pain is one of the most useful predictive symptoms of CAP in the community (together with fever, dyspnoea/tachypnoea, and new/focalising signs on physical examination of chest) when compared with the gold standard of radiological diagnosis of CAP.[1]

# rigors or night sweats (common)

Rigors or night sweats are usually present in people with CAP, but are less common in older patients. [1] [63]

# fever (common)

Fever is commonly seen in people with CAP, although older people may be afebrile. [1] [63] [65]

- A fever (>38°C [>100°F]) is one of the most useful predictive symptoms of CAP in the community (together with dyspnoea/tachypnoea, pleuritic chest pain, and new/focalising signs on physical examination of chest) when compared with the gold standard of radiological diagnosis of CAP.[1]
- Older people may be afebrile. [1]

# abnormal auscultatory findings (common)

New focal chest signs are frequently present on examination in people with CAP. [1] [63] [65]

- You may hear crackles, decreased breath sounds, dullness to percussion, and wheeze.
- Tachypnoea is one of the most useful predictive symptoms of CAP in the community (together with fever, dyspnoea, pleuritic chest pain, and new/focalising signs on physical examination of chest) when compared with the gold standard of radiological diagnosis of CAP.[1]

# confusion (common)

### Confusion is frequently seen in older people presenting with CAP. [1] [63] [65]

- Older people with CAP often present with non-specific symptoms such as confusion or worsening of underlying diseases, and may be afebrile.[1] [63] [64] [65]
- Atypical presentations (without obvious chest signs) of CAP may include confusion, such as in the case of **legionella pneumonia**, which may present as constitutional upset, diarrhoea, and confusion.[73]

# presence of risk factors (common)

Your history should cover the following risk factors to help assess the likelihood of CAP.[1] [63] [65]

(\*denotes a strong risk factor for CAP)

- Age ≥65 years\*
  - Incidence of CAP increases significantly with age. Advanced age is associated with a higher mortality from CAP.[10]
- Residence in a nursing home\*
  - Mortality rates due to pneumonia in nursing home residents have been reported to reach 55%.[83] [84]
  - Nursing home residents also have an increased risk of aspiration pneumonia.[85]

### Contact with children\*

- Regular contact with children is associated with an increased risk of CAP.[49]
- Respiratory chronic diseases
  - COPD\*, asthma, and bronchitis are associated with a 2-fold to 4-fold increased risk of CAP.[6]
  - COPD is an independent risk factor for mortality in patients with CAP.[37]

### Other chronic comorbidities

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- Chronic heart disease. [6] [37]
- **Diabetes** [6] [37] the risk of severe pneumococcal bacteraemia is higher in people with diabetes.[54]

#### Alcohol use/misuse\*

- People who consume alcohol at all or in higher amounts have an 83% higher risk of CAP compared with people who consume no alcohol or lower amounts (relative risk of 1.83).[43] For every 10-20 g higher alcohol intake per day, there is an 8% increase in the risk of CAP.[43]
- Smoking\*
  - Smoking is an independent risk factor for developing CAP.[41]
  - Passive smoking at home is also a risk factor for CAP in people aged 65 years or older.[42] [41]

#### Poor oral hygiene

• Poor oral hygiene (particularly dental dysaesthesia and wearing dental prosthesis) may contribute to a higher risk of CAP in adults.[87]

#### Proton pump inhibitors

• Associated with the occurrence of CAP.[46]

#### • H2 antagonists

- Associated with the occurrence of CAP.[48]
- Prescribed opioids
  - In particular, immunosuppressive opioids are associated with CAP.[59]

# Other diagnostic factors

### myalgia (common)

### Non-specific symptoms such as myalgia have been reported by people with CAP. [1]

• Older people with CAP frequently present with non-specific symptoms and worsening of preexisting conditions.[1]

# malaise (common)

### Non-specific symptoms such as malaise have been reported by people with CAP. [1]

 Older people with CAP frequently present with non-specific symptoms and worsening of preexisting conditions.[1]

# anorexia (common)

### Non-specific symptoms such as anorexia have been reported by people with CAP. [1]

• Older people with CAP frequently present with non-specific symptoms and worsening of preexisting conditions.[1]

# lethargy (common)

### Non-specific symptoms such as lethargy have been reported by people with CAP. [1]

• Older people with CAP frequently present with non-specific symptoms and worsening of preexisting conditions.[1]

# worsening of pre-existing conditions (common)

• Older people frequently present with non-specific symptoms and worsening of pre-existing conditions.[1]

# sore throat (uncommon)

Atypical presentations (without obvious chest signs) of CAP may include sore throat.

• Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea.[73]

# headache (uncommon)

Atypical presentations (without obvious chest signs) of CAP may include headache.

• Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea.[73]

### nausea (uncommon)

Atypical presentations (without obvious chest signs) of CAP may include nausea.

• Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea.[73]

# abdominal pain (uncommon)

Atypical presentations (without obvious chest signs) of CAP may include abdominal pain.

• Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea.[73]

# diarrhoea (uncommon)

Atypical presentations (without obvious chest signs) of CAP may include diarrhoea.

- Mycoplasma pneumonia in young adults may present as sore throat, headache, nausea, abdominal pain, and diarrhoea.[73]
- Legionella pneumonia may present as constitutional upset, diarrhoea, and confusion.[73]

# Investigations

## 1st test to order

### Test

#### chest x-ray

A definitive diagnosis of CAP requires evidence of consolidation on chest x-ray. [1] [63] [65] [75] #Perform a chest x-ray in all patients presenting in hospital as soon as possible and within 4 hours of admission.



Posterior-anterior chest radiograph showing right upper lobe consolidation in a patient with community-acquired pneumonia Durrington HJ, et al. Recent changes in the management of community acquired pneumonia in adults. BMJ 2008;336:1429.

• If the chest x-ray shows atypical changes or complicated pneumonia (e.g., cavitation, pleural effusion, multifocal consolidation), consider other imaging investigations (see our section on *Other tests to consider*).

#### **Practical tip**

A high-quality chest radiograph is very important to ensure accurate diagnosis and to avoid inappropriate antibiotic prescribing. One study reported that 29% of hospitalised patients treated for CAP did not have radiographic abnormalities.[88]

Bear in mind that it is more difficult to obtain a high-resolution image from a person with class III obesity (BMI  $\ge$ 40).

# Do not perform a chest x-ray in patients with suspected CAP seen in the community unless:[1] [65]

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### Result

new shadowing (consolidation)

### Diagnosis

Test	Result
<ul> <li>There is diagnostic doubt</li> <li>Progress following treatment is not satisfactory at review</li> <li>The patient is at risk of underlying lung pathology such as lung cancer.</li> </ul>	
<ul> <li>pulse oximetry</li> <li>Use pulse oximetry (preferably while breathing air) to assess ox ygen saturation in hospital to inform supportive treatment.</li> <li>Oxygen saturation &lt;94% in a patient with CAP is an adverse prognostic factor and may be an indication for oxygen therapy and urgent referral to hospital.[76]</li> <li>General practitioners should assess oxygenation via pulse oximetry.[71]</li> </ul>	<ul> <li>may reveal low arterial oxygen saturation</li> <li>oxygen saturation &lt;94% in a patient with CAP is an adverse prognostic factor and may be an indication for oxygen therapy and or urgent referral to hospital[76]</li> </ul>
<ul> <li>arterial blood gas (ABG)</li> <li>Measure ABG in patients with CAP receiving oxygen therapy with an SpO 2 &lt;94%, those with a risk of hypercapnic ventilatory failure (CO 2 retention), and all patients with high-severity CAP.</li> <li>Patients may be hypoxaemic and require supplemental oxygen.</li> <li>Oxygen saturation &lt;94% in a patient with CAP is an adverse prognostic factor and may be an indication for oxygen therapy and urgent referral to hospital.[76]</li> <li>Practical tip</li> </ul>	may reveal low arterial oxygen saturation
Always record the inspired oxygen concentration clearly as this is essential for interpreting blood gas results.	
urea and electrolytesRequest urea and electrolytes to inform disease severity and renal function in patients being investigated in hospital. [1] [65]• Chronic renal failure is a significant risk factor for mortality in patients with CAP.[56]General investigations are not necessary for the majority of patients 	<ul> <li>usually normal; elevated in patients with severe CAP</li> <li>urea &gt;7 mmol/L (&gt;19.6 mg/dL) counts for 1 point in the 6- point CURB-65 score to assess severity[1] [63] [65]</li> </ul>
full blood count Leukocytosis is often seen in people with CAP. General investigations are not necessary for the majority of patients with CAP who are managed in the community.[1] [63] [65]	<ul> <li>leukocytosis</li> <li>WBC count &gt; 15         x10<sup>9</sup> L indicates         a bacterial         aetiology (particularly         pneumococcal,)         although lower counts</li> </ul>

### Diagnosis

Test	Result	
	do not exclude a bacterial cause	
C-reactive protein (CRP)	<ul> <li>elevated</li> </ul>	
Order CRP as a baseline measurement and to help rule out other acute respiratory illnesses in patients being investigated in hospital.	<ul> <li>a level &gt;100 mg/L makes pneumonia likely[94]</li> <li>a level &lt;20 mg/L</li> </ul>	
<ul> <li>A failure of CRP to fall by 50% or more at day 4 is associated with an increased risk for 30-day mortality, need for mechanical ventilation and/or inotropic support, and complications.[96]</li> </ul>	with symptoms for more than 24 hours makes the presence of pneumonia highly	
General investigations are not necessary for the majority of patients with CAP who are managed in the community.[1] [63] [65]	unlikely[94]	
High levels of CRP do not necessarily indicate that pneumonia is bacterial or SARS-CoV-2, but low CRP levels make a secondary bacterial infection less likely.[111]		
liver function tests	usually normal; abnormal	
Take blood for a baseline measurement. Provides information about liver function.	in patients with underlying liver disease or legionella infection[1]	
<ul> <li>Chronic liver disease is a risk factor for pulmonary complications in patients hospitalised due to pneumococcal pneumonia.[58]</li> </ul>		
General investigations are not necessary for the majority of patients with CAP who are managed in the community.[1] [63] [65]		

## Diagnosis

### Other tests to consider

Test	Result
blood culture Order blood cultures, ideally before antibiotics are given, in all patients with moderate- or high-severity CAP (as determined by the CURB-65 score) presenting in hospital. [1] [63] [65]	growth of causative bacterial pathogen
<ul> <li>Blood cultures can be highly specific in determining the microbial aetiology [1] [63] [65]</li> <li>Bacteraemia is also a marker of illness severity. However, many patients with CAP do not have associated bacteraemia.[1] Microbial causes of CAP that can be associated with bacteraemia include:[1]</li> </ul>	
<ul> <li>Streptococcus pneumoniae (identified in approximately 60% of positive blood cultures)[103]</li> <li>Haemophilus influenzae (identified in 2% to 13% of positive cultures)[103]</li> <li>Staphylococcus aureus and Klebsiella pneumoniae.</li> </ul>	
Do not order blood cultures in patients with confirmed CAP who have low-severity disease and no comorbid conditions. [1] Empirical antibiotic therapy is associated with a good prognosis in these patients.[1]	
Debate: Blood cultures	
There is debate around the practicality of ordering routine blood cultures in patients hospitalised with CAP. This is mainly due to low sensitivity, cost, and the fact that results hardly ever influence antimicrobial management.	
<ul> <li>In a study of 355 patients admitted to hospital for CAP, the proportion of false-positive blood cultures was 10%, and the proportion of true positives was 9% (95% CI, 3.3% to 5.5%).[104]</li> <li>Antibiotic therapy was changed on the basis of blood</li> </ul>	
<ul> <li>culture results in only 5% of patients (95% CI, 3% to 8%).[104]</li> <li>However, despite these limitations, most experts still recommend blood cultures in patients with high-severity CAP.[1]</li> </ul>	
sputum culture (± Gram stain)	growth of causative bacterial
Take sputum samples for culture (± Gram stain) in all patients with moderate- and high-severity CAP (as determined by the CURB-65 score) presenting in hospital before starting antibiotics, and in patients who do not improve regardless of disease severity. [1] [63] [65]	pathogen
Order Gram stain of sputum cultures in patients with high- severity CAP or complications if available in your local laboratory.	

# Diagnosis

	Result
Gram stain is an immediate indicator of the likely pathogen and can nelp with interpreting culture results.[1]	
Do not order microbiological tests routinely in patients presenting with CAP in the community. [1] [63] [65]	
Evidence: Sputum Gram stain	
A prospective study of 1390 patients with bacteraemic CAP found a sensitivity for sputum Gram stain of: [105]	
<ul> <li>82% for pneumococcal pneumonia</li> <li>79% for <i>Haemophilus influenzae</i> pneumonia</li> <li>76% for staphylococcal pneumonia.</li> </ul>	
Specificities ranged from 93% to 96%.	
Practical tip	
Carrying out routine sputum Gram stains for all patients is unnecessary.[1] The test has a low sensitivity and specificity, and often does not contribute to initial management. Problems include:[1] • Patients may not be able to produce good specimens	
<ul> <li>Prior exposure to antibiotics</li> </ul>	
<ul> <li>Delays in transport and processing of samples, which</li> </ul>	
reduces the yield of bacterial pathogens	
<ul> <li>Difficulty interpreting the results due to contamination of</li> </ul>	
the sample by upper respiratory tract flora, which may include potential pathogens such as <i>Streptococcus</i> <i>pneumoniae</i> and 'coliforms' (especially in patients already given antibiotics).	
ry antigen testing for legionella and pneumococcus Consider pneumococcal and legionella urine antigen tests	positive for <i>Legionella</i> o pneumococcal antigens
n people with moderate- or high-severity CAP. [63] #Order egionella urine antigen testing in all patients with specific risk factors and during an outbreak (e.g, Legionnaires' disease) or during epidemic mycoplasma years. [1] [65]	
<ul> <li>Pneumococcal urinary antigen testing is useful for diagnosing pneumococcal pneumonia in adults and is less affected than blood/sputum cultures by prior antibiotic therapy.[1] [65]</li> <li>Legionella urinary antigen testing allows for rapid results early in the illness.[1] [65]</li> </ul>	
• For all patients who are positive for legionella urine antigen, order sputum cultures from respiratory samples (e.g., obtained from bronchoscopy) for Legionella species. This is to aid outbreak and source investigation with the aim of preventing further cases.[1] [65]	

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### Diagnosis

Test	Result
<ul> <li>Legionella antigen testing by enzyme immunoassay is highly specific (&gt;95%) and sensitive (80%) for detecting <i>Legionella pneumophila</i> serogroup 1, which is the most common cause of sporadic CAP and CAP due to foreign travel in the UK.[108]</li> </ul>	
Do not order microbiological tests routinely in patients presenting with CAP in the community. [1] [63] [65]	
Evidence: Urine antigen testing for pneumococcal pneumonia	
Studies have shown significantly greater sensitivity rates for the pneumococcal urine antigen test than for routine blood or sputum cultures. [106]	
<ul> <li>Results remain positive in 80% to 90% of patients for up to 7 days after starting antimicrobial treatment.[106]</li> </ul>	
polymerase chain reaction (PCR) and/or serological tests	detection of viral/atypical
Allows for rapid identification of the pathogen. Order PCR of sputum or other respiratory samples (e.g., nose and throat swabs) in patients with high-severity CAP:[1] [65]	pathogen antigens or antibodies
<ul> <li>If unresponsive to beta-lactam antibiotics</li> </ul>	
<ul> <li>If there is a strong suspicion of a respiratory virus (i.e.,</li> </ul>	
influenza A and B, parainfluenza 1-3, adenovirus, respiratory	
syncytial virus) or an 'atypical' pathogen:	
Mycoplasma pneumoniae	
Chlamydophila pneumoniae	
Chlamydophila psittaci	
<ul> <li>Coxiella burnetii</li> <li>Pneumocystis jirovecii (if at risk).</li> </ul>	
<b>Consider PCR in patients with low- or moderate-severity CAP</b> during outbreaks (e.g., Legionnaires' disease) or during epidemic mycoplasma, or when there is a particular clinical or epidemiological reason.[1] [65]	
Do not order microbiological tests routinely in patients presenting with CAP in the community. [1] [63] [65]	
During the COVID-19 pandemic, order a nucleic acid amplification test, such as real-time PCR, for SARS-CoV-2 in any patient with suspected infection whenever possible.[77] [78] See our topic [Coronavirus disease 2019 (COVID-19)].	

# Result

Diagnosis

### may show cavitations, pleural effusion, multifocal consolidation, neoplasm

### CT scan of chest

Test

Consider a CT scan of the chest when there is diagnostic doubt: for example, if the chest x-ray is of poor quality or there is an ill-defined consolidation. [1]

- Findings on chest x-ray that should prompt you to perform a CT scan include:
  - **Cavitation** CT helps identify alternative diagnoses such as tuberculosis, lung cancer, pulmonary infarct, septic pulmonary emboli, infected bulla, lung abscess

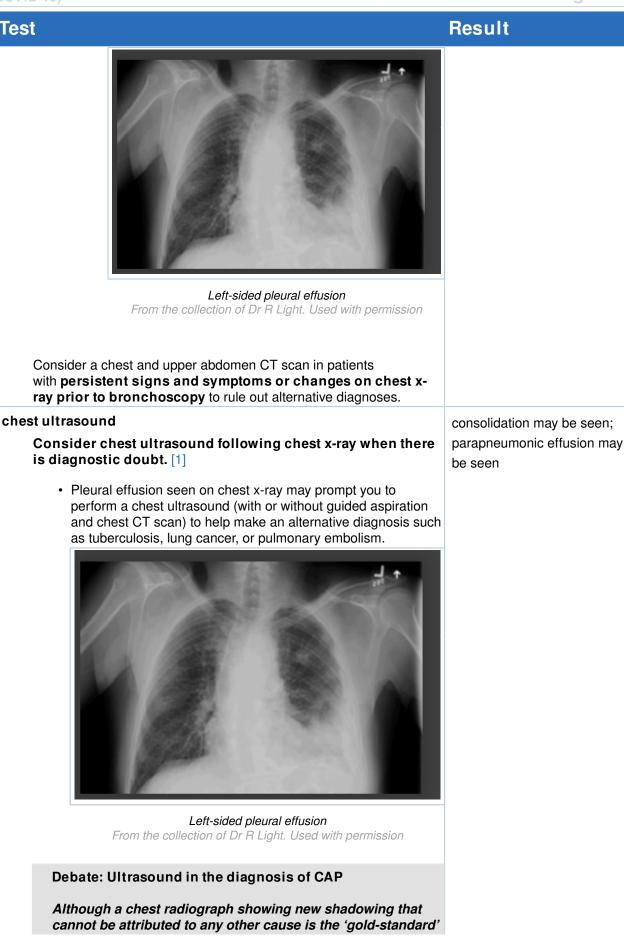


Chest radiograph showing left upper lobe cavitating pneumonia From the collection of Dr Jonathan Bennett. Used with permission

- Consolidation pattern (multifocal) CT helps identify alternative diagnoses such as staphylococcal infection, tuberculosis, aspiration pneumonia, allergic bronchopulmonary aspergillosis, cryptogenic organising pneumonia, or drug hypersensitivity reaction
- **Pleural effusion** CT (in conjunction with chest ultrasound and guided aspiration) helps identify parapneumonic effusion, empyema, tuberculosis, lung cancer
  - Approximately 40% of patients who are hospitalised for pneumonia develop a parapneumonic effusion.[90]

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### Diagnosis



## Diagnosis

COVID-19)	Diagnosi
Test	Result
for the diagnosis of pneumonia, it may not always be feasible in a community setting and it involves exposure to radiation.	
<ul> <li>Emerging evidence has shown that lung ultrasound is a possible accurate diagnostic test for people with CAP. However, the benefits of its use in practice over chest radiography are still unclear.</li> <li>A meta-analysis of 12 studies looking at the diagnostic accuracy of lung ultrasound in people with CAP found a sensitivity and specificity of 0.88 and 0.86, respectively.[93] However, there were limitations, such as the large variability in the findings and the lack of heterogeneity of the studies reviewed.</li> <li>Further evidence is required before recommendations can be made.</li> </ul>	
<ul> <li>thoracocentesis and pleural fluid culture</li> <li>Consider thoracocentesis in all patients with pleural effusion as this can reveal an infected pleural space consistent with a parapneumonic effusion or empyema. [1]</li> <li>[65]</li> <li>A positive Gram stain of pleural fluid indicates an empyema. In these patients, drain pleural fluid in those with an empyema or clear pleural fluid with pH &lt;7.2.[1]</li> </ul>	exudate; growth of causative bacterial species in case of empyema
<ul> <li>computer tomographic pulmonary angiography (CTPA)</li> <li>Consider CTPA to rule out pulmonary embolism if symptoms came on quickly (within minutes) or pain and breathlessness preceded infective symptoms. [92]</li> <li>CTPA has the best diagnostic accuracy of all advanced non-invasive imaging methods in the detection of pulmonary embolism.[112]</li> </ul>	may reveal a thrombus in a pulmonary artery; appears as a partial or complete intraluminal filling defect
bronchoscopy	• • • • • •
Consider bronchoscopy during recovery in patients with persisting signs and symptoms of CAP and radiological abnormalities at around 6 weeks after completing treatment. [1] [65] • The most common techniques are bronchoalveolar lavage (BAL) and protected specimen brushing (PSB).	<ul> <li>BAL: 10<sup>4</sup> colony-forming units (CFU)/mL indicates infection</li> <li>PSB: 10<sup>3</sup> CFU/mL has been recommended to distinguish colonisation from infection</li> </ul>
serum procalcitonin Consider ordering serum procalcitonin. Baseline procalcitonin is increasingly being used in critical care settings and in the emergency department to guide decisions on antibiotic treatment in patients with highly suspected sepsis and in those with suspected bacterial infection.[81] [97] [98] [99] [100]	may be elevated

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## Diagnosis

Test	Result
<ul> <li>Increased values of procalcitonin are correlated with bacterial pneumonia, whereas lower values are correlated with viral and atypical pneumonia. Procalcitonin is especially elevated in cases of pneumococcal pneumonia.[101] [102]</li> </ul>	
<ul> <li>Procalcitonin is a peptide precursor of calcitonin, which is responsible for calcium homeostasis. It is currently excluded from key guidelines, but increasingly used in practice.</li> </ul>	
point-of-care CRP	elevated
General investigations are not necessary for the majority of patients with CAP who are managed in the community.[1] [113] However, you should consider a point-of-care CRP if you cannot make a diagnosis of CAP from the clinical assessment and it is not clear whether antibiotics should be prescribed.[63]	
High levels of CRP do not necessarily indicate that pneumonia is bacterial or SARS-CoV-2, but low CRP levels make a secondary bacterial infection less likely.[111]	

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# Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Coronavirus disease 2019 (COVID-19)	<ul> <li>Residence in/travel history to an area with ongoing transmission, or close contact with a suspected/ confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>Differentiating community-acquired bacterial pneumonia from COVID-19 is not usually possible from signs and symptoms. However, patients with bacterial pneumonia are more likely to have rapid development of symptoms and purulent sputum. They are less likely to have myalgia, anosmia, or pleuritic pain.[109]</li> <li>This topic covers pneumonia caused by COVID-19 as a differential diagnosis only. For more detail on the diagnosis and management of community-acquired pneumonia caused by COVID-19, see our topic Coronavirus disease 2019 (COVID-19)</li> </ul>	<ul> <li>Real-time reverse transcription polymerase chain reaction (RT-PCR): positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA.</li> <li>It is not possible to differentiate COVID-19 from other causes of pneumonia on chest imaging.</li> </ul>
Acute bronchitis	<ul> <li>No dyspnoea, no lung crackles, mild presentation.</li> <li>Often related to a viral upper respiratory tract infection.</li> </ul>	<ul> <li>No consolidation on CXR, with frequency related to viral infection.</li> </ul>
Congestive heart failure	<ul> <li>Peripheral oedema, cardiomegaly, hypotension.</li> </ul>	Bilateral interstitial pattern     or pleural effusions seen on     CXR.
COPD exacerbation	<ul> <li>Increased expectoration and cough, and worsening of dyspnoea against a background of COPD. Patient is often a smoker.</li> </ul>	CXR shows hyperinflation.
Asthma exacerbation	<ul> <li>Symptoms and signs of bronchospasm, with worsening of underlying lung disease.</li> </ul>	No consolidation on CXR.

Condition	Differentiating signs /	Differentiating tests
	symptoms	
Bronchiectasis exacerbation	<ul> <li>Increased expectoration and cough, and worsening of dyspnoea, with worsening of underlying lung disease. Infections are typically recurrent.</li> </ul>	No consolidation on CXR.
Tuberculosis	<ul> <li>Typically a long history, often with constitutional symptoms. Many patients will have lived in an endemic area.</li> </ul>	Cavitation on CXR, enlarged lymph nodes, positive purified protein derivative (PPD) skin testing.
Lung cancer or lung metastases	<ul> <li>Constitutional symptoms are common.</li> </ul>	Consolidation on CXR may be multiple, with pleural effusion commonly seen.
Empyema	<ul> <li>Constitutional symptoms are common, usually associated with a recent respiratory infection.</li> </ul>	Pleural effusion seen on CXR. Microbiology of pleural fluid may reveal infecting organism.
Pulmonary embolism	<ul> <li>Suspect pulmonary embolism in a patient with acute onset of dyspnoea, pleuritic chest pain, or features of deep vein thrombosis. In general, symptoms developing within minutes are more suggestive of pulmonary embolism than of community-acquired pneumonia.</li> <li>Cough is usually non- productive.</li> <li>Fever is generally lower in pulmonary embolism (i.e., below 39°C [102.2°F]).[73]</li> </ul>	Multiple-detector computed tomographic pulmonary angiography (CTPA): direct visualisation of thrombus in a pulmonary artery; appears as a partial or complete intraluminal filling defect.
Pneumothorax	<ul> <li>May be difficult to differentiate on the basis of signs and symptoms. In general, symptoms developing within minutes are more suggestive of pneumothorax than of community-acquired pneumonia.</li> <li>Spontaneous pneumothorax may occur as a complication of pneumonia.</li> </ul>	CXR: presence of a visceral pleural line.[114]
Hypersensitivity pneumonitis	<ul> <li>May be difficult to differentiate on the basis of signs and symptoms.</li> </ul>	Immunological response to causative antigen: positive.

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Condition	Differentiating signs / symptoms	Differentiating tests
	<ul> <li>Acute hypersensitivity pneumonitis lasts only a few days and recurs with each additional exposure.</li> </ul>	

# Criteria

Determine disease severity (and therefore mortality risk) in patients with a working diagnosis of pneumonia using the CURB-65 score in hospital or the CRB-65 score in the community together with your clinical judgement. The score allows initiation of appropriate antibiotic therapy and confirms whether the patient can be managed in the community or needs to be admitted to hospital.

# CURB-65 score[115]

Recommended by the British Thoracic Society (BTS) and the National Institute for Health and Care Excellence (NICE) in the UK for use in the hospital setting, CURB-65 stratifies patients according to the presence or absence of five prognostic features.[1] [63] [65] Mortality at 30 days increases with the number of criteria that are met. Always use the CURB-65 score in conjunction with your clinical judgement.[1] [63] [65]

Scoring of the CURB-65 for CAP in hospital

- · Prognostic factors
  - Confusion (e.g., Abbreviated Mental Test score ≤8 [Abbreviated Mental Test Score]): 1 point
  - Urea >7 mmol/L (>19.6 mg/dL): 1 point
  - Respiratory rate ≥30 breaths/minute: 1 point
  - Blood pressure <90 mmHg systolic or <60 mmHg diastolic: 1 point</li>
  - Age ≥65 years: 1 point
- Score
  - Score 3-5: high-risk; 30-day mortality >15%
    - Score of 3 or more: discuss with senior colleague at the earliest opportunity and manage as high-severity pneumonia.
    - Score of 4-5: arrange emergency assessment by a critical care specialist.
  - Score 2: moderate-risk; 30-day mortality 3% to 15%
    - · Consider for short-stay inpatient treatment or hospital-supervised outpatient treatment.
  - Score 0-1: low-risk; 30-day mortality <3%</li>
    - Consider for outpatient treatment.

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Diagnosis

## CRB-65 score[115]

Recommended by the BTS and NICE in the UK to be used in the community setting, CRB-65 stratifies patients according to the presence or absence of four prognostic features. Always use the CRB-65 score in conjunction with your clinical judgement.[1] [63] [65]

Scoring of the CRB-65 for CAP in the community [115]

- · Prognostic factors
  - Confusion (e.g., Abbreviated Mental Test score ≤8 [Abbreviated Mental Test Score]): 1 point
  - Respiratory rate ≥30 breaths/minute: 1 point
  - Blood pressure <90 mmHg systolic or <60 mmHg diastolic: 1 point
  - Age ≥65 years: 1 point
- Score
  - Score 3-4: high-risk; 30-day mortality >10%
    - · Admit to hospital immediately.
  - Score 1-2: moderate-risk; 30-day mortality 1% to 10%
    - Consider hospital referral and assessment (particularly in those with a score of 2).
  - Score 0: low-risk; 30-day mortality <1%
    - Consider for treatment at home.

# Pneumonia severity index (PSI)[116]

The PSI score predicts the risk of 30-day mortality; patients with a high risk are managed in hospital, and those with the highest risk are managed in the intensive care unit. The PSI stratifies patients into 5 categories based on patient age, comorbidities, physical examination, and results of laboratory testing. The principal limitation is the high score accorded to variables such as age and comorbidities. In the UK, the BTS and NICE consider the simplicity of the calculation of the CURB-65 score to be an advantage over PSI.[1] [63] [65]

#### Scoring of the PSI for CAP [116]

- Demographics
  - Male: points = age in years
  - Female: points = age in years minus 10
  - Nursing home resident: +10 points
  - Liver disease: +20 points
  - Neoplastic disease: +30 points
  - Congestive heart failure: +10 points
  - Cerebrovascular disease: +10 points

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- Renal failure: +10 points
- Physical examination findings
  - Altered mental status: +20 points
  - Respiratory rate ≥30 breaths/minute: +20 points
  - Systolic blood pressure <90 mmHg: +20 points
  - Temperature <35°C (<95°F) or ≥40°C (≥104°F): +15 points
  - Pulse rate ≥125 beats/minute: +10 points
- · Laboratory and radiographic findings
  - Arterial pH <7.35: +30 points
  - Urea ≥10.7 mmol/L (≥30 mg/dL): +20 points
  - Sodium <130 mmol/L (<130 mEq/L): +20 points
  - Glucose ≥13.9 mmol/L (≥250 mg/dL): +10 points
  - Haematocrit <30%: +10 points
  - PaO <sub>2</sub> <60 mmHg (<90% O <sub>2</sub> saturation): +10 points
  - Pleural effusion: +10 points

Score

- Risk class I: 0 to 50 points: outpatients; 0.1% mortality
- · Risk class II: 51 to 70 points: outpatients; 0.6% mortality
- Risk class III: 71-90 points: short hospital stay for observation; 2.8% mortality
- Risk class IV: 91-130 points: hospital admission; 8.2% mortality
- Risk class V: >130 points: hospital admission; 29.2% mortality

# Recommendations

# Urgent

Think '**Could this be sepsis?**' based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[66] [67] [68] See Sepsis in adults .

- Use a systematic approach, alongside your clinical judgement, for assessment; urgently consult a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis.[67] [68] [69] [70]
- Refer to local guidelines for the recommended approach at your institution for assessment and management of the patient with suspected sepsis.
- Pneumonia is one of the main sources of sepsis.[80]

During the COVID-19 pandemic, for patients with suspected or confirmed COVID-19 pneumonia, see Coronavirus disease 2019 (COVID-19). Consider all patients with cough, fever, or other suggestive symptoms to have COVID-19 until proven otherwise.

• Pneumonia due to COVID-19 is not covered in this topic.

# Urgent: in hospital

Stratify patients with pneumonia confirmed by chest x-ray according to **mortality risk and disease severity using the CURB-65 score and your clinical judgement**. Use the score to help inform your management plan.

- Score of 3-5: high-severity.
  - Score of 3 or more: discuss with a senior colleague at the earliest opportunity and manage as high-severity pneumonia.[1] [63] [65]
  - Score of 4 or 5: arrange emergency assessment by a critical care specialist.[1] [65]
- Score of 2: manage as moderate-severity pneumonia.
- Score of 0 or 1: manage as low-severity pneumonia.

**Give empirical antibiotics immediately** to all patients with CAP confirmed by chest x-ray. Patients should receive antibiotics within **4 hours of presentation** to hospital.[1] [65] [117]

- High-severity CAP: give broad-spectrum intravenous antibiotics refer to your local protocol.
- Moderate- and low-severity CAP: give oral antibiotics (or intravenous if oral therapy is contraindicated) refer to your local protocol.

Give empirical antibiotics to patients with **life-threatening disease** based on a presumptive clinical diagnosis, then order an immediate chest x-ray to confirm the diagnosis.[1] [65]

 Follow your local protocol for investigation and treatment of all patients with suspected sepsis, or those at risk. Start treatment promptly.Determine urgency of treatment according to likelihood of infection and severity of illness, or according to your local protocol.[70][81]

Assess oxygen requirements. Prescribe oxygen if **oxygen saturation <94%** and maintain at target range.[1] [65] **In patients at risk of hypercapnia prescribe oxygen if oxygen saturation <88%**.[71]

Monitor controlled ox ygen therapy. An upper SpO <sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are **not at risk of hypercapnia**.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO <sub>2</sub> of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

Measure and record observations at least twice daily and more frequently (e.g., every hour) in those admitted to a critical care unit to inform your management plan.[1] [65]

Review all patients with high-severity CAP (high risk of death) at least every 12 hours until improvement.[1] **This should be done by a senior colleague and the medical team**.[1] [65]

# Urgent: in the community

Stratify patients according to mortality risk and disease severity using the **CRB-65 score** (see our *Diagnosis – recommendations* section for more information) and your **clinical judgement**.[1] [65]

- Score of 3 or more (high-severity): admit patient to hospital immediately.[1] [63] [65]
- Score of 1 or 2 (moderate-severity): refer to hospital. These patients are at increased risk of death, particularly those with a score of 2.[1] [63] [65]
- Score of 0 (low-severity): treat most patients at home.[1] [63] [65]

Consider treatment at home for patients with a CRB-65 score of 0 (low-severity), or a CRB-65 score of 1 or 2 (medium-severity) if they wish to be treated at home and they meet all of the following criteria:[1] [63] [65]

- · They are able to take oral medication safely and reliably
- · Their social circumstances make them suitable for treatment at home
- They do not have unstable comorbidities.

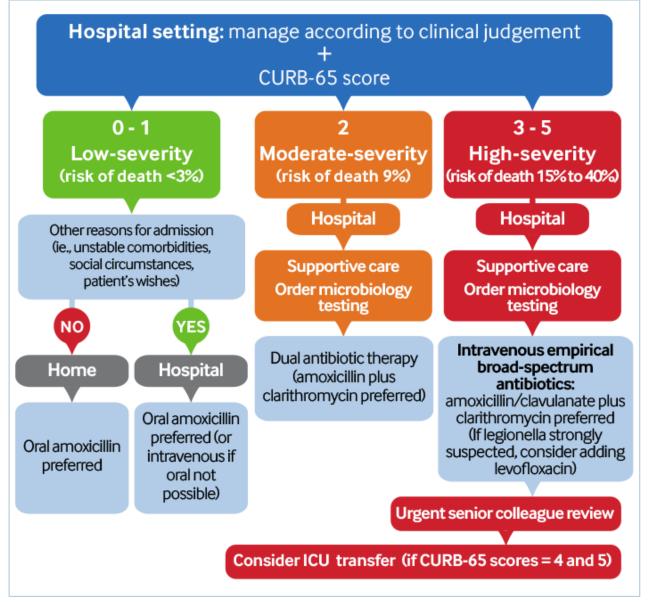
# Take a cautious approach when deciding whether it is safe to treat any patient with moderate-severity CAP (CRB-65 score of 1 or 2) in the community.

Give **empirical antibiotics prior to hospital transfer** (usually by blue-light ambulance in the UK) to patients with suspected CAP considered to be **life-threatening**.[1] [65] Follow your local protocol.

**Consider giving antibiotics prior to hospital transfer** (usually by blue-light ambulance in the UK) to patients with suspected CAP where there are likely to be **delays of over 6 hours** to hospital admission and treatment.[1] [65] Follow your local protocol.

# **Key Recommendations**

Risk assessment and management of CAP in the first 4 hours: hospital setting

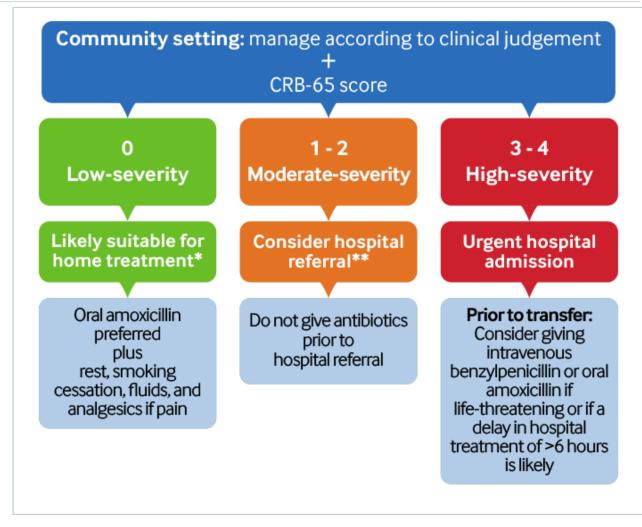


Risk assessment and management of CAP in the first 4 hours: hospital setting

Adapted from Lim WS, et al. Thorax. 2009 Oct;64(suppl 3):iii1-55

Risk assessment and management of CAP in the first 4 hours: community setting

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Risk assessment and management of CAP in the first 4 hours: community setting. \*Consider social circumstances, unstable comorbidities, ability to take oral treatment safely and reliably, and patient's wishes when deciding whether to treat patients at home. \*\*The majority of patients with moderate-severity CAP should be referred to hospital. However, you should consider social circumstances, ability to take oral treatment safely, unstable comorbidities, and patient's wishes when deciding on home treatment Adapted from Lim WS, et al. Thorax. 2009 Oct;64(suppl 3):iii1-55

### Supportive care

Give intravenous fluids to patients with volume depletion.[1] [65]

Arrange for patients with CURB-65 scores of 4 and 5 and an indication for intensive care unit (ICU) admission to be **transferred to ICU** and managed by ICU specialists together with respiratory physicians. [1] [65]

• Patients with respiratory failure despite appropriate oxygen therapy require urgent airway management and possible intubation.

Do not routinely give **non-invasive ventilation (NIV)** or **continuous positive airways pressure** (CPAP) **support** in patients with respiratory failure due to CAP.[1] [65] • If indicated, you should conduct a trial of non-invasive support only in a critical care area where immediate expertise is available to allow a rapid transition to invasive ventilation.[1]

Give simple analgesia (e.g., paracetamol) as appropriate (e.g., for pleuritic pain).[1] [65]

### Other treatments

Do not give corticosteroids routinely to patients with CAP of any severity.[1] [63] [65]

• **Discuss with a senior colleague** patients with **comorbidities** for which corticosteroids are indicated.[63]

## Failure to improve

Discuss with a senior colleague any patient who does not improve as expected.[1] [65]

- Consider repeat chest x-ray, C-reactive protein, white cell count, and further specimens for microbiology in patients who are not progressing satisfactorily after 3 days of treatment.[1] [65]
- Consider referral to a respiratory physician. [1] [65]

## Prognosis

For hospitalised patients, mortality rate ranges from 5% to 15%, but increases to between 20% and 50% in patients requiring admission to the ICU.[6] [118] Patients treated in the community generally have a good prognosis.[1]

# **Full Recommendations**

# **Risk stratification**

Determine disease severity in patients with a working diagnosis of CAP as severe pneumonia is associated with a high risk of complications and death. [64]

- Stratify patients into those with low-, moderate- or high-severity disease (see below).[1] [63] [65]
- Early identification of severity allows initiation of **appropriate antibiotic therapy**, as well as confirming whether the patient can be managed in the community or needs to be admitted to hospital where assisted ventilation in an intensive care setting may be necessary.[1] [63] [65]

### Practical tip

Think '**Could this be sepsis?**' based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[66] [67] [68] See Sepsis in adults .

- The patient may present with non-specific or non-localised symptoms (e.g., acutely unwell with a normal temperature) or there may be severe signs with evidence of multi-organ dysfunction and shock.[66] [67] [68]
- Remember that sepsis represents the severe, life-threatening end of infection.[79]
- Pneumonia is one of the main sources of sepsis.[80]

Use a systematic approach (e.g., National Early Warning Score 2 [NEWS2]), alongside your clinical judgement, to assess the risk of deterioration due to sepsis.[66] [68][69] [81] Consult local guidelines for the recommended approach at your institution.

Arrange urgent review by a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis:[70]

- Within 30 minutes for a patient who is critically ill (e.g., NEWS2 score of 7 or more, evidence of septic shock, or other significant clinical concerns).
- Within 1 hour for a patient who is severely ill (e.g., NEWS2 score of 5 or 6).

Follow your local protocol for investigation and treatment of all patients with suspected sepsis, or those at risk. Start treatment promptly. Determine urgency of treatment according to likelihood of infection and severity of illness, or according to your local protocol.[70][81]

In the community: refer for emergency medical care in hospital (usually by blue-light ambulance in the UK) any patient who is acutely ill with a suspected infection and is:[67]

- Deemed to be at high risk of deterioration due to organ dysfunction (as measured by risk stratification)
- At risk of neutropenic sepsis.

### Use your clinical judgement in conjunction with a scoring system:[1] [63] [65]

- CURB-65 in hospital
- CRB-65 in the community.

#### Debate: The importance of clinical judgement

#### Your clinical judgement is key when assessing severity in CAP using a scoring system.

- For example, consider a young person with a normal blood pressure and urea level, but a low oxygen saturation despite supplemental oxygen. This person could potentially have severe pneumonia, but you could miss this if you only use a scoring system in your assessment.[64]
- You should use mortality prediction tools such as CURB-65 and CRB-65 to supplement, rather than replace, clinical judgement when assessing severity in CAP.

Consult with a senior colleague regarding the decision to start antibiotics at the earliest opportunity. [1]

### In hospital

Assess severity using the CURB-65 score and your clinical judgement to identify patients with suspected CAP **at high risk of death** so that you can **prioritise immediate treatment** and consider whether the patient should be admitted.[1] [63] [65]

Assess severity regularly in all patients with CAP following hospital admission.[1] [65]

• An early opportunity for this is **by a senior colleague and the medical team** during the ward round following admission.[1]

### CURB-65 score: hospital setting

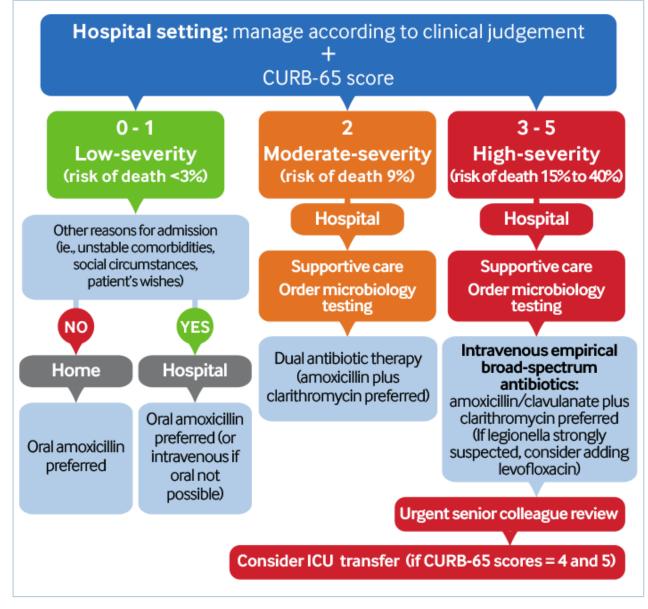
Score 1 point for each feature present:

- Confusion\*
- Urea >7 mmol/L (>19.6 mg/dL)
- Respiratory rate ≥30/minute
- Blood pressure (systolic <90 mmHg or diastolic ≤60 mmHg)
- Age ≥65 years.
- \*Use the Abbreviated Mental Test to assess for confusion. [Abbreviated Mental Test Score]
  - Each question scores 1 mark, with a total possible score of 10 marks.
  - A score of 8 or less has been used to define mental confusion in the CURB-65 severity score.[63]

Discuss patients with a CURB-65 score of 3 or more **with a senior colleague** at the earliest opportunity and manage as high-severity pneumonia (see below).[1] [63] [65]

**Arrange emergency assessment** of patients with a CURB-65 score of 4 or 5 by a critical care specialist.[1] [65]

### Risk assessment and management of CAP in the first 4 hours: hospital setting



Risk assessment and management of CAP in the first 4 hours: hospital setting Adapted from Lim WS, et al. Thorax. 2009 Oct;64(suppl 3):iii1-55

**Follow your local protocol when prescribing antibiotics.** The recommendations given here are based on British Thoracic Society (BTS) guidelines.[1] [65] See our *Management in hospital* section below for more detail on antibiotic regimens.

#### Evidence: Effectiveness of the CURB-65 mortality risk score

CURB-65 is an accurate prognostic tool for predicting mortality in patients with CAP, and it is recommended by the British Thoracic Society (BTS) and the National Institute for Health and Care Excellence (NICE) alongside clinical judgement. [1] [63] [65]

- It was developed from three prospective studies in the UK, New Zealand, and the Netherlands that included more than 1000 patients with CAP.[115]
- Validation studies have been carried out in several countries (including more than 3000 patients in total). They have shown increasing mortality with increasing CURB-65 scores, ranging from 0% to 1.1% (CURB-65 score = 0) to 17% to 60% (CURB-65 score = 5),[119] [120] [121] [122] and increasing need for mechanical ventilation with increasing CURB-65 scores, ranging from 0% (CURB-65 score = 0) to 11% (CURB-65 score = 5).[122]
  - In a study comparing CURB-65 to the pneumonia severity index (PSI), CURB-65 showed equal sensitivity and higher specificity (74.6% CURB-65 vs. 52.2% PSI) in predicting mortality due to CAP.[119]
  - Another study suggests that PSI may be more accurate than CURB-65 (and CRB-65) in predicting 30-day mortality in patients with CAP.[123]
- Despite emerging evidence for some benefits of PSI, both NICE and the BTS consider the simplicity of the calculation of the CURB-65 score to be an advantage over PSI. [1] [63] [65]

### In the community

Assess severity using the CRB-65 score together with your clinical judgement to decide whether to treat patients with suspected CAP at home or refer to hospital for assessment or hospital admission. [1] [63] [65]

#### CRB-65 score: community setting

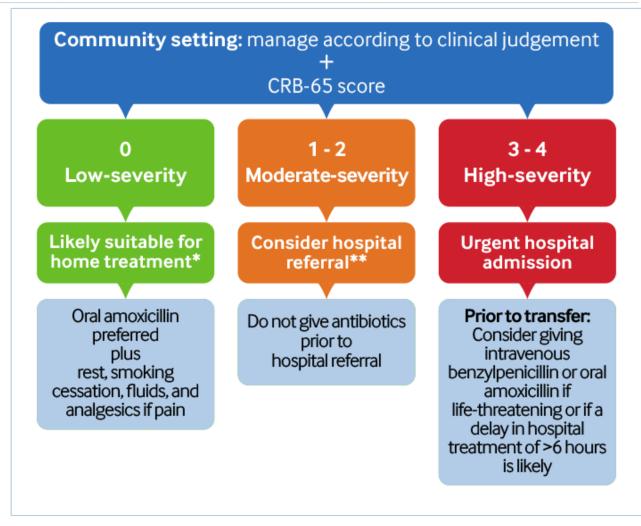
Score 1 point for each feature present:

- Confusion\*
- Respiratory rate ≥30/minute
- Blood pressure (systolic <90 mmHg or diastolic ≤60 mmHg)</li>
- Age ≥65 years.

\*Use the Abbreviated Mental Test to assess for confusion. [Abbreviated Mental Test Score]

- Each question scores 1 mark, with a total possible score of 10 marks.
- A score of 8 or less has been used to define mental confusion in the CRB-65 severity score.[63]

#### Risk assessment and management of CAP: community setting



Risk assessment and management of CAP in the first 4 hours: community setting. \*Consider social circumstances, unstable comorbidities, ability to take oral treatment safely and reliably, and patient's wishes when deciding whether to treat patients at home. \*\*The majority of patients with moderate-severity CAP should be referred to hospital. However, you should consider social circumstances, ability to take oral treatment safely, unstable comorbidities, and patient's wishes when deciding on home treatment Adapted from Lim WS, et al. Thorax. 2009 Oct;64(suppl 3):iii1-55

**Follow your local protocol when prescribing antibiotics.** The recommendations given here are based on BTS and NICE guidelines.[1] [65] [117] See our *Management in the community* section below for more detail on antibiotic regimens.

# Management in hospital

# Antibiotics

**Give empirical antibiotics to all patients with CAP confirmed by chest x-ray** immediately after diagnosis and within 4 hours of presentation to hospital.[1] [65] [117]

- Aim to give antibiotics to all patients with confirmed CAP before they leave the initial assessment area.[1] [65]
- Give empirical antibiotics to patients with **life-threatening disease** based on a **presumptive clinical diagnosis of CAP**, then order an immediate chest x-ray to confirm the diagnosis.[1] [65]

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- For these patients, follow your local protocol for investigation and treatment of all patients with suspected sepsis, or those at risk. Start treatment promptly. Determine urgency of treatment according to likelihood of infection and severity of illness, or according to your local protocol.[70][81] See Sepsis in adults .
- Pneumonia is one of the main sources of sepsis.[80]
- It is important to make an early, accurate diagnosis of infection and use antibiotics appropriately.

**Consult with a senior colleague** about your decision to start antibiotics at the earliest opportunity.[1] [65]

• Clearly document the indication for prescribing antibiotics in the medical notes.[1]

**De-escalate treatment as soon as appropriate**, including switching from intravenous to oral antibiotic therapy.[1] When making this decision consider response to treatment (see practical tip), change in disease severity, and contraindications to oral administration such as:[1] [65]

- Patient is unable to swallow (e.g., impaired swallowing reflex, impaired consciousness)
- Gastrointestinal malabsorption for functional or anatomical reasons.

**Review route of administration** initially on the ward round following admission and then daily thereafter.[1] [65]

### Practical tip

### Pointers to clinical improvement

The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

- Pulse rate <100 beats/minute
- · Resolution of tachypnoea
- · Clinically hydrated and taking oral fluids
- Resolution of fever for >24 hours
- 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.

Consider **narrowing the spectrum of antibiotics** or switching to **pathogen-targeted antibiotics** once a causative pathogen is identified.[1] [65]

### **Empirical antibiotics**

**Treat the majority of patients empirically** as the causative pathogen is only rarely identified at the initial assessment.[1] [65]

Prescribe an appropriate antibiotic regimen according to your local protocol to help reduce the development of antibiotic resistance and *Clostridium difficile* infection.[1] [65] To aid antibiotic stewardship, the British Thoracic Society (BTS) recommends:[1] [65]

- Give empirical broad-spectrum intravenous antibiotics only to patients with high-severity CAP, and de-escalate to narrow-spectrum antibiotics as soon as clinically appropriate, based on the results of early microbiological investigations.[1] [65]
  - This group comprises approximately one third of all patients admitted to hospital with confirmed CAP.[1]
- Give empirical antibiotics to all other patients and switch to pathogen-targeted antibiotics as soon as specific pathogens are identified.
- Consult with a microbiologist about appropriate antibiotic therapy.[1] [65]

**Consult local antibiotic protocols** to determine the most appropriate choice based on local pathogen prevalence and antibiotic resistance patterns.

Consider whether a correct diagnosis of CAP has been made if a patient does not respond to initial empirical antibiotics. [1] [65]

- Consider clinical and radiographic review to look for secondary diagnoses or complications of CAP such as pleural effusion/empyema, lung abscess, or worsening pneumonic shadowing.[1]
- Consider changing initial empirical antibiotics but first consider compliance with and adequate absorption of an oral regimen.[1]

The following recommendations are based on guidelines from the BTS and the National Institute for Health and Care Excellence (NICE).[1] [65] [117]

High-severity CAP (CURB-65 score: 3 or more)

Always manage patients with high-severity CAP in hospital. [1]

Give empirical broad-spectrum intravenous antibiotics immediately after diagnosis and within 4 hours of presentation to hospital.[1] [65] [117]

### Evidence: Time to first antibiotic within 4 hours of presentation

#### The BTS CAP care bundle study was carried out in 2013 in 16 UK hospital trusts.

- The CAP care bundle consisted of four elements:
  - A chest x-ray obtained within 4 hours of hospital admission in all adults with suspected CAP
  - Oxygen assessment and prescription in keeping with the BTS oxygen guideline[71]
  - · Severity assessment supported by the CURB-65 score
  - Timely and targeted antibiotics given according to CAP severity within 4 hours of admission.

The study compared patients with CAP receiving the CAP care bundle with those receiving standard care. Analysis of data from 2118 adults (median age 75.3 years) showed that significantly more patients in the CAP care bundle group received antibiotics within 4 hours of admission (adjusted odds ratio [OR] 1.52, 95% CI 1.08 to 2.14, P = 0.016) and that 30-day inpatient mortality was lower in this group (8.8% vs. 13.6%; adjusted odds ratio [OR] 0.59, 95% CI 0.37 to 0.95, P = 0.03).[124]

Give a broad-spectrum beta-lactamase-resistant penicillin (e.g., amoxicillin/clavulanate) plus a macrolide(e.g., clarithromycin).[1] [65]

- The BTS guideline recommends adding a fluoroquinolone to the existing empirical regimen (i.e., triple therapy) if the patient does not respond, or if legionella pneumonia is strongly suspected.[1] [65] However, in practice there are concerns about the risk of using a macrolide and fluoroquinolone together as they can both prolong the QT interval. Some clinicians therefore replace the macrolide in the original empirical regimen with a fluoroquinolone instead (i.e., dual therapy). Consider the safety issues associated with fluoroquinolone use. Consult with a microbiologist and senior colleague before treating these patients.
- More recent (2019) guidelines from NICE on antimicrobial prescribing in adults also recommend amoxicillin/clavulanate plus clarithromycin (or erythromycin) as first-line in people with high-severity CAP. These recommendations are based mainly on expert opinion as the evidence is limited.[117]

For **patients who are allergic to penicillin**, give a second-generation cephalosporin (e.g., cefuroxime) or a third-generation cephalosporin (e.g., cefotaxime or ceftriaxone) plus a macrolide (e.g., clarithromycin).[1] [65]

- A small number of patients are allergic to both penicillins and cephalosporins; consult an infectious disease consultant for selection of appropriate antibiotics in these patients.
- NICE guidelines on antimicrobial prescribing in adults recommend levofloxacin (after considering safety issues associated with fluoroquinolone use) as an alternative antibiotic for patients with highseverity CAP who are allergic to penicillin.[117]

# Review the need for intravenous antibiotics initially during the ward round following admission and then every day thereafter. [1] [65]

 NICE guidelines on antimicrobial prescribing in adults recommend reviewing intravenous antibiotics by 48 hours, and considering switching to oral treatment if possible.[117] Best practice is to review intravenous antibiotics every day; most intravenous antibiotics can be stopped and switched to oral treatment within 24 hours.

Switch to oral antibiotics as soon as clinical improvement occurs (see practical tip above for pointers to clinical improvement) and as long as there are no contraindications to oral administration such as:[1] [65]

- Patient is unable to swallow (e.g., impaired swallowing reflex, impaired consciousness)
- Gastrointestinal malabsorption for functional or anatomical reasons.

### Give antibiotic therapy for 5 days. [117] [125] NICE recommends: [117]

- Prescribing the shortest course that is likely to be effective to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects[117]
- Stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable. This should be based on your clinical judgement and the following criteria:[117] [126]
  - Fever in the past 48 hours, or more than one sign of clinical instability:
    - Systolic blood pressure <90 mmHg
    - Heart rate >100/minute
    - Respiratory rate >24/minute
    - Arterial oxygen saturation <90% or PaO 2 <60 mmHg in room air.

In some people, longer courses might be needed due to individual circumstances. In the UK, some hospitals require consultation with the microbiology team if considering extending the duration of antibiotic treatment beyond 5 days in high-severity CAP. Follow your local protocol.

• NICE guidelines do not provide an upper limit on antibiotic course length. This will be determined in individual circumstances, based on time taken to reach clinical stability.[117]

### Moderate-severity CAP (CURB-65 score: 2)

# Give antibiotics as soon as possible after diagnosis and within 4 hours of presentation to hospital. [1] [65] [117]

Consider patients with moderate-severity CAP for short-stay inpatient treatment or hospital-supervised outpatient treatment.[1] [65]

### Evidence: Time to first antibiotic within 4 hours of presentation

#### The BTS CAP care bundle study was carried out in 2013 in 16 UK hospital trusts.

- The CAP care bundle consisted of four elements:
  - A chest x-ray obtained within 4 hours of hospital admission in all adults with suspected CAP.
  - Oxygen assessment and prescription in keeping with the BTS oxygen guideline[71]
  - · Severity assessment supported by the CURB-65 score
  - Timely and targeted antibiotics given according to CAP severity within 4 hours of admission.
- The study compared patients with CAP receiving the CAP care bundle with those receiving standard care. Analysis of data from 2118 adults (median age 75.3 years) showed that significantly more patients in the CAP care bundle group received antibiotics ≤4 hours after admission (adjusted OR 1.52, 95% CI 1.08 to 2.14, P = 0.016) and that 30-day inpatient mortality was lower in this group (8.8% vs. 13.6%; adjusted OR 0.59, 95% CI 0.37 to 0.95, P = 0.03).[124]

Most patients with **moderate-severity CAP** can be treated with **dual oral antibiotic therapy**. The preferred choice is **amoxicillin plus a macrolide** (e.g., clarithromycin).[1] [65]

 NICE guidelines on antimicrobial prescribing in adults recommend monotherapy with amoxicillin in people with moderate-severity CAP, with the addition of clarithromycin (or erythromycin) only if an atypical pathogen is suspected. These recommendations are based mainly on expert opinion as the evidence is limited.[117]

Consider **monotherapy with a macrolide** for patients who have been **treated in the community and who have not responded** to an adequate course of amoxicillin prior to hospital admission.[1] [65]

Deciding whether the course of amoxicillin was adequate is tricky and involves clinical judgement.
 Consult a senior clinician before prescribing monotherapy within the first 24 hours of admission.[1] [65]

If **oral antibiotics are contraindicated** (e.g., patient is unable to swallow or has gastrointestinal malabsorption for functional or anatomical reasons), give intravenous amoxicillin or benzylpenicillin, plus clarithromycin.[1] [65]

For patients who are **allergic to penicillin or macrolides**, consider oral doxycycline.[1] [65] Alternative choices include oral levofloxacin or moxifloxacin (after considering safety issues associated with fluoroquinolone use).[1] [65]

• NICE guidelines on antimicrobial prescribing in adults with CAP recommend doxycycline or clarithromycin in people who are allergic to penicillin.[117]

For patients who are **allergic to penicillin in whom oral antibiotics are contraindicated**, give a second-generation cephalosporin (e.g., cefuroxime) or a third-generation cephalosporin (e.g., cefotaxime or ceftriaxone) plus clarithromycin, or intravenous levofloxacin as monotherapy.[1] [65]

If the **patient does not respond** to a combination of amoxicillin plus clarithromycin consider changing treatment to doxycycline or a fluoroquinolone with effective pneumococcal cover.[1] [65]

### More info: EMA and MHRA restrictions on the use of fluoroquinolone antibiotics

In November 2018, the European Medicines Agency (EMA) completed a review of serious, disabling, and potentially irreversible adverse effects associated with systemic and inhaled fluoroquinolone antibiotics. These adverse effects include tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.

- As a consequence of this review, the EMA now recommends that fluoroquinolone antibiotics be restricted for use in serious, life-threatening bacterial infections only. Furthermore, they recommend that fluoroquinolones should not be used for mild to moderate infections unless other appropriate antibiotics for the specific infection cannot be used, and should not be used in non-severe, non-bacterial, or self-limiting infections. Patients who are older, have renal impairment, or have had a solid organ transplant, and those being treated with a corticosteroid are at a higher risk of tendon damage. Co-administration of a fluoroquinolone and a corticosteroid should be avoided.[127] The UK-based Medicines and Healthcare products Regulatory Agency (MHRA) supports these recommendations.[128]
- For this reason, fluoroquinolones should only be considered in moderate-severity CAP when it is considered inappropriate to use other antibiotics that are commonly recommended for the treatment of CAP. **Consult with a microbiologist about whether a fluoroquinolone is an appropriate option for your patient.**

Review the need for intravenous antibiotics initially on the ward round following admission and then every day thereafter.[1] [65]

 NICE guidelines on antimicrobial prescribing in adults recommend reviewing intravenous antibiotics by 48 hours, and considering switching to oral treatment if possible.[117] Best practice is to review intravenous antibiotics every day; most intravenous antibiotics can be stopped and switched to oral treatment within 24 hours.

Switch to oral antibiotics as soon as clinical improvement occurs (see practical tip), and as long as there are no contraindications to oral administration such as:[1] [65]

- Patient is unable to swallow (e.g., impaired swallowing reflex, impaired consciousness)
- Gastrointestinal malabsorption for functional or anatomical reasons.

### Practical tip

### Pointers to clinical improvement

The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

- Pulse rate <100 beats/minute
- · Resolution of tachypnoea
- Clinically hydrated and taking oral fluids
- Resolution of fever for >24 hours
- 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.

### Give antibiotic therapy for 5 days. [117] [125] NICE recommends: [117]

- Prescribing the shortest course that is likely to be effective to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects
- Stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable. This should be based on your clinical judgement and the following criteria:[117] [126]
  - Fever in past 48 hours, or more than one sign of clinical instability:
    - Systolic blood pressure <90 mmHg
    - Heart rate >100/minute
    - Respiratory rate >24/minute
    - Arterial oxygen saturation <90% or PaO 2 <60 mmHg in room air.

One RCT found that in patients with moderately severe CAP who met clinical stability criteria, discontinuing beta-lactam treatment after 3 days was non-inferior to 8 days of treatment, suggesting that 3 days of antibiotics may be sufficient in immunocompetent, non-severely ill patients that are clinically improved at day 3.[129]

In some people, longer courses might be needed due to individual circumstances. In the UK, some hospitals require consultation with the microbiology team if considering extending the duration of antibiotic treatment beyond 5 days in moderate-severity CAP. Follow your local protocol.

• NICE guidelines do not provide an upper limit on antibiotic course length. This will be determined in individual circumstances, based on time taken to reach clinical stability.[117]

Low-severity CAP (CURB-65 score: 0-1)

Give antibiotics as soon as possible and within 4 hours of presentation to hospital.[1] [65] [117]

### Evidence: Time to first antibiotic within 4 hours of presentation

#### The BTS CAP care bundle study was carried out in 2013 in 16 UK hospital trusts.

- The CAP care bundle consisted of four elements:
  - A chest x-ray obtained within 4 hours of hospital admission in all adults with suspected CAP
  - Oxygen assessment and prescription in keeping with the BTS oxygen guideline[71]
  - · Severity assessment supported by the CURB-65 score
  - Timely and targeted antibiotics given according to CAP severity within 4 hours of admission.
- The study compared patients with CAP receiving the CAP care bundle with those receiving standard care. Analysis of data from 2118 adults (median age 75.3 years) showed that significantly more patients in the CAP care bundle group received antibiotics ≤4 hours after admission (adjusted OR 1.52, 95% CI 1.08 to 2.14, P = 0.016) and that 30-day inpatient mortality was lower in this group (8.8% vs. 13.6%; adjusted OR 0.59, 95% CI 0.37 to 0.95, P = 0.03).[124]

Most patients with **low-severity CAP** who are managed in hospital can be treated with **oral antibiotics**.[1] [65] **The preferred choice is amoxicillin**. [1] [65] Consider a macrolide (e.g., clarithromycin) or a tetracycline (e.g., doxycycline) for patients who are allergic to penicillin.[1] [65]

 NICE recommends clarithromycin (or erythromycin) or doxycycline as alternatives to amoxicillin for patients allergic to penicillin and for patients in whom amoxicillin is unsuitable (e.g., if atypical pneumonia is suspected). NICE recommendations are based mainly on expert opinion as the evidence is limited.[117]

If the oral route is contraindicated (e.g., impaired swallowing reflex, impaired consciousness, gastrointestinal malabsorption), consider **intravenous amoxicillin, benzylpenicillin, or clarithromycin**.[1] [65]

- Review the need for intravenous antibiotics initially during the ward round following admission and then every day after.[1] [65] NICE guidelines on antimicrobial prescribing in adults recommend reviewing intravenous antibiotics by 48 hours, and considering switching to oral treatment if possible.[117] Best practice is to review intravenous antibiotics every day; most intravenous antibiotics can be stopped and switched to oral treatment within 24 hours.
- Switch to oral antibiotics as soon as clinical improvement occurs (see practical tip), and as long as there are no contraindications to oral administration.[1] [117] [65]

### Practical tip

### Pointers to clinical improvement

The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

- Pulse rate <100 beats/minute
- · Resolution of tachypnoea
- Clinically hydrated and taking oral fluids
- Resolution of fever for >24 hours
- · 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.

If the **patient does not respond**to amoxicillin monotherapy, consider switching to, or adding, a macrolide (e.g., clarithromycin).[1] [65]

### Give antibiotic therapy for 5 days. [117] [125] NICE recommends: [117]

- Prescribing the shortest course that is likely to be effective to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects
- Stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable. This should be based on your clinical judgement and the following criteria:[117] [126]
  - Fever in past 48 hours, or more than one sign of clinical instability:
    - Systolic blood pressure <90 mmHg
    - Heart rate >100/minute
    - Arterial oxygen saturation <90% or PaO  $_{\rm 2}$  <60 mmHg in room air.

### Pathogen-targeted antibiotic treatment

Switch from empirical antibiotics to pathogen-targeted antibiotics as soon as **specific pathogens are identified** (unless there are legitimate concerns about dual-pathogen infection).[1] [65]

- Consult with a microbiologist about appropriate antibiotic therapy. [1] [65]
- Only about one third to one quarter of patients with CAP admitted to hospital will have their pneumonia defined microbiologically.[1] Among these patients:
  - Around 14% have an atypical pathogen, of which:[21]
    - 7% have Mycoplasma pneumoniae

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- 4% have Chlamydophila pneumoniae
- 3% have Legionella pneumophila
- Those with infections due to organisms such as *Mycoplasma*, *Chlamydophila*, and *Coxiella burnetii* will be diagnosed late in the illness on the basis of seroconversion, reducing the opportunity for early targeted therapy.[1] Among patients managed in the community, very few will be microbiologically defined.[1]

Consider switching treatment once the results of sensitivity testing are available or following consultation with a microbiologist, intensivist, or respiratory physician.[1]

### BTS recommendations for pathogen-targeted antibiotics [1] [65]

### Management

Pathogen	Preferred antibiotic	Alternative antibiotic
Mycoplasma pneumoniae Chlamydophila pneumoniae	Clarithromycin (orally or intravenously)	Doxycycline (orally) or a fluoroquinolone (orally or intravenously)
<i>Legionella</i> species	Fluoroquinolone (orally or intravenously)	Clarithromycin (orally or intravenously) or azithromyc (in countries where it is used for managing pneumonia)
Streptococcus pneumoniae	Amoxicillin (orally) or benzylpenicillin (intravenously)	Clarithromycin (orally) or cefuroxime or cefotaxime or ceftriaxone (intravenously)
Chlamydia psittaci Coxiella burnetii	Doxycycline (orally)	Clarithromycin (orally or intravenously)
Haemophilus influenzae	Non-beta-lactamase- producing: amoxicillin (orally or intravenously) Beta-lactamase-producing: amoxicillin/clavulanate (orally or intravenously)	Cefuroxime or cefotaxime or ceftriaxone (intravenously) o a fluoroquinolone (orally or intravenously)
Gram-negative enteric bacilli	Cefuroxime or cefotaxime or ceftriaxone (intravenously)	Fluoroquinolone (intravenously) or imipenem/ cilastatin (intravenously) or meropenem (intravenously)
Pseudomonas aeruginosa	Ceftazidime (intravenously)	Ciprofloxacin (intravenously) or piperacillin/tazobactam (intravenously)
	Gentamicin or tobramycin (dose monitoring required)	<b>plus</b> Gentamicin or tobramycin (dose monitoring required)
<i>Staphylococcus aureus</i> : non- MRSA	Flucloxacillin (intravenously) with or without Rifampicin (orally or intravenously)	
<i>Staphylococcus aureus</i> : MRSA	Vancomycin (intravenously; dose monitoring required) or	

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Pathogen	Preferred antibiotic	Alternative antibiotic
	linezolid (intravenously) or teicoplanin (intravenously)	
	with or without	
	Rifampicin (orally or intravenously)	

# Supportive care

Provide supportive care for patients treated in hospital. This may include the following measures. [1] [65]

## Oxygen

### Assess oxygen saturation in all patients by pulse oximetry (preferably while breathing air).

 Give oxygen if oxygen saturation <94% and maintain at target range.[1] [65] In patients at risk of CO 2 retention, give oxygen if oxygen saturation <88%. Early oxygen assessment is associated with improved prognosis.[71]

Monitor controlled ox ygen therapy. An upper SpO  $_2$  limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are not at risk of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO <sub>2</sub> of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

#### Evidence: Target oxygen saturation in acutely ill adults

#### Too much supplemental oxygen increases mortality.

Evidence from a large systematic review and meta-analysis supports conservative/ controlled oxygen therapy versus liberal oxygen therapy in acutely ill adults who are not at risk of hypercapnia.

- Guidelines differ in their recommendations on target oxygen saturation in acutely unwell adults who are receiving supplemental oxygen.
  - The 2017 British Thoracic Society (BTS) guideline recommends a target SpO <sub>2</sub> range of 94% to 98% for patients not at risk of hypercapnia, whereas the 2022 Thoracic Society of Australia and New Zealand (TSANZ) guideline recommends 92% to 96%.[71] [130]
  - The 2022 Global Initiative for Asthma (GINA) guidelines recommend a target SpO 2 range of 93% to 96% in the context of acute asthma exacerbations.
- A systematic review including a meta-analysis of data from 25 randomised controlled trials, published in 2018 found that in adults with acute illness, liberal oxygen therapy (broadly equivalent to a target saturation >96%) is associated with higher mortality than conservative oxygen therapy (broadly equivalent to a target saturation ≤96%).[72] In-hospital mortality was 11 per 1000 higher for the liberal oxygen therapy group versus the conservative therapy group (95% CI, 2 to 22 per 1000 more). Mortality at 30 days was also higher in the group who had received liberal oxygen (RR 1.14, 95% CI 1.01 to 1.29). The trials included adults with sepsis, critical illness, stroke, trauma, myocardial infarction, cardiac arrest, and patients who had emergency surgery. Studies that were limited to people with chronic respiratory illness or psychiatric illness, or patients on extracorporeal life support, receiving hyperbaric oxygen therapy, or having elective surgery, were all excluded from the review.
- An upper SpO<sub>2</sub> limit of 96% is therefore reasonable when administering supplemental oxygen to patients with acute illness who are not at risk of hypercapnia. However, a higher target may be appropriate for some specific conditions (e.g., pneumothorax, carbon monoxide poisoning, cluster headache, and sickle cell crisis).[132]
- In 2019 the BTS reviewed its guidance in response to this systematic review and meta-analysis and decided an interim update was not required.[113]
  - The committee noted that the systematic review supported the use of controlled oxygen therapy to a target.
  - While the systematic review showed an association between higher oxygen saturations and higher mortality, the BTS committee felt the review was not definitive on what the optimal target range should be. The suggested range of 94% to 96% in the review was based on the lower 95% confidence interval and the median baseline SpO <sub>2</sub> from the liberal oxygen groups, along with the earlier 2015 TSANZ guideline recommendation.
- Subsequently, experience during the COVID-19 pandemic has also made clinicians more aware of the feasibility of permissive hypoxaemia.[133]

- Management of oxygen therapy in patients in intensive care is specialised and informed by further evidence that is more specific to this setting.[134] [135] [136]
- **Measure arterial blood gases** in those with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO <sub>2</sub> retention), and all patients with high-severity CAP.[1] [65]

### Practical tip

Always record the inspired oxygen concentration clearly as this is essential for interpreting blood gas results.

## Standard intensive care unit (ICU) supportive care

Arrange for patients with **CURB-65 scores of 4 and 5 and an indication for ICU admission** to be **transferred to ICU** and managed by ICU specialists together with respiratory physicians.[1] [65]

• Patients with respiratory failure despite appropriate oxygen therapy require urgent airway management and possible intubation.

Do not routinely give non-invasive ventilation (NIV) or continuous positive airways pressure (CPAP) support in patients with respiratory failure due to CAP.[1] [65]

• If indicated, you should conduct a trial of non-invasive support only in a critical care area where immediate expertise is available to allow a rapid transition to invasive ventilation.[1] [65]

## Vasopressors

Start vasopressors if the patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure level ≥65 mmHg.[137]

### Intravenous fluids

Assess all patients for volume depletion and give intravenous fluids if required.[1] [65]

### Venous thromboembolism (VTE) prophylaxis

**Consider prophylaxis for VTE with a low molecular weight heparin** for all patients who are not fully mobile.[1] [65]

### **Nutritional support**

**Arrange nutritional support**(whether enteral, parenteral, or via nasogastric feeding) for patients with severe CAP who require a prolonged hospital stay.[1] [65]

### Airway clearance

Do not treat people with uncomplicated pneumonia with traditional airway clearance techniques routinely. If needed, offer these patients advice regarding expectoration of sputum.[1] [65]

**Consider airway clearance techniques** if the patient has difficulty expectorating sputum or if they have a pre-existing lung condition.[1] [65]

## Analgesia

Give simple analgesia (e.g., paracetamol) as appropriate (e.g., for **pleuritic pain**).[1] [65]

### Practical tip

Encourage patients with uncomplicated CAP (i.e., not complicated by the presence of parapneumonic effusion, empyema, abscess, pneumothorax, necrotising pneumonia, or bronchopleural fistula), whose medical condition allows them to, to sit out of bed. Initially aim for at least 20 minutes in the first 24 hours, and then increase mobility each subsequent day of hospitalisation.

# **Other treatments**

### Corticosteroids

Do not give corticosteroids routinely to patients with CAP of any severity. [1] [63] [65]

• **Discuss with a senior colleague** patients with comorbidities for which corticosteroids are indicated.[63]

### Debate: Corticosteroid treatment in CAP

Latest evidence suggests corticosteroids given as an adjunct to antibiotic treatment improve outcomes in adults with CAP but increases the risk of hyperglycaemia. The recommendation from NICE not to give corticosteroids routinely remains valid until further evidence is available.

- A Cochrane review including 17 studies evaluated the safety and efficacy of corticosteroids given as an adjunct to antibiotic treatment for adults and children with pneumonia (CAP, hospital-acquired pneumonia, and ventilator-associated pneumonia). The intervention included oral prednisolone in 3 trials and intravenous dexamethasone, hydrocortisone, or methylprednisolone in 13 trials. The findings suggest that corticosteroids significantly reduced mortality and morbidity in patients with high-severity CAP. They also reduced morbidity, although not mortality, in patients with moderate- or low-severity CAP. Hyperglycaemia was the most common adverse event in adults treated with corticosteroids; however, the authors concluded that overall the benefits outweigh the harms.[138]
- Two systematic reviews (published before the Cochrane review) also looked at the safety and efficacy of adjunctive glucocorticoids for patients with CAP.[139] [140] They showed no significant difference in all-cause mortality and reported significant reductions in length of ICU stay,[139] length of hospital stay,[139] [140] and length of time to clinical stability in the corticosteroid groups.[139] [140] One of the reviews reported an increased risk of hyperglycaemia in patients treated with corticosteroids.[140]
- NICE is due to review this area when the results of two ongoing trials have been published. For now, the recommendation not to give corticosteroids routinely remains valid.[63]

# Monitoring

**Measure observations** initially at least twice daily, and more frequently (e.g., every hour) in **those** admitted to a critical care unit (high-dependency unit or ICU).[1] [65] Monitor:

- Pulse
- Blood pressure
- · Respiratory rate
- Temperature
- Oxygen saturation (with a recording of the inspired oxygen saturation at the same time)
- Mental status.

Consider measuring a **baseline C-reactive protein concentration** in patients with CAP on admission to hospital, and repeat the test if clinical progress is uncertain after 48 to 72 hours.[1] [63] [65]

# **Review all patients with high-severity CAP** at least **every 12 hours** until clinical improvement occurs.[1] [65] **This should be done by a senior colleague and the medical team.** [1] [65]

### Practical tip

### Pointers to clinical improvement

The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

- Pulse rate <100 beats/minute
- · Resolution of tachypnoea
- · Clinically hydrated and taking oral fluids
- Resolution of fever for >24 hours
- 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.

Assess severity regularly in all patients with CAP following hospital admission.[1] [65] An early opportunity for this is the ward round following admission by a senior colleague and medical team.[1] [65]

For more information on complications related to CAP see our separate Complications section.

## Failure to improve

### Discuss with a senior colleague any patient who does not improve as expected. [1] [65]

- Consider repeat chest x-ray, C-reactive protein, white cell count, and further specimens for microbiology in patients not progressing satisfactorily after 3 days of treatment.[1] [65]
- Consider referral to a respiratory physician.[1] [65]

## Practical tip

The main reasons why patients do not improve as expected include:[1] [65]

- Incorrect diagnosis or complicating condition (e.g., pulmonary embolism, bronchial carcinoma, bronchiectasis)
- Unexpected pathogen or pathogens not covered by antibiotic choice (e.g., 'atypical' pathogens, pathogens resistant to commonly used antibiotics such as ampicillin-resistant *Haemophilus influenzae*)
- Antibiotic ineffective or causing allergic reaction (e.g., poor absorption of oral antibiotic, inadequate dose, antibiotic hypersensitivity)
- Impaired local (e.g., bronchiectasis, endobronchial obstruction, aspiration) or systemic (e.g., HIV infection, myeloma) defenses
- Local (e.g., parapneumonic effusion, empyema, lung abscess) or distant (e.g., metastatic infection, septicaemia, phlebitis at intravenous cannula site) complications of CAP
- Overwhelming infection
- Improvement expected too soon (e.g., in older patients).

# Discharge from hospital

Do not routinely discharge patients if they have had 2\* or more of the following findings present in the past 24 hours:[63]

- Temperature >37.5°C (>99.5°F)
- Heart rate >100/minute
- Respiratory rate ≥24/minute
- Systolic blood pressure ≤90 mmHg
- Oxygen saturation <90% on room air
- · Inability to maintain oral intake
- · Abnormal mental status.

(\*The BTS recommends basing your decision to discharge patients with CAP on 1 or more of the findings listed [unless they represent the usual baseline status for that patient] and uses a temperature threshold of 37.8°C [100.04°F]. See +Debate below.[1] [65])

**Consider delaying discharge** of patients with CAP **if their temperature is higher than 37.5** °C (99.5 ° F).[63]

#### Debate: Cut-off temperature for safe discharge

The BTS considers a temperature >37.8°C (>100.04°F), rather than the >37.5°C (>99.5°F) threshold recommended by NICE, as a finding that should prompt you to consider delaying discharge in a patient with CAP. [1] [65]

- The >37.5°C (>99.5°F) threshold that is recommended by NICE is based on the conclusions of a prospective cohort study that looked at the value of simple clinical variables for predicting short-term outcomes in patients with pneumonia.[63] [141]
- It found a cut-off of 37.5°C (99.5°F) to be strongly associated with 30-day mortality risk.
- For this reason we have based our recommendation on NICE guidance.

At discharge or at follow-up, **offer patients access to information about CAP**, such as a patient information leaflet.[1] [65]

Arrange a follow-up visit at around 6 weeks either with the patient's general practitioner or in a hospital clinic.[1] [65]

## Follow-up after discharge

**Request a repeat chest x-ray during recovery after about 6 weeks** for patients (regardless of whether they have been admitted to hospital):[1] [65]

- With persisting symptoms or physical signs
- Who are at **higher risk of underlying malignancy** (especially smokers and those aged >50 years).

Consider bronchoscopy during recovery in patients with persisting signs, symptoms, and radiological abnormalities at around 6 weeks after completing treatment.[1] [65]

# Management in the community

Use the **CRB-65 mortality risk tool and your clinical judgement** to determine which patients are suitable for management in the community (see our section above on *Risk stratification*).

Consider treatment at home for patients with a CRB-65 score of 0 (low-severity) or a CRB-65 score of 1 or 2 (medium-severity) if they wish to be treated at home and they meet all of the following criteria: [1] [63] [65]

- · They are able to take oral medication safely and reliably
- · Their social circumstances make them suitable for treatment at home
- They do not have unstable comorbidities.

Take a cautious approach, however, when deciding whether it is safe to treat any patient with moderate-severity CAP (CRB-65 score of 1 or 2) in the community. These patients are at increased risk of death, particularly those with a CRB-65 score of 2. You should refer the majority for management in hospital. [1] [63] [65]

• If you decide to treat the patient in the community, follow the same treatment recommendations given below for patients with suspected CAP presenting in the community (low-severity).

# Refer any patients presenting in the community with a CRB-65 score of 3 or more for immediate hospital admission (usually by blue-light ambulance in the UK). [1] [63] [65]

### Practical tip

If you need to refer a patient for emergency medical care in hospital, it is important to inform the hospital clinical team that the patient is on the way. This will enable the hospital to initiate appropriate treatment as soon as the patient arrives.

# Antibiotics

The following recommendations are **based on guidelines from the British Thoracic Society (BTS)** and the **National Institute for Health and Care Excellence (NICE)**.[1] [65] [117]

## Giving antibiotics prior to hospital transfer

### High-severity CAP (CRB-65 score 3 or 4)

Give empirical antibiotics prior to hospital transfer (usually by blue-light ambulance in the UK) to patients with suspected CAP considered to be life-threatening.[1] [65] Follow your local protocol.

- The first-line choice is intravenous benzylpenicillin or oral amoxicillin. Clarithromycin is an alternative for people who are allergic to penicillin.[1]
  - More recent (2019) guidelines from NICE on antimicrobial prescribing in adults recommend amoxicillin/clavulanate plus clarithromycin (or erythromycin) first-line in people with highseverity CAP. These recommendations are based mainly on expert opinion as the evidence is limited.[117]

Consider giving antibiotics prior to hospital transfer to patients with suspected highseverity CAP where there are likely to be delays of over 6 hours to hospital admission and treatment. [1] [65]

• Pre-admission antibiotics can negatively influence the results of subsequent microbiological investigations, but this is not seen as a reason for withholding antibiotics if a general practitioner considers it indicated.[1]

Moderate-severity CAP (CRB-65 score 1 or 2) and low-severity CAP (CRB-65 score 0)

**Do not give antibiotics** to patients with **moderate-severity CAP** or **low-severity CAP** prior to hospital referral.[1] [65]

## **Empirical antibiotics for home treatment**

Give empirical oral antibiotics to patients treated in the community.

- The first-line option is amoxicillin. [1] [65] [117]
- Alternative options for patients who are **allergic to penicillin** are a macrolide (e.g., clarithromycin) or a tetracycline (e.g., doxycycline).[1] [65]
  - NICE recommends clarithromycin (or erythromycin) or doxycycline as alternatives to amoxicillin for patients allergic to penicillin and for patients in whom amoxicillin is unsuitable (e.g., if atypical pneumonia is suspected). NICE recommendations are based mainly on expert opinion as the evidence is limited.[117]

## Consider adding or switching to a macrolide if the patient does not respond to amoxicillin. [1] [65]

- Consider whether a correct diagnosis of CAP has been made if a patient does not respond to initial empirical antibiotics.[1]
  - Consider clinical and radiographic review to look for secondary diagnoses or complications of CAP such as pleural effusion/empyema, lung abscess, or worsening pneumonic shadowing.[1]
  - Consider changing initial empirical antibiotics but first consider compliance with and adequate absorption of an oral regimen.[1]

### Give antibiotic therapy for 5 days. [117] [125] NICE recommends: [117]

- Prescribing the shortest course that is likely to be effective to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects
- Stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable. This should be based on your clinical judgement and the following criteria:[117] [126]
  - Fever in past 48 hours, or more than one sign of clinical instability:
    - Systolic blood pressure <90 mmHg
    - Heart rate >100/minute
    - Respiratory rate >24/minute
    - Arterial oxygen saturation <90% or PaO 2 <60 mmHg in room air.

# **General management**

Advise patients to rest, to drink plenty of fluids, and not to smoke.[1]

# Failure to respond

Advise patients (and their carers) to seek medical advice if:[117]

Symptoms worsen rapidly or significantly

- Symptoms do not start to improve within 3 days
- The person becomes systemically very unwell.

Around 10% of patients managed in the community do not respond to antibiotic therapy and require hospitalisation.[142]

Admit urgently to hospital any patient on antibiotic treatment with features of moderate- or highseverity infection.[1] [65]

# Follow-up

Order a **chest x-ray during recovery after about 6 weeks** for patients (regardless of whether patients have been admitted to hospital):[1] [65]

- With persisting symptoms or physical signs
- Who are at **higher risk of underlying malignancy** (especially people who smoke and those aged >50 years).

Consider **bronchoscopy** during recovery in patients with **persisting signs**, **symptoms**, **and radiological abnormalities at around 6 weeks after completing treatment**.[1] [65]

# Prognosis

For patients admitted to hospital, **mortality rate** ranges from 5% to 15%, but increases to 20% to 50% in patients requiring admission to the **intensive care unit** (ICU).[6] [118]

• Risk factors associated with increased 30-day mortality include bacteraemia, admission to the ICU, comorbidities (especially neurological disease), and infection with a potentially multidrug-resistant pathogen (e.g., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, Enterobacteriaceae).[34] [143] [144] [145]

Patients treated in the community generally have a good prognosis.[1] [65]

# Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: <u>see disclaimer</u>

Initial		( summary )
suspected CAP: presenting hospital with life-threatenin		
	1st	empirical intravenous antibiotic therapy
	plus	supportive care
suspected CAP: presenting hospital without life-threate illness		
	1st	supportive care while confirming diagnosis
suspected CAP: presenting community	in the	
·····■ high-severity (CI or 4)	RB-65 = 3 1st	urgent hospital admission
	consider	empirical antibiotic prior to hospital transfer
moderate-severi (CRB-65 = 1 or 2)		hospital referral
Iow-severity (CR	B-65 = 0) 1st	empirical oral antibiotic therapy
	plus	supportive care
	consider	hospital admission

# Community-acquired pneumonia in adults (non COVID-19)

Acute			( summary )
	CAP on chest x-ray: g in hospital		
	high-severity (CURB-65 = 3-5)	1st	empirical intravenous antibiotic therapy
		consider	fluoroquinolone
		plus	supportive care
		consider	switch to pathogen-targeted antibiotic therapy
	moderate-severity (CURB-65 = 2)	1st	empirical oral or intravenous antibiotic therapy
		plus	supportive care
		consider	switch to pathogen-targeted antibiotic therapy
	low-severity (CURB-65 = 0-1)	1st	empirical oral or intravenous antibiotic therapy
		plus	supportive care
		consider	switch to pathogen-targeted antibiotic therapy
	CAP on chest x-ray: g in the community		
		1st	continue empirical antibiotics or switch to pathogen-targeted antibiotic therapy

Management

MANAGEMENT

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# **Treatment algorithm**

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: <u>see disclaimer</u>

## Initial

suspected CAP: presenting in hospital with life-threatening illness

1st

#### empirical intravenous antibiotic therapy

» Give empirical antibiotics to patients presenting in hospital with **life-threatening** disease based on a presumptive clinical diagnosis of CAP.

# » Immediately order a chest x-ray to confirm the diagnosis. [1] [65]

• Once a diagnosis of CAP is confirmed, manage these patients as per the protocols below for patients with *confirmed CAP* on chest x-ray: presenting in hospital.

MANAGEMENT

### Practical tip

Think '**Could this be sepsis?**' based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[66] [67] [68] See Sepsis in adults .

- The patient may present with nonspecific or non-localised symptoms (e.g., acutely unwell with a normal temperature) or there may be severe signs with evidence of multi-organ dysfunction and shock.[66] [67] [68]
- Remember that sepsis represents the severe, life-threatening end of infection.[79]
- Pneumonia is one of the main sources of sepsis.[80]

Use a systematic approach (e.g., National Early Warning Score 2 [NEWS2]), alongside your clinical judgement, to assess the risk of deterioration due to sepsis.[66] [68] [69] [81] Consult local guidelines for the recommended approach at your institution.

Arrange urgent review by a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis:[70]

- Within 30 minutes for a patient who is critically ill (e.g., NEWS2 score of 7 or more, evidence of septic shock, or other significant clinical concerns).
- Within 1 hour for a patient who is severely ill (e.g., NEWS2 score of 5 or 6).

Follow your local protocol for investigation and treatment of all patients with suspected sepsis, or those at risk. Start treatment promptly. Determine urgency of treatment according to likelihood of infection and severity of illness, or according to your local protocol.[70] [81] In the community: refer for emergency medical care in hospital (usually by bluelight ambulance in the UK) any patient who is acutely ill with a suspected infection and is:[67]

- Deemed to be at high risk of deterioration due to organ dysfunction (as measured by risk stratification)
- At risk of neutropenic sepsis.

#### plus supportive care

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

» paracetamol: oral: 500-1000 mg orally every 4-6 hours when required, maximum 4000 mg/day; intravenous (<51 kg body weight): 15 mg/kg intravenously every 4-6 hours when required, maximum 60 mg/kg/ day; intravenous (≥51 kg body weight): 1000 mg intravenously every 4-6 hours when required, maximum 4000 mg/day (3000 mg/ day if risk factors for hepatotoxicity)

» **Provide supportive care**, which may include the following measures.[1] [65]

» Oxygen

» Prescribe oxygen if oxygen saturation <94% and maintain at target range.[1] [65] For patients at risk of CO 2 retention prescribe oxygen if oxygen saturation <88%.[71]</p>

» Monitor controlled ox ygen therapy. An upper SpO<sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are **not at risk** of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO 2 of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

Evidence: Target oxygen saturation in acutely ill adults

Too much supplemental oxygen increases mortality.

Evidence from a large systematic review and meta-analysis supports conservative/controlled oxygen therapy versus liberal oxygen therapy in acutely ill adults who are not at risk of hypercapnia.

• Guidelines differ in their

recommendations on target oxygen

saturation in acutely unwell adults who are receiving supplemental oxygen.

- The 2017 British Thoracic Society (BTS) guideline recommends a target SpO <sub>2</sub> range of 94% to 98% for patients not at risk of hypercapnia, whereas the 2022 Thoracic Society of Australia and New Zealand (TSANZ) guideline recommends 92% to 96%.[71] [130]
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- · A systematic review including a metaanalysis of data from 25 randomised controlled trials, published in 2018 found that in adults with acute illness, liberal oxygen therapy (broadly equivalent to a target saturation >96%) is associated with higher mortality than conservative oxygen therapy (broadly equivalent to a target saturation ≤96%).[72] In-hospital mortality was 11 per 1000 higher for the liberal oxygen therapy group versus the conservative therapy group (95% CI, 2 to 22 per 1000 more). Mortality at 30 days was also higher in the group who had received liberal oxygen (RR 1.14, 95% CI 1.01 to 1.29). The trials included adults with sepsis, critical illness, stroke, trauma, myocardial infarction, cardiac arrest, and patients who had emergency surgery. Studies that were limited to people with chronic respiratory illness or psychiatric illness, or patients on extracorporeal life support, receiving hyperbaric oxygen therapy, or having elective surgery, were all excluded from the review.
- An upper SpO <sub>2</sub> limit of 96% is therefore reasonable when administering supplemental oxygen to patients with acute illness who are not at risk of hypercapnia. However, a higher target may be appropriate for some specific conditions (e.g., pneumothorax, carbon monoxide

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poisoning, cluster headache, and sickle cell crisis).[132]

- In 2019 the BTS reviewed its guidance in response to this systematic review and meta-analysis and decided an interim update was not required.[113]
  - The committee noted that the systematic review supported the use of controlled oxygen therapy to a target.
  - While the systematic review showed an association between higher oxygen saturations and higher mortality, the BTS committee felt the review was not definitive on what the optimal target range should be. The suggested range of 94% to 96% in the review was based on the lower 95% confidence interval and the median baseline SpO <sub>2</sub> from the liberal oxygen groups, along with the earlier 2015 TSANZ guideline recommendation.
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- Management of oxygen therapy in patients in intensive care is specialised and informed by further evidence that is more specific to this setting.[134]
   [135] [136]
- Measure arterial blood gases in those with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO <sub>2</sub> retention), and all patients with highseverity CAP.[1] [65]

#### Practical tip

Always record the inspired oxygen concentration clearly as this is essential for interpreting blood gas results.

Fluid resuscitation

 Assess all patients for volume depletion and give intravenous fluids if required.[1]
 [65]

>>

# » Standard intensive care unit (ICU) supportive care

» Arrange for patients with an indication for ICU admission to be transferred to ICU and managed by ICU specialists together with respiratory physicians.[1] [65]

- Patients with respiratory failure despite appropriate oxygen therapy require urgent airway management and possible intubation.
- Do not routinely give non-invasive ventilation (NIV) or continuous positive airways pressure (CPAP) support in patients with respiratory failure due to CAP.[1] [65]
  - If indicated, you should conduct a trial of non-invasive support only in a critical care area where immediate expertise is available to allow a rapid transition to invasive ventilation.[1] [65]

#### » Vasopressors

 Start vasopressors if the patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure level greater than or equal to 65 mmHg.[137] See Sepsis in adults.

#### Analgesia

• Give simple analgesia as appropriate (e.g., for **pleuritic pain)**.[1] [65]

suspected CAP: presenting in hospital without life-threatening illness		
	1st	supportive care while confirming diagnosis
		Primary options

» paracetamol: oral: 500-1000 mg orally every 4-6 hours when required, maximum 4000 mg/day; intravenous (<51 kg body weight): 15 mg/kg intravenously every 4-6 hours when required, maximum 60 mg/kg/ day; intravenous (≥51 kg body weight): 1000 mg intravenously every 4-6 hours when required, maximum 4000 mg/day (3000 mg/ day if risk factors for hepatotoxicity)

# » Confirm diagnosis by chest x-ray before starting antibiotic therapy.

• In patients presenting in hospital without life-threatening illness, confirm the diagnosis by chest x-ray before starting antibiotics.[1] [65] Once diagnosis is confirmed, patients are managed as per the protocols below for patients with *confirmed CAP on chest x-ray: presenting in hospital.* 

» In the meantime, provide supportive care as necessary, which may include the following measures.[1] [65]

» Oxygen

» Prescribe oxygen if oxygen saturation <94% and maintain at target range.[1] [65] For patients at risk of hypercapnia prescribe oxygen if oxygen saturation <88%.[71]

» Monitor controlled ox ygen therapy. An upper SpO<sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are **not at risk** of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO 2 of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

# Evidence: Target oxygen saturation in acutely ill adults

Too much supplemental oxygen increases mortality.

Evidence from a large systematic review and meta-analysis supports conservative/controlled ox ygen therapy

#### versus liberal oxygen therapy in acutely ill adults who are not at risk of hypercapnia.

- Guidelines differ in their recommendations on target oxygen saturation in acutely unwell adults who are receiving supplemental oxygen.
  - The 2017 British Thoracic Society (BTS) guideline recommends a target SpO <sub>2</sub> range of 94% to 98% for patients not at risk of hypercapnia, whereas the 2022 Thoracic Society of Australia and New Zealand (TSANZ) guideline recommends 92% to 96%.[71]
  - The 2022 Global Initiative for Asthma (GINA) guidelines recommend a target SpO <sub>2</sub> range of 93% to 96% in the context of acute asthma exacerbations.[131]
- · A systematic review including a metaanalysis of data from 25 randomised controlled trials, published in 2018 found that in adults with acute illness, liberal oxygen therapy (broadly equivalent to a target saturation >96%) is associated with higher mortality than conservative oxygen therapy (broadly equivalent to a target saturation ≤96%).[72] In-hospital mortality was 11 per 1000 higher for the liberal oxygen therapy group versus the conservative therapy group (95% CI, 2 to 22 per 1000 more). Mortality at 30 days was also higher in the group who had received liberal oxygen (RR 1.14, 95% CI 1.01 to 1.29). The trials included adults with sepsis, critical illness, stroke, trauma, myocardial infarction, cardiac arrest, and patients who had emergency surgery. Studies that were limited to people with chronic respiratory illness or psychiatric illness, or patients on extracorporeal life support, receiving hyperbaric oxygen therapy, or having elective surgery, were all excluded from the review.
- An upper SpO <sup>2</sup> limit of 96% is therefore reasonable when administering supplemental oxygen

## Management

# Initial

to patients with acute illness who are not at risk of hypercapnia. However, a higher target may be appropriate for some specific conditions (e.g., pneumothorax, carbon monoxide poisoning, cluster headache, and sickle cell crisis).[132]

- In 2019 the BTS reviewed its guidance in response to this systematic review and meta-analysis and decided an interim update was not required.[113]
  - The committee noted that the systematic review supported the use of controlled oxygen therapy to a target.
  - While the systematic review showed an association between higher oxygen saturations and higher mortality, the BTS committee felt the review was not definitive on what the optimal target range should be. The suggested range of 94% to 96% in the review was based on the lower 95% confidence interval and the median baseline SpO <sub>2</sub> from the liberal oxygen groups, along with the earlier 2015 TSANZ guideline recommendation.
- Subsequently, experience during the COVID-19 pandemic has also made clinicians more aware of the feasibility of permissive hypoxaemia.[133]
- Management of oxygen therapy in patients in intensive care is specialised and informed by further evidence that is more specific to this setting.[134]
   [135] [136]
- **Measure arterial blood gases** in those with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO <sub>2</sub> retention), and all patients with highseverity CAP.[1] [65]

#### **Practical tip**

Always record the inspired oxygen concentration clearly as this is essential for interpreting blood gas results.

#### Fluid resuscitation

>>

· Assess all patients for volume depletion and give intravenous fluids if required.[1] [65]

#### Standard intensive care unit (ICU) >> supportive care

» Arrange for patients with an indication for ICU admission to be transferred to ICU and managed by ICU specialists together with respiratory physicians.[1] [65]

- Patients with respiratory failure despite appropriate oxygen therapy require urgent airway management and possible intubation.
- · Do not routinely give non-invasive ventilation (NIV) or continuous positive airways pressure (CPAP) support in patients with respiratory failure due to CAP.[1] [65]
  - If indicated, you should conduct a trial of non-invasive support only in a critical care area where immediate expertise is available to allow a rapid transition to invasive ventilation.[1] [65]

#### Vasopressors

- · Start vasopressors if the patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure level greater than or equal to 65 mmHg.[137] See our Sepsis in adults topic for more information.
- » Analgesia
  - · Give simple analgesia as appropriate (e.g., for pleuritic pain).[1] [65]

#### suspected CAP: presenting in the community



94

high-severity (CRB-65 = 3 · · · · · 💼 or 4)

1st

### urgent hospital admission

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 Refer patients presenting in the community with high-severity CAP (CRB-65 score of 3 or 4) for immediate hospital admission (usually by blue-light ambulance in the UK). [1] [63] [65]

 In hospital, once the diagnosis of CAP is confirmed by chest x-ray and the disease severity has been assessed, patients are managed as per the protocols below for patients with confirmed CAP on chest xray: presenting in hospital.

### **Practical tip**

If you need to refer a patient for emergency medical care in hospital, it is important to inform the hospital clinical team that the patient is on the way. This will enable the hospital to initiate appropriate treatment as soon as the patient arrives.

# consider empirical antibiotic prior to hospital transfer

Treatment recommended for SOME patients in selected patient group

» Give empirical antibiotics prior to hospital transfer (usually by blue-light ambulance in the UK) to any patients with suspected high-severity CAP considered to be lifethreatening, according to your local protocol.[1] [65]

• British Thoracic Society guidelines recommend intravenous benzylpenicillin or oral amoxicillin. Oral clarithromycin is an alternative for people who are allergic to penicillin.[1] [65]

» Consider giving empirical antibiotics **prior to hospital transfer** to patients with **suspected high-severity CAP** where there are likely to be **delays of over 6 hours to hospital admission and treatment**.[1] [65]

 Pre-admission antibiotics can negatively influence the results of subsequent microbiological investigations, but this is not seen as a reason for withholding antibiotics if a general practitioner considers it indicated.[1]

» Consult your local protocol for guidance on selection of antibiotic regimen.

# Community-acquired pneumonia in adults (non COVID-19)

nitial			
	moderate-severity	1st	hospital referral
	(CRB-65 = 1 or 2)		» Refer patients presenting in the community with moderate-severity CAP (CRB-65 score of 1 or 2) to hospital for assessment and management. These patients are at increased risk of death, particularly those with a score of 2.[1] [63] [65]
			• In hospital, once the diagnosis of CAP is confirmed by chest x-ray and the disease severity has been assessed, patients are managed as per the protocols below for patients with <i>confirmed CAP on chest x-ray: presenting in hospital.</i>
			» <b>Consider managing patients in the</b> <b>community</b> if they prefer to be treated at home and they meet the following criteria:[1] [63] [65]
			They are able to take oral medication
-			safely and reliably
-			Their social circumstances make them
			suitable for treatment at home
-			• They do not have unstable comorbidities.
			» Take a cautious approach, however, when deciding whether it is safe to treat any patient with moderate-severity CAP in the community. You should refer the majority for management in hospital.[1] [63] [65]
			• If you decide to treat the patient in the community, follow the same treatment recommendations given below for patients with suspected CAP: presenting in the community (low-severity).
	low-severity (CRB-65 = 0)	1st	empirical oral antibiotic therapy
			<ul> <li>» Give empirical oral antibiotics and manage people with low-severity CAP (CRB-65 score of 0) in the community. [1]</li> <li>[63] [65]</li> </ul>
			<ul> <li>The first-line option is amoxicillin. <ol> <li>[1] [65] Alternative options for patients who are allergic to penicillin are a macrolide (e.g., clarithromycin) or a tetracycline (e.g., doxycycline).[1] [65]</li> <li>If the patient does not respond to amoxicillin monotherapy, consider</li> </ol></li></ul>

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adding, or switching to, a macrolide (e.g., clarithromycin).[1] [65]

» Advise patients (and their carers) to seek medical advice if their symptoms worsen rapidly or significantly, their symptoms do not start to improve within 3 days, or they become systemically very unwell.[117]

 Admit urgently to hospital any patient on antibiotic treatment with features of moderate- or high-severity infection.[1] [65] Around 10% of patients managed in the community do not respond to antibiotic therapy and require hospitalisation.[142]

» Give antibiotic treatment for 5 days. [117] [125] The National Institute for Health and Care Excellence recommends stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable. This should be based on your clinical judgement and the following criteria:[117] [126]

- Fever in past 48 hours, or more than one sign of clinical instability:
  - Systolic blood pressure <90 mmHg
  - Heart rate >100/minute
  - Respiratory rate >24/minute
  - Arterial oxygen saturation <90% or PaO <sub>2</sub> <60 mmHg in room air.

» Consult local protocols for guidance on selection of antibiotic regimen.

#### plus supportive care

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

» paracetamol: oral: 500-1000 mg orally every 4-6 hours when required, maximum 4000 mg/day; intravenous (<51 kg body weight): 15 mg/kg intravenously every 4-6 hours when required, maximum 60 mg/kg/ day; intravenous (≥51 kg body weight): 1000 mg intravenously every 4-6 hours when required, maximum 4000 mg/day (3000 mg/ day if risk factors for hepatotoxicity)

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» Advise patients to rest, to drink plenty of fluids, and not to smoke.[1] [65]

» Give simple analgesia as appropriate (e.g., for **pleuritic pain**).[1] [65]

#### consider hospital admission

Treatment recommended for SOME patients in selected patient group

» Consider referring patients to hospital if:[1] [63] [65]

- They are not able to take oral medication safely and reliably
- Their social circumstances do not make them suitable for treatment at home
- They have unstable comorbidities
- They prefer to be treated in hospital.

» In hospital, once the diagnosis of CAP is confirmed by chest x-ray and the disease severity has been assessed, patients are managed as per the protocols below for patients with *confirmed CAP on chest x-ray: presenting in hospital.* 

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ute			
	CAP on chest x-ray: g in hospital		
Senting	j ili nospital		
	high-severity (CURB-65 = 3-5)	1st	empirical intravenous antibiotic therapy
-			» Always manage patients with high- severity CAP in hospital. [1] [65]
			» Give empirical broad-spectrum intravenous antibiotics immediately afted diagnosis. This should be within 4 hour of presentation to hospital. [1] [65] [117]
			» Prescribe an appropriate antibiotic regimen according to your local protocol to help reduce the development of antibiotic resistance and <i>Clostridium difficile</i> infection. Consult with a microbiologist. The British Thoracic Society (BTS) recommends:[1] [65]
			<ul> <li>A broad-spectrum beta-lactamase- resistant penicillin (e.g., amoxicillin/ clavulanate) plus a macrolide (e.g., clarithromycin).[1] [65]</li> <li>For patients who are allergic to penicillin, give a second-generation cephalosporin (e.g., cefuroxime) or a third-generation cephalosporin (e.g., cefotaxime or ceftriaxone) plus a macrolide (e.g., clarithromycin).[1] [65]</li> <li>A small number of patients are allergic to both penicillins and cephalosporins; consult an infectious disease consultant for selection of appropriate antibiotics in these patients.</li> </ul>
			» Review route of administration initially on th ward round following admission and then dail thereafter.[1] [65] De-escalate treatment as soon as appropriate, including switching from intravenous to oral therapy.[1] [65] When mak this decision consider response to treatment (see practical tip), change in disease severity and contraindications to oral administration su as:[1]
			<ul> <li>Patient is unable to swallow (e.g., impaired swallowing reflex, impaired consciousness)</li> <li>Gastrointestinal malabsorption for functional or anatomical reasons.</li> </ul>

## Management

## Acute

### Practical tip

#### Pointers to clinical improvement

The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

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

» Give antibiotic therapy for 5 days. [117] [125] The National Institute for Health and Care Excellence recommends stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable. [117] This should be based on your clinical judgement and the following criteria:[117] [126]

• Fever in past 48 hours, or more than one sign of clinical instability:

- Systolic blood pressure <90 mmHg</li>
- Heart rate >100/minute
- Respiratory rate >24/minute
- Arterial oxygen saturation <90% or PaO <sub>2</sub> <60 mmHg in room air.</li>

» In some people, longer courses might be needed due to individual circumstances.In the UK, some hospitals require consultation with the microbiology team if considering extending the duration of antibiotic treatment beyond 5 days in high-severity CAP. Follow your local protocol.

» Consult your local protocol for guidance on selection of antibiotic regimen.

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consider	fluoroquinolone
	Treatment recommended for SOME patients in selected patient group
	<ul> <li>Consult with a microbiologist and senior clinician before giving a fluoroquinolone.</li> </ul>
	• Consider safety issues associated with fluoroquinolone use. Fluoroquinolones are known to cause tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[127] [128]
	» The British Thoracic Society guideline recommends adding a fluoroquinolone to the existing empirical regimen (i.e., triple therapy) if the patient does not respond, or if legionella pneumonia is strongly suspected.[1] [65] However, in practice there are concerns about the risk of using a macrolide and a fluoroquinolone together as they can both prolong the QT interval. Therefore, some clinicians may replace the macrolide in the original empirical regimen with a fluoroquinolone instead (i.e., dual therapy).
plus	supportive care
	Treatment recommended for ALL patients in selected patient group
	Primary options
	» paracetamol: oral: 500-1000 mg orally every 4-6 hours when required, maximum 4000 mg/day; intravenous (<51 kg body weight): 15 mg/kg intravenously every 4-6 hours when required, maximum 60 mg/kg/ day; intravenous (≥51 kg body weight): 1000 mg intravenously every 4-6 hours when required, maximum 4000 mg/day (3000 mg/ day if risk factors for hepatotoxicity)
	» Provide supportive care, which may include the following measures.[1] [65]
	» Oxygen
	» Prescribe oxygen if oxygen saturation <94% and maintain at target range.[1] [65] For patients at risk of hypercapnia prescribe oxygen if oxygen saturation <88%.[71]

#### » Monitor controlled ox ygen therapy. An upper SpO <sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most

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patients with acute illness who are **not at risk** of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO 2 of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

Evidence: Target oxygen saturation in acutely ill adults

Too much supplemental oxygen increases mortality.

Evidence from a large systematic review and meta-analysis supports conservative/controlled oxygen therapy versus liberal oxygen therapy in acutely ill adults who are not at risk of hypercapnia.

- Guidelines differ in their recommendations on target oxygen saturation in acutely unwell adults who are receiving supplemental oxygen.
  - The 2017 British Thoracic Society (BTS) guideline recommends a target SpO <sub>2</sub> range of 94% to 98% for patients not at risk of hypercapnia, whereas the 2022 Thoracic Society of Australia and New Zealand (TSANZ) guideline recommends 92% to 96%.[71]
     [130]
  - The 2022 Global Initiative for Asthma (GINA) guidelines recommend a target SpO <sub>2</sub> range of 93% to 96% in the context of acute asthma exacerbations.[131]
- A systematic review including a metaanalysis of data from 25 randomised controlled trials, published in 2018 found that in adults with acute illness, liberal oxygen therapy (broadly equivalent to a target saturation >96%) is associated with higher mortality than conservative oxygen therapy (broadly

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equivalent to a target saturation ≤96%).[72] In-hospital mortality was 11 per 1000 higher for the liberal oxygen therapy group versus the conservative therapy group (95% CI, 2 to 22 per 1000 more). Mortality at 30 days was also higher in the group who had received liberal oxygen (RR 1.14, 95% CI 1.01 to 1.29). The trials included adults with sepsis, critical illness, stroke, trauma, myocardial infarction, cardiac arrest, and patients who had emergency surgery. Studies that were limited to people with chronic respiratory illness or psychiatric illness, or patients on extracorporeal life support, receiving hyperbaric oxygen therapy, or having elective surgery, were all excluded from the review.

- An upper SpO <sub>2</sub> limit of 96% is therefore reasonable when administering supplemental oxygen to patients with acute illness who are not at risk of hypercapnia. However, a higher target may be appropriate for some specific conditions (e.g., pneumothorax, carbon monoxide poisoning, cluster headache, and sickle cell crisis).[132]
- In 2019 the BTS reviewed its guidance in response to this systematic review and meta-analysis and decided an interim update was not required.[113]
  - The committee noted that the systematic review supported the use of controlled oxygen therapy to a target.
  - While the systematic review showed an association between higher oxygen saturations and higher mortality, the BTS committee felt the review was not definitive on what the optimal target range should be. The suggested range of 94% to 96% in the review was based on the lower 95% confidence interval and the median baseline SpO <sub>2</sub> from the liberal oxygen groups, along with the earlier 2015 TSANZ guideline recommendation.
- Subsequently, experience during the COVID-19 pandemic has also made

#### clinicians more aware of the feasibility of permissive hypoxaemia.[133]

- Management of oxygen therapy in patients in intensive care is specialised and informed by further evidence that is more specific to this setting.[134]
   [135] [136]
- Measure arterial blood gases in those with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO <sub>2</sub> retention), and all patients with highseverity CAP.[1] [65]
- Fluid resuscitation

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- Assess all patients for volume depletion and give intravenous fluids if required.[1] [65]
- .

# » Standard intensive care unit (ICU) supportive care

» Arrange for patients with CURB-65 scores of 4 and 5 and an indication for ICU admission to be transferred to ICU and managed by ICU specialists together with respiratory physicians.[1] [65]

- Patients with respiratory failure despite appropriate oxygen therapy require urgent airway management and possible intubation.
- Do not routinely give non-invasive ventilation (NIV) or continuous positive airways pressure (CPAP) support in patients with respiratory failure due to CAP.[1] [65]
  - If indicated, you should conduct a trial of non-invasive support only in a critical care area where immediate expertise is available to allow a rapid transition to invasive ventilation.[1] [65]

#### Vasopressors

>>

 Start vasopressors if the patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure level greater than or equal to 65 mmHg.[137]

# » Venous thromboembolism (VTE) prophylaxis

- Consider prophylaxis for VTE with a low molecular weight heparin for all patients who are not fully mobile.[1] [65] In practice in the UK, prescription of heparin will be prompted if appropriate once you have recorded your VTE risk assessment in the patient's electronic record.
- Nutritional support
  - Arrange nutritional support (whether enteral, parenteral, or via nasogastric feeding) for patients with severe CAP who require a prolonged hospital stay.[1] [65]
- Airway clearance
  - Do not treat people with uncomplicated pneumonia with traditional airway clearance techniques routinely. If needed, offer these patients advice regarding expectoration of sputum.[1] [65]
  - Consider airway clearance techniques if the patient has difficulty expectorating sputum or if they have a pre-existing lung condition.[1] [65]

#### Analgesia

• Give simple analgesia as appropriate (e.g., for **pleuritic pain**).[1]

# consider switch to pathogen-targeted antibiotic therapy

Treatment recommended for SOME patients in selected patient group

#### » Consult with a microbiologist about appropriate pathogen-targeted antibiotic therapy. [1] [65]

 Switch from empirical antibiotics to pathogen-targeted antibiotics as soon as specific pathogens are identified (unless

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there are legitimate concerns about dualpathogen infection).[1] [65]

» Only about one third to one quarter of patients with CAP admitted to hospital will have their pneumonia defined microbiologically.[1] Among these patients:

- Around 14% have an atypical pathogen, of which:[21]
  - 7% have Mycoplasma pneumoniae
  - 4% have Chlamydophila
  - pneumoniae3% have Legionella pneumophila .
- Those with infections due to Mycoplasma, *Chlamydophila*, and Coxiella burnetii will be diagnosed late in the illness on the basis of seroconversion, reducing the opportunity for early targeted therapy.[1]

» Consider switching the choice of agent once the results of sensitivity testing are available or following consultation with a microbiologist, intensivist, or respiratory physician.[1] [65]

Pathogen	Preferred antibiotic	Alternative antibiotic
Mycoplasma pneumoniae Chlamydophila pneumoniae	Clarithromycin (orally or intravenously)	Doxycycline (orally) or a fluoroquinolone (orally or intravenously)
<i>Legionella</i> species	Fluoroquinolon (orally or intravenously)	eClarithromycin (orally or intravenously) or azithromycin (in countries where it is used for managing pneumonia)
Streptococcus pneumoniae	Amoxicillin (orally) or	Clarithromycin (orally) or

#### » BTS recommendations for pathogentargeted antibiotics [1] [65]

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# Community-acquired pneumonia in adults (non COVID-19)

# Management

	Preferred antibiotic	Alternative antibiotic
	benzylpenicillin (intravenously)	cefuroxime or cefotaxime or ceftriaxone (intravenously
naittaai	Doxycycline (orally)	Clarithromycir (orally or intravenously)
influenzae	Non-beta- lactamase- producing: amoxicillin (orally or intravenously) Beta- lactamase- producing: amoxicillin/ clavulanate (orally or intravenously)	Cefuroxime or cefotaxime or ceftriaxone (intravenously or a fluoroquinolor (orally or intravenously)
enteric bacilli	Cefuroxime or cefotaxime or ceftriaxone (intravenously)	Fluoroquinolo (intravenously or imipenem/ cilastatin (intravenously or meropenen (intravenously
neruginosa	Ceftazidime (intravenously) <b>plus</b> Gentamicin or tobramycin (dose monitoring required)	Ciprofloxacin (intravenously or piperacillin/ tazobactam (intravenously <b>plus</b> Gentamicin or tobramycin (dose monitoring required)

# Community-acquired pneumonia in adults (non COVID-19)

# Management

9			
	Pathogen	Preferred antibiotic	Alternative antibiotic
	Staphylococcu aureus : non- MRSA	Flucloxacillin (intravenously)	
		with or without	
		Rifampicin (orally or intravenously)	
	<i>Staphylococcu aureus</i> : MRSA	(intravenously; dose monitoring	
		required) or linezolid (intravenously) or teicoplanin (intravenously)	
		with or without	
		Rifampicin (orally or	
		intravenously)	
e-severity 1st 5 = 2)	empirical oral therapy	or intravenous	antibiotic
	» Consider patie CAP for short-s or hospital-sup treatment.[1] [6]	tay inpatient tr pervised outpat	eatment
	<ul> <li>Give antibio after diagnosis hours of prese [117]</li> </ul>	s. This should	be within 4
	» Give broad-sp antibiotics.	oectrum empiri	cal oral
	can be tre therapy.[1 Society g amoxicil	ents with moderat ated with dual or [65] British Th juidelines reco lin plus a macr ycin).[1] [65]	al antibiotic oracic mmend

MANAGEMENT

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- For patients who are allergic to penicillin or macrolides, consider oral doxycycline.[1] [65] Alternative choices include oral levofloxacin or moxifloxacin (after considering safety issues associated with fluoroquinolone use).[1] [65]
- If oral antibiotics are contraindicated (e.g., patient is unable to swallow or has gastrointestinal malabsorption for functional or anatomical reasons) give intravenous amoxicillin or benzylpenicillin plus clarithromycin.[1] [65]
- For patients who are allergic to penicillin in whom oral antibiotics are contraindicated, give a secondgeneration cephalosporin (e.g., cefuroxime) or a third-generation cephalosporin (e.g., cefotaxime or ceftriaxone) plus clarithromycin, or intravenous levofloxacin monotherapy.[1] [65]
- If the patient does not respond to a combination of amoxicillin and clarithromycin, consider changing treatment to doxycycline or a fluoroquinolone with effective pneumococcal cover (e.g., levofloxacin, moxifloxacin).[1] [65]

#### More info: EMA and MHRA restrictions on the use of fluoroquinolone antibiotics

In November 2018, the European Medicines Agency (EMA) completed a review of serious, disabling, and potentially irreversible adverse effects associated with systemic and inhaled fluoroquinolone antibiotics. These adverse effects include tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.

 As a consequence of this review, the EMA now recommends that fluoroquinolone antibiotics be restricted for use in serious, life-threatening bacterial infections only. Furthermore, they recommend that fluoroquinolones should not be used for mild to moderate infections unless other appropriate antibiotics for the specific infection cannot be used, and should not be used in non-

severe, non-bacterial, or self-limiting infections. Patients who are older, have renal impairment, or have had a solid organ transplant, and those being treated with a corticosteroid are at a higher risk of tendon damage. Coadministration of a fluoroquinolone and a corticosteroid should be avoided.[127] The UK-based Medicines and Healthcare products Regulatory Agency (MHRA) supports these recommendations.[128]

• For this reason, fluoroquinolones (e.g., levofloxacin, moxifloxacin) should only be considered in **moderateseverity CAP** when it is considered inappropriate to use other antibiotics that are commonly recommended for the treatment of CAP. **Consult with a microbiologist about whether a fluoroquinolone is an appropriate option for your patient.** 

» Consider monotherapy with a macrolide for patients who have been treated in the community and who have not responded to an adequate course of amoxicillin prior to hospital admission.[1] [65]

 Deciding whether the course of amoxicillin was adequate is tricky and involves clinical judgement. Consult a senior clinician before prescribing monotherapy within the first 24 hours of admission. [1] [65]

» Review the need for intravenous antibiotics initially on the ward round following admission and then every day thereafter.[1] [65]

 NICE guidelines on antimicrobial prescribing in adults recommend reviewing intravenous antibiotics by 48 hours, and considering switching to oral treatment if possible.[117] Best practice is to review intravenous antibiotics every day; most intravenous antibiotics can be stopped and switched to oral treatment within 24 hours.

» Switch to oral antibiotics as soon as clinical improvement occurs (see practical tip), and as long as there are no contraindications to oral administration (e.g., patient is unable to swallow or has gastrointestinal malabsorption for functional or anatomical reasons).[1] [65]

### Management

### Acute

#### Practical tip

#### Pointers to clinical improvement

The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

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

» Give antibiotic therapy for 5 days. [117] [125] The National Institute for Health and Care Excellence recommends stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable.[117] This should be based on your clinical judgement and the following criteria:[117] [126]

- Fever in past 48 hours, or more than one sign of clinical instability:
  - Systolic blood pressure <90 mmHg
  - Heart rate >100/minute
  - Respiratory rate >24/minute
  - Arterial oxygen saturation <90% or PaO <sub>2</sub> <60 mmHg in room air.

» In some people, longer courses might be needed due to individual circumstances. In the UK, some hospitals require consultation with the microbiology team if considering extending the duration of antibiotic treatment beyond 5 days in moderate-severity CAP. Follow your local protocol.

» Consult your local protocol for guidance on selection of antibiotic regimen.

#### plus supportive care

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

» paracetamol: oral: 500-1000 mg orally every 4-6 hours when required, maximum 4000 mg/day; intravenous (<51 kg body weight): 15 mg/kg intravenously every 4-6 hours when required, maximum 60 mg/kg/ day; intravenous (≥51 kg body weight): 1000 mg intravenously every 4-6 hours when required, maximum 4000 mg/day (3000 mg/ day if risk factors for hepatotoxicity)

» Provide supportive care, which may include the following measures.[1] [65]

» Oxygen

» Prescribe oxygen if oxygen saturation <94% and maintain at target range.[1] [65] For patients at risk of hypercapnia prescribe oxygen if oxygen saturation <88%.[71]

» Monitor controlled ox ygen therapy. An upper SpO<sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are **not at risk** of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO 2 of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

Evidence: Target oxygen saturation in acutely ill adults

Too much supplemental oxygen increases mortality.

Evidence from a large systematic review and meta-analysis supports conservative/controlled oxygen therapy versus liberal oxygen therapy in acutely ill adults who are not at risk of hypercapnia.

• Guidelines differ in their

recommendations on target oxygen

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saturation in acutely unwell adults who are receiving supplemental oxygen.

- The 2017 British Thoracic Society (BTS) guideline recommends a target SpO <sub>2</sub> range of 94% to 98% for patients not at risk of hypercapnia, whereas the 2022 Thoracic Society of Australia and New Zealand (TSANZ) guideline recommends 92% to 96%.[71] [130]
- The 2022 Global Initiative for Asthma (GINA) guidelines recommend a target SpO <sub>2</sub> range of 93% to 96% in the context of acute asthma exacerbations.[131]
- · A systematic review including a metaanalysis of data from 25 randomised controlled trials, published in 2018 found that in adults with acute illness, liberal oxygen therapy (broadly equivalent to a target saturation >96%) is associated with higher mortality than conservative oxygen therapy (broadly equivalent to a target saturation ≤96%).[72] In-hospital mortality was 11 per 1000 higher for the liberal oxygen therapy group versus the conservative therapy group (95% CI, 2 to 22 per 1000 more). Mortality at 30 days was also higher in the group who had received liberal oxygen (RR 1.14, 95% CI 1.01 to 1.29). The trials included adults with sepsis, critical illness, stroke, trauma, myocardial infarction, cardiac arrest, and patients who had emergency surgery. Studies that were limited to people with chronic respiratory illness or psychiatric illness, or patients on extracorporeal life support, receiving hyperbaric oxygen therapy, or having elective surgery, were all excluded from the review.
- An upper SpO <sub>2</sub> limit of 96% is therefore reasonable when administering supplemental oxygen to patients with acute illness who are not at risk of hypercapnia. However, a higher target may be appropriate for some specific conditions (e.g., pneumothorax, carbon monoxide

poisoning, cluster headache, and sickle cell crisis).[132]

- In 2019 the BTS reviewed its guidance in response to this systematic review and meta-analysis and decided an interim update was not required.[113]
  - The committee noted that the systematic review supported the use of controlled oxygen therapy to a target.
  - While the systematic review showed an association between higher oxygen saturations and higher mortality, the BTS committee felt the review was not definitive on what the optimal target range should be. The suggested range of 94% to 96% in the review was based on the lower 95% confidence interval and the median baseline SpO <sub>2</sub> from the liberal oxygen groups, along with the earlier 2015 TSANZ guideline recommendation.
- Subsequently, experience during the COVID-19 pandemic has also made clinicians more aware of the feasibility of permissive hypoxaemia.[133]
- Management of oxygen therapy in patients in intensive care is specialised and informed by further evidence that is more specific to this setting.[134]
   [135] [136]
- Measure arterial blood gases in those with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO <sub>2</sub> retention), and all patients with highseverity CAP.[1] [65]
- >>

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- » Fluid resuscitation
  - Assess all patients for volume depletion and give intravenous fluids if required.[1]
     [65]

#### Venous thromboembolism (VTE) prophylaxis

- Consider prophylaxis for VTE with a low molecular weight heparin for all patients who are not fully mobile.[1] [65]
- Airway clearance
  - Do not treat people with uncomplicated pneumonia with traditional airway clearance techniques routinely. If needed, offer these patients advice regarding expectoration of sputum.[1] [65]
  - Consider airway clearance techniques if the patient has difficulty expectorating sputum or if they have a pre-existing lung condition.[1] [65]

» Analgesia

• Give simple analgesia as appropriate (e.g., for **pleuritic pain**).[1] [65]

# consider switch to pathogen-targeted antibiotic therapy

Treatment recommended for SOME patients in selected patient group

#### » Consult with a microbiologist about appropriate pathogen-targeted antibiotic therapy. [1] [65]

• Switch from empirical antibiotics to pathogen-targeted antibiotics as soon as specific pathogens are identified (unless there are legitimate concerns about dualpathogen infection).[1] [65]

» Only about one third to one quarter of patients with CAP admitted to hospital will have their pneumonia defined microbiologically.[1] Among these patients:

- Around 14% have an atypical pathogen, of which[21]
  - 7% have Mycoplasma pneumoniae
  - 4% have Chlamydophila pneumoniae
  - 3% have Legionella pneumophila
- Those with infections due to *Mycoplasma*, *Chlamydophila*, and *Coxiella burnetii* will be diagnosed late in the illness on

the basis of seroconversion, reducing the opportunity for early targeted therapy.[1]

» Consider switching the choice of agent once the results of sensitivity testing are available or following consultation with a microbiologist, intensivist, or respiratory physician.[1] [65]

#### » BTS recommendations for pathogentargeted antibiotics [1] [65]

Pathogen	Preferred antibiotic	Alternative antibiotic
Mycoplasma pneumoniae Chlamydophila pneumoniae	Clarithromycin (orally or intravenously)	Doxycycline (orally) or a fluoroquinolone (orally or intravenously)
<i>Legionella</i> species	Fluoroquinolon (orally or intravenously)	Clarithromycin (orally or intravenously) or azithromycin (in countries where it is used for managing pneumonia)
Streptococcus pneumoniae	Amoxicillin (orally) or benzylpenicillin (intravenously)	Clarithromycin (orally) or cefuroxime or cefotaxime or ceftriaxone (intravenously)
Chlamydia psittaci Coxiella burnetii	Doxycycline (orally)	Clarithromycin (orally or intravenously)
Haemophilus influenzae	Non-beta- lactamase- producing: amoxicillin (orally or intravenously)	Cefuroxime or cefotaxime or ceftriaxone (intravenously) or a fluoroquinolone

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# Community-acquired pneumonia in adults (non COVID-19)

Ac

### Management

		Preferred	Alternative
	Pathogen	antibiotic	antibiotic
	•		
		Beta- lactamase-	(orally or
		producing:	intravenously)
		amoxicillin/ clavulanate	
		(orally or	
		intravenously)	
(	Gram-negative	Cefuroxime	Fluoroquinolo
	enteric bacilli	or cefotaxime	(intravenously
		or ceftriaxone	or imipenem/
		(intravenously)	cilastatin
			(intravenously
			or meropenen
			(intravenously
	Pseudomonas	Ceftazidime	Ciprofloxacin
	aeruginosa	(intravenously)	(intravenously
		plus	or piperacillin/
		-	tazobactam (intravenously
		Gentamicin or tobramycin	Intravenously
		or tobramycin (dose	plus
		monitoring	Gentamicin
		required)	or tobramycin
			(dose
			monitoring
			required)
	Staphylococcus	Flucloxacillin	
	aureus : non-	(intravenously)	
	MRSA	with or	
		without	
		Rifampicin	
		(orally or	
		intravenously)	
	Staphylococcus aureus :		
	MRSA	(intravenously;	
		dose monitoring	
		required)	
		or linezolid	

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Cl	ute				
			Pathogen	Preferred antibiotic	Alternative antibiotic
				or teicoplanin (intravenously)	
				with or without	
				Rifampicin (orally or	
				intravenously)	
	Iow-severity (CURB-65 = 0-1)	1st	empirical oral therapy	or intravenous	antibiotic
			discharged for t	with low-severity reatment at home ng patients if:[1] [	e. However,
			<ul> <li>They are not able to take oral medicati safely and reliably</li> </ul>		
			-	ial circumstances	do not make
			them suit	able for treatment	t at home
				e unstable comor	
			<ul> <li>They pref</li> </ul>	er to be treated ir	n hospital.
			<ul> <li>Give antibiotics as soon as possib</li> <li>This should be within 4 hours of</li> <li>presentation to hospital. [1] [63] [65]</li> </ul>		
				with <b>low-severit</b> spital can be treat [65]	
			<ul> <li>[1] [65] C clarithron doxycycli allergic</li> <li>If the pati amoxicilli adding, o</li> </ul>	<b>ferred choice is</b> onsider a macroli hycin) or a tetracy ne) for <b>patients</b> <b>to penicillin</b> .[1] ent <b>does not res</b> n monotherapy, c r switching to, a r hycin).[1] [65]	de (e.g., cline (e.g., <b>who are</b> [65] p <b>ond</b> to onsider
****************			impaired swallo consciousness, consider <b>intrav</b>	e is contraindicat wing reflex, impai gastrointestinal n enous amoxici lin, or clarithro	red nalabsorption) I <b>lin,</b>
				need for intrave itially during th	

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# following admission and then every day after.[1]

 NICE guidelines on antimicrobial prescribing in adults recommend reviewing intravenous antibiotics by 48 hours, and considering switching to oral treatment if possible.[117] Best practice is to review intravenous antibiotics every day; most intravenous antibiotics can be stopped and switched to oral treatment within 24 hours.

» Switch to oral antibiotics as soon as clinical improvement occurs (see practical tip), and as long as there are no contraindications to oral administration.

#### **Practical tip**

**Pointers to clinical improvement** The following clinical features should prompt you to consider switching from intravenous to oral antibiotic therapy:[1] [65]

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

» Give antibiotic therapy for 5 days. [117] [125] The National Institute for Health and Care Excellence recommends stopping treatment after 5 days unless microbiological results suggest a longer course or the patient is not clinically stable.[117] This should be based on your clinical judgement and the following criteria:[117] [126]

- Fever in past 48 hours, or more than one sign of clinical instability:
  - Systolic blood pressure <90 mmHg</li>

- Heart rate >100/minute
- Respiratory rate >24/minute
- Arterial oxygen saturation <90% or PaO <sub>2</sub> <60 mmHg in room air.

» Consult local protocols for guidance on selection of antibiotic regimen.

#### plus

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

supportive care

» paracetamol: oral: 500-1000 mg orally every 4-6 hours when required, maximum 4000 mg/day; intravenous (<51 kg body weight): 15 mg/kg intravenously every 4-6 hours when required, maximum 60 mg/kg/ day; intravenous (≥51 kg body weight): 1000 mg intravenously every 4-6 hours when required, maximum 4000 mg/day (3000 mg/ day if risk factors for hepatotoxicity)

» Provide supportive care, which may include the following measures.[1] [65]

» Oxygen

» Prescribe oxygen if oxygen saturation <94% and maintain at target range.[1] [65] For patients at risk of hypercapnia prescribe oxygen if oxygen saturation <88%.[71]

» Monitor controlled ox ygen therapy. An upper SpO<sub>2</sub> limit of 96% is reasonable when administering supplemental oxygen to most patients with acute illness who are **not at risk** of hypercapnia.

- Evidence suggests that liberal use of supplemental oxygen (target SpO <sub>2</sub> >96%) in acutely ill adults is associated with higher mortality than more conservative oxygen therapy.[72]
- A lower target SpO 2 of 88% to 92% is appropriate if the patient is at risk of hypercapnic respiratory failure.[71]

# Evidence: Target oxygen saturation in acutely ill adults

Too much supplemental oxygen increases mortality.

Evidence from a large systematic review and meta-analysis supports conservative/controlled ox ygen therapy versus liberal ox ygen therapy in acutely ill adults who are not at risk of hypercapnia.

- Guidelines differ in their recommendations on target oxygen saturation in acutely unwell adults who are receiving supplemental oxygen.
  - The 2017 British Thoracic Society (BTS) guideline recommends a target SpO <sub>2</sub> range of 94% to 98% for patients not at risk of hypercapnia, whereas the 2022 Thoracic Society of Australia and New Zealand (TSANZ) guideline recommends 92% to 96%.[71]
     [130]
  - The 2022 Global Initiative for Asthma (GINA) guidelines recommend a target SpO <sub>2</sub> range of 93% to 96% in the context of acute asthma exacerbations.[131]
- · A systematic review including a metaanalysis of data from 25 randomised controlled trials, published in 2018 found that in adults with acute illness, liberal oxygen therapy (broadly equivalent to a target saturation >96%) is associated with higher mortality than conservative oxygen therapy (broadly equivalent to a target saturation ≤96%).[72] In-hospital mortality was 11 per 1000 higher for the liberal oxygen therapy group versus the conservative therapy group (95% CI, 2 to 22 per 1000 more). Mortality at 30 days was also higher in the group who had received liberal oxygen (RR 1.14, 95% CI 1.01 to 1.29). The trials included adults with sepsis, critical illness, stroke, trauma, myocardial infarction, cardiac arrest, and patients who had emergency surgery. Studies that were limited to people with chronic respiratory illness or psychiatric illness, or patients on extracorporeal life support, receiving hyperbaric oxygen therapy, or having elective surgery, were all excluded from the review.

- An upper SpO <sub>2</sub> limit of 96% is therefore reasonable when administering supplemental oxygen to patients with acute illness who are not at risk of hypercapnia. However, a higher target may be appropriate for some specific conditions (e.g., pneumothorax, carbon monoxide poisoning, cluster headache, and sickle cell crisis).[132]
- In 2019 the BTS reviewed its guidance in response to this systematic review and meta-analysis and decided an interim update was not required.[113]
  - The committee noted that the systematic review supported the use of controlled oxygen therapy to a target.
  - While the systematic review showed an association between higher oxygen saturations and higher mortality, the BTS committee felt the review was not definitive on what the optimal target range should be. The suggested range of 94% to 96% in the review was based on the lower 95% confidence interval and the median baseline SpO <sub>2</sub> from the liberal oxygen groups, along with the earlier 2015 TSANZ guideline recommendation.
- Subsequently, experience during the COVID-19 pandemic has also made clinicians more aware of the feasibility of permissive hypoxaemia.[133]
- Management of oxygen therapy in patients in intensive care is specialised and informed by further evidence that is more specific to this setting.[134]
   [135] [136]
- **Measure arterial blood gases** in those with SpO <sub>2</sub> <94%, those with a risk of hypercapnic ventilatory failure (CO 2 retention), and all patients with highseverity CAP.[1] [65]
- » Fluid resuscitation

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 Assess all patients for volume depletion and give intravenous fluids if required.[1] [65]

>>

#### Venous thromboembolism (VTE) prophylaxis

- Consider prophylaxis for VTE with a low molecular weight heparin for all patients who are not fully mobile.[1] [65]
- » Airway clearance
  - Do not treat people with uncomplicated pneumonia with traditional airway clearance techniques routinely. If needed, offer these patients advice regarding expectoration of sputum.[1] [65]
  - Consider airway clearance techniques if the patient has difficulty expectorating sputum or if they have a pre-existing lung condition.[1] [65]
- » Analgesia
  - Give simple analgesia as appropriate (e.g., for **pleuritic pain**).[1] [65]

# consider switch to pathogen-targeted antibiotic therapy

Treatment recommended for SOME patients in selected patient group

» **Consult with a microbiologist** about appropriate pathogen-targeted antibiotic therapy.[1] [65]

• Switch from empirical antibiotics to pathogen-targeted antibiotics as soon as specific pathogens are identified (unless there are legitimate concerns about dualpathogen infection).[1] [65]

» Only about one third to one quarter of patients with CAP admitted to hospital will have their pneumonia defined microbiologically.[1] Among these patients:

- Around 14% have an atypical pathogen, of which:[21]
  - 7% have Mycoplasma pneumoniae
  - 4% have Chlamydophila pneumoniae

• 3% have Legionella pneumophila

• Those with infections due to *Mycoplasma*, *Chlamydophila*, and *Coxiella burnetii* will be diagnosed late in the illness on the basis of seroconversion, reducing the opportunity for early targeted therapy.[1]

» Consider switching the choice of agent once the results of sensitivity testing are available or following consultation with a microbiologist, intensivist, or respiratory physician.[1]

#### » BTS recommendations for pathogentargeted antibiotics [1] [65]

Pathogen	Preferred antibiotic	Alternative antibiotic
Mycoplasma pneumoniae Chlamydophila pneumoniae	Clarithromycin (orally or intravenously)	Doxycycline (orally) or a fluoroquinolone (orally or intravenously)
<i>Legionella</i> species	Fluoroquinolon (orally or intravenously)	Clarithromycin (orally or intravenously) or azithromycin (in countries where it is used for managing pneumonia)
Streptococcus pneumoniae	Amoxicillin (orally) or benzylpenicillin (intravenously)	Clarithromycin (orally) or cefuroxime or cefotaxime or ceftriaxone (intravenously)
Chlamydia psittaci Coxiella burnetii	Doxycycline (orally)	Clarithromycin (orally or intravenously)

# Community-acquired pneumonia in adults (non COVID-19)

### Management

	Pathogen	Preferred antibiotic	Alternative antibiotic
	Haemophilus influenzae	Non-beta- lactamase- producing: amoxicillin (orally or intravenously) Beta- lactamase- producing: amoxicillin/ clavulanate (orally or intravenously)	Cefuroxime or cefotaxime or ceftriaxone (intravenously or a fluoroquinolor (orally or intravenously)
	ram-negative nteric bacilli	Cefuroxime or cefotaxime or ceftriaxone (intravenously)	Fluoroquinolo (intravenously or imipenem/ cilastatin (intravenously or meropener (intravenously
	Pseudomonas aeruginosa	Ceftazidime (intravenously) <b>plus</b> Gentamicin or tobramycin (dose monitoring required)	Ciprofloxacin (intravenously or piperacillin tazobactam (intravenously <b>plus</b> Gentamicin or tobramycin (dose monitoring required)
a	<i>taphylococcus ureus</i> : non- IRSA	Flucloxacillin (intravenously) with or without Rifampicin (orally or intravenously)	

# Community-acquired pneumonia in adults (non COVID-19)

### Management

Pathogen
Staphylococ aureus : MRSA

# confirmed CAP on chest x-ray: presenting in the community

1st

#### continue empirical antibiotics or switch to pathogen-targeted antibiotic therapy

» Continue empirical antibiotics in patients with CAP confirmed by chest x-ray in the community. However, where a pathogen has been identified, follow your local antibiotic protocol for the identified organism(s).[1] [65]

#### » BTS recommendations for pathogentargeted antibiotics [1] [65]

Pathogen	Preferred antibiotic	Alternative antibiotic
Mycoplasma pneumoniae Chlamydophila pneumoniae	Clarithromycin (orally or intravenously)	Doxycycline (orally) or a fluoroquinolone (orally or intravenously)
<i>Legionella</i> species	Fluoroquinolon (orally or intravenously)	eClarithromycin (orally or intravenously) or azithromycin (in countries

MANAGEMENT

Pathogen	Preferred antibiotic	Alternative antibiotic
ratilogen	antibiotic	
		where it is used for managing pneumonia)
Streptococcus pneumoniae	Amoxicillin (orally) or benzylpenicillin (intravenously)	Clarithromycin (orally) or cefuroxime or cefotaxime or ceftriaxone (intravenously)
Chlamydia psittaci Coxiella burnetii	Doxycycline (orally)	Clarithromycin (orally or intravenously)
Haemophilus influenzae	Non-beta- lactamase- producing: amoxicillin (orally or intravenously) Beta- lactamase- producing: amoxicillin/ clavulanate (orally or intravenously)	Cefuroxime or cefotaxime or ceftriaxone (intravenously) or a fluoroquinolone (orally or intravenously)
Gram-negative enteric bacilli	Cefuroxime or cefotaxime or ceftriaxone (intravenously)	Fluoroquinolon (intravenously) or imipenem/ cilastatin (intravenously) or meropenem (intravenously)
Pseudomonas aeruginosa	Ceftazidime (intravenously) <b>plus</b> Gentamicin or tobramycin (dose	Ciprofloxacin (intravenously) or piperacillin/ tazobactam (intravenously) <b>plus</b>

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Pathogen	Preferred antibiotic	Alternative antibiotic
	monitoring required)	Gentamicin or tobramycin (dose monitoring required)
Staphylococcus	Flucloxacillin	
<i>aureus</i> : non- MRSA	(intravenously)	
	with or without	
	Rifampicin	
	(orally or	
	intravenously)	
Staphylococcus aureus : MRSA	Vancomycin (intravenously; dose monitoring required) or linezolid (intravenously) or teicoplanin (intravenously)	
	with or without	
	Rifampicin	
	(orally or	
	intravenously)	

» In community settings, the diagnosis of CAP is based on signs and symptoms of lower respiratory tract infection, focal chest signs, and illness severity, and management is based on a suspected diagnosis.[1] [63] [65] However, a chest x-ray is indicated in the community if:[1] [63] [65]

- There is diagnostic doubt
- The patient is deemed to be at risk of underlying lung pathology (e.g., they have risk factors for lung cancer)

 Progress following treatment is not satisfactory at review.

# Emerging

### **Newer antibiotics**

Given the concerns over increasing drug resistance and safety issues (e.g., fluoroquinolones) with existing antibiotics, there is a need for further research on new therapeutic agents. Newer antibiotic agents are detailed in this section. Current guidelines do not recommend them yet as they require further validation. Therefore, these agents are still considered to be emerging. Despite this, some of these newer antibiotics are approved by the European Medicines Agency (EMA) for the treatment of CAP and may be considered under specialist guidance.

## Lefamulin

A first-in-class pleuromutilin antibiotic available in oral and intravenous formulations. It inhibits bacterial protein synthesis via interactions with the A- and P- sites of the peptidyl transferase centre of the 50S subunit. Lefamulin offers a unique spectrum of activity covering Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Legionella pneumophila, Chlamydia pneumoniae, Mycoplasma pneumoniae, Staphylococcus aureus (including methicillin-resistant S aureus [MRSA]), beta-haemolytic streptococci (including Spyogenes and Sagalactiae), and Enterococcus faecium (including vancomycinresistant enterococci). It lacks cross-resistance with other antibiotic classes for S pneumoniae and S aureus .[146] [147] [148] The safety and efficacy of lefamulin has been evaluated in two phase 3 clinical trials where it was found to be non-inferior to moxifloxacin (with or without linezolid) in terms of primary efficacy endpoints (early clinical response, investigator assessment of clinical response). It was considered safe and well tolerated.[149] [150] However, it has the potential to cause QT interval prolongation and should not be used in patients with known prolongation of the QT interval, ventricular arrhythmias, or who are on other drugs that prolong the QT interval. Lefamulin is approved by the EMA for the treatment of CAP in adults; however, its exact place in management is not clear as yet. One systematic review suggests a role for lefamulin as an alternative agent to beta-lactams and macrolides in bacterial CAP and an alternative to amoxicillin and doxycycline in the outpatient setting.[151]

## Delafloxacin

A new fluoroquinolone antibiotic approved by the EMA for the treatment of adults with CAP when it is considered inappropriate to use other antibiotics that are commonly recommended for the treatment of CAP. One phase 3 study that found delafloxacin was non-inferior to moxifloxacin.[152]

## Omadacycline

A new modernised tetracycline antibiotic with broad-spectrum activity, designed to overcome tetracycline resistance. Like other antibiotics in the tetracycline class, omadacycline may cause discolouration of deciduous teeth, and inhibition of fetal bone growth when administered during pregnancy.[153] It has been found to be noninferior to moxifloxacin in terms of efficacy in adults with CAP.[153] Omadacycline is approved in the US by the FDA for the treatment of CAP in adults; however, it was refused approval for this indication in Europe in October 2018.

## Ceftobiprole

A broad-spectrum parenteral cephalosporin that has microbiological activity against most typical bacterial pathogens causing CAP, including MRSA. A phase III study found that ceftobiprole was non-inferior to ceftriaxone with or without linezolid for the treatment of CAP.[154]

### Nemonoxacin

A non-fluorinated, broad-spectrum quinolone. It has greater antimicrobial activity than the fluoroquinolones (e.g., levofloxacin) against MRSA, methicillin-sensitive *Staphylococcus epidermidis* (MSSE), methicillin-resistant *S epidermidis* (MRSE), *S pneumoniae*, and *Enterobacter faecalis*. One systematic review

found that it is as effective and well tolerated as levofloxacin in patients with CAP.[155] Nemonoxacin is not currently approved in Europe or the US, but may be available in other countries.

## Solithromycin

A fluoroketolide with antimicrobial activity against gram-positive and gram-negative bacteria commonly associated with CAP. A completed phase II study showed that solithromycin had similar efficacy to that of levofloxacin in adults with bacterial CAP with pneumonia severity index scores of II to IV.[156] It has also been found to be non-inferior to moxifloxacin.[157] Solithromycin is currently in phase III development for the treatment of bacterial CAP.

## Statins

There is evidence to suggest that statins may reduce the risk of CAP and its complications due to their immunomodulatory effects. Data suggest that patients with CAP who are taking a statin on hospital admission have a reduced risk of inpatient mortality.[158] One meta-analysis found that statins may decrease mortality associated with CAP, as well as reduce the need for mechanical ventilation or intensive care unit admission.[159] However, whether statin use can reduce the risk of pneumonia is unclear and further studies are required. It is important to note that statins interact with macrolides, an antibiotic class commonly used for the treatment of CAP. These drugs should not be used in combination as macrolides inhibit the metabolism of statins via the CYP3A4 pathway and therefore increase the risk of myopathy and rhabdomyolysis.

# **Primary prevention**

Pneumonia prevention is focused on the pathogens that cause disease, through vaccination and by managing the risks associated with disease development.

The main means of prevention are pneumococcal and influenza vaccination of at-risk people and smoking cessation.[1]

In terms of vaccination, the UK Health and Security Agency (UKHSA) recommends:[60]

- Pneumococcal vaccination
  - Adults aged 65 or over and at-risk groups: a single dose of 23-valent pneumococcal polysaccharide vaccine (PPV23). At-risk groups are those with:[60]
    - Asplenia or dysfunction of the spleen
    - Chronic respiratory, heart, liver disease, or neurological conditions
    - Stage 4 or 5 chronic kidney disease (including haemodialysis)
    - Diabetes
    - · Immunosuppression due to disease or treatment
    - · Cochlear implants
    - Complement disorders.
  - At-risk patients should be offered pneumococcal immunisation at every opportunity (for example, when immunising against influenza or at routine consultations), and especially at discharge from hospital.

#### Influenza vaccination

- Adults aged 65 or over, and at-risk groups: annual influenza vaccine provided they do not have a contraindication. At risk groups are pregnant women and those with:[60]
  - Asplenia or dysfunction of the spleen

- Chronic respiratory, heart, liver, or neurological disease
- Stage 3, 4, or 5 chronic kidney disease (including haemodialysis)
- Diabetes
- Immunosuppression due to disease or treatment
- Complement disorders.

Further information on vaccines, vaccination procedures, special patient populations, and current vaccination schedules in the UK can be found in the latest UK Health and Security Agency vaccination schedule. [UKHSA complete routine immunisation schedule.] Vaccination schedules vary by location; consult local guidance for recommendations.

Smoking cessation is important for all patients, but particularly for those at risk of pneumonia and influenza. Offer advice according to national smoking cessation guidelines.[1] [NICE: stop smoking interventions and services]

• Cigarette smoking, both active and passive, is a recognised independent risk factor for CAP.[1]

There is insufficient evidence to determine the effect of vitamin C or vitamin D supplementation in the prevention (or treatment) of pneumonia.[61] [62]

## Secondary prevention

For all patients with CAP who smoke, offer advice according to national smoking cessation guidelines. [NICE: stop smoking interventions and services] Explain to patients how smoking impairs natural mechanisms for eliminating pathogens and debris.[1]

## Patient discussions

Advise patients to rest, to drink plenty of fluids, and not to smoke.[1] [65]

- Adequate hydration and preservation of the cough reflex during convalescence are important. The cough reflex is necessary to remove micro-organisms from the respiratory tract before it reaches the lung.
- Explain that adherence to treatment is important in patients with CAP, even after they experience clinical improvement.

At discharge, offer patients access to information about CAP, such as a patient information leaflet.[1] [65] For all patients with CAP who smoke, offer advice according to national smoking cessation guidelines. [NICE: stop smoking interventions and services]

In the community, advise patients (and their carers) to **seek medical advice** if their **symptoms #vorsen rapidly or significantly; symptoms do not start to improve within 3 days; or they become systemically very unwell**.[63]

 Around 10% of patients managed in the community do not respond to antibiotic therapy and require hospitalisation.[142]

## Monitoring

## Monitoring

## In hospital

#### Discuss with a senior colleague any patient who does not improve as expected. [1] [65]

- Consider repeat chest radiograph, C-reactive protein, white cell count, and further specimens for microbiology in patients not progressing satisfactorily after 3 days of treatment.[1] [65]
- Consider referral to a respiratory physician. [1] [65]

#### Practical tip

The main reasons why patients **do not improve as expected** include:[1] [65]

- Incorrect diagnosis or complicating condition (e.g., pulmonary embolism, bronchial carcinoma, bronchiectasis)
- Unexpected pathogen or pathogens not covered by antibiotic choice (e.g., 'atypical' pathogens, pathogens resistant to commonly used antibiotics such as ampicillin-resistant *Haemophilus influenzae*)
- Antibiotic ineffective or causing allergic reaction (e.g., poor absorption of oral antibiotic, inadequate dose, antibiotic hypersensitivity)
- Impaired local (e.g., bronchiectasis, endobronchial obstruction, aspiration) or systemic (e.g., HIV infection, myeloma) defenses
- Local (e.g., parapneumonic effusion, empyema, lung abscess) or distant (e.g., metastatic infection, septicaemia, phlebitis at intravenous cannula site) complications of CAP
- Overwhelming infection
- Improvement expected too soon (e.g., in older patients).

In patients with high-severity CAP who are not responding to beta-lactam antibiotics or for whom an atypical or viral pathogen is suspected, order polymerase chain reaction (or other antigen detection test) of sputum or other respiratory tract sample.[1] [65]

• Consider initial and follow-up viral and atypical pathogen serology.[1] [65]

## In the community

Advise patients (and their carers) to **seek medical advice** if their **symptoms worsen rapidly or significantly; symptoms do not start to improve within 3 days; or they become systemically very unwell**.[63]

 About 10% of patients managed in the community do not respond to antibiotic therapy and require hospitalisation.[142]

Admit urgently to hospital any patient on antibiotic treatment with features of moderate- or high-severity infection.[1] [65]

## Discharge and follow-up

Do not request a repeat chest radiograph before discharge from hospital in patients who have recovered satisfactorily from CAP.[1] [65]

Arrange a follow-up visit at around 6 weeks either with the patient's general practitioner or in a hospital clinic.[1] [65]

- Request a repeat chest radiograph during recovery after about 6 weeks for patients (regardless of whether they have been admitted to hospital):[1] [65]
  - · With persisting symptoms or physical signs
  - Who are at higher risk of underlying malignancy (especially smokers and those aged >50 years).
- Consider bronchoscopy in patients with persisting signs, symptoms, and radiological abnormalities at around 6 weeks after completing treatment.[1] [65]

## Complications

Complications	Timeframe	Likelihood			
septic shock	short term	medium			
Commonly complicates severe CAP. Patients have fever, leukocytosis, tachypnoea, tachycardia. Can					

progress rapidly to multi-organ failure and shock. Follow your local protocol for investigation and treatment of all patients with suspected sepsis, or those at risk. Start treatment promptly. Determine urgency of treatment according to likelihood of infection and severity of illness, or according to your local protocol.[70] [81]

acute respiratory distress syndrome (ARDS)	short term	medium
Pneumonia can be complicated by ARDS, which is a condition o severe lung inflammation.	f non-cardiogenic pulr	nonary oedema and
Associated with a 30% to 50% mortality, and treated with low tida mechanical ventilation.[6]	al volume plateau pres	ssure limited
antibiotic-associated Clostridium difficile colitis	short term	medium
May occur as a result of interruption of the normal bowel flora fro diarrhoea, abdominal pain, and leukocytosis. Stool immunoassa Ideally, causative antibiotics should be stopped, and treatment is fidaxomicin.	y for C difficile enzym	nes is diagnostic.
heart failure	short term	medium
The incidence of heart failure in hospitalised patients with CAP w little information about risk factors for the occurrence of cardiac o		
little information about risk factors for the occurrence of cardiac or age, pre-existing congestive heart failure, severity of CAP, and th in hospitalised patients are possible risk factors.[164] [165] [166] disease, use of pneumococcal and influenza vaccine may reduce	complications in patier le use of insulin by glu In patients with know e morbidity and morta	nts with CAP. Older acose sliding scales n cardiovascular
little information about risk factors for the occurrence of cardiac or age, pre-existing congestive heart failure, severity of CAP, and th in hospitalised patients are possible risk factors.[164] [165] [166]	complications in patier le use of insulin by glu In patients with know e morbidity and morta short term	its with CAP. Older icose sliding scales n cardiovascular lity.
little information about risk factors for the occurrence of cardiac or age, pre-existing congestive heart failure, severity of CAP, and th in hospitalised patients are possible risk factors.[164] [165] [166] disease, use of pneumococcal and influenza vaccine may reduce acute coronary syndrome	complications in patier le use of insulin by glu In patients with know e morbidity and morta short term	its with CAP. Older icose sliding scales n cardiovascular lity.
little information about risk factors for the occurrence of cardiac of age, pre-existing congestive heart failure, severity of CAP, and the in hospitalised patients are possible risk factors.[164] [165] [166] disease, use of pneumococcal and influenza vaccine may reduce acute coronary syndrome The incidence of acute coronary syndrome in hospitalised patient cardiac arrhythmias	complications in patier ne use of insulin by glu In patients with know e morbidity and morta <b>short term</b> nts with CAP was 5.3% <b>short term</b>	ts with CAP. Older cose sliding scales n cardiovascular lity. low 6 in one study.[163]
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little information about risk factors for the occurrence of cardiac of age, pre-existing congestive heart failure, severity of CAP, and the in hospitalised patients are possible risk factors.[164] [165] [166] disease, use of pneumococcal and influenza vaccine may reduce acute coronary syndrome The incidence of acute coronary syndrome in hospitalised patien cardiac arrhythmias The incidence of incident cardiac arrhythmia in hospitalised patien necrotising pneumonia Regarded as a rare complication of CAP in adults. Associated wi aureus, Streptococcus pyogenes, Nocardia species, Klebsiel	complications in patier ne use of insulin by glu In patients with know e morbidity and morta <b>short term</b> ents with CAP was 5.3% <b>short term</b> ents with CAP was 4.7 <b>short term</b> ith pathogens such as <i>la pneumoniae</i> , and	its with CAP. Older icose sliding scales n cardiovascular lity. in one study.[163] iow % in one study.[163] iow Staphylococcus Streptococcus

pleural effusion are complicated with empyema.

Complications	Timeframe	Likelihood			
Pleural effusion is considered to be an indicator of pneumonia severity and is clearly associated with an increased risk of treatment failure.[1] [169]					
lung abscess variable low					
A rare complication, frequently requiring prolonged antibiotic therapy and, in some cases, surgical drainage.					
pneumothorax	variable	low			
A rare complication of CAP in adults. Pneumothorax is associated with bacterial pneumonia caused by staphylococcus, streptococcus, and other type of bacteria, which may cause the collapse of a lung.					

# Prognosis

For patients admitted to hospital, mortality rate ranges from 5% to 15%, but increases to 20% to 50% in patients requiring admission to the intensive care unit (ICU).[6] [118] Patients treated in the community generally have a good prognosis.[1]

Risk factors associated with increased 30-day mortality include bacteraemia, admission to the ICU, comorbidities (especially neurological disease), and infection with a potentially multidrug-resistant pathogen (e.g., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, Enterobacteriaceae).[34] [143] [144] [145]

Readmission rates in patients with CAP range from 7% to 12%.[160] [161] In most cases, exacerbation of comorbidities (mainly cardiovascular, pulmonary, or neurological disease) is responsible for readmission.

Prognostic biomarkers such as pro-adrenomedullin, prohormone forms of atrial natriuretic peptide, cortisol, procalcitonin, and C-reactive protein are being studied as predictors of mortality; however, further studies are required before these biomarkers are used for this function in clinical practice.[162]

## **Diagnostic guidelines**

## United Kingdom

### Pneumonia in adults: diagnosis and management

Published by: National Institute for Health and Care Excellence

Last published: 2023

Annotated edition (2015) of the BTS Guideline for the management of CAP in adults (2009)

Published by: British Thoracic Society

Last published: 2015

BTS guidelines for the management of community acquired pneumonia in adults

Published by: British Thoracic Society

Last published: 2009

**North America** 

### Diagnosis and treatment of adults with community-acquired pneumonia

Published by: American Thoracic Society; Infectious Diseases Society Last published: 2019 of America

### Asia

### Diagnosis and treatment of community-acquired pneumonia in adults

Published by: Chinese Thoracic Society; Chinese Medical Association Last published: 2017

## Treatment guidelines

## **United Kingdom**

### Pneumonia in adults: diagnosis and management

Published by: National Institute for Health and Care Excellence Last published: 2023

### Complete routine immunisation schedule

Published by: UK Health and security agency

### Pneumonia (community-acquired): antimicrobial prescribing

Published by: National Institute for Health and Care Excellence	Last published: 2019
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Annotated edition (2015) of the BTS Guideline for the management of CAP in adults (2009)

Published by: British Thoracic Society

BTS guidelines for the management of community acquired pneumonia in adults

Published by: British Thoracic Society

### Europe

Management of community-acquired pneumonia in immunocompetent adults: updated Swedish guidelines 2017

 Published by:
 Swedish Society of Infectious Diseases
 Last published: 2018

#### Management of community-acquired pneumonia in adults

Published by:Dutch Working Party on Antibiotic Policy;DutchLast published:2018Association of Chest Physicians

Guidelines for the management of adult lower respiratory tract infections

Published by: European Respiratory Society

Last published: 2011

Last published: 2022

Last published: 2015

Last published: 2009

### North America

### Diagnosis and treatment of adults with community-acquired pneumonia

Published by: American Thoracic Society; Infectious Diseases Society Last published: 2019 of America

### Guideline for antibiotic use in adults with community-acquired pneumonia

Published by: Korean Society of Infectious Diseases; Korean Society Last published: 2018 for Chemotherapy

### Diagnosis and treatment of community-acquired pneumonia in adults

Published by: Chinese Thoracic Society; Chinese Medical Association Last published: 2017

### Executive summary of the Gulf Cooperation Council practice guidelines for the management of community-acquired pneumonia

Published by: Gulf Cooperation Council Community-acquired Pneumonia Working Group

Guidelines for the management of community acquired pneumonia in adults, revised edition

Published by: Committee for The Japanese Respiratory Society

### Africa

### Guideline for management of community-acquired pneumonia in adults

Published by: South African Thoracic Society

Last published: 2017

Last published: 2007

Last published: 2006

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### Asia

## **Online resources**

- 1. Coronavirus disease 2019 (COVID-19) (external link)
- 2. UKHSA complete routine immunisation schedule. (external link)
- 3. NICE: stop smoking interventions and services (external link)
- 4. Abbreviated Mental Test Score (*external link*)

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## Images



Figure 1: Posterior-anterior chest radiograph showing right upper lobe consolidation in a patient with community-acquired pneumonia

Durrington HJ, et al. Recent changes in the management of community acquired pneumonia in adults. BMJ 2008;336:1429.



## Figure 2: Chest radiograph showing left upper lobe cavitating pneumonia

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#### Figure 3: Left-sided pleural effusion

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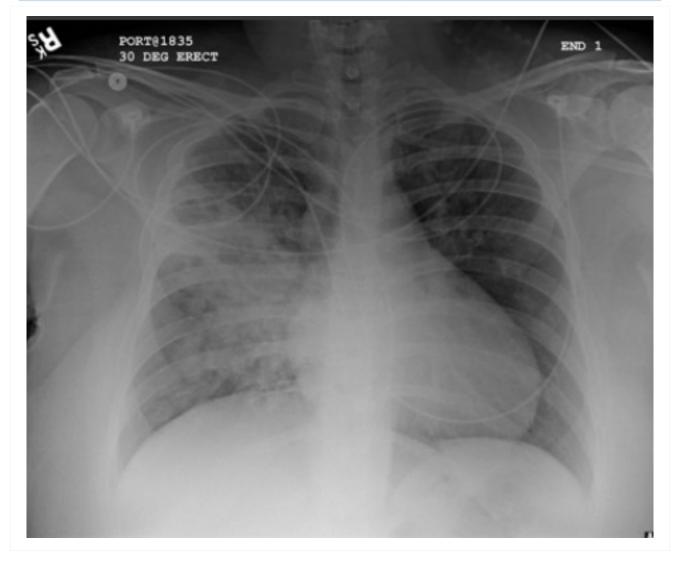


Figure 4: Increased opacification of the right perihilar region and superior segment of the right lower and upper lobes consistent with worsening aspiration pneumonia

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#### Images

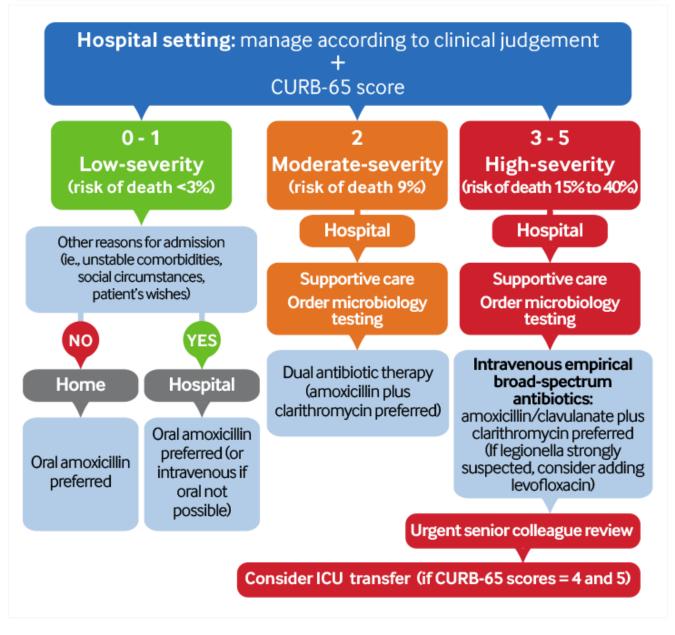


Figure 5: Risk assessment and management of CAP in the first 4 hours: hospital setting

Adapted from Lim WS, et al. Thorax. 2009 Oct;64(suppl 3):iii1-55

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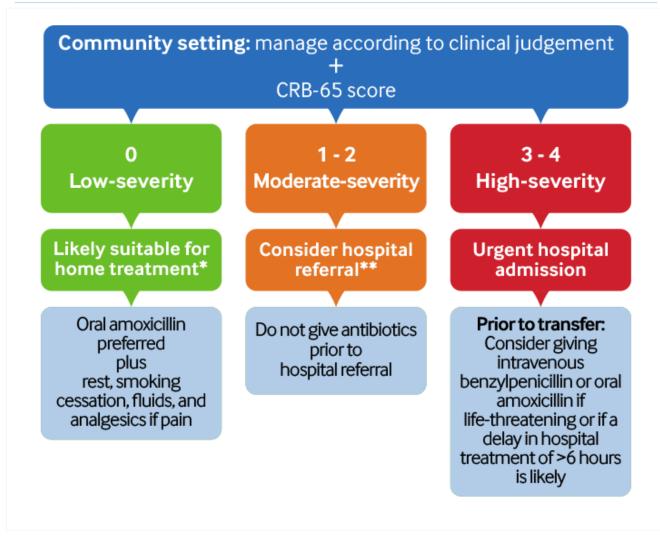


Figure 6: Risk assessment and management of CAP in the first 4 hours: community setting. \*Consider social circumstances, unstable comorbidities, ability to take oral treatment safely and reliably, and patient's wishes when deciding whether to treat patients at home. \*\*The majority of patients with moderate-severity CAP should be referred to hospital. However, you should consider social circumstances, ability to take oral treatment safely, unstable comorbidities, and patient's wishes when deciding on home treatment

Adapted from Lim WS, et al. Thorax. 2009 Oct;64(suppl 3):iii1-55

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