Community-acquired pneumonia

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Community-acquired pneumonia is a major global health challenge that disproportionately affects vulnerable populations, including older people, immunocompromised people, those with chronic conditions, and young children. Once considered solely an acute illness, community-acquired pneumonia is now recognised as a disease with long-term complications, including cardiovascular events, respiratory impairment, and cognitive decline. Advances, such as nucleic acid amplification tests (NAATs) and the broader availability of point-of-care lung ultrasound, allow for rapid pathogen detection and personalised treatment. However, substantial uncertainties remain regarding the role of NAATs, lung ultrasounds, and serum biomarkers in clinical practice. Antibiotics are the cornerstone of community-acquired pneumonia treatment, but the roles of adjunctive therapies, including corticosteroids and immunomodulators, remain incompletely defined. Comprehensive community-acquired pneumonia management emphasises personalised treatment, rehabilitation after the acute episode, routine cardiovascular screening, and strengthening preventive measures, such as vaccination. As precision medicine advances, integrating diagnostics and tailored therapies will improve outcomes and reduce the global burden of community-acquired pneumonia.

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Introduction

Community-acquired pneumonia is the leading infectious cause of morbidity and mortality worldwide, with an estimated global incidence of 4350/100 000 population in 2021.[1] It disproportionately affects vulnerable people, including older people, very young children, immunocompromised individuals, and those with chronic comorbidities.[2] Data from 2021 suggest that community-acquired pneumonia is responsible for approximately 2·2 million deaths annually, or 27·7 deaths per 100 000 people.[2] The highest mortality rates are observed in lower-middle-income countries (LMICs), where disparities in health-care access, air quality, and vaccination coverage exacerbate the disease burden.[2–4]

Although community-acquired pneumonia is a large public health concern, there are numerous challenges associated with its diagnosis, treatment, and long-term management. Clinically, no gold standard exists that allows clinicians to quickly and accurately diagnose bacterial pneumonia, which often leads to the overuse of empirical antimicrobial therapies.[5] This overuse is related to rising antibiotic resistance, increased risk of adverse clinical outcomes, inaccurate diagnosis, and follow-up challenges.[6] Current recommendations emphasise using local epidemiology data and validated risk factors to guide empirical therapy, aiming to balance adequate coverage with minimising resistance development.[7,8] Strengthening the implementation of rapid diagnostic tools and improving adherence to clinical guidelines are crucial in addressing this persistent challenge and mitigating these issues.

Advances in diagnostics and therapeutics are transforming the clinical management of community-acquired pneumonia, moving away from one-size-fits-all approaches towards personalised strategies that are adapted to the level of care needed and account for clinical severity, demographics, comorbidities, and pathogen detection. Nucleic acid amplification tests (NAATs; table 1) could revolutionise pathogen identification and enable the rapid and accurate detection of bacterial and viral pathogens (including co-infection). These diagnostic breakthroughs, accelerated by the widespread adoption of molecular testing during the COVID-19 pandemic, are increasingly being incorporated into clinical practice.[25–27] This shift could guide individualised treatment plans that are tailored to pathogen-specific therapies and patient risk profiles, potentially reducing the burden of antimicrobial resistance and improving outcomes. However, interpretation of results continues to be challenging depending on the sample used for the test, since there is controversy about whether the identified pathogens correspond to colonising or infecting microorganisms. Additionally, concerns exist about the availability of these technologies in countries with few health-care resources.

Personalised treatment approaches for community-acquired pneumonia are urgently needed to address its complexity and heterogeneity. Stratifying patients on the basis of clinical severity, serum biomarkers (eg, procalcitonin or C-reactive protein), and risk factors for specific pathogens—such as *Pseudomonas aeruginosa* or meticillin-resistant *Staphylococcus aureus*—has become

Search strategy and selection criteria

We conducted a comprehensive literature search in PubMed covering publications from Jan 1, 1990, to May 1, 2025. The search included combinations of the terms "pneumonia", "community-acquired pneumonia", or "CAP" along with "diagnosis", "therapy", "antibiotics", "prevention", and "vaccines." No filters were applied for language or publication date. To ensure a thorough review, we manually screened the reference lists of relevant narrative and systematic reviews focused on community-acquired pneumonia to identify additional key articles and international clinical guidelines. Furthermore, we consulted the websites of WHO and other international health agencies to gather essential documents that might not have been indexed in PubMed.

	Detected pathogens (n)	Viruses	Bacteria	Resistance genes	Sample type	Time to results*	Sensitivity	Specificity
FilmArray respiratory panel[9,10]	Ten	Adenovirus, coronaviruses (229E, HKU1, NL63, and OC43), human metapneumovirus, human rhinovirus and enterovirus, influenza A (H1, H1–2009, and H3), influenza B, parainfluenza 1–4, and RSV	*Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*	..	Nasopharyngeal swab	60 min	90%	95%
FilmArray pneumonia panel[11–13]	33	Influenza A (H1, H3, and H1–2009), influenza B, coronaviruses (229E, HKU1, NL63, and OC43), human metapneumovirus, human rhinovirus and enterovirus, RSV, and parainfluenza 1–4	*Streptococcus pneumoniae*, *Staphylococcus aureus* (including MRSA), *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Escherichia coli*, *Moraxella catarrhalis*, *Legionella pneumophila*, other *Legionella* spp, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae*	*mecA*/*C*, *MREJ*, *blaKPC*, *blaNDM*, *blaOXA-48-like*, *blaVIM*, and *blaIMP*	Bronchoalveolar lavage, sputum, or endotracheal aspirate	60 min	>96·2 %	>98·3%
Xpert Xpress FLU/RSV[14]	Three	Influenza A (subtypes H1, H3, and H1–2009), influenza B, and RSV	..	..	Nasopharyngeal swab	30 min	>95%	>95%
ePlex respiratory pathogen panel[15–17]	20	Adenovirus, coronaviruses (229E, HKU1, NL63, and OC43), human metapneumovirus, human rhinovirus and enterovirus, influenza A (H1, H3, and H1–2009), influenza B, parainfluenza 1–4, and RSV	*Bordetella pertussis*, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*	..	Nasopharyngeal swab	90 min	90%	95%
Simplexa Flu A/B & RSV direct[14]	Three	Influenza A and influenza Bl	..	..	Nasopharyngeal swab	60 min	>90%	95%
Verigene respiratory pathogens flex test[18–20]	12	Influenza A (H1, H3, and H1–2009), influenza B, RSV, adenovirus, human metapneumovirus, human rhinovirus and enterovirus, and parainfluenza 1–4	*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, and *Legionella pneumophila*	..	Nasopharyngeal swab	120 min	>90%	95%
Xpert MTB/RIF[21–23]	One	..	*Mycobacterium tuberculosis*	Rifampicin resistance	Sputum or other clinical samples	120 min	86·3%	85·3%
RT-LAMP for SARS-CoV-2[24]	One	SARS-CoV-2	..	..	Nasopharyngeal swab or saliva	30–60 min	97%	81%

MRSA=meticillin-resistant *Staphylococcus aureus*. RSV=respiratory syncytial virus. SARS=severe acute respiratory syndrome. *All times are approximate.

Table 1: **Commercially available nucleic acid amplification tests to identify causal pathogens in patients with community-acquired pneumonia**

essential.[28,29] Biomarkers' potential to inform the empirical use of antimicrobials remains a subject of ongoing study. Furthermore, accounting for local epidemiology, including variations in pathogen prevalence and antimicrobial resistance patterns, is essential to optimise empirical therapy. For example, the prevalence of some microorganisms has declined with the broader adoption of vaccination strategies, which have changed their epidemiology in North America and parts of Europe.[30] However, *Streptococcus pneumoniae* remains a dominant pathogen in many low-income settings and is the most frequently identified bacterial pathogen in patients with community-acquired pneumonia worldwide.[31,32] Similarly, globally, respiratory viruses account for an increasing proportion of microbiologically proven community-acquired pneumonia and are now detectable in up to 30% of cases due to advances in molecular diagnostics.[33,34]

The evolving understanding of community-acquired pneumonia's pathophysiology challenges its conventional characterisation as only an acute infection. Increasing evidence links it to long-term complications—including cardiovascular events, persistent respiratory dysfunction, and cognitive decline—particularly among older adults and those with severe community-acquired pneumonia.[35–41] These findings highlight the need to reframe community-acquired pneumonia as a disease with potential chronic sequelae that requires comprehensive management strategies, extending beyond the acute phase to include long-term follow-up and prevention.[42–44]

As community-acquired pneumonia continues to impose a substantial global health burden, integrating advanced diagnostics, personalising treatment strategies, and focusing on long-term outcomes is a transformative shift in its management. This Seminar

explores these developments, emphasising global epidemiology, pathophysiological insights, diagnostics, and therapeutic innovations that redefine our approach to community-acquired pneumonia in acute and chronic contexts. By leveraging these advances, clinicians can move closer to achieving the goal of precise, patient-centred care for this pervasive and complex disease.

Epidemiology and risk factors

Community-acquired pneumonia's incidence varies widely depending on demographic and geographical factors and contributes to a considerable health-care burden, especially when it causes hospitalisation or admission to an intensive care unit (ICU).

Biological and environmental risk factors and social determinants

Key biological risk factors for developing community-acquired pneumonia have been identified and include older age, previous history of pneumonia (including COVID-19), smoking, chronic lung conditions (eg, chronic obstructive pulmonary disease [COPD] and asthma), chronic cardiovascular disease, and diabetes.[45–47] Immunosuppression due to illness or treatment also elevates the risk for community-acquired pneumonia. Lifestyle factors, such as the misuse of alcohol or neurological depressants (which increase the risk of bronchoaspiration and swallowing disorders) and poor nutrition weaken immune defences, further increasing susceptibility, with air pollution particularly affecting people in urban and industrial areas.[48] Likewise, socioeconomic status, health-care access, housing quality, and education substantially affect incidence, severity, and outcomes.[49–51] Individuals from lower-income backgrounds often face higher rates of community-acquired pneumonia related to inadequate housing, restricted access to health care, and increased exposure to pollutants that compromise respiratory health.[51] Crowded living conditions and restricted access to health care can promote pathogen transmission and delay diagnosis and treatment, thereby worsening outcomes. Additionally, low health literacy has been associated with reduced acceptance of preventive behaviours and strategies, including vaccination.[52,53]

Incidence and severe disease requiring ICU admission

The incidence of community-acquired pneumonia is high in older populations and individuals with chronic diseases.[47] In high-income countries, incidence is approximately 1188·6/100 000 population, which increases among those aged 70 years and older to around 4846·6/100 000 population.[1,2,54] The European community-acquired pneumonia incidence rate is 1664·0/100 000 in the general population, with rates rising steeply in those older than 70 years and reaching up to 5062·9/100 000 population.[45,55,56] Of the patients hospitalised with community-acquired pneumonia, 13–22% have severe commnity-acquired pneumonia and often require ICU care, with respiratory failure, septic shock, and multiorgan dysfunction driving high mortality rates.[55–57] In the USA, patients with community-acquired pneumonia treated in ambulatory settings reach an average cost of US$2394 per episode.[58] Although patients with in-hospital community-acquired pneumonia reach a mean cost of $17736, with a mean length of stay of 5·7 days for patients without complications,[59] these costs can increase to $51219 for patients that develop complications.[60] In 2020, the all-cause readmission rate was 8·8% at 30 days and 20·1% at 180 days.[59] 30-day mortality rates of community-acquired pneumonia vary substantially depending on several factors; nevertheless, in recent years, mortality rates have decreased to between 4·1% and 9·6% among hospitalised patients.[61,62] However, the 30-day mortality rate for patients with community-acquired pneumonia who need ICU admission can be up to 49·4%.[55,63–65]

Pathogen detection rate

Despite extensive diagnostic testing, a specific pathogen can only be identified in less than half of patients with community-acquired pneumonia,[33] underscoring key knowledge gaps. As molecular diagnostics improve and real-time, reverse transcriptase quantitative PCR and multiplex real-time PCR assays are more broadly used,[27] identification of the microbiological causes of community-acquired pneumonia is expected to increase. This increase might improve diagnostic yields even in patients who have already received antimicrobials, which often renders cultures negative, leading to better targeted treatments.[66,67]

Bacterial causes

Although *S pneumoniae* is the most frequently detected bacterial cause of community-acquired pneumonia worldwide, other causative bacterial pathogens include *S aureus, Haemophilus influenzae, Chlamydia pneumoniae, Mycoplasma pneumoniae,* and Enterobacteriaceae spp, the last being among the less common causes.[1,2,33,68] However, depending on various factors, including comorbidities, lifestyle habits, immunosuppression, and previous colonisation, other causal agents—such as *P aeruginosa* and *Legioxphila*—could be prevalent.[1,2,33,68,69] Notably, the incidence of *S pneumoniae* has declined due to the widespread use of pneumococcal vaccination, reducing pneumococcal pneumonia rates and contributing to population-level herd immunity.[26] Regional vaccination recommendations and uptake differences affect *S pneumoniae* prevalence in patients with community-acquired pneumonia; it causes approximately 30% of community-acquired pneumonia cases in Europe but only 10–15% of cases in the USA, where higher pneumococcal vaccination rates are reported.[33] However, in LMICs, vaccination strategies are less effective, contributing to a higher prevalence of *S pneumoniae*.[4,70–72] *H influenzae* also remains a prevalent pathogen in community-acquired

pneumonia; however, vaccination strategies, demographic factors, and external events (eg, the COVID-19 pandemic) influence the dynamics of its detection and reporting.[73,74] The introduction of the *H influenzae* type b vaccine has led to decreased *H influenzae* type b infections; however, an increase in non-Hib serotypes has been observed.[75,76] These changes in trends of *H influenzae* identification suggest that the COVID-19 pandemic could have influenced the infection landscape, possibly due to changes in health-care seeking behaviours, public health measures, or viral–bacterial interactions.[77]

Viral causes

Advances in molecular diagnostics have increased the detection of respiratory viruses in community-acquired pneumonia, with studies indicating that viruses are present in approximately a third of adults with community-acquired pneumonia, with rhinovirus and influenza A and B accounting for 9%.[33] Other viruses frequently identified include respiratory syncytial virus (mainly in older people and children), human metapneumovirus, parainfluenza viruses, coronaviruses (229E, OC43, NL63, HKU1, and severe acute respiratory syndrome [SARS]), hantavirus, cytomegalovirus, herpes simplex virus, and varicella zoster virus.[78,79]

Acknowledging the complex interplay between viral and bacterial infections in community-acquired pneumonia is essential as viral infections can potentially predispose individuals to secondary bacterial infections. The cooperative existence between viruses and bacteria involves mechanisms such as impairment of the host immune response and disruption of epithelial barrier integrity, leading to more severe clinical manifestations and an increased risk of respiratory failure.[80,81] This risk highlights the need for research to better understand viral contributions to community-acquired pneumonia pathogenesis.[33,34,78]

Pathophysiology

Community-acquired pneumonia occurs when pathogens (ie, bacteria, viruses, or fungi) proliferate rapidly in the lower respiratory tract, provoking robust local and systemic inflammation and subsequently leading to tissue destruction. Pathogens access the lower respiratory tract by inhalation of airborne particles (in the case of viral pathogens) or aspiration of pharyngeal secretions.[82] Subclinical aspiration of pharyngeal contents is common even among healthy, asymptomatic individuals,[83] explaining the presence of viable oropharynx-associated bacteria in the lungs of healthy volunteers.[82,84] Current microbiological studies using culture-dependent or culture-independent techniques do not support the conventional distinction between aspiration pneumonia and other community-acquired pneumonias.[85] Essentially, all bacterial community-acquired pneumonias arise via aspiration and the mere presence of microbes in the lungs cannot explain the disease's pathogenesis. Bacterial pneumonia occurs when a sufficient burden of specific microbes with pathogenic potential accesses the lower respiratory tract, exceeding the host's complementary mechanisms of microbial clearance (ie, cough, mucociliary clearance, and immune defences). Although the healthy lung environment is nutrient-poor for reproducing microbes, the onset of pneumonia alters this landscape: the influx of oedema and mucus to the airspaces provides a nutrient-rich medium that fosters microbial proliferation.[82]

Under physiological conditions, resident macrophages in the alveolar space clear pathogenic microorganisms.[86] If the phagocytes' capacity is exceeded, closely coordinated inflammatory pathways are triggered.[87] This triggering leads to the expression of early inflammatory cytokines, including IL-1β, and chemokines, including IL-8,[86,88] driving the recruitment of neutrophils and inflammatory monocytes from systemic circulation. The lytic enzymes, oxidants, and extruded nuclear material from these cells damage the delicate alveolar epithelium, leading to plasma protein fluid leakage and disruption of gas exchange.[89] These pathological features drive the clinical picture of pneumonia, with breathlessness, pyrexia and, as severity increases, hypoxia and hypercarbia.

Although neutrophils are considered central to the development of acute lung injury,[89] it is also recognised that injury can develop in patients with neutropenia.[90] Data from a preprint published in 2024 identified a wider group of patients with lung injury without alveolar neutrophilia.[91] Evidence of macrophage–lymphocyte pathology in COVID-19[92] and enrichment for respiratory viruses in the non-neutrophil phenotype identified by Jeffery and colleagues[91] indicates multiple pathways by which similar clinical presentations could arise. There is increasing interest in identifying the divergent immunological mechanisms underlying common clinical syndromes[93] with an aim to personalise immunomodulatory therapies. However, these approaches almost exclusively focus on blood immune profiling.[93] Given the compartmentalised nature of lung inflammation, tailoring therapies based on blood indices could result in misapplication.[94]

Patients who develop severe manifestations of pneumonia seldom die of refractory hypoxaemia. The mechanisms of extrapulmonary organ failure are diverse but include direct bacterial invasion and bacteraemia,[95] systemic inflammatory activation with complement activation and cytokine release, immunoparesis,[96] and an inability to clear primary or secondary pathogens. The development of extrapulmonary organ failures, such as acute kidney and liver injury or cardiovascular failure and shock, portends poorly and helps explain the substantial global mortality burden of community-acquired pneumonia.

Clinical features and diagnostic approaches

Inflammatory infiltration of the alveolar space drives the clinical symptomatology of community-acquired

pneumonia. However, this disease presents with marked variability in its respiratory and systemic manifestations between patients. Symptom severity largely depends on the intensity of the host's immune response, with younger, immunocompetent patients presenting with more pronounced clinical features.[97] Both respiratory and systemic symptoms can be mild or absent among patients with impaired immune responses due to comorbidities (eg, HIV/AIDS), iatrogenesis (eg, corticosteroids), or other factors (eg, older age).[97] Notably, the absence of classic pneumonia symptoms does not exclude the diagnosis in these populations.

Respiratory manifestations dominate community-acquired pneumonia's clinical presentation. Cough (often productive of sputum), dyspnoea, and pleuritic chest pain are hallmark features (figure 1). Physical examination findings commonly include tachypnoea, adventitious breath sounds (rales or rhonchi), and evidence of consolidation, including dullness to percussion or egophony.[8,33]

The diagnostic approach for community-acquired pneumonia is variable in the literature and can be attributed to an absence of a gold standard definition; nevertheless, some features are globally accepted and the most common diagnosis criteria involve identifying pulmonary clinical signs (ie, classic pneumonia symptoms and radiological signs of pulmonary consolidation) alongside systemic features, such as abnormal body temperature (>38°C or <36°C),[101–104] tachypnoea, and tachycardia.[103–105] Detection of systemic inflammation might extend to laboratory parameters, including total leukocyte counts (<4000/μL or >10 000/μL) and neutrophil counts (>15% band-type neutrophils), and elevated C-reactive protein or procalcitonin concentrations. No single clinical sign has good predictive

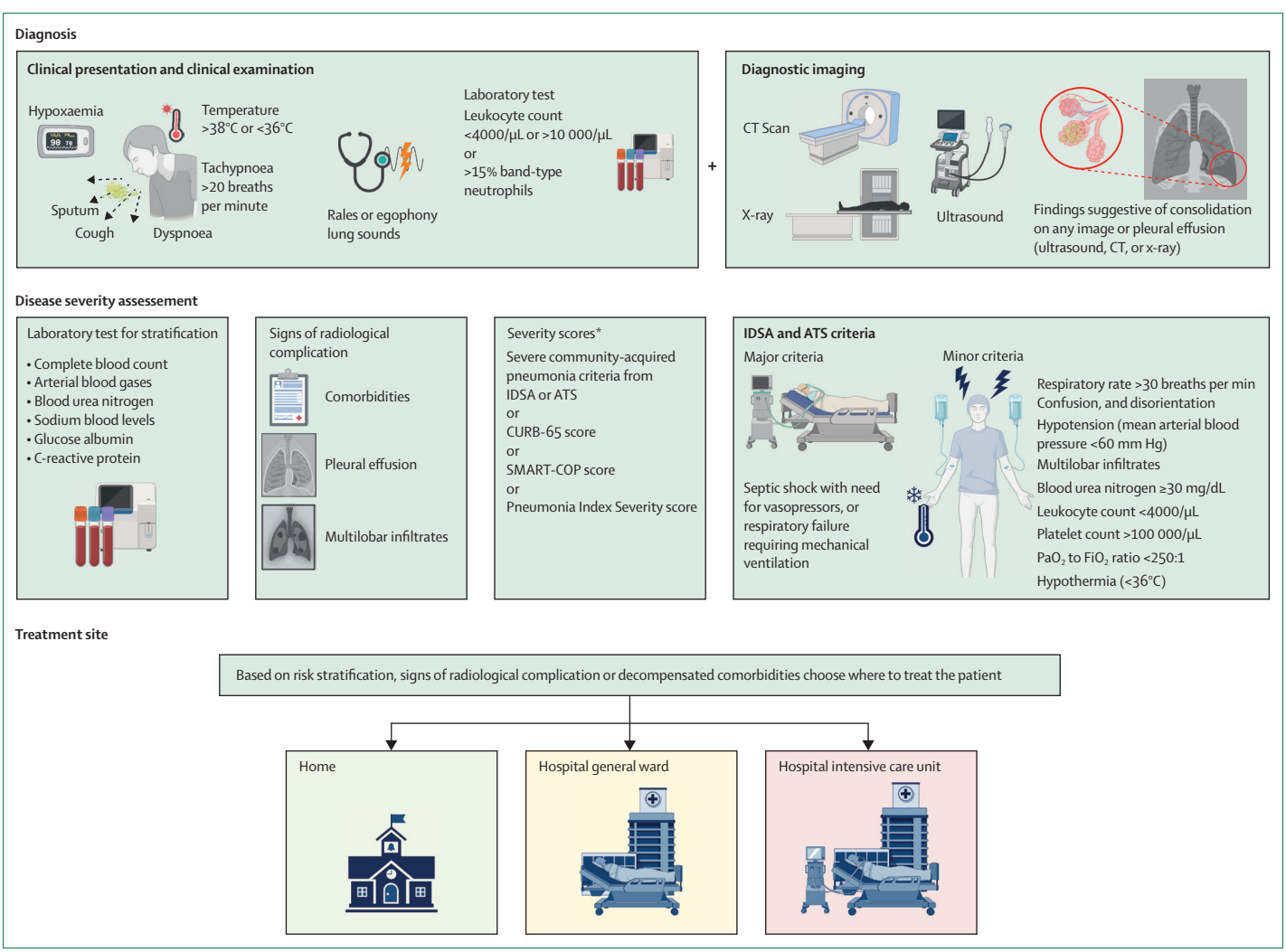

Figure 1: **Considerations for diagnosis and treatment initiation of patients with community-acquired pneumonia**
ATS=American Thoracic Society. FiO_2=fraction of inspired oxygen. IDSA=Infectious Diseases Society of America. PaO_2=partial pressure of oxygen in arterial blood. *The IDSA and ATS criteria[8] are preferred, but the SCAP score,[8] CURB-65 score,[98] SMART-COP,[99,100] or Pneumonia Index Severity score[98] can also be used.

power for identifying patients with radiographical infiltrates, although the absence of abnormal pulmonary examination and physiology has good negative predictive power.[101] Hence, clinical examination alone cannot confirm a pneumonia diagnosis but can support ruling it out. Likewise, older or immunocompromised patients might not have fever, could present with non-specific findings (such as confusion or functional decline), or could present with atypical pneumonia, with mild respiratory symptoms such as a dry cough, sore throat, mild fever, and more severe extrapulmonary symptoms, including confusion, diarrhoea, headache, and myalgia.[106,107] Community-acquired pneumonia is a leading cause of sepsis and patients with severe cases might present with hypotension, altered mental status, and other organ dysfunctions alongside respiratory failure.[102]

A meta-diagnostic analysis of C-reactive protein and procalcitonin in community-acquired pneumonia published in 2022 found that both tests had a modest diagnostic performance.[103] At a cutoff of 50 mg/L, C-reactive protein had a sensitivity and specificity of 75% and at a cutoff of 0·5 µg/L, procalcitonin had a sensitivity of 44% and a specificity of 93%. This diagnostic performance is insufficient to guide the initiation of antimicrobial therapy; US guidelines,[8] European and South American guidelines,[108] and other studies recommend against using biomarkers to guide antimicrobial initiation.[8,109–111] Procalcitonin has a proven role in antimicrobial de-escalation in sepsis arising from severe community-acquired pneumonia and other severe infections,[112–115] but the role of C-reactive protein is less clear.[113,116,117] Treatment algorithms guided by these biomarkers drastically reduced the duration of antibiotic therapy in hospitalised patients with community-acquired pneumonia compared with standard care.[112–116] The median number of days on antibiotics was reduced to 4·0 days in the C-reactive protein group and 5·5 days in the procalcitonin group compared with 7·0 days in the control group.[116] A 2022 meta-analysis suggested that these biomarkers can serve as reliable tools to support the de-escalation of antimicrobial therapy in community-acquired pneumonia, contributing to shorter antibiotic courses and potentially mitigating the development of antimicrobial resistance and adverse drug effects.[116] Nonetheless, the interpretation of these biomarkers should be complemented by thorough clinical evaluation to ensure optimal therapeutic decision making.[118,119]

Given the imperfect diagnostic performance of clinical and laboratory measures, showing alveolar infiltration is a key step in securing a diagnosis; it can be achieved through chest radiography, CT imaging, or lung ultrasound (figure 1). Radiographical assessment is recommended for all patients in the US guidelines,[120] although it is only recommended for hospitalised patients in the UK guidelines.[121] Although plain chest radiology is frequently used as the standard for radiological assessment of community-acquired pneumonia, it is insensitive compared with CT imaging[103] and infiltrates are not specific for pulmonary infection. CT imaging is advised in the Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) guidelines for uncertain or inconclusive cases.[8] Lung ultrasound has better sensitivity (pooled value 92%, 95% CI 88–95) and specificity (89%, 81–95) than plain radiology (specificity 49%, 40–58; sensitivity 92%, 86–95).[103] The finding of dynamic air bronchograms is considered a pathognomonic sonographical feature of pneumonia. Nevertheless, the most common signs are lung consolidation or interstitial patterns.[122–124] However, although lung ultrasound is often helpful in the resuscitation room and ICU, it does not have sufficient sensitivity to rule out pneumonia and depends on the operator's experience and expertise.[122–126] It is important to highlight that the ATS 2025 guidelines explicitly recognise lung ultrasound as an acceptable diagnostic alternative to chest radiography when local expertise and equipment are available, particularly in settings with restricted radiographical access.[127]

Notably, in a survey of international practice of severe pneumonia diagnosis published in 2024, a third of ICU clinicians did not consider radiographical infiltrates mandatory to diagnose pneumonia.[27]

The definitive diagnosis of community-acquired pneumonia is secured by identifying a respiratory pathogen in combination with the clinical, radiological, and laboratory features outlined above, even though a gold standard definition of pneumonia remains absent. Microbiological sampling is generally not required for low-severity disease managed in the community, as the results do not affect management.[78,87] Blood and sputum samples are commonly obtained for culture in patients hospitalised with community-acquired pneumonia,[128] although the yield from such cultures is low (blood samples 7% and sputum samples 18%). Antigen detection is available for identifying specific pathogens, notably urinary antigen testing for *S pneumoniae* and *L pneumophila*, and a growing number of respiratory viruses on upper-respiratory swabs.[129] Antigen testing has good positive predictive value; however, false negatives are common and these tests do not rule out other co-infecting organisms. As a result, antigen testing has restricted effects on antimicrobial prescribing and there is concern that it might lead to the inappropriate narrowing of the antimicrobial spectrum and an increased risk of relapse.[130]

The growing availability of NAATs has improved viral detection. Tests for SARS-CoV-2 and influenza are recommended for mild and severe community-acquired pneumonia, but only when viruses are actively circulating or exposure is suspected.[8] When these tests are done at admission, they decrease time to antimicrobial use, antiviral initiation, and length of stay.[8,105,131,132] Expanded viral tests (ie, beyond SARS-CoV-2 and influenza) could be done for patients with severe community-acquired pneumonia to guide treatment by cause.[132–134]

NAATs are also increasingly available in multiorganism syndromic formats, with panels increasingly extended to cover conventional bacteria, respiratory viruses, and atypical microorganisms.[66] The evidence that syndromic NAATs affect antimicrobial prescribing for hospitalised patients with community-acquired pneumonia is uncertain, with divergent trial results.[9–11,135,136] Patient context (ie, management in the community, severity of illness, and emergency department, ward, or ICU settings) alongside biomarker assessment as part of embedded antimicrobial stewardship approaches is likely required to achieve changes in antimicrobial prescribing.[112,113] There are only a few trials of NAATs in patients with severe community-acquired pneumonia managed in the ICU and none have yet been published in full. However, abstract reports from Voiriot and colleagues[12] and observational data[13] suggest improved antimicrobial targeting is possible.[13] Nonetheless, there is not enough evidence to support antimicrobial withdrawal and some guidelines do not recommend NAAT use.[8,135]

Assessment of disease severity

Severe community-acquired pneumonia is the most life-threatening form of community-acquired pneumonia and is characterised by high morbidity and mortality.[137] It often presents with clinical features, such as respiratory distress, multilobar infiltrates on imaging, septic shock, and acute respiratory failure. With its heightened mortality, guidelines advise risk stratification and early ICU admission.[99,108,138] The most widely accepted criteria for defining severe community-acquired pneumonia are those from the IDSA and ATS and have both major criteria (need for invasive mechanical ventilation or septic shock requiring vasopressors) and minor criteria (respiratory rate >30 breaths per min; arterial oxygen pressure to fraction of inspired oxygen ratio of <250:1; multilobar infiltrates; confusion or disorientation; uraemia with blood urea nitrogen ≥20 mg/dL; leukocyte [white blood cell] count <4000/μL; thrombocytopenia [platelets <100 000/μL], hypothermia [core temperature <36°C]; and hypotension requiring aggressive fluid resuscitation)[8]. Severe community-acquired pneumonia is diagnosed with one major or three or more minor criteria.[8,120] However, other severity scores, such as the CURB-65, Pneumonia Severity Index, SMART-COPS, APS II, and Pneumonia Shock score, are available (table 2).[38] Notably, the current clinical practice guidelines emphasise the clinician's judgement in tailoring management on the basis of specific risk profiles.[108] A substantial challenge with risk scoring is that although the scores are good for predicting mortality and thus help establish if hospitalisation is needed, they are typically less effective at predicting the need for ICU admission and organ support.[143] Attempts to improve the prediction of the need for ICU have found the Sequential Organ Failure Assessment score to be the most effective,[144] although in many cases, this is simply identifying organ failure manifesting at the time of hospital presentation.

	Primary use	Setting	Variables included	Score range	Risk stratification	Key strengths	Key limitations
CURB-65[98,139]	Assess mortality and the need for admission in community-acquired pneumonia	Outpatient and emergency department	Confusion, urea >7 mmol/L, respiratory rate ≥30 breaths per min, blood pressure < 90 systolic or ≤ 60 diastolic, and age ≥65 years	0–5	0–1 low risk (outpatient); 2 consider admission; ≥3 severe (consider ICU)	Simple and fast	Does not consider comorbidities or most laboratory tests
Pneumonia Severity Index[98,140]	Predict 30-day mortality in community-acquired pneumonia	Inpatient and emergency department	20 variables: age, sex, comorbidities, physical examination, laboratory tests (pH, sodium, glucose, and haematocrit), and radiographical findings	I–V (0 to >130 points)	I–II low risk; III moderate; IV–V high risk, consider hospital or ICU admission	Highly validated	Complex, time consuming, and must be done without a calculator
SMART-COP[100]	Predict the need for IRVS	Emergency department and ICU	Systolic blood pressure <90 mm Hg, multilobar infiltrates, albumin <35 g/L, increase in respiratory rate, heart rate >125 beats per min, confusion, low PaO_2, and pH <7·35	0–16	0–2 low risk; 3–4 moderate risk; ≥5 high risk of IRVS	Strong predictor of ICU needs, even in younger adults	Not a mortality tool
SAPS II[141]	General severity of illness score (ICU mortality)	ICU	17 variables: age, Glasgow Coma Scale, heart rate, systolic blood pressure, core temperature, FiO_2, PaO_2, urine output, laboratory tests, and chronic diseases	0–163	Higher scores means higher predicted mortality	Highly validated	It requires full lab and physiological data and is not pneumonia-specific
Pneumonia Shock score [38,142]	Predict ICU mortality in septic shock due to community-acquired pneumonia	ICU	Hypoxaemia (PaO_2 to FiO_2 ratio), lactate >4 mmol/L, acute renal failure, vasopressors, confusion, and thrombocytopenia	0–6	0–1 low risk; 2–3 intermediate; ≥4 high mortality risk	Designed specifically for severe pneumonia with shock and incorporates organ failure	It does not evaluate the risk of long-term outcomes[38]

ICU=intensive care unit. PaO_2=partial pressure of oxygen in arterial blood. FiO_2=fraction of inspired oxygen. IRVS=intensive respiratory or vasopressor support.

Table 2: **Details of CURB-65, Pneumonia Severity Index, SMART-COP, SAPS II, and Pneumonia Shock score**

Assessing illness severity helps establish how quickly antimicrobials and supportive treatments should be initiated. Simultaneously, clinicians should evaluate the likely causative organisms and consider the risks of multidrug-resistant or opportunistic pathogens, which might require targeted antimicrobial strategies. Risk factors for infection with multidrug-resistant organisms include known carriage of them and recent (<90 days) receipt of intravenous antibiotics during hospitalisation.[78] Opportunistic pathogens should be considered among patients who are profoundly immunocompromised (eg, HIV infection with low CD4 count, neutropenia following chemotherapy, and solid organ or haematopoietic stem cell recipients). However, it is essential to recognise that sporadic and epidemic causes of community-acquired pneumonia are also common among these patient groups.

Treatment

Antimicrobial therapy

Treatment is dependent on the severity of illness and the likely causative pathogens. Initial therapy is empirical because the causative pathogen is usually unknown at presentation. Typical pathogens are generally covered with a β-lactam antibiotic, assuming no history of allergy, with local resistance patterns determining the specific agents.[108] Coverage for intracellular organisms, including for patients with severe community-acquired pneumonia and with suspected atypical infections, is recommended with fluoroquinolones or macrolides.[8] Some quinolones, such as levofloxacin cover both Gram-positive and Gram-negative typical and atypical pathogens. Most guidelines advise macrolides over fluoroquinolones, primarily on the basis on data from observational studies (figure 2).[145]

The potential immunomodulatory effects of macrolides were investigated in the ACCESS trial, in which 68% of patients who took clarithromycin twice a day for 7 days met the composite primary endpoint (a decrease in respiratory symptom severity score and SOFA score, procalcitonin, or both) at day 4 compared with 38% of patients in the placebo group.[146] However, it remains uncertain if these improvements in surrogate outcomes translate into tangible benefits for patients, such as enhanced quality of life, faster functional recovery, or reduced mortality. In a randomised trial comparing β-lactam monotherapy to β-lactam plus macrolide therapy in patients with moderate severity, community-acquired pneumonia, time to stability did not include the predefined non-inferiority limit and favoured combination therapy; however, this effect appeared to be restricted to patients with atypical infections or more severe pneumonia (Pneumonia Severity Index category IV).[147] Another RCT found that, in patients with community-acquired pneumonia admitted to non-ICU wards, a strategy of preferred empirical treatment with β-lactam monotherapy was non-inferior to strategies with a β-lactam–macrolide combination or fluoroquinolone monotherapy concerning 90-day mortality.[148] A systematic review of observational data concerning mortality found that dual therapy (ie, β-lactam plus macrolide) was associated with a reduced mortality risk in patients with community-acquired pneumonia.[149] These findings suggest that macrolides can be effective as immunomodulatory agents in treating community-acquired pneumonia, particularly in severe cases, and should be used for patients requiring hospital admission.

Standard empirical treatment should be modified for patients at risk of carrying multidrug-resistant organisms. However, the severity of illness alone is no justification for using anti-pseudomonal or anti-meticillin-resistant *S aureus* agents, such as piperacillin and tazobactam or cefepime and vancomycin, in patients without risk factors for multidrug-resistant organism infection or carriage. Clinicians should shift the perspective to individualised patient assessment by evaluating specific risk factors for multidrug-resistant organisms, previous colonisation, disease severity, and comorbidities to select the best antimicrobial regimen while avoiding the universal use of broad-spectrum regimens.[62,150,151] When empirical multidrug-resistant organism treatment is started, it should be de-escalated rapidly if screening tests are negative. Additionally, there is no reason to specifically cover anaerobes empirically, even in the presence of aspiration.[108] It has even been suggested that anaerobic coverage might disrupt the healthy microbiome in these patients, increasing the risk of adverse outcomes.[152,153]

Antiviral therapies targeting SARS-CoV-2 have the strongest evidence. For example, remdesivir might help prevent progression to severe disease, but has no significant benefit in patients requiring invasive mechanical ventilation or extra corporeal membrane oxygenation.[154] Of note, during the COVID-19 pandemic, some critically ill patients presented with a hyper-inflammatory profile, clinically presenting with acute respiratory distress syndrome following the cessation of viral replication.[155] However, patients with severe community-acquired pneumonia from SARS-CoV-2 infection are now frequently immunocompromised and their illness could be related to viral replication, hyperinflammation, or both.[154,156] Whether the trial findings obtained during the pandemic apply to the current case-mix is unclear. Although high-quality evidence for treating severe community-acquired pneumonia arising from influenza is scarce,[157] recommendations for treatment are provided by WHO[157] and cluster patients into those with non-severe and severe symptomatic influenza. Patients with non-severe influenza should not receive antiviral treatment and baloxavir is only suggested for patients with non-severe influenza with a risk of progression to severe influenza.[157,158] The recommendation for patients with severe symptomatic influenza is to take oseltamivir and other antivirals are not recommended,[158] although the low quality of the evidence for these recommendations is recognised.

	Home	Hospital general ward	Hospital intensive care unit
Tests to prescribe	• COVID-19 or influenza testing (only if there is a potential exposure or it is common in the community)	• COVID-19 or influenza testing (only if there is a potential exposure or it is common in the community) • Respiratory cultures and Gram stain • Blood cultures • C-reactive protein • MRSA nasal swab (only if risk factors for MRSA are present*)	• COVID-19 and influenza testing • Respiratory cultures and Gram stain • Blood cultures • MRSA nasal swab • Pneumococcal urinary antigen • *Legionella* urinary antigen • C-reactive protein (following up every 48–72 h) • Procalcitonin and expanded respiratory viral and bacterial testing (nucleic acid amplification testing) • Invasive lower respiratory test (only if patient under invasive mechanical ventilation and not improving with initial treatment)
Empirical treatments	• Amoxicillin or doxycycline If patient has chronic lung disease or asplenia: • Amoxicillin and clavulanate or oral cephalosporine + • Macrolide or doxycycline If patient is allergic: • Respiratory fluoroquinolone If respiratory viral PCR positive and no comorbidity: • Avoid empirical antibacterials† If comorbidity present: • Consider empirical antibacterials†	• β-lactam (ampicillin + sulbactam or ceftriaxone) + • Macrolide If patient is allergic: • Respiratory fluoroquinolone If patient had previous MRSA or *P aeruginosa* infection or previous hospitalisation with parenteral antimicrobials: • Vancomycin or linezolid + cefepime or piperacillin/tazobactam + macrolide (alternatives are ceftazidime, imipenem, or meropenem)	• Vancomycin or linezolid + • Cefepime or piperacillin/tazobactam (alternatives are ceftazidime, imipenem, or meropenem) + • Oseltamivir
Antimicrobial duration, change of regimen, and steroids	• 3–5 day antibiotic course • Follow-up visit 1 week after treatment completion • Reconsult if warning signs present‡ • No steroids	• 3-5 days depending on time to stability • At least 7 days if confirmation of MRSA or *P aeruginosa* • Longer than 7 days if complications—eg, emphysema, effusion, abcess, or unusual pathogens • Once microorganism is confirmed, targeted therapy should be initiated • No steroids	• 7–10 days tailored based on the patient's clinical progress and microbiological findings • Once microorganism is confirmed, targeted therapy should be initiated • Start steroids within 24 h of meeting severity criteria; do no start steroids if the patient has a positive influenza test
When to transition to oral antimicrobial medication and when to discharge the patient	• Oral antimicrobials from the beginning • No in-hospital management	• As soon as the patient is improving and able to tolerate oral therapy and if the antimicrobial is available to oral administration • Hospital discharge when they have met day stability criteria§	• As soon as the patient is improving and able to tolerate oral therapy and if the antimicrobial is available to oral administration • ICU discharge when considered by the treating physician • Hospital discharge when they have met 3 day stability criteria§

Figure 2: **Considerations for taking care of patients with community-acquired pneumonia**
The treatment site is established based on risk stratification, signs of radiological complication, or decompensated comorbidities. Stability criteria: afebrile (<37·8 °C), heart rate less than 100 beats per min, respiratory rate less than 24 breaths per min, no hypoxaemia (ie, peripheral oxygen saturation >90% or partial pressure of oxygen >60 mm Hg), and systolic blood pressure greater than 90 mm Hg. ICU=intensive care unit. MRSA=meticillin-resistant *Staphylococcus aureus*. *P aeruginosa=Pseudomonas aeruginosa*. *Risk factors are previous MRSA infection, hospitalisation in the past 90 days, intravenous antibiotic use in the past 90 days, and high local MRSA prevalence.[8] †Advice from the 2025 American Thoracic Society guideline on the diagnosis and management of community-acquired pneumonia.[127] ‡Warning signs are continued fever, high respiratory rate, or low blood pressure. §Patients must meet all criteria by day 3 to be considered for hospital discharge.

The scarcity of high-quality evidence in non-SARS-CoV-2 viral pneumonia requires large-scale clinical trials on treating severe viral pneumonia. Bacterial co-infection with *S aureus* is a common complication of severe influenza. Some guidelines recommend empirical antibacterial therapy to cover common bacterial pathogens, whereas others do not encourage antimicrobials without biomarkers to support the decision.[8,158,159] Co-infection with *Aspergillus* species can occur, especially in patients with severe viral pneumonia (ie, COVID-19 and influenza) who have risk factors such as prolonged mechanical ventilation, corticosteroid use, or underlying chronic respiratory disease. Initiation of empirical antifungal therapy should be guided by clinical suspicion and diagnostic findings.[33,160,161] Bacterial co-infection at the time of presentation with COVID-19 is rare, but secondary infection in the form of nosocomial pneumonia is common.[162,163] In patients with confirmed severe viral community-acquired pneumonia, guidelines recommend joint antimicrobial and antiviral treatment to cover for bacterial co-infection, with early de-escalation when bacterial co-infection is subsequently ruled out.[8,105,108]

Depending on the patient's treatment setting (ie, outpatient, inpatient, or ICU), the availability of microbiological tests, and the types of samples (ie, nasopharyngeal swab, sputum, blood cultures, urine, and bronchoalveolar lavage) for culture and molecular diagnostics, samples should be collected before initiating empirical antimicrobial therapy, although this should not delay the administration of antimicrobials.[164] Microbiological testing allows for subsequent narrowing of the therapeutic spectrum as the causative pathogens are identified and resistance profiles are established.

The optimal duration of therapy remains uncertain. The duration of antimicrobial treatment depends on where the patient will be treated, how soon the patient is clinically stable, changes in serum biomarkers, local epidemiology, and individualised assessment of risk factors. The recommended duration ranges depending on if the patient is treated as an outpatient (3 to 5 days), is in-hospital without ICU requirement (5 to 7 days), or is admitted to the ICU (7 to 10 days).[8] For patients in the ICU with severe community-acquired pneumonia, antibiotics should be given for at least 5 days once clinical stability is achieved, with extension only for specific indications, such as necrotising pneumonia, empyema, bacteriaemia, *S aureus* infection, *P aeruginosa* infection, suspected *Legionella* infection, or slow clinical response.[127] These times should be adjusted according to the patient's response to treatment. Although studies support short antimicrobial courses (eg, 3 days) in out-of-hospital environments,[165] the median duration remains 5 days. For patients who require in-hospital treatment, if there is a good clinical response, 5 days of antimicrobial therapy is the most evidence-based recommendation[166] when the antibiotic chosen is appropriate (ie, the right drug for the correct infection) and adequate (ie, therapeutic drug concentrations in the lung are accomplished). Prolonged antimicrobial courses (>7 days) should be avoided except in specific indications, such as severe community-acquired pneumonia, *S aureus* bacteraemia, or pleural collections that cannot be drained.[8] Current clinical guidelines recommend using clinical stability, supplemented by biomarkers, to guide the duration and limit prolonged antimicrobial therapy.[8]

Immunomodulation and adjunctive therapies

The immune system aims to rapidly restore immune homoeostasis by balancing disease resistance (eradicating pathogens with collateral tissue damage) and disease tolerance (limiting the severity of infection without directly affecting pathogen burden).[167] Thus, adjuvant treatment with corticosteroids, a broad immunosuppressant, targeted immunomodulatory drugs, or antimicrobial therapies could be beneficial.[168]

The use of corticosteroids is based on their potential to reduce mortality, decrease the need for mechanical ventilation, reduce the length of stay, and improve clinical stability. However, hyperglycaemia, secondary effects (eg, secondary infections and gastrointestinal bleeding), and the potential increased risks of hospital readmission are negative aspects.[169–172] Studies on corticosteroids in community-acquired pneumonia vary widely in selection criteria, drug type, timing, dosage, duration of treatment, and choice of primary endpoint. Most trials have been either underpowered or stopped early due to no signals for benefit or low recruitment rates.[173,174] Notably, the CAPE COD study found that treatment with hydrocortisone reduced the 28-day mortality in patients with severe community-acquired pneumonia.[175] A data-driven analysis of randomised trials found that steroids (compared with no steroids) were associated with lower 30-day mortality rates in patients with community-acquired pneumonia, especially in those with high C-reactive protein at admission.[173]

The ongoing international platform REMAP-CAP trial, which evaluates treatments for patients with community-acquired pneumonia in pandemic and non-pandemic settings, found that a 7-day course of hydrocortisone did not reduce mortality in patients with severe community-acquired pneumonia.[176] However, adding this study to a meta-analysis did not alter the conclusion that corticosteroids reduced short-term mortality and probably reduced longer-term mortality.[170] The overlap between severe community-acquired pneumonia, septic shock, and acute respiratory distress syndrome further complicates the interpretation of the evidence and patients might be treated with corticosteroids for these indications. Future studies should focus on diseases rather than syndromes, address the heterogeneity of treatment effects, use prognostic and predictive enrichment,[74,177] and aim to identify treatable traits,[156] thereby establishing which corticosteroid treatment strategy benefits each patient. This uncertainty is reflected in the current US and European and South American guidelines, which advise the use of corticosteroids as adjunctive therapy in cases of concurrent septic shock but are ambivalent on their use in non-shock, inflammatory, severe community-acquired pneumonia states,[173,174] although these guidelines were published before the most recent trials and meta-analyses were available. Consistent with 2025 ATS guidelines, systemic corticosteroids are not recommended for patients with non-severe community-acquired pneumonia.[127] By contrast, for severe community-acquired pneumonia, corticosteroids are suggested, except for influenza pneumonia, for which observational data suggest potential harm and no randomised controlled trials exist (conditional, low-quality evidence).[127]

Targeted immune modulation is commonly used in oncology and chronic autoimmune diseases but has been infrequently used in the ICU until recently. The reduced mortality from the IL-6 receptor JAK-STAT and complement-5a pathway blockade in COVID-19 suggests that such adjuvant therapies might also benefit other causes of severe community-acquired pneumonia.[156] There are currently no established immune modulation

therapies for severe bacterial community-acquired pneumonia. Notably, the REMAP-CAP platform is currently investigating the use of tocilizumab and baricitinib in severe influenza pneumonia.[178]

Compared with placebo, adjunctive therapy with simvastatin was safe but did not improve clinical outcomes in patients with acute respiratory distress syndrome that was primarily driven by pneumonia in the HARP-2 trial, as established by a frequentist analysis.[179] In a secondary post-hoc analysis using latent class analysis, a hyperinflammatory subphenotype was identified that was associated with improved survival in the simvastatin group.[180] In 2684 critically ill patients with COVID-19 in REMAP-CAP, there was a high likelihood (95·9% posterior probability of superiority) of a reduction in organ support-free days for simvastatin compared with control. At 90 days, the hazard ratio for survival with simvastatin was 1·12 (95% credible interval 0·95–1·32), yielding a 91·9% posterior probability of superiority to control.[181] However, these patients were almost uniquely of a hypoinflammatory subphenotype. The effects of simvastatin observed in the HARP-2 and REMAP-CAP trials appear to differ, suggesting a potential divergence in outcomes depending on the causative pathogens. These differences might be influenced by the patient's inflammatory subphenotype; however, the nature of these phenotypes and their extension to the pulmonary compartment[91,94] remains to be fully defined, thus highlighting the need for future research in this area. In summary, future clinical trials should prospectively stratify patients by inflammatory subphenotype to better interpret these findings and assess if simvastatin yields differential effects among biologically distinct groups.

There is currently insufficient evidence to support the use of other adjunctive therapies outside well conducted clinical trials, including thrombomodulin, colony-stimulating factors, immunoglobulins, and mesenchymal stem cells.

Management of complications and long-term follow-up

Managing complications and long-term follow-up care is an essential component of community-acquired pneumonia treatment and reflects the growing recognition of its post-acute sequelae.[39] Although conventionally considered an acute infection, community-acquired pneumonia often has lasting effects, necessitating a structured and multidisciplinary approach to ensure optimal recovery and prevent long-term morbidity.

Respiratory complications are among the most common long-term consequences of community-acquired pneumonia. Patients with severe disease frequently have prolonged pulmonary dysfunction, including impaired gas exchange, reduced lung capacity, and an increased risk of chronic conditions, such as bronchiectasis and exacerbations of COPD.[43,44] Early rehabilitation, including respiratory physiotherapy, can accelerate recovery, improve lung function, and reduce the risk of recurrent infections.[182–184] Follow-up imaging is not recommended in patients with community-acquired pneumonia whose symptoms have resolved within 5–7 days.[8] However, imaging follow-up 4–6 weeks after treatment to identify residual abnormalities is suggested, especially in patients with persistent symptoms or risk factors for lung cancer, as early detection of malignancies could have been obscured by initial pneumonia.[8]

Cardiovascular complications are a substantial burden following community-acquired pneumonia, with studies consistently showing an elevated risk of myocardial infarction, arrhythmias, heart failure, and stroke in the weeks to months after hospitalisation.[37,185,186] This increased risk is thought to result from systemic inflammation, endothelial dysfunction, and prothrombotic states induced by the acute infection.[37,185,186] Consequently, all patients recovering from community-acquired pneumonia should undergo regular cardiovascular screening, particularly those with pre-existing cardiac conditions or risk factors, such as diabetes, hypertension, and smoking.[187,188] Interventions to optimise cardiovascular health, including lifestyle modifications, pharmacological management of risk factors, and routine follow-up with cardiology when indicated, are essential to reduce long-term morbidity and mortality.

The systemic effects of community-acquired pneumonia extend beyond the respiratory and cardiovascular systems. Many survivors, particularly older adults and those who require intensive care, have post-intensive care syndrome—characterised by physical weakness—cognitive impairment, and psychological disorders, such as depression and post-traumatic stress.[43,44] Emerging syndromes, such as post-COVID-19 condition, have also been studied and can include neurological symptoms that persist even after lung inflammation appears to have resolved.[42,189] Rehabilitation programmes that address physical and cognitive deficits are vital for enhancing functional recovery and improving quality of life. Close monitoring for these complications also allows timely interventions to address unmet needs.

A comprehensive approach to community-acquired pneumonia follow-up should include vaccinating to reduce the risk of recurrence, addressing modifiable risk factors such as smoking and alcohol use, and improving access to primary care. By emphasising early rehabilitation, ongoing screening for cardiovascular and systemic complications, and holistic patient management, clinicians can mitigate the long-term effects of community-acquired pneumonia, reduce hospital readmissions, and enhance overall survival and quality of life.

Current guidelines

The accumulation of knowledge around community-acquired pneumonia diagnosis and management in the past decade has been reflected in the updated recommendations of international guidelines, which are

***Panel*: Objectives of future research areas**

- New antibiotics: address antibiotic resistance in pathogens that cause community-acquired pneumonia
- Discontinuing antibiotics: safely initiate and stop antibiotics when viral community-acquired pneumonia is confirmed; biomarkers could be used to guide antimicrobials
- Steroids in severe community-acquired pneumonia: establish their benefit–risk balance in treating inflammatory severe community-acquired pneumonia
- Avoiding anti-anaerobes: minimise unnecessary antibiotic exposure without anaerobe risk
- Immune phenotypes: develop consensus immune phenotypes, including those in the lung compartment; use these consensuses to stratify trials and personalise therapies
- Shorter antibiotic treatments: assess the efficacy of shorter antibiotic courses and a safe switch to oral antimicrobials
- New antiviral agents: evaluate novel antiviral therapies for viral community-acquired pneumonia
- Immunostimulants: study their effects, particularly in immunocompromised patients
- High-flow nasal oxygen: assess its role in managing respiratory distress
- Socioeconomic and environmental influences: investigate how factors such as income, education, and housing affect risk of community-acquired pneumonia; develop targeted interventions
- Emerging pathogens and global trends: understand how travel, climate, and social factors shape pathogen prevalence
- Early diagnostics for viral versus bacterial community-acquired pneumonia: improve diagnostic tools to guide antibiotic use and reduce disparities in treatment quality in resource-constrained settings
- Host microbiome and susceptibility: explore the microbiome's role in the risk of community-acquired pneumonia and its potential for enhancing immunity
- Effects of immunosuppressive therapies: develop prevention strategies for immunosuppressed patients across socioeconomic backgrounds
- Neurological effects: elucidate the mechanisms by which neurological complications occur after severe disease

discussed in the sections above. Two guidelines from major groups released in the past five years are from the ATS and IDSA in 2019,[8] and the European Respiratory Society (ERS), European Society of Intensive Care Medicine, European Society of Clinical Microbiology and Infectious Diseases, and Latin American Thoracic Association in 2023.[108] The major shifts from previous versions and other older guidelines, such as those from the British Thoracic Society[110] and ERS, include differentiated recommendations for community-acquired pneumonia and severe community-acquired pneumonia,[8] improving diagnostic stewardship to enhance resource allocation and reduce costs. The guidelines shift the clinical approach towards one in which risk profiles, clinical presentation, and tailored testing are prominent.

Controversies and uncertainties

Several controversies and uncertainties persist in managing community-acquired pneumonia, particularly in severe cases in which clinical decision making is complex. As noted above, the evidence for adjunctive therapies—such as corticosteroids, macrolides, and immunomodulatory agents—remains scarce and the benefits are uncertain. Ongoing and forthcoming clinical trials will hopefully resolve this uncertainty. It is possible that therapies targeted at well defined phenotypes with specific disease mechanisms could prove most effective.

Other areas of uncertainty are the mechanisms that drive systemic complications, such as cardiovascular events, cognitive decline, and long-term respiratory dysfunction. Although systemic inflammation and immune dysregulation are thought to play key roles, the precise pathways remain poorly understood. For instance, the relationship between the acute inflammatory response and the heightened risk of myocardial infarction and stroke observed after community-acquired pneumonia has not been fully elucidated. This inadequate mechanistic clarity hampers the development of targeted interventions to mitigate these complications.

The management of severe community-acquired pneumonia is further complicated by gaps in knowledge regarding the factors that contribute to adverse outcomes. Although advanced age, comorbidities, and delayed ICU admission are recognised risk factors, the interplay of genetic predispositions, host immune responses, and local epidemiological factors requires further study. In addition, the scarcity of robust data on the effectiveness of personalised therapies, such as biomarker-guided treatment, limits their implementation in routine practice.

Finally, the evolving landscape of molecular diagnostics raises questions about their effects on community-acquired pneumonia management. Although NAATs have improved pathogen identification, their integration into clinical workflows, influence on antibiotic stewardship, and effects on patient-centred outcomes require establishment through real-world studies. Resolving these uncertainties is essential to advancing community-acquired pneumonia care and improving patient outcomes.

Outstanding research questions

The field has essential research questions that span clinical, socioeconomic, and environmental factors. The rising threat of antibiotic resistance underscores the need for new antibiotics and protocols for safely initiating and discontinuing antibiotics in patients with confirmed, viral, community-acquired pneumonia. Likewise, there is a need to standardise the use of biomarkers to guide antimicrobials. Additionally, the efficacy of shorter antibiotic courses, early and safe switches to oral antimicrobials, the potential benefits of steroids in severe community-acquired pneumonia, and the avoidance of anti-anaerobic antibiotics in community-acquired pneumonia warrant further exploration (panel).

Broader determinants of risk, such as income, education, and housing quality, are crucial to understanding community-acquired pneumonia disparities (eg, in prevalence, disease severity, access to treatment, and treatment quality). Targeted public health interventions

could mitigate these risks, particularly in underserved communities. Meanwhile, the role of the host microbiome in community-acquired pneumonia susceptibility and if it can be modified to enhance immunity remains an important area of investigation.

Emerging pathogens associated with community-acquired pneumonia require study, particularly regional variations, as well as the impacts of global travel and climate change. Enhanced diagnostics to differentiate between viral and bacterial community-acquired pneumonia could guide appropriate antibiotic use and reduce disparities in care. Ultimately, as immunosuppressive therapies become increasingly prevalent, understanding their effects on the risk of community-acquired pneumonia in diverse socioeconomic contexts is crucial for developing targeted prevention strategies.

Contributors

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LFR reports grants or contracts from GSK, Pfizer, and MSD; consulting fees from GSK and Pfizer; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from GSK and Pfizer; payment for expert testimony from GSK and Pfizer; and support for attending meetings and/or travel from GSK and Pfizer. ACM reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Biomerieux, Fischer and Paykel, ThermoFisher, and Boston Scientific, and participation on a Data Safety Monitoring Board or Advisory Board for Cambridge Infection Diagnostics. CS-M reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Pfizer and support for attending meetings and/or travel from Pfizer. LPGD reports grants or contracts from Horizon 2020; support for attending meetings and/or travel from the European Society of Intensive Care Medicine (ESICIM), the International Symposium on Intensive Care and Emergency Medicine, the European Respiratory Society, and the University of Pittsburgh Medical Center; and a leadership or fiduciary role in other board, society, committee, or advocacy group, paid or unpaid with WHO, ESICIM, the European Clinical Research Alliance for Infectious Diseases, and the Dutch Society for Intensive Care Medicine. IM-L reports consulting fees from Mundipharma and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from MSD and Gilead. RPD declares no competing interests.

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