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Title: Community-Acquired Pneumonia in Adults: Evolving Epidemiology and Advances in Diagnosis, Treatment, and Prevention

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Clinical Question Box

Which recent advances in epidemiology, diagnosis, treatment, and prevention of adult community-acquired pneumonia should inform clinical practice?

Changes in respiratory pathogen circulation and pneumococcal serotypes highlight the importance of continued surveillance. Lung ultrasonography and AI-assisted imaging can support diagnosis, while molecular testing improves pathogen identification. mNGS may provide additional benefits in selected patients with severe CAP, although evidence for routine use remains limited. Current evidence supports shorter antibiotic courses in clinically stable nonsevere CAP and adjunctive corticosteroids in selected patients with severe disease. The clinical benefits of macrolide immunomodulation and the comparative effectiveness of higher-valency pneumococcal vaccines require further investigation.

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Abstract

Community-acquired pneumonia (CAP) remains a major cause of hospitalization and death among adults, yet its clinical landscape is changing. This narrative review examines evidence published primarily between 2023 and October 2026 on epidemiology, diagnosis, treatment, and prevention of adult CAP. Post-pandemic surveillance indicates substantial regional shifts in CAP incidence, respiratory pathogen circulation, and pneumococcal serotype distribution, although the persistence of these trends remains uncertain. Updated guidelines recognize lung ultrasonography as an alternative to chest radiography in settings with adequate expertise. AI-assisted chest radiography supports diagnostic assessment, while metagenomic next-generation sequencing may improve pathogen identification in selected patients with severe CAP. Randomized trials show that rapid multiplex molecular testing increases etiologic detection and may accelerate pathogen-directed treatment, but reductions in antibiotic exposure and improvements in patient-centered outcomes have not been consistent. Treatment advances include shorter antibiotic courses for clinically stable nonsevere CAP, biomarker-assisted discontinuation in selected patients, and conditional use of systemic corticosteroids for severe CAP. Evidence for clarithromycin-associated early response and host-directed immunomodulation requires further validation of clinical benefits and patient selection. Higher-valency pneumococcal conjugate vaccines broaden serotype coverage, whereas evidence directly demonstrating superior protection against clinically confirmed CAP remains limited. These developments favor selective application of diagnostic tools, individualized treatment decisions, and continued pathogen-specific surveillance, with future research prioritizing safety and clinically meaningful outcomes.

Keywords: Community-acquired pneumonia; Lung ultrasonography; Multiplex polymerase chain reaction; Antibiotic stewardship; Corticosteroids; Pneumococcal vaccination

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Introduction

Community-acquired pneumonia (CAP) remains a major cause of hospitalization and mortality in adults, particularly in older people and those with chronic illness. Persistent diagnostic uncertainty and heterogeneous clinical presentations continue to complicate management.[1] Following the coronavirus disease 2019 (COVID-19) pandemic, changes in respiratory pathogen circulation and pneumococcal serotype distribution have prompted renewed epidemiological surveillance. Rapid molecular testing and higher-valency vaccines have also introduced new opportunities, although their effects on CAP-specific outcomes require careful evaluation.

Recent evidence and guideline updates have challenged conventional decisions regarding antibiotic duration, adjunctive corticosteroids, and macrolide-associated immunomodulation. Importantly, improvements in diagnostic or intermediate outcomes have not consistently translated into better patient-centered outcomes.[2] This review focuses on clinically relevant advances reported predominantly from 2023 through October 2026 in the epidemiology, diagnosis, treatment, and prevention of adult CAP. It distinguishes diagnostic accuracy and immunogenicity findings from evidence of patient-centered clinical benefit. Relevant literature was identified through PubMed, with emphasis on recent clinical practice guidelines, randomized trials, and major observational studies.

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Evolving Epidemiology and Etiology of Community-Acquired Pneumonia

Recent surveillance studies reveal substantial temporal and geographic variation in adult CAP incidence, pathogen detection, and pneumococcal serotype distribution (Table 1)[3-11]. Differences in CAP definitions, enrollment criteria, diagnostic testing, and surveillance periods preclude direct comparison of incidence and pathogen prevalence across these cohorts.

Changes in CAP Burden Following the COVID-19 Pandemic

A Shanghai cohort of 61,230 adults aged 20–74 years documented CAP incidence rates of 50.8, 24.2, and 95.9 cases per 1,000 person-years before, during, and after pandemic-related interventions, respectively.[3] Because CAP was identified through clinical records and diagnostic codes and the post-intervention period was brief, these estimates should not be interpreted as proof of a sustained increase. German prospective multicenter surveillance of radiologically confirmed, hospitalized CAP in 2021–2023 estimated annual incidence rates of 490 per 100,000 adults and 1,538 per 100,000 among those aged at least 65 years.[4] The incidence was higher in the final surveillance year despite a decline in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated cases. Changes in ascertainment, exposure, and health-care utilization remain important alternative explanations for regional trends.

Shifting Patterns of CAP Pathogens

The etiology of adult CAP is increasingly characterized by the recognition of respiratory viral infections, bacterial–viral coinfections, and changing pathogen distributions (Figure 1). In a Norwegian prospective study of 384 adults with confirmed CAP, comprehensive testing identified a pathogen of probable or proven significance in 81.3%; respiratory viruses were detected in 48.4%, Haemophilus influenzae in 30.7%, and Streptococcus pneumoniae in 16.7%. Such estimates depend on specimen selection and diagnostic methods, and should not be treated as fixed pathogen proportions across settings.[8] In the CAPNETZ cohort of 1,388 adults with CAP (2020–2023), at least one respiratory virus was detected in 26.2%, including SARS-CoV-2 (15.1%), rhinovirus/enterovirus (4.6%), influenza (1.6%), and respiratory syncytial virus (RSV; 1.2%).[5] Viral detection may vary with

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timing, assay selection, specimen quality, and circulating strains; it should not be equated automatically with sole causation of pneumonia.

Changing Pneumococcal Serotype Distribution

In a UK prospective cohort of 5,186 adults hospitalized with CAP (2013–2023), pneumococcal disease was identified in 42.2%. Among pneumococcal CAP cases, the proportion attributable to serotype 3 increased from 13.4% to 48.8%.[6] These figures describe relative serotype distribution, not an increase in the absolute incidence of serotype 3 pneumonia.

A US prospective surveillance study of 2,016 adults hospitalized with CAP identified pneumococcal pneumonia in 13.8%; serotypes included in the 21-valent pneumococcal conjugate vaccine (PCV21) accounted for 9.8% of all CAP cases.[7] A Japanese multicenter study of 583 adults with culture-confirmed pneumococcal pneumonia found serotypes 3 (12.5%) and 35B (12.0%) to be the most frequent, illustrating substantial geographic variation in vaccine-type coverage.[12] Serotype distribution should not be conflated with vaccine effectiveness.

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Recent Advances in the Diagnosis of Community-Acquired Pneumonia

Recent advances in CAP diagnosis and treatment encompass bedside imaging, molecular diagnostics, and individualized therapeutic strategies (Figure 2).

Lung Ultrasonography for CAP Diagnosis

Lung ultrasonography (LUS) has gained a stronger role as a bedside imaging option. The American Thoracic Society (ATS) CAP guideline update, released online in 2025 and published in print in 2026, conditionally accepts LUS as an alternative to chest radiography in suspected CAP when trained personnel are available, on low-certainty evidence.[13] A 2025 meta-analysis of eight studies using computed tomography (CT) as the reference standard estimated LUS sensitivity and specificity at 90.0% (95% confidence interval [CI], 81.3–96.2%) and 90.8% (79.9–97.7%), respectively, compared with 72.6% (61.7–82.4%) and 82.0% (65.5–93.9%) for chest radiography.[14] The comparative accuracy estimates are limited by observational designs, selective CT verification, and heterogeneity; improved clinical outcomes have not been established.

Artificial Intelligence-Assisted Chest Imaging

Artificial intelligence (AI)-assisted chest radiography may identify pulmonary opacities and prioritize image review, but its clinical value should be distinguished from a stand-alone diagnosis of CAP. A 2025 meta-analysis of 15 chest radiography studies, including 10 evaluating pneumonia detection, reported pooled sensitivity of 88% and specificity of 90% for AI-based pneumonia detection.[15] In a 2026 prospective crossover reader study involving 1,200 patients, four commercial AI systems did not improve overall diagnostic accuracy, although interpretation time decreased for some readers.[16] Radiographic abnormalities cannot independently establish pneumonia etiology, and evidence that AI-assisted interpretation improves CAP-specific management or patient-important outcomes remains limited.

Rapid Molecular Diagnostics and Pathogen Identification

Randomized trials of multiplex polymerase chain reaction (mPCR) testing have demonstrated improved pathogen identification and, in some settings, more targeted antimicrobial prescribing, but benefits for antibiotic exposure and clinical outcomes have been inconsistent (Table 2)[17-22]. Cartuliares

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et al. randomized 294 patients with suspected CAP: receipt of no or narrow-spectrum antibiotics within four hours did not differ significantly between mPCR and standard care (62.8% vs. 59.6%; P = 0.134).[17]

In Markussen et al., 374 adults with suspected CAP were randomized; among the 200 patients with CAP and lower respiratory samples, pathogen-directed therapy within 48 hours was more frequent with syndromic testing (47.4% vs. 15.5%).[18] However, targeting included both escalation and de-escalation and did not demonstrate shorter overall antibiotic therapy. In 242 hospitalized adults with CAP, Abelenda-Alonso et al. observed greater etiological detection with mPCR than conventional testing (63.9% vs. 26.0%), without a significant reduction in antibiotic days of therapy (median 10.04 vs. 11.33 days; P = 0.093) or 30-day mortality.[19]

Metagenomic Next-Generation Sequencing in Selected Patients

Metagenomic next-generation sequencing (mNGS) may extend pathogen identification in selected patients with severe or diagnostically unresolved CAP. In a multicenter randomized trial of 349 ICU patients with severe CAP, adding bronchoalveolar lavage fluid mNGS to conventional testing shortened the reported time to clinical improvement (10 vs. 13 days) and increased clinical improvement by day 14 (62.0% vs. 46.5%); other secondary outcomes did not differ significantly.[23] A 2026 systematic review of 74 pneumonia studies (10,566 participants) found higher pathogen detection with mNGS than with conventional testing (78.9% vs. 43.2%), but all studies had risk-of-bias or applicability concerns in at least one domain, and most did not specify pneumonia subtype.[24] A cohort of 541 patients with suspected CAP likewise concluded that mNGS was not necessary as a routine test in all suspected cases.[25] Results require interpretation alongside clinical findings to distinguish causative infection from colonization or contamination; specimen selection, turnaround time, and cost further limit universal application. Greater pathogen detection alone does not establish reductions in antibiotic exposure or mortality, and evidence of improved clinical outcomes with mNGS remains limited to selected populations.

Integration of Molecular Diagnostics and Biomarkers into Clinical Decision-Making

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The MULTI-CAP trial studied mPCR combined with a procalcitonin (PCT)-guided algorithm in severe CAP. Among 385 evaluable patients, days alive without antibiotics through day 28 did not differ significantly (median 19 days in both groups), despite a shorter cumulative antibiotic duration in the intervention group.[20] This discrepancy illustrates why process measures should not be substituted for clinical outcomes. The 2026 CAP-NEXT multicenter cluster-randomized, controlled before–after study did not demonstrate a significant reduction in broad-spectrum antibiotic exposure using point-of-care mPCR (adjusted risk ratio [RR], 0.89; 95% CI, 0.75–1.04).[21] The low-dose chest CT intervention also did not significantly reduce broad-spectrum antibiotic exposure (adjusted RR, 1.12; 95% CI, 0.90–1.38). Testing was performed in only 67% of assigned intervention patients, illustrating the importance of implementation fidelity. This design should be distinguished from individual-patient randomized controlled trials (RCTs).

Molecular assays detect genetic material rather than proving causation: colonization, mixed infection, prior antibiotic therapy, and pathogens outside the assay panel complicate interpretation. A positive viral result does not exclude bacterial coinfection, and a negative bacterial panel cannot independently rule it out. The 2026 European Respiratory Society/European Society of Clinical Microbiology and Infectious Diseases (ERS/ESCMID) statement emphasizes the need to embed rapid tests within clinically actionable stewardship pathways.[26]

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Recent Advances in the Treatment of Community-Acquired Pneumonia

Recent randomized trials have evaluated biomarker-guided antibiotic discontinuation, adjunctive corticosteroids, and macrolide-based immunomodulation, with findings that vary by clinical population and outcome (Table 3)[27-32].

Pathogen-Directed Antibiotic Optimization

The updated ATS guideline conditionally suggests withholding empirical antibiotics in otherwise healthy outpatients with clinical and imaging evidence of CAP when a respiratory virus is detected, while recommending antibiotics for virus-positive patients with comorbidities and for hospitalized patients; the certainty of evidence is very low.[13] The Infectious Diseases Society of America (IDSA) did not endorse the virus-positive CAP recommendations in full and instead emphasized individualized, dynamic assessment of bacterial coinfection risk in patients with nonsevere disease.[33] Clinical severity and the consequences of delayed treatment remain central to these decisions.

In 2026, Baghdadi et al. randomized 107 hospitalized patients receiving antibiotics for suspected community-acquired respiratory infection and low PCT or positive viral testing. A stewardship intervention interpreting post-test bacterial pneumonia probability reduced antibiotic exposure from 11.6 to 7.5 days of therapy (P = 0.006), and increased discontinuation by day 5 (76% vs. 49%).[22] Its population was not restricted to radiologically confirmed CAP, and the study was not powered for uncommon safety outcomes. These findings support actionable interpretation rather than test adoption alone.

Short-Course and Biomarker-Guided Antibiotic Therapy

The ATS guideline update conditionally suggests fewer than five days (at least three days) of treatment for nonsevere CAP after documented clinical stability (including improving vital signs, oxygenation, and oral intake), whereas severe CAP should receive at least five days.[13] Complicated pneumonia and selected pathogens warrant longer treatment. A 2026 meta-analysis of 21 RCTs involving 5,812 adults found comparable clinical success for short (≤5 days) versus longer (>5 days) treatment (RR 1.00; 95% CI, 0.98–1.02), although severe and complicated cases were underrepresented.[34]

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In a three-arm randomized trial of 468 non-intensive care unit (ICU) patients with CAP, median antibiotic duration was four days under a C-reactive protein (CRP)-guided algorithm, 5.5 days under a PCT-guided algorithm, and seven days with usual care.[27] Neither biomarker should be interpreted in isolation: a low initial value does not safely exclude bacterial disease, and trials of treatment discontinuation should not be extrapolated to withholding initial antibiotics in severe CAP.

Corticosteroid Therapy in Severe CAP

In CAPE COD (2023), 795 evaluable ICU patients with severe CAP were randomized to hydrocortisone or placebo; 28-day mortality was 6.2% versus 11.9% (P = 0.006), alongside lower rates of subsequent intubation and vasopressor initiation.[28] The findings supported early adjunctive therapy in selected severe presentations. REMAP-CAP (2025), however, stopped enrollment in its fixed seven-day intravenous hydrocortisone domain for futility. Among 658 randomized participants (536 assigned hydrocortisone, 122 control), 90-day mortality was 15.0% versus 9.8%, respectively.[29] Given the adaptive design, unequal allocation, and uncertainty intervals, this finding does not establish steroid-associated harm, but does not replicate a large survival benefit.

In contrast, the SONIA pragmatic trial in 18 Kenyan hospitals randomized 2,180 adults with CAP to ten days of oral glucocorticoids plus standard care or standard care alone; 30-day mortality was 22.6% versus 26.0% (hazard ratio [HR], 0.84; 95% CI, 0.73–0.97).[30] Its broader case mix, predominantly ward-based low-resource setting, and flexible glucocorticoid regimens differ substantially from ICU trials.

A 2026 network meta-analysis comparing corticosteroid dose categories across 32 trials and 9,746 participants did not identify a clear difference between higher- and lower-dose regimens for short-term mortality (RR 0.98; 95% CI, 0.83–1.16). This indirect comparison does not establish equivalence and provides limited guidance regarding optimal regimens.[35] Differences in illness severity, ICU versus ward settings, treatment timing, and response-adapted intravenous, fixed-duration intravenous, or oral glucocorticoid regimens may explain discordant results; steroid use should remain population-specific, accounting for hyperglycemia risk. No prospectively validated biomarker currently identifies the subgroup most likely to benefit.

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Macrolides and Emerging Host-Directed Immunomodulatory Strategies

The ACCESS trial randomized 278 adults with CAP and systemic inflammation to clarithromycin or placebo in addition to standard care. The prespecified composite of early clinical and inflammatory improvement by 72 hours occurred in 68% and 38%, respectively (odds ratio [OR], 3.40; 95% CI, 2.06–5.63).[31] This is not evidence of a mortality benefit.

A 2026 mechanistic analysis of the ACCESS cohort described changes in interleukin-1-related signaling and antigen presentation.[36] A separate proteomic analysis identified modulation of circulating interleukin-6 and suggested heterogeneous host responses.[37] These are secondary analyses of the same randomized cohort, not independent efficacy trials; inflammatory endotype-guided macrolide use requires prospective validation. Macrolides remain antimicrobial agents with potential benefits and harms, including QT prolongation, drug interactions, and selection of resistance. The relative contribution of antibacterial and host-directed mechanisms remains uncertain; evidence from clarithromycin cannot be generalized automatically to every macrolide or to uncomplicated CAP.

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Recent Advances in the Prevention of Community-Acquired Pneumonia

New-Generation Pneumococcal Conjugate Vaccines

The clinical precedent for pneumococcal conjugate vaccines derives from the CAPiTA trial, which demonstrated protection against vaccine-type pneumococcal CAP with the 13-valent pneumococcal conjugate vaccine (PCV13).[38] In contrast, contemporary trials of higher-valency formulations principally rely on immunogenicity and immune bridging. A phase 3 study in 1,421 adults aged at least 60 years in East Asia found the 20-valent pneumococcal conjugate vaccine (PCV20) noninferior to PCV13 for all shared serotypes and to the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for six of seven additional serotypes.[39] Clinical CAP was not the trial endpoint.

In STRIDE-3 (n = 2,663), the PCV21 elicited noninferior immune responses to PCV20 for ten shared serotypes and superior responses for ten of eleven PCV21-unique serotypes.[40] STRIDE-9 subsequently provided immunogenicity data in 450 Japanese older adults.[41] Neither study established superior protection against clinically confirmed CAP; furthermore, PCV21 omits serotype 4, which may matter in selected populations.

Recent German CAPNETZ surveillance adds evidence of residual vaccine-type disease: among 1,504 tested adults with CAP during 2020–2023, serotype 3 was the most frequent pneumococcal vaccine serotype (52 cases), and vaccine-type distributions differed by age and risk status. These findings support region-specific vaccine selection based on prevalent serotypes, product-specific serotype coverage, and vaccination history rather than valency alone.[42] Adult recommendations have also evolved. In the United States, the Advisory Committee on Immunization Practices expanded routine pneumococcal conjugate vaccination to adults aged 50 years or older, with vaccine choice influenced by immunization history and clinical risk.[43]

Other Respiratory Vaccination Strategies

In the expanded DAN-RSV pragmatic randomized trial (n = 513,358 across two seasons), a bivalent respiratory syncytial virus prefusion F (RSVpreF) vaccine reduced RSV-related respiratory hospitalization (estimated effectiveness 70.3%; 95% CI, 49.7–83.2%).[44] However, there was no

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statistically conclusive reduction in all-cause respiratory hospitalization, and the outcome was not all-cause radiologically confirmed CAP.

Two 2025 pragmatic trials compared high- with standard-dose influenza vaccination. DANFLU-2 (332,438 adults) did not significantly reduce the composite of influenza or pneumonia hospitalization (relative effectiveness 5.9%; 95.2% CI, −2.1 to 13.4), with nearly identical pneumonia hospitalization rates.[45] GALFLU (103,169 unique adults) reported 23.7% relative effectiveness (95% CI, 6.6–37.7%) for the same composite, but the prespecified event threshold was not reached and analyses were descriptive.[46] These results do not establish a consistent reduction in CAP-specific hospitalization.

A 2026 evidence review estimated effectiveness of updated COVID-19 vaccines against COVID-19-associated hospitalization in adults aged at least 65 years at 53.0% (95% CI, 37.0–65.0%).[47] This is pathogen-specific protection, not direct evidence for reducing all-cause CAP; it therefore merits only brief coverage in this review.

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Conclusions

Recent advances in adult CAP have improved diagnostic assessment and supported more individualized treatment strategies. AI-assisted imaging and molecular diagnostics offer new opportunities for diagnosis, although improvements in pathogen detection have not consistently translated into better clinical outcomes. Current evidence supports shorter antibiotic courses in clinically stable nonsevere CAP, while corticosteroid use in severe disease requires careful patient selection. Evolving pneumococcal serotypes highlight the importance of surveillance, whereas the clinical benefits of higher-valency vaccines remain to be established. Future research should prioritize the clinical effectiveness and safety of these interventions.

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Generative AI Declaration

During the preparation of this manuscript, the authors used DeepSeek for drafting, literature summarization, language editing, and manuscript formatting. The authors subsequently reviewed and edited the content as necessary and assume full responsibility for the accuracy and integrity of the published work.

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466 Table 1. Epidemiological and Etiological Studies in Adult CAP

Study	Setting and design	Assessment	Main results	Clinical considerations
Wang et al., 2026	China (2016–2023); cohort, ages 20–74 y (n=61,230).	CAP identified from clinical records and codes.	CAP incidence/1,000 person-years: 50.8 before, 24.2 during, 95.9 after NPIs.	Code-based diagnosis and brief post-NPI follow-up limit trend inference.
Theilacker et al., 2026	Germany (2021–2023); prospective hospitalized-CAP surveillance (4,319 eligible).	Radiographic CAP; pathogen testing in 1,479.	Annual CAP admissions/100,000: 490 adults, 1,538 at ≥65 y; pneumococcal and RSV-associated CAP rose 8.6- and 10-fold.	Admission, sampling, and healthcare-use patterns may affect estimates.
Dähne et al., 2024	Germany (2020–2023); prospective CAPNETZ cohort (n=1,388).	Respiratory-virus testing over time.	Virus detection: 26.2%; SARS-CoV-2 15.1%, rhinovirus/enterovirus 4.6%, influenza 1.6%, RSV 1.2%.	Detection varies by assay/timing; viral positivity does not prove causation.
Markussen et al., 2024	Norway (2020–2023); prospective confirmed-CAP cohort (n=384).	Routine tests plus syndromic pneumonia PCR.	Probable/proven pathogen: 81.3% vs. 62.8% by routine tests; viruses 48.4%.	Broader panels increase yield; cohort comparisons depend on testing scope.
Maeda et al. (APSG-J2), 2026	Japan (2022–2024); 7 hospitals, CAP/ARI admissions (n=3,047).	Multiplex PCR in 1,499; catchment-based admission rates.	Among those tested: RSV 2.8%, influenza 3.3%. RSV-CAP/ARI admissions at ≥65 y: 29 and 36/100,000 person-years (years 1/2).	Combined CAP/ARI outcomes; PCR uptake 49.2%.
Ippolito et al. (SIS-NET ICU), 2026	Italy (2025); prospective severe-CAP cohort, 13 ICUs (n=150).	Pathogens, organ support, and ICU outcomes.	Mortality 21%; rapid tests in 63%; treatment changed in ≈40% of evaluable tested patients.	Selected ICU patients; test-linked treatment changes were observational.
Lansbury et al., 2025	UK (2013–2023); hospitalized-CAP cohort (n=5,186).	Serotype-specific pneumococcal urine antigens.	Pneumococcal CAP 42.2%; serotype 3 share rose from 13.4% to 48.8%.	Serotype share does not indicate absolute incidence or vaccine efficacy.
Grijalva et al., 2025	US (2018–2022); prospective hospitalized-CAP cohort (n=2,016).	Routine microbiology plus serotype-specific urine antigens.	Pneumococcal CAP 13.8%; PCV21-type CAP 9.8% of all CAP; annual CAP admissions 340/100,000.	Vaccine-type prevalence does not measure vaccine effectiveness.
Karssen et al., 2026	Germany (2022–2024); prospective 7-hospital CAP cohort (n=514).	Pneumococcal urine antigen and serotype-specific assays.	Pneumococci 16.5%; of 74 serotype detections, V116 vs. PCV20 coverage: 86.9% vs. 75.8% (difference 10.8%; 95% CI −3.2 to 24.8).	Serotype coverage is not efficacy; difference was not significant.

467 ARI, acute respiratory infection; CAP, community-acquired pneumonia; CI, confidence interval;
468 ICU, intensive care unit; NPIs, nonpharmaceutical interventions; PCR, polymerase chain reaction;
469 PCV20, 20-valent pneumococcal conjugate vaccine; PCV21, 21-valent pneumococcal conjugate
470 vaccine; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome
471 coronavirus 2; V116, 21-valent pneumococcal conjugate vaccine (PCV21).
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473 Table 2. Clinical Studies of Molecular Diagnostics and Test-Informed Antibiotic Stewardship

Study	Population and design	Decision evaluated	Reported endpoint	Clinical interpretation
Cartuliares et al., 2023	Multicenter RCT; suspected CAP (n=294).	Initial antibiotic choice at 4 h; point-of-care mPCR vs. standard tests.	Early antibiotic choice unchanged (P=0.134).	4-h decision only; subsequent treatment duration not addressed.
Markussen et al., 2024	Multicenter RCT; suspected CAP (n=374); sampled CAP subgroup (n=200).	Pathogen-directed adjustment by 48 h; syndromic PCR vs. routine tests.	More targeted treatment (47.4% vs. 15.5%).	Includes escalation and de-escalation; no shorter courses.
Abelenda-Alonso et al., 2024	Four-hospital RCT; hospitalized CAP (n=242).	Respiratory mPCR added to routine testing.	Detection increased (63.9% vs. 26.0%); course length not significantly reduced.	Diagnostic gain did not establish a mortality benefit.
MULTI-CAP, 2025	Open-label multicenter RCT; ICU CAP (406 randomized; 385 evaluable).	mPCR linked to a PCT-guided algorithm vs. usual care.	≈3 fewer antibiotic days; primary endpoint unchanged.	Combined biomarker strategy in ICU; not evidence for mPCR alone.
CAP-NEXT, 2026	Cluster-randomized before–after study; 910 intervention, 2,084 controls.	Point-of-care mPCR plus treatment advice vs. standard care.	Broad-spectrum use unchanged (adjusted RR 0.89; 95% CI 0.75–1.04).	PCR uptake 67%; cluster design and implementation limit inference.
Baghdadi et al., 2026	Two-center pragmatic RCT; suspected respiratory infection (n=107).	Stewardship interpretation of low PCT/positive viral tests vs. usual care.	Antibiotic duration decreased (7.5 vs. 11.6 days).	Decision support helped; broader respiratory-infection cohort and small sample limit CAP inference.

474 CAP, community-acquired pneumonia; CI, confidence interval; ICU, intensive care unit; mPCR,
475 multiplex polymerase chain reaction; PCR, polymerase chain reaction; PCT, procalcitonin; RCT,
476 randomized controlled trial; RR, risk ratio. Diagnostic yield and antibiotic prescribing are diagnostic
477 or stewardship endpoints, not direct measures of patient-important clinical benefit; primary endpoints
478 differed by trial.
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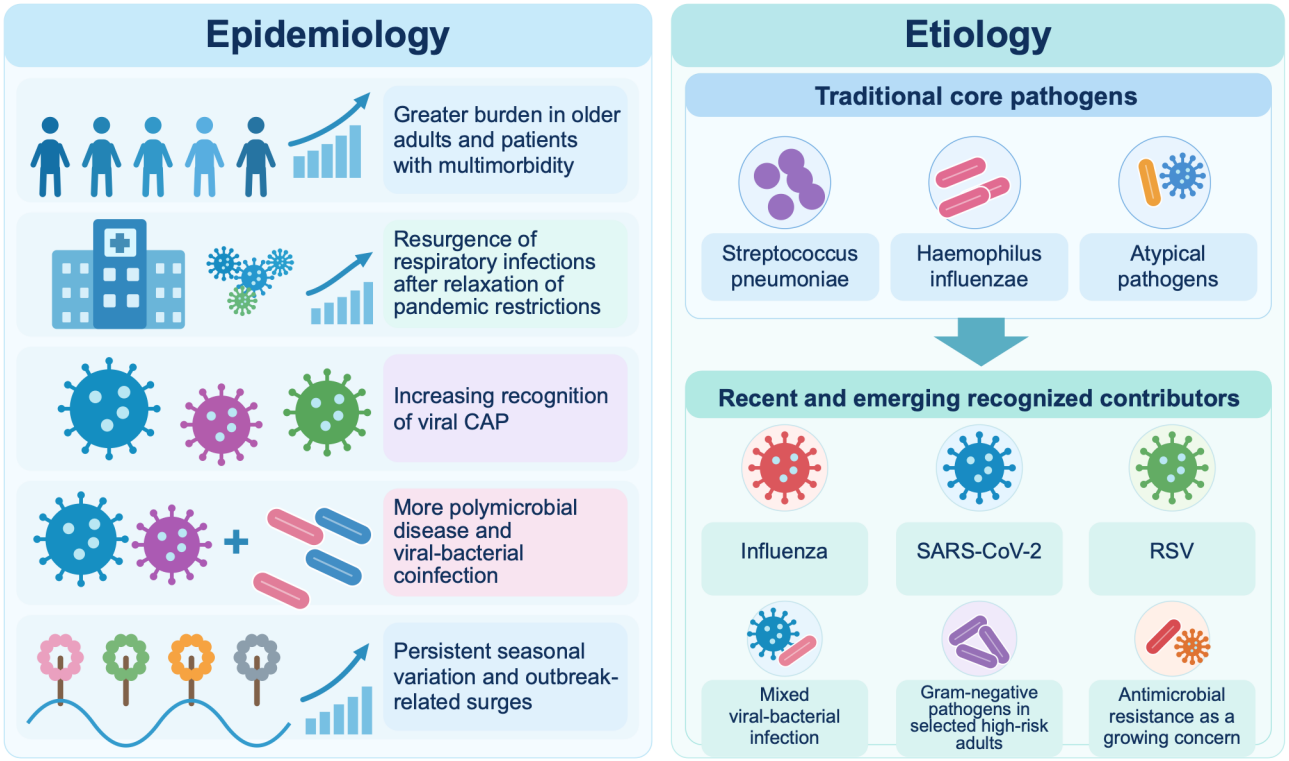
480 Table 3. Randomized Treatment Trials in Adult CAP

Trial	Population and design	Regimen compared	Reported endpoint	Comparative interpretation
Dinh et al. (PTC), 2021	Day-3 stable non-ICU CAP; double-blind noninferiority RCT (n=310).	Stop β-lactam at day 3 vs. continue to day 8.	Day-15 cure noninferior (77% vs. 68%).	Requires day-3 stability; not generalizable to severe or unstable CAP.
CAPE COD, 2023	Severe ICU CAP; double-blind RCT (n=795 evaluable).	Response-adapted IV hydrocortisone vs. placebo.	28-day mortality lower (6.2% vs. 11.9%).	Response-adapted dosing differs from REMAP-CAP's fixed regimen.
ACCESS, 2024	CAP with systemic inflammation; double-blind RCT (n=278).	Clarithromycin plus standard care vs. placebo.	Improved 72-h clinical/inflammatory composite (OR 3.40).	Early composite; mortality benefit unproven and mechanism uncertain.
Duijkers et al., 2024	Hospitalized non-ICU CAP; three-arm RCT (n=468).	CRP- or PCT-guided discontinuation vs. usual care.	Median antibiotic days: 4.0 (CRP), 5.5 (PCT), 7.0 (usual care).	Guides discontinuation, not initial empirical prescribing.
REMAP-CAP, 2025	Severe ICU CAP; adaptive platform RCT (n=658; 536/122 allocated).	Fixed 7-day IV hydrocortisone vs. no steroid.	90-day survival benefit not shown; enrollment stopped for futility.	Unequal allocation and Bayesian design; regimen and endpoint differ from CAPE COD.
SONIA, 2025	Predominantly ward-based CAP; pragmatic RCT in Kenya (n=2,180).	10-day oral glucocorticoids plus care vs. care alone.	30-day mortality lower (HR 0.84; 95% CI 0.73–0.97).	Ward-based, low-resource setting limits direct ICU extrapolation.

481 CAP, community-acquired pneumonia; CI, confidence interval; CRP, C-reactive protein; HR, hazard
482 ratio; ICU, intensive care unit; IV, intravenous; OR, odds ratio; PCT, procalcitonin; RCT,
483 randomized controlled trial. Mortality and clinical cure are patient-important endpoints; antibiotic
484 duration and early clinical/inflammatory composites are stewardship or intermediate outcomes.
485 Primary endpoints differed by trial.
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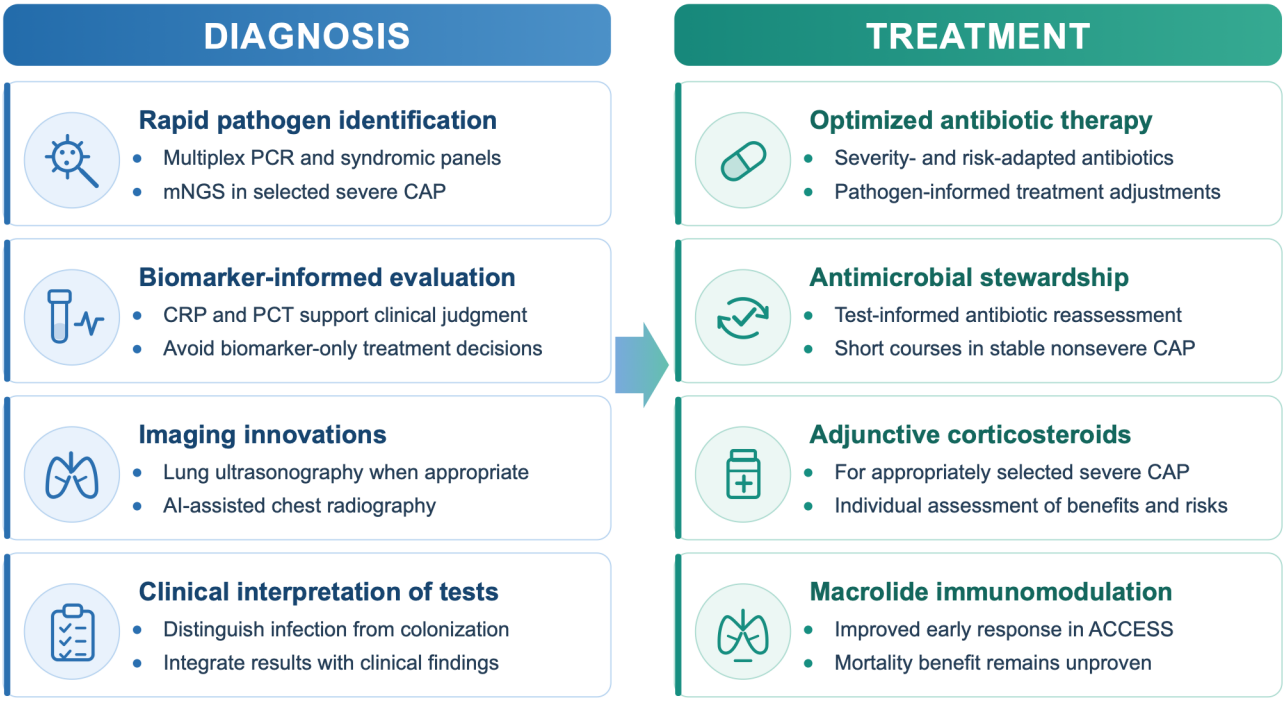
Figure 1. Changes in the Epidemiology and Etiology of CAP



CAP, community-acquired pneumonia; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

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492 Figure 2. Recent Advances in the Diagnosis and Treatment of Adult CAP



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494 AI, artificial intelligence; CAP, community-acquired pneumonia; CRP, C-reactive protein; mNGS,
495 metagenomic next-generation sequencing; PCR, polymerase chain reaction; PCT, procalcitonin
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