Community-Acquired Pneumonia Outside the Intensive Care Unit: Clinical Characteristics and Impact of Rapid Molecular Diagnostics in the Italian SIS-NET Study

Luca Pipitò , Ilenia Giacchino , Chiara Vincenza Mazzola , Emanuele Nicastri , Teresa M.A. Fasciana , Massimo Puoti , Vincenzo Malagnino , Marco Iannetta , Delia Goletti , Maria Grazia Bocci , Antonella Minutolo , Clementina Cocuzza , Marco Merli , Prezioso Carla , Matteo Velardo , Marina Campione , Michael Damiano , Michele Spinicci , Bruno Tassone , Sandro Grelli , Marco Falcone , Laura Rindi , Alessandro Russo , Angela Quirino , Lorenzo Zammarchi , Dolores Limongi , Gian Maria Rossolini , Loredana Sarmati , Giovanni M. Giammanco , Antonino Giarratano , Antonio Cascio , SIS-NET Working Group

PII: S1201-9712(26)00623-5
DOI: https://doi.org/10.1016/j.ijid.2026.108988
Reference: IJID 108988

To appear in: *International Journal of Infectious Diseases*

Received date: 11 May 2026
Revised date: 10 July 2026
Accepted date: 15 July 2026

Please cite this article as: Luca Pipitò , Ilenia Giacchino , Chiara Vincenza Mazzola , Emanuele Nicastri , Teresa M.A. Fasciana , Massimo Puoti , Vincenzo Malagnino , Marco Iannetta , Delia Goletti , Maria Grazia Bocci , Antonella Minutolo , Clementina Cocuzza , Marco Merli , Prezioso Carla , Matteo Velardo , Marina Campione , Michael Damiano , Michele Spinicci , Bruno Tassone , Sandro Grelli , Marco Falcone , Laura Rindi , Alessandro Russo , Angela Quirino , Lorenzo Zammarchi , Dolores Limongi , Gian Maria Rossolini , Loredana Sarmati , Giovanni M. Giammanco , Antonino Giarratano , Antonio Cascio , SIS-NET Working Group, Community-Acquired Pneumonia Outside the Intensive Care Unit: Clinical Characteristics and Impact of Rapid Molecular Diagnostics in the Italian SIS-NET Study, *International Journal of Infectious Diseases* (2026), doi: https://doi.org/10.1016/j.ijid.2026.108988

Highlights

- Most non-ICU CAP admissions involve elderly patients with multimorbidity
- Rapid molecular testing shortened hospital stay despite unchanged antibiotics
- Quality lower respiratory samples for optimal pathogen detection are hard to obtain

Community-Acquired Pneumonia Outside the Intensive Care Unit: Clinical Characteristics and Impact of Rapid Molecular Diagnostics in the Italian SIS-NET Study

Luca Pipitò [1,2], Ilenia Giacchino [1,3], Chiara Vincenza Mazzola [1,2], Emanuele Nicastri [4], Teresa M. A. Fasciana [1,3], Massimo Puoti [5,6], Vincenzo Malagnino [7], Marco Iannetta [7], Delia Goletti [8], Maria Grazia Bocci [4], Antonella Minutolo [9], Clementina Cocuzza [5], Marco Merli [6], Prezioso Carla [10], Matteo Velardo [11], Marina Campione [11], Michael Damiano [11], Michele Spinicci [12], Bruno Tassone [13], Sandro Grelli [9], Marco Falcone [15], Laura Rindi [16], Alessandro Russo [13,14], Angela Quirino [17], , Lorenzo Zammarchi [12], Dolores Limongi [10], Gian Maria Rossolini [12], Loredana Sarmati [6], Giovanni M. Giammanco [1,3], Antonino Giarratano [11], Antonio Cascio [1,2 *] and SIS-NET Working Group[†]

* Corresponding author E-mail: antonio.cascio03@unipa.it

[1]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties "G D'Alessandro", University of Palermo, 90133 Palermo, Italy.

[2]Infectious and Tropical Disease Unit, AOU Policlinico "P. Giaccone", 90127 Palermo, Italy.

[3]Microbiology and Virology Unit, AOU Policlinico "P. Giaccone", Palermo, Italy

[4]High Intensity Care Infectious Diseases, National Institute for Infectious Diseases 'Lazzaro Spallanzani' IRCCS, Rome, Italy

[5]School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy

[6]Division of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Piazza dell'Ospedale Maggiore, 3, 20162 Milan, Italy

[7]Infectious Diseases Unit, Department of Systems Medicine, Tor Vergata University, 00133 Rome, Italy

[8]Translational Research Unit, Department of Epidemiology, Preclinical Research and Advanced Diagnostics, National Institute for Infectious Diseases "Lazzaro Spallanzani" IRCCS, Rome, Italy

[9]Department of Experimental Medicine, University of Rome Tor Vergata.

[10]Laboratory of Microbiology, IRCCS San Raffaele Roma, Via di Val Cannuta 247, 00166 Rome, Italy

[11]Department of Precision Medicine in Medical, Surgical and Critical Care (Me.Pre.C.C), University of Palermo, 90127 Palermo, Italy

[12]Department of Experimental and Clinical Medicine, University of Florence, 50134 Florence, Italy

[13]Department of Medical and Surgical Sciences, "Magna Graecia" University, Catanzaro, Italy.

[14]Infectious and Tropical Disease Unit, "Renato Dulbecco" Teaching Hospital, Catanzaro, Italy

[15]Infectious Diseases Unit, Department of Clinical and Experimental Medicine, Azienda Ospedaliero Universitaria Pisana, University of Pisa, 56126 Pisa, Italy

[16]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, 56126 Pisa, Italy

[17]Clinical Microbiology Unit, Department of Health Sciences, “Magna Graecia” University of Catanzaro, “Renato Dulbecco” University Hospital, 88100, Catanzaro, Italy

[†]Eleonora Bono (eleonora.bono@community.unipa.it), Giulio D’Agati (giulio.dagati@community.unipa.it), Mariachiara Ippolito (mariachiara.ippolito@unipa.it), Matilde Todaro (matilde.todaro@unipa.it), Mario Giuffré (mario.giuffre@unipa.it) , Nicola Cotugno (nicola.cotugno@opbg.net), Paolo Palma (paolo.palma@opbg.net), Lucia Graziani (grazianilu@aou-careggi.toscana.it), Luca Di Candia (luca.dicandia@studenti.unicz.it), Giovanni Matera (mmatera@unicz.it), Alessandro Bartoloni (alessandro.bartoloni@unifi.it).

Keywords

Community-acquired pneumonia; non-ICU hospitalization; rapid molecular diagnostics; hospital length of stay; Italy

Abstract

Objectives: To describe the clinical, radiological, and microbiological characteristics of community-acquired pneumonia (CAP) managed outside the ICU and evaluate the impact of rapid microbiological diagnostics on hospital outcomes in a multicenter Italian cohort. **Method**s: In this prospective observational study conducted across seven Italian centers (October 2024–October 2025), 176 adults hospitalized with CAP outside the ICU and a PaO_2/FiO_2 ratio <300 were enrolled. Demographic, clinical, laboratory, radiological, microbiological, therapeutic, and outcome data were collected. Syndromic respiratory panels were performed in a subset of patients. Secondary outcomes included factors associated with in-hospital mortality and time to live discharge within 28 days. **Results:** Patients were predominantly elderly (mean age 69.7±14.4 years) with high comorbidity burden (Charlson Comorbidity Index 4.9±2.1). Dyspnea, fever, and cough were the most frequent symptoms. Microbiological testing was performed in 48% of cases; viral pathogens were detected more often than bacteria (42.3% vs 27.0%), with viral–bacterial co-detection in 14.1%. In-hospital mortality was 2%, and 3% required ICU transfer. Rapid microbiological testing was independently associated with earlier discharge (HR 1.67, 95%CI 1.17–2.38; p=0.005), while chronic corticosteroid

therapy predicted longer hospitalization. **Conclusions:** CAP outside the ICU mainly affects elderly multimorbid patients. Rapid molecular diagnostics may facilitate earlier discharge by supporting clinical decision-making.

1. Introduction

Community-acquired pneumonia remains one of the leading causes of hospitalization, intensive care unit (ICU) admission, and infection-related mortality worldwide [1]. Despite advances in supportive care and antimicrobial therapy, in-hospital mortality for severe CAP remains unacceptably high, reaching up to 49.4 % in the most critically ill patients [1]. This burden is further amplified by the aging population and the increasing prevalence of chronic comorbid conditions, which significantly influence disease severity, diagnostic complexity, therapeutic decisions, and clinical outcomes [1], [2].

Patients hospitalized with CAP frequently present with multiple comorbidities, including chronic respiratory disease, cardiovascular disorders, diabetes mellitus, chronic kidney disease, and immunosuppressive conditions [1], [2]. These factors not only increase susceptibility to severe infection but also complicate clinical management by affecting host response, microbiological etiology, and tolerance to standard therapies [3]. Consequently, early risk stratification and timely initiation of appropriate treatment are essential components of CAP management [1], [2].

Current international guidelines recommend prompt empiric broad-spectrum antibiotic therapy targeting core pathogens, combined with early supportive care measures [1], [2]. However, establishing an etiological diagnosis in CAP remains challenging. Conventional microbiological techniques often have low diagnostic sensitivity, particularly in patients who have received prior antibiotic therapy or who are unable to provide high-quality lower respiratory tract samples. As a result, clinicians frequently rely on empiric treatment strategies, which may limit opportunities for antimicrobial optimization and stewardship.

In recent years, the introduction of rapid multiplex molecular diagnostic panels has represented a major innovation in the diagnostic approach to pneumonia [1], [2], [4], [5]. These assays enable simultaneous detection of a wide range of bacterial and viral pathogens, as well as selected resistance markers, with a significantly shorter turnaround time than traditional culture methods. Although molecular testing has demonstrated high analytical sensitivity, its clinical impact on patient-centered outcomes such as length of hospital stay, antibiotic exposure, and mortality remains incompletely defined, particularly in real-world settings and in patients with CAP [4]. Moreover, the interpretation of results from upper respiratory tract specimens requires caution, as detection of colonizing organisms does not predict lower respiratory tract infection.

Another ongoing area of debate in CAP management concerns the role of adjunctive therapies, including systemic corticosteroids, and their interaction with host factors such as age and comorbidity burden [5], [6]. Identifying clinical and management host-related factors associated with prolonged hospitalization may help refine treatment strategies and optimize resource utilization.

In this context, we conducted a multicenter observational study within the Italian Severe Infections and Sepsis clinical Network (SIS-NET) to describe the clinical characteristics, diagnostic approaches, antimicrobial management, and outcomes of patients hospitalized with community-acquired pneumonia.

SIS-NET is a nationally coordinated, multicentre research infrastructure established to enhance the surveillance, diagnosis, and clinical characterization of severe infections across Italy. The network was initiated to address gaps in coordinated epidemiological monitoring and to support multicentre observational and diagnostic-prognostic studies of severe infectious diseases, with the goal of informing tailored therapeutic strategies and improving clinical outcomes.

2. Methods

2.1. Study design and ethical approval

This multicentre, prospective non-interventional observational study was conducted across 7 Italian centers between October 2024 and October 2025. The study protocol was reviewed and approved by the ethics committees of all participating institutions, and the study was conducted in accordance with the Declaration of Helsinki and local regulatory requirements. Written informed consent was obtained from all participants before enrolment. Clinical and microbiological information of the patients was collected according to the expected standard of care at each center.

2.2. Setting and participants

Consecutive adult patients admitted to internal medicine or infectious diseases wards with a diagnosis of CAP were screened for eligibility. Inclusion criteria were age ≥18 years, infection onset within 48 hours of hospitalization, a PaO_2/FiO_2 (P/F) ratio <300, and no hospital admission within the preceding 30 days. Exclusion criteria were a life expectancy of less than six months and institutionalized status.

2.3. Data collection and microbiological testing

At baseline, data were collected on demographic characteristics (age, sex), comorbidities, clinical presentation, radiological findings, vital signs, laboratory parameters, and arterial blood gas results. Information on previous antibiotic therapy, initiation of empirical antibiotic treatment, oxygen support administered, corticosteroid therapy, and microbiological investigations was recorded. Comorbidities and disease severity were assessed using the Charlson Comorbidity Index (CCI), the APACHE II, and the Sequential Organ Failure Assessment (SOFA) score, respectively.

Microbiological testing included analyses of respiratory specimens using standard bacterial and fungal cultures and/or molecular assays on sputum and/or nasopharyngeal swabs (NPS) at the clinician's discretion and in accordance with the center's standard of care.

Across all participating centers, molecular analyses were performed using at least one of the following molecular diagnostic methods: the BioFire FilmArray® (BioMérieux) platform or the

Arrow Seegene multiplex real-time PCR platform. The molecular diagnostic platforms are summarized in Supplementary Tables 1–4. Blood cultures were analyzed using automated systems enabling rapid detection of microorganisms in blood. Conventional bacterial and fungal cultures were performed on BAL and sputum samples following standard laboratory procedures. Antimicrobial susceptibility test (AST) results were interpreted according to EUCAST clinical breakpoints.

2.4. Follow-up and outcomes

All patients were prospectively followed, with reassessment of vital signs, laboratory parameters, arterial blood gas analysis, and therapeutic modifications at days 3 and 7 after enrolment.
The final clinical outcome was defined as either hospital discharge or in-hospital death.

The primary outcome was to describe the clinical, radiological, and microbiological characteristics of CAP. Secondary outcomes included identification of factors associated with in-hospital mortality and with time to live discharge, censored at 28 days.

2.5 Statistical analysis

Descriptive statistics were used to characterize the study population. Continuous variables were presented as mean and standard deviation (SD) when approximately normally distributed, and as median with first and third quartiles [Q1–Q3, IQR] when their distribution departed from normality. Categorical variables were summarized as absolute frequencies and percentages. For all estimates, 95% confidence intervals (CIs) were reported to quantify statistical uncertainty.

To identify factors associated with hospital length of stay, both univariable and multivariable Cox proportional hazards regression analyses were performed. Time zero was defined as the date of enrolment. The event of interest was discharge alive from the hospital. Patients who died or were transferred to the ICU during hospitalization were censored at the time of these events. The proportional hazards assumption was assessed for each covariate. Explanatory variables included

demographic characteristics, comorbidities, clinical and laboratory parameters at admission, and performance of rapid molecular respiratory testing.

Variables with p-values < 0.10 in univariable analyses were considered candidates for inclusion in the multivariable model. The final multivariable model was selected according to the lowest Akaike Information Criterion (AIC). Hazard ratios (HRs) greater than 1 indicate a higher hazard of discharge (shorter hospital stay), whereas HRs less than 1 indicate a lower hazard of discharge (prolonged hospital stay).

The association between rapid molecular testing and antibiotic therapy modifications (escalation, de-escalation, or no change) was assessed using the chi-squared test; when expected cell counts were fewer than 5, Fisher's exact test was used. The association between rapid molecular testing and antibiotic duration exceeding 7 days was assessed using binary logistic regression.

Missing data were handled using complete-case analysis. All analyses were performed using R Statistical Software (version 4.5), with statistical significance set at $p < 0.05$.

3. Results

3.1. Patients' characteristics

During the study period, 176 patients were enrolled, of whom 57.4% (*n* =101) were male. The mean age was 69.7 ± 14.4 years. The most common presenting symptoms on admission were dyspnea (*n* = 106, 60%), fever (n = 78, 44%), and cough (n = 70, 39%). Altered sputum production was reported in 9% of patients (*n* = 17), a confusional state in 5% (*n* = 9), and other symptoms in 22% (*n* = 40). Notably, 42% of patients (*n* = 74) had received prior antibiotic therapy before admission, with a median duration of 3 days [IQR 1–5].

Comorbidities were frequent, with a mean CCI of 4.9 ± 2.1. Average APACHE II and SOFA scores were 9.8 ± 3.5 and 2.1 ± 1.6, respectively. The prevalence of individual comorbidities is depicted in Figure 1, with chronic obstructive pulmonary disease (COPD), diabetes mellitus, and chronic

kidney disease being the most common. Active smoking was reported in 25% of patients, while 33% were former smokers. Eight patients were HIV-positive, of whom three had progressed to AIDS. Chronic corticosteroid therapy was reported in 21.5% of patients, and 12.7% were receiving other immunosuppressive drugs at home.

The median white blood cell (WBC) count was 9.9 ×10⁹/L [IQR 7.8–13.4]. C-reactive protein (CRP) and procalcitonin (PCT) median levels were 13.3 mg/dL [IQR 0.7–87.8] and 0.1 ng/mL [IQR 0–0.3], respectively. At admission, 18.8% of patients (*n* = 33) were on long-term home oxygen therapy; hypercapnic respiratory failure was detected in 15% (*n* = 26).

All patients required supplemental oxygen during hospitalization, with 92% (n = 162) receiving low-flow oxygen, 5% (n = 9) receiving high-flow oxygen, and 3% (n = 5) receiving non-invasive ventilation.

3.2. Imaging findings

Chest imaging was performed using radiography (X-ray) and computed tomography (CT). Chest X-ray was performed in 16% of cases (*n* = 28), revealing pulmonary infiltrates in 64%. The predominant radiographic patterns included consolidative opacities (*n* = 12, 43%), non-specific findings (*n* = 16, 57%), ground-glass opacities (*n* = 2, 7%), and pleural effusion (*n* = 5, 18%). Bilateral involvement was observed in 32% (*n* = 9) and unilateral involvement in 18% (*n* = 5), with the lower lobes most frequently affected.

Chest CT was reported in 62% (*n* = 110) of patients with pulmonary infiltrates, in 95 cases (86%). The most common CT patterns included consolidative lesions (*n* = 54, 49%), ground-glass opacities (*n* = 51, 46%), pleural effusion (*n* = 34, 31%), and hilar lymphadenopathy (*n* = 33, 30%). Less frequent findings included peribronchial nodules, bronchiectasis, cavitary lesions, and interstitial pneumonia, each observed in ≤5% of cases. Lobar distribution showed a predominance in the lower lobes (right lower lobe, *n* = 53, 48%, left lower lobe, *n* = 52, 47%), followed by left upper, right

upper, and middle lobes (*n* = 33, 30%; *n* = 36, 33%; n = 26, 24%). In 24% (*n* = 26) of cases, the type of radiological investigation performed at enrollment to confirm pneumonia was not specified in the case report form.

3.3. Microbiological findings

Microbiological investigations were performed in 85 patients (48.3%). Specimen types collected, testing methods applied per specimen type, and pathogens identified are detailed in Table 1. Considering all specimen types and diagnostic methods, viral pathogens predominated over bacterial isolates (*n* = 36, 42.3% vs n = 23, 27.0%). When analysis was restricted to sputum specimen detection rates, the virus detection rate was 31.2% (10/32), slightly higher than for bacteria (9/32, 28.1%), underscoring the critical influence of specimen type on microbiological yield. Among the nine sputum samples that tested positive for bacterial growth on culture, a rapid microbiological test was also performed in eight cases, yielding concordant results. Blood cultures were performed in 17 cases; one was positive (5.9%), while a pleural fluid culture was performed in one case and was positive.

Concordance between upper and lower respiratory tract specimens could not be reliably assessed, as paired sampling was rarely available.

3.4. Antimicrobial and antiviral therapy

Empirical antimicrobial therapy was administered to 88% of patients, *n* = 155 (Figure 2). Ceftriaxone-based regimens were most frequently prescribed, including ceftriaxone plus doxycycline (*n* = 23, 15%), ceftriaxone plus a macrolide (*n* = 17, 11%), and ceftriaxone monotherapy (*n* = 11, 7%). Piperacillin/tazobactam regimens were used as monotherapy in 9% (n = 14) of cases and in combination with doxycycline (*n* = 14, 9%), macrolides (*n* = 6, 4%), linezolid (*n* = 3, 2%), levofloxacin (*n* = 3, 2%), or linezolid plus doxycycline (*n* = 3, 2%). Triple therapy, including piperacillin/tazobactam, doxycycline, and vancomycin, was used in 1% of cases (*n* = 1).

Fluoroquinolone monotherapy with levofloxacin was administered in 6% (*n* = 9), doxycycline monotherapy in 3% (*n* = 5), macrolide combined with amoxicillin/clavulanate in 2% (*n* = 3), and amoxicillin monotherapy in 1% (*n* = 1). Broad-spectrum and reserve antibiotics were used less frequently, including ceftobiprole-based regimens (*n* = 6, 4%), trimethoprim–sulfamethoxazole (*n* = 3, 2%), meropenem (*n* = 3, 2%), ceftazidime/avibactam (*n* = 3, 2%), and cefiderocol with linezolid (*n* = 1, 1%). Oseltamivir was administered in 8% of patients (*n* = 12), mostly in combination with antibacterial agents. Switch of empirical antibiotic therapy occurred in 34 cases (19%), with 17 (10%) de-escalations and 17 (10%) escalations. Antibiotic modifications were not influenced by molecular respiratory testing (p = 0.223). Median duration of empirical and targeted therapy was 9 days [IQR 3.5–12] and 9 days [IQR 6.5–15.5], respectively. Corticosteroid therapy was administered in 28% of patients (n = 49), using various regimens including methylprednisolone, prednisone, hydrocortisone, and betamethasone. Corticosteroid use was significantly associated with the presence of dyspnea (OR 2.185, 95% CI 1.037–4.604; p = 0.037), as well as with higher APACHE II scores (11.20 vs. 9.30, p = 0.002) and SOFA scores (2.87 vs. 1.85, p < 0.001) at baseline. In contrast, it was not associated with higher CCI values (p = 0.283) or with specific comorbidities.

In a multivariable analysis adjusted for potential confounders (age and use of immunosuppressive therapy), including dyspnea, APACHE II score, and SOFA score, only a higher SOFA score remained independently associated with corticosteroid administration in our population (AOR 1.334, 95% CI 1.025–1.737; p = 0.032).

In-hospital mortality was low, with only four deaths (2%) reported. Five patients (3%) required transfer to the intensive care unit (ICU) during hospitalization. Healthcare-associated infections occurred in 10% of patients (*n* = 18), including bacteremia (*n* = 6, 3%), urinary tract infections (*n* = 4, 2%), and other infections (*n* = 10, 6%).

3.5. Factors associated with hospital discharge and impact of rapid molecular testing on antimicrobial management

In univariable Cox regression analysis, the presence of cough at admission was associated with a higher hazard of hospital discharge (HR 2.08), indicating a shorter length of stay. Performance of a rapid molecular respiratory test was also associated with an increased hazard of discharge (HR 1.85). Higher mean platelet volume was similarly associated with earlier discharge (HR 1.41). Conversely, chronic corticosteroid therapy was associated with a reduced hazard of discharge (HR 0.55).

In the multivariable Cox proportional hazards model, performance of a rapid diagnostic test remained independently associated with earlier discharge (HR 1.67, 95% CI 1.17–2.38; p = 0.005). Increasing age was associated with longer hospitalization (HR per 10-year increase: 0.89, 95% CI 0.79–1.00; p = 0.054). Chronic corticosteroid therapy was independently associated with a prolonged hospital stay (HR 0.59, 95% CI 0.38–0.91; p = 0.016), as shown in Table 2.

The association between rapid molecular testing and modifications to antibiotic treatment was further explored. Among 168 patients with available data, no statistically significant association was observed between rapid testing and antibiotic escalation, de-escalation, or lack of change (χ^2 test, p = 0.223), although escalation appeared numerically less frequent among patients who underwent rapid testing (see Table 3).

Similarly, rapid molecular testing was not associated with a total antibiotic duration exceeding 7 days. Patients who underwent rapid testing had comparable odds of receiving prolonged antibiotic therapy compared with those who did not (OR 0.99, 95% CI 0.55–1.80; p = 0.984).

Discussion

In this multicentre prospective study conducted within the Italian SIS-net network, we provide a contemporary real-world overview of CAP managed outside the ICU. Our cohort reflects a clinically complex population, characterized by advanced age (mean 69.7 years) and a high burden of comorbidities (mean CCI 4.9), including chronic respiratory and cardiovascular diseases, diabetes, and chronic kidney disease. A substantial proportion of patients were receiving chronic corticosteroids (21.5%) or other immunosuppressive therapies (12.7%). These findings are consistent with current epidemiological data indicating that CAP disproportionately affects elderly and multimorbid individuals, in whom host-related factors play a key role in disease severity and outcomes [1], [2], [5], [7].

A central finding of our study is the difficulty in achieving an etiological diagnosis of CAP in routine non-ICU practice. Many factors influenced the rate of etiological diagnosis in our cohort:

(i) microbiological investigations were requested in fewer than half of the patients, (ii) lower respiratory tract samples were obtained only in a minority (32/85), and (iii) 42% of our patients had received antibiotics before admission, a factor that likely further reduced culture sensitivity and contributed to the low bacterial detection rate.

These observations align with well-recognized limitations in the diagnostic work-up of CAP, particularly among elderly and frail patients, who frequently are unable to provide adequate sputum specimens and in whom invasive sampling is seldom feasible [2].

In our study, molecular testing was performed extensively on nasopharyngeal swabs, usually with viral panels. In contrast, sputum samples were more often analyzed using both culture and molecular methods.

However, while some evidence supports the diagnostic contribution of upper airway PCR, particularly for atypical pathogens and pneumococcus [8], results across studies remain heterogeneous, with concordance rates highly dependent on patient population and sampling

strategy [9], [10]. Notably, a previous study found that the predictive value of upper airway detection for CT-confirmed pneumonia has been inconsistent in elderly patients [11].

In our study, viral pathogens were detected more frequently than bacteria, and viral–bacterial co-detection was observed in a relevant proportion of cases (14.1%). However, the clinical relevance of multiple simultaneous detections remains uncertain and may contribute to therapeutic ambiguity rather than clarity. Furthermore, microbiological investigations were performed in fewer than half of the cohort, lower respiratory tract specimens were available only in a minority of patients, and molecular testing was conducted predominantly on upper respiratory tract samples. These methodological limitations may have influenced pathogen detection rates. In particular, the higher detection of viral pathogens may reflect the diagnostic approach rather than the true etiology of CAP, as viruses identified in upper respiratory tract specimens do not necessarily represent causative pathogens of lower respiratory tract infection.

When analysis was further restricted to sputum samples, arguably more representative of lower respiratory infection, detection rates for viruses decreased to 33%, whereas bacterial detection increased to 33%, suggesting a more balanced etiological distribution.

Although our analysis showed that rapid molecular respiratory testing was independently associated with earlier hospital discharge, it did not translate into measurable improvements in antimicrobial management. Specifically, no association was observed with antibiotic escalation, de-escalation, or duration. However, these findings should be interpreted with caution in light of several study limitations, including the relatively small proportion of patients who underwent rapid molecular testing, the predominant use of upper rather than lower respiratory tract specimens, and the observational design, which precludes causal inference. Furthermore, turnaround time for molecular testing was not prospectively recorded. This represents an important limitation, as the clinical impact of rapid molecular diagnostics largely depends on the timely availability of test results, which directly influences clinicians' ability to modify management and optimize patient care.

Our findings are consistent with previous randomized and observational studies showing heterogeneous or limited impact of molecular diagnostics on antibiotic use and clinical outcomes [12], [13], [14]. In the emergency department (NCT04660084), PCR testing improved pathogen-directed therapy without affecting antibiotic duration or length of stay [12]. In the ICU-based MULTI-CAP trial, multiplex PCR combined with procalcitonin did not reduce antibiotic exposure or improve outcomes [13], and another randomized trial using non-invasive samples failed to demonstrate reductions in antibiotic use or hospitalization [14].

Our findings showed that the benefit of rapid testing may be indirect, potentially supporting clinical decision-making and discharge planning rather than driving antimicrobial optimization.

In our cohort, antibiotic de-escalation occurred in less than 20% of cases, despite the availability of microbiological data in a subset of patients. This highlights a persistent gap between diagnostic information and antimicrobial stewardship. Several factors may contribute, including the difficulty in interpreting molecular results, especially from upper respiratory tract samples, and the high rate of prior antibiotic exposure, which is known to reduce culture yield [4], [15].

Multidrug-resistant pathogens were rarely identified, and escalation to reserve antibiotics was uncommon, supporting that, in non-ICU CAP within our epidemiological context, routine broad-spectrum escalation may not be justified.

In our cohort, corticosteroid use appeared to be primarily driven by markers of acute organ dysfunction rather than baseline comorbidity burden. The independent association with higher SOFA scores suggests that clinicians may preferentially reserve corticosteroid therapy for patients with more severe systemic involvement, reflecting a pragmatic, severity-based approach. This finding aligns with the ongoing uncertainty regarding the role of corticosteroids in CAP, where their use remains heterogeneous and often guided by clinical judgment rather than standardized criteria. However, the role of corticosteroids in CAP remains debated [5], [6], and our results underscore the complexity of interpreting their impact in heterogeneous real-world populations.

Finally, chronic corticosteroid therapy was independently associated with delayed discharge, likely reflecting both underlying disease severity and impaired immune response.

Our study has several important limitations that must be carefully considered. First, microbiological testing was not systematically performed, and lower respiratory tract samples were obtained in a minority of patients, substantially limiting etiological attribution. Second, the high rate of pre-hospital antibiotic exposure likely reduced the yield of bacterial cultures. Third, rapid microbiological testing was performed predominantly on upper respiratory specimens, which may overestimate viral involvement and cannot reliably distinguish colonization from infection. Fourth, paired upper–lower respiratory sampling was not available, preventing robust concordance analysis. Fifth, turnaround times for molecular assays were not recorded, precluding assessment of their operational impact. Sixth, the small number of deaths limited the power to explore mortality predictors. Finally, the observational design prevents causal inference regarding the association between rapid testing and hospital length of stay, and residual confounding cannot be excluded.

In conclusion, in this multicentre real-world cohort of CAP managed outside the ICU, patients were predominantly elderly and multimorbid, and host-related factors, particularly age and chronic corticosteroid therapy, were key determinants of prolonged hospitalization. Our microbiological findings underscore the persistent difficulty of establishing a definitive etiological diagnosis in non-ICU CAP, especially when lower respiratory tract specimens are unavailable. Rapid microbiologic respiratory testing was independently associated with earlier hospital discharge but did not significantly influence antibiotic modification or duration. The findings of this study indicate that, within the context of routine medical practice, the significance of rapid diagnostics may lie primarily in its support of clinical decision-making rather than solely in antimicrobial stewardship.

Our findings suggest that, within routine clinical practice, rapid molecular respiratory testing is associated with earlier hospital discharge. However, because of the observational design, non-standardized testing strategy, incomplete microbiological sampling, and the potential for residual

confounding, these findings should be interpreted as demonstrating an association rather than a causal relationship. Future studies should focus on optimized sampling strategies, integration with biomarkers and clinical algorithms, and prospective evaluation of diagnostic-driven care pathways to fully realize the potential of molecular testing in CAP.

Author contributions

LP: Writing – original draft, Investigation, Data collection, Writing – review & editing; IG: Investigation, Data collection, Writing – review & editing; CVM: Investigation, Data collection; EN: Investigation, Data collection, Writing – review & editing; TMAF: Investigation, Data collection, Writing – review & editing; MV: Formal analysis, Statistical analysis; MC: Formal analysis, Statistical analysis; MD: Formal analysis, Statistical analysis; VM: Investigation, Data collection; MI: Investigation, Data collection; DG: Investigation, Data collection; MGB: Investigation, Data collection; AM: Investigation, Data collection; CC: Investigation, Data collection; MM: Investigation, Data collection; PC: Investigation, Data collection; MS: Investigation, Data collection; BT: Investigation, Data collection; SG: Investigation, Data collection; MF: Investigation, Data collection; LR: Investigation, Data collection; AR: Investigation, Data collection; AQ: Investigation, Data collection; MP: Investigation, Data collection; LZ: Investigation, Data collection; DL: Investigation, Data collection; GMR: Investigation, Data collection; LS: Investigation, Data collection; GMG: Conceptualization, Supervision, Writing – review & editing; AG: Project administration; AC: Conceptualization, Supervision, Writing – review & editing; SIS-NET Working Group: Investigation, Data collection.

Funding

This study did not receive any funding.

Institutional Review Board Statement

This study was approved by the Ethics Committee “Palermo 1”, Palermo, Italy (The SIS-NET-ID Study -Verbal n.23 19/09/2024 and n. 25 30/10/2024).

Informed Consent Statement

Written informed consent has been obtained from the patient enrolled in the study

Data availability

Data will be made available upon request to corresponding author.

Conflict of interest

The authors have no competing interests to declare that are relevant to the content of this article.

References

[1] Reyes LF, Conway Morris A, Serrano-Mayorga C, Derde LPG, Dickson RP, Martin-Loeches I. Community-acquired pneumonia. The Lancet 2025;406:2371–88. https://doi.org/10.1016/S0140-6736(25)01493-X.

[2] Vaughn VM, Dickson RP, Horowitz JK, Flanders SA. Community-Acquired Pneumonia: A Review. JAMA 2024;332:1282. https://doi.org/10.1001/jama.2024.14796.

[3] Ferriero AM, Di Lella R, Farroni C, Aiello A, Giarratano A, Todaro M, et al. Host-pathogen interaction in community-acquired pneumonia: a focus on the immune response. Front Cell Infect Microbiol 2026;16:1731074. https://doi.org/10.3389/fcimb.2026.1731074.

[4] Moy A-C, Kimmoun A, Merkling T, Berçot B, Caméléna F, Poncin T, et al. Performance evaluation of a PCR panel (FilmArray® Pneumonia Plus) for detection of respiratory bacterial pathogens in respiratory specimens: A systematic review and meta-analysis. Anaesthesia Critical Care & Pain Medicine 2023;42:101300. https://doi.org/10.1016/j.accpm.2023.101300.

[5] Niederman MS, Torres A. Severe community-acquired pneumonia. Eur Respir Rev 2022;31:220123. https://doi.org/10.1183/16000617.0123-2022.

[6] Fujishima S. Current corticosteroid therapeutic strategy for community-acquired pneumonia in adults: indications, dosage, and timing. J Intensive Care 2025;13:37. https://doi.org/10.1186/s40560-025-00809-8.

[7] Grifoni A, Alonzi T, Alter G, Noonan DM, Landay AL, Albini A, et al. Impact of aging on immunity in the context of COVID-19, HIV, and tuberculosis. Front Immunol 2023;14:1146704. https://doi.org/10.3389/fimmu.2023.1146704.

[8] Saarela E, Renko M, Uhari M, Pokka T, Kauma H, Ruuska TS. Multiplex PCR for respiratory bacteria in acute care. APMIS 2024;132:444–51. https://doi.org/10.1111/apm.13403.

[9] Serigstad S, Knoop ST, Markussen DL, Ulvestad E, Bjørneklett RO, Ebbesen MH, et al. Diagnostic utility of oropharyngeal swabs as an alternative to lower respiratory tract samples for PCR-based syndromic testing in patients with community-acquired pneumonia. J Clin Microbiol 2023;61:e00505-23. https://doi.org/10.1128/jcm.00505-23.

[10] Robert S, Lhommet C, Le Brun C, Garot D, Legras A, Mankikian J, et al. Diagnostic performance of multiplex PCR on pulmonary samples versus nasopharyngeal aspirates in community-acquired severe lower respiratory tract infections. Journal of Clinical Virology 2018;108:1–5. https://doi.org/10.1016/j.jcv.2018.08.001.

[11] Prendki V, Huttner B, Marti C, Mamin A, Fubini PE, Meynet MP, et al. Accuracy of comprehensive PCR analysis of nasopharyngeal and oropharyngeal swabs for CT-scan-confirmed pneumonia in elderly patients: a prospective cohort study. Clinical Microbiology and Infection 2019;25:1114–9. https://doi.org/10.1016/j.cmi.2018.12.037.

[12] Markussen DL, Serigstad S, Ritz C, Knoop ST, Ebbesen MH, Faurholt-Jepsen D, et al. Diagnostic Stewardship in Community-Acquired Pneumonia With Syndromic Molecular Testing: A Randomized Clinical Trial. JAMA Netw Open 2024;7:e240830. https://doi.org/10.1001/jamanetworkopen.2024.0830.

[13] Voiriot G, Argaud L, Cohen Y, Tuffet S, Chauvelot L, Souweine B, et al. Combined use of a multiplex PCR and serum procalcitonin to reduce antibiotic exposure in critically ill patients with community-acquired pneumonia: the MULTI-CAP randomized controlled trial. Intensive Care Med 2025;51:1417–30. https://doi.org/10.1007/s00134-025-08014-9.

[14] Abelenda-Alonso G, Calatayud L, Rombauts A, Meije Y, Oriol I, Sopena N, et al. Multiplex real-time PCR in non-invasive respiratory samples to reduce antibiotic use in community-acquired pneumonia: a randomised trial. Nat Commun 2024;15:7098. https://doi.org/10.1038/s41467-024-51547-8.

[15] Weishampel ZA, Nagahawatte A, Wijayaratne G, Wickramasinghe SS, Nicholson B, Anderson J, Vanderburg S, et al. Use of the BIOFIRE® FILMARRAY® Pneumonia plus Panel to characterize the etiology of lower respiratory tract infections among hospitalized patients in

Southern Province, Sri Lanka. BMC Infect Dis 2025;25:1178. https://doi.org/10.1186/s12879-025-11562-6.

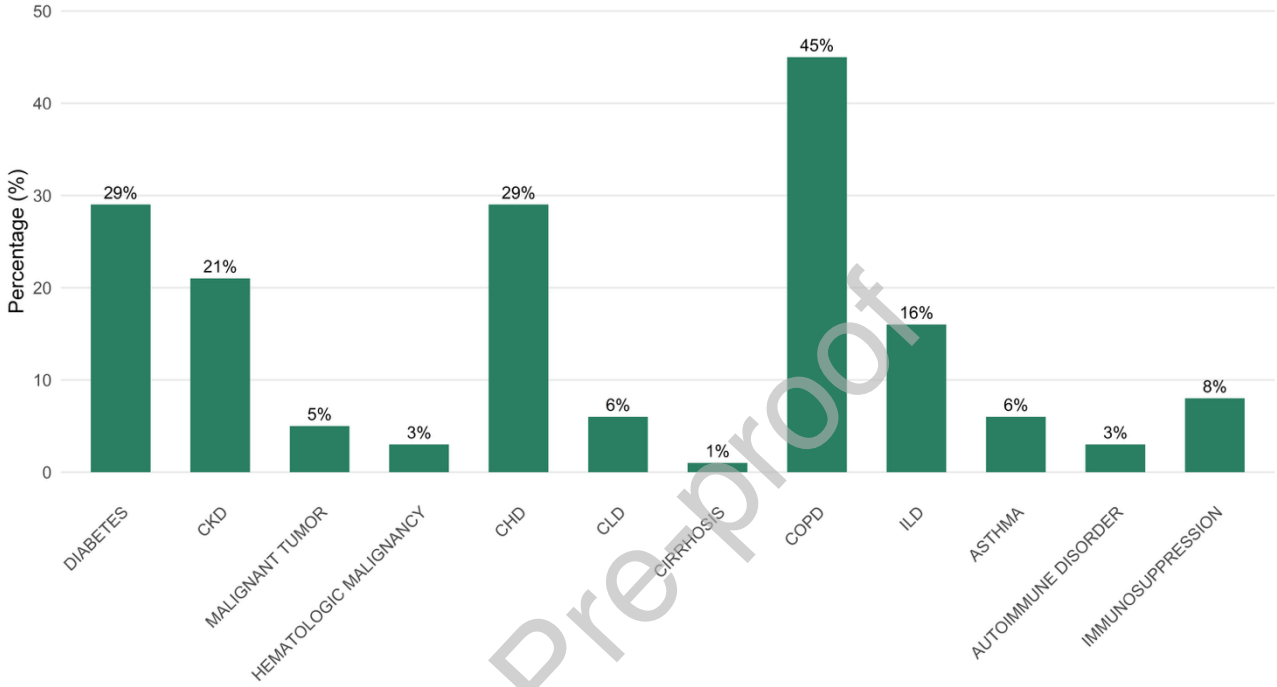

Figure 1. Prevalence of individual comorbidities in the study cohort. Chronic obstructive pulmonary disease (COPD) was the most frequent comorbidity, followed by chronic heart disease (CHD) and diabetes (equal prevalence), chronic kidney disease (CKD), interstitial lung disease (ILD), immunosuppression, chronic liver disease (CLD), asthma, autoimmune disorders, hematologic malignancy, and cirrhosis.

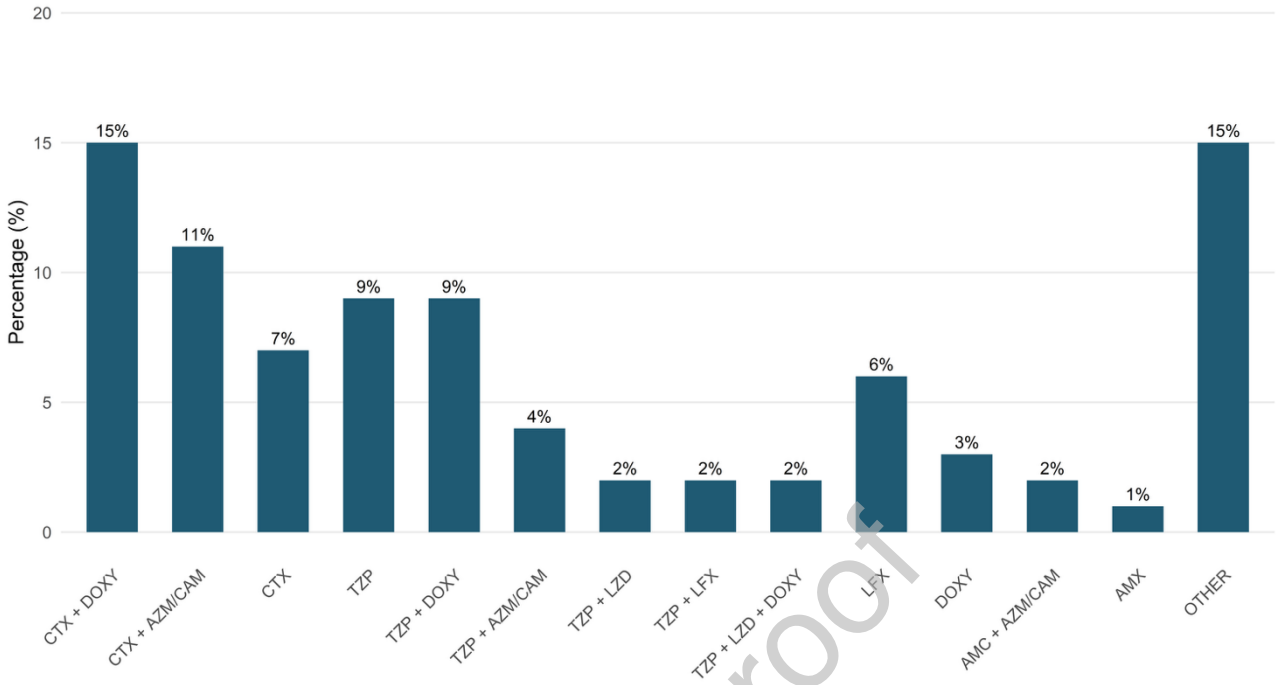

Figure 2. Empiric antibiotic therapy: overall frequency of administered antibiotics.

AZM: azithromycin; CAM: clarithromycin; CTX: ceftriaxone; Doxy: doxycycline; TZP: piperacillin/tazobactam; LZD: linezolid; LFX: levofloxacin; AMX: amoxicillin.

Table 1. Microbiological findings. The 'Sputum only' column reflects lower respiratory tract detection rates on the small number of sputum specimens (n = 32).

Panel A — Specimen types collected (total cohort: N = 176 patients)		
Specimen type	Patients, n (%)	
Nasopharyngeal swab	52 (29.5%)	
Sputum	32 (18.1%)	
Blood culture	17 (9.7%)	
Unspecified respiratory sample	17 (9.7%)	
Pleural fluid	1 (0.6%)	
Any microbiological sample	85 (48.3%)	
Panel B — Testing methods by specimen type		
Specimen / Method	total specimens	% positivity
Nasopharyngeal swab (n = 52)		
Viral molecular testing	50 (96.2%)	23/50 (46.0%)
Bacterial molecular testing	25 (48.1%)	8/25 (32.0%)
Rapid antigen testing	2 (3.8%)	1 (50.0%)
Sputum (n = 32)		

Culture	30 (94.0%)	9/30 (30.0%)
Viral molecular testing	29 (91.0%)	7/29 (24.1%)
Bacterial molecular testing	28 (87.5%)	8/28 (28.6%)
Panel C — Pathogens identified by any method		
Pathogen	All specimens, n=85	Sputum only, n=32
VIRUSES		
SARS-CoV-2	10 (11.8%)	—
Rhinovirus	9 (10.6%)	3 (9.3%)
Influenza A virus	8 (9.4%)	2 (6.2%)
Human metapneumovirus	5 (5.9%)	2 (6.2%)
Respiratory syncytial virus	4 (4.7%)	2 (6.2%)
Parainfluenza virus	2 (2.3%)	—
Adenovirus	1 (1.2%)	—
Coronavirus	1 (1.2%)	1 (3.1%)
Influenza B virus	1 (1.2%)	—
Any virus detected	36 (42.3%)	10 (31.2%)
≥ 2 viruses detected	5 (5.9%)	1 (3.1%)
BACTERIA & FUNGI		
Haemophilus influenzae	9 (10.6%)	4 (12.5%)
Streptococcus pneumoniae	6 (7.0%)	3 (9.4%)
Pseudomonas aeruginosa	3 (3.5%)	—
Mycoplasma pneumoniae	3 (3.5%)	1 (3.1%)
Staphylococcus aureus	3 (3.5%)	1 (3.1%)
Legionella spp.	2 (2.3%)	2 (6.25%)
Klebsiella pneumoniae	1 (1.2%)	—
Acinetobacter baumannii	1 (1.2%)	1 (3.1%)
Pneumocystis jirovecii	1 (1.2%)	—
Cryptococcus neoformans	1 (1.2%)	—
Any bacterial/fungal pathogen identified	24 (28.2%)	10 (31.2%)
≥ 2 bacteria detected	8 (9.4%)	2 (6.25%)
CO-DETECTION		
Viral–bacterial co-detection	12 (14.1%)	4 (12.5%)

Table 2. Multivariable Cox proportional hazards model for time to alive hospital discharge. HR > 1 indicates a higher hazard of discharge (shorter hospital stay); HR < 1 indicates a lower hazard of discharge (prolonged hospital stay). Event: discharge alive; censoring: in-hospital death or transfer to ICU.

Variable	Level of variable	HR	95% CI (low–high)	p-value
Rapid diagnostic test performed	Yes vs No	1.67	1.17 – 2.38	0.005
Age, years	Per 10-year increase	0.89	0.79 – 1.00	0.054
Chronic corticosteroid use	Yes vs No	0.59	0.38 – 0.91	0.016

Table 3. Rapid test and antibiotic therapy associations. Among patients with relevant data, the chi-squared test revealed no clear association between rapid molecular tests and changes in antibiotic treatment. However, escalation appeared less common among patients who underwent rapid testing.

Rapid test	No change	De-escalation	Escalation	Total
No FAST	73	10	13	96
FAST	61	7	4	72
Total	134	17	17	168

Conflict of Interest

The authors have declared no conflict of interest

Corresponding author

Antonio Cascio, PhD, MD *(Corresponding Author)*

Infectious and Tropical Disease Unit

AOU Policlinico "P. Giaccone" – University of Palermo

Via del Vespro 129, 90127 Palermo, Italy

Phone: +39 091 23890632

Email: antonio.cascio03@unipa.it