Title:
"Clinical Utility and Cost-Effectiveness of Molecular Diagnostic-Guided Antimicrobial Therapy in Sepsis: A Retrospective Cohort Study".

Abstract:
Background: Rapid molecular diagnostics enable early identification of pathogens and resistance genes in bacteremia and sepsis, but their impact on antimicrobial stewardship (AMS) outcomes requires evaluation.
Methods: Retrospective cohort of 200 sepsis and bateremia patients who underwent molecular testing (FilmArray/Xpert). Primary outcome: hospital length of stay. Secondary outcomes: costs, mortality. **Exposure:** MM-guided adequate therapy (optimized per AMS principles and attributed to MM results). Analysis: Chi^2, U de Mann Whitney, Lineal regression; Negative binomial regression adjusted for age, ICU admission, and adequate empirical therapy.
Results: Sample: 200 patients, 76 patients (38%) received MM-guided adequate therapy. After adjustment, this was associated with a 30.3% reduction in hospital stay (IRR 0.697, 95% CI: 0.558-0.872, p=0.002), 7-day reduction in ICU stay (p<0.001), and 14-day reduction in total hospitalization stay, median total cost savings of 3,094.3 PEN per patient (63.1% reduction, p<0.001) and median ICU cost savings of 3,561.1 PEN per patient (50.5% reduction, p=0.025). De-escalation was achieved in 30.3% vs 13.7% (p<0.001). Mortality showed a favorable but non-significant trend (a RR 0.612, p=0.271).
Conclusions: Molecular diagnostic-guided antimicrobial therapy optimization significantly reduces hospital length of stay, ICU utilization, and costs while promoting antimicrobial de-escalation in sepsis patients. These findings support the clinical utility and cost-effectiveness of rapid molecular diagnostics in AMS programs.

Key words: Sepsis, Length of Stay, Mortality, Cost-Effectiveness Analysis.

Introduction

The global burden of sepsis remains overwhelming: estimates from the Global Burden of Disease Study place its annual incidence in the tens of millions of cases and millions of deaths, with a greater impact in low- and middle-income regions; the WHO has called for strengthening prevention, diagnosis, and surveillance as public health priorities.[1,2] In this context, the Sepsis definition underscores the organ dysfunction induced by a dysregulated response to infection and reinforces the urgency of promptly initiating adequate antimicrobial therapy, as delays are associated with worse outcomes.[3]

Molecular microbiology is a technique that provides speed and precision in detecting and analyzing the genetic material of microbes; it does so through the use of syndromic multiplex PCR panels, identifying pathogens directly from blood cultures and detecting the presence of resistance genes. By reducing hours and even days to identification and resistance profiling, these tests allow clinicians to de-escalate or escalate antibiotics with greater safety and therapeutic precision, especially when combined with antimicrobial stewardship programs (ASP) or with clinical decision support systems (CDSS).[4,5] The estimated turnaround times according to global evidence suggest that rapid molecular tests, when integrated with antimicrobial optimization teams, reduce the waiting time for effective therapy, contribute to decreasing mortality, hospital and ICU length of stay, and costs through reduction in bed-days and unnecessary exposure to broad-spectrum antibiotics; nevertheless, effects vary according to the technology, context, and the intensity of the clinical intervention required.[4,6]

In Latin America, the use of molecular microbiology for diagnosing patients with suspected sepsis has been increasing, with private healthcare facilities being those that have implemented and reported the greatest use of this technique, due to the costs, infrastructure, and professional training gaps that its implementation requires in laboratories. The benefits of this technique are consistent with what is reported in the international literature, especially when the use of molecular tests is embedded in care algorithms and particularly when accompanied by ASPs[7]; however, it should be noted that the literature still corresponds to single-center observational studies with modest sample sizes and heterogeneous populations, demonstrating the need for multicenter evaluations that measure more outcomes and that simultaneously compare public and private settings.[6,8] Consequently, cost studies have shown mixed results: some found significant savings for patients with sepsis, while others found no difference in costs between control and intervention groups.[9]

In Peru, although molecular capacity was boosted and expanded during and after the pandemic, molecular microbiology applied to sepsis and its impact on mortality, length of stay, and costs is still limited and scattered, which creates an opportunity for local research and economic evaluation that should be explored. This manuscript aims to help close this gap, since when we consider the diagnostic possibility of sepsis, time becomes a fundamental factor to ensure optimal management, and molecular microbiology emerges as a tool that promises to gain critical time by identifying the pathogen, enabling faster adjustment of antibiotic therapy, thereby generating clinical and economic impact. For this reason, we are interested in understanding: What is the role of molecular microbiology in patients with sepsis, and how does it affect antibiotic treatment, clinical outcomes, and associated costs?

Materials and methods

Patients and Study Design

This study is observational and retrospective, conducted in a private level III-1 hospital center in the province of Lima. Patients of all ages who met the Sepsis-3 criteria (suspected infection with an acute increase of ≥2 SOFA points), admitted to general hospitalization wards, the intensive care unit, and intermediate care units with more than 48 hours of length of stay, and with positive results in both conventional blood culture and molecular tests, from October 2019 to December 2023, were included; COVID cases were excluded. During the study period, patients underwent both the conventional method and the FilmArray molecular assay, and informed consent from patients or their relatives was not required due to the characteristics of the study. Blood culture results involving bacteria of low clinical relevance such as *S. epidermidis*and other CoNS (coagulase-negative staphylococci), as well as results classified as contamination, were also excluded. This study was approved by the Ethics Committee of the University of Tacna (Resolution FACSA-CEI/004-02-2025). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Definitions and Data Collection

Sepsis was defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection[10], and bacteremia as the presence of bacteria in the bloodstream[11]. In this study, only bacteria of clinical relevance were considered, excluding cases of *S. epidermidis* and other coagulase-negative staphylococci (CoNS) that were classified as contaminants, unless they met the established criteria for clinical significance: at least two positive blood cultures for CoNS within a 5-day period, or one positive culture plus clinical evidence of infection (abnormal leukocyte count and abnormal temperature or blood pressure)[12]. For CoNS cases responsible for nosocomial infections, compliance with the following criteria was assessed: presenting one or more positive results identifying a CoNS from the same blood sample or from samples obtained within one week, plus three signs and/or symptoms of SIRS, or presenting two SIRS signs and symptoms and additionally having a central venous catheter[13].

Regarding appropriate treatment, it was operationally defined as the selection of an antibiotic with in vitro activity against the causal microorganism and lacking genes presumed to confer resistance to the antibiotic used; and appropriate or molecular microbiology–guided treatment refers to the antibiotic chosen based on molecular microbiology results, demonstrating in vitro activity, and being optimized in the context of an antimicrobial stewardship program (ASP), whose objective is to improve clinical outcomes by enhancing antimicrobial prescribing practices, reducing inappropriate use, and containing resistance[14].

With respect to the variables, the dependent variable is treatment guided by molecular microbiology, and the independent variables are mortality, hospital length of stay, and costs. Other data collected included age, sex, origin, the unit where the patient was hospitalized, diagnosis, sepsis source, use of empirical therapy, the bacterium identified, appropriate treatment, the class of antibiotics used, use of mechanical ventilation, presence of shock, and the costs associated with antibiotic therapy and hospital stay.

Conventional and Molecular Microbiological Testing

Blood samples were inoculated into aerobic and anaerobic culture bottles following standard protocols and incubated. Positive blood cultures were subjected to rapid molecular analysis using the FilmArray Blood Culture Identification (BCID) Panel (BioFire Diagnostics, LLC, Salt Lake City, UT, USA) or the Xpert® MRSA/SA cartridge (Cepheid LLC, Sunnyvale, CA, USA), selected according to Gram stain results. Assays were performed according to manufacturer instructions, with strict attention to reagent preparation, sample volume (200 μL), and assay conditions (temperature and duration).

Bacterial identification was carried out using VITEK MS MALDI-TOF. All isolates underwent phenotypic susceptibility testing using automated systems (Vitek 2.0) and/or disk diffusion (Kirby-Bauer), applying Clinical and Laboratory Standards Institute (CLSI) breakpoints for the corresponding year. Carbapenemase detection was performed via colorimetric methods (Blue Carba [ANLIS-Malbran]); positive samples were confirmed using the OKNVI RESIST-5 immunochromatographic assay (Coris Bioconcept) to determine carbapenemase type.

Impact of Molecular Microbiology Testing

During the study period, we observed that the use of empirical antimicrobial therapy is a constant when there is clinical suspicion of sepsis. Given its direct relationship and possible effect on the dependent variable, its association with the outcomes was evaluated, but it was not significant, leading us to conclude that it is not a confounding variable, although it is directly associated with the exposure.

Our study primarily evaluated whether therapy guided by the molecular test showed significant differences in the variables: hospital length of stay, mortality, and costs; we observed that with molecular tests, adjustments in antibiotic therapy are more precise, and escalation and de-escalation were performed in a shorter time than in those who waited for the results of conventional culture, due to the shorter turnaround times. This ultimately translates into reduced use of broad-spectrum antimicrobials, reduced length of stay, and consequently lower costs. It is important to mention that the determination of appropriateness based on molecular microbiology was performed by two (02) infectious disease physicians who reviewed the patients' clinical records and compared their therapies with the recommendations of the antimicrobial stewardship programs (ASP). Discrepancies were resolved by a third reviewer to reach consensus, in order to maintain the objectivity of the evaluation.

Statistical Analysis

The statistical analysis was performed using SPSS software version 27. From a population of 485, the estimated sample size was 215, determined with Epidat software version 4.2 with 80% power for cohort sample calculations. A descriptive analysis was carried out, presenting categorical variables through frequencies and percentages, and numerical variables with measures of central tendency and dispersion. The distribution of continuous variables was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. For outcome frequencies lower than 10%, the Odds Ratio (OR) was calculated; in general, a p value < 0.05 was considered significant, and a 95% confidence interval (CI) was used.

In the inferential analysis, to compare variables between groups, we used the Chi-square test, Fisher's exact test for categorical variables, and the Mann–Whitney U test for numerical variables, after confirming their distribution. As measures of association, the crude relative risk (RR) was calculated, and the adjusted risk was estimated using log-binomial regression. Confounding variables were

identified through the Mantel–Haenszel method and log-binomial regression; multivariate analyses were also performed using negative binomial regression and generalized linear models.

To control for disease severity, patients were stratified according to their severity (ICU admission, mechanical ventilation, appropriate empirical treatment, appropriate treatment, among others) to assess whether the benefits of molecular tests varied according to disease severity.

Results

From the estimated sample of 215, a total of 200 cases were considered valid for statistical analysis because they met the inclusion criteria. Among the valid cases, two groups were identified: those whose antibiotic therapy was guided by the molecular microbiology (MM) report, representing 38% (76), hereafter referred to as group 1, and those whose therapy was not guided by MM, representing 62% (124), group 2. The objectives of the study were to determine the impact of guided therapy on mortality, hospital length of stay, and costs.

Demographic and clinical characteristics

Among the 200 patients, 61.5% were male and 38.5% female. Adults aged 65 years and older represented the most affected age group (45.5%), with a median age of 62.5 years. Most patients (97.5%) resided in Lima. Overall mortality in the sample was 14%. A total of 71.6% of patients required admission to the intensive care unit (ICU) or intermediate care unit. Empirical antibiotic therapy was appropriate in 67% of cases, and post-result therapy was appropriate in 93.5%. Therapy escalation or de-escalation occurred in 20% of cases. Mechanical ventilation was required in 32.5% of patients, and 7.5% presented with septic shock. The median total hospital length of stay was 13.5 days, and the median ICU stay was 8 days. Statistically significant differences between the two groups were observed in variables including age, hospital unit, appropriateness of therapy, escalation/de-escalation, mechanical ventilation, total and ICU length of stay, and costs.(Table 01).

Table 01. Clinical and demographic characteristics.

	Group 1 **Guided Treatment for MM** n=76(38.0%)	**Group 2** **Not Guided Treatment for MM** n=124(62.0%)	**p-value**
Sex			
Male	48(63.1%)	75(60.4%)	0.706[a]
Female	28(36.9%)	49(39.6%)	
Age*	66[1;95]	57,5[1;95]	0.029[b]
Age group			
<18 years	8(25.2%)	23(74.2%)	
Adults	27(34.6%)	51(65.4%)	0.119[c]
older adults	41(45.1%)	50(54.9%)	
Procedence			
Lima	77(100.0%)	118(95.2%)	
Province	0(0.0%)	5(0.04%)	
Foreing	0(0.0%)	1(0.01%)	

HSPU			
ICU	46(60.5%)	96(77.4%)	0,011[a]
Hospitalization	30(39.5%)	28(22.6%)	
Main diagnostic			
Pneumonia sepsis	16(21.1%)	40(32.2%)	
Abdominal sepsis	9(11.8%)	11(8.8%)	
skin sepsis	6(7.8%)	9(7.2%)	0.012[c]
Urinary tract sepsis	35(46.1%)	30(24.2%)	
Other sepsis	6(7.8%)	14(11.2%)	
Sepsis without focus	4(5.2%)	20(16.1%)	
Mortality	8(10.5%)	20(16.1%)	0.268[a]
Appropriate treatment	76(100.0%)	111(90.9%)	0,007[d]
Adequate empirical treatment	52(68.4%)	82(66.1%)	0,738[a]
Escalate/de-escalate	23(30.3%)	17(13.7%)	<0,001[b]
Use of mechanical ventilator	19(25.0%)	46(37.0%)	0,076[a]
Septic shock	6(7.9%)	9(7.3%)	0,868[a]
Hospital stay(days)*			
Total hospitalization stay	8[3;69]	22[2;168]	<0,001[c]
ICU+hospitalization stay	11[3;69]	29[2;168]	0.004[b]
ICU stay	4,5[0;137]	11.5[0;146]	0,003[b]
Cost*			
Total cost	1,811.2[185.72;71,528.46]	4,905.5[114.06;58,629.9]	<0,001[b]
ICU cost	3,485.7[1,008;71,528.5]	7,046.8[650.95;58,629.9]	0,025[b]
Antibiotic cost	89.7[0.44;26,151.0]	139.5[0.22;17,862.3]	0,029[b]

HSPU: Health Service Provider Unit; ICU: Intensive care unit; *Mediana; RIQ: Rango intercuartílico; a: $Chi_{2.}$: b: U de Mann Whitney; c: Phi y V de Cramer; d: Fisher's exact test.

Laboratory and treatment characteristics

The bacteria identified in the molecular microbiology reports, according to prevalence, were *E. coli* 33.6%, *Pseudomonas aeruginosa* 9%, *Staphylococcus aureus* 9%, and *Klebsiella pneumoniae* 4.5%. The classes of antibacterials most commonly used in empirical therapy were: carbapenems 39%, cephalosporins 32%, and glycopeptides 12.5%; and in post–molecular result/blood culture therapy they were: carbapenems 35.5%, cephalosporins 33%, and glycopeptides 31%. It is important to mention that these frequencies also show the same trend in each of the groups studied (Table 02).

Table 02. Laboratory and treatment characteristics.

	Group 1 Guided Treatment for MM	**Group 2 Not Guided Treatment for MM**

	n=76(38.0%)	n=124(62.0%)
Bacteria identified		
Escherichia coli	40(52.6%)	26(21.3%)
Haemophilus influenzae	1(1.3%)	0(0.0%)
Klebsiela pneumoniae	2(2.6%)	7(5.7%)
Pseudomona aeruginosa	0(0.0%)	18(14.5%)
Serratian marcescens	1(1.3%)	5(4.0%)
Staphylococcus aureus	7(9.2%)	11(9.0%)
Streptococcus pneumoniae	1(1.3%)	4(3.3%)
Others Staphylococcus	4(5.2%)	17(13.9%)
Others Pseudomonas	0(0.0%)	1(0.8%)
Others Streptococcus	1(1.3%)	10(8.2%)
Others Enterobacters	6(7.8%)	12(9.8%)
Others grups	3(3.9%)	12(9.8%)
Empirical antibiotic		
Aminoglycoside	5(6.6%)	9(6.0%)
Penicillin with beta-lactamase inhibitor	5(6.6%)	10(6.7%)
Carbapenem	30(39.5%)	48(32.4%)
Cefphalosporin	23(30.2%)	41(27.7%)
Fluoroquinolone	1(1.3%)	2(1.3%)
Glycopeptide	6(7.8%)	19(12.8%)
Others	5(6.5%)	5(3.4%)
Antibiotic post report		
Aminoglycoside	6(6.5%)	17(8.1%)
Penicillin with beta-lactamase inhibitor	10(10.8%)	11(5.2%)
Carbapenem	37(40.2%)	34(30.2%)
Cefphalosporin 3ra gen	24(26.1%)	42(20.1%)
Fluoroquinolone	0(0.0%)	9(4.3%)
Others	4(4.4%)	15(5.4%)

Outcome evaluation

Mortality associated with antimicrobial therapy in sepsis

In the risk assessment, the mortality variable did not show significant differences between both groups ($p = 0.271$), recording 10.5% for the group whose antibiotic therapy was guided by MM versus 16.1% for the group that was not guided by MM (Table 03).

Table 03. Outcome mortality associated with guided treatment for MM.

	RR/OR (IC)	p-value
Mortality		
Adjusted RR (95% CI)	0.612 (0,255;1,468)[e]	0.271[e]
Mechanic Ventilation		
Adjusted RR (95% CI)	1.769(0.938;3.336)[f]	0.780[f]
Hospital stay(days)*		
Adjusted OR (95% CI)	0.957 (0,930;0,984)[f]	0,002[f]
ICU stay(days)		
Adjusted OR (95% CI)	0.981 (0,965;0,997)[f]	0,020[f]

RR: Relative risk; OD: Odds ratio; a:Chi2; e:Mantel Haenszel; f:Binary logistic regression.

Hospital length of stay associated with antimicrobial therapy in sepsis

Regarding the variables, total hospital stay recorded a median of 8 days for the group whose antibiotic therapy was guided by MM versus 22 days for the group that was not guided by MM, with an OR of 0.957 and a crude p-value of $p<0.001$ using the Mann–Whitney U test, and an adjusted p-value of $p=0.002$ after binary logistic regression. Similarly, ICU stay showed a median of 4.5 days for the group whose antibiotic therapy was guided by MM versus 11 days for the group not guided by MM, with an OR of 0.981, a crude p-value of $p=0.003$, and an adjusted p-value of $p=0.020$. These findings indicate that therapy guided by molecular microbiology reports is a protective factor and is associated with a reduction of 14 days in total hospital stay and 6.5 days in ICU stay (Table 03).

A negative binomial regression was also performed to adjust for age, ICU admission, and adequate empirical therapy. It was observed that appropriate therapy guided by MM reduced hospital stay by 32.2% ($p<0.001$); age also showed a 6% reduction, as did adequate empirical treatment, which reduced hospital stay by 15.5%. Only ICU admission prolonged hospital stay by 234%. Additionally, the use of mechanical ventilation and the presence of shock were evaluated as potential confounding variables; the results showed weak significance, with adjusted p-values of 0.890 and 0.959, respectively (Table 04).

Table 04. Outcome length of stay associated with guided treatment for MM.

	IRR (95%CI)	p-value
Treatment Adequate for MM	0.697(0.558-0.872)	0.002[h]
Age	0.994(0.990-0.998)	0.004[h]
ICU admission	3.34(2.622-4.255)	<0.001[h]
Adequate empirical	0.845(0.678-1.052)	0.132[h]

IRR: Incidence rate ratio; h: Negative Binomial Regression.

Costs associated with antimicrobial therapy in sepsis

Regarding costs, the main variables evaluated were total cost, ICU cost, and antibiotic therapy cost, all of which showed significant differences between groups. Total cost had a median of 1,811.2 PEN for the group whose antibiotic therapy was guided by MM versus 4,905.5 PEN for the group not guided by MM, with a p-value of $p<0.001$ obtained using the Mann–Whitney U test. ICU cost showed a median of 3,485.7 PEN for the group guided by MM versus 7,046.8 PEN for the non-MM-guided group, with a p-value of $p=0.025$ by the Mann–Whitney U test. Finally, the cost of antibiotic therapy had a median of 89.7 PEN for the MM-guided group compared with 139.5 PEN for the non-MM-guided group, with a p-value of $p=0.029$, also obtained using the Mann–Whitney U test (Table 01).

A multivariate analysis was performed using linear regression and goodness-of-fit assessment, yielding an $R^2 = 0.837$, which explains 84% of the cost variation. Potential confounding variables—such as total hospital stay, ICU stay, and ICU admission—were also evaluated. ICU admission was identified as the primary driver of increased costs, whereas total and ICU stay increased cost per day by +1.8% and +1.4%, respectively. On the other hand, when costs were associated with the dependent variable, no significant differences were observed; however, the beta coefficient ($\beta = -0.086$) indicates an inverse relationship, suggesting that antibiotic therapy guided by MM tends to be cost-saving (Table 05).

Table 05. Outcome length of stay associated with guided treatment for MM.

	IRR (95%CI)	p-value
Treatment Adequate for MM	0.697(0.558-0.872)	0.002[h]
Age	0.994(0.990-0.998)	0.004[h]
ICU admission	3.34(2.622-4.255)	<0.001[h]
Adequate empirical	0.845(0.678-1.052)	0.132[h]
Mechanic Ventilation	0.240(0.647-1.746)	0.890[h]

IRR: Incidence rate ratio; Model Fit: $R^2 = 0.837$ g: Linear Regression on Log-transformed Costs.

Discussion

The retrospective cohort included 215 patients, with 200 valid results for statistical analysis, as they met the inclusion criteria. The sample was composed mostly of males (61.5%) and older adults (45.5%), with a high proportion of patients requiring ICU/IMCU care (71%), which suggests a profile of complex cases with high resource demand; it may also reflect the presence of less stringent ICU admission criteria in private healthcare facilities due to their lower demand. The predominant sources of sepsis onset were urinary tract infection and pneumonia. In Group 1, whose antibiotic therapy was guided by MM, a higher frequency of UTI-related sepsis was recorded (46.1%), followed by pneumonia (21.1%); in Group 2, whose therapy was not guided by the molecular result, the same sources of infection were reported but in reversed order. Both groups presented a microbiological spectrum led by E. coli (33%), Staphylococcus aureus (9%), Pseudomonas aeruginosa (9%), followed by Klebsiella pneumoniae (4.5%), a pattern consistent with mixed community and nosocomial etiologies in adult sepsis.[15,16,17]

Overall mortality was 14% (RR 0.612; 95%CI 0.255–1.468; p=0.271), indicating no association with the exposure analyzed; and although mortality was numerically lower in the MM-guided group (10.5% versus 16.1%), this difference was not statistically significant (p=0.271). The study may have been underpowered to detect clinically meaningful differences in mortality, and a post-hoc power analysis would be required to confirm this hypothesis. However, this tendency toward reduced risk of death in those applying MM is consistent with the literature and may be explained by the timely use of antimicrobial stewardship programs.[18] When analyzing the overall rate and the group-specific rate, it is markedly lower than that described in other studies of sepsis and severe sepsis/septic shock in ICUs (≈56% and lower rates that do not fall below 30% in Latin America), differences that may be attributable to greater severity of clinical presentation and to the selection of ICU patients in those series.[16,19]

The current microbiological and therapeutic context supports the need for early decision-making, given that the predominant bacteria are Gram-negative and require the use of empirical antibiotic therapy. Carbapenems and cephalosporins were used most frequently, reflecting the need for broad coverage in an environment with resistant bacteria, followed by post-result adjustments based on either molecular microbiology or conventional methods. In our study, the same antibiotic classes were used—along with glycopeptides—in both empirical and post-result therapy; however, this does not imply that therapies remained unchanged, but rather that modifications involved escalation or de-escalation based on clinical and laboratory criteria. It is important to note that in Lima, Peru, ESBL-producing bacteremias are associated with higher mortality, obligating clinicians to balance initial broad-spectrum coverage followed by timely de-escalation—a strategy that MM could facilitate by reducing the waiting time for effective therapy.[20]
This finding is physiologically plausible and aligns with current guidelines that emphasize early cultures, timely initiation of antibiotics, and reassessment to narrow coverage when appropriate.[18] Current evidence also links de-escalation with reduced nephrotoxicity, decreased late ICU admission, and a modest reduction in adjusted mortality, reinforcing clinical safety by optimizing antimicrobials with early and actionable data.[21] Since it is known that each hour of delay in effective therapy increases the risk of death from septic shock, it is reasonable that molecular tools contribute to shorter lengths of stay by accelerating therapeutic adequacy, even if the effect on mortality was not demonstrable in this cohort. It should also be noted that the diagnostic precision of molecular tests guides therapy in shorter time frames, and timely effective therapy within the first hour is associated with a 79.9% survival rate, with each hour of delay associated with a mean reduction of –7.6%.[22]

Regarding the impact of molecular microbiology (MM) as a guide to achieving effective therapy, in our study it was associated with substantial reductions in clinical and economic burden: the median total hospital length of stay was 8 days in Group 1 vs. 22 days in Group 2, demonstrating a significant difference between the groups (RR = 0.957; 95%CI: 0.930–0.984; p adjusted = 0.002) and a reduction of 14 days among those whose therapy was guided by MM. A similar pattern was observed in the ICU: Group 1 recorded 4.5 days of stay versus 11.5 days in Group 2, also showing a significant difference (RR = 0.981; 95%CI: 0.965–0.997; p adjusted = 0.020), likewise demonstrating that MM-guided therapy contributes to a 7-day reduction in ICU stay and consolidates itself as a protective factor. This is supported by the "time-to-actionable-information" mechanism, which facilitates early de-escalation/adjustment and safe discharge decisions,[18] and is particularly noteworthy considering that Group 1 had a higher median age than Group 2 (66 vs. 57.5 years). A Negative Binomial Regression model was applied to identify confounders and relevant factors, evaluating age, ICU admission, and adequate empirical therapy. We observed that the latter was not a confounder but rather an effect modifier that enhances the benefit of MM-guided adequate therapy. This finding is important because it alters the effect of the dependent variable on hospital length of stay, especially when empirical antibiotic therapy is inadequate. This was assessed through stratified analysis, where Group 1 recorded a median of 8 days and Group 2 of 21 days, demonstrating a significant 13-day

reduction—a 30.3% decrease (p=0.002)—thus establishing a true clinical benefit. When comparing our results with a sepsis management cohort in a Brazilian ICU, where de-escalation was infrequent and no reductions in mortality or length of stay were observed, our findings contrast sharply due to the reduction in hospitalization and ICU days. This difference could plausibly be attributed to the integration of MM, which has the potential to shorten actionable timeframes, coupled with a possible combination of less extreme cases in our cohort.[19]

The economic savings paralleled the reductions in ICU stay, total costs, and antibiotic costs. The median total cost for Group 1 was 1,811.2 PEN versus 4,905.5 PEN in Group 2, with $p < 0.001$; the median ICU stay cost was 3,485.7 PEN versus 7,046.8 PEN in Group 2 ($p = 0.025$); and the median antibiotic cost was 89.7 PEN for Group 1 versus 139.5 PEN for Group 2 ($p = 0.029$). These findings are plausible, as length of stay is the primary determinant of hospital expenditure; therefore, reducing duration and narrowing antibiotic spectrum lowers total costs. It is also known that such reductions do not adversely impact mortality in patients with severe sepsis and/or septic shock when compared with continued broad-spectrum therapy.[23] Peruvian and local studies further confirm that prolonged hospitalization and antibiotics constitute the major cost components in critical infections.[20,24] Likewise, the reduction in hospital days and expenditure among patients whose antibiotic therapy was guided by MM contrasts with other ICU sepsis-management cohorts lacking rapid diagnostics, where microbiological data were key to improving efficiency.[16,19] Our cost results were also adjusted using Linear Regression with goodness-of-fit analysis to identify potential confounders, determining that costs are driven primarily by ICU admission and length of stay—both of which are reduced through MM-guided therapy, thereby indirectly lowering overall expenditure. Model adjustment yielded an $R^2 = 0.837$, explaining 84% of the cost variability, despite the considerable clinical heterogeneity and high fixed costs inherent to critical care settings. In summary, MM appears to function as a catalyst for achieving earlier, more precise, and more effective therapy, resulting in fewer bed-days and reduced antibiotic spending.[24]

Finally, we must conclude that the implementation of molecular microbiology tests is a cost-effective intervention[25] because it demonstrates a reduction in costs associated with antimicrobial treatment of sepsis and hospital stay, due to reduced waiting time for results and diagnostic precision[26] by identifying pathogens and their resistances efficiently and effectively, enabling early diagnosis and precise treatment. Regarding mortality, no significant differences were found; in this scenario, it is prudent to maintain both molecular and conventional tests in clinical practice until sufficient evidence supports transitioning to new technologies.

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Conflict of interest statement
The authors declare that they have no conflicts of interest regarding the publication of this article.

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