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ORIGINAL RESEARCH

Role of Rapid Molecular Diagnostic Testing in Antimicrobial Stewardship: Effects on Antibiotic De-escalation, Length of Hospital Stay, and Mortality

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Abstract

Background: Rapid molecular diagnostics may accelerate antimicrobial optimization in bloodstream infection, but their incremental clinical value in hospitals with existing stewardship services remains uncertain.

Methods: We analysed a nonrandomized cohort from eight anonymised hospitals in the United States between January and December 2023. Of 480 patients, 269 underwent rapid molecular testing and 211 conventional testing; stewardship was present in both groups. The primary endpoint was de-escalation within 72 hours among patients with final susceptibility profiles allowing narrower therapy. Multivariable logistic and gamma regressions adjusted for demographics, comorbidity, critical illness, isolate resistance, effective empirical therapy, and hospital.

Results: Among 416 eligible patients, 72-hour de-escalation occurred in 173/237 (73.0%) rapid-pathway patients versus 25/179 (14.0%) conventional-pathway patients (adjusted odds ratio [aOR] 21.11, 95% CI 11.71–38.04). Median actionable-result time was 18.5 versus 57.6 hours. Broad-spectrum antibiotic days were lower with rapid testing (adjusted mean ratio 0.86, 95% CI 0.80–0.92). Neither post-draw length of stay (adjusted mean ratio 0.92, 95% CI 0.84–1.02) nor 30-day mortality (aOR 0.70, 95% CI 0.36–1.35) differed significantly.

Conclusions: Rapid molecular testing embedded in stewardship was associated with faster de-escalation and reduced broad-spectrum exposure, without demonstrable mortality or length-of-stay benefit. Residual confounding limits causal interpretation.

Keywords: bloodstream infection; rapid molecular diagnostics; antimicrobial stewardship; antibiotic de-escalation; hospital length of stay; mortality; observational cohort.

Introduction

Bloodstream infection is a time-sensitive clinical syndrome in which pathogen identification and prompt selection of active antimicrobial therapy must be balanced against avoidable exposure to broad-spectrum agents. Invasive bacterial infection contributes substantially to the worldwide burden of antimicrobial resistance, while delays in effective therapy have been linked to poorer outcomes among severely ill patients [1–2]. Clinicians therefore initiate empirical antibiotics before definitive microbiological information is available. This pragmatic approach protects patients at immediate risk but also creates a period during which treatment may be unnecessarily broad, toxic, or ineffective.

Conventional blood-culture workflows require microbial growth followed by species identification and phenotypic susceptibility testing. The elapsed time between specimen collection and an actionable report frequently extends beyond the early therapeutic decision window. Rapid molecular diagnostic testing can shorten this interval by identifying selected organisms and resistance determinants directly from positive culture broth or, for some platforms, blood specimens. Its benefit is not automatic: a result must reach clinicians, be interpreted in clinical context, and trigger an appropriate antimicrobial action. Professional guidance accordingly advocates pairing rapid diagnostics with active antimicrobial stewardship rather than treating the assay as an isolated technology [3,9–12].

Earlier syntheses linked molecular rapid diagnostics to shorter time to effective therapy and, in some settings, lower mortality or shorter hospitalisation [4–5]. The systematic review and meta-analysis by Timbrook and colleagues found that the mortality association was more evident in studies incorporating antimicrobial stewardship; studies without stewardship did not demonstrate a statistically significant mortality reduction [4]. Heterogeneous designs, local microbiology workflows, differences in baseline stewardship services and selection of patients for testing complicate interpretation. Randomised and implementation studies have demonstrated improvements in antimicrobial decisions but have not consistently established reductions in mortality or length of stay [6–8,13–24].

The question is particularly relevant to health systems where molecular testing is selectively available and where stewardship input is already provided to patients managed with conventional microbiology. In such circumstances, comparison of testing pathways should assess not only diagnostic turnaround but also clinically meaningful treatment changes, subsequent antimicrobial exposure, duration of hospitalization, and survival. We therefore evaluated a multicentre observational cohort of patients with bloodstream infection managed through either rapid molecular or conventional diagnostic pathways, both supported by stewardship review. The primary objective was to compare de-escalation within 72 hours among patients whose final susceptibility profile permitted narrowing. Secondary objectives were to assess the timing of diagnostic and stewardship actions, broad-spectrum antibiotic exposure, post-draw hospital stay, in-hospital death, and 30-day all-cause mortality.

Methods

Study design, setting, and participants. We analysed a de-identified, patient-level multicentre observational cohort conducted between January and December 2023 across eight hospitals in the United States. To protect institutional confidentiality, participating hospitals are identified only by the codes H01–H08; no hospital names are disclosed. The analytic dataset contained 480 unique patient records. Individual encounter dates, enrolment logs, and molecular platform names were not included in the data export; consequently, individual accrual timing and assay-specific details could not be independently reconstructed from the dataset. We treated the index blood draw as time zero and included all 480 complete patient rows, excluding the embedded dictionary and blank worksheet rows. Every recorded patient had an identified bloodstream isolate. This was an analysis of observed clinical pathways, not a randomized diagnostic trial [37].

Exposure and comparator. The exposure was the diagnostic pathway planned at index assessment, coded as rapid molecular testing or conventional testing. The accompanying data dictionary states that clinical selection and hospital availability determined exposure and that both groups received antimicrobial stewardship. The comparison is therefore incremental rapid testing plus stewardship versus conventional microbiology plus stewardship, not stewardship versus no stewardship. The dataset does not name individual assays or specify their pathogen and resistance-gene panels; diagnostic sensitivity, assay-specific agreement, and laboratory operating hours could not be evaluated. The recorded time to a result represents the time until an actionable identification/resistance report, irrespective of the component providing the information.

Clinical variables. Baseline covariates comprised age, sex (0, female; 1, male), Charlson Comorbidity Index excluding age points, admission to intensive care at the index assessment, Sequential Organ Failure Assessment (SOFA) score, presence of a multidrug-resistant isolate, organism category, and receipt of an effective empirical antibiotic at blood draw. The Charlson index and SOFA score were treated as markers of pre-exposure comorbidity and acute illness severity, respectively [38–39]. The six predefined organism categories were Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Staphylococcus aureus, and Enterococcus faecium; no A. baumannii isolate was present in the exported records.

Outcomes and operational definitions. The primary endpoint was recorded de-escalation within 72 hours from blood draw, assessed only in patients designated eligible on the final susceptibility profile. Eligibility meant that narrower treatment was microbiologically permissible than the empirical regimen, not that every patient was clinically suitable for narrowing at that moment. De-escalation was defined as initiation of a narrower regimen before discharge or inpatient death. Secondary endpoints included any recorded de-escalation among eligible patients, time from blood draw to blood-culture positivity, actionable reporting, stewardship review and de-escalation, days of broad-spectrum treatment, and post-draw hospital length of stay. Time to effective therapy equalled zero when the empirical regimen was active at index; therefore, this interval was summarized separately among those initially lacking effective coverage. Death during hospitalization and all-cause death within 30 days were separate outcomes; the latter included post-discharge deaths and was complete in the export. Clostridioides difficile infection within 30 days was exploratory.

Data integrity and descriptive analysis. We screened the 480 patient rows for duplicate identifiers, invalid exposure and outcome codes, missing fields, and discordance between the de-escalation indicator and its recorded time. No patient-level covariate or endpoint was missing, apart from de-escalation time being structurally blank for the 200 patients without a de-escalation event. We excluded the 64 patients coded ineligible from eligibility-specific analyses rather than treating them as failures. Continuous outcomes were described by medians and interquartile ranges (IQRs), or means and standard deviations when informative; categorical outcomes were summarized as counts and percentages. The Mann–Whitney U test compared selected continuous distributions and Fisher's exact test compared sparse binary endpoints. Tests were two-sided, with 0.05 used as a descriptive threshold, not a causal decision rule.

Multivariable modelling. Prespecified associations with binary endpoints were estimated using logistic generalized linear models; continuous positive endpoints (broad-spectrum days, length of stay, and diagnostic turnaround) were analysed using gamma generalized linear models with a log link. All primary adjusted models incorporated diagnostic pathway, age, sex, Charlson index, intensive-care status, SOFA score, multidrug resistance, effective empirical therapy, and hospital fixed effects (seven hospital indicator variables). Heteroskedasticity-consistent HC3 standard errors were used. Results are presented as adjusted odds ratios (aORs) for binary outcomes or adjusted mean ratios (aMRs) for positive continuous measures, with 95% confidence intervals. The principal sensitivity analysis removed hospital fixed effects; additional descriptive stratification considered baseline intensive-care status and hospital. Because there were only eight institutions and relatively few deaths, the adjusted clinical outcome analyses are interpreted as exploratory; none should be taken as a causal effect or a fully validated prognostic model.

Ethics and reporting. Ethics approval for the study was obtained from the relevant institutional ethics review bodies. All patient-level records in the analytic dataset were de-identified, and the identities of the eight participating U.S. hospitals are withheld for institutional confidentiality. The manuscript was prepared in accordance with relevant elements of the STROBE reporting recommendations for observational cohort studies [37].

Results

Cohort composition and baseline characteristics. All 480 unique records were eligible for descriptive analysis; 269 (56.0%) followed the rapid molecular pathway and 211 (44.0%) followed conventional testing. The data were distributed across eight hospitals, each contributing 52–67 patients. Baseline age was comparable between groups (mean 53.1 years in each), whereas patients selected for rapid testing had more acute illness: 98 of 269 (36.4%) were in intensive care compared with 37 of 211 (17.5%) conventional-pathway patients; the corresponding mean SOFA scores were 4.1 and 2.9. Multidrug-resistant isolates were recorded in 74/269 (27.5%) and 60/211 (28.4%), respectively. Effective empirical therapy was in place at the blood draw in 209/269 (77.7%) and 160/211 (75.8%). De-escalation eligibility was defined for 237/269 (88.1%) and 179/211 (84.8%) patients. Detailed characteristics appear in Table 1.

Diagnostic turnaround and stewardship response. Blood-culture positivity occurred at broadly similar times: median 15.4 hours (IQR 12.7–18.7) in the rapid group and 14.6 hours (11.5–18.3) in the conventional group. In contrast, the actionable result was available at 18.5 hours (15.9–21.6) after the index draw with rapid testing versus 57.6 hours (49.4–68.8) under conventional testing. Stewardship reviewed results at medians of 20.5 hours (17.7–23.9) and 62.9 hours (53.7–72.5), respectively. Both result and review intervals differed markedly on unadjusted comparisons (both $P<0.001$); adjusted gamma models yielded an actionable-result aMR of 0.32 (95% CI 0.31–0.33) and review aMR of 0.33 (0.32–0.34). These process measures indicate that the observed advantage was concentrated after culture positivity, consistent with the role of faster identification and resistance information (Table 2; Figure 1).

De-escalation. The primary endpoint occurred in 173/237 (73.0%) eligible rapid-testing patients and 25/179 (14.0%) eligible conventional-testing patients. The unadjusted absolute risk difference was 59.0 percentage points (95% CI 50.7–65.8), and the unadjusted odds ratio was 16.65 (95% CI 9.99–27.75; Fisher exact $P<0.001$). After covariate adjustment including hospital, rapid testing remained associated with earlier de-escalation (aOR 21.11, 95% CI 11.71–38.04; $P<0.001$). Any de-escalation before discharge or inpatient death occurred in 174/237 (73.4%) versus 106/179 (59.2%) eligible patients (aOR 2.01, 95% CI 1.29–3.15; $P=0.002$). Among patients in whom de-escalation

occurred, median times were 29.3 hours (IQR 25.4–35.3) and 82.5 hours (72.8–96.7), respectively; these conditional times exclude those never de-escalated and therefore should not be read as an unbiased time-to-event comparison. The direction of the early de-escalation association was preserved in both ICU and non-ICU descriptive strata and across each hospital.

Antibiotic exposure and effective treatment. Median broad-spectrum use was 6 days (IQR 5–8) under rapid testing and 7 days (5–9) with conventional testing; mean exposure was 6.38 versus 7.39 days. The adjusted mean ratio was 0.86 (95% CI 0.80–0.92; P<0.001), consistent with approximately 14% less broad-spectrum exposure after adjustment. Among the 111 patients whose empirical therapy was not active at blood draw, time to first effective therapy was a median 22.5 hours (IQR 19.6–25.7; n=60) under rapid testing versus 62.6 hours (54.2–72.4; n=51) under conventional testing. This subgroup metric captures a clinically important shift but is conditioned on baseline effectiveness and was not designated a confirmatory outcome (Table 2).

Hospital stay, mortality, and safety. Median post-draw hospital stays were 11.7 days (IQR 8.1–16.1) in the rapid-testing group and 12.2 days (8.4–17.4) in the conventional group (unadjusted Mann–Whitney P=0.295). The adjusted stay ratio was 0.92 (95% CI 0.84–1.02; P=0.101). In-hospital deaths occurred in 25/269 (9.3%) and 20/211 (9.5%); 30-day deaths occurred in 31/269 (11.5%) and 26/211 (12.3%), respectively. The adjusted odds of 30-day mortality were not significantly different (aOR 0.70, 95% CI 0.36–1.35; P=0.282), nor were in-hospital mortality odds (aOR 0.70, 95% CI 0.34–1.45; P=0.333). Thirty-day C. difficile infection occurred in 9/269 (3.3%) versus 11/211 (5.2%) (aOR 0.86, 95% CI 0.32–2.33; P=0.768), with wide confidence intervals. Table 3 and Figure 2 summarize these clinical associations.

Sensitivity analyses and model interpretation. The early de-escalation estimate remained large when hospital indicators were omitted (aOR 20.79, 95% CI 11.76–36.75), while the corresponding 30-day mortality estimate remained uncertain (aOR 0.70, 95% CI 0.39–1.26). Across intensive-care strata, early de-escalation was observed in 56/82 ICU patients with rapid testing versus 3/29 receiving conventional testing, and in 117/155 versus 22/150 non-ICU patients. These are unadjusted subgroup descriptions rather than formal interaction tests. No missing baseline records required imputation. As expected in a clinically selected cohort, adjusted estimates differ from crude mortality comparisons, underscoring the importance of case-mix differences and the limits of residual-confounding control.

Discussion

In this eight-hospital observational cohort, rapid molecular testing embedded within an existing stewardship workflow was strongly associated with earlier narrowing of antibiotic treatment when the final susceptibility profile allowed it. Actionable microbiological information reached clinicians more than a day earlier, and the stewardship review followed soon afterward. The overall percentage of eligible patients who were ever de-escalated increased more modestly than the proportion de-escalated within 72 hours. This distinction is meaningful: the most defensible advantage of rapid testing in the present data is acceleration of an appropriate treatment decision, rather than assurance that every ultimately eligible patient will be narrowed.

Our findings align with mechanistic expectations and substantial prior work showing that faster diagnostic information is more useful when integrated with a responsive stewardship service. The randomized trial by Banerjee and colleagues showed improvements in antimicrobial optimization through multiplex blood-culture testing and stewardship communication, while studies of adding rapid PCR panels to established stewardship programs demonstrated shorter decision intervals [6–8]. The randomized RAPIDS-GN study and phenotypic rapid susceptibility investigations broadened the evidence base for earlier optimization of Gram-negative bacteremia, although patient-level clinical outcomes have varied [7,16,19]. The present study extends that operational comparison to an observational multicentre sample in which stewardship was present on both diagnostic pathways.

The magnitude of the early de-escalation association warrants cautious interpretation. An aOR above 20 reflects a highly separated timing distribution, with most observed rapid-pathway de-escalations preceding 72 hours and most conventional-pathway actions occurring later. An odds ratio of this size should not be confused with a 20-fold probability or a causal effect. The absolute difference of approximately 59 percentage points is more interpretable clinically. Furthermore, selection for rapid testing was not random: the rapid cohort included substantially more ICU patients and higher SOFA scores. We adjusted for available severity markers and hospital, but residual confounding by infection source, shock, immunosuppression, prior antimicrobial exposure, laboratory staffing, formulary restrictions, and local prescribing behaviours remains possible.

A shorter diagnostic interval is not synonymous with a clinically justified de-escalation in every patient. Resistance-marker panels provide incomplete susceptibility information; a negative gene result cannot universally establish phenotypic susceptibility, and species identification alone may be insufficient for safe narrowing in complicated infection. Decisions depend on source control, organism, illness trajectory, antimicrobial penetration, and clinician assessment. The dataset defines eligibility retrospectively from the final susceptibility profile, meaning the primary endpoint conditions on information observed after exposure assignment. Consequently, even though eligibility reflects the recorded possibility of narrowing, it does not necessarily equal a

prospective bedside decision threshold. Diagnostic and antimicrobial stewardship principles require documenting the reason for maintaining broad coverage when clinical conditions demand it [3,9–12].

Evidence from pathogen-specific settings is informative but not interchangeable. Investigations of vancomycin-resistant enterococcal bloodstream infection and resistant Gram-negative bacteremia have reported earlier active treatment after rapid identification or susceptibility testing, although these studies differ in intervention and case mix [25–28,35]. Other implementation reports emphasize that alert design, active pharmacist notification, and local stewardship capacity determine how much of a laboratory time saving reaches the patient [29–34,36,40–41]. This reinforces why the comparator in the current analysis matters: both pathways incorporated stewardship, whereas some earlier evaluations compared combined testing-and-stewardship initiatives with routine care lacking an equivalent clinical response mechanism. The current estimates therefore should not be generalized to laboratories with no active stewardship service.

The finding of fewer broad-spectrum antibiotic days is consistent with several intervention studies and reflects an antimicrobial-sparing benefit beyond diagnostic speed itself [13–15,24,27–31]. Reducing unnecessary broad-spectrum exposure may contribute to better individual tolerability and to antimicrobial-resistance mitigation over time. Nevertheless, the current dataset captures only total broad-spectrum days; it does not distinguish agents, dosage, appropriateness, route changes, discharge prescriptions, or specific resistance-selection events. The exploratory C. difficile endpoint was uncommon and its uncertainty interval was wide. It would therefore be unjustified to infer prevention of adverse antimicrobial effects or resistant infections from these measurements alone.

The apparent absence of a statistically demonstrable mortality or length-of-stay benefit is equally important. Previous meta-analyses have suggested better survival or shorter hospitalization when rapid diagnostics are coupled with stewardship, while controlled studies have shown heterogeneity across settings [4–5,21–23]. In the current cohort, a high proportion of both groups already received effective antibiotics at the index draw, leaving less opportunity for any diagnostic intervention to change survival. Severe baseline illness and non-antimicrobial determinants of hospitalization—organ dysfunction, source control, rehabilitation, and discharge logistics—could obscure benefits of faster treatment optimization. The 30-day mortality estimate (aOR 0.70) was compatible with benefit, little effect, or residual confounding, and cannot establish either superiority or equivalence. Likewise, the 95% confidence interval for adjusted post-draw stay spanned a modest reduction through almost no difference.

This analysis has several strengths. The cohort contains complete baseline severity measures, explicit separation of microbiologic eligibility from observed de-escalation, both inpatient and 30-day mortality, and standardized blood-draw–anchored process intervals. Including eight hospital indicators reduces confounding by measured between-centre differences. We also avoided inflating event rates by coding ineligible patients as de-escalation failures, and we distinguished time to effective therapy among initially inactive regimens from those already treated effectively. The consistency of the early-de-escalation association across hospitals and ICU strata supports its descriptive robustness, albeit without eliminating selection bias.

Several limitations restrict causal interpretation and readiness for external validation. Although the study was conducted from January to December 2023, the analytic dataset lacked individual calendar dates, screening logs, detailed recruitment criteria, molecular assay platform specifications, shift-level testing availability, and descriptions of individual stewardship interventions. The denominator of all potentially eligible bloodstream-infection encounters cannot therefore be reconstructed. There is no source-level ascertainment record for culture contaminants, repeat episodes, polymicrobial infections, or missing patients. Hospital fixed effects address average site differences but not unmeasured within-site selection; HC3 confidence intervals do not substitute for small-cluster causal inference. Conditioning de-escalation time on patients who experienced the event creates selection issues, and discharge or inpatient death may compete with de-escalation. Only 45 in-hospital deaths, 57 deaths within 30 days, and 20 C. difficile events limited precision for clinical endpoints. Because the recorded hospital-stay endpoint ends at inpatient death as well as discharge, a shorter stay is not automatically favourable. Independent validation of source data, variable coding, and the prespecified analysis protocol would further strengthen the interpretation of these observational results.

For stewardship teams, the implementation implication is to measure an entire sequence of events rather than the time taken by the analyser alone. A result that is issued rapidly but awaits clinical review may provide little patient-level value; conversely, a conventional result that prompts immediate expert review may still allow appropriate adjustment. In this cohort the median interval between actionable reporting and stewardship review was short in each pathway, suggesting that the differential arose primarily from earlier microbiological reporting. A reproducible quality-improvement programme could audit time to specimen collection, positivity, identification, interpretation, recommended change, prescription modification, and administration of the revised regimen. It could also record the proportion of recommendations accepted and the explicit reasons for deferral. These process measures would help distinguish successful de-escalation from inappropriate early narrowing and identify whether benefit is sustained overnight and on weekends.

The two mortality metrics also require separate interpretation. In-hospital mortality depends partly on

discharge practice and therefore cannot substitute for the more complete 30-day follow-up recorded here. Nevertheless, even 30-day all-cause mortality may be insensitive to benefits confined to a minority who lack active empirical therapy. Treatment effects could differ substantially for resistant Gram-negative organisms, methicillin-resistant staphylococci, or enterococci, but the available sample was not designed to estimate those pathogen-specific interactions reliably. Organism-level testing, a prespecified analytic protocol, and external replication would be preferable to post hoc subgroup claims.

Future prospective research should standardize the intervention as a test-and-action pathway, specify molecular platforms and resistance targets, and measure time from culture positivity to verified clinician action. Explicit documentation of clinician recommendations and acceptance, inappropriate narrowing, antimicrobial adverse effects, infection source, and pathogen-specific susceptibility would improve interpretability. Where feasible, random or quasi-random assignment of rapid-testing availability at the hospital or ward level could reduce confounding. Pragmatic trials powered for patient-important outcomes are required to determine whether the consistently observed process improvement produces durable reductions in mortality, resistant infections, hospital occupancy, or cost.

Conclusion

In this January–December 2023 multicentre U.S. cohort, rapid molecular bloodstream-infection testing linked to antimicrobial stewardship was associated with substantially earlier antibiotic de-escalation and less broad-spectrum exposure than conventional testing with stewardship. Hospital length of stay and mortality did not differ significantly after adjustment. These findings support faster diagnostic-to-treatment workflows while highlighting that clinical-outcome benefits remain uncertain in a nonrandomized observational study. Future research should validate these associations and clarify the contributions of specific molecular platforms and implementation pathways.

Declarations

Ethics approval: Ethical approval was obtained from the relevant institutional ethics review bodies. The analytic records were de-identified, and participating hospitals are not identified by name.

Table 1. Baseline characteristics by planned diagnostic pathway.

Baseline characteristic	Conventional (n=211)	Rapid molecular (n=269)
Age, years, median (IQR)	54 (34–70)	52 (33–71)
Male sex, n (%)	114/211 (54.0%)	132/269 (49.1%)
Charlson index, median (IQR)	1 (0–2)	1 (0–2)
ICU at index, n (%)	37/211 (17.5%)	98/269 (36.4%)
SOFA score, median (IQR)	3 (1–4)	4 (2–6)
Multidrug-resistant isolate, n (%)	60/211 (28.4%)	74/269 (27.5%)
Effective empirical treatment, n (%)	160/211 (75.8%)	209/269 (77.7%)
De-escalation eligible, n (%)	179/211 (84.8%)	237/269 (88.1%)
Escherichia coli isolate, n (%)	41 (19.4%)	46 (17.1%)
Klebsiella pneumoniae isolate, n (%)	48 (22.7%)	53 (19.7%)
Acinetobacter baumannii isolate, n (%)	0 (0.0%)	0 (0.0%)
Pseudomonas aeruginosa isolate, n (%)	34 (16.1%)	53 (19.7%)
Staphylococcus aureus isolate, n (%)	45 (21.3%)	54 (20.1%)
Enterococcus faecium isolate, n (%)	43 (20.4%)	63 (23.4%)

IQR, interquartile range; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment. Characteristics are descriptive; exposure was not randomized.

Table 2. Diagnostic reporting, stewardship response, and treatment timing: median (IQR).

Process interval from blood draw	Conventional (n=211)	Rapid molecular (n=269)
Blood-culture positivity, h	14.6 (11.5–18.2)	15.4 (12.7–18.7)
Actionable identification/resistance, h	57.6 (49.3–68.8)	18.5 (15.9–21.6)
Stewardship review, h	62.9 (53.7–72.5)	20.5 (17.7–23.9)
Time to effective therapy if initially inactive, h	62.6 (54.1–72.3)	22.5 (19.6–25.7)
Time to de-escalation among observed events, h	82.5 (72.8–96.7)	29.3 (25.4–35.3)

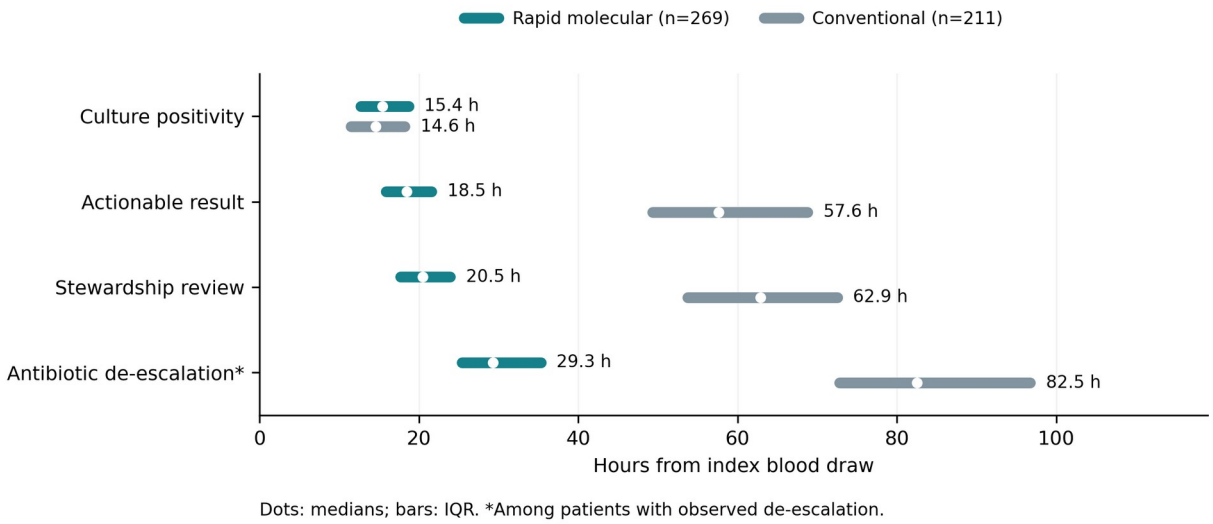
For initially inactive empirical therapy, n=51 conventional and n=60 rapid molecular. For observed de-escalation, n=106 conventional and n=174 rapid molecular. Conditional event-time summaries are descriptive and subject to selection by the occurrence of de-escalation.

Table 3. Treatment and clinical outcomes with adjusted pathway associations.

Outcome	Conventional	Rapid molecular	Adjusted ratio (95% CI)	P value
De-escalation ≤72 h among eligible	25/179 (14.0%)	173/237 (73.0%)	aOR 21.11 (11.71–38.04)	<0.001
Any de-escalation among eligible	106/179 (59.2%)	174/237 (73.4%)	aOR 2.01 (1.29–3.15)	0.002
Broad-spectrum antibiotic days, median (IQR)	7.0 (5.0–9.0)	6.0 (5.0–8.0)	aMR 0.86 (0.80–0.92)	<0.001
Post-draw hospital stay, days, median (IQR)	12.2 (8.4–17.4)	11.7 (8.1–16.1)	aMR 0.92 (0.84–1.02)	0.101
In-hospital death	20/211 (9.5%)	25/269 (9.3%)	aOR 0.70 (0.34–1.45)	0.333
All-cause death by 30 days	26/211 (12.3%)	31/269 (11.5%)	aOR 0.70 (0.36–1.35)	0.282
C. difficile infection by 30 days	11/211 (5.2%)	9/269 (3.3%)	aOR 0.86 (0.32–2.33)	0.768

aOR, adjusted odds ratio; aMR, adjusted mean ratio; CI, confidence interval. All models adjust for age, sex, Charlson index, ICU, SOFA, multidrug resistance, effective empirical therapy, and hospital fixed effects; HC3 robust standard errors. No adjusted estimate should be interpreted as a causal effect.

Figure 1. Time from index blood draw to key microbiology and treatment milestones by pathway.



Dots: medians; bars: IQR. *Among patients with observed de-escalation.

Figure 2. Adjusted associations between diagnostic pathway and stewardship/clinical outcomes.

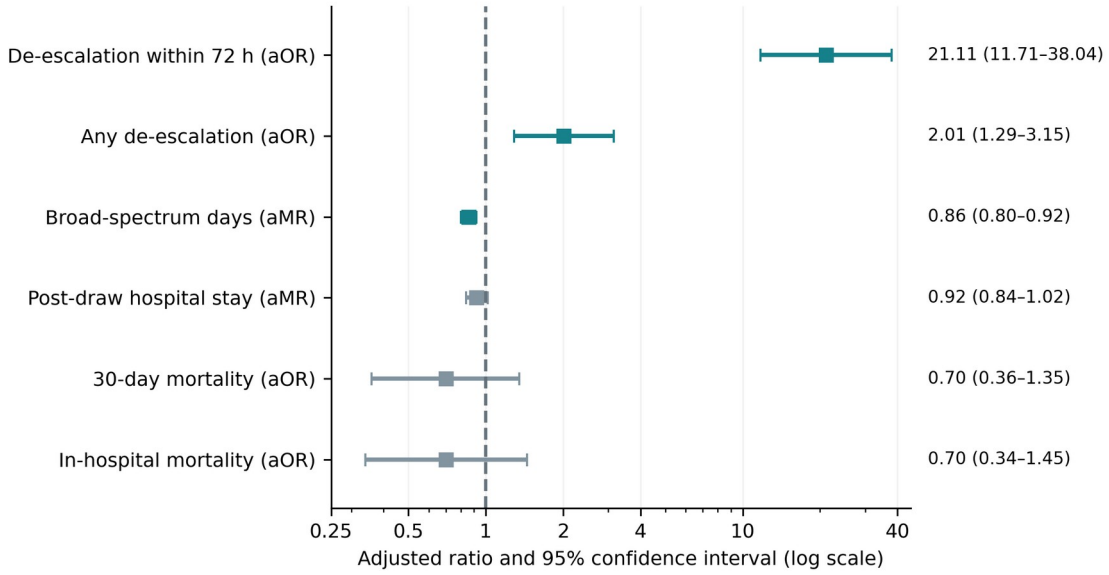


Figure 2: aOR, adjusted odds ratio for binary outcomes; aMR, adjusted mean ratio for continuous outcomes. Ratios above 1 favour rapid testing only for desirable de-escalation events; ratios below 1 favour rapid testing for adverse outcomes or longer exposure. Vertical dashed reference line = no association. All models include baseline covariates and hospital indicators.

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