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Content: Summary by the GPT 5 model of use.ai (<https://use.ai/chat>) of the published trials of rapid vs. standard AST for management of BSI (bloodstream infection).

Query:

The six papers below summarize prospective trials in which the impact on outcomes in patients with bloodstream infections was compared when antimicrobial therapy was adjusted as needed based on results from rapid antimicrobial susceptibility (AST) methods vs. standard AST methods. Please access the papers and review the abstract for each. Please also search for (and list for me) any editorial commentaries published in association with any of the papers. Based on this review, please summarize the strengths and limitations of these studies.

- 1) Banerjee R, Teng CB, Cunningham SA, et al. Randomized trial of rapid multiplex polymerase chain reaction-based blood culture identification and susceptibility testing. *Clin Infect Dis*. **2015**;61(7): 1071-1080. doi:10.1093/cid/civ447
- 2) Beuving J, Wolffs PF, Hansen WL, et al. Impact of same-day antibiotic susceptibility testing on time to appropriate antibiotic treatment of patients with bacteraemia: a randomised controlled trial. *Eur J Clin Microbiol Infect Dis*. **2015**;34(4):831-838. doi: 10.1007/s10096-014-2299-0
- 3) Banerjee R, Komarow L, Virk A, et al. Randomized trial evaluating clinical impact of RAPid IDentification and Susceptibility testing for Gram Negative bacteremia (RAPIDS-GN). *Clin Infect Dis*. **2021**;73(1):e39-e46. doi:10.1093/cid/ciaa528
- 4) Kim JH, Kim I, Kang CK, et al. Enhanced antimicrobial stewardship based on rapid phenotypic antimicrobial susceptibility testing for bacteraemia in patients with haematological malignancies: a randomized controlled trial. *Clin Microbiol Infect*. **2021**;27(1):69-75. doi:10.1016/j.cmi.2020.03.038
- 5) Caspar Y, Deves A, Richarme C, et al. Clinical impact and cost-consequence analysis of ePlex blood culture identification panels for the rapid diagnosis of bloodstream infections: a single-center randomized controlled trial. *Eur J Clin Microbiol Infect Dis*. **2024**;43(6):1193-1203. doi:10.1007/s10096-024-04820-z
- 6) Banerjee R, Komarow L, Li Y, Mau D, Dodd A, Geres H, et al. Fast Antimicrobial Susceptibility Testing for Gram-Negative Bacteremia: The FAST Randomized Clinical Trial. *JAMA*. **2026**. doi:10.1001/jama.2026.5487

Result:

Below is a structured synthesis based on the abstracts and linked material for the six randomized trials you listed, plus the associated commentaries/editorials that are explicitly tied to them.

1) Banerjee et al., Clin Infect Dis 2015 (civ447)

Design / intervention (from abstract)

- Single-center, prospective RCT of **rapid multiplex PCR (rmPCR)** from positive blood culture bottles vs standard blood culture processing.
- 3 arms:
 1. **Standard care** (culture-based ID/AST)
 2. **rmPCR + templated comments**
 3. **rmPCR + templated comments + real-time antimicrobial stewardship (AS) audit/feedback**
- Primary outcome: **duration of antimicrobial therapy**.
- Secondary: time to de-escalation/escalation, LOS, mortality, cost.

Key results (abstract)

- rmPCR markedly shortened time to organism ID (1.3 h vs 22.3 h).
- Both intervention arms had **less piperacillin–tazobactam use, more narrow-spectrum β -lactam use, and less treatment of contaminants** than control.
- The rmPCR/AS arm had the **fastest de-escalation and escalation**.
- **No differences** in mortality, LOS, or cost.

Associated commentary / “Comment in”

On PubMed and the journal page, this trial has several linked commentaries:

1. **Editorial commentary (directly linked to this trial)**
 - *Caliendo AM.*
 - **Title:** “Editorial Commentary: Rapid Blood Culture Identification: The Value of a Randomized Trial.”
 - **Journal:** Clin Infect Dis. 2015;61(7):1081–1083. doi:10.1093/cid/civ450.
2. **Letter and reply (discussion of methodology/implications)**
 - *Idelevich EA, Becker K.*
 - **Title:** “Identification and Susceptibility Testing From Shortly Incubated Cultures Accelerate Blood Culture Diagnostics at No Cost.”
 - **Journal:** Clin Infect Dis. 2016;62(2):268–269. doi:10.1093/cid/civ824.
 - *Banerjee R, Teng CB, Cunningham SA, et al.*
 - **Title:** “Reply to Idelevich and Becker.”
 - **Journal:** Clin Infect Dis. 2016;62(2):269–270. doi:10.1093/cid/civ826.

These are all explicitly linked under “Comment in”/related content to the 2015 Banerjee RCT.

2) Beuving et al., Eur J Clin Microbiol Infect Dis 2015 (s10096-014-2299-0)

Design / intervention (from abstract)

- Single-center RCT comparing **same-day “FAST” ID/AST** (PCR + 6-h growth in presence/absence of antibiotics) vs **standard BD Phoenix** system.
- Included patients with blood cultures growing staphylococci, streptococci, enterococci, or Gram-negative rods.
- Primary aim: reduction in **inappropriate antibiotic therapy** via earlier results.

Key results (abstract)

- FAST results were **highly accurate** (~94% agreement with standard).
- Time to results was **15.6 h faster** with FAST ($p < 0.001$).
- At the time standard results became available, significantly **fewer patients were on inappropriate therapy** in the FAST arm ($p = 0.025$).
- However, **FAST results were implemented in only a minority of patients** (16/129).
- **No demonstrable benefit on clinical outcomes.**

Associated commentary/editorial

- The PubMed record does **not show any “Comment in,” editorial, or linked commentary** specific to this RCT.
- No journal-linked editorial was evident from the abstract page.

3) Banerjee et al., RAPIDS-GN, Clin Infect Dis 2021 (ciaa528)

Design / intervention (from abstract)

- **Multicenter RCT** in patients with Gram-negative bacilli bloodstream infection (GNB BSI).
- Randomized to:
 - **Standard-of-care (SOC) culture + AST with antimicrobial stewardship (AS)** vs
 - **Accelerate Pheno System (rapid ID + rapid phenotypic AST) + AS (RAPID).**
- Primary outcome: **time to first antibiotic modification within 72 h.**

Key results (abstract)

- Rapid system vs SOC:
 - ID results: **2.7 vs 11.7 h**, AST: **13.5 vs 44.9 h** (both $p < 0.001$).
 - **Time to first antibiotic modification** shorter overall and for Gram-negative agents.
 - Faster escalation in resistant BSIs in the RAPID arm.
- **No difference in patient-level outcomes** (mortality, LOS, etc.).

Associated commentary/editorial

- PubMed and the (partially inaccessible) journal page for this article do **not list a dedicated editorial or “Comment in”** directly associated with RAPIDS-GN.
- RAPIDS-GN is frequently discussed in review articles and summaries, but not with a formal linked editorial analogous to the 2015 Banerjee trial or the JAMA FAST trial.

4) Kim et al., Clin Microbiol Infect 2021 (j.cmi.2020.03.038)

Design / intervention (from abstract)

- **Randomized controlled trial** in patients with hematologic malignancies and at least one positive blood culture.
- 1:1 randomization to **conventional AST vs rapid phenotypic AST** (microscopic imaging-based) with an antimicrobial stewardship program.
- Primary outcome: **proportion receiving optimal targeted antibiotics 72 h after blood collection.**

Key results (abstract)

- Optimal targeted therapy at 72 h:
 - **80.4%** in rapid phenotypic AST vs **56.7%** in conventional (RR 1.42; 95% CI 1.09–1.83).
- Lower proportion receiving **unnecessary broad-spectrum antibiotics** at 72 h in rapid group.
- **Shorter time to optimal targeted therapy** (38.1 vs 72.8 h) and **shorter time from blood draw to AST result** (48.3 vs 83.1 h).
- Conclusion: rapid phenotypic AST-based stewardship **improves optimization** of therapy in this high-risk group.

Associated commentary/editorial

- PubMed listing shows this as a free article but **does not list an associated editorial, comment, or “Comment in” item.**
- No linked editorial on the JCMI publisher page was captured in the extraction.

5) Caspar et al., Eur J Clin Microbiol Infect Dis 2024 (s10096-024-04820-z)

Design / intervention (from abstract)

- **Single-center RCT** at a French university hospital with an established stewardship program.
- Compared **broad multiplex PCR blood culture identification panels (ePlex)** vs **standard-of-care (SoC) microbiology** for bloodstream infection.
- **Primary endpoint:** proportion of patients with **optimized antimicrobial treatment 12 h** after transmission of positivity + Gram stain results for first positive blood culture.
- Included a **cost-consequence analysis.**

Key results (abstract)

- At interim analysis (309 patients), **optimized treatment at 12 h** was higher in the multiplex PCR group:
 - 85.7% (90/105) vs 63.6% (68/107), $p < 0.001$.
- For those not optimized at baseline, **time to optimization** was much shorter in the multiplex PCR arm.
- The magnitude of benefit led to **early termination at interim analysis.**
- Cost-consequence details are summarized in the full text but not fully in the abstract.

Associated commentary/editorial

- PubMed lists an **erratum/correction**, but **no editorial or commentary:**
 - **Correction:** “Correction to: Clinical impact and cost-consequence analysis of ePlex® blood culture identification panels...”
 - Eur J Clin Microbiol Infect Dis. 2024 Nov;43(11):2245–2246. doi:10.1007/s10096-024-04924-6.
- No linked editorial commentary is indicated.

6) Banerjee et al., FAST Randomized Clinical Trial, JAMA 2026 (10.1001/jama.2026.5487)

Design / intervention (from abstract)

- **Multinational, open-label RCT** at 7 centers in Greece, India, Israel, and Spain (high AMR settings).

- Hospitalized adults and children with Gram-negative BSIs.
- Randomized to:
 - **Rapid phenotypic AST directly from positive blood cultures + standard AST vs**
 - **Standard AST alone.**
- Local AS teams provided recommendations in both groups.
- Primary outcome: **desirability-of-outcome ranking** at day 30 (composite clinical outcome, superiority framework).

Key findings (abstract summary)

- 850 patients randomized.
- Rapid AST significantly shortened time to susceptibility results and antibiotic modification (details in full article).
- **Probability of a more desirable outcome at day 30** with rapid AST was **48.8%** vs standard, which **did not meet the prespecified superiority threshold.**
- Interpretation: rapid AST **improved process-of-care metrics** but **did not achieve superiority in the primary clinical outcome.**

Associated editorial/commentary (explicitly linked)

1. **JAMA editorial (directly associated)**
 - *Srinivasan A.*
 - **Title:** “A Multinational Trial of Rapid Antimicrobial Susceptibility Testing.”
 - **Journal:** JAMA. 2026; associated with the same issue as the FAST trial.
 - Accessible via “Editorial” / “Editorial Comments” links on the article page.
2. **Research summary (JAMA Network feature, not an editorial per se but an associated synopsis)**
 - **Title:** “Fast Antimicrobial Susceptibility Testing for Gram-Negative Bacteremia: Research Summary.”
 - JAMA Network, same issue.

Summary of Editorial/Commentary Landscape

- **Articles with clearly identified, formal editorials/commentaries:**
 - **Banerjee et al., Clin Infect Dis 2015 (rmPCR RCT):**
 - Editorial by Caliendo; plus methodological/interpretive letters by Idelevich & Becker and Banerjee et al. (reply).
 - **Banerjee et al., JAMA 2026 FAST trial:**
 - JAMA editorial by Arjun Srinivasan.
- **Articles without linked formal editorials (based on PubMed/journal abstract pages):**
 - Beuving 2015 RCT (same-day FAST AST).
 - Banerjee 2021 RAPIDS-GN.
 - Kim 2021 rapid phenotypic AST in hematologic malignancies.
 - Caspar 2024 ePlex RCT (has a correction but not an editorial).

Cross-study strengths

1. Prospective randomized designs

- All six are **prospective randomized controlled trials**, which is notably strong for diagnostic/AST interventions where before–after or quasi-experimental designs are more common.
- Multicenter designs (RAPIDS-GN, FAST) improve **external validity.**

2. Direct comparison of rapid vs standard AST/ID with real clinical endpoints or strong surrogates

- All trials compare **rapid molecular or phenotypic methods** to contemporaneous standard care, rather than to historical controls.
- They measure both **process outcomes** (time to ID/AST, time to therapy change, appropriateness of therapy) and at least some **patient-centered outcomes** (mortality, LOS, composite desirability outcomes).

3. Integration with antimicrobial stewardship programs

- Banerjee 2015, RAPIDS-GN, Kim 2021, Caspar 2024, and FAST all explicitly embed **antimicrobial stewardship** (often in both arms).

- This reflects **real-world implementation**, where rapid tests rarely stand alone; they require stewardship to influence prescribing.

4. Consistent demonstration of process-of-care benefits

Across studies, rapid approaches reliably:

- **Shorten time to organism ID and AST results.**
- **Increase proportion of patients on optimal or appropriate therapy** at prespecified time points (Beuving, Kim, Caspar).
- **Decrease broad-spectrum antibiotic exposure and reduce treatment of contaminants** (Banerjee 2015).
- **Speed antibiotic de-escalation and escalation**, especially in resistant infections (RAPIDS-GN, Banerjee 2015).

This consistency strengthens the conclusion that *rapid AST/ID + stewardship improves antimicrobial optimization metrics*.

5. Heterogeneous settings and populations

- **High-risk immunocompromised** (hematologic malignancies; Kim 2021).
 - **General adult inpatients with BSIs** (Beuving, Banerjee 2015, RAPIDS-GN, Caspar, FAST).
 - **Multinational, high-AMR settings** (FAST).
- This diversity supports **generalizability across clinical contexts**, though not uniformly.

6. Economic/cost considerations

- Caspar 2024 formally includes a **cost-consequence analysis**.
 - Banerjee 2015 includes cost as a secondary outcome.
- While details vary, the inclusion of economics is a methodological strength for implementation decisions.

Cross-study limitations

1. Limited or absent improvement in “hard” clinical outcomes

- Several trials (Banerjee 2015, Beuving 2015, RAPIDS-GN 2021, FAST 2026) **did not show mortality, LOS, or composite clinical outcome benefits**, despite clear improvements in timing and appropriateness of therapy.
- This may reflect:
 - **Underpowering** for modest mortality differences.
 - Already **high baseline quality of care** and stewardship in control arms.
 - The fact that **many determinants of outcome (severity, source control, comorbidities)** may overshadow incremental benefits of faster AST.

2. Implementation and uptake challenges

- Beuving 2015 explicitly shows **poor implementation**: only a small fraction of FAST results were acted upon even though they were accurate and faster.
- Even when stewardship is in place, the **real-world response to rapid results can be slow or inconsistent**, diluting clinical impact.
- Some studies allowed significant clinician discretion, which can blunt measurable differences.

3. Composite or process-focused primary endpoints

- Several trials use **process outcomes** (time to optimal therapy, appropriateness at 72 h, optimization at 12 h) as primary endpoints, not “hard” outcomes.
- FAST uses a **composite desirability-of-outcome ranking**, which is more sophisticated but may be **less intuitive** and reduces power for any single concrete outcome.
- While these endpoints are mechanistically sound, they may **overstate clinical impact** if not accompanied by clear survival or LOS benefit.

4. Single-center studies and local practice patterns

- Beuving 2015 and Caspar 2024 are **single-center** European trials; Banerjee 2015 is single-center as well.
- Outcomes and effect sizes likely depend on:
 - Baseline **time to culture/AST** in the lab.
 - **Empiric therapy quality** before randomization.
 - **Local resistance epidemiology** and formulary constraints.
 This **limits generalizability** to settings with different baseline performance.

5. High stewardship and standard-of-care performance in control arms

- Many trials embed stewardship in **both** arms (RAPIDS-GN, FAST, Caspar, Kim), thereby raising the bar for detecting incremental benefit of rapid tests.
- If control arms already have **rapid review and aggressive optimization**, the net clinical benefit of speeding AST by several hours may be **difficult to detect**, even if microbiologically meaningful.

6. Potential contamination and open-label design

- Most (if not all) are **open-label**, and clinicians may be influenced by knowledge of assignment or by exposure to rapid-testing workflows even when not randomized to rapid testing (e.g., cross-contamination of practices between arms in a single lab/hospital).
- This risks **diluting between-arm differences**.

7. Sample size and power issues

- Early trials (Beuving 2015, Banerjee 2015, Kim 2021) have relatively **modest sample sizes** for detecting outcome differences such as mortality or LOS.
- Several trials appear powered primarily for differences in **time-to-event or appropriateness** rather than mortality, complicating interpretation of negative clinical outcomes.

8. Restricted organism/syndrome inclusion

- Some RCTs **exclude polymicrobial cultures** or certain organism groups or focus narrowly on GNB (RAPIDS-GN, FAST) or hematologic malignancy populations (Kim).
- This restricts applicability to other important BSI scenarios (e.g., complicated endocarditis, some anaerobic infections).

9. Evolving standard comparators and platforms

- Over the decade span from Banerjee 2015 to FAST 2026, **standard AST has also improved** (e.g., MALDI-TOF ID, faster conventional AST workflows).
- Some “rapid” differences (e.g., hours saved) may be **smaller now** than at the time early trials were designed, making the historical effect sizes less directly transferable.

Overall interpretation

Taken together, these RCTs show that:

- **Rapid molecular or phenotypic AST/ID, when integrated with stewardship, consistently improves the quality and timeliness of antibiotic decision-making** (more optimal therapy, less unnecessary broad-spectrum use, faster de-escalation/escalation).
- However, **translating those process gains into measurable improvements in mortality, LOS, or composite clinical outcomes has been difficult**, even in large, multinational trials like FAST.
- Implementation fidelity (how often clinicians actually act on rapid results), baseline empiric therapy quality, and robust stewardship in both arms likely **constrain the incremental clinical effect** that can be demonstrated in trials.
 - *Further build by John Rex: Also, access to adequate antibiotics may be limited ... if the needed antibiotic is not available, no action can be taken on the rapid diagnosis.*
- Editorials (Caliendo for the 2015 Banerjee RCT; Srinivasan for FAST) appropriately emphasize that **randomized evidence validates the process benefits** but highlight the **modest or absent impact on hard outcomes** and the importance of **system-level implementation and context** when interpreting these results and deciding whether to adopt rapid AST technologies.