



**CLINICAL MICROBIOLOGY
KRONOBERG AND BLEKINGE**
SWEDISH NRL FOR PHENOTYPIC AST
EUCAST DEVELOPMENT LABORATORY



**WHO Collaborating Centre
for Standardization of
Antimicrobial Susceptibility Testing**



EURL
PUBLIC HEALTH
ANTIMICROBIAL RESISTANCE (AMR)
IN BACTERIA

Scientific support for rapid diagnostics, with focus on rapid AST

NordicAST 2026, Malmö

Oskar Ekelund

Clinical microbiology Kronoberg/Blekinge

Växjö/Karlskrona, Sweden

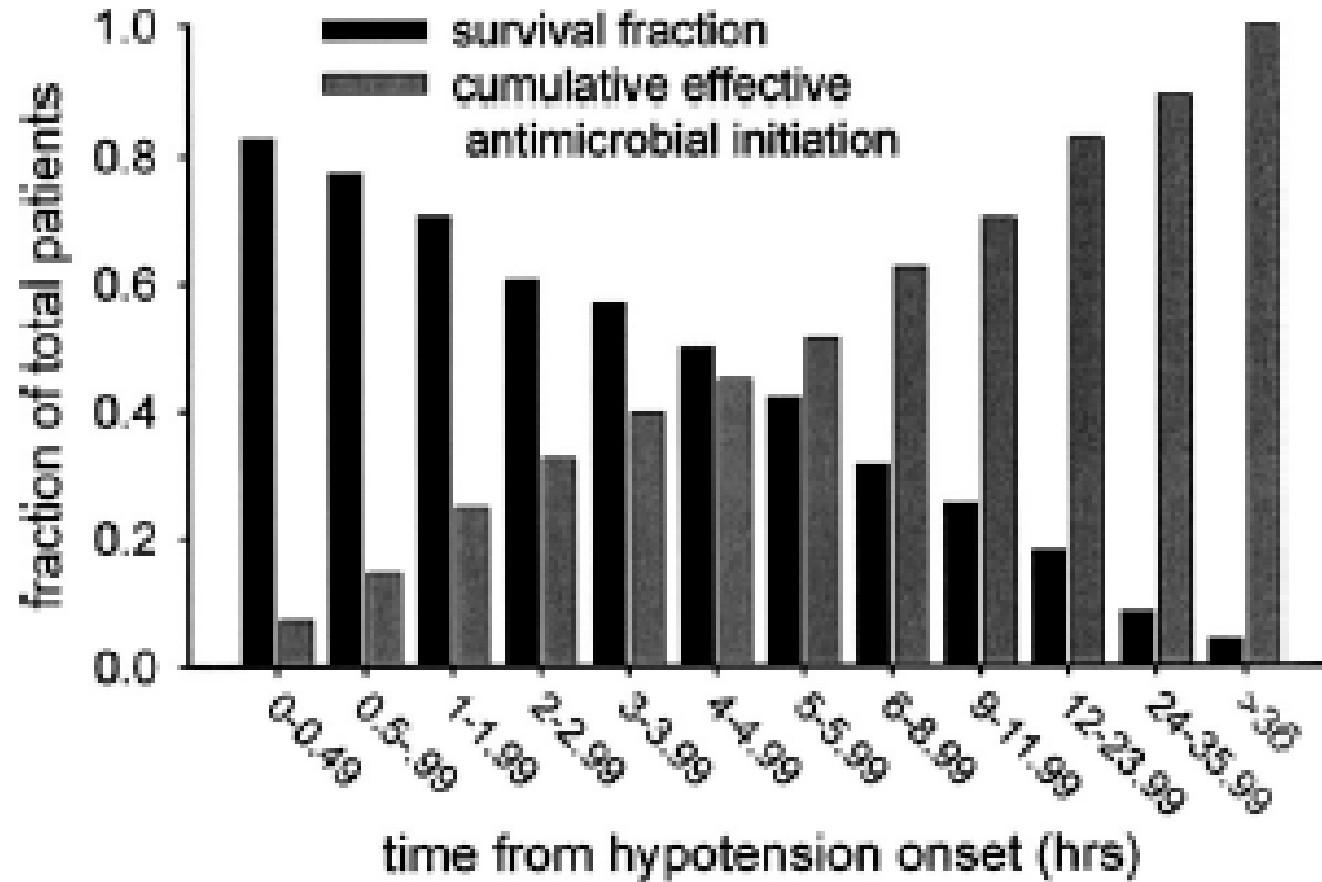
**No single diagnostic test will in itself
improve survival of patients**

Outline - the more comprehensive version

- How important is the time to adequate treatment in severe bacterial infections?
- The impact of rapid diagnostics on outcome in bloodstream infections
- The impact of rapid AST on outcome in bloodstream infections
- May access to rapid AST affect our choice of empirical therapy?

- Is rapid AST worth the effort?
- If so, when and how?

The need for early targeted therapy in sepsis



The need for early targeted therapy in sepsis

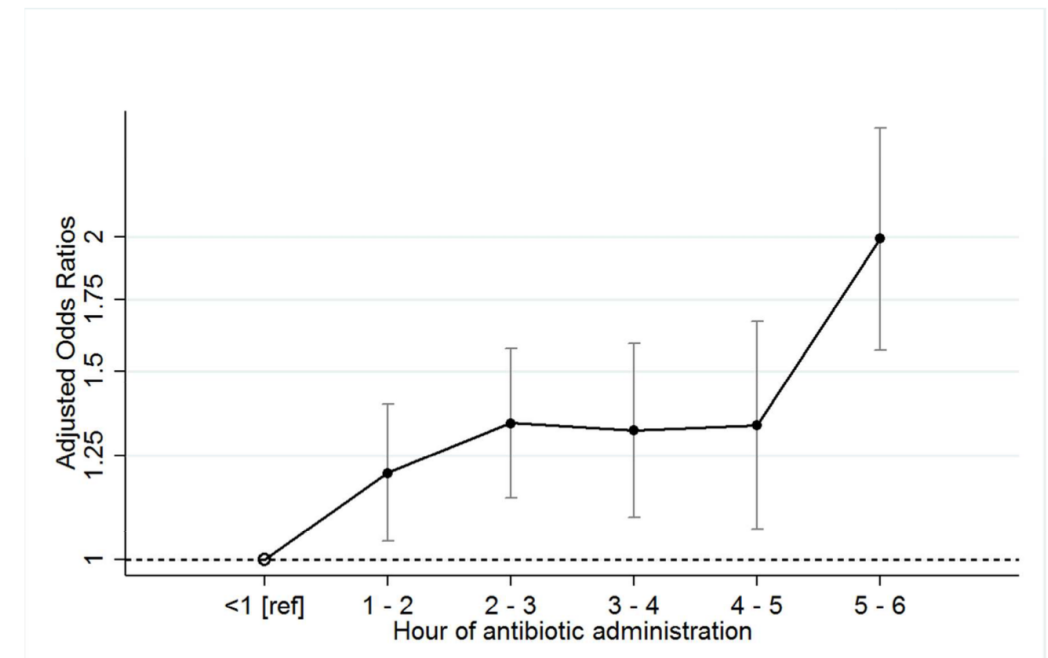
Retrospective study of 35 000 patients with septicemia, severe septicemia (n=18210) and septic shock (n=4 668) Absolute increase in mortality per hour delay:

0,3% septicemia

0,4% severe septicemia

1,8% septic shock

Figure 2. Adjusted odds ratios for hospital mortality comparing patients within each hourly antibiotic administration group with the reference group of patients given antibiotics in <1 hour. Y-axis is on logarithmic scale.



Association of Treatment at Bloodstream

Jasper Van Heuverswyn, ^{1,a}

Results. We found an association in favor of early treatment at landmark after bloodstream infection with an adjusted odds ratio 1.17 [95% confidence interval 1.01 - 1.37] in patients with high or low SOFA score.

Landmark time	Therapy		Risk of mortality	
	Inappropriate therapy Events (Episodes)	Appropriate therapy Events (Episodes)	Adjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Total cohort				
1 hour	750 (7022)	447 (3266)	0.83 (.72 - .95)	
3 hours	530 (4699)	631 (5346)	1.00 (.87 - 1.15)	
6 hours	392 (3404)	730 (6458)	1.05 (.91 - 1.22)	
12 hours	323 (2594)	752 (7129)	1.17 (1.01 - 1.37)	
24 hours	227 (1755)	776 (7837)	1.24 (1.04 - 1.47)	
48 hours	150 (1092)	784 (8461)	1.41 (1.15 - 1.74)	
72 hours	99 (657)	768 (8908)	1.67 (1.30 - 2.15)	
Low SOFA score				
1 hour	133 (2716)	49 (957)	0.90 (.63 - 1.29)	
3 hours	100 (1858)	79 (1721)	1.01 (.73 - 1.39)	
6 hours	78 (1374)	96 (2151)	1.06 (.76 - 1.46)	
12 hours	66 (1009)	108 (2479)	1.20 (.86 - 1.68)	
24 hours	43 (617)	120 (2823)	1.23 (.84 - 1.82)	
48 hours	33 (385)	124 (3064)	1.52 (.98 - 2.34)	
72 hours	18 (239)	129 (3230)	1.29 (.73 - 2.27)	
High SOFA score				
1 hour	617 (4306)	398 (2309)	0.81 (.70 - .95)	
3 hours	430 (2841)	552 (3625)	0.99 (.85 - 1.16)	
6 hours	314 (2030)	634 (4307)	1.05 (.89 - 1.24)	
12 hours	257 (1585)	644 (4650)	1.17 (.98 - 1.39)	
24 hours	184 (1138)	656 (5014)	1.24 (1.01 - 1.51)	
48 hours	117 (707)	660 (5397)	1.36 (1.07 - 1.73)	
72 hours	81 (418)	639 (5678)	1.78 (1.34 - 2.35)	

mortality was 11.8%. No association was found at the 1, 3 and 6 hours treatment (adjusted odds ratio 0.83, 1.00, 1.05 respectively). At 12, 24, 48 and 72 hours, an association in favor of early treatment was found (adjusted odds ratio 1.17, 1.24, 1.41, 1.67 respectively).

Mortality impact of further delays in active targeted antibiotic therapy in bacteraemic patients that did not receive initial active empiric treatment: results from the prospective, multicentre cohort PROBAC.



Sandra De la Rosa Riestra , Pedro María Martínez Pérez-Crespo ,
María Teresa Pérez Rodríguez , Adrián Sousa ,
Josune Goikoetxea , José María Reguera Iglesias ,
Carlos Armiñanzas , Inmaculada López-Hernández ,
Luis E. López-Cortés , Jesús Rodríguez-Baño , the PROBAC group

<u>Delay in active therapy</u>	<u>Adjusted OR for mortality</u>	<u>P value</u>
Day 3 or after	1.53	0.006
Day 4 or after	2.26	<0.001
Day 5 or after	4.33	<0.001
Day 6 or after	11.38	<0.001

We conclude that delayed administration of active targeted antibiotic treatment in patients is associated with a deleterious impact in the prognosis of patients; these results reinforce the importance of rapid reporting of blood culture results and of specialized advice in the management of BSI.

DOI: <https://doi.org/10.1016/j.ijid.2024.107072>



**Time indeed seems to be of
importance**



**Can we shorten time to targeted
treatment and improve clinical outcome
by introducing rapid diagnostics?**



16 June 2025

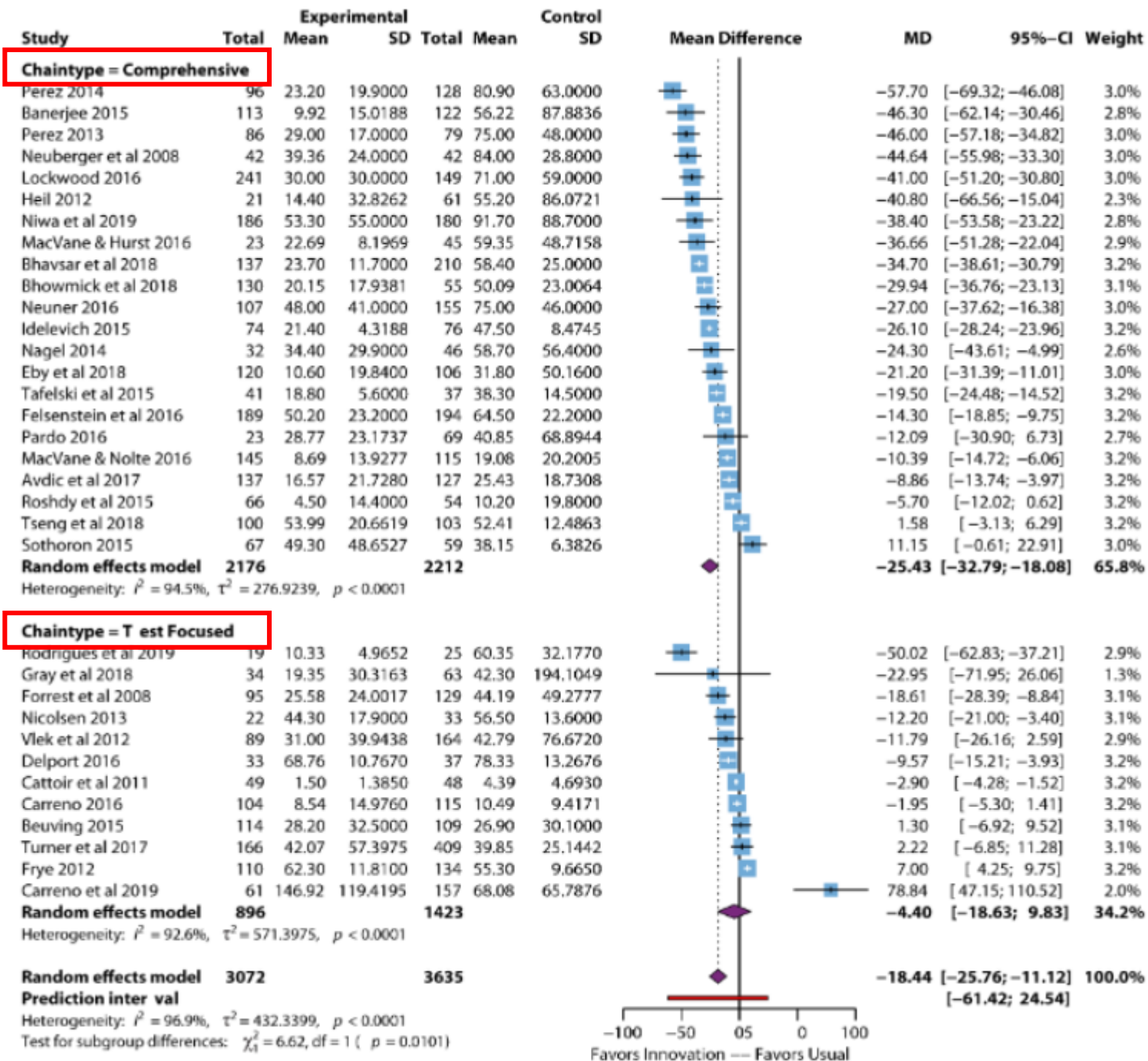
The American Society for Microbiology's evidence-based laboratory medicine practice guidelines for the diagnosis of bloodstream infections using rapid tests: a systematic review and meta-analysis

Donna M. Wolk,¹ J. Scott Parrott,² N. Esther Babady,³ A. Brian Mochon,^{4,5} Ryan Tom,⁶ Christen Diel,⁷ Jennifer Dien Bard,⁸ Amanda Harrington,⁹ D. Jane Hata,¹⁰ Amity L. Roberts,¹¹ Lindsay Boyce,¹² J. Kristie Johnson¹³

Endpoints:

1. Time to targeted therapy
2. Length of stay (total / ICU / infection-related)
3. Mortality

<https://doi.org/10.1128/cmr.00137-24>



Time to targeted therapy
 $\Delta - 18.4 \text{ h (} p < 0.001 \text{)}$

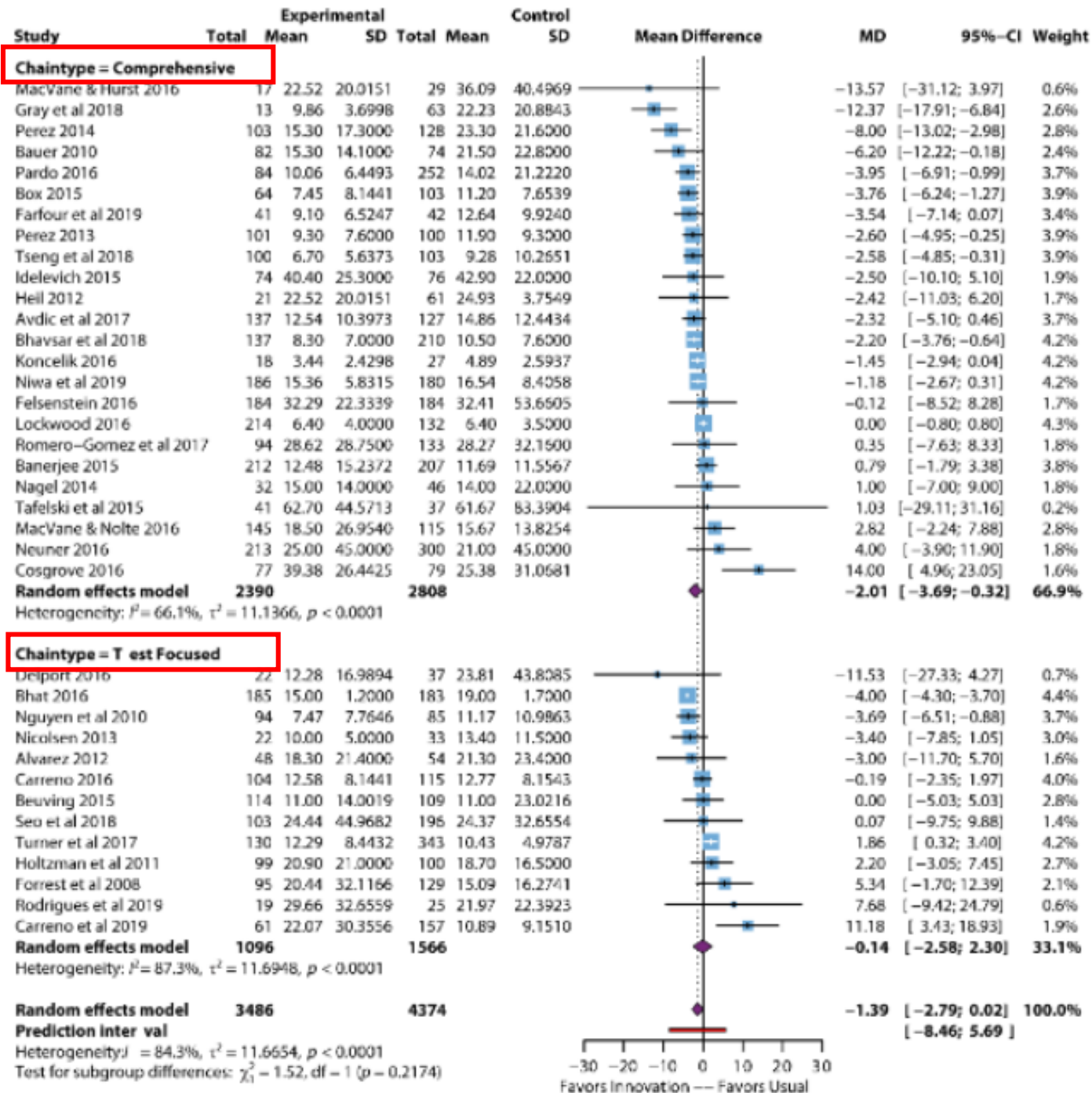
$\Delta - 25.4 \text{ h (} p < 0.001 \text{)}$

$\Delta - 4.4 \text{ h (n.s.)}$

TABLE 4 Characteristics of outlier studies for time to targeted therapy outcomes^a

Studies	Intervention chain type	Comments
Overperforming studies		
Banerjee et al. (48)	Comprehensive	Active antimicrobial stewardship program
Bhavsar et al. (55)	Comprehensive	Active antimicrobial stewardship program
Lockwood et al. (51)	Comprehensive	Active antimicrobial stewardship program
Neuberger et al. (50)	Comprehensive	Positive results were called to the physician
Perez et al. (49)	Comprehensive	Active antimicrobial stewardship program
Perez et al. (47)	Comprehensive	Active antimicrobial stewardship program
Rodrigues et al. (69)	Test focused	Active antimicrobial stewardship program in place before the intervention
Underperforming studies		
Beuving et al. (77)	Test focused	The test only resulted in changes in antibiotics in 12 patients.
Carreno et al. (76)	Test focused	Only septic patients were included. Inconsistent communication
Carreno et al. (46)	Test focused	No power calculations; low numbers
Cattoir et al. (75)	Test focused	No power calculations; small sample size
Frye et al. (79)	Test focused	Only positive intervention was called to the provider by the laboratory
Sothoron et al. (68)	Comprehensive	Most patients in both arms were placed on effective antibiotic(s) shortly after blood collection.
Tseng et al. (67)	Comprehensive	Changes were only made on Gram stain or AST.
Turner et al. (78)	Test focused	No active antimicrobial stewardship program

^aAdditional details are included in the Narrative Summary Table (Table S1).



Length of stay

1. Total n.s.
2. ICU n.s.

3. Infection-related
 $\Delta - 1.8$ d ($p < 0.001$),
 only if comprehensive
 approach

TABLE 5 Characteristics of outlier studies for length of stay outcomes^a

Studies	Intervention chain type	Comments
Hospital LOS		
Overperforming studies		
Bhat et al. (87)	Test-focused	This was a controlled interventional study in a pediatric patient population using a laboratory-developed test that <u>performed significantly better than the conventional microbiology methods.</u>
Rivard et al. (92)	Comprehensive	The molecular result triggered <u>a real-time electronic message to the antimicrobial stewardship team.</u>
Underperforming studies		
Carreno et al. (46)	Comprehensive	The antimicrobial stewardship team received reports of molecular results twice daily (8 a.m. and 1 p.m.). They saw improved clinical response times but no LOS, TTT, or mortality change. The authors believe <u>the intervention group was more complex than the comparator group.</u>
Cosgrove et al. (86)	Comprehensive	This was a controlled interventional study. The authors <u>shortened the manufacturer’s test protocol by 60 minutes</u> but saw no impact on LOS.
Gray et al. (70)	Comprehensive	The study saw no difference in the LOS, but they did see a significant decrease in the LOS, though in the ICU setting. <u>Testing was performed on <i>Enterococcus</i> species only.</u>
Turner et al. (78)	Test-focused	In the <u>absence of an antimicrobial stewardship program</u> , the use of molecular testing alone did not impact the LOS. However, the study was not powered enough to evaluate LOS properly.

Recommendations for the use of rapid diagnostic tests to decrease TTT

Recommendation 1

To decrease TTT in patients with a positive blood culture, the panel recommends that clinical laboratories implement rapid diagnostics (Evidence quality: Moderate; Recommendation strength: Strong) in combination with a comprehensive plan to actively communicate the actionable test result(s) (Evidence quality: Strong; Recommendation strength: Strong).

Remarks

The panel does NOT recommend using rapid diagnostics tests alone, without active communication, to improve TTT.

**Do these results also apply to rapid
AST?**

[Intervention Review]

Rapid versus standard antimicrobial susceptibility testing to guide treatment of bloodstream infection

Vanessa Anton-Vazquez¹, Paul Hine², Sanjeev Krishna¹, Marty Chaplin², Timothy Planche³

¹Institute of Infection and Immunity, St George's University of London, London, UK. ²Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK. ³Medical Microbiology Department, SouthWest London Pathology, Jenner Wing St George's Hospital, London, UK

Main results

We included six trials, with 1638 participants. For rapid antimicrobial susceptibility testing compared to conventional methods, there was little or no difference in mortality between groups (RR 1.10, 95% CI 0.82 to 1.46; 6 RCTs, 1638 participants; low-certainty evidence). In subgroup analysis, for rapid genotypic or molecular antimicrobial susceptibility testing compared to conventional methods, there was little or no difference in mortality between groups (RR 1.02, 95% CI 0.69 to 1.49; 4 RCTs, 1074 participants; low-certainty evidence). For phenotypic rapid susceptibility testing compared to conventional methods, there was little or no difference in mortality between groups (RR 1.37, 95% CI 0.80 to 2.35; 2 RCTs, 564 participants; low-certainty evidence).

Authors' conclusions

The theoretical benefits of rapid susceptibility testing have not been demonstrated to directly improve mortality, time-to-discharge, or time-to-appropriate antibiotic in these randomized studies. Future large prospective studies should be designed to focus on the most clinically meaningful outcomes, and aim to optimize blood culture pathways.

A closer look at the Cochrane metaanalysis

- 4 of 6 trials focused on targeted genotypic testing in Gram-

We need trials on rapid AST in bloodstream infections

- 1) due to Gram-negative pathogens
- 2) in areas where resistance rates are significant
- 3) in combination with functioning AMS programs

- **Rapid species ID + rapid AST + AMS program: *"...may have played a role in reducing time-to-appropriate antibiotics..."***

Fast Antimicrobial Susceptibility Testing for Gram-Negative Bacteremia

The FAST Randomized Clinical Trial

Ritu Banerjee, MD, PhD; Lauren Komarow, MS; Yixuan Li, PhD, MS; Donald Mau, MLA; Andrew Dodd, MS; Holly Geres, BS; Kerryl Greenwood-Quaintance, EdD; Amos Adler, MD; Shrikala Baliga, MD; Michal Chowers, MD; George Chrysos, MD; Olympia Zarkotou, MD, PhD; Mical Paul, MD; Spyros Pournaras, MD, PhD; Dolores Sousa Regueiro, MD; Scott Evans, MS, PhD; Henry Chambers, MD; Vance G. Fowler Jr, MD, MHS; Robin Patel, MD; for the Antibacterial Resistance Leadership Group

JAMA. doi:10.1001/jama.2026.5487

Published online April 18, 2026.

Seven medical centres in countries with a high prevalence of resistance, 18 months:

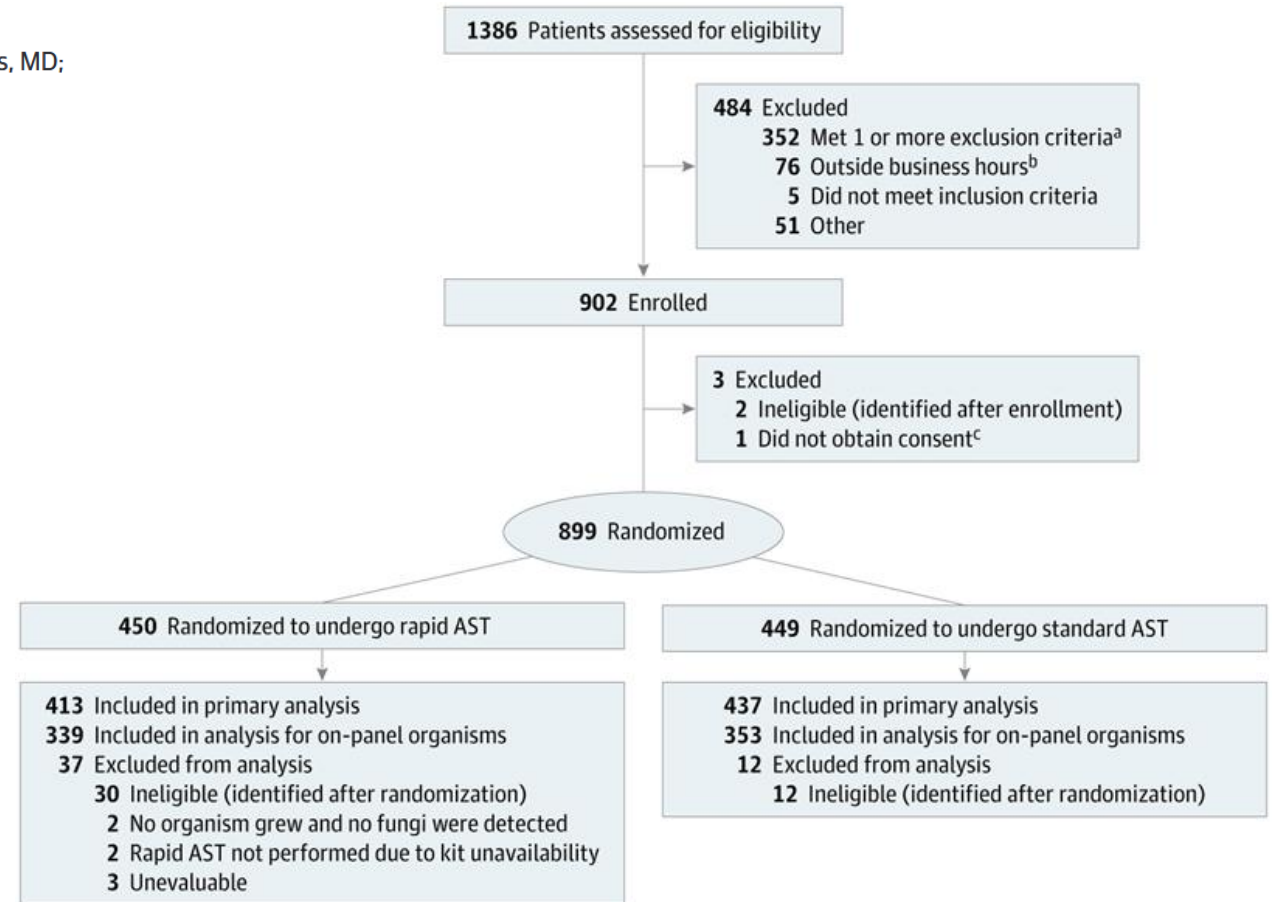
Spain	(n=1)
Greece	(n=3)
India	(n=1)
Israel	(n=2)

Intervention:

Introduction on VITEK Reveal rapid AST

Primary endpoint:

Desirability of outcome ranking (DOOR) at day 30 after randomization



QUESTION Does rapid antimicrobial susceptibility testing (AST) improve clinical outcomes compared with standard AST among individuals with bloodstream infections caused by gram-negative bacilli (GNB)?

CONCLUSION Rapid blood culture AST for GNB was not superior to standard AST in achieving a more desirable outcome among patients with bloodstream infections, but the subgroup with carbapenem-resistant infections had a greater proportion discharged at 30 days.

POPULATION

486 Males
364 Females



Patients of any age with GNB in blood cultures and hospitalized at the time of the blood culture result

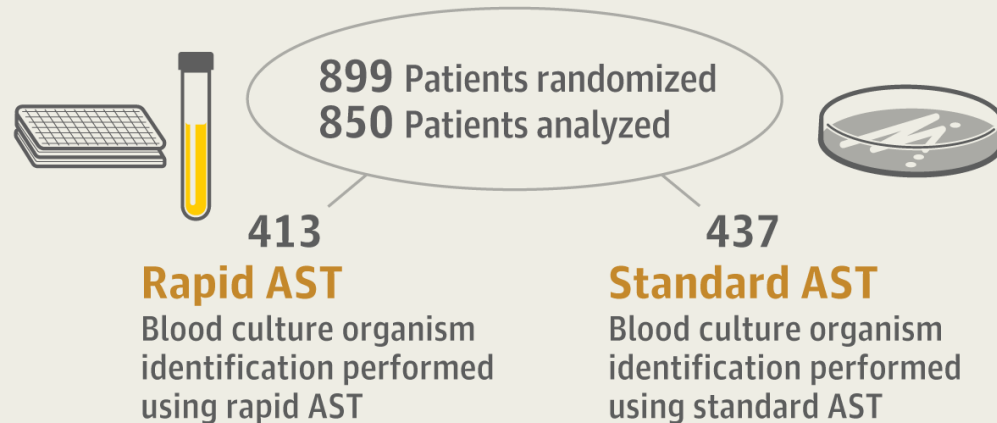
Median age: 72 years

LOCATIONS

7
Medical centers
worldwide



INTERVENTION



PRIMARY OUTCOME

Desirability of outcome ranking (DOOR), the probability that a patient in the rapid AST group would achieve a more desirable outcome than a patient in the standard AST group, at day 30; superiority was concluded if the lower limit of the 95% CI exceeded 50%

FINDINGS

Patients alive at 30 days

	Rapid AST	Standard AST
Alive without deleterious events	47%	49%
Alive with ≥ 1 deleterious events	28%	28%

Rapid AST did not demonstrate superiority over standard AST:

DOOR probability, **48.8%**
(95% CI, 45.3% to 52.4%)

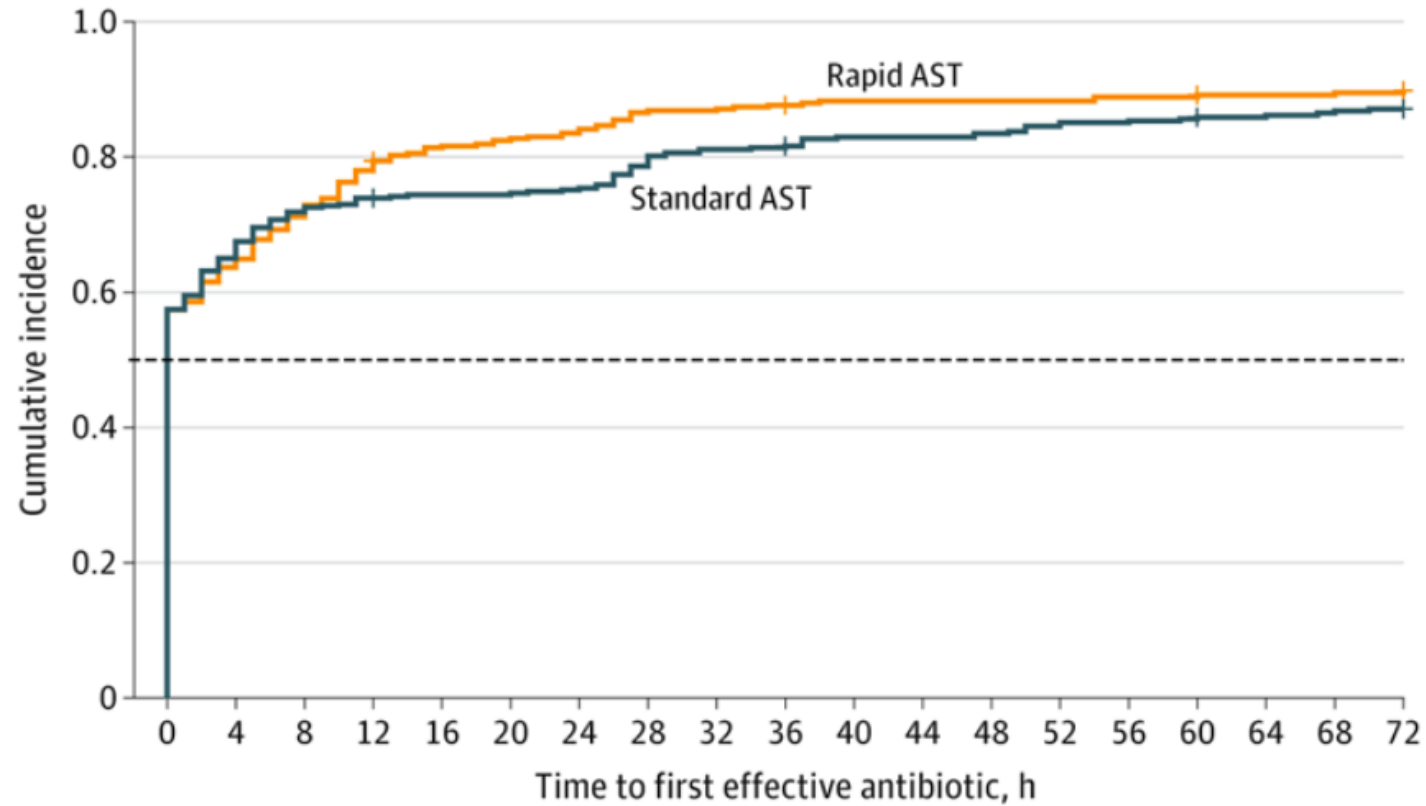
eTable 4. Antibiotics administered within three days of randomization by country, as randomized population

Antibiotic	Greece (N=406)	India (N=91)	Israel (N=291)	Spain (N=62)	Total (N=850)
Amikacin	76 (19)	6 (7)	69 (24)	1 (2)	152 (18)
Amoxicillin intravenous or oral	0	0	6 (2)	0	6 (1)
Amoxicillin/clavulanate	0	1 (1)	11 (4)	8 (13)	20 (2)
Ampicillin	1 (0)	0	22 (8)	0	23 (3)
Ampicillin/sulbactam	18 (4)	0	0	0	18 (2)
Aztreonam	10 (2)	1 (1)	0	0	11 (1)
Cefazolin	0	0	21 (7)	0	21 (2)
Cefepime	8 (2)	1 (1)	0	3 (5)	12 (1)
Cefiderocol	3 (1)	0	0	0	3 (0)
Cefoperazone/sulbactam	0	8 (9)	0	0	8 (1)
Cefotaxime	1(0)	2 (2)	0	3 (5)	6 (1)
Cefoxitin	2 (0)	0	0	0	2 (0)
Ceftaroline	3 (1)	0	0	0	3 (0)
Ceftazidime	5 (1)	0	5 (2)	1 (2)	11 (1)
Ceftazidime/avibactam	52 (13)	1 (1)	1 (0)	1 (2)	55 (6)
Ceftizoxime	0	1 (1)	0	0	1 (0)
Ceftolozane/tazobactam	6 (1)	0	1 (0)	1 (2)	8 (1)
Ceftriaxone	35 (9)	21 (23)	93 (32)	25 (40)	174 (20)
Cefuroxime	1 (0)	0	60 (21)	0	61 (7)
Chloramphenicol	0	0	6 (2)	0	6 (1)
Ciprofloxacin intravenous or oral	26 (6)	1 (1)	27 (9)	4 (6)	58 (7)
Colistin	88 (22)	1 (1)	2 (1)	0	91 (11)
Ertapenem	4 (1)	0	22 (8)	28 (45)	54 (6)
Fosfomycin	0	1 (1)	0	0	1 (0)
Gentamicin	3 (1)	0	28 (10)	1 (2)	32 (4)
Imipenem	1 (0)	0	3 (1)	2	6 (1)
Imipenem/cilastatin	1 (0)	0	0	0	1 (0)
Imipenem/cilastatin/relebactam	3 (1)	0	0	0	3 (0)
Levofloxacin intravenous or oral	16 (4)	0	2 (1)	0	18 (2)
Meropenem	169 (42)	28 (31)	26 (9)	18 (29)	241 (28)
Meropenem/vaborbactam	11 (3)	0	0	0	11 (1)
Moxifloxacin	4 (1)	0	0	0	4 (0)
Piperacillin	0	0	4 (1)	0	4 (0)
Piperacillin/tazobactam	178 (44)	23 (25)	85 (29)	16 (26)	302 (36)
Polymyxin B	0	1 (1)	0	0	1 (0)
Tigecycline	36 (9)	2 (2)	0	0	38 (4)
Trimethoprim/sulfamethoxazole intravenous or oral	7 (2)	0	7 (2)	2 (3)	16 (2)

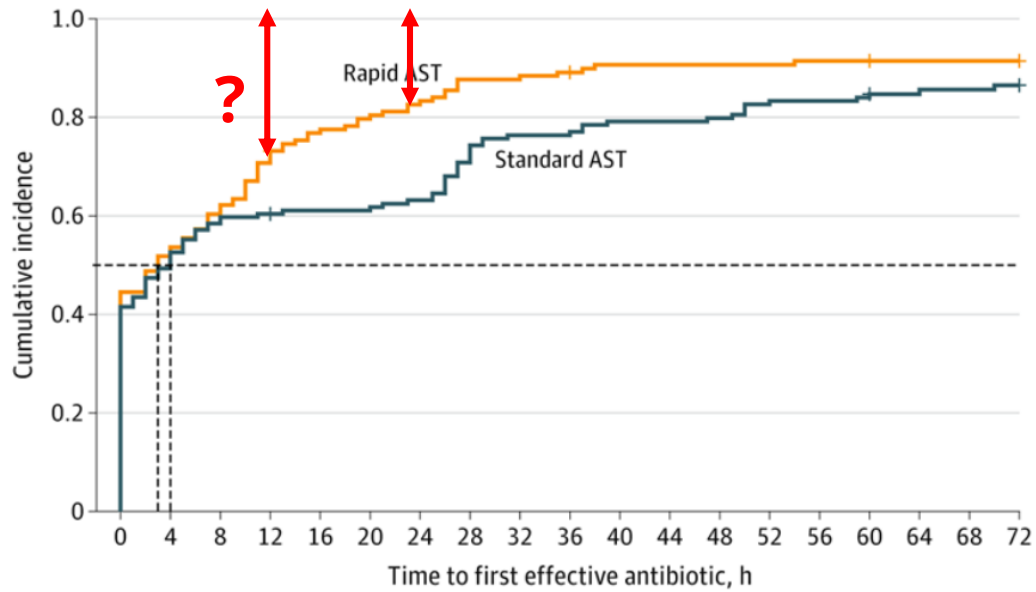


Figure 3. Survival Curves of Cumulative Incidence of Time to Receipt of First Effective Antibiotic Within 3 Days After Gram Stain Result

A As-randomized population



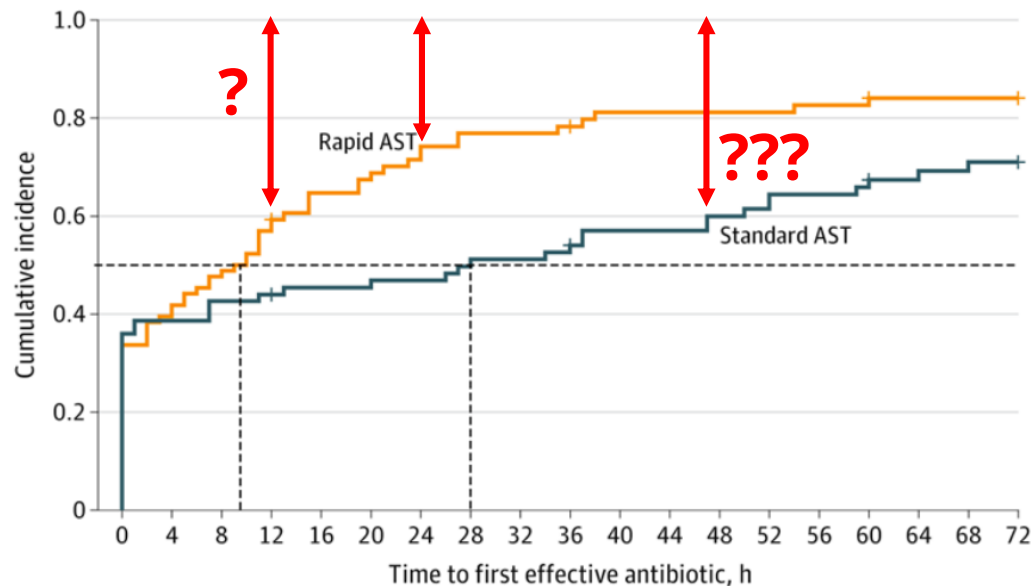
B Patients with cephalosporin-resistant organism



Cephalosporin-resistant pathogens:

	% inadequate Rx	
	R-AST	S-AST
At 12 h:	29%	40%
At 24 h:	15%	34%
At 36 h:	9%	22%

C Patients with carbapenem-resistant organism



Carbapenem-resistant pathogens:

	% inadequate Rx	
	R-AST	S-AST
At 12 h:	43%	56%
At 24 h:	24%	49%
At 36 h:	19%	44%

Observations from reading this paper

Large proportion of patients were not given adequate therapy in spite of availability to AST results – why?

AMS team only available office hours (not weekends)

Unavailability of some important antibiotics:

Greece: Aztreonam not available (for months) - NDMs

Greece/India: Sulbactam/durlobactam not approved

10-15% of patients classified as receiving "appropriate" antibiotics were on colistin/polymyxin based regimens (newer BL/BLI antibiotics not available)

Technical observations

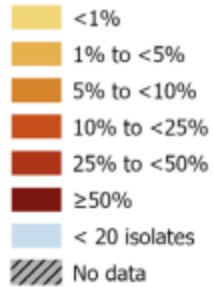
Direct MALDI only performed in 1 of 7 centres

➔ Rapid AST in some centres initiated only after MALDI from sub-cultured colonies

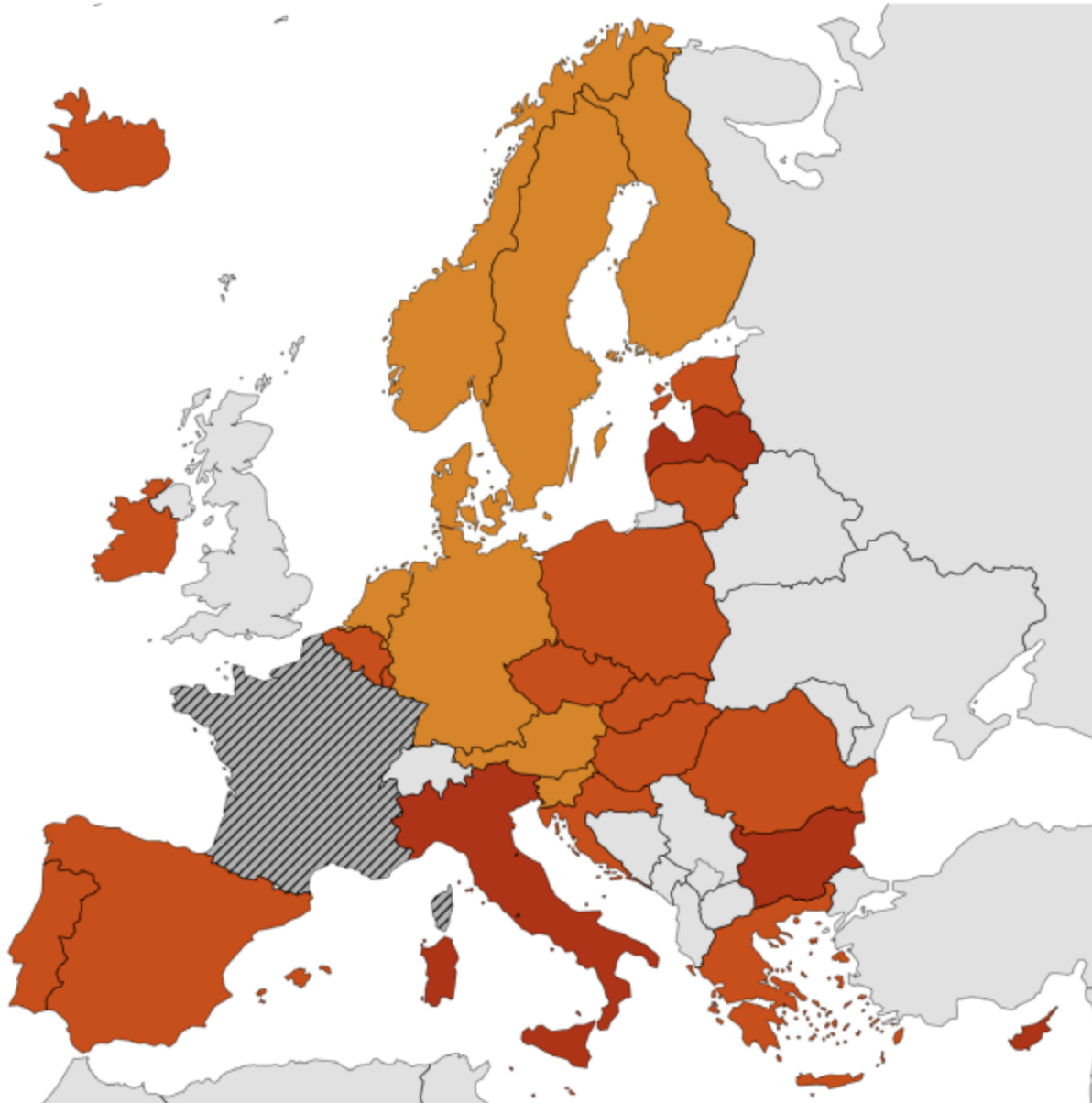
No information on preanalytical logistics (time to incubation?)

**May access to rapid AST affect our
choice of empirical therapy?**

Figure 2. *Escherichia coli*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2023



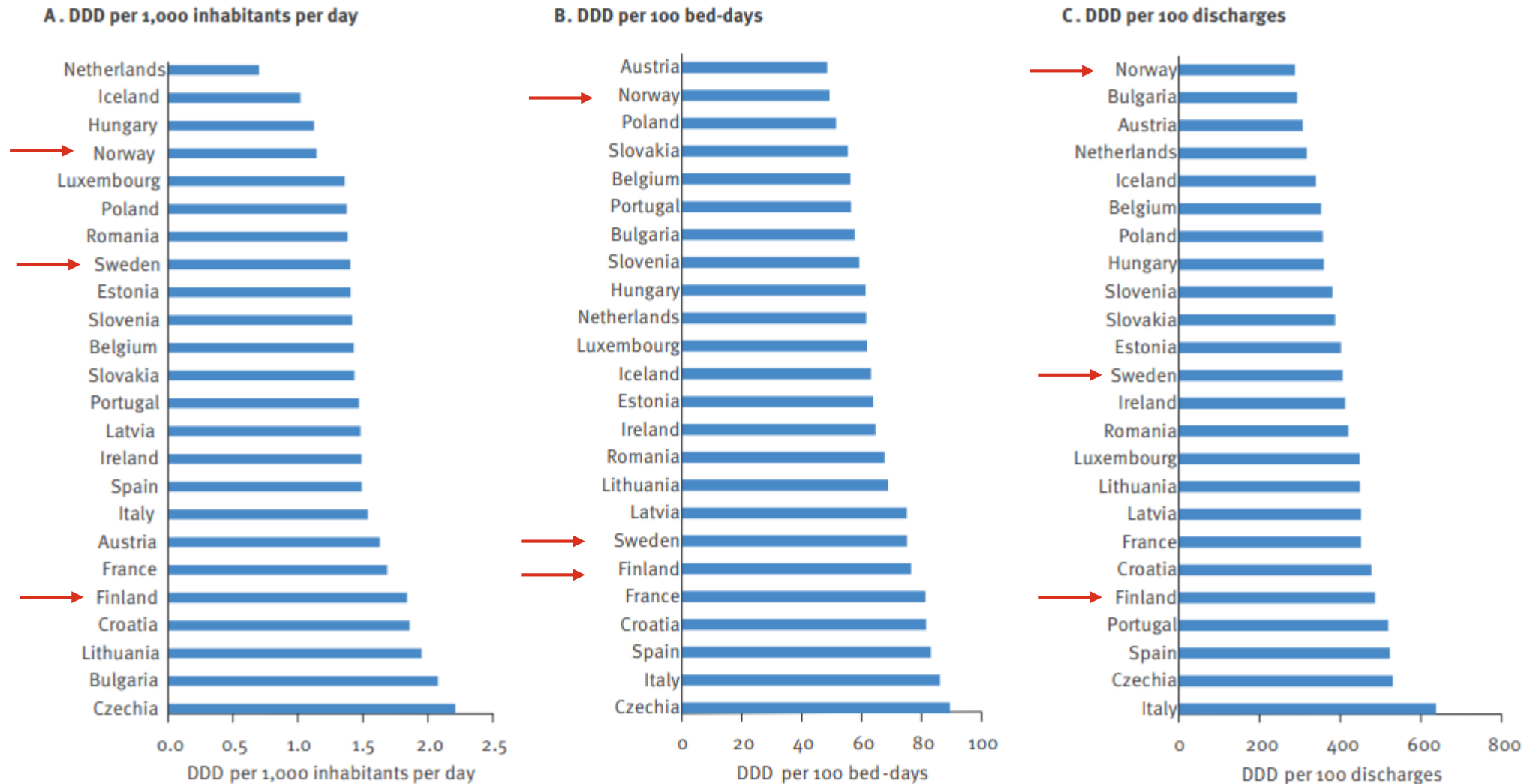
Countries not visible in the main map extent



Administrative boundaries: © EuroGeographics. The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. Map produced by ECDC on 13 September 2024

FIGURE 1

Hospital sector antibiotic consumption rates expressed and ranked according to defined daily doses per (A) 1,000 inhabitants per day, (B) 100 bed-days and (C) 100 discharges, 24 EU/EEA countries, 2021



High clinical severity

Co-morbidities

**High prevalence of antimicrobial
resistance**

**Short expected time to etiological
diagnosis, including AST results**

Broader

Narrower



EMPIRICAL TREATMENT



Sampling/transportation 1h-
eternity

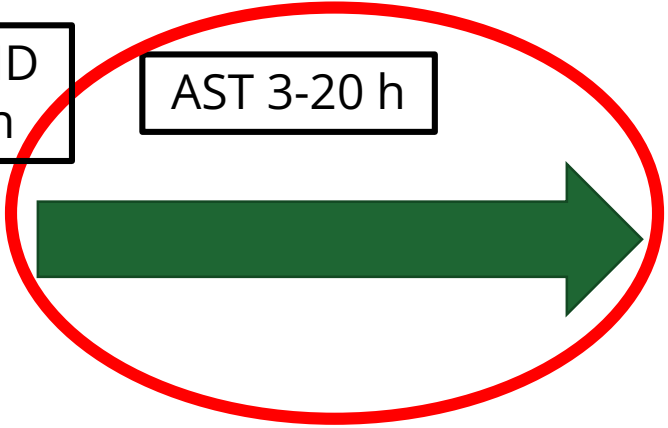
Enrichment 6-48 h

Species ID
0.5-24 h

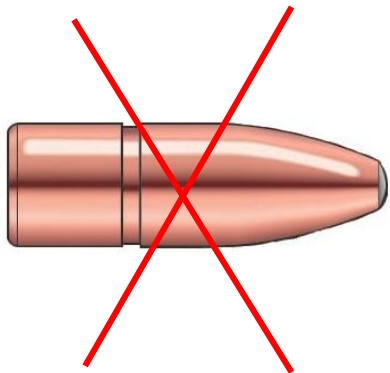
AST 3-20 h



Arion vulgaris
0.048 km/h



RAPID BSI DIAGNOSTICS, INCL. LOGISTICS, RAPID AST, COMMUNICATION ETC.



BUNDLE DEAL



When do we need rapid AST in the Nordics?

When we intend to use the results of it

When we have adequate logistics in place

24/7 cabinets, transportation time etc.

When we have ensured effective means of communication of AST results

When we combine it with an ambitious antimicrobial stewardship program

When we are serious about keeping empirical therapy as narrow as possible

...then we need rapid AST



WHO Collaborating Centre
for Standardization of
Antimicrobial Susceptibility Testing



**CLINICAL MICROBIOLOGY
KRONOBERG AND BLEKINGE**
SWEDISH NRL FOR PHENOTYPIC AST
EUCAST DEVELOPMENT LABORATORY



EURL
PUBLIC HEALTH
ANTIMICROBIAL RESISTANCE (AMR)
IN BACTERIA

Thank you for your attention!

oskar.ekelund@kronoberg.se