

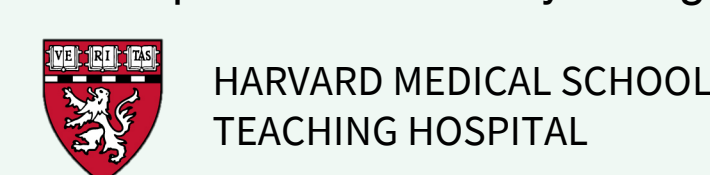
Accuracy of direct antimicrobial susceptibility testing from positive blood cultures in children and its utility as an antimicrobial stewardship tool



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Objective

- We evaluated the accuracy of direct susceptibility testing (DST) to assess its potential as an antimicrobial stewardship tool

Conclusions

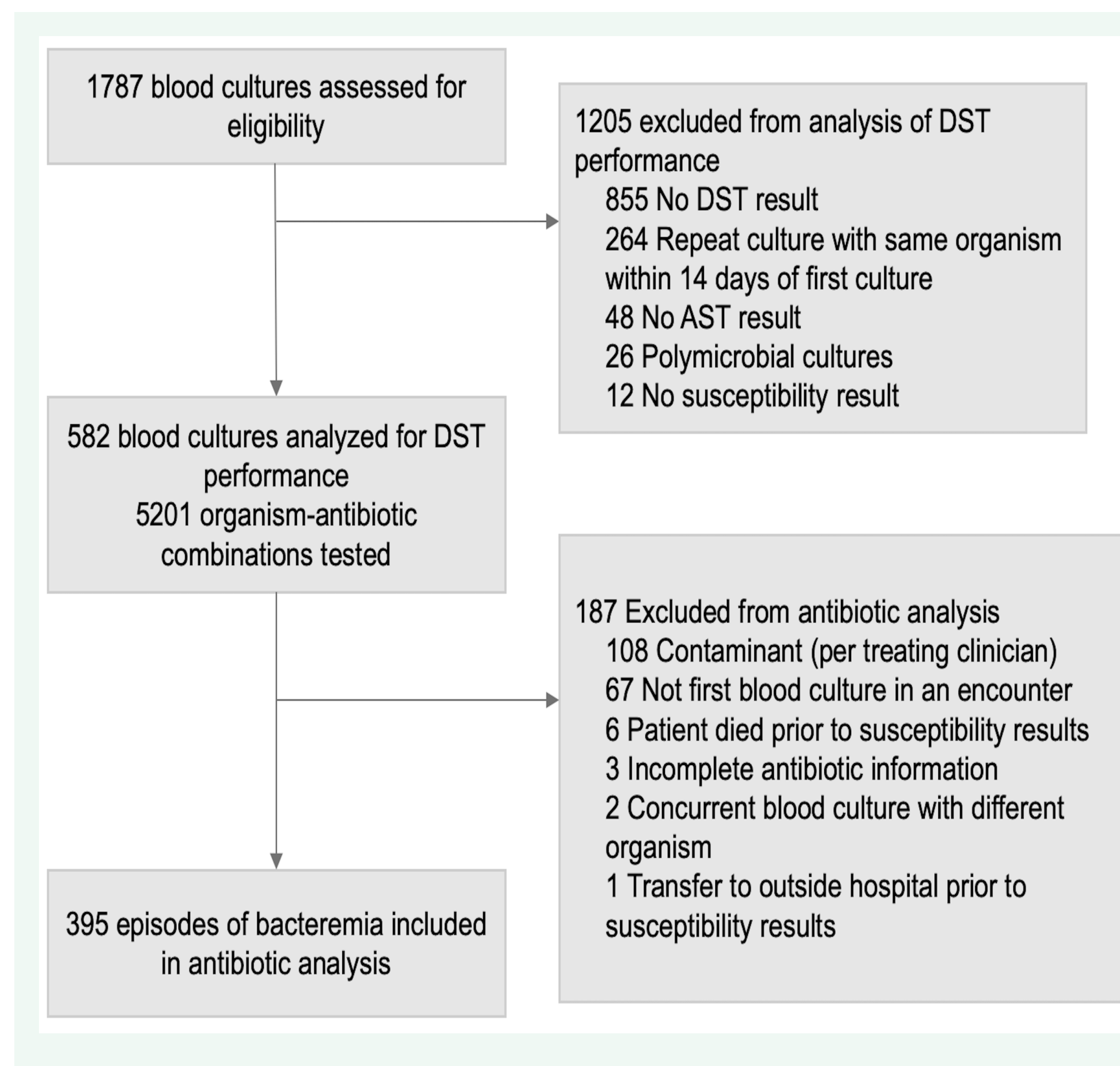
- Direct susceptibility testing is a low-cost, easy to use, phenotypic test to evaluate blood culture susceptibility
- Direct susceptibility testing is highly predictive of susceptibility for common organism-antibiotic combinations
- Direct susceptibility testing provides actionable information one day earlier than conventional methods and has potential as an antimicrobial stewardship tool

Background

- Empiric treatment of bacteremia is often with broad antibiotics
- Accurate, earlier susceptibility results could reduce unnecessarily broad antibiotic use
- DST uses disk diffusion testing on Mueller Hinton agar plate with non-standardized inoculum directly from blood cultures

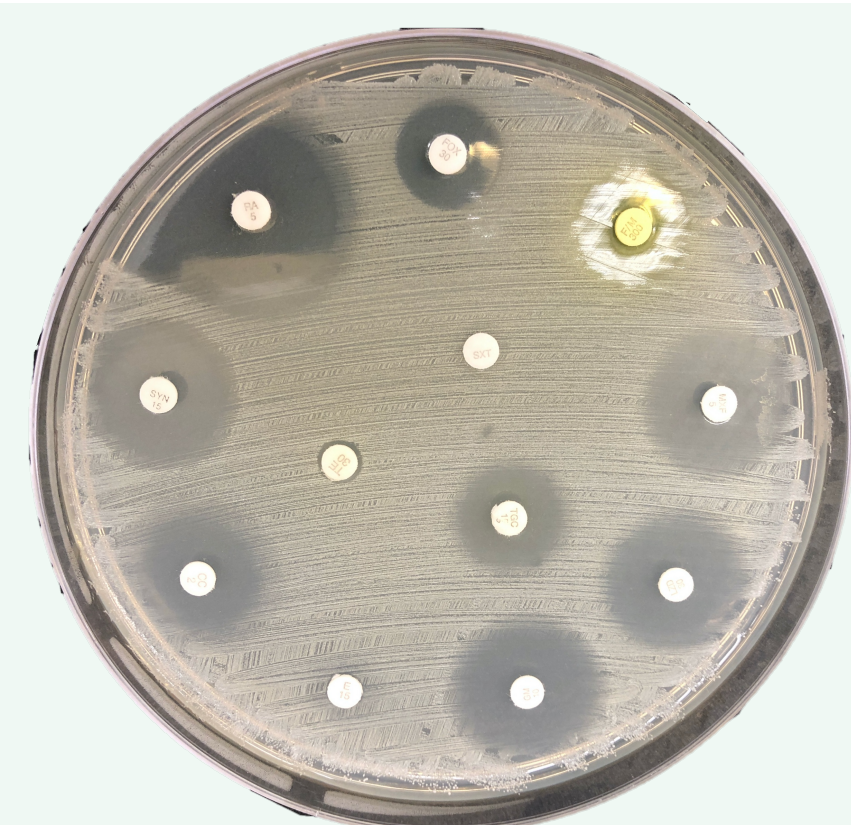
Methods

- Retrospective cohort study
- 582 blood cultures from 495 pediatric patients
- Sensitivity, specificity, positive predictive value and negative predictive value were calculated using gold standard of standardized antimicrobial susceptibility testing (AST) via Vitek 2
- We reviewed prescribed antibiotics and evaluated changes in the Antibiotic Spectrum Index at 3 different time points relative to susceptibility results
- Examples of ASI include oxacillin=1, cefazolin=3, ceftriaxone=5, vancomycin=5, meropenem=10



Results

- DST results were available a median of 21 hours before AST results
- DST had positive predictive values (ability to predict susceptibility) of ≥96% for most organism-antibiotic pairs
- Negative predictive values were variable
- The spectrum of antibiotics was narrowed in 31% of eligible cases after DST, and a further 38% after AST result



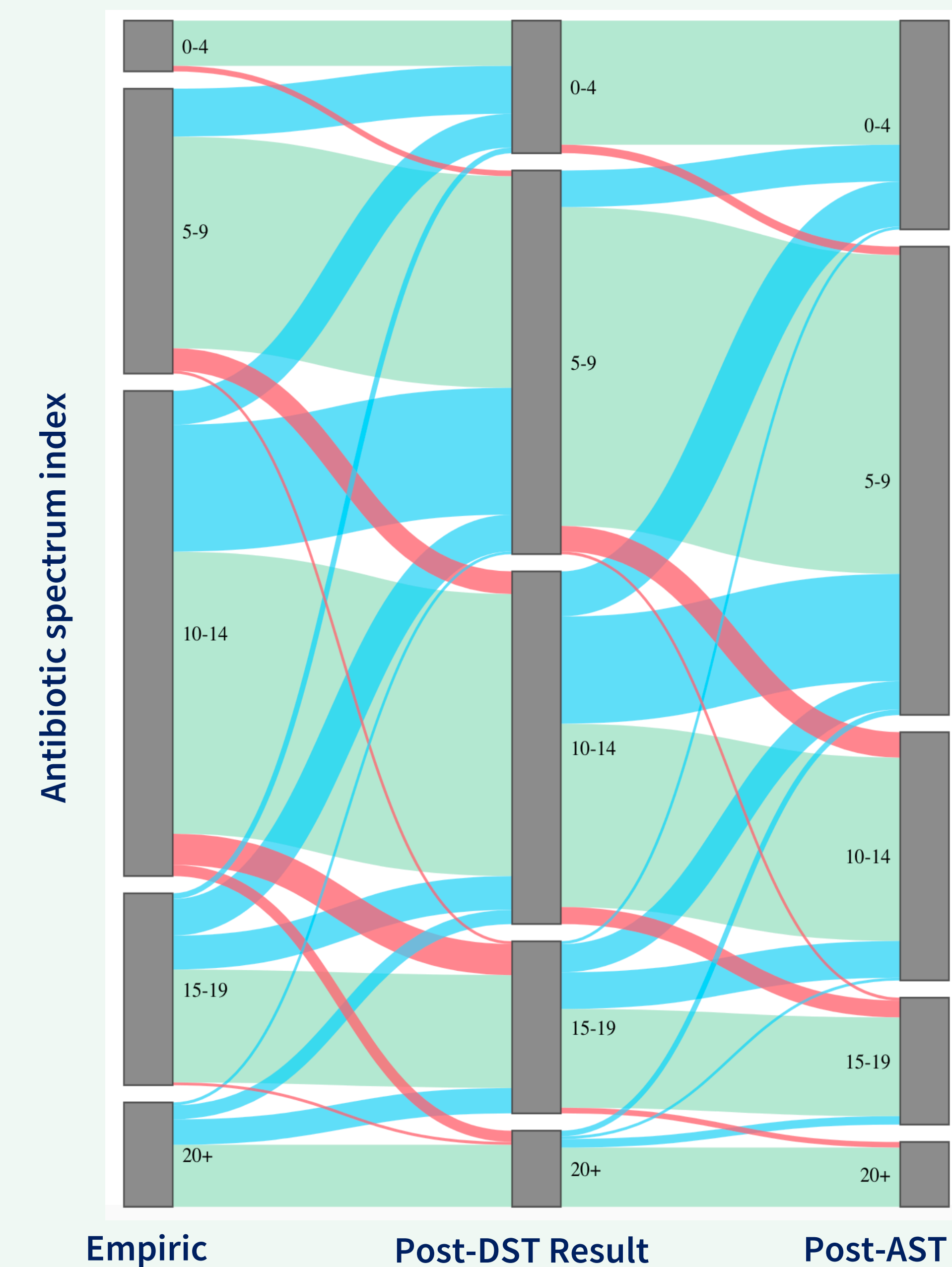
Example of direct susceptibility testing using Mueller Hinton agar plate

Predictive values of direct susceptibility testing (DST) of clinical isolates from patients with bacteremia to identify organism susceptibility to specific antibiotics

Antibiotic (number of isolates tested)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Staphylococcus aureus				
Clindamycin (137)	86 (75,93)	27 (17,39)	54 (45,63)	64 (47,82)
Oxacillin (137)	100 (96,100)	60 (45,74)	81 (74,89)	100 (100,100)
SXT (137)	100 (97,100)	25 (1,81)	98 (95,100)	100 (100,100)
Coagulase-negative staphylococci^a				
Clindamycin (254)	88 (80,94)	81 (75,87)	73 (65,86)	92 (88,97)
Oxacillin (251)	97 (89,100)	89 (83,93)	73 (63,82)	99 (97,100)
SXT (254)	100 (97,100)	76 (71,86)	81 (75,87)	100 (100,100)
Pseudomonas aeruginosa				
Cefepime (17)	100 (78,100)	100 (16,100)	100 (100,100)	100 (100,100)
Ceftazidime (17)	100 (74,100)	80 (28,100)	92 (78,100)	100 (100,100)
Ciprofloxacin (17)	93 (68,100)	50 (1,99)	93 (81,100)	50 (0,100)
Gentamicin (17)	100 (78,100)	50 (1,99)	94 (82,100)	100 (100,100)
Meropenem (17)	100 (72,100)	83 (36,100)	92 (76,100)	100 (100,100)
TZP (17)	100 (72,100)	100 (48,100)	100 (100,100)	100 (100,100)
Enterobacteriales^b				
Cefepime (135)	100 (97,100)	77 (55,92)	96 (92,99)	100 (100,100)
Ceftriaxone (110)	99 (93,100)	64 (46,79)	85 (77,92)	96 (88,100)
Ciprofloxacin (161)	99 (95,100)	62 (48,75)	83 (77,90)	97 (92,100)
Gentamicin (149)	99 (97,100)	100 (74,100)	100 (100,100)	100 (100,100)
Meropenem (149)	100 (97,100)	5 (1,16)	72 (65,79)	100 (100,100)
TZP (84)	99 (93,100)	75 (35,97)	97 (94,100)	86 (60,100)
Enterobacter cloacae complex				
Cefepime (20)	100 (82,100)	100 (48,100)	100 (100,100)	100 (100,100)
Gentamicin (20)	100 (82,100)	100 (22,100)	100 (100,100)	100 (100,100)
Meropenem (20)	100 (78,100)	0 (0,52)	75 (56,94)	N/A
Escherichia coli				
Ampicillin (45)	100 (66,100)	81 (64,92)	56 (32,81)	100 (100,100)
Cefepime (37)	100 (87,100)	70 (35,93)	90 (79,100)	100 (100,100)
Ceftazidime (44)	100 (90,100)	55 (23,83)	87 (76,98)	100 (100,100)
Ceftriaxone (43)	97 (82,100)	79 (49,95)	90 (80,100)	92 (76,100)
Ciprofloxacin (45)	100 (88,100)	81 (54,96)	91 (81,100)	100 (100,100)
Gentamicin (44)	100 (90,100)	100 (63,100)	100 (100,100)	100 (100,100)
Klebsiella pneumonia				
Cefepime (35)	100 (87,100)	75 (35,97)	93 (84,100)	100 (100,100)
Ceftazidime (41)	100 (86,100)	44 (20,70)	74 (59,88)	100 (100,100)
Ceftriaxone (40)	100 (86,100)	53 (27,79)	78 (64,92)	100 (100,100)
Ciprofloxacin (41)	100 (85,100)	53 (29,76)	71 (55,87)	100 (100,100)
Gentamicin (41)	100 (91,100)	100 (16,100)	100 (100,100)	100 (100,100)
Meropenem (40)	100 (86,100)	13 (2,38)	63 (48,78)	100 (100,100)
TZP (34)	96 (82,100)	67 (22,96)	93 (84,100)	80 (45,100)

Positive predictive value = accuracy of susceptibility on DST in identifying susceptibility on final AST result; Negative predictive value = accuracy of DST in identifying non-susceptibility (either intermediate or resistant) on AST result. Sensitivity = ability of DST to identify susceptible AST results (i.e. among susceptible (by AST) isolates, the percentage identified as susceptible by DST). Specificity = ability of DST to identify non-susceptible AST results (i.e. among non-susceptible (by AST) isolates, the percentage identified as non-susceptible by DST). SXT: trimethoprim-sulfamethoxazole. TZP: piperacillin-tazobactam.

Distribution of spectrum of antibiotics ordered to treat bacteremia in pediatric patients



Antibiotic spectrum, as measured by the antibiotic spectrum index (ASI), is represented in this Sankey diagram on the Y-axis. The height of each group indicates the proportion of patients with an aggregate antibiotic spectrum falling in that category at three time points. The ASI of empiric antibiotics was measured just before the DST result to provide time for a treating physician to settle on an empiric regimen (Empiric). The ASI with the DST result was measured just before the AST result (Post-DST result). The ASI with the AST result was measured 24 hours after the AST result was available (Post-AST result). Bands between the columns indicate the proportion of patients whose ASI decreased, remained the same, or increased between two time points.

Characteristics and laboratory results of patients treated for bacteremia

	n (%)
Age	
0 to <2 months	52 (13)
2 months to <1 year	64 (16)
1 year to 5 years	102 (26)
6 years to 10 years	49 (12)
11 years to 18 years	83 (21)
Older than 18 years	45 (11)
Race	
Asian	22 (4.4)
Black or African American	40 (8.1)
White	233 (47)
Other	107 (21.6)
Unknown	94 (18.9)
Ethnicity	
Hispanic or Latinx	29 (7)
Not Hispanic or Latinx	231 (58)
Unknown	135 (34)
Sex	
Male	250 (63)
Female	145 (37)
Primary Service	
Medical	145 (37)
Oncology/transplant	77 (19)
Surgical	116 (29)
Intensive care unit	57 (14)
White blood cell count, cells/ul ^a (median, IQR)	8.1 (4.4,14.2)
Severe neutropenia (ANC<500), n (%)	58 (18)
C-reactive protein, mg/dL ^b (median, IQR)	6.8 (2.3,15.3)

^an=330, ^bn=193

Organisms included in evaluation of direct susceptibility testing performance (n=582)

Organism	n (%)
Acinetobacter species	6 (1.0)
Citrobacter species	6 (1.0)
Enterobacter species	25 (4.3)
Escherichia coli	46 (7.9)
Escherichia vulneris	1 (0.2)
Klebsiella species ^a	53 (9.1)
Pantoea species	1 (0.2)
Proteus mirabilis	2 (0.3)
Pseudomonas aeruginosa	17 (2.9)
Pseudomonas fluorescens group	1 (0.2)
Salmonella species	7 (1.2)
Salmonella typhi	4 (0.7)
Serratia liquefaciens	1 (0.2)
Serratia marcescens	16 (2.7)
Staphylococcus aureus	137 (23.5)
Coagulase-negative staphylococci ^b	259 (44.5)

^aincludes *Klebsiella oxytoca/Raoutella ornithinolytica* (n=10), *Klebsiella pneumoniae* (n=41), *Klebsiella variicola* (n=1).

^bincludes *Staphylococcus capitis* (n=20), *Staphylococcus epidermidis* (n=176), *Staphylococcus haemolyticus* (7), *Staphylococcus hominis* (n=44), *Staphylococcus pettenkoferi* (n=4), and *Staphylococcus warneri* (n=8).