Use of selective reporting of antimicrobial susceptibilities and its impact on antimicrobial resistance surveillance — National Healthcare Safety Network, 2017–2018

May 23rd, 2019

Hsiu Wu, MD

Selective and cascade reporting

- Selective reporting (SR): an antimicrobial stewardship strategy to guide the appropriate use of antimicrobial agents by limiting the antimicrobial susceptibility testing (AST) results available to prescribers

- Cascade reporting (CR): a type of SR, which AST results of secondary antimicrobial agents (eg. broader spectrum, more costly) are only reported if an organism is resistant to primary agents

- Reporting criteria are often developed by a multidisciplinary health care team of a healthcare facility

CLSI M39-A4 (2014)

SR or CR is recommended in 2016 IDSA/SHEA antibiotic stewardship implementation guidelines

XV. Should ASPs Work With the Microbiology Laboratory to Perform Selective or Cascade Reporting of Antibiotic Susceptibility Test Results?

Recommendation

16. We suggest selective and cascade reporting of antibiotics over reporting of all tested antibiotics *(weak recommendation, low-quality evidence).*

Comment: Although data are limited that demonstrate direct impact of those strategies on prescribing, some form of selective or cascaded reporting is reasonable. After implementation, ASPs should review prescribing to ensure there are no unintended consequences.

M100 standards of the Clinical and Laboratory Standards Institute (CLSI) suggested groupings of antimicrobial agents considered for testing and reporting by microbiology labs

- **Group A:** agents considered appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results
- **Group B:** agents may warrant primary testing, but may be reported only selectively
- **Group C:** alternative or supplemental antimicrobial agents
- **Group U:** certain agents that are used only or primarily for treating UTIs

CLSI M100 29th Edition (2019)

Objectives

- Assessed the extent of SR use and its impact on national antimicrobial resistance (AR) surveillance

Methods

Data source

- Data source: NHSN AR Option
  - AST results of 20 designated organisms cultured from blood, cerebrospinal fluid (CSF), lower respiratory tract (LRT), or urine cultures
  - Data extracted from Laboratory Information System (LIS) or Electronic Health Records (EHR) that directly linked with LIS
- Data included for the analysis
  - AST results for CLSI group A and B agents of Enterobacteriaceae and *Staphylococcus aureus* isolates from urine and blood cultures reported to NHSN AR Option from January 2017 through December 2018

Definitions

- Drugs that are considered to be routinely reported in a hospital:
  - the drug of which the AST results were reported most frequently among all drugs and reported in ≥90% isolates of given pathogen and specimen source in the hospital

Hospitals that performed selective reporting (SR)

- Hospital reported ≥30 isolates and had ≥1 agent(s) were tested and reported among ≥90% isolates of the organism were included for SR analysis

- SR hospital: the difference of %reported is >20% between the drug of interest and the most commonly reported drug in the hospital

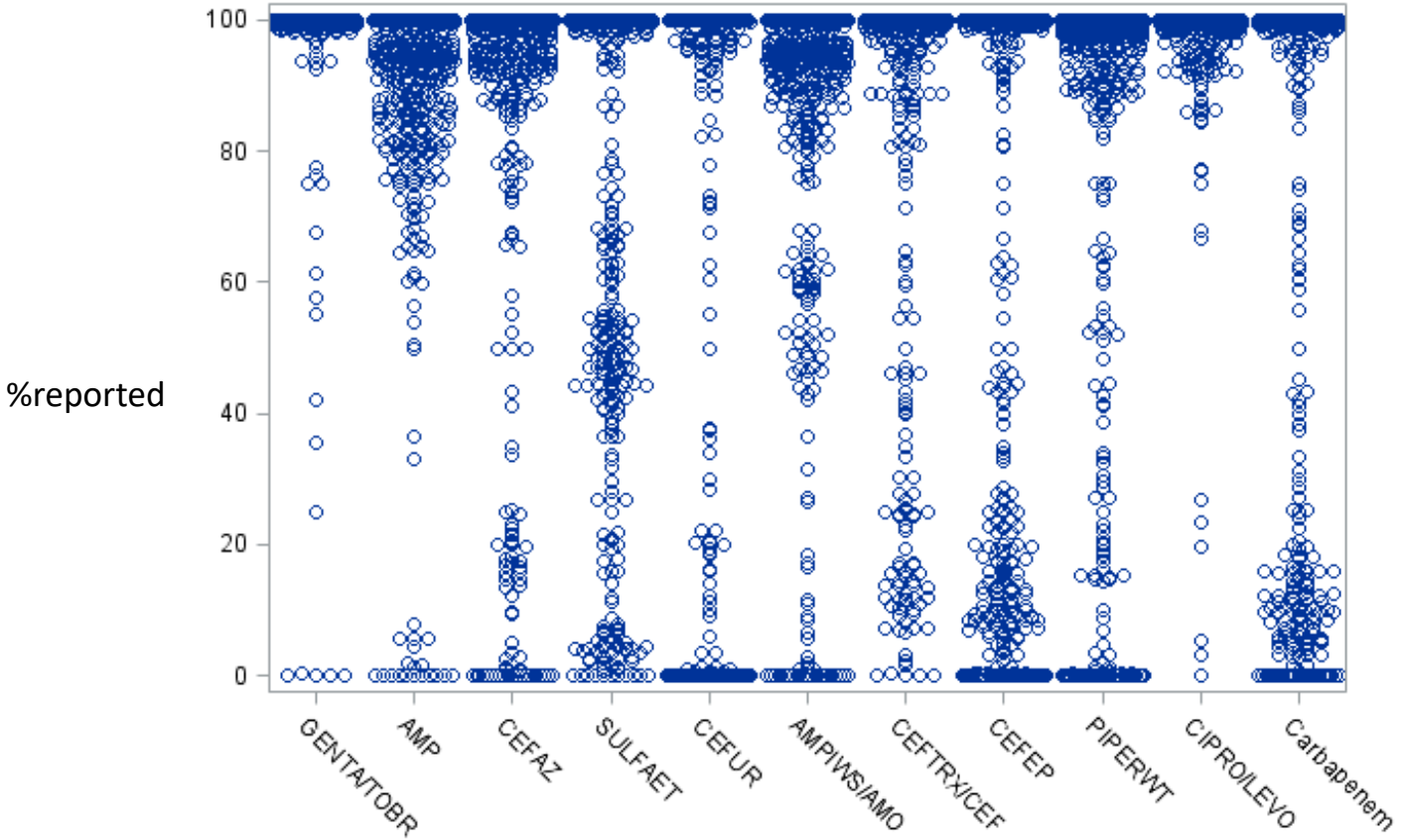
- Non-SR hospital: the difference of %reported in the hospital is ≤20% between the drug of interest and the routinely reported drug

Analyses

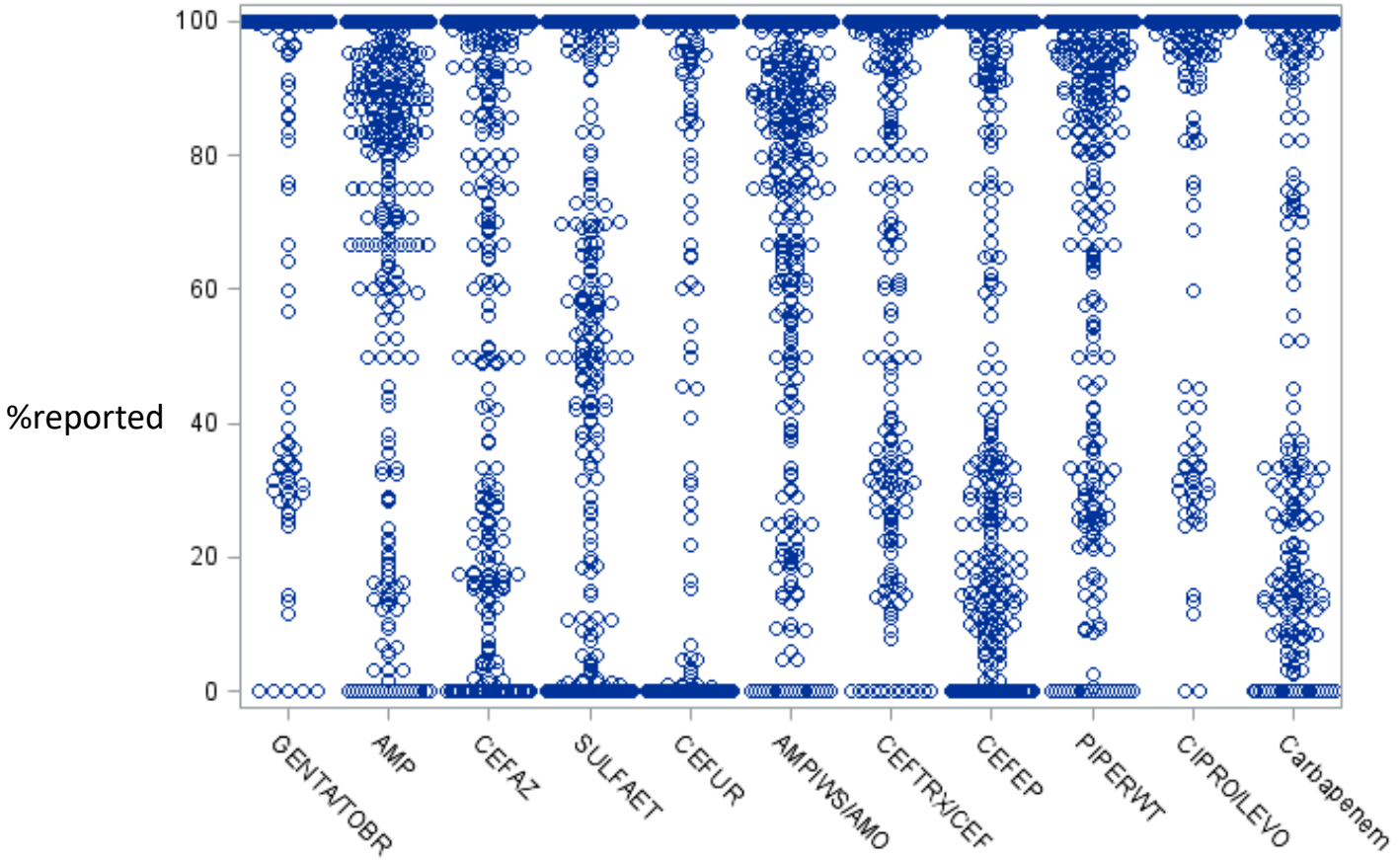
- Calculate the number of hospitals in which the AST results were considered reported routinely by drug
- Calculate the proportion of hospitals that showed patterns of SR
- Compare distribution of antibiograms among SR and non-SR hospitals
  - Wilcoxon Rank-Sum test
- Among isolates in SR hospitals, identify isolate and patient characteristics that are associated with reporting of susceptibility results
  - Prevalence ratios
  - Log binomial regression

Results: reporting of Enterobacteriaceae susceptibilities

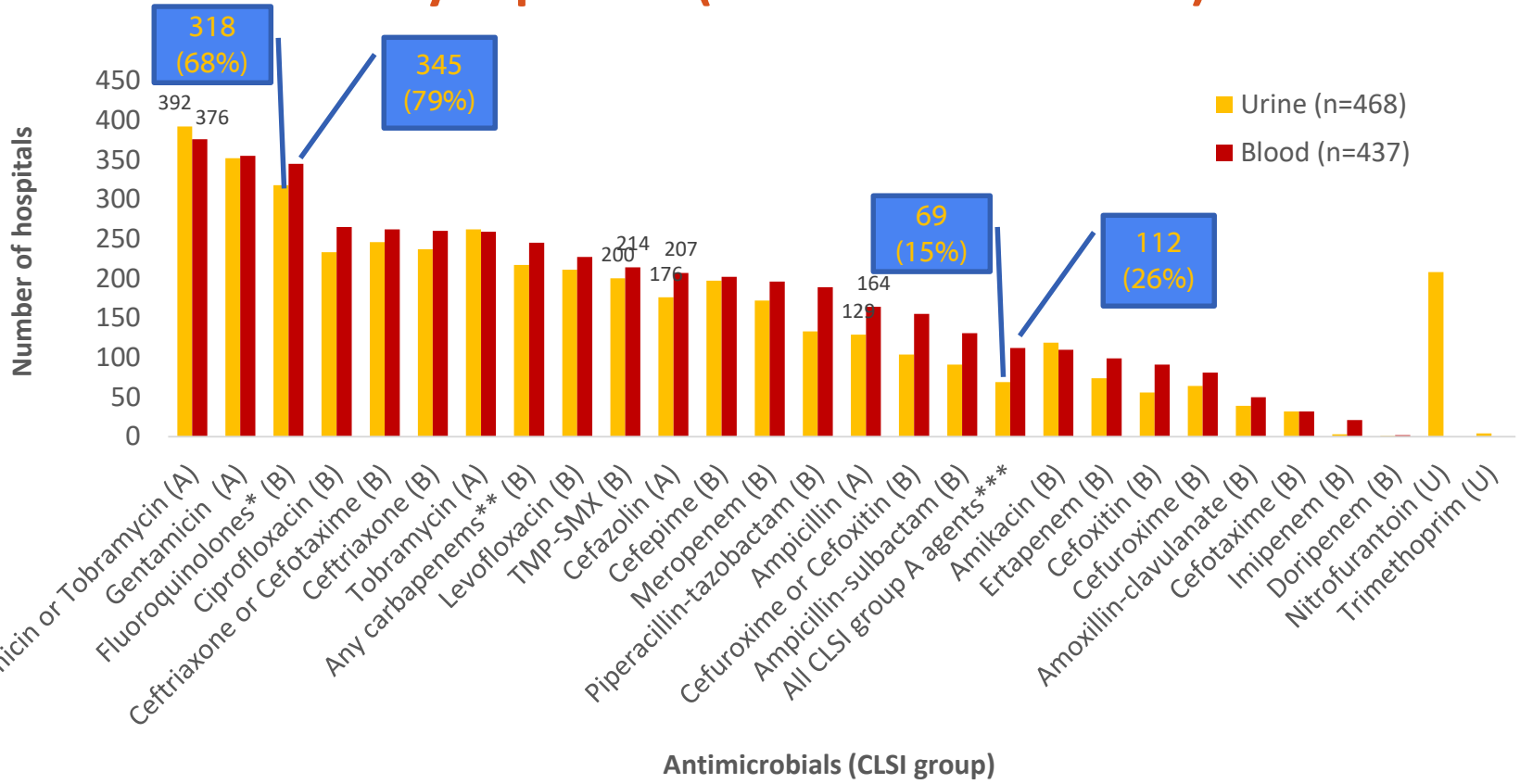
%reported varies across hospitals and antimicrobials (urine cultures)



%reported varies across hospitals and antimicrobials (blood cultures)

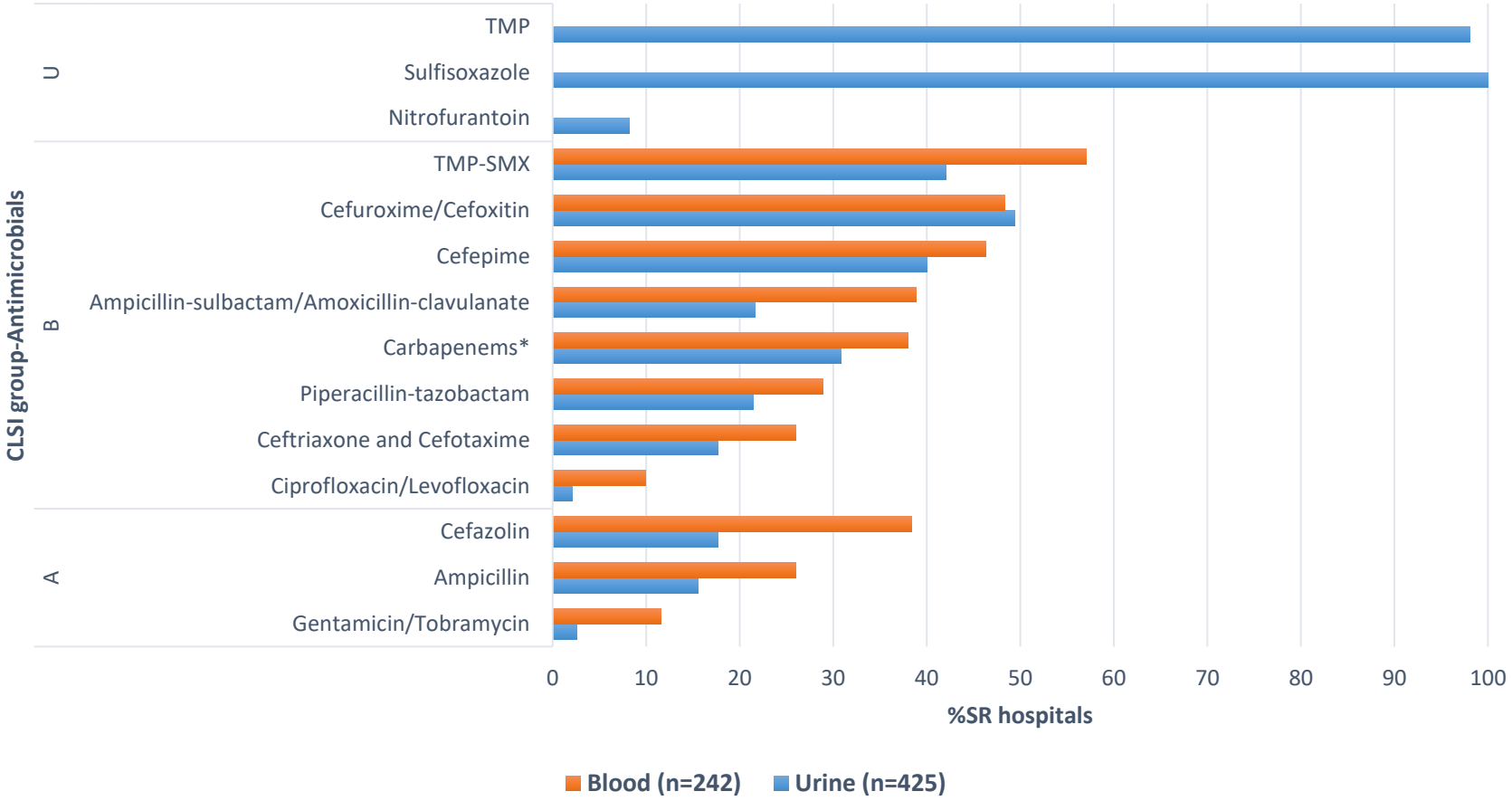


Number of hospitals in which the susceptibility of the drug was considered routinely reported (Enterobacteriaceae)



*Ciprofloxacin or Levofloxacin **Doripenem, Ertapenem, Imipenem, or Meropenem *Ampicillin, Cefazolin, Gentamicin, or Tobramycin

Percentage of hospitals with a pattern of SR for antimicrobials—Enterobacteriaceae



*Doripenem, Ertapenem, Imipenem, or Meropenem

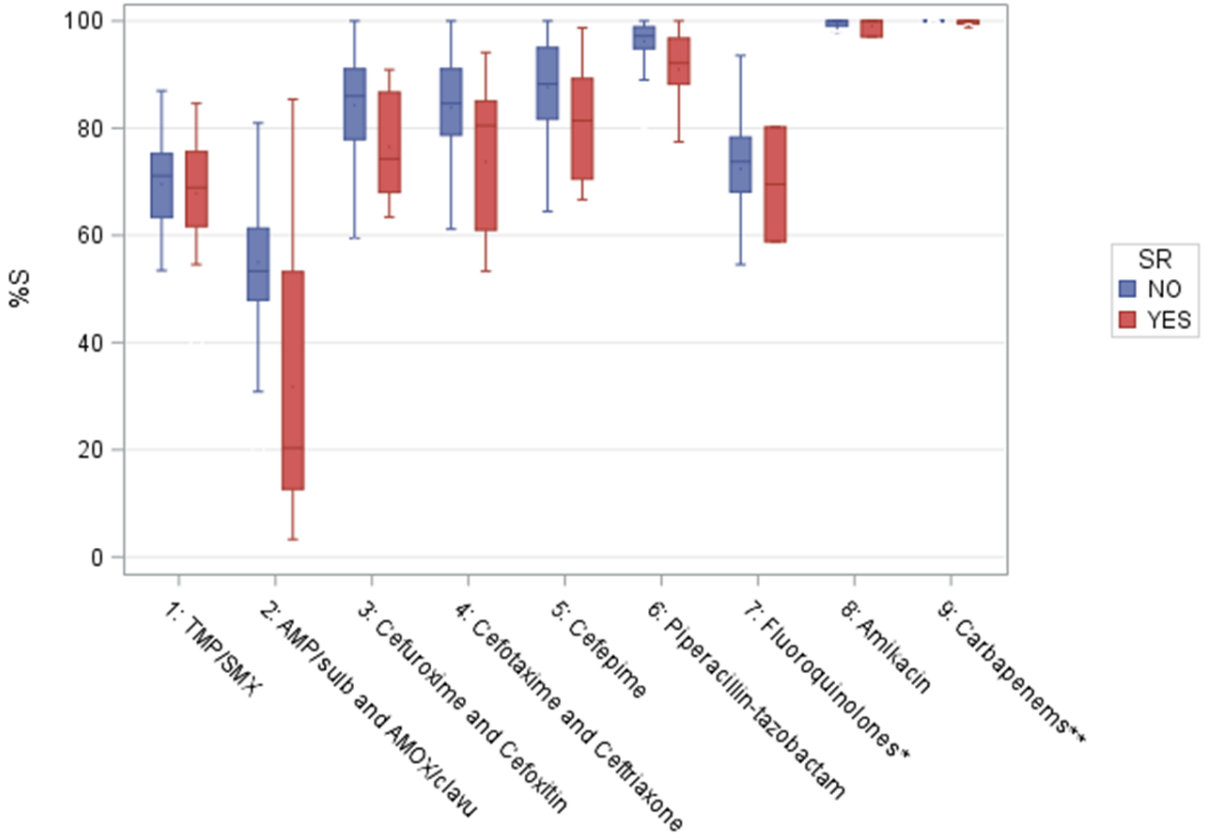
Hospital-level %S among *E. coli* isolates: SR versus non-SR (urine)

CLSI group	Antimicrobials	*E. coli* isolates from urine cultures				
		SR hospitals %S, median (IQR)	n	Non-SR hospitals %S, median (IQR)	n	*p*-value†
A	Ampicillin	47.0 (42.0–56.4)	47	49.2 (44.3–54.4)	350	0.318
	Cefazolin	65.9 (0–94.6)	42	85.9 (81.1–90.1)	329	0.0004
	Gentamicin or Tobramycin	88.5 (84.8–94.6)	6	89.3 (86.6–92.0)	403	
B	TMP-SMX	72.0 (67.5–76.0)	238	73.1 (68.4–78.5)	138	0.0369
	Ampicillin-sulbactam or Amoxicillin-clavulanate	17.0 (12.6–57.7)	62	57.5 (52.7–62.7)	321	<0.0001
	Cefuroxime or Cefoxitin	83.9 (73.7–91.2)	25	87.8 (83.1–91.9)	207	0.0201
	Ceftriaxone or Cefotaxime	65.1 (34.1–83.7)	45	88.6 (83.6–92.5)	342	<0.0001
	Cefepime	53.7 (22.2–85.6)	71	93.3 (89.6–95.9)	246	<0.0001
	Piperacillin-tazobactam	92.8 (87.7–95.0)	42	96.8 (95.3–98.0)	324	<0.0001
	Any carbapenems*	100 (100–100)	64	100 (100–100)	286	0.704
	Fluoroquinolones**	71.1 (26.2–79.4)	7	75.8 (70.1–81.3)	404	
	Amikacin	98.9 (96.9–100)	64	99.9 (99.5–100)	164	0.0002

† *p* values based on Wilcoxon Rank Sum test, only shown if the numbers of hospitals are ≥20 for both SR and non-SR groups

*Doripenem, Ertapenem, Imipenem, or Meropenem **Ciprofloxacin or Levofloxacin

Hospital-level %S (median, quartiles, and range) among urine *E. coli* isolates: SR vs non-SR



*Ciprofloxacin and Levofloxacin **Doripenem, Ertapenem, Imipenem, and Meropenem

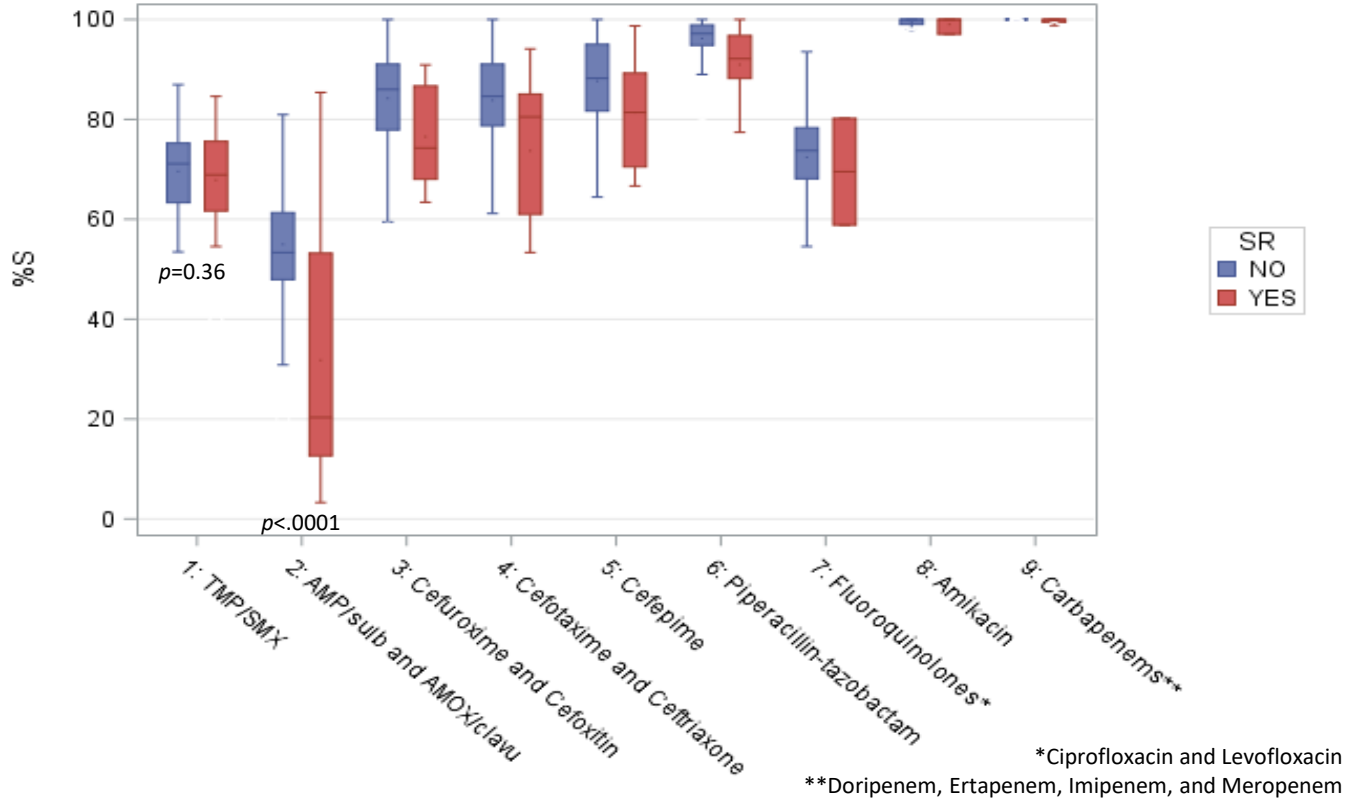
Hospital-level %S among *E. coli* isolates: SR versus non-SR (blood)

		E. coli isolates from blood cultures				
		SR hospitals		Non-SR hospitals		
CLSI group	Antimicrobials	%S, median (IQR)	n	%S, median (IQR)	n	*p*-value†
A	Ampicillin	43.4 (32.6–54.9)	10	44.6 (39.2–51.9)	144	
	Cefazolin	51.9 (22.6–75.0)	11	79.8 (70.0–85.9)	117	
	Gentamicin or Tobramycin	82.6 (82.4–90.3)	3	86.6 (81.4–90.4)	163	
B	TMP-SMX	68.9 (61.7–75.6)	46	71.1 (63.3–75.2)	75	0.363
	Ampicillin-sulbactam or Amoxicillin-clavulanate	20.3 (12.6–53.2)	38	53.3 (47.9–61.3)	117	<0.0001
	Cefuroxime or Cefoxitin	74.3 (68.0–86.7)	8	86.0 (77.9–91.1)	100	
	Ceftriaxone or Cefotaxime	85.1 (80.5–94.1)	9	84.6 (78.7–91.1)	138	
	Cefepime	81.4 (70.5–89.2)	10	88.2 (81.7–95.0)	100	
	Piperacillin-tazobactam	92.1 (88.2–96.8)	14	97.2 (94.8–98.9)	127	
	Any carbapenems*	100 (99.5–100)	2	100 (100–100)	166	
	Fluoroquinolones**	69.6 (58.8–80.2)	14	73.4 (68.1–78.3)	110	
	Amikacin	100 (97.1–100)	3	100 (99.0–100)	62	

† *p* values based on Wilcoxon Rank Sum test, only shown if the numbers of hospitals are ≥20 for both SR and non-SR groups

*Doripenem, Ertapenem, Imipenem, or Meropenem **Ciprofloxacin or Levofloxacin

Hospital-level %S (median, quartiles, and range) among blood *E. coli* isolates: SR vs non-SR



*Ciprofloxacin and Levofloxacin

**Doripenem, Ertapenem, Imipenem, and Meropenem

p values are based on Wilcoxon Rank Sum test and only shown if the numbers of hospitals are ≥20 in both SR and non-SR groups

Factors associated with reporting of cefepime susceptibility results among hospitals showed a pattern of SR

	Urine (n=104,270) aPR	*p*-value	Blood (n=11,002) aPR	*p*-value
Non-susceptibility to ≥1 narrow-spectrum* antimicrobials				
No	reference		reference	
Yes	3.03 (2.91–3.15)	<.0001	4.53 (4.06–5.06)	<.0001
Pathogen				
E. coli	reference		reference	
Enterobacter spp.	2.11 (2.03–2.19)	<.0001	2.12 (1.97–2.27)	<.0001
Citrobacter freundii	1.86 (1.74–1.99)	<.0001	1.46 (1.17–1.86)	0.001
Serratia marcescence	1.52 (1.37–1.69)	<.0001	1.76 (.157–1.97)	<.0001
Morganella morganii	1.51 (1.38–1.64)	<.0001	1.66 (1.38–1.99)	<.0001
K. oxytoca	0.90 (0.82–0.99)	0.026	1.04 (0.88–1.23)	0.661
Proteus mirabilis	0.64 (0.60–0.68)	<.0001	1.01 (0.86–1.19)	0.879
K. pneumoniae	0.64 (0.61–0.67)	<.0001	0.73 (0.66–0.81)	<.0001
Patient location				
ED and 24-hour observation units	reference		reference	
Intensive care units	1.17 (1.11–1.24)	<.0001	1.08 (0.98–1.19)	0.119
Other inpatient locations	1.14 (1.10–1.17)	<.0001	1.10 (1.02–1.18)	0.009
Age				
<16 years	reference		reference	
≥16 years	1.04 (0.98–1.10)	0.214	1.05 (0.89–1.22)	0.576
Gender				
Female	reference		reference	
Male	1.18 (1.141.21)	<.0001	1.02 (0.97–1.09)	0.404

*ampicillin, cefazolin, cefuroxime, cefoxitin, ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicillin/ clavulanate, or nitrofurantoin for urine; ampicillin, cefazolin, cefuroxime, cefoxitin, ceftriaxone, cefotaxime, ampicillin/sulbactam, amoxicilin/ clavulanate for blood

Factors associated with reporting of ampicillin susceptibility results among hospitals show a pattern of SR

		Urine (n=37,125)		Blood (n=6,053)	
		aPR	*p*-value	aPR	*p*-value
Pathogen					
	E. coli	reference		reference	
	Enterobacter spp.	0.11 (0.09–0.14)	<.0001	0.37 (0.28–0.48)	<.0001
	Citrobacter freundii	0.85 (0.10.1–0.21)	<.0001	0.33 (0.13–0.83)	0.0185
	Serratia marcescence	0.13 (0.08–0.20)	<.0001	0.25 (0.15–0.42)	<.0001
	Morganella morganii	0.37 (0.31–0.44)	<.0001	0.63 (0.40–0.99)	0.046
	K. oxytoca	0.60 (0.53–0.68)	<.0001	1.32 (1.09–1.60)	0.004
	Proteus mirabilis	0.96 (0.03–0.99)	0.01	1.14 (0.99–1.32)	0.068
	K. pneumoniae	0.09 (0.09–0.11)	<.0001	0.28 (0.23–0.34)	<.0001
Patient location					
	ED and 24-hour observation units	reference		reference	
	ICUs	1.09 (1.04–1.14)	0.0003	0.79 (0.82–1.16)	0.791
	Other inpatient locations	1.08 (1.06–1.11)	<.0001	0.97 (0.85–1.10)	0.610
Age					
	<16 years	reference		reference	
	≥16 years	1.26 (1.19–1.34)	<.0001	0.59 (0.49–0.70)	<.0001
Gender					
	Female	reference		reference	
	Male	0.91 (0.89–0.94)	<.0001	1.0 (0.92–1.09)	0.984

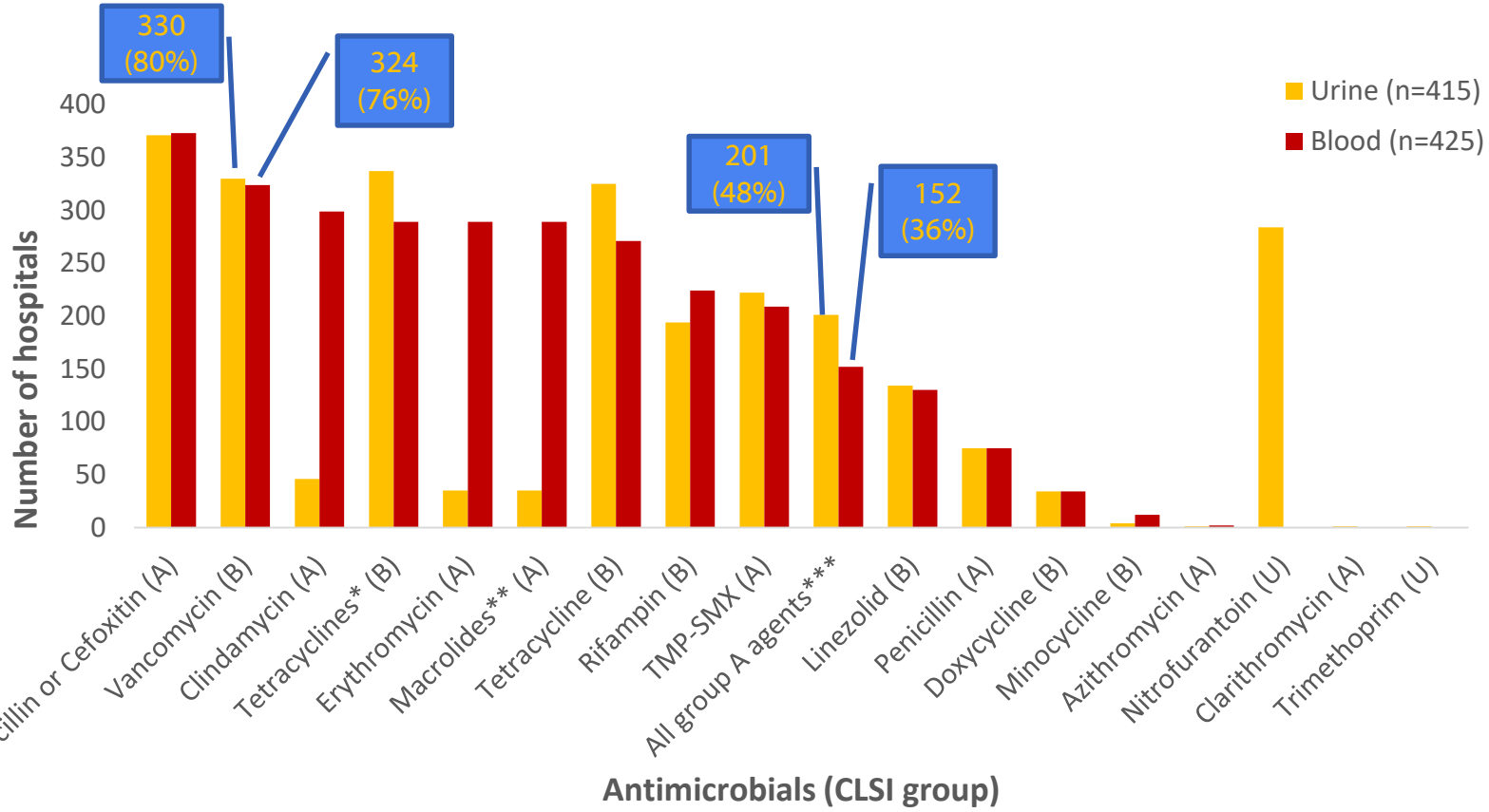
Summary (Enterobacteriaceae)

- AST reporting varies greatly across hospitals and antimicrobials
- Only 15% and 26% hospitals routinely reported susceptibility results of all CLSI group A agents in urine and blood cultures, respectively
- Fluoroquinolones, although in group B, are routinely reported in most hospitals
- Antibiograms of hospitals with patterns of SR showed lower %S in many antimicrobials
- Among hospitals with a pattern of SR for cefepime, isolates with non-susceptibility to narrower-spectrum antimicrobials and ampC producing species* are more likely to report of cefepime susceptibilities
- Age, gender, and patient locations are also associated with reporting of cefepime and/or ampicillin susceptibility results

**Enterobacter spp., Citrobacter freundii, Serratia marcescence, or Morganella morganii*

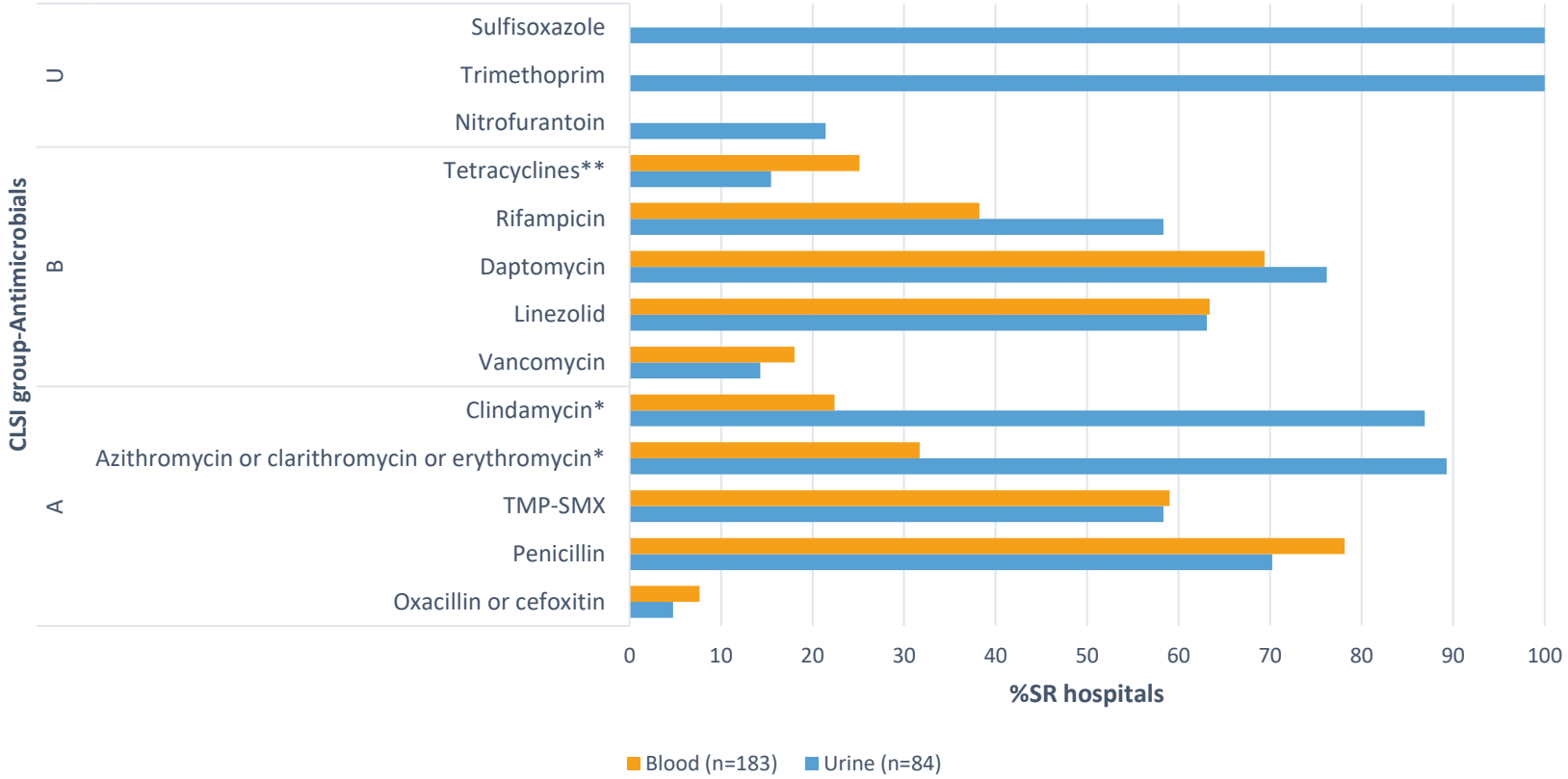
Results: reporting of *Staphylococcus aureus* susceptibilities

Number of hospitals in which the susceptibility of the drug was considered routinely reported (*S. aureus*)



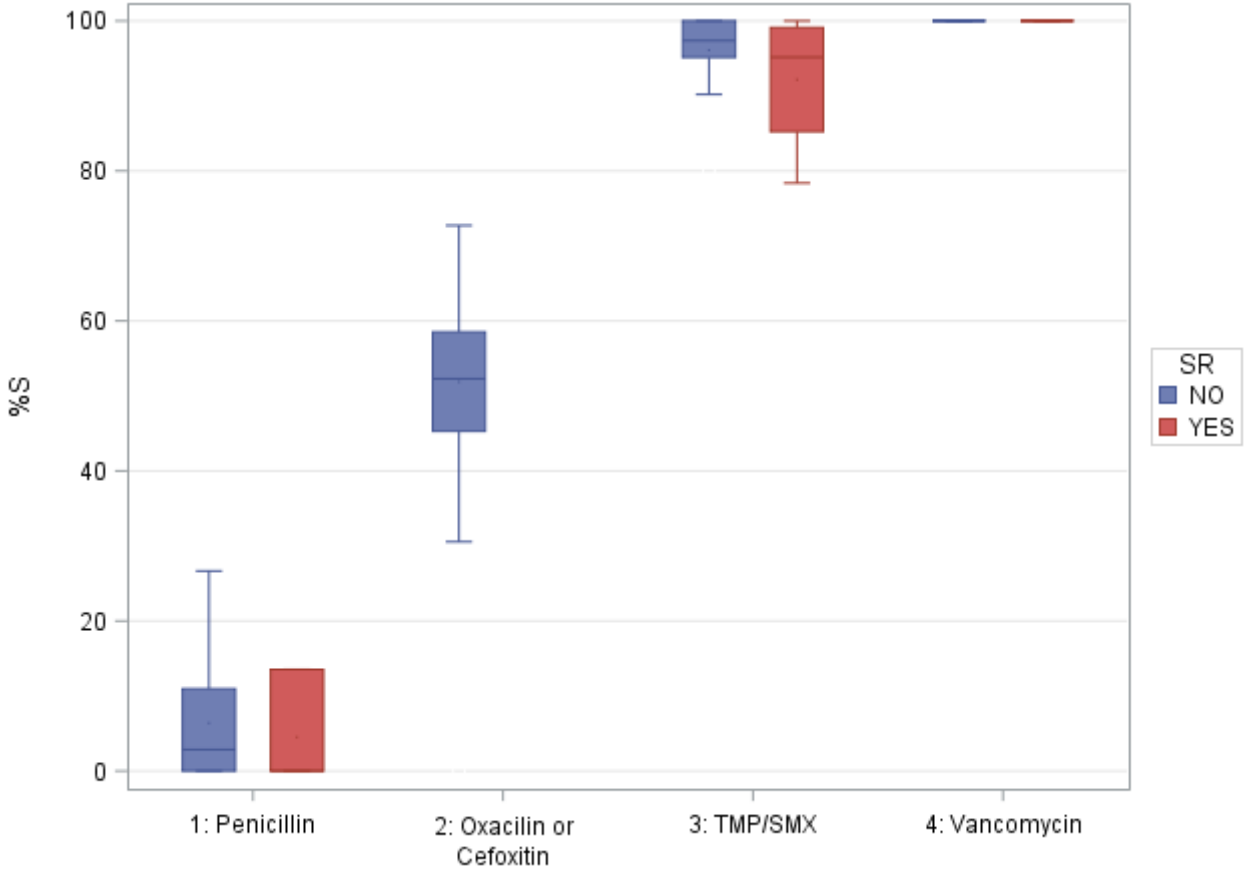
*Doxycycline, Minocycline, or Tetracycline **Azithromycin, Clarithromycin, or Erythromycin ***For blood cultures: Oxacillin/Cefoxitin or Penicillin with susceptible results, TMP-SMX, Clindamicin, and Macrolides; for urine cultures: Oxacillin/Cefoxitin or Penicillin with susceptible results, and TMP-SMX

Percentage of hospitals with a pattern of SR for antimicrobials— *Staphylococcus aureus*



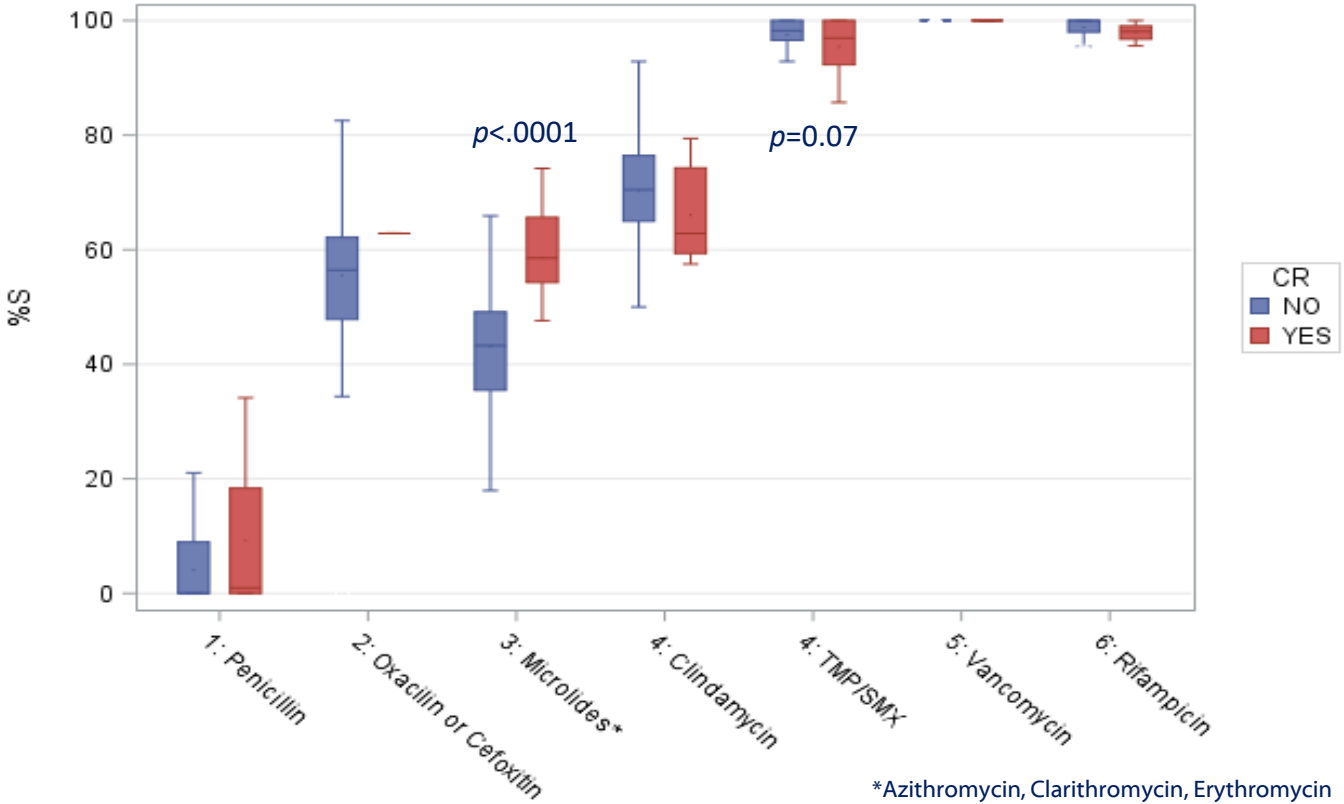
*Routine testing for urine not required by the CLSI **Doxycycline, Minocycline, or Tetracycline

Hospital-level %S (median, quartiles, range) among *S. aureus* isolates: SR *vs* non-SR (urine)



p values are based on Wilcoxon Rank Sum test and only shown if the numbers of hospitals are ≥20 in both SR and non-SR groups

Hospital-level %S (median, quartiles, range) among *S. aureus* isolates: SR *vs* non-SR (blood)



*Azithromycin, Clarithromycin, Erythromycin

p values are based on Wilcoxon Rank Sum test and only shown if the numbers of hospitals are ≥20 in both SR and non-SR groups

Factors associated with reporting of vancomycin susceptibility results among SR hospitals

		Urine (n=657)		Blood (n=2,876)	
		aPR	P-value	aPR	*p*-value
Non-susceptibility to narrower-spectrum agents*					
	No	reference		reference	
	Yes	5.67 (3.93–8.19)	<.0001	4.41 (3.85–5.06)	<.0001
Patient location					
	ED and 24-hour observation units	reference		reference	
	Intensive care units	1.34 (1.02–1.77)	0.039	1.30 (1.19–1.42)	<.0001
	Other inpatient locations	1.17 (0.97–1.40)	0.974	1.07 (0.97–1.17)	0.175
Age					
	<16 years	reference		reference	
	≥16 years	1.03 (0.60–1.78)	0.905	1.63 (1.28–2.08)	<.0001
Gender					
	Female	reference		reference	
	Male	0.93 (0.79–1.10)	0.385	0.98 (0.91–1.05)	0.527

*Penicillin, oxacillin/cefoxitin, TMP-SMX, doxycycline, minocycline, or tetractycline

Factors associated with reporting of macrolide susceptibility results among SR hospitals

		Blood (n=14,773)	
		aPR	*p*-value
Non-susceptibility to oxacillin/cefoxitin			
	No	1.29 (1.26–1.31)	<.0001
	Yes	reference	
Patient location			
	ED and 24-hour observation units	1.04 (1.02–1.06)	0.0003
	Intensive care units	0.96 (0.93–0.99)	0.008
	Other inpatient locations	reference	
Age			
	<16 years	1.12 (1.09–1.15)	<.0001
	≥16 years	reference	
Gender			
	Female	reference	
	Male	1.00 (0.99–1.02)	0.635

Summary (*S. aureus*) (1)

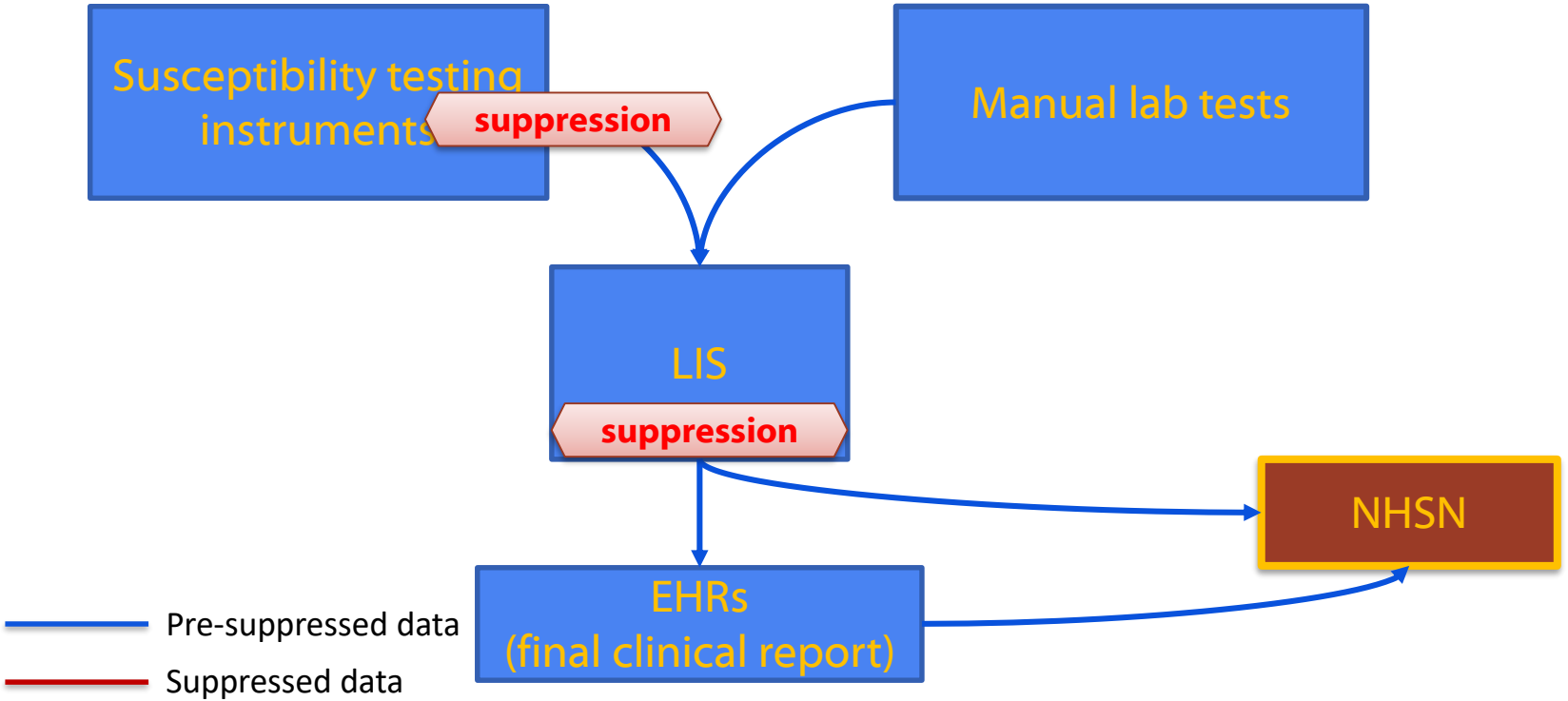
- AST reporting varies across hospitals and antimicrobials
- Only 48% and 36% hospitals routinely reported susceptibility results of all CLSI group A agents for urine and blood cultures, respectively
- Vancomycin, although in group B, is routinely reported in ~80% of all hospitals
- Many SR hospitals were unable to generate antibiograms for certain antimicrobials due to insufficient isolates with AST results that were partially reported

Summary (*S. aureus*) (2)

- Among isolates reported from hospitals with a pattern of SR for vancomycin, non-susceptibility to anti-MSSA agents, age, and isolates collected from ICU patients are more likely to report vancomycin susceptibilities
- Among blood isolates reported from hospitals with a pattern of SR for macrolides, susceptibility to OX/CEFOX, outpatient locations, and isolates collected from pediatric patients are more likely to report macrolide susceptibilities

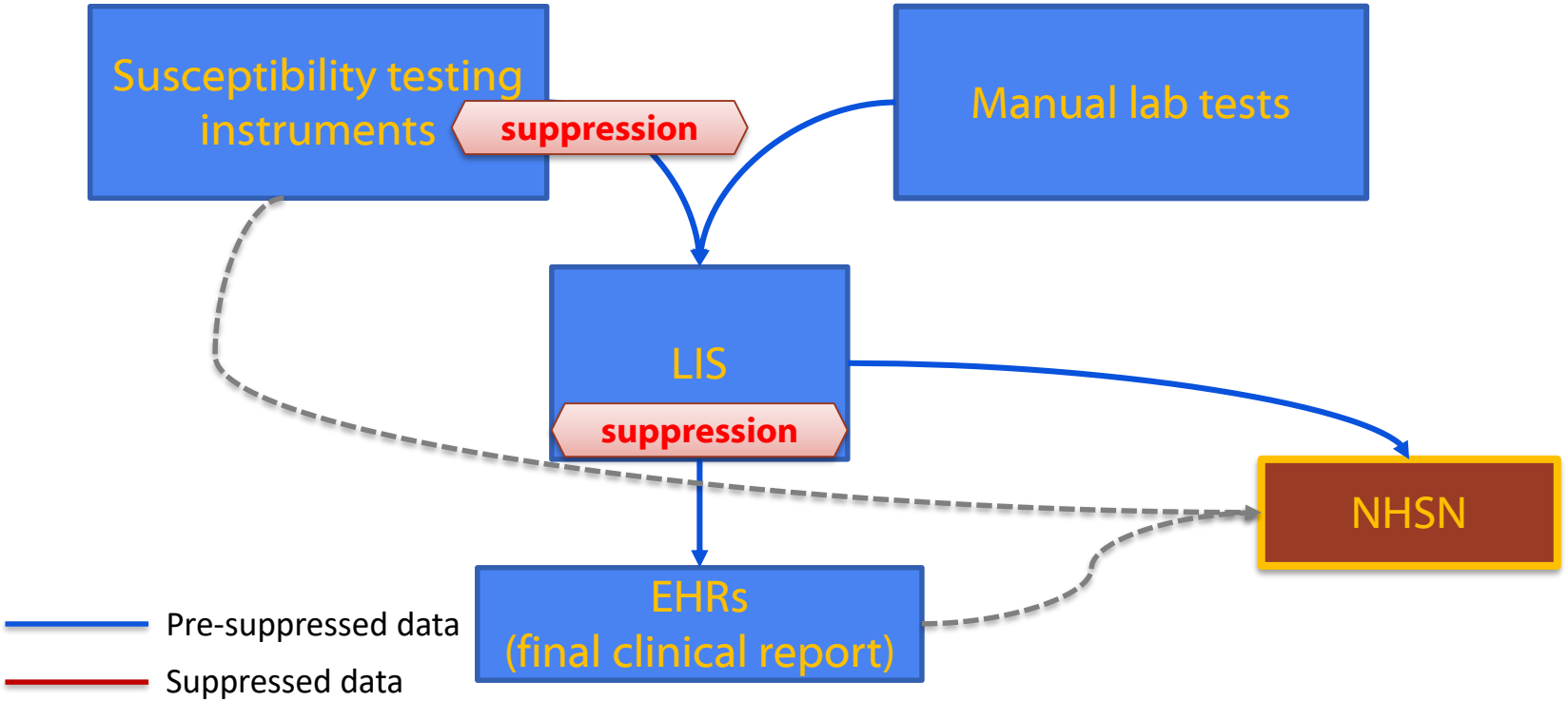
Discussion

Data captured and submitted to NHSN



*Laboratory Information System **Electronic Health Records

Data captured and submitted to NHSN



*Laboratory Information System **Electronic Health Records

Limitations

- Cross-sectional study using the final data reported to NHSN from 2017 through 2018
  - Changes of reporting behaviors during this time period can not be detected
  - The timing when the AST was reported during clinical courses is unavailable
- Use the reporting pattern to identify hospitals performed SR
  - Hospitals that practice SR with small differences of %reported between antimicrobials might be misclassified
  - Hospitals that performed SR but submitted pre-suppressed data to NHSN are classified as non-cascade hospitals
  - Reporting logics for individual facilities are not available
  - Unable to differentiate non-reporting from non-testing
- Only include urine and blood cultures from ED and inpatient locations

Conclusions

- A significant proportion of hospitals that reported to NHSN AR Option showed patterns of SR of various antimicrobials across Enterobacteriaceae and *S. aureus* isolated from urine and blood cultures
- CLSI M100 standards for reporting AST results are used inconsistently
- Among hospitals performed SR, reporting of certain AST results are associated with several patient and isolate factors which could include species identification, susceptibility to other antmicrobials, patient location, age, and gender — suggesting the existence of cascade reporting and selection biases in calculating antibiograms
- Antibiograms are not comparable between SR and non-SR hospitals

Recommendations

- Guidelines/recommendations from antimicrobial stewardship perspective to guide SR practices are needed
- Further investigation to understand the implementation of SR, regarding decision making process, information system and laboratory capacity to support SR, is needed
- For antimicrobial resistance surveillance purposes, technical solutions that can enable hospitals to obtain pre-suppressed AST data are needed
- SR should be taken into account in national AR surveillance, specifically for benchmarking and inter-hospital comparisons

Thank you

HsiuWu@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.