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Understanding the Hospital Antibiogram

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Learning Objectives

- Review the CLSI M39 guidelines for antibiogram development
- Discuss how to utilize a hospital antibiogram to guide empiric antibiotic selection and to detect bacterial resistance patterns
- Discuss how rates of MRSA, VRE, and other resistant organisms can be calculated using antibiogram data
- Describe how individual and hospital antibiograms may be used to foster prudent antimicrobial prescribing and optimize antimicrobial stewardship

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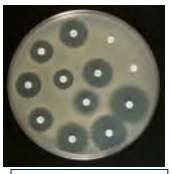
Common Definitions

Breakpoint = the MIC or zone size used to differentiate between susceptible, intermediate, or resistant antimicrobial susceptibility results (also called interpretive criteria)

Broth Microdilution (Vitek)



Disk Diffusion (Kirby Bauer)

CLSI M02, M07, M11, M39, M100

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Common Definitions

- **Susceptible (S)** = MIC is below S breakpoint; concentrations represented by MIC are easily achieved using standard doses of the antibiotic; high probability of clinical success
- **Intermediate (I)** = MICs above S breakpoint and approach R breakpoint; higher doses of antibiotic are needed or antibiotic needs to concentrate at infection site; response rates lower than S isolates
- **Resistant (R)** = MICs are above R breakpoint; concentrations represented by the MIC are not achieved with maximal doses of antibiotic and/or MIC falls in the range where resistance mechanisms are probable; treatment will likely fail

CLSI M100-S23, 2013

Common Definitions

- **Antibiogram** = a laboratory report that displays the overall susceptibility profile of a bacterial isolate to a variety of antibiotics
- **Cumulative Antibiogram** = a cumulative report that lists the percentage of isolates susceptible to a variety of antibiotics that includes data from patients receiving care at a particular institution/clinic over a defined period of time
  - Used to guide the selection of empiric antibiotic therapy
  - Used to identify the emergence of resistance or to monitor resistance trends over time

CLSI M02, M07, M11, M39, M100

Individual Isolate Antibiogram

Specimen: Urine
Culture Result: > 10^5 *Escherichia coli*
Susceptibilities:

Drug	MIC	Interpretation
Ampicillin	> 32	Resistant
Cefazolin	1	Susceptible
Ciprofloxacin	0.25	Susceptible
Tobramycin	1	Susceptible
Bactrim	≤ 10	Susceptible

History of Antibiogram Development

Prior to the publication of CLSI's M39-A in May 2002, there were no guidelines or standardized methods for antibiogram preparation

- Resistance rates may have been incorrectly conveyed leading to inappropriate empiric antibiotic selection
- Data could not be compared between institutions due to differences in methodology

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CLSI M39: Cumulative Antibiogram Development Guidelines

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CLSI M39

- Guideline for antibiogram development that provides recommendations for the collection, analysis and presentation of ***cumulative*** antimicrobial susceptibility test data
- Issues addressed:
  - Frequency of data analysis
  - Method for handling multiple isolates from the same patient
  - Species to be included in the report
  - Format for data presentation

Scope of M39-A

Recommendations set forth in the guideline are intended to be used by:

- Clinical microbiologists, physicians, pharmacists, epidemiologists and infection control personnel to analyze and present antimicrobial susceptibility test data
- Clinicians and prescribers when making clinical decisions regarding empiric antibiotic therapy
- Laboratory information systems (LIS) and manufacturers of diagnostic software to design information systems for the storage and analysis of antimicrobial susceptibility test data

Primary Aim of CLSI M39:

To guide clinicians in the selection of appropriate ***empiric*** antimicrobial therapy

Desirable Characteristics of Data Analysis Software

- Susceptibility test result data files should be available in a consistent format utilizing consistent codes in order to facilitate data analysis and interpretation
- Data should be preserved and communicated clearly if more than one isolate is recovered or more than one panel is used for susceptibility testing
- Data should be easily importable and modifiable

Important Information for Individual Culture Data

Patient Demographics

- Unique patient identifier
- Health care facility
- Date of birth or age
- Gender
- Patient location

Specimen Information

- Specimen identifier
- Specimen type
- Date of collection
- Body site

Organism Information

- Organism identification
- Isolate number
- Ability to compare results over time
- Supplemental information

Susceptibility Data

- MIC or zone size with interpretation for all antibiotics tested
- All susceptibility testing methods used

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Summary Recommendations for Antibiogram Development

- Compile, analyze and present data at least annually
- Include only final, verified results
- Include only diagnostic (NOT surveillance) isolates
- Include only the first isolate per patient per reporting period
- Include only species with testing data for ≥ 30 isolates per reporting period

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Summary Recommendations for Antibiogram Development

- Include only antimicrobial agents routinely tested (not agents selectively tested)
- Report only %S, not %I (except for viridans strep and penicillin)
- *Streptococcus pneumoniae*
  - Report %S using meningitis and nonmeningitis breakpoints for ceftriaxone, cefotaxime and penicillin (also report %S for oral pen)
- *Staphylococcus aureus*
  - Report %S for all isolates and MRSA subset

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Annual Reporting

- In order to provide current susceptibility information to guide appropriate empiric antibiotic selection, data should be analyzed and reported at least yearly
- More frequent analysis may be needed when:
  - Large numbers of isolates have been tested
  - New antimicrobial agents have been tested
  - Clinically relevant changes occur

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Data to Include Within Antibiogram Tables

- Include only **final, verified susceptibility test results** from diagnostic specimens
  - Do not include isolates from surveillance cultures
- Susceptibility results for all isolates should be verified **prior** to being reported in the patient's medical record and the antibiogram
  - Many commercial susceptibility testing systems contain verification software
  - Appendix A - Suggestions for verification of antimicrobial susceptibility test results

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Appendix A: Verification of Results

Appendix A. Suggestions for Confirmation of Resistant (R), Intermediate (I), or Nonsusceptible (NS) Antimicrobial Susceptibility Test Results and Organism Identification

Organism or Organism Group	Resistance Phenotype Detected[a]	Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[b]		
		Category I	Category II	Category III
		Not reported or only rarely reported to date	Uncommon in most institutions	May be common, but is generally considered of epidemiological concern
		Action Steps:		
		• Confirm ID and susceptibility.[c] • Report to infection control. • Send to public health laboratory. • Save isolate. *Note: May be appropriate to notify infection control of preliminary findings before confirmation of results.*	• Confirm ID and susceptibility if uncommon in your institution.[c] • Check with infection control in your facility to determine if special reporting procedures or further action are needed. • Check with your local public health department to determine which isolates should be reported to them and when isolates should be sent to the public health laboratory.	• Confirm ID and susceptibility if uncommon in your institution.[c] • Check with infection control in your facility to determine if special reporting procedures or further action are needed.
Any Enterobacteriaceae	Carbapenem – I or R[d]		x	
	Amikacin, gentamicin, and tobramycin – R			x
Escherichia coli *Klebsiella* spp. *Proteus mirabilis*	Extended-spectrum cephalosporin[e] – I or R			x
Salmonella and *Shigella* spp.[f]	Cephalosporin III – I or R		x	
	Fluoroquinolone – I or R		x	
Acinetobacter baumannii	Colistin polymyxin – R		x	
	Carbapenem – I or R			x
Pseudomonas aeruginosa	Colistin polymyxin – I or R		x	
	Amikacin, gentamicin, and tobramycin – R Carbapenem – I or R			x

CLSI M39-A4, 2014

Appendix A: Verification of Results

Appendix A. (Continued)

Organism or Organism Group	Resistance Phenotype Detected[a]	Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[a]		
		Category I	Category II	Category III
		Not reported or only rarely reported to date	Uncommon in most institutions	May be common, but is generally considered of epidemiological concern
Stenotrophomonas maltophilia	Trimethoprim-sulfamethoxazole – I or R.		x	
Haemophilus influenzae	Carbapenem – NS Ceftaroline – NS Extended-spectrum cephalosporin[c] – NS Fluoroquinolone – NS	x		
	Amoxicillin-clavulanate – R. Ampicillin – R and β-lactamase negative		x	
Neisseria gonorrhoeae	Extended-spectrum cephalosporin[c] – NS		x	
	Fluoroquinolone – I or R.			x
Neisseria meningitidis	Ampicillin or penicillin – R. Extended-spectrum cephalosporin[c] – NS Meropenem – NS	x		
	Ampicillin or penicillin – I Azithromycin – NS Chloramphenicol – I or R. Fluoroquinolone – I or R. Minocycline – NS Rifampin – I or R.		x	
Enterococcus spp.	Daptomycin – NS Linezolid – R.		x	
	Vancomycin – R. High-level aminoglycoside – R.			x
Staphylococcus aureus	Vancomycin MIC = 8 μg/mL[d]		x[d]	
	Ceftaroline – R. Daptomycin – NS Linezolid – R. Quinupristin-dalfopristin – I or R. Vancomycin MIC = 4 μg/mL		x	
	Oxacillin – R.			x
Staphylococcus, coagulase-negative	Daptomycin – NS Linezolid – R. Quinupristin-dalfopristin – I or R. Vancomycin – I or R[f]		x	

CLSI M39-A4, 2014

Which Isolates Should be Included From Each Patient?

- Include only the **first isolate of a given species per patient per reporting period** regardless of:
  - Body site
  - Antimicrobial susceptibility testing profile
  - Phenotypic characteristics
- Analytic software should be able to select "first isolates" when calculating susceptibility rates

Rationale Behind First Isolate Per Patient Recommendation

- Multiple isolates of the same organism are frequently cultured from the same patient from successive specimens
  - Inclusion of multiple isolates from the same patient can bias susceptibility data (overestimate resistance)
  - May lead to overestimation of the risk of acquiring a resistant strain and the use of more broad spectrum empiric antibiotic therapy
- Multiple isolate information is valuable for detecting emerging resistance and for infection control purposes

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Susceptibility Rates Depending on Calculation Method Utilized

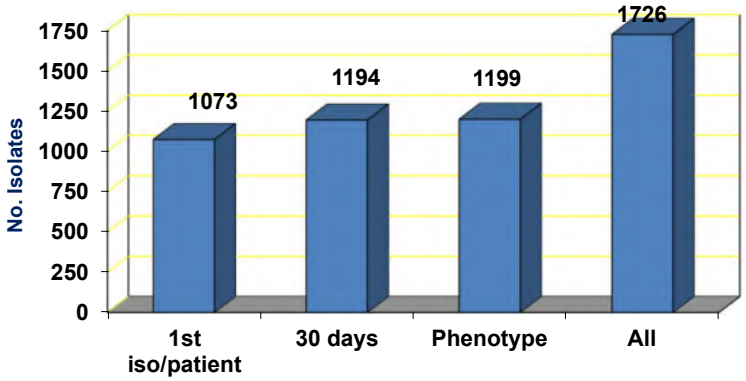
Calculation Method	N	%S
Isolate-based estimate		
All isolates	1892 isolates	54
Patient-based estimates		
Most susceptible	1019 patients	69
First isolate	1019 patients	67
Weighted average	1019 patients	66
Most resistant	1019 patients	64
Episode-based estimates		
First isolate, 30-day interval	1060 episodes	66
First isolate, 7-day interval	1262 episodes	61
Phenotype-based estimates		
First isolate, major or minor differences in oxacillin only	1070 "strains"	66
First isolate, major differences in any antimicrobial agent	1311 "strains"	61

Abbreviation: %S, percent susceptible.

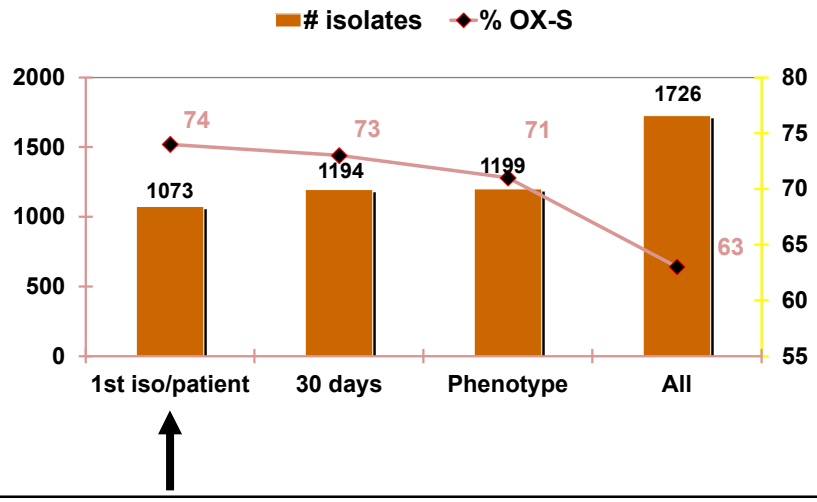
CLSI M39-A4, 2014

S. aureus - Oxacillin Handling Duplicates

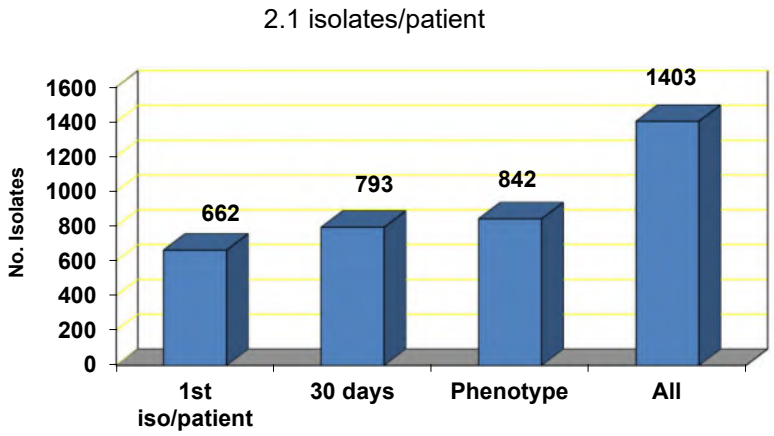
1.6 isolates/patient



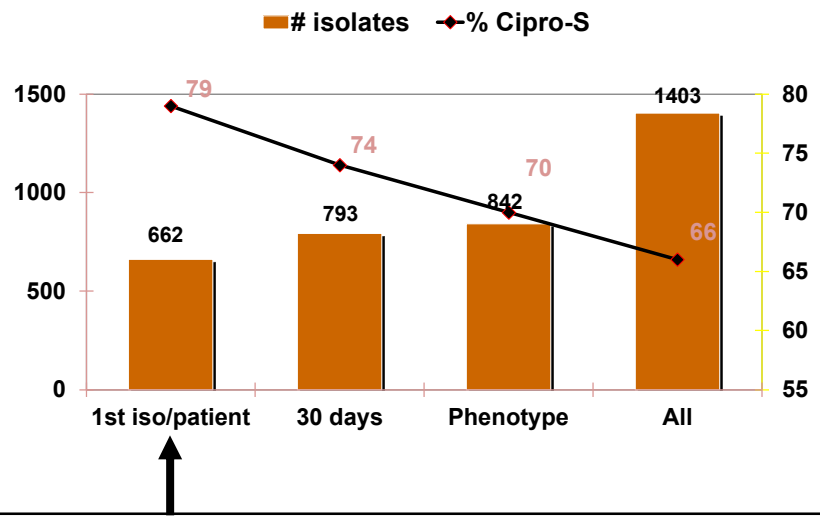
S. aureus – Oxacillin Handling Duplicates



P. aeruginosa – Ciprofloxacin Handling Duplicates



P. aeruginosa – Ciprofloxacin Handling Duplicates



Verifying the Removal of Duplicate Isolates

Line listings of susceptibility data should be used to manually calculate number of isolates and susceptibility rates and then compared with computer-generated reports to ensure that it is calculating the data correctly

- Initial use of the program
- When changes are made to the analytical software or MIC/disk diffusion interpretive criteria
- For select organisms where multiple cultures are often performed

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Verification of Results

Appendix C. Example of Using a Line Listing to Verify Susceptibility Rates Determined by the Analysis Software

Table C1. Statistics Generated for *Streptococcus pneumoniae* by the Analysis Software

Organism	n	CRO Meningitis	CRO Nonmeningitis	CLI	ERY	LVX	MEM	PEN Meningitis	PEN Nonmeningitis	PEN oral	SXT	VAN
spn	35	77% S	94% S	77% S	60% S	100% S	74% S	54% S	100% S	54% S	71% S	100% S
		17% I	6% I					NA		29% I		
		6% R	0% R					46% R		17% R		

Abbreviations: %I, percent intermediate; %R, percent resistant; %S, percent susceptible; CLI, clindamycin; CRO, ceftriaxone; ERY, erythromycin; LVX, levofloxacin; MEM, meropenem; NA, not applicable; PEN, penicillin; spn, *S. pneumoniae*, SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Table C2. Line Listing of All Isolates of This Organism Stored in the Database. Most patients had a single isolate; although two patients, highlighted in gray, had two isolates each.

Abbreviations: BAL, bronchoalveolar lavage; CLI, clindamycin; CRO, ceftriaxone; CSF, cerebrospinal fluid; ERY, erythromycin; I, intermediate; LVX, levofloxacin; MEM, meropenem; PEN, penicillin; R, resistant; S, susceptible; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

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Number of Isolates Needed

- Include only species with testing data for **≥ 30 isolates per reporting period**
- If fewer than 30 isolates are available:
  - Determine if inclusion of organism is essential → if so, include data with footnote
  - Consider combining species (e.g., *Shigella* spp.)
  - Consider combining data from multiple years
  - Consider using data from alternate sources (e.g., State Department of Health, local/regional hospital, published)

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< 30 Isolate Footnote:

"Please exercise discretion when interpreting the susceptibility of organisms with < 30 bacterial isolates"

Antimicrobial Agents to Report on the Antibiogram

- Include only antimicrobial agents that have been routinely tested against the population of isolates to be analyzed
- Assure that each antimicrobial agent reported is appropriate for the species
- Store data used for surrogate testing, but report % susceptibility for the agent represented by the surrogate
  - Cefoxitin disk – present % S for oxacillin

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Antibiogram Example

Memorial Medical Center
1 January – 31 December 2012 Cumulative Antimicrobial Susceptibility Report*
Percent Susceptible

Gram-Negative Organisms	No. Strains	Amikacin	Ampicillin	Cefazolin	Cefotaxime	Ceftazidime	Ciprofloxacin	Nitrofurantoin†	Gentamicin	Meropenem	Piperacillin-tazobactam	Trimethoprim-sulfamethoxazole	Tobramycin
Acinetobacter baumannii	32	80	R	R	34	52	51	–‡	60	80	46	58	59
Citrobacter freundii	49	100	R	R	72	67	90	78	100	99	67	67	100
Enterobacter aerogenes	31	100	R	R	68	69	92	85	91	99	74	95	91
Enterobacter cloacae	76	99	R	R	61	62	92	81	90	99	77	84	90
Escherichia coli	1433	99	36	68	96	94	72	98	91	99	51	65	92
Klebsiella pneumoniae	543	99	R	72	91	92	84	74	94	95	86	81	94
Morganella morganii	44	100	R	R	85	81	99	R	100	99	64	75	100
Proteus mirabilis	88	100	87	80	99	99	89	R	90	100	70	73	93
Pseudomonas aeruginosa	397	97	R	R	R	76	75	R	80	80	85	R	83
Salmonella spp.	32	–	88	–	97	97	90	–	–	100	91	86	–
Serratia marcescens	50	100	R	R	82	94	95	R	94	99	94	91	89
Shigella spp.	33	–	64	–	100	100	95	–	–	100	84	69	–
Stenotrophomonas maltophilia	72	R	R	R	R	63	6	R	R	R	–	98	R

* The percent susceptible for each organism/antimicrobial combination was generated by including the first isolate of that organism encountered on a given patient.
† Nitrofurantoin data from testing urine isolates only.
‡ (–) drug not tested or drug not indicated.

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Antibiogram Example

Memorial Medical Center
1 January – 31 December 2012 Cumulative Antimicrobial Susceptibility Report*
Percent Susceptible

Gram-Negative Organisms	No. Strains	β-lactams						Aminoglycosides			FQs	Other	
		Ampicillin	Cefazolin	Cefotaxime	Ceftazidime	Meropenem	Piperacillin-tazobactam	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Nitrofurantoin†	Trimethoprim-sulfamethoxazole
Acinetobacter baumannii	32	R	R	34	52	80	46	80	60	59	51	–‡	58
Citrobacter freundii	49	R	R	72	67	99	67	100	100	100	90	78	67
Enterobacter aerogenes	31	R	R	68	69	99	74	100	91	91	92	85	95
Enterobacter cloacae	76	R	R	61	62	99	77	99	90	90	92	81	84
Escherichia coli	1433	36	68	96	94	99	51	99	91	92	72	98	65
Klebsiella pneumoniae	543	R	72	91	92	99	86	99	94	94	84	74	81
Morganella morganii	44	R	R	85	81	99	64	100	100	100	99	R	75
Proteus mirabilis	88	87	80	99	99	100	70	100	90	93	89	R	73
Pseudomonas aeruginosa	397	R	R	R	76	80	85	97	80	83	75	R	R
Salmonella spp.	32	88	–	97	97	100	91	–	–	–	90	–	86
Serratia marcescens	50	R	R	82	94	99	94	100	94	89	95	R	91
Shigella spp.	33	64	–	100	100	100	84	–	–	–	95	–	69
Stenotrophomonas maltophilia	72	R	R	R	63	R	R	R	R	R	6	R	98

* The percent susceptible for each organism/antimicrobial combination was generated by including the first isolate of that organism encountered on a given patient.
† Nitrofurantoin data from testing urine isolates only.
‡ (–) drug not tested or drug not indicated.
Abbreviations: FQ, fluoroquinolone; R, intrinsic resistance.

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Supplemental Drug Testing

- Additional antibiotics may be tested for susceptibility against isolates displaying significant resistance to routine agents, or upon clinician request
  - Example: Colistin susceptibility testing on *Pseudomonas aeruginosa* resistant to all antibiotics on primary testing panel
- Results should not be routinely included in antibiogram since they have only been tested against a subset of isolates

Selective Reporting Example

GRAM NEGATIVE BACILLI - INTENSIVE CARE UNITS (INCLUDING MICU, CCU, SICU, PICU, and IICU)

	# Tested	Amikacin	Gentamicin	Tobramycin	Ampicillin	Amp/Sulb	Pip/Tazobac	Cefazolin	Cefoxitin	Ceftazidime	Ceftriaxone	Cefepime	Ciprofloxacin	Levofloxacin	Aztreonam**	Meropenem	Trimeth/Sulfa	Colistin	Nitrofurantoin*
MIC Breakpoint (µg/ml)		≤ 16	≤ 4	≤ 4	≤ 8	≤ 8	≤ 16	≤ 8	≤ 8	≤ 4	≤ 1	≤ 8	≤ 1	≤ 2		≤ 1	≤ 40	≤ 2	≤ 32
Pseudomonas aeruginosa breakpoint		≤ 16	≤ 4	≤ 4			≤ 64			≤ 8		≤ 8	≤ 1	≤ 2		≤ 2		≤ 2	
Acinetobacter baumannii	5	50†	**60**	80		80	**20**			40		**40**	**40**	**40**		**40**	**40**	100†	
Enterobacter cloacae	38	97	95	95			86			82	82	97	95	95		100	89		
Escherichia coli	120	100	95	93	50	62	94	84	88	93	90	93	77	77		100	77		93
Klebsiella pneumoniae	60	97	98	95		80	85	90	87	95	95	93	93	93		95	90		25
Proteus mirabilis	26	100	**85**	96	85	88	100	92	96	96	100	96	81	81		100	81		
Pseudomonas aeruginosa	36	100	100	100			94			89		92	89	83		92			

NT = Not tested or current automated susceptibility test results are unreliable
* Nitrofurantoin should only be used for the treatment of uncomplicated urinary tract infections
** Aztreonam and ceftazidime display similar susceptibility patterns so that aztreonam susceptibility may be inferred from ceftazidime susceptibility
† Susceptibility selectively performed against 2 Multidrug-Resistant (MDR) strains

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Suggested Supplemental Analyses by Organism

Organism	Suggested Analyses
Streptococcus pneumoniae	**Penicillin**: calculate and list %S using meningitis, non-meningitis, and oral penicillin breakpoints **Ceftriaxone, cefotaxime, cefepime:** calculate and list %S using meningitis and non-meningitis breakpoints
Viridans Streptococcus	**Penicillin:** for isolates from sterile sites, calculate and list separately %S and %I
Staphylococcus aureus	Consider including separate analysis for MSSA and MRSA; indicate % of *S. aureus* isolates that are MRSA
***Enterococcus* spp.**	Consider separating analysis for *E. faecalis* and *E. faecium;* indicate % of Enterococci that are VRE
Klebsiella pneumoniae	Consider reporting data by resistance mechanism (ESBL- or KPC-producing) and/or hospital unit to illustrate potentially useful antibiotics for empiric therapy

Streptococcus pneumoniae Supplemental Analysis

Example:

Organism	No. Strains	%S									
		AMX	CTX	CRO	CLI	ERY	LVX	PEN (IV)	PEN (oral)	SXT	VAN
S. pneumoniae	110	94	–*	–*	81	64	99	–*	64	69	100
Meningitis	110	–	85	84	–	–	–	64	–	–	–
Nonmeningitis	110	–	95	96	–	–	–	84	–	–	–

* Breakpoints differ for cefotaxime, ceftriaxone, and penicillin based on diagnosis. Cefotaxime, ceftriaxone, and penicillin meningitis applies to susceptibility of pneumococci for patients who have meningitis; cefotaxime, ceftriaxone, and penicillin nonmeningitis applies to susceptibility of pneumococci for patients who do not have meningitis.

Abbreviations: %S, percent susceptible; AMX, amoxicillin; CLI, clindamycin; CRO, ceftriaxone; CTX, cefotaxime; ERY, erythromycin; IV, intravenous; LVX, levofloxacin; No., number; PEN, penicillin; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

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MRSA and VRE

GRAM-POSITIVE COCCI - INPATIENT (EXCLUDING INTENSIVE CARE UNITS)

	# Tested	Ampicillin	Clindamycin	Gentamicin Synergy*	Streptomycin Synergy*	Rifampin **	Oxacillin ***	Penicillin	Vancomycin	Linezolid	Trimethoprim-Sulfamethoxazole
Staph aureus MIC Breakpoint (µg/ml)			≤ 0.5			≤ 1	≤ 2	≤ 0.12	≤ 2	≤ 4	≤ 40
Coag-Neg Staph MIC Breakpoint (µg/ml)							≤ 0.25		≤ 4		
Enterococcus MIC Breakpoint (µg/ml)		≤ 8						≤ 8	≤ 4	≤ 2	
Methicillin-Susceptible *Staph aureus* (MSSA)	161	-	90	-	-	100	100	25	100		98‡
Methicillin-Resistant *Staph aureus* (MRSA)	112	-	77	-	-	99	0	0	100		100‡
Coagulase Negative Staphylococcus	197	-	68	-	-	99	46	18	100		
Enterococcus Vancomycin-Susceptible	167	97	-	83	87		-	97	100		
Enterococcus Vancomycin-Resistant (VRE)	32	33	-	55	47		-	33	0	100†	

41% of Inpatient *Staph aureus* isolates are MRSA; 16% of Inpatient *Enterococci* are VRE

* If susceptible, an aminoglycoside (gentamicin or streptomycin) may be used with a cell wall active agent (ampicillin/vancomycin) for the treatment of serious Enterococcal infections (such as endocarditis).
** Rifampin should not be used alone.
*** Penicillin-resistant, oxacillin-susceptible strains are susceptible to other penicillinase-stable penicillins (nafcillin), cephalosporins (cefazolin), beta-lactamase inhibitor combinations, and carbapenems. Oxacillin-resistant staphylococci are resistant to most currently-available beta-lactam antibiotics.
‡ Trimethoprim-sulfamethoxazole (Bactrim) should only be considered for treatment of skin and soft tissue infections due to these organisms.
† Susceptibility only performed against 27 isolates

Klebsiella pneumoniae Segregated Data Analysis

Example:

Organism	No. Strains	%S									
		AMK	AMP	CFZ	CRO	CIP	GEN	IPM	PTZ	TET	SXT
K. pneumoniae (All)	1163	63	R	44	48	46	74	64	53	84	46
K. pneumoniae (Extended-spectrum cephalosporin resistant)	233	30	R	0	0	6	48	100	0	84	3
K. pneumoniae (Carbapenem-resistant)	361	5	R	0	0	0	28	0	0	82	0
K. pneumoniae (**Not** resistant to extended-spectrum cephalosporins or carbapenems)	569	100	R	84	99	94	96	100	88	87	95

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CRO, ceftriaxone; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; TET, tetracycline; R, resistant; SXT, trimethoprim-sulfamethoxazole.

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Additional Data Stratification

- **By nursing unit or site of care** → data segregated by patient location at time specimen was collected for culture
- **By organism's resistance profile**
- **By specimen type or infection site** → urine isolates, bloodstream isolates; only include antibiotics useful for these infections
- **By clinical service or patient population**

Data Stratified by Patient Location/Infection Type

Appendix D. Examples of Supplemental Analyses – Stratifying Cumulative Antibiogram Data by Various Parameters

Example D1. *Staphylococcus aureus* by patient location

Organism	Location	No. Strains	%S							
			CLI	DAP	ERY	OXA	PEN	LNZ	SXT	VAN
S. aureus	OP	781	86	99	54	75	4	99	96	100
	IP	461	66	99	42	53	5	99	95	100
	ICU	231	70	99	44	54	5	99	96	100

Abbreviations: %S, percent susceptible; CLI, clindamycin; DAP, daptomycin; ERY, erythromycin; ICU, intensive care unit; IP, inpatient (non-ICU); LNZ, linezolid; No., number; OP, outpatient; OXA, oxacillin; PEN, penicillin; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Example D2. Urine isolates from inpatients and from outpatients for selected uropathogens

Organism	Location	No. Strains	%S						
			AMP	CFZ	CTX	CIP	NIT	GEN	SXT
Escherichia coli	OP	1205	56	91	98	84	98	90	72
	IP	436	39	83	93	62	97	78	60
Klebsiella pneumoniae	OP	517	R	95	97	95	50	97	86
	IP	138	R	77	85	91	52	88	70
Proteus mirabilis	OP	271	83	95	100	88	R	96	82
	IP	32	74	94	94	81	R	88	75
Pseudomonas aeruginosa	OP	131	R	R	R	67	R	84	R
	IP	169	R	R	R	56	R	75	R

Abbreviations: %S, percent susceptible; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CTX, cefotaxime; GEN, gentamicin; IP, inpatient (non-ICU); NIT, nitrofurantoin; No., number; OP, outpatient; R, resistant; SXT, trimethoprim-sulfamethoxazole.

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Data Stratified by Infection Type

Example D3. Bloodstream isolates for selected pathogens from all patients (continued)

Organism	No. Strains	%S										
		AMK	AMP	CFZ	CAZ	CTX	CIP	GEN	IPM	PTZ	SXT	TOB
E. coli	120	100	54	77	95	95	71	84	100	90	70	90
K. pneumoniae	73	100	R	81	92	86	84	87	99	82	75	94
P. aeruginosa	41	94	R	–	79	R	71	84	79	87	R	88

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CAZ, ceftazidime; CFZ, cefazolin; CIP, ciprofloxacin; CTX, cefotaxime; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; R, resistant; SXT, trimethoprim-sulfamethoxazole; TOB, tobramycin.

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Other Presentation Issues

- Susceptibility panels may differ for testing of isolates from different body sites or groups
  - Include data on highest number of bacteria - antibiotic combinations tested
  - May be useful to report susceptibility of subsets separately if not tested against all antibiotics
- Presenting data when a change in testing protocol is implemented during the analysis period

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Handling Variations in Drug Panels

Organism	No. Strains	%S								
		AMP	CFZ	CRO	CIP	GEN	IPM	LVX*	PTZ	SXT
E. coli (All)	3636	61	92	99	92	93	100	80	96	76
E. coli (Nonurine)	292	44	82	96	80	87	100	80	93	62
E. coli (Urine)	3417	63	93	99	93	94	100	NT	97	77

* Tested on nonurine isolates only (n = 292). Therefore, results should not be compared to those of other antimicrobial agents listed, all of which were tested against both urine and nonurine isolates.

Abbreviations: %S, percent susceptible; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CRO, ceftriaxone; GEN, gentamicin; IPM, imipenem; LVX, levofloxacin; No., number; PTZ, piperacillin-tazobactam; SXT, trimethoprim-sulfamethoxazole.

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Handling Variations in Drug Panels

Organism	No. Strains	%S									
		AMP	CFZ	CPM*	CRO	CTZ	CIP	GEN	IPM	PTZ	SXT
E. cloacae	44	R	R	86	75	76	93	95	98	84	90
E. coli	378	49	90	96	95	95	77	91	100	86	74
K. pneumoniae	97	R	94	96	94	93	95	100	98	95	86
P. aeruginosa	73	R	R	86	R	85	79	91	93	92	R

* Added to test panel August 2012. Results for CPM should not be compared directly to those of other agents because CPM was not tested on all isolates.

Abbreviations: %S, percent susceptible; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CPM, cefepime; CRO, ceftriaxone; CTZ, ceftizoxime; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; R, resistant; SXT, trimethoprim-sulfamethoxazole.

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Other Presentation Formats

- Presenting data for particular units, patient types, or facilities
  - Isolates from ICU patients, Burn Unit patients and LTCF patients are often more resistant
- Notification of intrinsic resistance
- Tables or graphs of emerging resistance trends
  - Resistance over several years
  - Useful for display of resistance trends in MRSA, *Pseudomonas aeruginosa*, ESBLs, KPCs, etc.

Intrinsic Resistance

Organism \ Antimicrobial Agent	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Piperacillin	Ticarcillin	Cephalosporin I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Tetracyclines	Nitrofurantoin	Polymyxin B Colistin
Citrobacter freundii	R	R	R			R	R	R			
Citrobacter koseri	R	R	R	R	R						
Enterobacter aerogenes	R	R	R			R	R	R			
Enterobacter cloacae	R	R	R			R	R	R			
Escherichia coli	There is no intrinsic resistance to β-lactams in this organism.										
Escherichia hermannii	R				R						
Hafnia alvei	R	R	R			R	R				
Klebsiella pneumoniae	R				R						
Morganella morganii	R	R				R		R	R	R	R
Proteus mirabilis	There is no intrinsic resistance to β-lactams in this organism.								R	R	R
Proteus penneri	R					R		R	R	R	R
Proteus vulgaris	R					R		R	R	R	R
Providencia rettgeri	R	R				R			R	R	R
Providencia stuartii	R	R				R			R	R	R
Salmonella and *Shigella* spp.	There is no intrinsic resistance to β-lactams in these organisms; see Table 2A, comment (6) for reporting.										
Serratia marcescens	R	R	R			R	R	R		R	R
Yersinia enterocolitica	R	R			R	R					

M100-S21 Appendix B: Intrinsic Resistance - *Enterobacteriaceae*

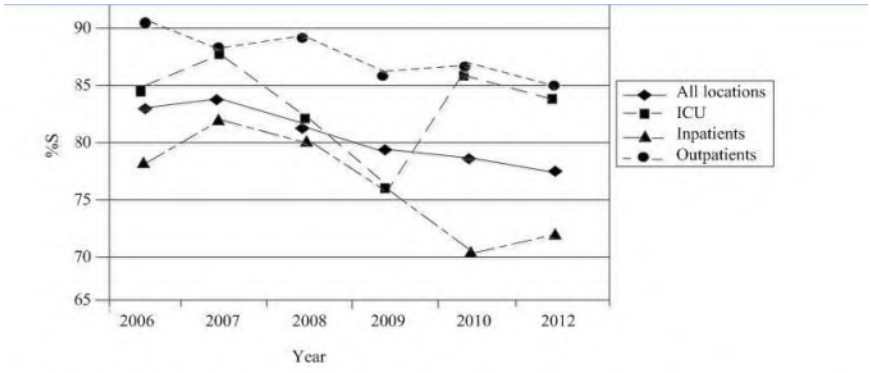
Displaying Intrinsic Resistance in a Unit Specific Antibiogram

GRAM NEGATIVE BACILLI - BURN UNIT

	# Tested	Amikacin	Gentamicin	Tobramycin	Ampicillin	Amp/Sulb	Pip/Tazobac	Cefazolin	Cefoxitin	Ceftazidime	Ceftriaxone	Cefepime	Ciprofloxacin	Levofloxacin	Aztreonam**	Imipenem	Meropenem	Trimeth/Sulfa	Colistin
MIC Breakpoint (µg/ml)		≤ 16	≤ 4	≤ 4	≤ 8	≤ 8	≤ 16	≤ 8	≤ 8	≤ 8	≤ 8	≤ 8	≤ 1	≤ 2	≤ 8	≤ 4	≤ 4	≤ 40	≤ 2
Pseudomonas aeruginosa breakpoint		≤ 16	≤ 4	≤ 4			≤ 64	-		≤ 8		≤ 8	≤ 1	≤ 2	≤ 8	≤ 4	≤ 4		≤ 2
Acinetobacter baumannii	16	60†	13	69		31	13			0		13	13	13		13	NT	13	90†
Enterobacter cloacae	15	100	100	100			47			47	47	100	100	100		100	100	100	
Escherichia coli	23	100	87	91	35	43	100‡	87	87	91	91	96	78	78		100	100	83	
Klebsiella pneumoniae	15	100	100	100		87	100	100	93	100	100	100	100	100		100	100	93	
Pseudomonas aeruginosa	14	100	86	100			79			71		86	79	79		71	93		

Black boxes signify intrinsic resistance; NT = Not tested or current automated susceptibility test results are unreliable
* Nitrofurantoin should only be used for the treatment of uncomplicated urinary tract infections
** Aztreonam and ceftazidime display similar susceptibility patterns so that aztreonam susceptibility may be inferred from ceftazidime susceptibility
† Susceptibility only selectively performed against 10 Multidrug-Resistant (MDR) strains; ‡ Susceptibility performed on only 19 isolates

Emerging Resistance Trends



Abbreviation: ICU, intensive care unit.

Figure F1. Five-Year Trend – Oxacillin %S for *Staphylococcus aureus* From All Locations and by Patient Care Area 2006 to 2012

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Emerging Resistance Trends

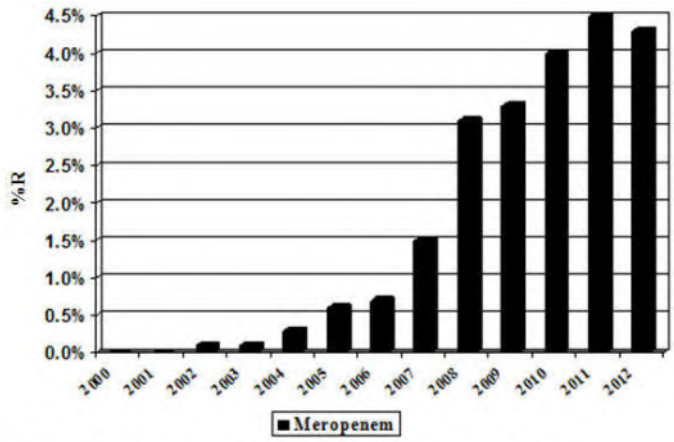

Figure F3. *Klebsiella pneumoniae* – Meropenem %R 2000 to 2012

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Constructing the Antibiogram

- **Cover page:** facility included, inclusive dates of report, contact information
- **Unit or site-specific susceptibility tables:** ICUs, outpatient, urine, blood, etc.
  - **Name and number of bacteria isolated:** gives indication of relative frequency of organism as cause of infection
  - **Antibiotics tested against the organism:** consider including breakpoints

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Constructing the Antibiogram

- Percent of organisms susceptible to a particular antibiotic
- Footnotes for explanation of data, abbreviations, and therapeutic guidance
- Other optional information
  - Dosing information
  - Cost of antimicrobial therapy
  - Empiric antibiotics of choice by infection chart

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Empiric Antibiotics of Choice

Eskenazi Health

Recommended Empiric Antibiotic Regimens by Infection for Adult Patients

Infection and Suspected Organisms	Recommended Regimen	Alternative Regimen
Community Acquired Pneumonia *Streptococcus pneumoniae, Haemophilus influenzae, Legionella pneumophila, etc* *Pseudomonas aeruginosa* - consider in patients with structural lung disease, recent hospitalization, recent antibiotic therapy, or need for ICU admission	Ceftriaxone + Azithromycin Piperacillin-Tazobactam or Cefepime + Levofloxacin 750mg Daily	Levofloxacin 750mg Daily (normal renal function) Piperacillin-Tazobactam, Cefepime or Meropenem + Tobramycin + Azithromycin or Levofloxacin 750mg Daily
HAP/VAP* = Early onset (< 5 days), no risk for MDR pathogens, any severity *Streptococcus pneumoniae, Haemophilus influenzae,* MSSA, antibiotic sensitive enteric Gram-negative bacilli **HAP/VAP/HCAP* = Late onset (≥ 5 days) or risk factors for MDR pathogens**, any severity** Same as early onset PLUS MDR pathogens such as *Pseudomonas aeruginosa, Klebsiella pneumoniae,* MRSA	Ceftriaxone or Levofloxacin Piperacillin/tazobactam (preferred in ICU patients) or Cefepime +/- Tobramycin or Ciprofloxacin† + Vancomycin (if MRSA suspected)	Cefepime Meropenem or Cefepime + Tobramycin or Ciprofloxacin† + Vancomycin (if MRSA suspected)
Urinary Tract Infections - Community *Escherichia coli, Proteus mirabilis*	Nitrofurantoin, Ciprofloxacin or Levofloxacin	Trimethoprim-Sulfamethoxazole or Cephalexin
Urinary Tract Infections - Nosocomial *Escherichia coli, Enterobacter* spp, *Serratia marcescens, Pseudomonas aeruginosa, etc*	Ceftriaxone or Cefepime	Aztreonam
Acute Bacterial Meningitis - Adults *Streptococcus pneumoniae, Neisseria meningitidis*	Ceftriaxone + Vancomycin (+ Ampicillin if *Listeria* is suspected)	Vancomycin + Meropenem
Cellulitis - without open skin wound *Staphylococcus aureus* (MSSA), β-hemolytic streptococcus (*S. pyogenes, etc*)	Nafcillin or Cefazolin	Clindamycin or Vancomycin
Cellulitis - with abscess formation or pustules Same as above including possible CA-MRSA	Vancomycin	Trimethoprim-Sulfamethoxazole or Clindamycin
Diabetic Foot Infections§ - ulcer with ≥ 2 features of inflammation (erythema, warmth, pain, purulence, induration)		
Description	**Likely Causative Organisms**	**Empiric Therapy**
Mild‡ = Cellulitis extends < 2 cm around ulcer, infection limited to skin/superficial tissue; patient without SIRS	β-hemolytic Streptococcus, *S. aureus*	PO cephalexin, dicloxacillin, amoxicillin/clavulanate; use clindamycin or TMP/SMX if MRSA suspected
Moderate‡ = Cellulitis extending > 2 cm or involving structures deeper than skin/SC tissue (e.g., abscess, septic arthritis, osteomyelitis, fasciitis); patient without SIRS	β-hemolytic Streptococcus, *S. aureus* Consider Enterobacteriaceae if on antibiotics within past 30 days Consider obligate anaerobes if necrotic wound that has not been debrided	- Cefazolin (or vancomycin if patient has MRSA risk factors listed below) - Consider ceftriaxone alone if Enterobacteriaceae suspected - Add PO metronidazole if anaerobes suspected
Severe = Local infection with signs of SIRS manifested by ≥ 2 of the following: temp >38°C or <36°C, heart rate >90 beats/min, respiratory rate >20 breaths/min, WBC >12,000 or <4,000 cells/μL or >10% immature (band) forms	β-hemolytic Streptococcus, *S. aureus* (MSSA, MRSA), Enterobacteriaceae, *P. aeruginosa*	Vancomycin PLUS Piperacillin/ tazobactam; meropenem; ceftazidime/cefepime and PO metronidazole; OR levofloxacin/ciprofloxacin with PO metronidazole

ONCE CULTURE RESULTS ARE AVAILABLE, PLEASE STREAMLINE ANTIBIOTIC THERAPY

Review of Completed Antibiogram

- Ensure that all abbreviations are defined
- Data are included only for antibiotics that are appropriate for the organism (Table 2 in CLSI M100)
- Data are not included for antibiotics that are clinically inappropriate for an organism despite *in vitro* susceptibility (e.g., 1st generation cephalosporins and *Salmonella*)

Distribution of the Antibiogram

- The antibiogram should be made available to all prescribers of antibiotics, pharma-cists, Infection Control and Microbiology Lab personnel
  - Pocket guide
  - Within EMR or posted at nursing stations, order entry terminals, medical team rooms
  - Institutional website
  - PDA applications
- P&T, ID Subcommittee presentation

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Statistical Applications to the Antibiogram

- Establish confidence intervals to quantify the precision of %S estimate to guide therapy and policy decisions
- Determine the statistical significance of susceptibility changes over time
  - Statistically-significant differences may not always be clinically/epidemiologically important
  - Are differences due to changes in the organism or to changes in population, culturing practices or lab testing?

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Estimating Confidence Intervals

Table H1. 95% CIs for Selected Sample Sizes*

Sample Size	Susceptible or Resistant Rate																	
	10%		20%		30%		40%		50%		60%		70%		80%		90%	
10	0	43	5	52	10	61	17	69	24	76	31	83	39	90	48	95	57	100
20	2	31	7	42	14	52	22	61	30	70	39	78	48	86	58	93	69	98
30	3	26	9	38	17	48	25	58	33	67	42	75	52	83	62	91	74	97
40	3	24	10	35	18	46	26	55	35	65	45	74	54	82	65	90	76	97
50	4	22	11	33	19	44	28	54	37	63	46	72	56	81	67	89	78	96
60	4	20	12	32	20	43	29	53	38	62	47	71	57	80	68	88	80	96
70	5	20	12	31	20	42	29	52	39	61	48	71	58	80	69	88	80	95
80	5	19	13	30	21	41	30	51	39	61	49	70	59	79	70	87	81	95
90	5	18	13	30	21	40	30	50	40	60	50	70	60	79	70	87	82	95
100	5	18	13	29	22	40	31	50	40	60	50	69	60	78	71	87	82	95
200	7	15	15	26	24	37	33	47	43	57	53	67	63	76	74	85	85	93
400	7	13	16	24	26	35	35	45	45	55	55	65	65	74	76	84	87	93
600	8	13	17	23	26	34	36	44	46	54	56	64	66	74	77	83	87	92
1000	8	12	18	23	27	33	37	43	47	53	57	63	67	73	77	82	88	92

* CIs were calculated using the Agresti-Coull interval.
Abbreviation: CI, confidence interval.

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Assessing the Significance of Susceptibility Changes Over Time

Table H2. Percent Susceptible Decreases

Initial %S	Sample Size							
	10	20	50	100	200	400	600	1000
98	–	–	84	90	93	95	95	96
95	–	65	78	85	89	91	92	92
90	30	55	72	78	82	85	86	87
80	20	45	60	66	71	73	75	76
70	10	30	48	55	60	63	64	65
60	0	20	38	45	49	52	54	55
50	0	15	28	35	39	42	44	45
40	NS	5	20	25	30	33	34	35
30	NS	0	12	17	20	23	24	25
20	NS	NS	4	9	12	14	15	16
10	NS	NS	NS	2	4	5	6	7

Abbreviations: %s, percent susceptible; NS, nonsusceptible.

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Reporting Strategies to Guide Appropriate Antibiotic Use

Selective reporting – reporting certain antimicrobial susceptibility test results from an individual patient's isolate based on defined criteria such as organism identification, site of infection, and overall susceptibility profile

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Selective Reporting Examples for *Streptococcus pneumoniae*

Antibiotic	CSF	Blood and Sterile Site	Respiratory
Penicillin G	X	X*	X*
Ceftriaxone	X	X*	X*
Vancomycin	X	X	
Erythromycin			X
Levofloxacin/ Moxifloxacin		X	X
Doxycycline			X

* Report susceptibility using meningitis and non-meningitis breakpoints

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Selective Reporting Examples for *Enterococcus*

Antibiotic	Urine VSE	Blood VSE	Urine VRE	Blood VRE
Ampicillin	X	X	X	X
Vancomycin	X	X	X	X
Gent-syn		X		X
Strepto-syn		X		X
Nitrofurantoin	X		X	
Linezolid			X	X
Quinu/dalfo				X
Daptomycin				X

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Selective Reporting Examples for Gram-Negative Bacteria

Antibiotic	Enterobacteriaceae	*Pseudomonas aeruginosa*
Ampicillin	X	
Piperacillin	X	X
Cefazolin	X	
Ceftriaxone	X	
Ceftaz/Cefepime		X
Meropenem	X	X
Aminoglycosides	X	X
Cipro/Levofloxacin	X	X
TMP-SMX	X	

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Selective Reporting by Specimen Type

Antibiotic	Enterobacteriaceae	
	Blood	Urine
Ampicillin	X	X
Piperacillin	X	
Cefazolin	X	X
Ceftriaxone	X	X
Ceftaz/Cefepime		
Meropenem	X	
Aminoglycosides	X	X
Cipro/Levofloxacin	X	X
TMP-SMX	X	X

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Selective Reporting Example

Specimen: Urine
Culture Result: > 10^5 *Escherichia coli*
Susceptibilities:

Drug	MIC (µg/ml)	Interpretation
Ampicillin	> 32	Resistant
Pip/tazo	8	Susceptible
Cefazolin	1	Susceptible
Ceftriaxone	1	Susceptible
Cefepime	1	Susceptible
Meropenem	0.5	Susceptible
Ciprofloxacin	0.25	Susceptible
Tobramycin	1	Susceptible
Amikacin	2	Susceptible
Bactrim	≤ 10	Susceptible

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Selective Reporting Example

Specimen: Urine
Culture Result: > 10^5 *Escherichia coli*
Susceptibilities:

Drug	MIC (µg/ml)	Interpretation
Ampicillin	> 32	Resistant
Cefazolin	1	Susceptible
Ciprofloxacin	0.25	Susceptible
Tobramycin	1	Susceptible
Bactrim	≤ 10	Susceptible
Nitrofurantoin	16	Susceptible

Reporting Strategies to Guide Appropriate Antibiotic Use

Cascade reporting – reporting susceptibility results for second-line, broader spectrum and more costly agents ONLY IF an organism is resistant to primary agents

Enterobacteriaceae
Cascade Reporting Rules

Ampicillin R	**Report:** Amox/clav, Amp/sulb, Piperacillin, Pip/tazo
Cefazolin R	**Report:** Ceftriax, Ceftaz, Cefepime, Aztreonam, Imipenem
Gent R	**Report:** Tobramycin and/or Amikacin

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Cascade Reporting Example

Specimen: Urine
Culture Result: > 10^5 *Escherichia coli*
Susceptibilities:

Drug	MIC (mcg/ml)	Interpretation
Ampicillin	> 32	Resistant
Cefazolin	1	Susceptible
Ciprofloxacin	0.25	Susceptible
Nitrofurantoin	16	Susceptible
Bactrim	10	Susceptible

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Conclusions

- Antibiogram development is a multi-disciplinary process
- Utilizing standardized guidelines for antibiogram development enhances the accuracy, integrity and comparability of the data
- Cumulative antimicrobial susceptibility data reports are useful for guiding appropriate empiric antimicrobial use

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Understanding the Hospital Antibiogram

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