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The Nuts and Bolts of Antibiograms in Long-Term Care Facilities

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- M39 Working group member

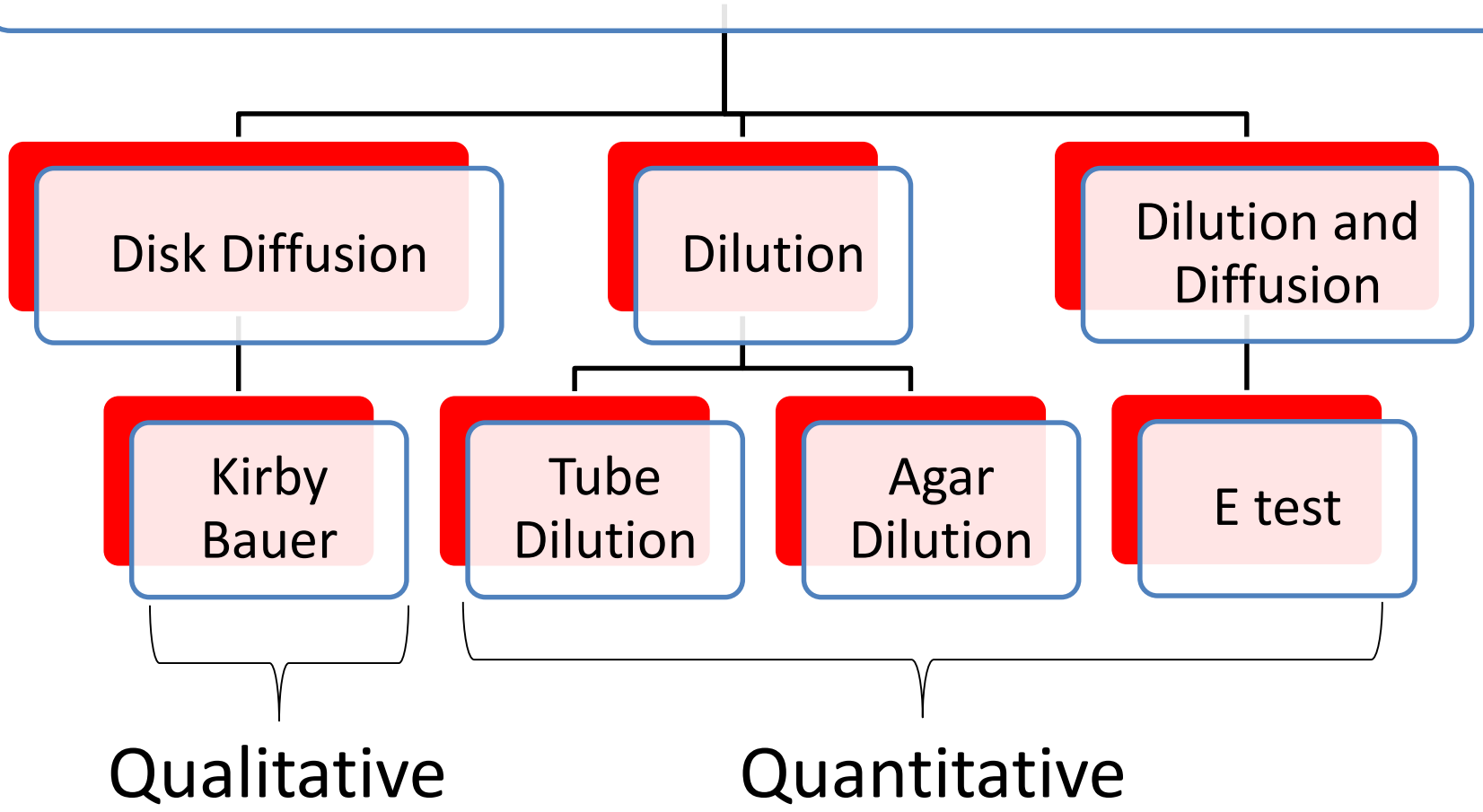
Objectives

- Review core concepts of antibiotic susceptibility and cumulative antibiotic susceptibility data/antibiograms
- Identify best practices for developing and maintaining annual antibiograms in long-term care
- Define how cumulative susceptibility data/antibiograms can be used in surveillance programs.

Antimicrobial Susceptibility Test

- Only performed on bacteria in which susceptibility to standardized treatment is not predictable.
  - Predictable
    - *β-Streptococcus*
  - Not-predictable
    - *E. coli*
- Antibiotics reported
  - Cascading antibiotics
  - Additional antibiotics fro MDROs
  - What methods
  - Breakpoints used

Antibiotic Susceptibility Testing



Terminology

- Sensitive
  - Based on the pharmaco-dynamics of an antimicrobial agent administered according to the normally recommended dosage and the organism causing an infection, the agent *will most likely inhibit the organism in vivo*.
- Intermediate (indeterminate)/Susceptible Dose Dependent
  - *…..might inhibit the organism in vivo.* /Use higher dose
  -
- Resistant
  - *…..will most likely not inhibit the organism in vivo.*
- Non-Susceptible
  - *…..Not enough data to know if it is likely to inhibit the organism in vivo.*
- Epidemiological Cutoff Values
  - Determines the MIC of Wildtype and non-WT.

Where does the data come from?

- Microbiology AST instruments
- Microbiology LIS
- Electronic Health Records (EHR)
- Clinical decision support system (CDSS)

3 Types of Cumulative AST Data Reports

1. Traditional Antibiogram
2. Enhanced Antibiogram

Local Level – A single facility

3. Non-Traditional Antibiograms
   - Combined Antibiograms
   - Antimicrobial Resistance Surveillance Programs

Regional, National or Global

What Is An Antibiogram?

- Presentation of cumulative antimicrobial susceptibility testing (AST) data from a single institution on an annual basis

Appendix E1. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents Listed Alphabetically (Hypothetical Data)

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									
Pseudomonas aeruginosa	397	97	R	R									
Salmonella spp.	32	–	88	–									
Serratia marcescens	50	100	R	R									
Shigella spp.	33	–	64	–									
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.
Abbreviations: No., number; R, intrinsic resistance.

"Routine" Cumulative antibiogram
Generally…all isolates from a facility

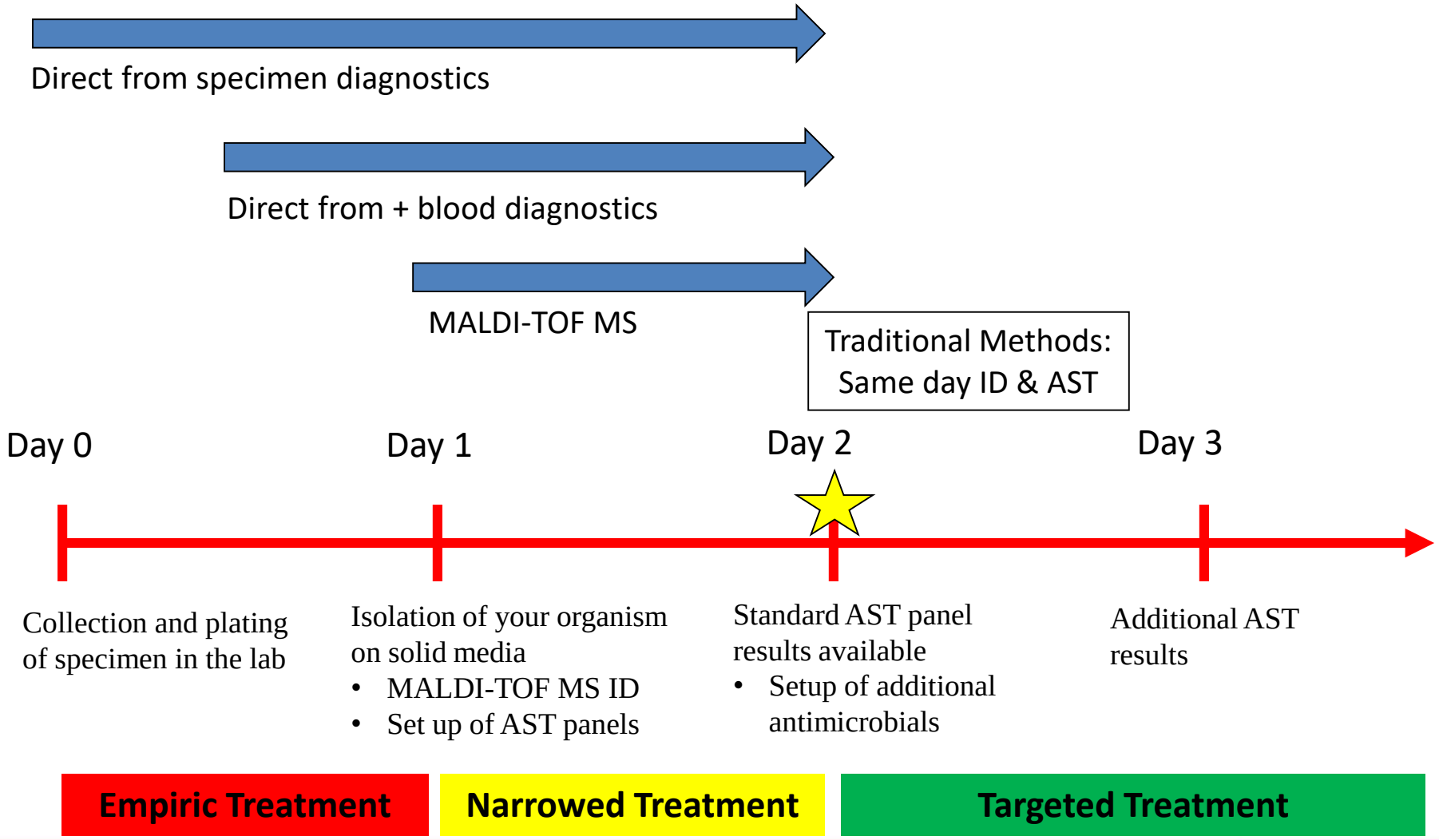
The Why? - Purpose of the Antibiogram

- To help clinicians choose initial empiric therapy

- Many more applications
  - Dr. Kim Claeys presentation on February 6th discussed using the antibiogram for Antimicrobial Stewardship applications

Importance & Reliance on Antibiograms Grow!

Courtesy of Trish Simner

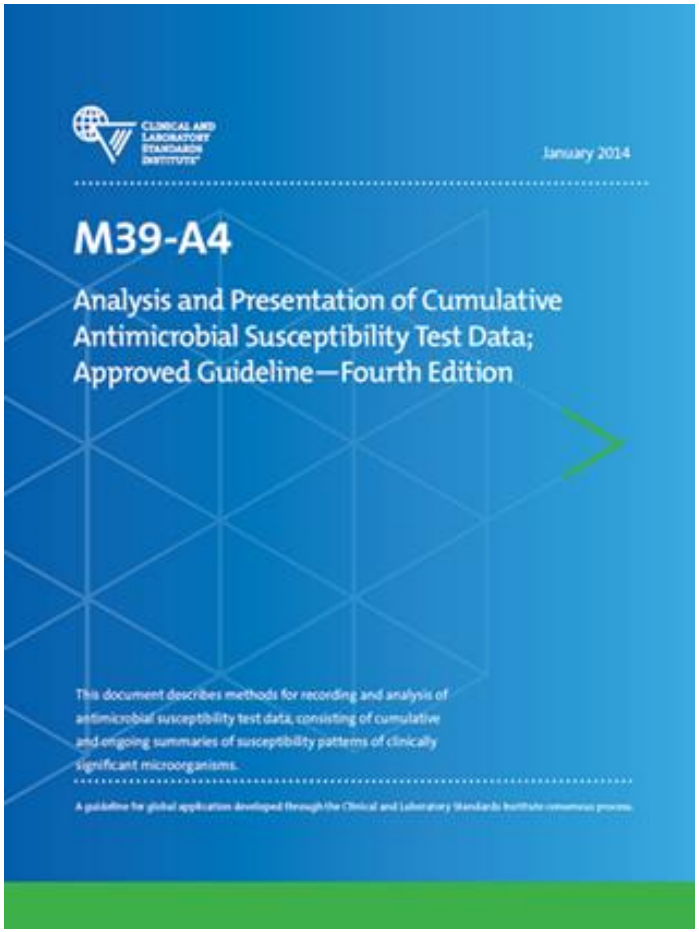


Who is Responsible for Creating the Antibiogram?

- Traditionally the microbiology laboratory
  - Driven by access to the data from AST instruments or the LIS
- Shifting towards stronger collaborations with Antimicrobial Stewardship Programs
  - Automated EHR based antibiograms
- Should be a collaborative effort
  - Clinical microbiologists, pharmacists, physicians, IT specialists

Where Do You Start?

- M39-A4: Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline-Fourth Edition
- M39-A5 currently being worked on. 2019-2020
  - A newly created section on LTC



Preparation of Cumulative Antibiogram Recommendations

- WHEN?-Analyze/present data at least **annually**
- Include only verified **final results**
- Include only species with **≥ 30** isolates
- Include **diagnostic** (not surveillance) isolates
- Include the **1st isolate/patient**; no duplicate isolates
- Only include **routinely tested** antimicrobial agents
- Report only **%S** and do not include I%

The Cumulative Antibiogram Report

- Analyzes data from **routine antimicrobial susceptibility tests** performed in the clinical laboratory
- Separate report prepared for each **healthcare facility**
- Primarily used to guide **empiric therapy**
- Sometimes used to **monitor resistance**
  - Changes in %S from year to year
- **Highly impacted** by
  - patient population served
  - culturing practices
    - If cultures only performed when patients fail therapy
  - Laboratory antimicrobial susceptibility testing and reporting policies
  - Temporal outbreaks

Organism Specific Recommendations

Bug/Drug	Presentation of Data
Streptococcus pneumoniae and penicillin	List the %S using oral, meningitis and non-meningitis breakpoints
Streptococcus pneumoniae and cefotaxime, ceftriaxone, cefepime	List the %S using meningitis and nonmeningitis breakpoints
Viridans group streptococci and penicillin	List both the %S and %I
Staphylococcus aureus	List %S for all isolates and the methicillin-resistant *S. aureus* (MRSA) subset
E. coli, K. pneumoniae and *P. mirabilis* and cefazolin	List % S using urine and non-urine breakpoints

Stratification of Antibiograms

- Nursing site or site of care
  - ICU, burn unit, ED, outpatient clinic
- Specimen type of infection site
  - Urine, blood
- Clinical service or patient population
  - Surgical, pediatric, transplant, cancer

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Answers to Commonly Asked Questions

How do I Apply Intrinsic Resistance?

B1. *Enterobacteriaceae*

Organism \ Antimicrobial Agent	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Piperacillin	Ticarcillin	Cephalosporins I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Polymyxin B Colistin	Aminoglycosides
Citrobacter freundii	R	R	R			R	R	R						
Citrobacter koseri	R			R	R									
Enterobacter cloacae complex[a]	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* (formerly *Enterobacter*) *aerogenes	R	R	R			R	R	R						
Klebsiella pneumoniae	R				R									
Morganella morganii	R	R				R		R	[b]		R	R	R	
Proteus mirabilis	There is no intrinsic resistance to penicillins and cephalosporins in this organism.								[b]	R	R	R	R	
Proteus penneri	R					R		R	[b]	R	R	R	R	
Proteus vulgaris	R					R		R	[b]	R	R	R	R	
Providencia rettgeri	R	R				R			[b]	R	R	R	R	
Providencia stuartii	R	R				R			[b]	R	R	R	R	[c]

The most up-to-date Intrinsic Resistance tables are located in the current M100 document.

What Do You Do With Susceptible Dose Dependent (SDD) Results?

- SDD: an interpretive category defined by a breakpoint that susceptibility of an isolate is dependent on the dosing regimen that is used in the patient
  - Cefepime and *Enterobacteriaceae*
  - Fluconazole and *C. albicans, C. glabrata, C. parapsilosis*, & *C. tropicalis*
  - New in 2019:
    - Daptomycin and *Enterococcus* spp
    - Ceftaroline and *Staphylococcus aureus*
  - Report both % S & %SDD either in the Table or as a footnote

	N	% S Cefepime	%SDD Cefepime
Escherichia coli	574	92[a]	3
Klebsiella pneumoniae	132	84[b]	2

[a]: "In addition, to the 92% S results, 3% were SDD (MIC 4 to 8 µg/mL) and 5% were R (MIC >16 µg/mL) to cefepime"

Why Do We Need a Minimum of N=30?

- Less statistical validity of data
  - Small numbers can skew the data

How Reliable is a Report of 80% Susceptible for *E. coli* and Ciprofloxacin?

Sample size	% S (95% CI)
10	44 to 97
100	71 to 87
1000	77 to 82

What Do I Do If We Don't Reach N≥30?

- So what can you do?
  - Analyze multiple years – add footnote
  - Report the results from N < 30 with a footnote
    - "Calculated from fewer than the standard recommendation of 30 isolates"
  - Group several species within a genus together
  - Aggregate data from multiple smaller facilities with a similar patient population in the same geographic area

Discuss more LTCF specific later

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Enhanced Antibiogram

What Are Enhanced Antibiograms?

- Segregating cumulative antibiogram data by one or more of the following:
  - Location – e.g., Inpatient vs Outpatient or ICU vs Oncology vs Non-ICU/Non-Oncology Wards
  - Specimen type – e.g. urine or blood specific
  - Clinical condition – e.g. cystic fibrosis, burn patients
  - Patient Age – e.g., pediatrics vs adults
  - Resistance Phenotype – e.g., MRSA, MSSA, carbapenem-resistant *Enterobacteriaceae*
  - Organism – e.g. anaerobe antibiogram
  - ASP Antibiograms – e.g. novel agents or last resort agents (colistin)
- Resistance Profiles
  - % Susceptible for combinations of drugs
  - % Susceptible for groups of organisms (e.g., all GNR from blood)

Combination of Antimicrobial Agents

Organism		% Susceptible							
	No. Strains	CIP	CTZ	IMP	TOB	CTZ and/or CIP	IMP and/or CIP	CTZ and/or TOB	IMP and/or TOB
Pseudomonas aeruginosa	814	69	80	79	86	86	84	91	91

Organisms resistance characteristics

Organism	No. Strains	% Susceptible								
		CLI	DOX	ERY	GEN	OXA	PEN	RIF	SXT	VAN
All *S. aureus*	1317	80	98	50	93	68	13	98	96	100
Oxacillin-resistant *S. aureus* (MRSA)	449	44	96	4	79	0	0	95	94	100
Oxacillin-susceptible *S. aureus* (MSSA)	904	97	99	72	99	100	18	99	97	100

Organism	No. Strains	% Susceptible									
		AMK	AMP	CFZ	CRO	CIP	GEN	IMP	PTZ	TET	SXT
K. pneumoniae (all)	1163	63	-	44	48	46	74	64	53	84	46
K. pneumoniae (ESBL-producing)	233	30	-	0	0	6	48	100	0	84	3
K. pneumoniae (KPC-producing)	361	5	-	0	0	0	28	0	0	82	0
K. pneumoniae (non-ESBL or KPC-producing)	569	100	-	84	99	94	96	100	88	87	95

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Non-Traditional Antibiograms

What About Non-Traditional Antibiograms?

- Accumulate AST data outside of a single institution
  - Combined Regional Antibiograms
  - Antimicrobial Resistance Surveillance Programs (ARSP)
    - Creating an ARSP report – New in M39-A5

Characteristic	Routine Antibiogram	Non-Traditional Antibiogram
Study Period	Annually	Defined by study
# of Institutions	One	Multiple
Presentation	Table	Report with I, M&M, R and D

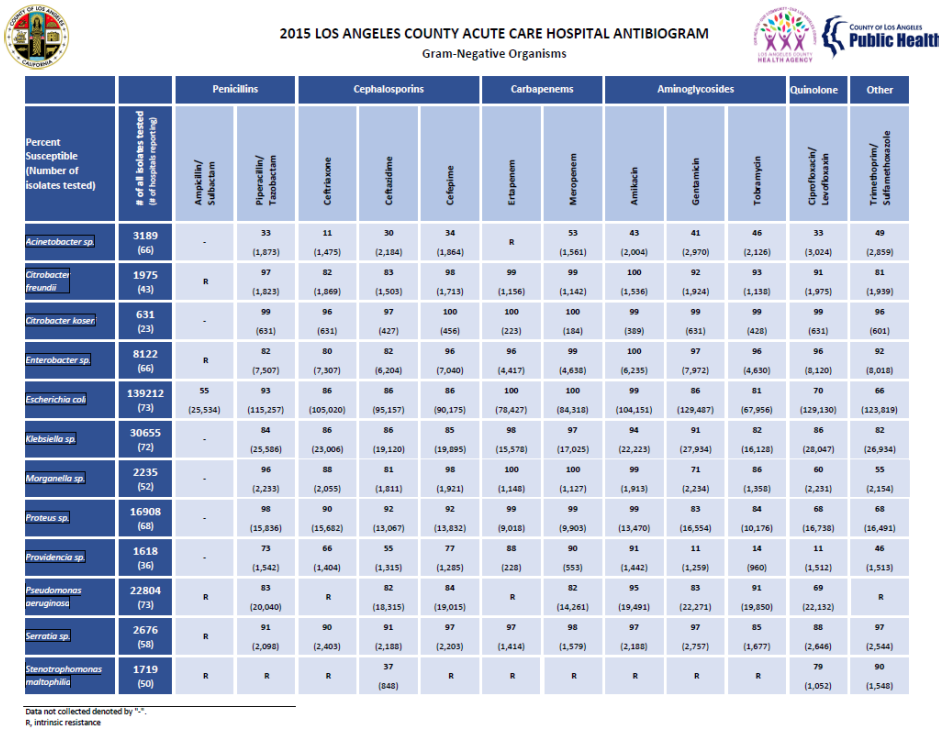
When To Consider Utilizing Non-Traditional Antibiogram Data?

- The use of a local cumulative antibiogram **is preferred to guide initial empiric therapy**

- Non-Traditional antibiogram data:
  - Used when local AST data are not available, are limited in size or scope
  - Used as a benchmark to compare local data to regional and national findings

Combined REGIONAL Antibiogram

- Compilation of data from facility-level antibiograms
- Susceptibility was defined by local labs in all circumstances
- Created a report with an Introduction, Methodology Notes, Antibiogram Table & Breakdown by Individual Organisms
- Methodology Notes Included:
  - Differences in breakpoints (eg cephalosporin & carbapenem breakpoints)
- Differences in agents within a class (eg ciprofloxacin vs levofloxacin)



2015 LOS ANGELES COUNTY ACUTE CARE HOSPITAL ANTIBIOGRAM

Gram-Negative Organisms

		Penicillins		Cephalosporins			Carbapenems		Aminoglycosides			Quinolone	Other
Percent Susceptible (Number of isolates tested)	# of all isolates tested (# of hospitals reporting)	Ampicillin/ Sulbactam	Piperacillin/ Tazobactam	Ceftriaxone	Ceftazidime	Cefepime	Ertapenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin/ Levofloxacin	Trimethoprim/ Sulfamethoxazole
Acinetobacter sp.	3189 (66)	-	33 (1,873)	11 (1,475)	30 (2,184)	34 (1,864)	R	53 (1,561)	43 (2,004)	41 (2,970)	46 (2,126)	33 (3,024)	49 (2,859)
Citrobacter freundii	1975 (43)	R	97 (1,823)	82 (1,869)	83 (1,503)	98 (1,713)	99 (1,156)	99 (1,142)	100 (1,536)	92 (1,924)	93 (1,138)	91 (1,975)	81 (1,939)
Citrobacter koseri	631 (23)	-	99 (631)	96 (631)	97 (427)	100 (456)	100 (223)	100 (184)	99 (389)	99 (631)	99 (428)	99 (631)	96 (601)
Enterobacter sp.	8122 (66)	R	82 (7,507)	80 (7,307)	82 (6,204)	96 (7,040)	96 (4,417)	99 (4,638)	100 (6,235)	97 (7,972)	96 (4,630)	96 (8,120)	92 (8,018)
Escherichia coli	139212 (73)	55 (25,534)	93 (115,257)	86 (105,020)	86 (95,157)	86 (90,175)	100 (78,427)	100 (84,318)	99 (104,151)	86 (129,487)	81 (67,956)	70 (129,130)	66 (123,819)
Klebsiella sp.	30655 (72)	-	84 (25,586)	86 (23,006)	86 (19,120)	85 (19,895)	98 (15,578)	97 (17,025)	94 (22,223)	91 (27,934)	82 (16,128)	86 (28,047)	82 (26,934)
Morganella sp.	2235 (52)	-	96 (2,233)	88 (2,055)	81 (1,811)	98 (1,921)	100 (1,148)	100 (1,127)	99 (1,913)	71 (2,234)	86 (1,358)	60 (2,231)	55 (2,154)
Proteus sp.	16908 (68)	-	98 (15,836)	90 (15,682)	92 (13,067)	92 (13,832)	99 (9,018)	99 (9,903)	99 (13,470)	83 (16,554)	84 (10,176)	68 (16,738)	68 (16,491)
Providencia sp.	1618 (36)	-	73 (1,542)	66 (1,404)	55 (1,315)	77 (1,285)	88 (228)	90 (553)	91 (1,442)	11 (1,259)	14 (960)	11 (1,512)	46 (1,513)
Pseudomonas aeruginosa	22804 (73)	R	83 (20,040)	R	82 (18,315)	84 (19,015)	R	82 (14,261)	95 (19,491)	83 (22,271)	91 (19,850)	69 (22,132)	R
Serratia sp.	2676 (58)	R	91 (2,098)	90 (2,403)	91 (2,188)	97 (2,203)	97 (1,414)	98 (1,579)	97 (2,188)	97 (2,757)	85 (1,677)	88 (2,646)	97 (2,544)
Stenotrophomonas maltophilia	1719 (50)	R	R	R	37 (848)	R	R	R	R	R	R	79 (1,052)	90 (1,548)

Data not collected denoted by "-".
R, intrinsic resistance

http://publichealth.lacounty.gov/acd/AntibiogramData.htm

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Applications of Cumulative AST Data

Many Applications of Cumulative AST data

Stake Holder	Application
Physicians	Empiric therapy decisions
Clinical Microbiology Laboratories	Benchmarking, quality control, role of rapid diagnostics
Antimicrobial Stewardship Programs	Antimicrobial therapy recommendations and formulary decisions
Infection Prevention and Control	Benchmarking to evaluate infection control practices
Pharmaceutical Industry	Informs new drug development
Regulatory	Informs regulatory practices
Public Health	Monitoring changes in resistance levels and public health interventions

Courtesy of Trish Simner

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Increasing Awareness of Antibiograms

Increasing Awareness of Antibiogram Data

Methods for Antibiogram Data Dissemination
Pocket guides/booklets
Laminated posters
Hospital newsletter article
Posting within hospital intranet/EMR
Email to all prescribers
Smartphone or tablet applications
Presentations

Increasing Awareness of Antibiogram Data

Appendix G – provides stepwise instructions on presenting the local cumulative antibiogram data to healthcare professionals

- Explain purpose of the local cumulative antibiogram with a brief description of how the report is prepared
- Describe any software limitations
- Describe the rationale used for separating data into subgroups for the report
- Present graphs and charts for trends that are monitored each year

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Recommendations in the New M39-A5 for LTC

Optimizing Culturing Practices in LTCF

- *Suspected Urinary Tract Infection* – To avoid over-culturing, consider developing a policy with the LTCF reference lab to determine if culture can be performed ONLY on urine specimens with significant pyuria (auto-reflex to culture).
- *Suspected Pneumonia* – Obtain an expectorated sputum sample, if possible, for Gram stain and culture.
- *Suspected Skin and Soft Tissue Infection* – If the skin infection is associated with an abscess or area of purulence, send a sample of the pus to the lab for culture.

Responsibility for Cumulative Antibiogram Development

- The willingness of the referral lab to either develop the antibiogram or provide susceptibility reports for antibiogram development should be determined.
  - Guidelines that will be followed for antibiogram development (e.g., CLSI M39)
  - Information (e.g., bacteria, antibiotics, etc.) that should be included in the antibiogram
  - Method for collection of cumulative susceptibility data
  - Method for data analysis, presentation and formatting (e.g., time period of antibiogram, data segregation techniques, the utility of infection-specific reports, etc)
- Multiple Referral Labs
  - Variations in laboratory practice must be considered (breakpoints)
  - Data formatted the same way
  - Appropriate and correct data from each laboratory

Data Analysis Techniques

- First Isolate per Patient
  - First isolate per reporting period
- Handling of small numbers (≤30)
  - Consider combining data from multiple years
  - Consider combining species, if applicable
  - Consider using data from other sources
  - Evaluate current culturing practices to assure that all patients with suspected infection are being cultured appropriately.
  - Consider constructing a cumulative antibiogram from patients in the general community in age category 65 and older.

More information and resources on the development of a LTCF Antibiogram

- https://www.ahrq.gov/nhguide/toolkits/help-clinicians-choose-the-right-antibiotic/index.html

Summary

- M39-A4 provides guidelines for creating a cumulative antibiogram
- There are 3 types of cumulative antibiograms
- Cumulative antibiograms can be stratified by different patient, hospital, or organism characteristics
- New Guidelines specific for LTCF will be in the new edition of M39-A5 coming out in 2020