Creation and Use of Antibiograms

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Objectives

1. Introduce the New CLSI M39-Ed5 Document

2. Highlight Some of the Changes in the M39-Ed5 Document

3. Review The Various Types of Antibiograms in M39-Ed5

4. Discuss in Detail Some of the Enhanced Antibiograms in M39-Ed5

Disclosure

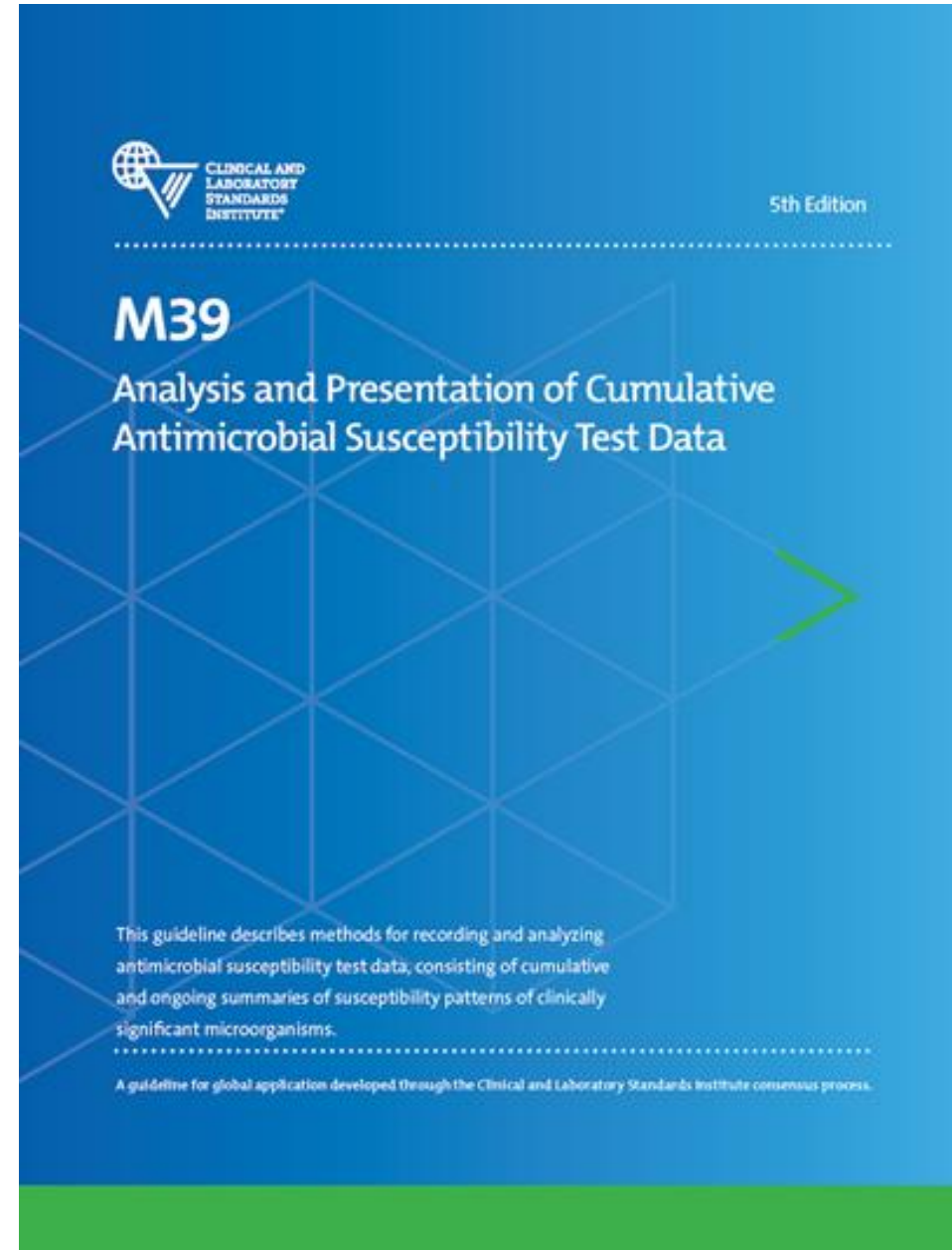**Raymond P. Podzorski, Ph.D., D(ABMM)**
April 26, 2022

No relevant financial relationships do disclose.

Recommendations M39-Ed5

Purpose of M39-Ed5

The primary aim of M39 is to guide the preparation and use of antibiograms by clinicians for selecting the most appropriate antimicrobial agents for empirical therapy for initial infections when definitive antimicrobial susceptibility test (AST) results are not available.

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Contents of M39-Ed5

The M39 guideline includes recommendations for:

Data
- **Collection**
- **Storage**
- **Analysis**
- **Presentation**

Preparation of reports
- **Routine and enhanced antibiograms**
- **Guide selection of empirical antimicrobial therapy**

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Contents of M39-Ed5

M39 describes:

Methods for recording and analyzing AST data
- **Consisting of cumulative and ongoing summaries (antibiograms)**
- **Susceptibility patterns of clinically significant microorganisms**

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Overview of Changes to M39-Ed5

- Adding definitions for "cumulative antimicrobial susceptibility test report" and "antibiogram"
- How to extract data from different sources for antibiogram preparation
- Combining results from rapid diagnostics and antimicrobial resistance marker testing with the antibiogram for empirical therapy selection
- Developing antibiograms for multiple facilities
- Describing ways in which antimicrobial stewardship programs may use antibiogram data
- Preparing cumulative susceptibility data for peer-reviewed publications
- Using statistical analysis techniques
- Adding general comment explaining the use of the "^" with intermediate breakpoints for applicable antibiotics known to concentrate in the urine
- Deleting recommendation to list percent intermediate in addition to percent susceptible for penicillin with viridans group streptococci
- Adding a section on epidemiological cutoff values

Overview of Changes M39-Ed5

Document has been rewritten and reorganized with some new material.
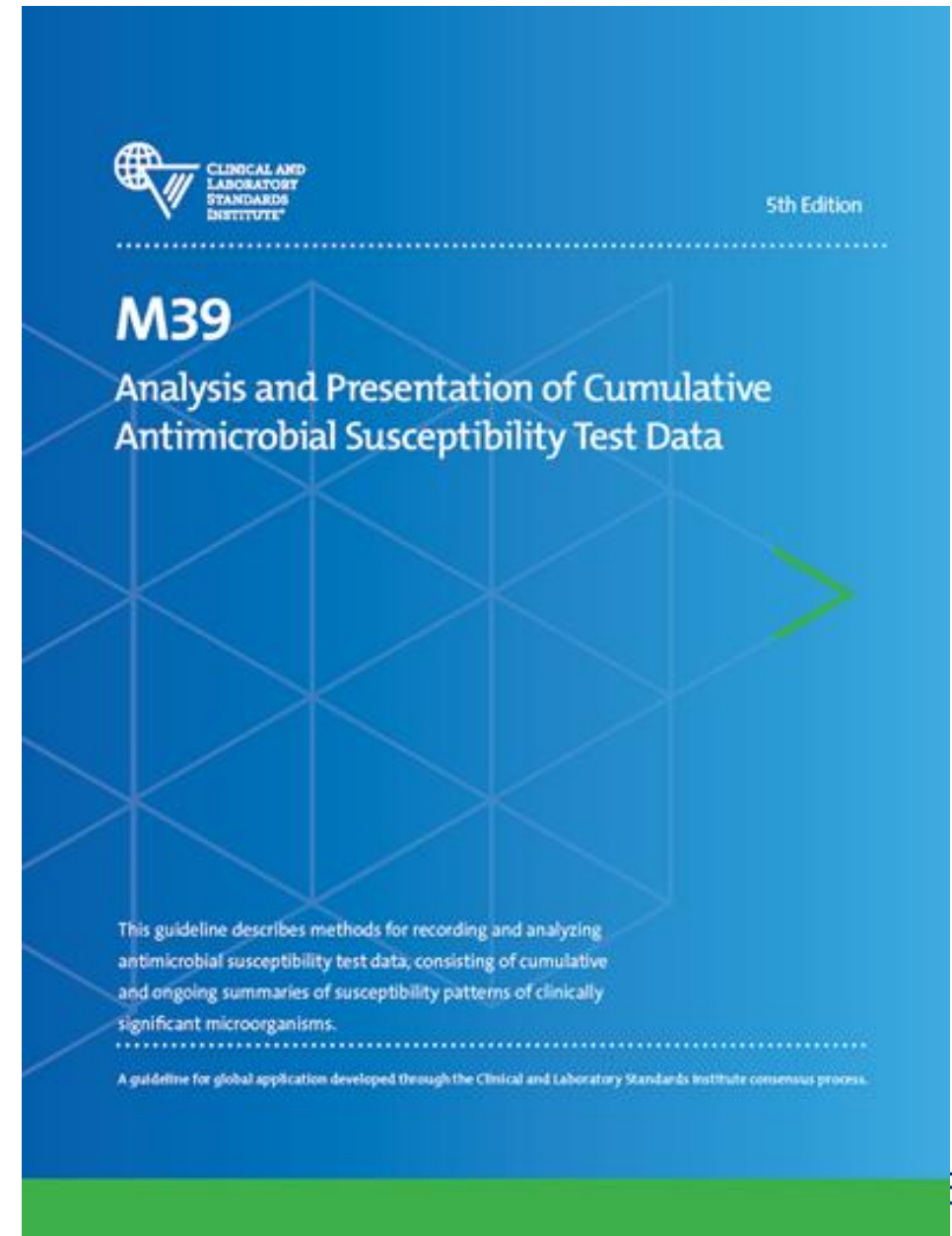
8 Use of Cumulative Antimicrobial Susceptibility Reports

The following sections provide suggestions for educational efforts to facilitate understanding and use of the cumulative antimicrobial susceptibility test data report.

8.1 Use of the Report

The cumulative antimicrobial susceptibility test data report should only be used as a general guide for empirical antimicrobial therapy until such time that specific antimicrobial susceptibility test results for a patient's infecting organism become available. Clinical application of the cumulative antimicrobial susceptibility test data in an initial choice of antimicrobial agents depends on a variety of factors, including the organism, the antimicrobial agent, patient characteristics, site of infection, and the other clinical parameters. Thus, the patient's physician uses the susceptibility data as one, but not the only, criterion for drug choice.

The cumulative antibiogram is increasing in importance as ASPs evolve in health care facilities. Individuals responsible for ASPs and those preparing cumulative antibiograms must work together to ensure these reports are prepared, distributed, and used optimally.

Part V. Using the Routine and Enhanced Antibiogram

⑩ Using the Antibiogram to Guide Empirical Therapy of Initial Infections

10.1 Percent Susceptibility Threshold to Guide Empirical Antimicrobial Therapy

The routine or enhanced antibiogram can be used as a general guide for empirical antimicrobial therapy selection until definitive antimicrobial susceptibility test results become available. There are limited clinical data that define the %S value needed for optimal coverage for empirical therapy. When specific empirical therapy is selected, antibiogram data should be considered with other factors such as:

Types of Antibiograms

1. Routine CLSI
2. Enhanced CLSI

What is a Routine Antibiogram?

Antibiogram prepared in accordance with Chapter 3 in the current CLIS M39-Ed5 document.

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Routine Antibiogram

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFTRX	CEFEPIME	CIPRO	GENT	MERO	PIP/TAZ	TOB	TMP/SMX	NITRO^U
Citrobacter freundii	76	R	R	87***	100	97	96	100	91	99	88	96
Citrobacter koseri	108	R	•	100	100	100	100	100	100	100	100	90
Enterobacter cloacae cmplx.	115	R	R	85***	96	98	99	100	87	99	93	31
Escherichia coli	3,648	66	72	96	99	89	95	100	98	95	84	97
*Klebsiella aerogenes**	58	R	R	88***	100	98	100	98	86	100	100	10
Klebsiella oxytoca	111	R	67	99	100	99	100	100	99	99	94	85
Klebsiella pneumoniae	515	R	88	99	99	97	99	100	97	99	95	36
Morganella morganii	38	R	R	97	100	89	95	100	100	97	84	R
Proteus mirabilis	241	90	93	99	100	95	95	100	100	95	93	R
Serratia marcescens	63	R	R	97***	100	94	100	100	100	98	94	100	R

*** Use with caution, *Enterobacter spp.*, *K. aerogenes*, *C. freundii*, and *S. marcescens* may develop resistance to Ceftriaxone during prolonged therapy as a result of derepression of Amp C β-lactamase

• no data

* *Klebsiella* (formally *Enterobacter*) *aerogenes*

GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFEPIME	MERO
Pseudomonas aeruginosa	292	91	97	99	94	97	97

What is an Enhanced Antibiogram?

Enhanced antibiograms are cumulative antimicrobial susceptibility test data in which the data have been extracted, stratified, and displayed to answer specific clinical questions or to help guide empirical abx therapy in select patient populations or infection types.

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What Are Some Enhanced Antibiograms?

1. Stratified Antibiogram
2. Cross-Table Combination Antibiogram
3. Weighted-Incidence Syndromic Combination Antibiogram - WISCA

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What is a Stratified Antibiogram?

Antibiogram that analyzes a specific subset of bacterial isolates, e.g., those from specific location (ED, ICU), those from a specific source (urine, blood), those from a specific age of patient.

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Routine Antibiogram
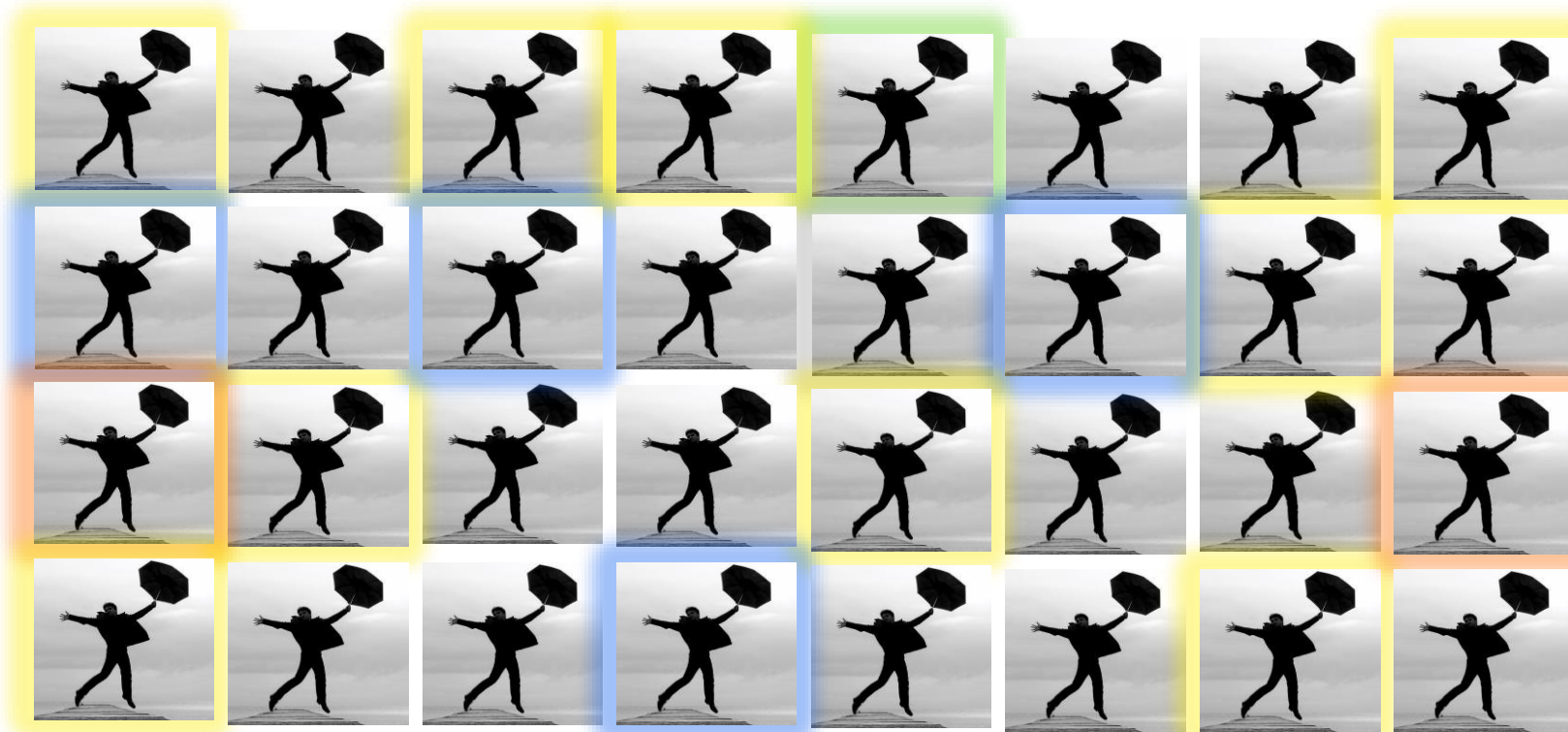
UTI   Resp   Wound   Blood   Tissue

Stratified Antibiogram

E. coli

P. mirabilis   K. oxytoca

C. freundii

E. faecalis

E. cloacae

E. coli
E. faecalis

E. faecalis

K. pneumoniae

UTI

Stratified Antibiogram

Urine Isolates Only

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFZLN	CEFTRX	CEFEPIME	CIPRO	GENT	ERTAPEN	PIP/TAZ	TMP/SMX	NITRO
Escherichia coli	96	55	58	93	100	100	70	93	100	95	80	98
Enterobacter spp.	31	R	R	R	100***	100	100	100	100	100	75	0
Klebsiella pneumoniae	30	R	89	100	100	100	100	100	100	100	100	33
Proteus mirabilis	33	83	100	100	100	100	83	83	100	100	83	R

*** Use with caution, *Enterobacter spp.*, *K. aerogenes*, *C. freundii*, and *S. marcescens* may develop resistance to Ceftriaxone during prolonged therapy as a result of derepression of Amp C β-lactamase

GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFPIME	AMK	MERO
Pseudomonas aeruginosa	30	100	75	100	100	100	75	75

UTI

Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America

Microbiology and Laboratory Diagnostics

XIV. Should ASPs Work With the Microbiology Laboratory to Develop Stratified Antibiograms, Compared With Nonstratied Antibiograms?

Recommendation

15. We suggest development of stratified antibiograms over solely relying on nonstratified antibiograms to assist ASPs in developing guidelines for empiric therapy (weak recommendation, low-quality evidence).

Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America

Microbiology and Laboratory Diagnostics

XIV. Should ASPs Work With the Microbiology Laboratory to Develop Stratified Antibiograms, Compared With Nonstratied Antibiograms?

Recommendation

Comment: Although there is limited evidence at this time that stratified antibiograms (eg, by location or age) lead to improved empiric antibiotic therapy, stratification can expose important differences in susceptibility, which can help ASPs develop optimized treatment recommendations and guidelines.

What is a Cross-Table/Combination Antibiogram?

Antibiogram that takes into account cross resistance among bacteria with respect to susceptibility.

1. Dual Cross-Table Antibiogram
2. Cross-Table Antibiogram
3. Combination Antibiogram (CLSI)
4. Cross-Susceptibility Table

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Routine Antibiogram

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFTRX	CEFEPIME	CIPRO	GENT	MERO	PIP/TAZ	TOB	TMP/SMX	NITRO^U
Citrobacter freundii	76	R	R	87***	100	97	96	100	91	99	88	96
Citrobacter koseri	108	R	•	100	100	100	100	100	100	100	100	90
Enterobacter cloacae cmplx.	115	R	R	85***	96	98	99	100	87	99	93	31
Escherichia coli	3,648	66	72	96	99	89	95	100	98	95	84	97
*Klebsiella aerogenes**	58	R	R	88***	100	98	100	98	86	100	100	10
Klebsiella oxytoca	111	R	67	99	100	99	100	100	99	99	94	85
Klebsiella pneumoniae	515	R	88	99	99	97	99	100	97	99	95	36
Morganella morganii	38	R	R	97	100	89	95	100	100	97	84	R
Proteus mirabilis	241	90	93	99	100	95	95	100	100	95	93	R
Serratia marcescens	63	R	R	97***	100	94	100	100	98	94	100	R

*** Use with caution, *Enterobacter spp*., *K. aerogenes*, *C. freundii*, and *S. marcescens* may develop resistance to Ceftriaxone during prolonged therapy as a result of derepression of Amp C β-lactamase

• no data

* *Klebsiella* (formally *Enterobacter*) *aerogenes*

GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFPIME	MERO
Pseudomonas aeruginosa	292	91	97	99	94	97	97

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St. Mary's Hospital/ED Gram Negative Rod Dual Cross-Table Antibiogram

	Cefepime	Pip/Tazo	Meropen	Cipro	Tobra
Cefepime	**95.90%**	98.30%	99.20%	97.70%	98.50%
Pip/Tazo		**94.60%**	99.30%	98.70%	99.30%
Meropen			**98.90%**	99.60%	99.70%
Ciproflox				**87.70%**	96.50%
Tobra					**94.70%**

1,492 "Unique" Gram negative bacteria from January – December

Enterobacterales and *P. aeruginosa* mostly

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What is a Weighted-Incidence Syndromic Combination Antibiogram?

Antibiogram that shows for a given infectious condition (syndrome) the likelihood of adequate antibiotic coverage using either monotherapy or combination therapy taking into account the local weighted incidence of the infecting agents.

1. Weighted-Incidence Syndromic Combination Antibiogram
2. Stratified Antibiogram by Infection site (CLSI)

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Routine Antibiogram

UTI Resp Wound Blood Tissue

Routine Antibiogram

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFTRX	CEFEPIME	CIPRO	GENT	MERO	PIP/TAZ	TOB	TMP/SMX	NITRO[U]
Citrobacter freundii	76	R	R	87***	100	97	96	100	91	99	88	96
Citrobacter koseri	108	R	•	100	100	100	100	100	100	100	100	90
Enterobacter cloacae cmplx.	115	R	R	85***	96	98	99	100	87	99	93	31
Escherichia coli	3,648	66	72	96	99	89	95	100	98	95	84	97
*Klebsiella aerogenes**	58	R	R	88***	100	98	100	98	86	100	100	10
Klebsiella oxytoca	111	R	67	99	100	99	100	100	99	99	94	85
Klebsiella pneumoniae	515	R	88	99	99	97	99	100	97	99	95	36
Morganella morganii	38	R	R	97	100	89	95	100	100	97	84	R
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*** Use with caution, *Enterobacter spp.*, *K. aerogenes*, *C. freundii*, and *S. marcescens* may develop resistance to Ceftriaxone during prolonged therapy as a result of derepression of Amp C β-lactamase

• no data

* *Klebsiella* (formally *Enterobacter*) *aerogenes*

GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFPIME	MERO
Pseudomonas aeruginosa	292	91	97	99	94	97	97

 UTI

 Resp

 Wound

 Blood

 Tissue

Weighted-Incidence Syndromic Combination Antibiogram

UTI   Resp   Wound   Blood   Tissue

Weighted-Incidence Syndromic Combination Antibiogram

UTI
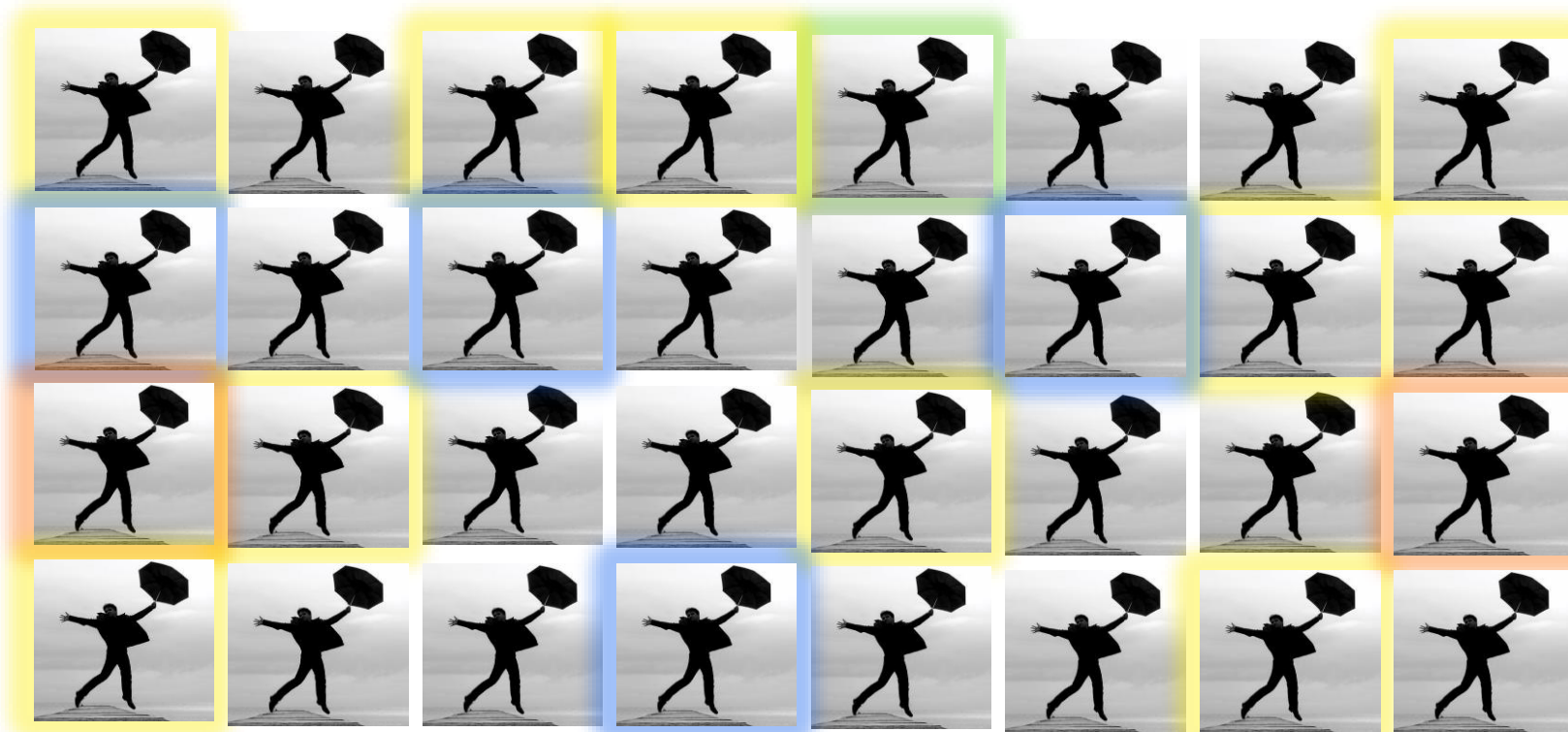
Weighted-Incidence **Syndromic Combination Antibiogram**

E. coli

P. mirabilis   *K. oxytoca*

C. freundii

E. faecalis

E. cloacae

E. faecalis

E. coli
E. faecalis

K. pneumoniae

UTI

Choose the abxs that are important

Weighted-Incidence Syndromic Combination Antibiogram

K. oxytoca   E. coli   E. cloacae

E. coli   P. mirabilis   E. coli   E. faecalis

T/S

Covered by specific regime, e.g., T/S

Total numbers of cases in the data set

Equals percent infections covered

K. oxytoca   E. coli   E. cloacae

E. coli   P. mirabilis   E. coli   E. faecalis

T/S

CIP

Infect Control Hosp Epidemiol 2012;33(4):381-388

TABLE 4. Weighted-Incidence Syndromic Combination Antibiogram

	Infections covered, %		
Antimicrobial regimen	UTI	ABI	P^a
Trimethoprim-sulfamethoxazole	55	...	...
Ciprofloxacin (+MTZ)[b]	62	37	<.001
Cefazolin (+MTZ)[b]	62	47	<.001
Ceftriaxone (+MTZ)[b]	71	59	<.001
Ertapenem	71	63	<.001
Ceftazidime (+MTZ)[b]	76	65	<.001
Ampicillin-sulbactam	83	68	<.001
Ampicillin and gentamicin (+MTZ)[b]	84	81	.10
Cipro + MTZ + vancomycin	...	84	...
Ceftazidime (+MTZ)[b] + vancomycin	88	93	<.001
Ertapenem + vancomycin	...	88	...
Piperacillin-tazobactam	89	88	.70
Piperacillin-tazobactam + vancomycin	91	93	.04
Meropenem	91	91	.72
Meropenem + vancomycin	93	96	<.001

NOTE. Listed are 15 common antimicrobial regimens and the percentage of the time that a regimen would cover all recovered organisms in an individual patient's infection. This was cal-

Weighted-Incidence Syndromic Combination Antibiogram

TABLE 3. Traditional Antibiogram for the Study Site over the Entire Study Period

	Staphylococcus aureus	Enterococcus species	Beta-hemolytic Streptococcus group B	Streptococcus pneumoniae	Escherichia coli	Klebsiella pneumoniae	Proteus mirabilis	Pseudomonas aeruginosa	Citrobacter species	Enterobacter cloacae	Klebsiella oxytoca	Enterobacter aerogenes	Serratia marcescens	Morganella morganii
Ampicillin	13	96	97	69	54	0	80	...	2	0	1	0	0	0
Trimethoprim-sulfamethoxazole	99	...	...	...	75	90	85	...	90	90	95	98	91	80
Fluoroquinolone	74	69	...	98	84	97	85	85	96	96	98	99	97	91
Cefazolin	65	...	...	...	92	96	90	...	47	1	76	3	1	0
Ceftriaxone	...	...	100	...	97	98	97	...	94	88	98	94	99	99
Ertapenem	...	...	...	...	100	100	100	...	100	99	100	100	100	99
Ceftazidime	...	...	...	...	97	98	96	97	94	89	99	94	99	99
Ampicillin-sulbactam	...	...	...	...	82	93	97	...	66	29	91	24	5	15
Piperacillin-tazobactam	...	...	...	...	98	96	100	97	94	92	96	92	99	99
Meropenem	...	...	...	...	100	99	100	94	98	100	100	100	100	...

NOTE. Data are percent of isolates susceptible. This antibiogram includes the first unique bacterial isolates from any body site, from all outpatient locations (including emergency room) for the entire study period. Ellipses indicate that there are less than 100 sensitivity tests done for this combination of medication and organism over the study period. The 14 most frequently isolated organisms, excluding coagulase negative Staphylococcus, are shown.

T/S WISCA = 55% Covered

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Weighted-Incidence Syndromic Combination Antibiogram

TABLE 3. Traditional Antibiogram for the Study Site over the Entire Study Period

	Staphylococcus aureus	Enterococcus species	Beta-hemolytic Streptococcus group B	Streptococcus pneumoniae	Escherichia coli	Klebsiella pneumoniae	Proteus mirabilis	Pseudomonas aeruginosa	Citrobacter species	Enterobacter cloacae	Klebsiella oxytoca	Enterobacter aerogenes	Serratia marcescens	Morganella morganii
Ampicillin	13	96	97	69	54	0	80	...	2	0	1	0	0	0
Trimethoprim-sulfamethoxazole	99	...	...	...	75	90	85	...	90	90	95	98	91	80
Fluoroquinolone	74	69	...	98	84	97	85	85	96	96	98	99	97	91
Cefazolin	65	...	...	...	92	96	90	...	47	1	76	3	1	0
Ceftriaxone	...	...	100	...	97	98	97	...	94	88	98	94	99	99
Ertapenem	...	...	...	...	100	100	100	...	100	99	100	100	100	99
Ceftazidime	...	...	...	...	97	98	96	97	94	89	99	94	99	99
Ampicillin-sulbactam	...	...	...	...	82	93	97	...	66	29	91	24	5	15
Piperacillin-tazobactam	...	...	...	...	98	96	100	97	94	92	96	92	99	99
Meropenem	...	...	...	...	100	99	100	94	98	100	100	100	100	...

NOTE.   Data are percent of isolates susceptible. This antibiogram includes the first unique bacterial isolates from any body site, from all outpatient locations (including emergency room) for the entire study period. Ellipses indicate that there are less than 100 sensitivity tests done for this combination of medication and organism over the study period. The 14 most frequently isolated organisms, excluding coagulase negative Staphylococcus, are shown.

CIP WISCA = 62% Covered

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Weighted-Incidence Syndromic Combination Antibiogram

How Do You Make One?

UTI   Resp   Wound   Blood

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Weighted-Incidence Syndromic Combination Antibiogram
How Do You Make One?

Step 1

Get the electronic health records of a select patient population (syndrome) who had a final diagnosis code consistent UTI and had a positive urine culture.

UTI

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Weighted-Incidence Syndromic Combination Antibiogram
How Do You Make One?

Step 2

E. coli

P. mirabilis   *K. oxytoca*

C. freundii

E. faecalis

For the selected patient population collect culture and susceptibility data. For each case, determine whether the infection would be "covered" by one or more of the antibiotics reported for the specific source of the infection.

E. cloacae

E. coli
E. faecalis

E. faecalis

K. pneumoniae

UTI

Choose the antibiotics for treatment of UTIs

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Weighted-Incidence Syndromic Combination Antibiogram

Step 3

Put the data in a usable reporting format.

TABLE 4. Weighted-Incidence Syndromic Combination Antibiogram

Antimicrobial regimen	Infections covered, %		
	UTI	ABI	P^a
Trimethoprim-sulfamethoxazole	55	...	...
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Ampicillin-sulbactam	83	68	<.001
Ampicillin and gentamicin (+MTZ)[b]	84	81	.10
Cipro + MTZ + vancomycin	...	84	...
Ceftazidime (+MTZ)[b] + vancomycin	88	93	<.001
Ertapenem + vancomycin	...	88	...
Piperacillin-tazobactam	89	88	.70
Piperacillin-tazobactam + vancomycin	91	93	.04
Meropenem	91	91	.72
Meropenem + vancomycin	93	96	<.001

NOTE. Listed are 15 common antimicrobial regimens and the percentage of the time that a regimen would cover all recovered organisms in an individual patient's infection. This was cal-

Weighted-Incidence Syndromic Combination Antibiogram

Preparation Method Using Cumulative Susceptibility Test Data

1. Determine the "Syndrome" you are looking to cover in your patient population.

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Weighted-Incidence Syndromic Combination Antibiogram

How Do You Make One?

UTI   Resp   Wound   Blood

Weighted-Incidence Syndromic Combination Antibiogram

UTI

Weighted-Incidence Syndromic Combination Antibiogram

2. Stratify the Routine Antibiogram by Syndrome

Urine Isolates Only

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFZLN	CEFTRX	CEFEPIME	CIPRO	GENT	ERTAPEN	PIP/TAZ	TMP/SMX	NITRO
Escherichia coli	96	55	58	93	100	100	70	93	100	95	80	98
Enterobacter spp.	31	R	R	R	100***	100	100	100	100	100	75	0
Klebsiella pneumoniae	30	R	89	100	100	100	100	100	100	100	100	33
Proteus mirabilis	33	83	100	100	100	100	83	83	100	100	83	R

*** Use with caution, *Enterobacter spp*., *K. aerogenes*, *C. freundii*, and *S. marcescens* may develop resistance to Ceftriaxone during prolonged therapy as a result of derepression of Amp C β-lactamase

GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFPIME	AMK	MERO
Pseudomonas aeruginosa	30	100	75	100	100	100	75	75

UTI

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Weighted-Incidence Syndromic Combination Antibiogram

3. Identify the Antibiotics of Interest

Urine Isolates Only

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFZLN	CEFTRX	CEFEPIME	CIPRO	GENT	ERTAPEN	PIP/TAZ	TMP/SMX	NITRO
Escherichia coli	96	55	58	93	100	100	70	93	100	95	80	98
Enterobacter spp.	31	R	R	R	100***	100	100	100	100	100	75	0
Klebsiella pneumoniae	30	R	89	100	100	100	100	100	100	100	100	33
Proteus mirabilis	33	83	100	100	100	100	83	83	100	100	83	R

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GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFPIME	AMK	MERO
Pseudomonas aeruginosa	30	100	75	100	100	100	75	75

UTI

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Weighted-Incidence Syndromic Combination Antibiogram
4. Make the Calculations

Total		Number Isolates Susceptible		
		Cipro	A/C	T/S
96	*E. coli*	67	56	77
33	*P. mirabilis*	30	29	33
30	*K. pneumoniae*	25	30	25
159		122	115	135
		159	159	159
			WISCA	
	Percent Coverage	77%	72%	85%

Urine culture Stratified Antibiogram

E. coli	Cipro S=70%, A/C S=58%, T/S S=80%
P. mirabilis	Cipro S=91%, A/C S=89%, T/S S=100%
K. pneumoniae	Cipro S=83%, A/C S=100%, T/S S=83%

Weighted-Incidence Syndromic Combination Antibiogram Stratified Antibiogram

Urine Isolates Only

GRAM NEGATIVE	N	AMP	AMP/SUL	CEFZLN	CEFTRX	CEFEPIME	CIPRO	GENT	ERTAPEN	PIP/TAZ	TMP/SMX	NITRO
Escherichia coli	96	55	58	93	100	100	70	93	100	95	80	98
Enterobacter spp.	31	R	R	R	100***	100	100	100	100	100	75	0
Klebsiella pneumoniae	30	R	89	100	100	100	100	100	100	100	100	33
Proteus mirabilis	33	83	100	100	100	100	83	83	100	100	83	R

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GRAM NEGATIVE	N	CIPRO	GENT	TOB	PIP/TAZ	CEFPIME	AMK	MERO
Pseudomonas aeruginosa	30	100	75	100	100	100	75	75

		WISCA		
Percent Coverage		**Cipro**	**A/C**	**T/S**
		77%	**72%**	**85%**

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Conclusions

- **A new edition (Ed5) of the CLSI M39, Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data, document has recently been released.**
- **The new M39 document has been rewritten and reorganized with some new material.**
- **The new M39 document talks about Routine Antibiograms and Enhanced Antibiograms, but there is not a lot of detail on how to create some of the Enhanced Antibiograms.**
- **Three Enhanced Antibiograms described in the new M39 document, a Stratified Antibiogram, a Cross-table Antibiogram, and a Weighted-Incidence Syndromic Combination Antibiogram were discussed.**

Questions?

Thank you!