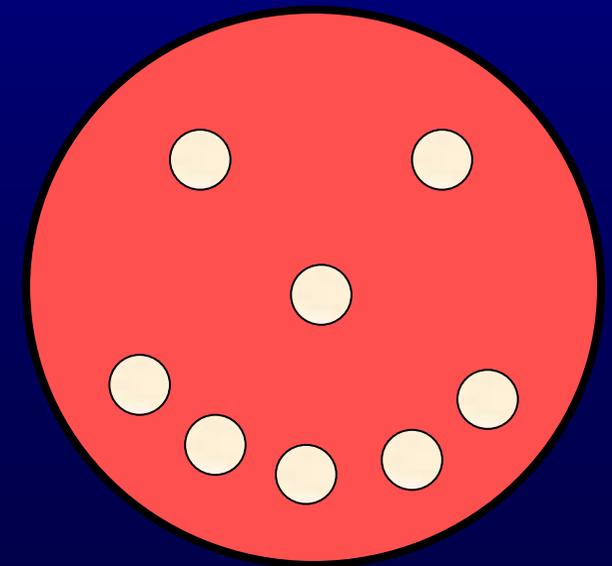


# Cumulative Susceptibility Test Data

## Local Antibiograms

## Surveillance Data

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# Cumulative Susceptibility Test Data Options

Local Level

Routine  
Antibiogram

“Enhanced”  
Antibiogram

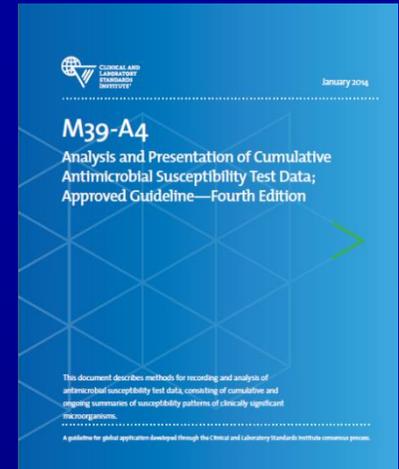


Regional, National, Global Level

Surveillance  
Data



# “Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data”



CLSI M39-A4 2014.

- ...describes preparation of a cumulative antibiogram report to be used to support clinical decisions re: empiric therapy of initial infections
- ...discusses utility of surveillance data

# Routine Antibigram

## 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	Cefoxime	Ceftazidime	Ciprofloxacin	Nitrofurantoin†	Gentamicin	Meropenem	Piperacillin-tazobactam	Trimethoprim-sulfamethoxazole	Tobramycin
<i>Acinetobacter baumannii</i>	32	80	R	R	34	52	51	–‡	60	80	46	58	59
<i>Citrobacter freundii</i>	49	100	R	R	72	67	90	78	100	99	67	67	100
<i>Enterobacter aerogenes</i>	31	100	R	R	68	69	92	85	91	99	74	95	91
<i>Enterobacter cloacae</i>	76	99	R	R	61	62	92	81	90	99	77	84	90
<i>Escherichia coli</i>	1433	99	36	68	96	94	72	98	91	99	51	65	92
<i>Klebsiella pneumoniae</i>	543	99	R	72	91	92	84	74	94	95	86	81	94
<i>Morganella morganii</i>	44	100											
<i>Proteus mirabilis</i>	88	100											
<i>Pseudomonas aeruginosa</i>	397	97											
<i>Salmonella</i> spp.	32	–	88	–	97	97	90	–	–	100	91	80	–
<i>Serratia marcescens</i>	50	100	R	R	82	94	95	R	94	99	94	91	89
<i>Shigella</i> spp.	33	–	64	–	100	100	95	–	–	100	84	69	–
<i>Stenotrophomonas maltophilia</i>	72	R	R	R	R	63	6	R	R	R	–	98	R

**“Routine” Cumulative antibiogram  
Generally...one big report**

\* 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.

**CLSI M39-A4.**

# ***What is suggested in CLSI M39-A4? (1)***

- ❑ Analyze/present data at least annually**
- ❑ Include only final, verified results**
- ❑ Include only species with  $\geq 30$  isolates**
- ❑ Include diagnostic (not surveillance) isolates**
- ❑ Include the 1<sup>st</sup> isolate/patient, irrespective of**
  - body site**
  - overall antimicrobial susceptibility profile**
- ❑ Include only drugs routinely tested**
- ❑ Calculate %S (do not include %I)**

**Most debated  
criterion**

## ***What is suggested in CLSI M39-A4? (2)***

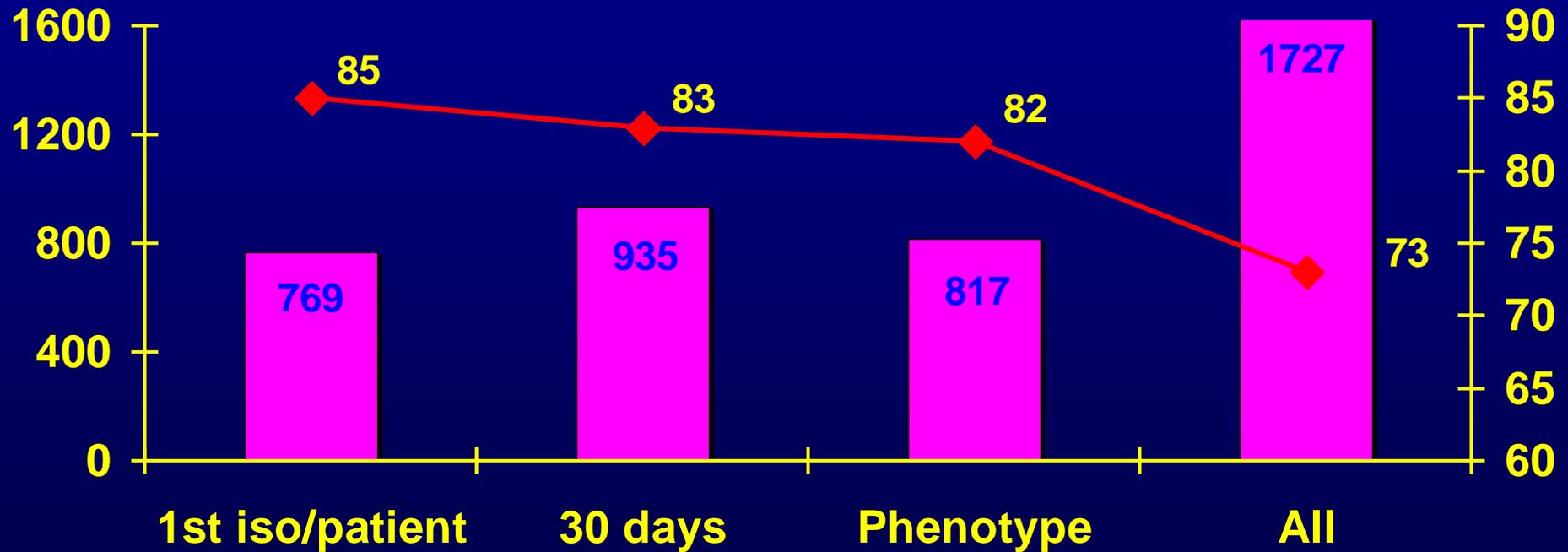
- ❑ ***Staphylococcus aureus*** – list %S for all *S. aureus* and MRSA subset
- ❑ ***Streptococcus pneumoniae***
  - list %S for cefotaxime / ceftriaxone / penicillin w/ meningitis and non-meningitis breakpoints
  - list %S for penicillin w/ oral breakpoints, if appropriate
- ❑ ***Viridans streptococcus*** - list %S and list %I for penicillin

# How do various methods for excluding duplicates impact %S?

*P. aeruginosa* - meropenem

2.2 isolates/patient

# isolates    % Mero-S



M39-A4

UCLA 2013

# Special Circumstance.....

Organism	N	% Susceptible				
		Clin	Ery	Ox	T-S	Van
All <i>S. aureus</i>	1648*	72	53	69	99	100
MSSA	529	80	71	100	99	100
MRSA	1160	54	13	0	96	100

\*"All" NOT sum of MRSA and MSSA because:

- analyzed 1<sup>st</sup>/iso/patient from each subset, e.g., OX-R *S. aureus*
- 41 pts had both MRSA and MSSA

# Key Points

## Cumulative Antibigrams (1)

- ◆ If “N” is small, limitations of %S data must be understood
- ◆ If comparing %S for several drugs, all must be tested and analyzed for each organism even if drugs are not routinely reported on each patient report

# Example: Small “N”

## *Pseudomonas aeruginosa* - cefepime

Patients	N	% S <sup>1</sup>	95% CI
All	769	85	83-88
Outpatients <sup>2</sup>	469	87	84-90
Inpatients	178	82	76-88
Med ICU	34	73	56-90 <sup>3</sup>

<sup>1</sup> First isolate/pt (CLSI M39-A4)

<sup>2</sup> Includes ER patients

<sup>3</sup> We can be 95% confident that between 56% and 90% of *P. aeruginosa* isolates are susceptible to cefepime

**Must be careful of small “N” with subsets of data**

# Potential for Skewed Data - Example:

Only drugs selectively reported are used for antibiogram

## *E. coli* - %Susceptible

N	Amk	Amp	Cfaz	Cftrx	Gent	Mero	T-S	Notes
1356	48 <sup>1</sup>	35	30	65	74	90 <sup>2</sup>	55	Amk and Mero %S only from isolates where drugs were reported - <b>SKEWED</b>
1356	86	35	30	65	74	96	55	Amk and Mero %S from all isolates tested – <b>OK!</b>

<sup>1</sup> Amikacin only reported on gentamicin-I or -R isolates (n=353)

<sup>2</sup> Meropenem only reported on ceftriaxone-I or -R isolates (n=475)

# Key Points

## Cumulative Antibigrams (2)

- ◆ **Cumulative antibiogram data can be impacted by...**
  - Patient population served
  - Culturing practices
  - Antimicrobial susceptibility testing policies
  - Temporal outbreaks

# Enhanced Antibiogram

# To answer specific questions, there is an increased interest in...

- ◆ **Segregating** cumulative antibiogram data by one or more of the following:
  - **Location** – e.g., outpatient vs. inpatient, unit specific
  - **Specimen type** - e.g., urine, blood
  - **Clinical condition** - e.g., cystic fibrosis, burn patients
  - **Patient age** – e.g., pediatrics vs. adults
  - **Resistance phenotype** – e.g., MRSA, MSSA; *K. pneumoniae*: all, carbapenem-R, carbapenem-S
- ◆ **Resistance profiles**
- ◆ % Susceptible for **combinations** of drugs
- ◆ % Susceptible for **groups of organisms** (e.g., all GNR from blood)

*What agents would be appropriate for empiric therapy of cystitis in women?*

Question ????

## Uncomplicated Cystitis and Pyelonephritis (UTI)

 Share this Guideline

Published: Clinical Infectious Diseases ;  
2011 ; 52 : e103 -e120



### "Guidelines for Antimicrobial Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women"

Panel of International Experts was convened by the Infectious Diseases Society of America (IDSA) in collaboration with the European Society for Microbiology and Infectious Diseases (ESCMID) to update the 1999 Uncomplicated Urinary Tract Infection Guidelines by the IDSA. Co-sponsoring organizations include the American Congress of Obstetricians and Gynecologists, American Urological Association, Association of Medical Microbiology and Infectious Diseases—Canada, and the Society for Academic Emergency Medicine. The focus of this work is treatment of women with acute uncomplicated cystitis and pyelonephritis, diagnoses limited in these guidelines to premenopausal, non-pregnant women with no known urological abnormalities or co-morbidities. [Link to full text guideline](#)

<http://www.idsociety.org>

Infectious Diseases Society of America

## Recommend (Acute Cystitis)

Nitrofurantoin  
TMP-SMX  
Fosfomycin

Fluoroquinolone  
 $\beta$ -lactam (oral)

**Uncomplicated UTIs (uUTIs)  
IDSA Guidelines**

# **IDSA Recommendations for “Empiric” Rx of Acute Cystitis / Pyelonephritis**

- ◆ **Ciprofloxacin** for pyelonephritis:  
Use alternative if %R >10%
- ◆ **Trimethoprim-sulfa** for cystitis:  
Use alternative if %R >20%

# *E. coli* - % Susceptible<sup>1</sup>

Category	N	Cip	FM	T-S	CZ
All isolates	4167	77	93	71	92
18-40 yo female outpatient urine	797	90	95	79	96
>65 yo outpatient urine	1260	70	91	68	92

<sup>1</sup> First isolate/pt (CLSI M39-A4)

# Variability in Urine C&S Ordering Practices

Clinical Scenario	No. (%) of general practitioners who said they would order C&S
Probable uncomplicated UTI	165/278 (59%)
Previous treatment failure in older woman <sup>1</sup>	262/291 (90%)

<sup>1</sup> more likely to have resistant organisms

Hillier et al. 2006. J Antimicrob Chemother. 58:1303.

- Patient with uUTI often not cultured
- Data in our routine cumulative antibiogram likely reflects patients with more problematic UTIs

*How many patients had MDR  
Acinetobacter baumannii and  
which drugs are most active  
against Acinetobacter baumannii?*

Question ????

# *Acinetobacter baumannii*

## % Susceptible<sup>1</sup> (N=73)

A-S	P-T	Ceftaz	Mero	Amk	Gent	Tob	Cip	T-S
51	43	44	58	58	50	54	47	51

<sup>1</sup> First isolate/pt (CLSI M39-A4)

# ***Acinetobacter baumannii***

**(N=73 patients; 8 had multiple isolates with >1 profile)**

<b>Resistance Profile</b>	<b># patients</b>	<b>%<sup>1</sup></b>
<b>NO Resistance</b>	<b>28</b>	<b>38.4</b>
<b>Amk, A-S, Ceftaz, Cip, Mero</b>	<b>24</b>	<b>32.9</b>
<b>A-S, Ceftaz, Cip, Mero</b>	<b>5</b>	<b>6.8</b>
<b>Ceftaz</b>	<b>4</b>	<b>5.5</b>
<b>Cip</b>	<b>3</b>	<b>4.1</b>
<b>Amk, A-S, Ceftaz, Cip</b>	<b>3</b>	<b>4.1</b>
<b>Other (10 profiles)</b>	<b>14</b>	<b>19.3</b>

**Drugs examined:**  
**Amk - amikacin**  
**A-S – amp-sulbactam**  
**Ceftaz - ceftazidime**  
**Cip - ciprofloxacin**  
**Mero - meropenem**

**<sup>1</sup>of 73 patients with *A. baumannii***

*What two drugs might best "cover"  
Pseudomonas aeruginosa isolates?*

Question ????

# *Pseudomonas aeruginosa* % Susceptible<sup>1</sup> (N=769)

Cip	Cfpm	Mero	Tob	Cfpm and/or Cip	Mero and/or Cip	Cfpm and/or Tob	Mero and/or Tob
73	77	72	94	94	91	97	96

<sup>1</sup> First isolate/pt (CLSI M39-A4)

*What agents are most active against bloodstream isolates of gram-negative rods (GNR)?*

Question ????

# Bloodstream Isolates of GNR

## Bloodstream Isolates, % Susceptible<sup>1</sup>

Organism*	N	Cftrx	Cftaz	P-T	Mero	Amk	Tob	Cip
<i>E. coli</i>	107	79	79	95	100	100	83	61
<i>K. pneumoniae</i>	63	92	91	87	95	97	94	94
<i>E. cloacae</i>	30	73	72	77	100	100	97	100
<i>P. aeruginosa</i>	29	-	89	79	86	100	97	76

\* Only a few representative species listed here as example.

<sup>1</sup> First isolate/pt (CLSI M39-A4)

# Bloodstream Isolates of GNR

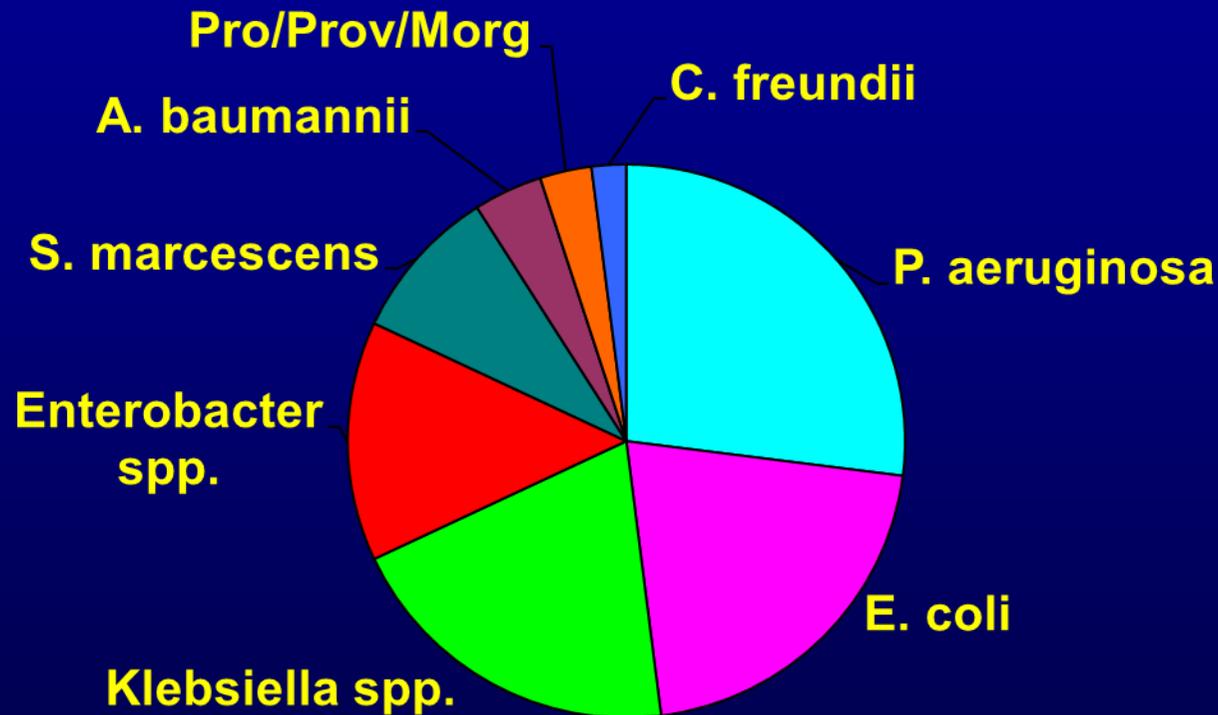
**Bloodstream Isolates, % Susceptible<sup>1</sup>**  
**All Species Combined (N = 339 patients)**

Organism	Cftrx	Cftaz	P-T	Mero	Amk	Tob	Cip
All GNR	72	80	84	92	94	86	77

*What percentage of piperacillin-tazobactam-R blood and respiratory isolates would be covered by adding a second agent?*

Question ????

# GNR Blood and Respiratory Isolates (N=977)



# GNR Blood and Respiratory Isolates (N=977)

<b>Pip-Tazo %S</b>	<b>Add</b>	<b>%S gained</b>	<b>Total % Covered with 2 drugs</b>
<b>79.6</b>	<b>Ciprofloxacin</b>	<b>14.3</b>	<b>93.9</b>
	<b>Tobramycin</b>	<b>18.4</b>	<b>98.0</b>
	<b>Amikacin</b>	<b>20.4</b>	<b>100</b>

*How many patients had  
Carbapenem-resistant  
Enterobacteriaceae (CRE)?*

Question ????

# *Klebsiella pneumoniae* Isolates % Susceptible<sup>1</sup> (N=886)

Cz	P-T	Cftrx	Mero	Amk	Gent	Tob	Cip	T-S
90	90	94	98	98	95	92	91	85

<sup>1</sup> First isolate/pt (CLSI M39-A4)

# Number of CRE Patients

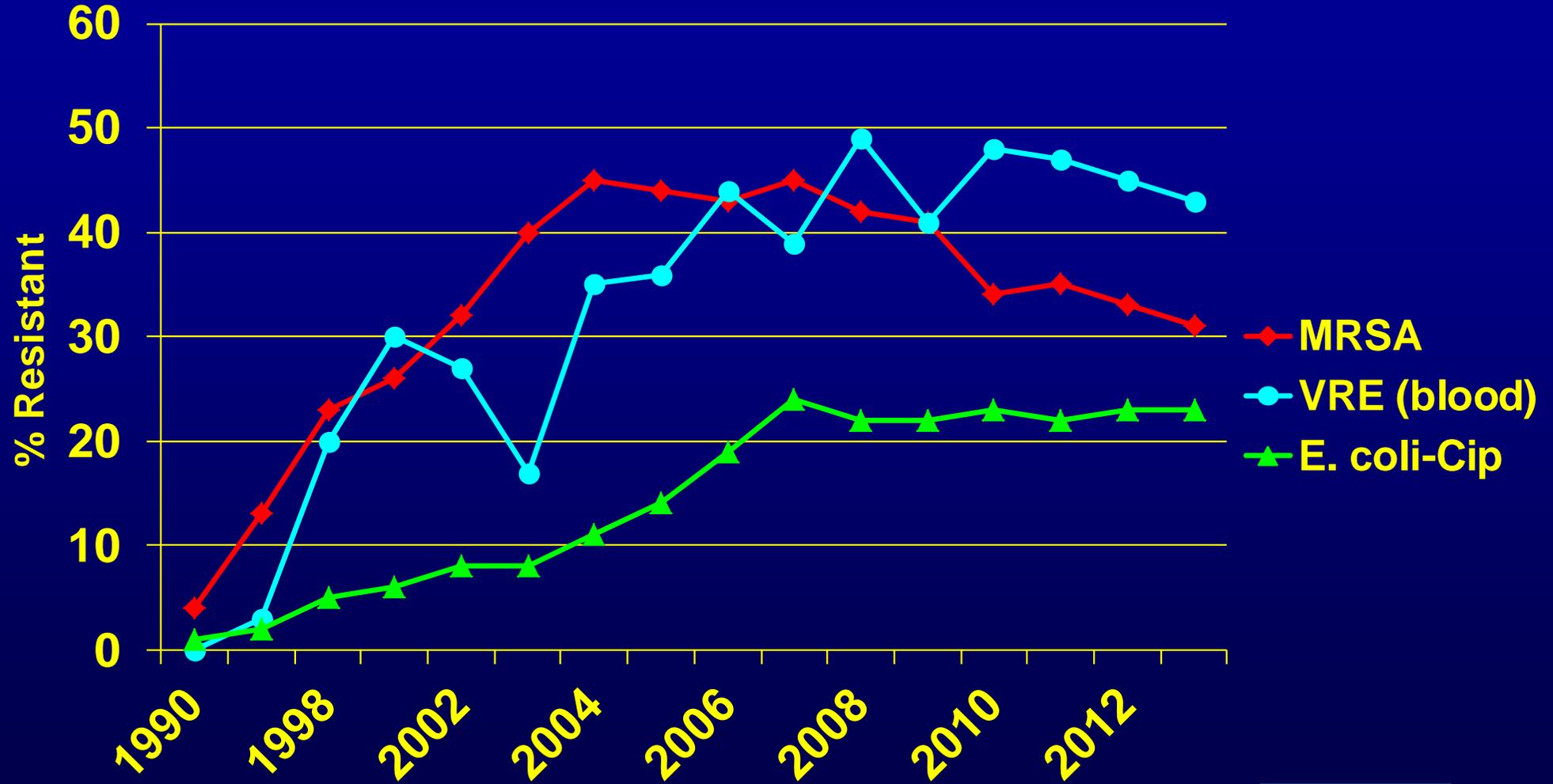


Examine all isolates (not just first isolate/patient).  
Number of Enterobacteriaceae/year tested = approximately 5000 isolates.

*Has there been an increase in  
resistant isolates?*

Question ????

# Resistance Trends



**Surveillance Data  
Antimicrobial Resistance**

# ***When might we use local antibiogram vs. surveillance data?***

<b>Local Antibiogram Data</b>	<b>Surveillance Data</b>
<b>Antibiotic Stewardship</b>	<b>When local not available*</b>
<b>Empiric therapy policies</b>	<b>To benchmark with local data</b>
<b>Formulary decisions</b>	<b>Learn about current resistance trends</b>

- \* Local antibiogram data may not be available for:**
- Organisms with predictable AST profiles (e.g. *Streptococcus pyogenes*)**
  - Organisms infrequently isolated (*Streptococcus pneumoniae*)**
  - Agents not routinely tested (new drugs)**
  - Organisms “selectively” tested (anaerobes)**
  - Isolates from patients in select facilities (e.g., nursing homes)**

# *When analyzing surveillance data, must ask questions...*

- ◆ *Were isolates from specimens obtained...*
  - as part of “routine care”?
  - as part of a controlled “surveillance study”?
- ◆ *What types of patients?*
- ◆ *What time frame?*
- ◆ *What geographic area?*
- ◆ *How was testing done? What breakpoints were used?*
- ◆ *Was testing done at a centralized laboratory?*
- ◆ *How were results analyzed?*

# Cumulative Antibiogram - Anaerobes

## Appendix D. Cumulative Antimicrobial Susceptibility Report for Anaerobic Organisms

Isolates collected from selected US hospitals  
1 January 2010 – 31 December 2012<sup>a</sup>

### *Bacteroides fragilis* Group

Anaerobic Organisms	Number of Strains	Ampicillin-sulbactam		Number of Strains	Piperacillin-tazobactam		Number of Strains	Cefoxitin		Number of Strains	Ertapenem		Number of Strains	Imipenem		Number of Strains	Meropenem	
		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R
Percent Susceptible (%S) and Percent Resistant (%R) <sup>b</sup>		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R
Breakpoints in µg/mL		≤ 8/4	≥ 32/16		≤ 32/4	≥ 128/4		≤ 16	≥ 64		≤ 4	≥ 16		≤ 4	≥ 16		≤ 4	≥ 16
<i>B. fragilis</i>	768	90	3	1497	98	1	1403	87	3	770	97	2	234	98	1	1503	96	1
<i>B. thetaiotaomicron</i>	349	80	4	467	79	8	469	48	8	348	98	1	134	99	1	470	98	1
<i>B. ovatus</i>	77	88	1	127	95	4	130	58	9	77	95	1	52	100	0	130	98	0
<i>B. vulgatus</i>	106	70	5	174	97	2	153	82	7	106	99	1	56	100	0	153	98	1
<i>B. uniformis</i>	94	88	4	128	95	2	129	60	9	94	100	0	24	100	0	128	99	0
<i>B. eggerthii</i>	60	93	0	70	89	11	73	34	21	60	100	0				72	100	0
<i>Parabacteroides distasonis</i>	220	66	20	265	56	30	265	42	15	220	97	2	33	97	0	265	97	2
<i>B. fragilis</i> group without <i>B. fragilis</i>	906	78	8	1231	81	11	1219	53	10	905	98	1	299	99	0	1218	98	1
<i>B. fragilis</i> group (all 7 species listed)	2580	82	6	3959	87	7	3841	65	7	2580	98	1	832	99	1	3939	98	1

# Summary

- ◆ CLSI M39-A4 contains guidelines for preparation of cumulative antibiogram reports.
- ◆ Failure to eliminate repeat isolates on a given patient can skew cumulative antibiogram data.
- ◆ One must use caution in interpreting %S results when “N” is small.
- ◆ One must use caution in interpreting %S results when not all drugs are tested on all isolates presented in the cumulative antibiogram.
- ◆ Supplemental analysis of cumulative antibiograms may provide useful information to guide empiric therapy decisions in select patient populations.
- ◆ Surveillance data for antimicrobial resistance is helpful when local data are not available and to follow geographic resistance trends.

**Thank You!**

