Here, There, and Everywhere

Surveillance of Wisconsin Organisms for Trends in Antimicrobial Resistance and Epidemiology

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The presenter states no conflict of interest and has no financial relationship to disclose relevant to the content of this presentation.

OUTLINE

I. Impetus

II. Past efforts in Wisconsin

III. A new approach

- Advantages of MIC
- Epidemiology

IV. Region-specific findings and future directions

Impetus

MAJOR ARTICLE

US Outpatient Antibiotic Prescribing Variation According to Geography, Patient Population, and Provider Specialty in 2011

Lauri A. Hicks,[1] Monina G. Bartoces,[1] Rebecca M. Roberts,[1] Katie J. Suda,[2] Robert J. Hunkler,[3] Thomas H. Taylor Jr,[1] and Stephanie J. Schrag[1]

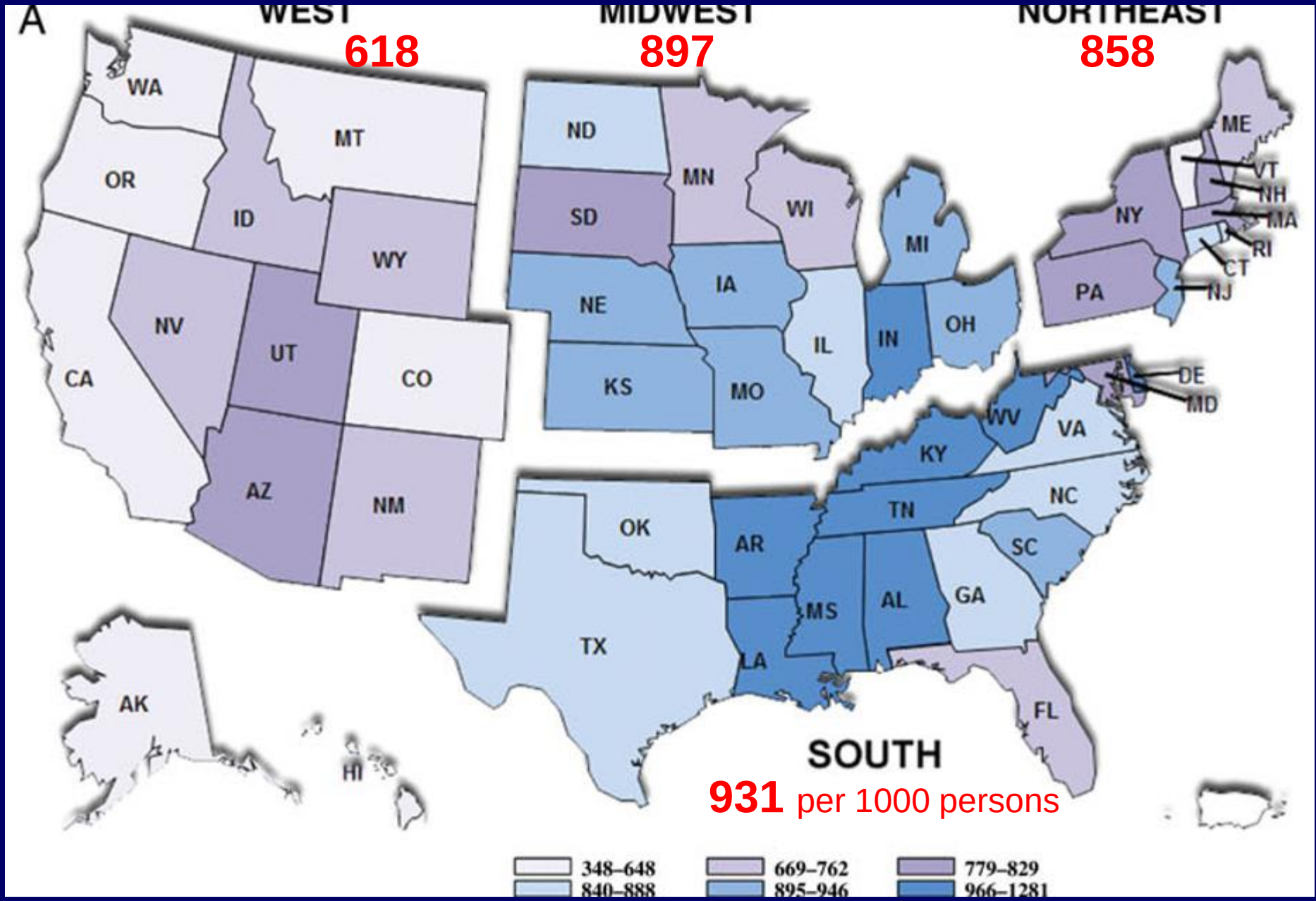
[1]Centers for Disease Control and Prevention, Atlanta, Georgia; [2]Department of Veterans Affairs, University of Illinois at Chicago; and [3]IMS Health, Plymouth Meeting, Pennsylvania

(See the Editorial Commentary by Metlay on pages 1317–8.)

Prescriptions per 1000 persons:

penicillins 193
macrolides 190
cephalosporins 114
quinolones 89
β-lactams (increased activity) 69
tetracyclines 68
trimethoprim-sulfamethoxazole 65

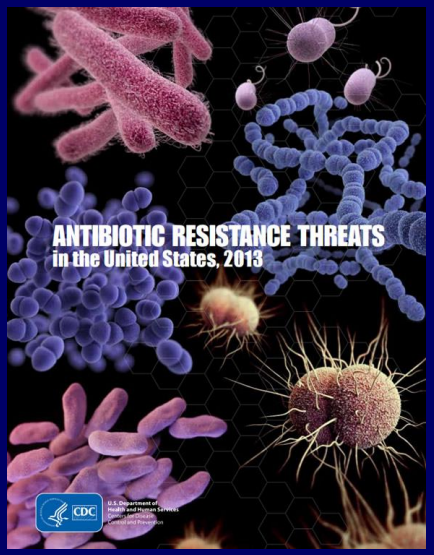
Clin. Infect. Dis. **60:** 1308-1316; 2015



Clin. Infect. Dis. **60:** 1308-1316; 2015

FOUR-PRONGED APPROACH (CDC)

- Prevent infections; prevent spread
  - Immunization
  - Hand hygiene
  - Food preparation
  - Judicious antimicrobial use
- Resistance tracking
  - Data gathering
  - Epidemiology
- Stewardship
  - Humans (~50%)
  - Animals (more)
- Research and development
  - New antibiotics
  - New laboratory diagnostics



CDC; Antibiotic Resistance Threats in the United States, 2013

Past efforts in Wisconsin

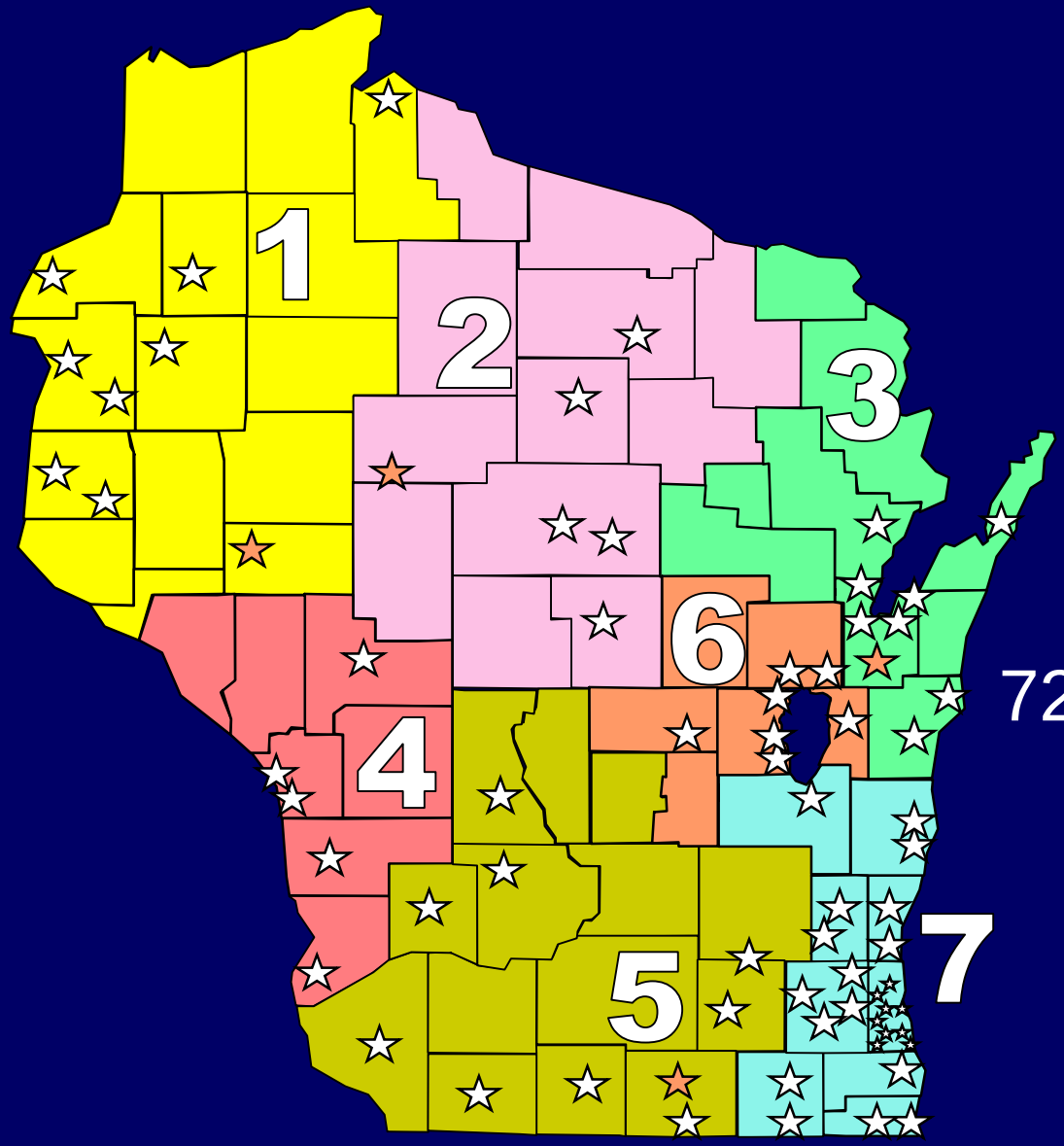
ORIGINAL RESEARCH

Surveillance of Wisconsin Antibacterial Susceptibility Patterns

Erik Munson, PhD; Timothy K. Block, MT; Erin J. Bowles, MT; Michael Costello, PhD; Richard Dern, MS; Thomas R. Fritsche, MD, PhD; Michael A. Helgesen, MT; Joshua L. Kro[illegible], MLS; Raymond P. Podzorski, PhD; Karen Siebers, MT; Brian Simmons, MLS; Mary A. Smith, MLS; Frances Spray-Larson, P[illegible]D, MLT; Tam T. Van, PhD; David M. Warshauer, PhD

WMJ **115:** 29-36; 2016

2013 ANTIBIOGRAM SURVEY



72 healthcare entities; 7 regions
Volunteer basis
Data compilation

~75,000 *E. coli*
~30,000 *S. aureus*

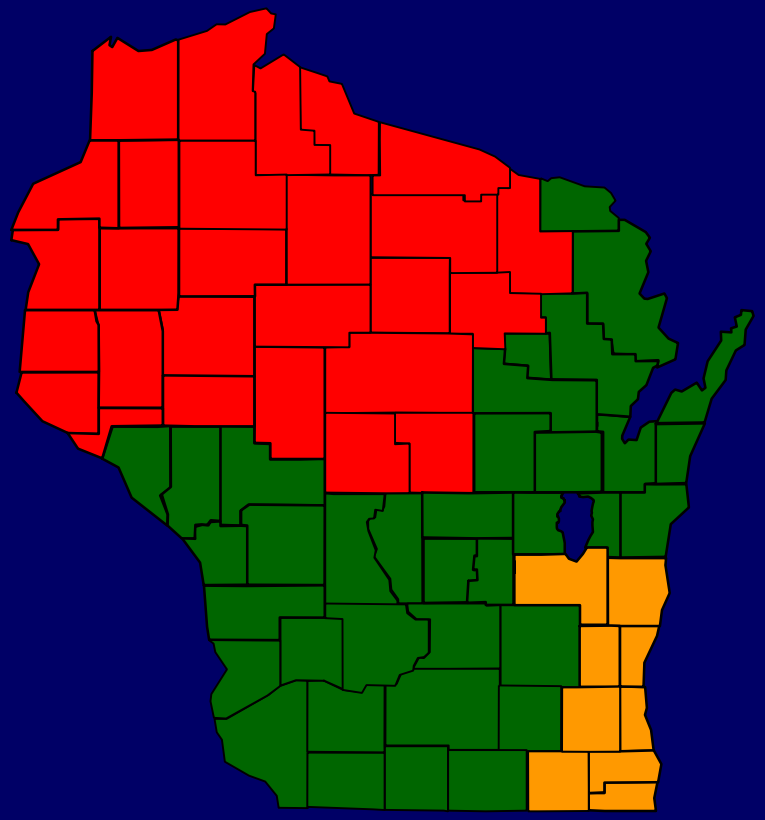
GRAM-NEGATIVE ORGANISMS

Organism	% of Antibiograms
Escherichia coli	100
Klebsiella pneumoniae	90
Klebsiella oxytoca	33
Proteus mirabilis	75
Enterobacter cloacae	49
Enterobacter aerogenes	18
Citrobacter koseri	10
Citrobacter freundii	28
Morganella morganii	6
Serratia marcescens	17
Pseudomonas aeruginosa	83

GRAM-NEGATIVE ANTIMICROBIALS

Agent	% of Antibiograms
levofloxacin	93
ciprofloxacin	82
moxifloxacin	1
ampicillin	88
ampicillin-sulbactam	92
amoxicillin	1
amox-clavulanate	29
piperacillin	25
piperacillin-tazo	86
cefazolin	93
cefoxitin	32
cefotetan	3
cefuroxime	17
ceftriaxone	97

Agent	% of Antibiograms
cefotaxime	4
ceftazidime	75
cefepime	82
aztreonam	53
gentamicin	99
tobramycin	89
amikacin	56
tetracycline	14
imipenem	65
meropenem	61
ertapenem	46
trimethoprim-sulfa	100
nitrofurantoin	90



2013

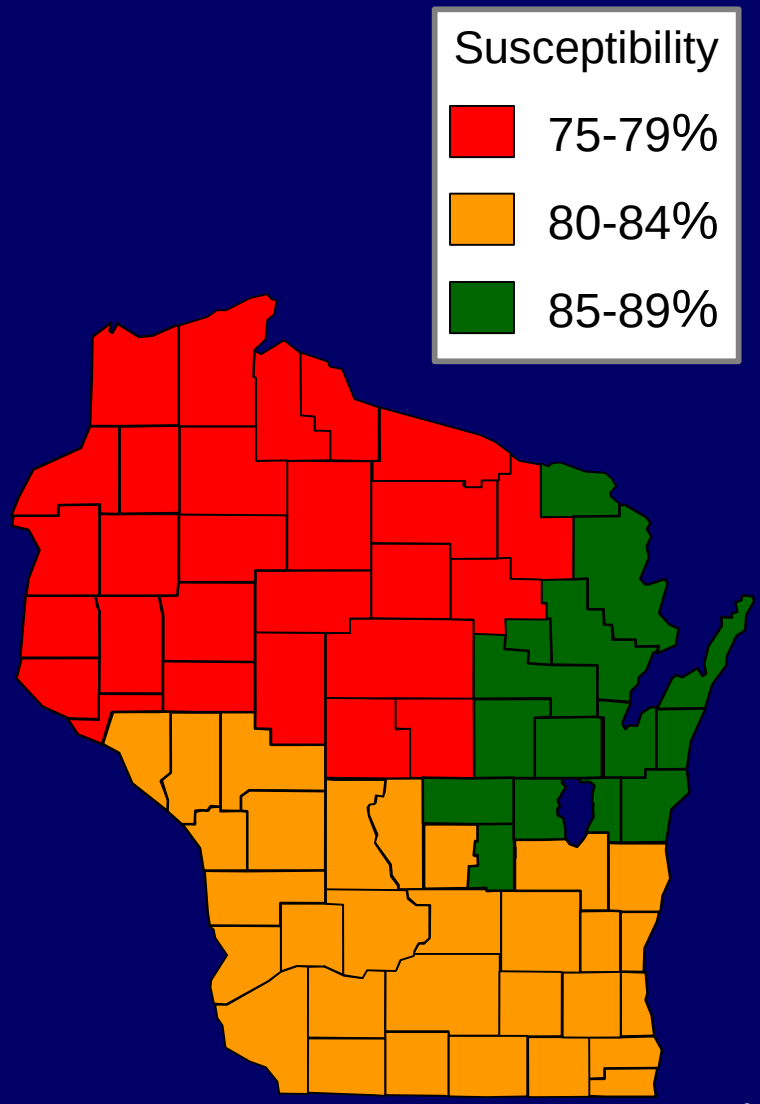
P. mirabilis

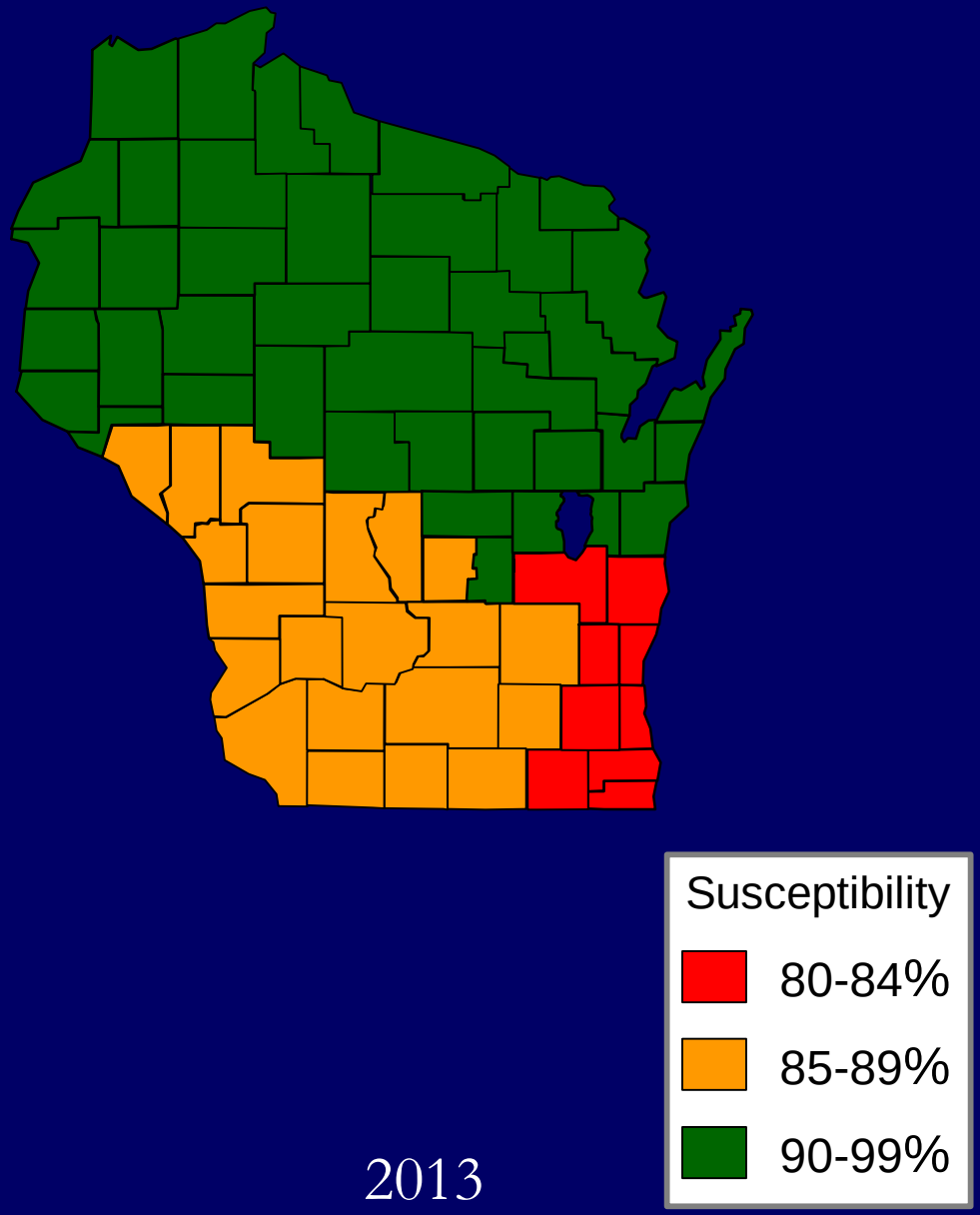
ciprofloxacin

2013

P. mirabilis

trimethoprim-sulfamethoxazole





2013

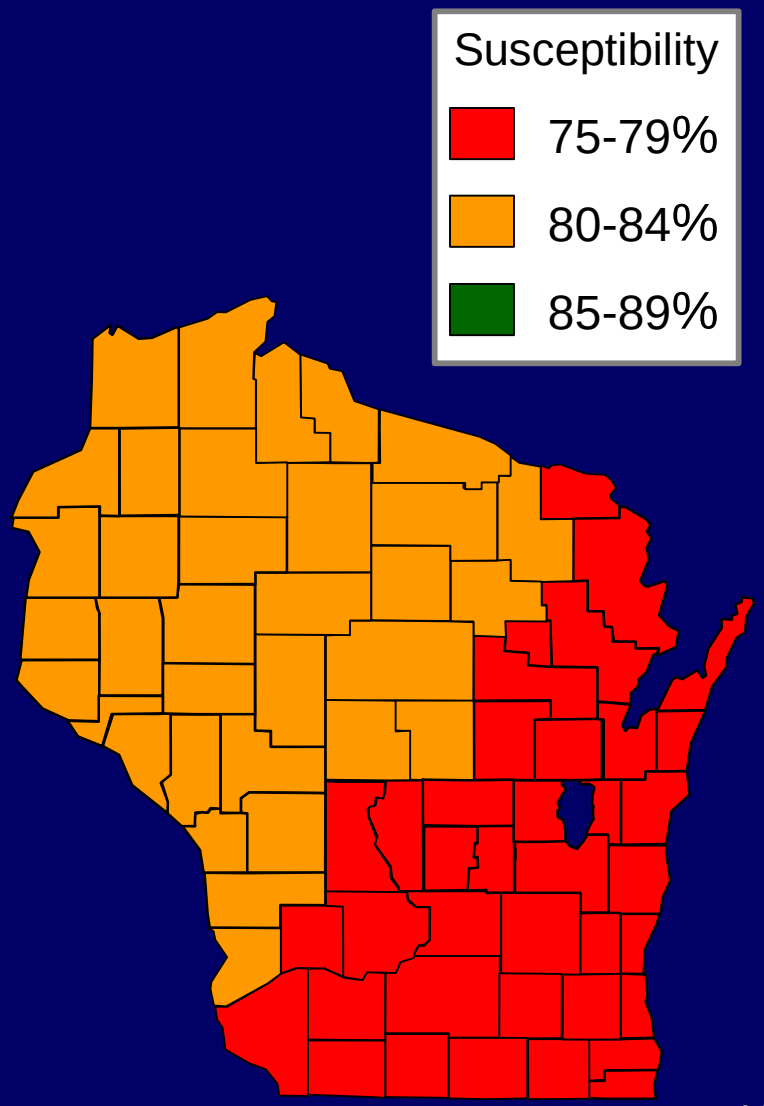
P. aeruginosa

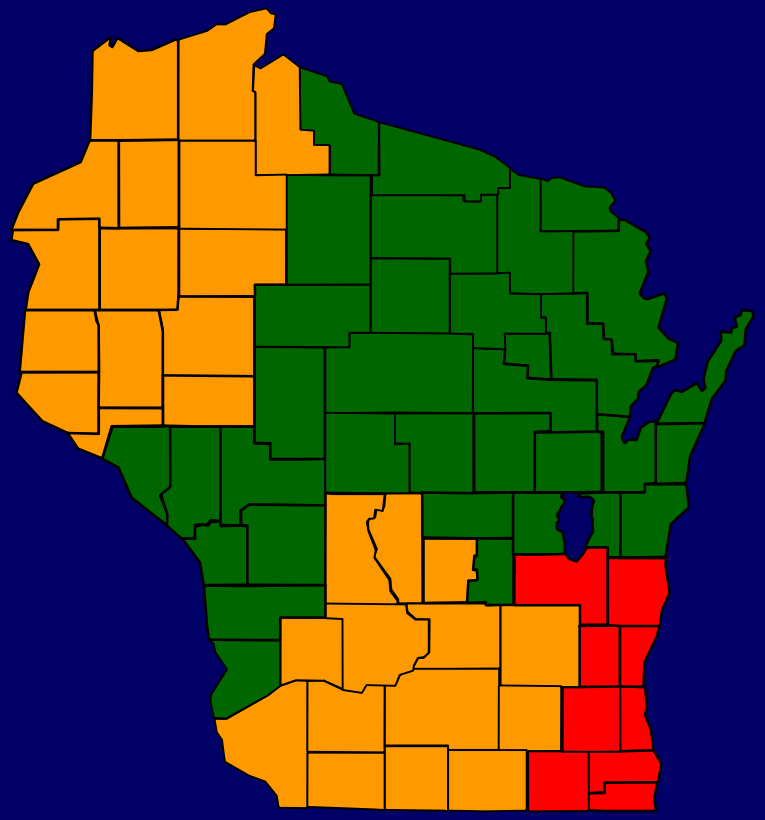
gentamicin

2013

P. aeruginosa

ciprofloxacin

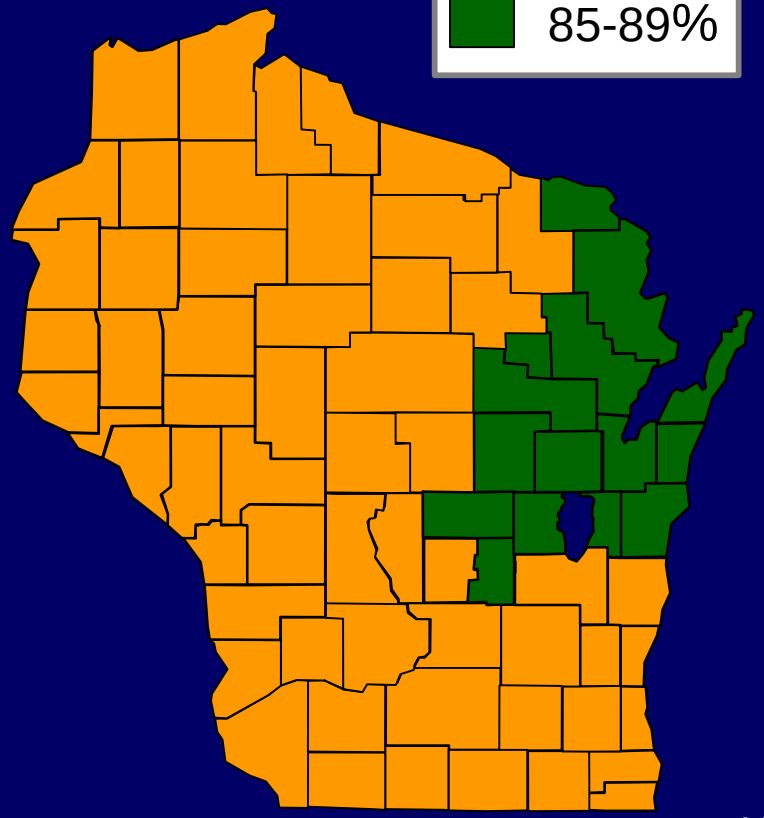




Susceptibility
75-79%
80-84%
85-89%

2009
E. coli
levofloxacin

2013
E. coli
levofloxacin

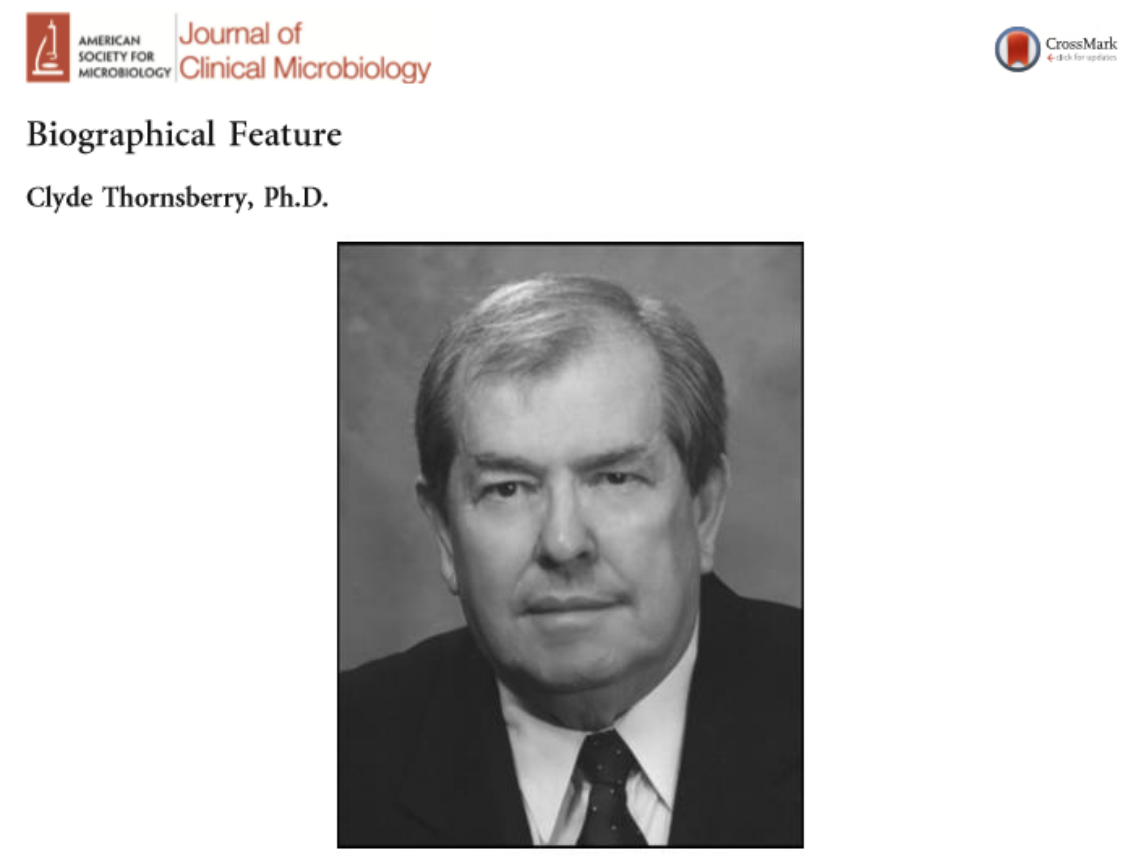


Susceptibility
75-79%
80-84%
85-89%

LIMITATIONS/CAVEATS

- Laboratory validation, testing, reporting
- Variable testing methods; formats
- Raw data or result of cascading?
- These are not true “resistance” data
- Inpatient versus outpatient?
- “Rule of 30” for antibiogram (selection bias?)

A new approach



AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

CrossMark

Biographical Feature

Clyde Thornsberry, Ph.D.

"Once an antibiotic is discovered, your job is not done. You need to monitor your product for development of resistance and do surveillance."

J. Clin. Microbiol. **54:** 250-253; 2016

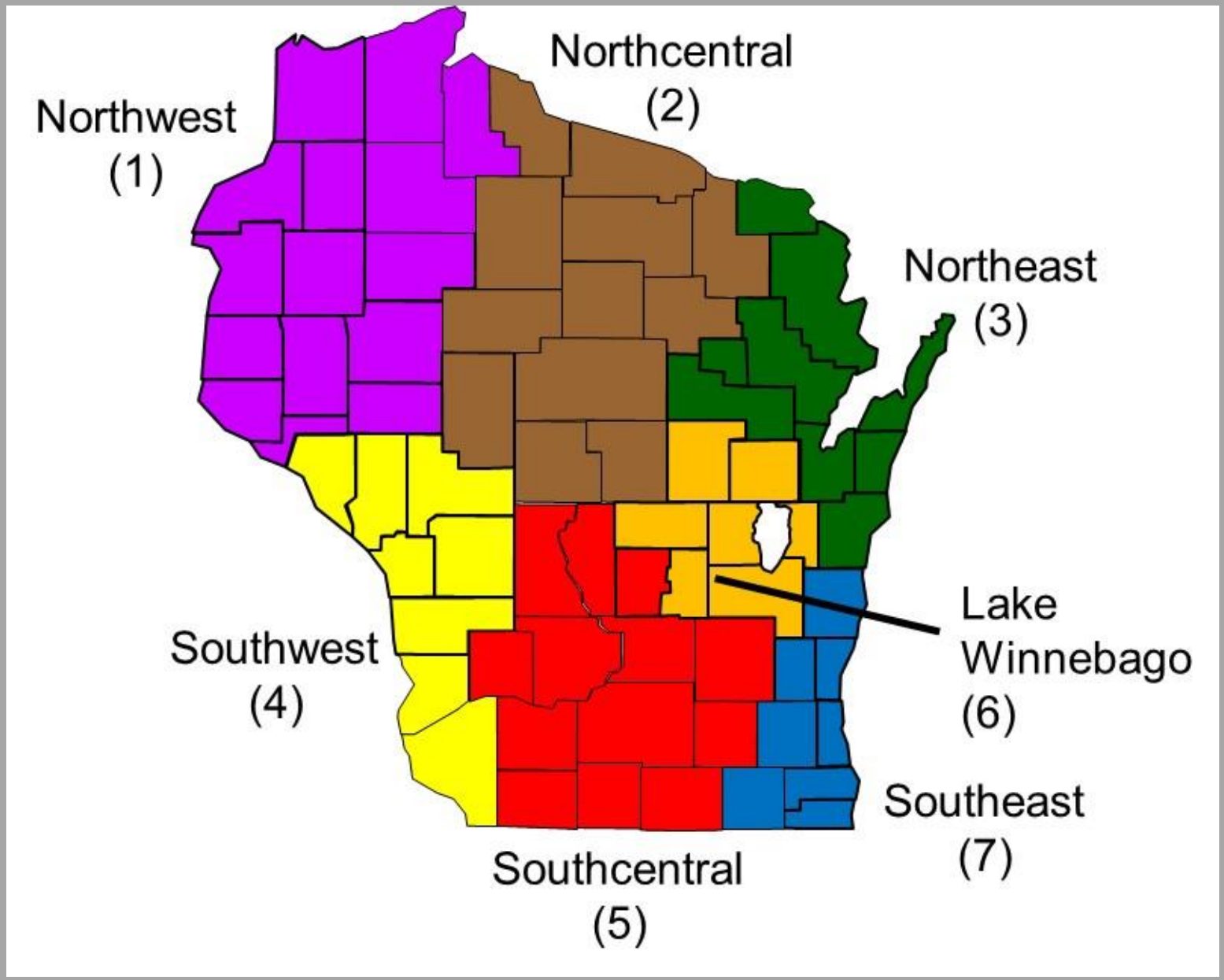
RATIONALE FOR STUDY SITE

- Based on seven-region WCLN model
- Two “rural” plus one “major population center”

  38% of laboratories from municipalities <15,000
  58% of laboratories from municipalities <35,000

- Caveats

  Limited number of stand-alone microbiology labs
  “Rural” laboratories in Fox Valley, Milwaukee
  Concerns over ‘quota’


Northwest
(1)
Northcentral
(2)
Northeast
(3)
Lake
Winnebago
(6)
Southwest
(4)
Southeast
(7)
Southcentral
(5)

REQUEST

- Number of clinical isolates per year
- Preference skin and soft tissue, respiratory tract, bloodstream isolates

  Consecutive isolates
  Non-duplicate isolates
  Urines accepted to reach quota

- Supply limited demographic information

  No “engagement” in “human subjects research”
  Data use agreement

METHODS

- Custom frozen broth microdilution panels; Testing and reporting per CLSI M100 series

MHB (Gram-negative)

CIP	LEV	CFZ	FOX
CAZ	CAX	FEP	AMP
A/S	AZT	P/T	MER
ERT	GEN	TOB	NIT
T/S			

MHB (*Staphylococcus* sp.)

PEN	TET	GEN	TAR
VAN	DOX	LEV	DAL
CLI (D)	ERY	LZD	TEL
FOX	DAP	T/S	

- Database management at Marquette University
- %S, %I (%DD), %R; MIC_{50}, MIC_{90} determination

Expressed as S/I (or susceptible dose-dependent)/R
(selected agents may not possess intermediate breakpoint
rare agents only possess susceptible breakpoint)

Antimicrobial (testing range μg/mL)

Data from your location

Data from your region

Cumulative data from Wisconsin

PIP-TAZOBACTAM (8-256)				CLSI breakpoints 16 / 32-64 / 128		
Location	**n**	**MIC_{50}**	**MIC_{90}**	**%S**	**%I**	**%R**
St. Elsewhere						
Region 6						
Wisconsin						

Median MIC

90th percentile MIC

Advantages of the MIC

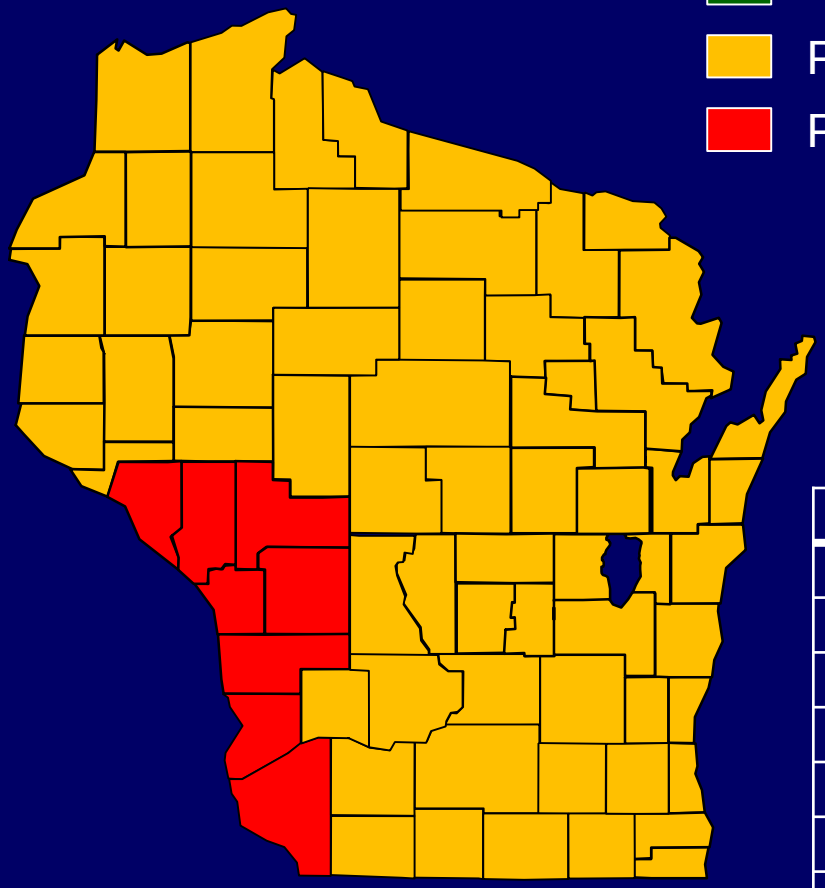
1	2	3	4	5	6	7	8	9	10	11	12
LEV 32	LEV 16	LEV 8	LEV 4	LEV 2	**LEV 1**	LEV 0.5	LEV 0.25	AMP 64	AMP 32	**AMP 16**	AMP 8
CIP 32	CIP 16	CIP 8	CIP 4	CIP 2	CIP 1	**CIP 0.5**	CIP 0.25	TOB 16	**TOB 8**	TOB 4	TOB 2
CFZ 64	CFZ 32	CFZ 16	CFZ 8	**CFZ 4**	CFZ 2	CFZ 1	A/S 64	A/S 32	**A/S 16**	A/S 8	A/S 4
FEP 64	FEP 32	FEP 16	**FEP 8**	**FEP 4**	FEP 2	FEP 1	CAX 8	CAX 4	**CAX 2**	CAX 1	CAX 0.5
CAZ 64	CAZ 32	CAZ 16	**CAZ 8**	CAZ 4	CAZ 2	P/T 256	P/T 128	**P/T 64**	**P/T 32**	P/T 16	P/T 8
ERT 8	ERT 4	ERT 2	**ERT 1**	ERT 0.5	ERT 0.25	FOX 32	**FOX 16**	FOX 8	NIT 128	**NIT 64**	NIT 32
MER 16	MER 8	MER 4	**MER 2**	MER 1	MER 0.5	T/S 16	T/S 8	T/S 4	T/S 2	T/S 1	**POS**
AZT 64	AZT 32	AZT 16	**AZT 8**	AZT 4	AZT 2	GEN 32	GEN 16	**GEN 8**	GEN 4	GEN 2	NEG

2018 *S. aureus* OBSERVATIONS

DOXYCYCLINE (0.5-32)						CLSI breakpoints 4/8/16
Location	n	MIC_{50}	MIC_{90}	%S	%I	%R
Northwest	45	≤ 0.5	≤ 0.5	95.6	4.4	0.0
Northcentral	44	≤ 0.5	≤ 0.5	95.5	4.5	0.0
Northeast	45	≤ 0.5	≤ 0.5	100	0.0	0.0
Southwest	45	≤ 0.5	4	91.1	8.9	0.0
Southcentral	44	≤ 0.5	≤ 0.5	95.5	4.5	0.0
Lake Winnebago	44	≤ 0.5	≤ 0.5	100	0.0	0.0
Southeast	43	≤ 0.5	≤ 0.5	93.0	7.0	0.0
Wisconsin	310	≤ 0.5	≤ 0.5	95.8	4.2	0.0

Clin. Med. Research in press

2018 *S. aureus* OBSERVATIONS



- Percentage susceptible 5% or more greater than state mean
- Percentage susceptible ±5% of state mean
- Percentage susceptible 5% or more less than state mean

tetracycline
state mean 93.5%

TETRACYCLINE (0.5-32)						CLSI breakpoints 4/8/16
Location	n	MIC_{50}	MIC_{90}	%S	%I	%R
Northwest	45	≤ 0.5	1	93.3	0.0	6.7
Northcentral	44	≤ 0.5	≤ 0.5	95.5	0.0	4.5
Northeast	45	≤ 0.5	≤ 0.5	97.8	2.2	0.0
Southwest	45	≤ 0.5	32	84.4	2.2	13.3
Southcentral	44	≤ 0.5	≤ 0.5	95.5	0.0	4.5
Lake Winnebago	44	≤ 0.5	≤ 0.5	97.7	2.3	0.0
Southeast	43	≤ 0.5	≤ 0.5	90.7	0.0	9.3
Wisconsin	310	≤ 0.5	≤ 0.5	93.5	0.6	5.8

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FLUOROQUINOLONES

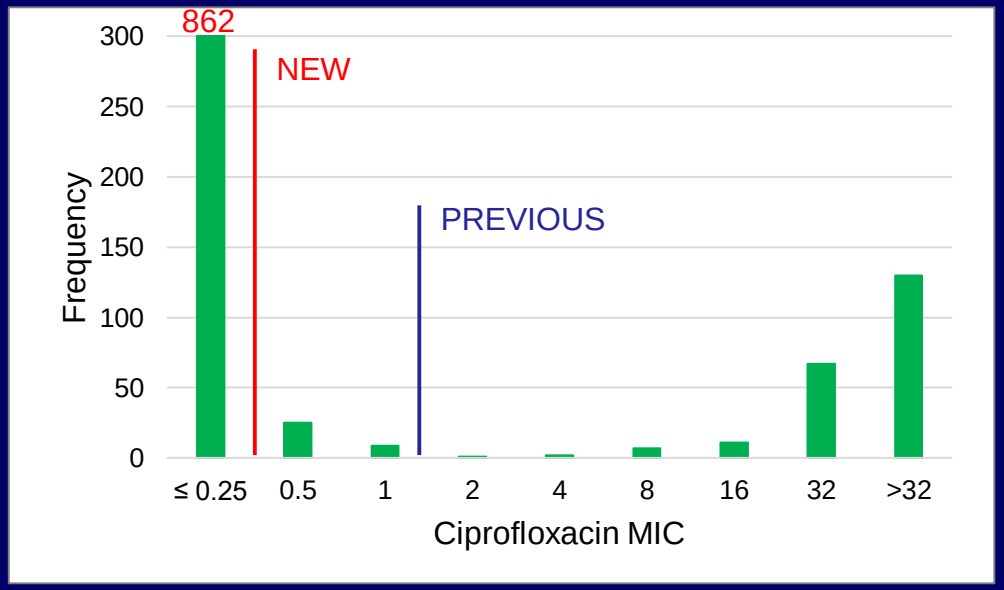
Organism	Method	Ciprofloxacin Previous			Ciprofloxacin New		
		S	I	R	S	I	R
Enterobacteriaceae	BMD	≤ 1	2	≥ 4	≤ 0.25	0.5	≥ 1
P. aeruginosa	BMD	≤ 1	2	≥ 4	≤ 0.5	1	≥ 2
Enterobacteriaceae	DD	≥ 21	16-20	≤ 15	≥ 26	22-25	≤ 21
P. aeruginosa	DD	≥ 21	16-20	≤ 15	≥ 25	19-24	≤ 18

Organism	Method	Levofloxacin Previous			Levofloxacin New		
		S	I	R	S	I	R
Enterobacteriaceae	BMD	≤ 2	4	≥ 8	≤ 0.5	1	≥ 2
P. aeruginosa	BMD	≤ 2	4	≥ 8	≤ 1	2	≥ 4
Enterobacteriaceae	DD	≥ 17	14-16	≤ 13	≥ 21	17-20	≤ 16
P. aeruginosa	DD	≥ 17	14-16	≤ 13	≥ 22	15-21	≤ 14

CLSI M100; 29th ed.; 2019

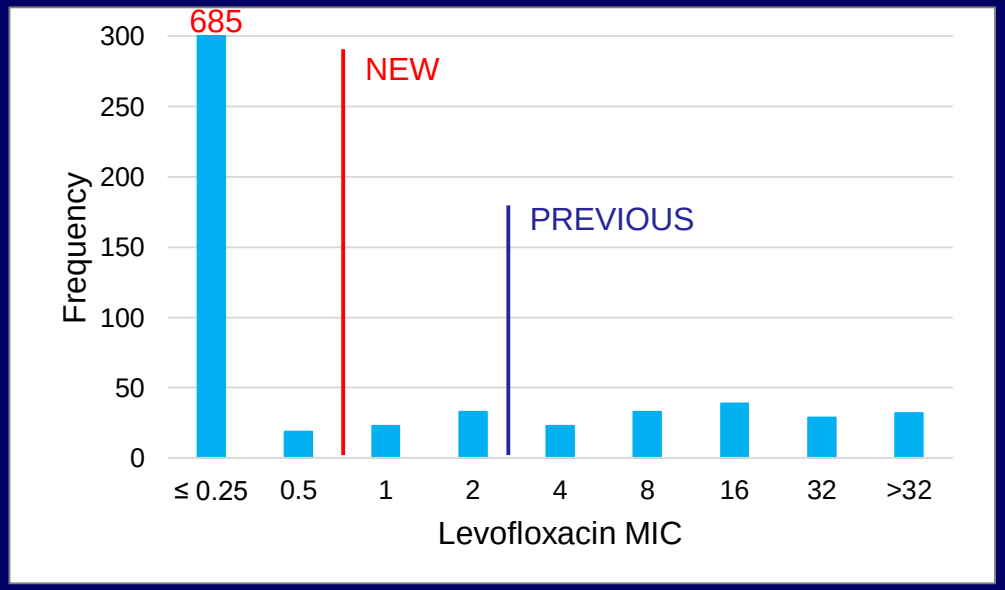
WISCONSIN SURVEILLANCE

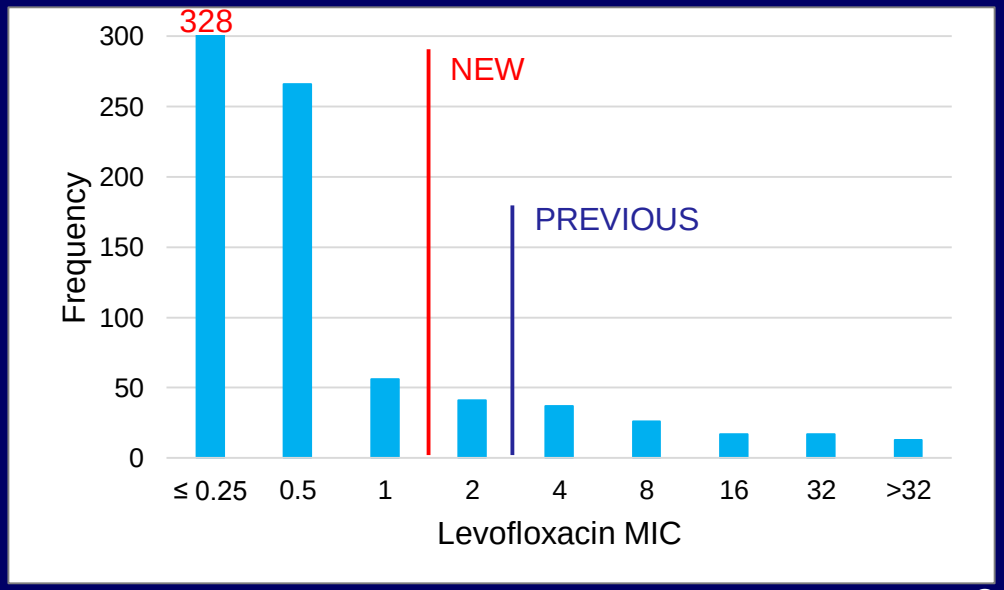
Organism	n	Ciprofloxacin Previous			Ciprofloxacin New		
		%S	%I	%R	%S	%I	%R
Escherichia coli	1114	80.4	0.1	19.5	77.4	2.2	20.4
Proteus mirabilis	916	78.5	3.6	17.9	76.0	1.4	22.6
Pseudomonas aeruginosa	801	86.8	3.7	9.5	82.4	4.4	13.2



WISCONSIN SURVEILLANCE

Organism	n	Levofloxacin Previous			Levofloxacin New		
		%S	%I	%R	%S	%I	%R
Escherichia coli	1114	80.6	0.4	18.9	79.5	0.9	19.6
Proteus mirabilis	916	83.0	2.5	14.5	76.9	2.5	20.6
Pseudomonas aeruginosa	801	86.3	4.6	9.1	81.1	5.1	13.7



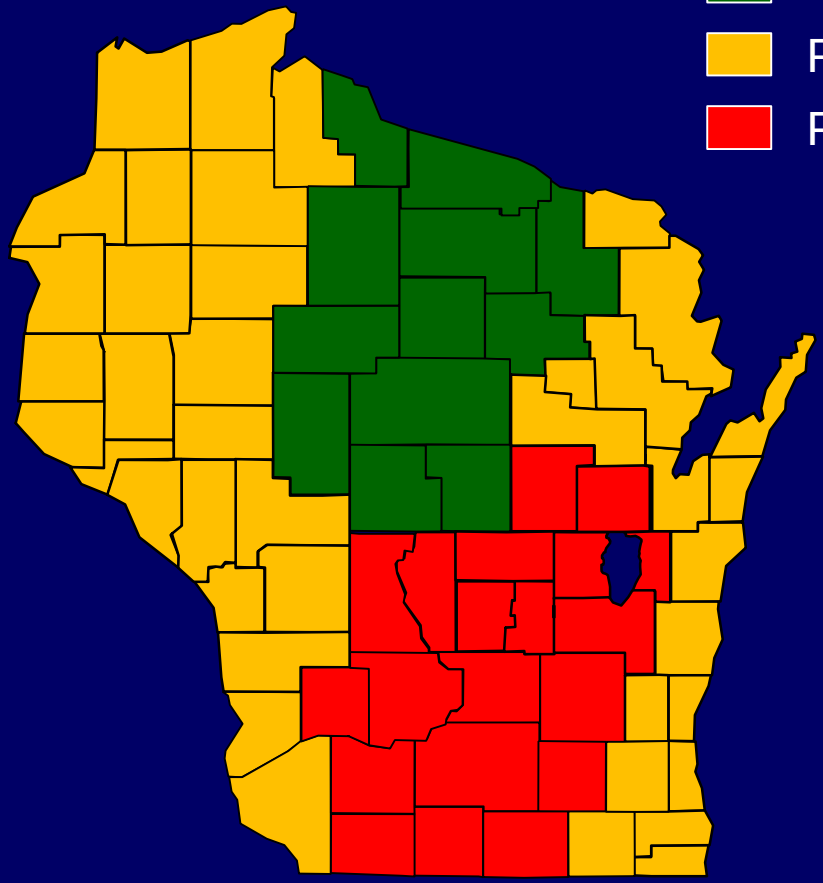


E. coli / CIPROFLOXACIN

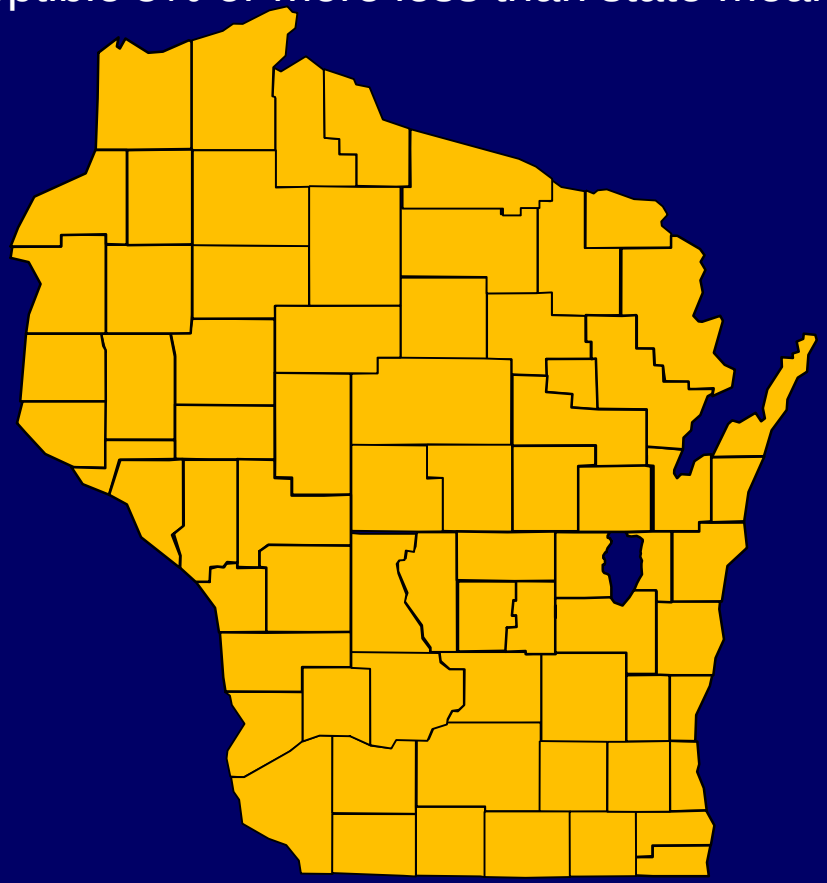
Percentage susceptible 5% or more greater than state mean

Percentage susceptible ±5% of state mean

Percentage susceptible 5% or more less than state mean



Previous
state mean 80.4%



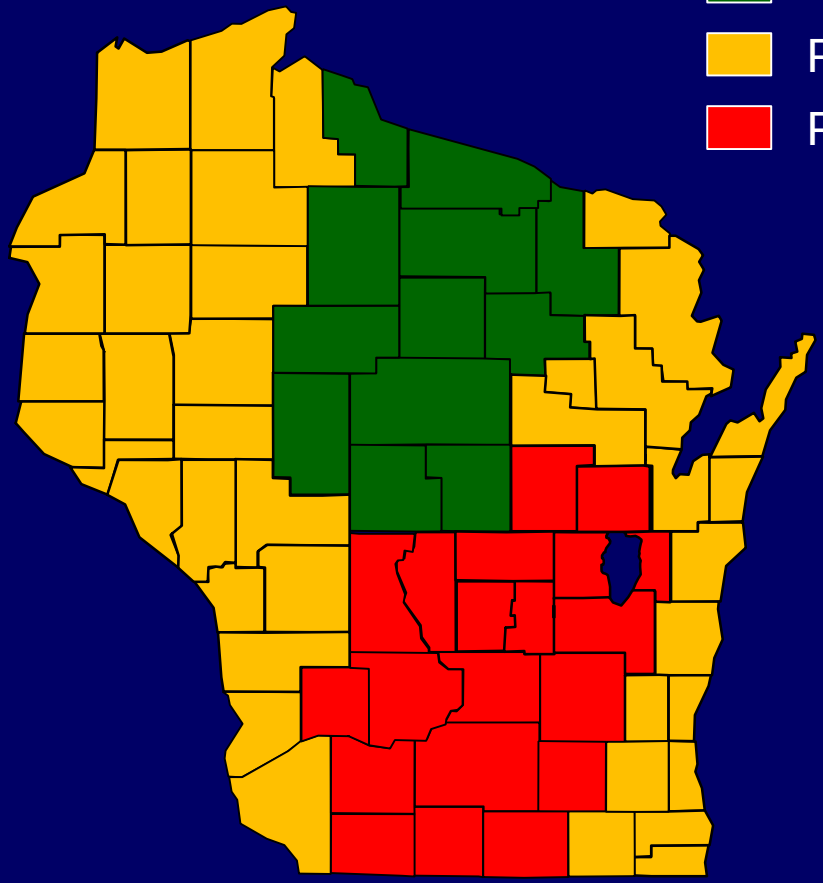
New
state mean 77.4%

E. coli / LEVOFLOXACIN

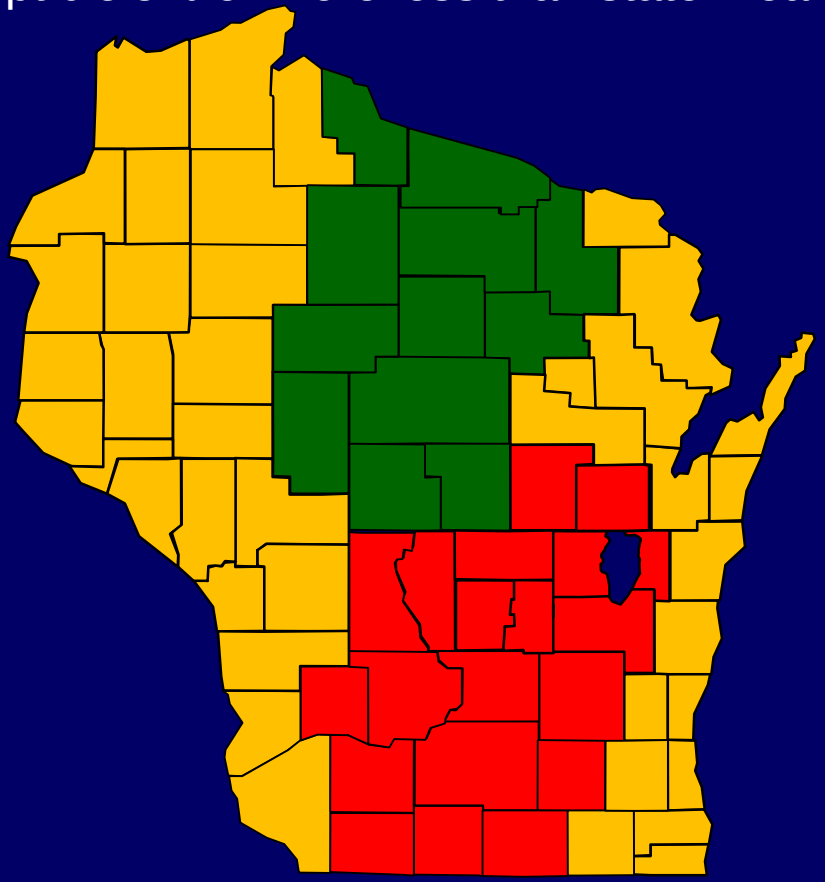
Percentage susceptible 5% or more greater than state mean

Percentage susceptible ±5% of state mean

Percentage susceptible 5% or more less than state mean



Previous
state mean 80.6%



New
state mean 79.5%

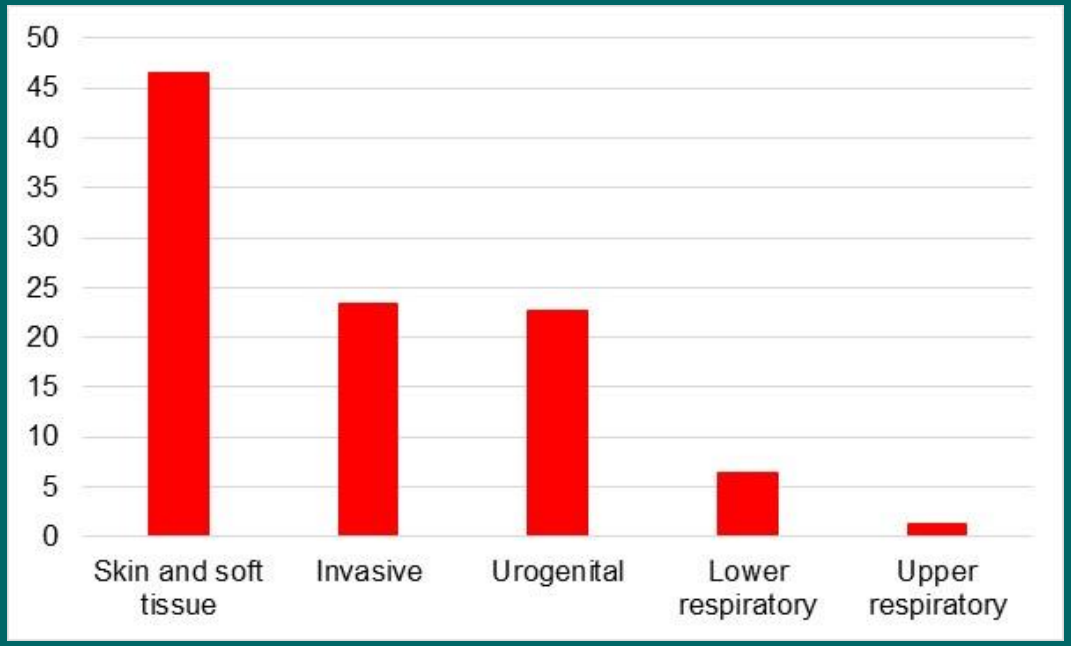
CEFTAROLINE

Organism	Method	Ceftaroline Previous			Ceftaroline New		
		S	I	R	S	SDD	R
S. aureus (incl. MRSA)	BMD	≤ 1	2	≥ 4	≤ 1	2-4	≥ 8
S. aureus (incl. MRSA)	DD	≥ 24	21-23	≤ 20	≥ 25	20-24	≤ 19

MIC	Number of Wisconsin Isolates
≤ 0.12	126
0.25	133
0.5	49
1	1
2	0
4	1
8	0

Surveillance of Wisconsin Organisms for Trends in Antimicrobial Resistance and Epidemiology (SWOTARE)

Epidemiology

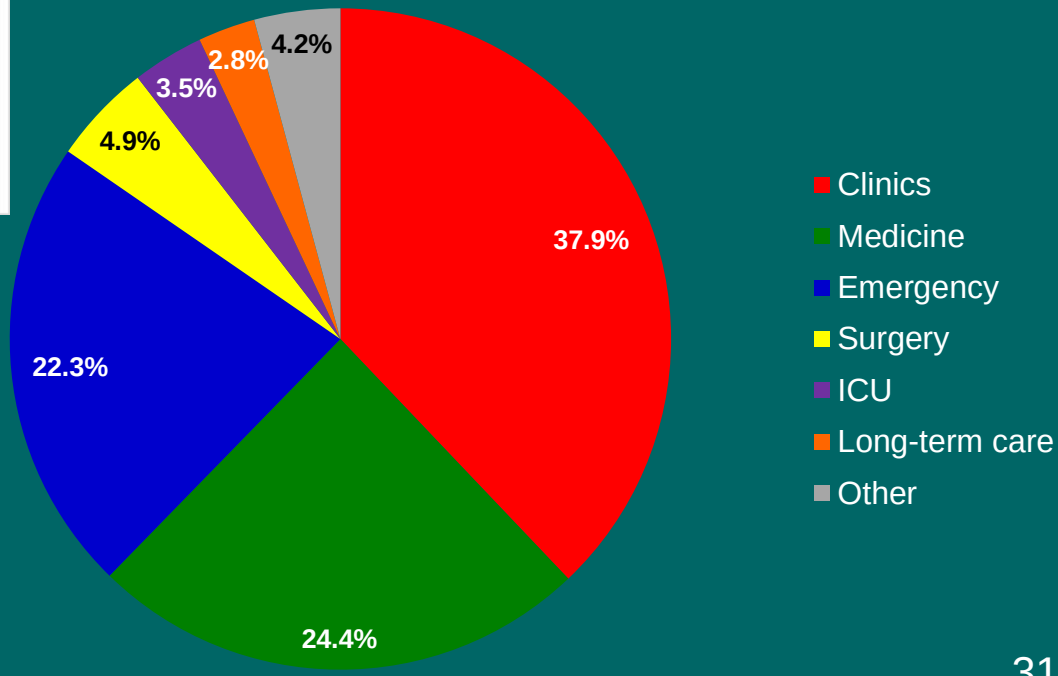


52.3%

47.7%

median 67

mean 63.2



OUTPATIENT VERSUS INPATIENT

Proteus mirabilis

LEVOFLOXACIN (0.25-32)						CLSI breakpoints 2/4/8
Location	n	MIC_{50}	MIC_{90}	%S	%I	%R
Outpatient	155	≤ 0.25	4	89.0	1.9	9.1
Inpatient	116	≤ 0.25	>32	69.0	3.4	27.6
Wisconsin		≤ 0.25	16	81.0	2.5	16.5

LEVOFLOXACIN (0.25-32)						CLSI breakpoints 2/4/8
Location	n	MIC_{50}	MIC_{90}	%S	%I	%R
Clinics	109	≤ 0.25	16	86.2	1.8	11.9
Medicine	64	≤ 0.25	>32	67.2	4.7	28.1
Emergency	46	≤ 0.25	1	95.6	2.2	2.2
ICU	10	0.5	8	70.0	10.0	20.0
Long-term care	23	2	>32	65.2	0.0	34.8
Surgery	13	≤ 0.25	32	92.3	0.0	7.7
Wisconsin		≤ 0.25	16	81.0	2.5	16.5

Gundersen Med. J. **10:** 41-48; 2017

Proteus mirabilis BY AGE

CIPROFLOXACIN (0.25-32)						CLSI breakpoints 1/2/4
Age	n	MIC_{50}	MIC_{90}	%S	%I	%R
20-39	25	≤ 0.25	1	92.0	0.0	8.0
40-59	60	≤ 0.25	16	80.0	1.7	18.3
60-79	110	≤ 0.25	32	72.7	3.6	23.6
≥ 80	71	≤ 0.25	32	67.6	8.5	23.9
Wisconsin		≤ 0.25	32	75.6	4.3	20.1

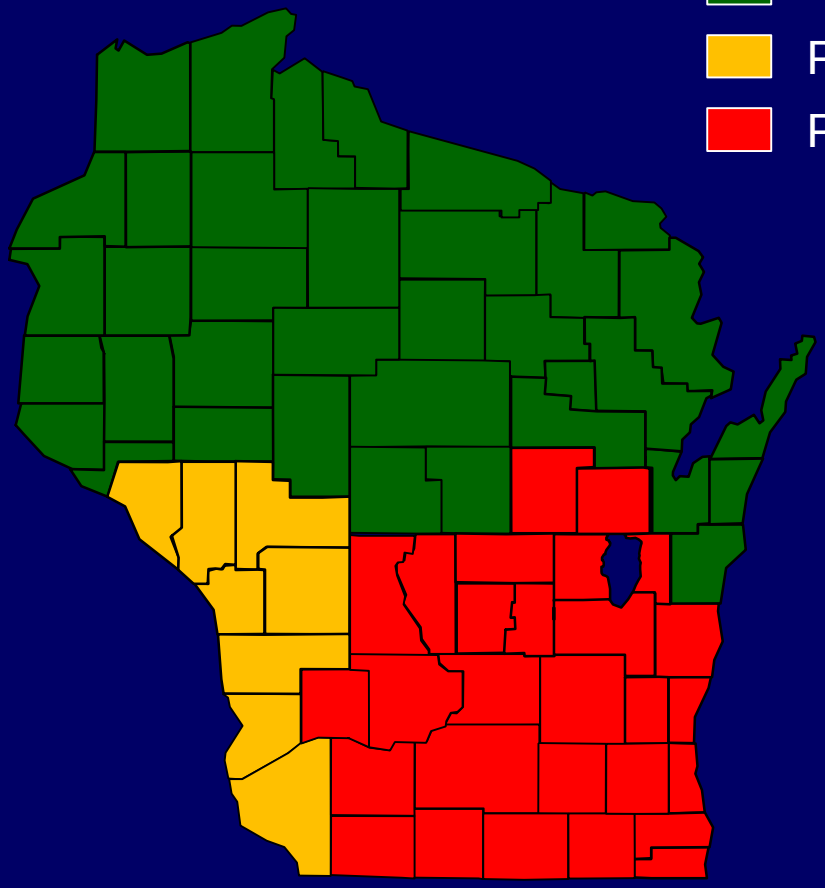
P = 0.04 for susceptibility rate of 20-39 years vs. 60-79 years
P = 0.02 for susceptibility rate of 20-39 years vs. ≥ 80 years

TRIMETHOPRIM-SULFA (1-16)						CLSI breakpoints 2/4
Age	n	MIC_{50}	MIC_{90}	%S	%I	%R
20-39	25	≤ 1	≤ 1	100		0.0
40-59	60	≤ 1	>16	85.0		15.0
60-79	110	≤ 1	>16	77.3		22.7
≥ 80	71	≤ 1	>16	80.3		19.7
Wisconsin		≤ 1	>16	82.4		17.6

P = 0.04 for susceptibility rate of 20-39 years vs. 40-59 years
P = 0.008 for susceptibility rate of 20-39 years vs. 60-79 years
P = 0.02 for susceptibility rate of 20-39 years vs. ≥ 80 years

Gundersen Med. J. **10:** 41-48; 2017

2018 *S. aureus* OBSERVATIONS



- Percentage susceptible 5% or more greater than state mean
- Percentage susceptible ±5% of state mean
- Percentage susceptible 5% or more less than state mean

cefoxitin
state mean 62.3%

CEFOXITIN (2-8)					CLSI breakpoints 4/8
Age	n	MIC_{50}	MIC_{90}	%S	%R
0-19	41	4	>8	63.4	36.6
20-39	54	8	>8	44.4	55.6
40-59	62	4	>8	69.4	30.6
60-79	108	4	>8	68.5	31.5
≥ 80	45	4	>8	57.8	42.2

P = 0.007 for susceptibility rate of 20-39 years vs. 40-59 years
P = 0.003 for susceptibility rate of 20-39 years vs. 60-79 years

Clin. Med. Research in press

A Day in the Life

ACKNOWLEDGMENTS

WCLN STUDY SITES

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