Surveillance of Wisconsin Antibacterial Susceptibility Patterns

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ABSTRACT

Background: Antimicrobial resistance presents a threat to quality patient care. Knowledge of local antibacterial susceptibility patterns can guide clinicians in empiric antibacterial administration and assist pharmacists and infectious disease physicians in development of appropriate therapeutic pathways.

Methods: To characterize Wisconsin antibacterial susceptibility patterns and elucidate geographic or temporal variation in antibacterial resistance, a retrospective, observational analysis of antibiogram data was performed. Seventy-two members of the Wisconsin Clinical Laboratory Network (WCLN) submitted antibiograms describing clinically significant isolates tested in calendar year 2013 to the WCLN Laboratory Technical Advisory Group.

Results: In the context of commonly reported antibacterial agents, data were compiled for approximately 75,800 isolates of *Escherichia coli*; 13,300 *Klebsiella pneumoniae*; 6300 *Proteus mirabilis*; 2800 *Enterobacter cloacae*; 8400 *Pseudomonas aeruginosa*; 30,000 *S aureus*; 11,200 coagulase-negative *Staphylococcus* spp; and 13,800 *Enterococcus* spp. *P mirabilis* isolates from northern Wisconsin were more likely to demonstrate resistance than those in the southern region. In contrast, *P aeruginosa* isolates from southern Wisconsin had decreased susceptibility to a number of agents when compared to other regions. Temporal trending in decreased *E coli* and *P mirabilis* susceptibility to fluoroquinolones and trimethoprim-sulfamethoxazole was observed. Increased methicillin-resistant *Staphylococcus aureus* (MRSA) rates were observed in northwest and southeast Wisconsin. In general, northeast Wisconsin exhibited less frequency of antibacterial resistance.

Conclusions: Geographic variation exists with respect to antibacterial resistance, particularly in areas of Wisconsin adjacent to large population centers of neighboring states. Antibacterial surveillance in Wisconsin is indicated on a regular basis to assess emerging trends in antibacterial resistance. Existing WCLN infrastructure allows for such investigations.

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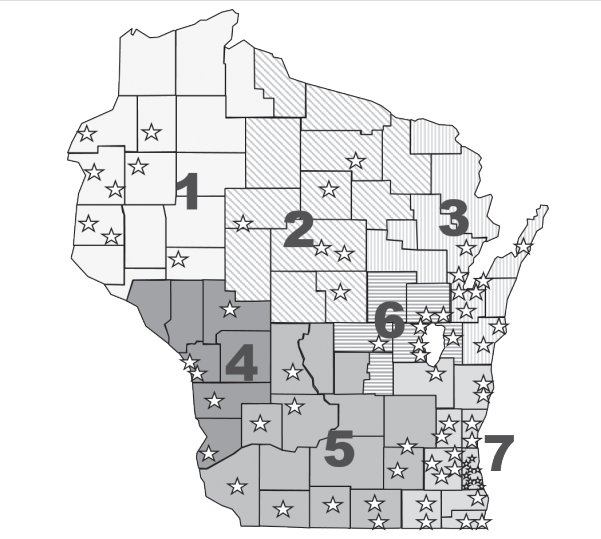
INTRODUCTION

Subsequent to the domestic terrorism events of 2001, the Wisconsin State Laboratory of Hygiene (WSLH) established a network of clinical laboratories throughout the state, known as the Wisconsin Clinical Laboratory Network (WCLN), to ensure a timely and effective response to clinical laboratory and public health needs. The WCLN is arbitrarily subdivided into 7 regions (Figure 1), with 7 clinical laboratory representatives (as well as a number of at-large clinical microbiologists) serving collectively as members of the WCLN Laboratory Technical Advisory Group (LabTAG). The mission of the WCLN has subsequently evolved into updating and training statewide colleagues on novel diagnostic options and actively participating in disease surveillance. Greater than 130 clinical laboratories, including entities without clinical microbiology services, comprise the WCLN.

Hicks et al[1] revealed that upwards of 260 million outpatient courses of antimicrobial agents were prescribed by physicians in 2011, with nearly 25% of these regimens prescribed by family practice clinicians. While the upper Midwest was not targeted as a region that could benefit from enhanced surveillance or intervention strategies with respect to overall prescription practices,[1] the high frequency of outpatient and family practice-based prescribing patterns may potentiate antimicrobial resistance in addition to that potentiated by high acuity-of-illness inpatient settings.[2] As such, surveillance of antibacterial susceptibility patterns

Figure 1. Wisconsin Clinical Laboratory Network (WCLN) Bioterrorism Preparedness Team Regions and Health Care Locations That Supplied 2013 Antibiogram Data for Antibacterial Susceptibility Surveillance



Numbers = WCLN Bioterrorism Preparedness Team Regions
Stars = Health care locations

Table 1. Regional Population Distribution and Rates of *E coli* and *S aureus* Isolate Contribution

Region	Population (2010 Census)	Reported Isolates/ 100,000 population	
		E coli	S aureus
1	565,926	1054	433
2	469,647	2655	1077
3	507,821	1641	729
4	268,520	2394	950
5	1,149,375	927	320
6	489,263	1628	611
7	2,237,110	1072	472

Shows Wisconsin Clinical Laboratory Network (WCLN) Biopreparedness Team Region population distribution and rates of *E coli* and S *aureus* isolate contribution per 100,000 population to cumulative WCLN antibacterial susceptibility surveillance.

at a statewide level, both in higher- and lower-density population settings, can be important for clinician-initiated empiric therapy, development of clinical pharmacy therapeutic recommendations, and selection of antibacterial susceptibility testing formats by the clinical microbiology laboratory. To this end, this report documents a local, data-driven antibacterial susceptibility surveillance project with the goal of generating a statewide Wisconsin antibiogram.

MATERIALS AND METHODS

Request for Antibiogram Data

During December 2014, LabTAG members extended invitations to clinical laboratories within respective Bioterrorism Preparedness Team Regions (subsequently referred to as "region") for hospital-specific antibiogram data. Tertiary and university-based clinical entities were excluded from participation, as a portion of their patient population may reside in locales outside of the respective region. Data were requested from clinically significant isolates recovered in calendar year 2013. To determine potential temporal changes in antibacterial susceptibility patterns, sites were requested to provide data, if available, from clinically significant isolates analyzed in 2009 and 2005. However, these data were excluded from analysis if the submitting entities were unable to provide 2013 antibiogram data.

Selection of Organisms for Analysis

Seventy-two entities submitted antibiograms from 2013 for consideration (Figure 1). Clinical and Laboratory Standards Institute (CLSI) states that an organism with an n value of ≥ 30 is optimal for annual antibiogram inclusion.[3] Furthermore, multiple single species isolates from the same patient are excluded from individual antibiogram inclusion. With respect to this study, a given Gram-negative bacillus meeting these criteria was reported on 6% to 100% of submitted antibiograms. *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* were reported on ≥ 50% of all submitted antibiograms and were considered for further data analysis. With the exception of *E cloacae*, the aforementioned organisms were reported on ≥ 57% of antibiograms submitted from a given region.

With respect to Gram-positive cocci, increased variation was observed in antibiogram reporting. For purposes of antibiogram generation, 63% of healthcare entities categorized *Staphylococcus aureus* as methicillin-resistant *S aureus* (MRSA) and methicillin-susceptible *S aureus* (MSSA). Therefore, all antimicrobial-specific susceptibility data for MRSA and MSSA were combined and reported as *S aureus* for the surveillance project. In analogous fashion, all permutations of non-*S aureus* species (including agents such as *S epidermidis, S saprophyticus, S lugdunensis, S warneri*, and the generic classification of coagulase-negative *Staphylococcus* spp) were combined and reported as coagulase-negative *Staphylococcus* spp. Finally, as only 50% of entities throughout Wisconsin identified enterococci to the species level, data specific to *Enterococcus faecalis, E faecium, E casseliflavus,* and *E gallinarum* were combined as *Enterococcus* spp.

Selection of Antibacterial Agents for Analysis

Thirteen antibacterials were reported on ≥ 75% of submitted Gram-negative bacilli antibiograms and were included in the final statewide compilation. Represented (sub)classes included fluoroquinolone, penicillin, β-lactam/β-lactamase inhibitor combination, cephem, aminoglycoside, nitrofuran, and folate pathway inhibitor. Within a given region, these 13 antibacterials were reported on ≥ 52% of antibiograms (data not illustrated). Two exceptions to this generalization were reporting of ceftazidime and tobramycin in region 4 (each on 40% of antibiograms). Imipenem, reported on 65% of submitted antibiograms through-

Table 2. 2013 Wisconsin Gram-negative Bacilli Antibacterial Susceptibility Surveillance

	Percentage Susceptible				
	Escherichia coli (max n 75,804)	*Klebsiella pneumoniae* (max n 13,360)	*Proteus mirabilis* (max n 6375)	*Enterobacter cloacae* (max n 2831)	*Pseudomonas aeruginosa* (max n 8493)
Gentamicin	94	99	93	99	87
Tobramycin	95	99	93	99	96
Levofloxacin	82	98	81	97	77
Ciprofloxacin	82	98	77	97	79
Ampicillin	61		83		
Ampicillin-sulbactam	68	89	91		
Piperacillin-tazobactam	97	97	99	87	93
Cefazolin	90	96	89		
Ceftriaxone	97	98	97	84	
Ceftazidime	97	98	96	86	90
Cefepime	98	98	98	98	82
Imipenem	99	99		98	87
Trimethoprim-sulfamethoxazole	81	94	83	92	
Nitrofurantoin	94	37		28	

out the state, also was included on the final compilation to sample carbapenem activity against selected Enterobacteriaceae and *P aeruginosa*.

Ten antibacterials (representing penicillin, fluoroquinolone, folate pathway inhibitor, tetracycline, macrolide, aminoglycoside, lincosamide, nitrofuran, and glycopeptide [sub]classes) were reported on ≥73% of submitted Gram-positive cocci antibiograms and included in the compilation. On a given region basis, these 10 antibacterials were reported on ≥56% of antibiograms. One exception to this generalization was reporting of gentamicin in region 2 (33% of antibiograms). Data from ampicillin, reported as a first-line agent against *Enterococcus* spp by 46% of entities, also were included on a limited basis.

Table 3. 2013 Wisconsin Gram-positive Cocci Antibacterial Susceptibility Surveillance

	Percentage Susceptible		
	Staphylococcus aureus (max n 30,982)	*coagulase-negative Staphylococcus* (max n 11,299)	*Enterococcus spp* (max n 13,893)
Penicillin	12	10	89
Ampicillin			93
Methicillin	62	49	
Levofloxacin	65	60	66
Gentamicin	98	90	
Erythromycin	47	39	
Clindamycin	72	63	
Nitrofurantoin	99	99	93
Trimethoprim-sulfamethoxazole	98	66	
Tetracycline	94	85	
Vancomycin	99	99	93

Analysis

Mean percentage susceptibility data were calculated for given organism/antibacterial combinations solely on the basis of all percentage susceptible data submitted from a region, irrespective of n values. The significance test of proportions determined whether region-specific variances in Gram-negative bacilli and Gram-positive cocci antibacterial surveillance from 2009 to 2013 were significant. The alpha level was set at 0.05 before the investigations commenced and all *P* values are 2-tailed.

RESULTS

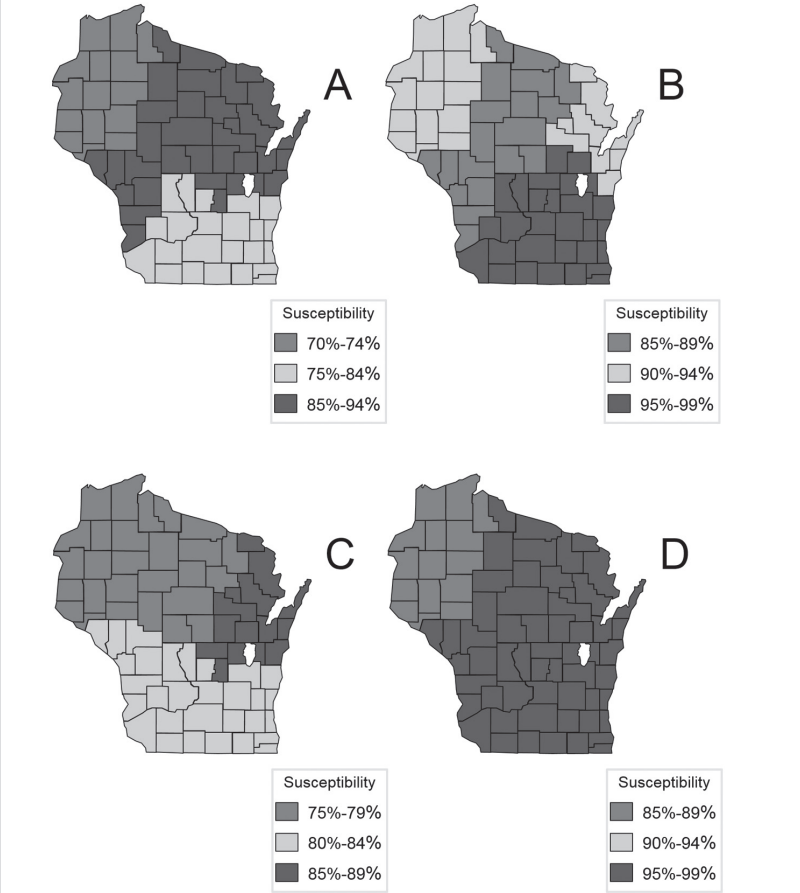
Representation Across Regions

To assess bias potential toward large population regions, frequency of *E coli* and *S aureus* antibiogram reporting per 100,000 population was calculated for each region on the basis of 2010 US Census data. Five of 7 regions contributed 927 to 1641 reports of *E coli*-specific data per 100,000 population, including region 7 (Table 1). Regions 2 and 4 contributed 2655 and 2394 *E coli* isolates per 100,000 population, respectively, to this project. In similar fashion, 320 to 729 isolates of *S aureus* per 100,000 population were submitted from 5 of 7 regions. Regions 2 and 4 submitted data from 1077 and 950 *S aureus* isolates per 100,000 population, respectively.

Wisconsin Gram-negative Bacilli Antibacterial Surveillance, 2013

Susceptibility data from 75,804 isolates of *E coli* were compiled (Table 2). Noteworthy findings included susceptibility rates of 61% to ampicillin, 68% to ampicillin-sulbactam, and 94% to nitrofurantoin. Susceptibility rates compiled from 13,360 *K pneumoniae* revealed increased susceptibility rates to fluoroquinolone agents (levofloxacin, ciprofloxacin) and trimethoprim-sulfamethoxazole when compared to commonly encountered enteric Gram-negative bacilli such as *E coli* and *P mirabilis*. *In vitro* activity of ampicillin and ampicillin-sulbactam against 6375 isolates of

Figure 2. Geographic Variation in *P mirabilis* Susceptibility to Ampicillin (A), Tobramycin (B), Trimethoprim-Sulfamethoxazole (C), and Third- and Fourth-Generation Cephems (D), Wisconsin 2013



P mirabilis was increased over that observed in *E coli*. Analysis of 2831 isolates of *E cloacae* revealed increased rates of cefepime susceptibility when compared to ceftriaxone and ceftazidime. On a statewide basis, piperacillin-tazobactam and tobramycin exhibited best *in vitro* activity against a compilation of 8493 *P aeruginosa* isolates. Susceptibility rates to fluoroquinolone agents were generally lower than aminoglycosides (gentamicin, tobramycin).

Wisconsin Gram-positive Cocci Antibacterial Surveillance, 2013

Susceptibility data from 30,982 isolates of *S aureus* revealed a statewide MRSA rate of 38% (Table 3). Data also revealed high rates of *S aureus* susceptibility to trimethoprim-sulfamethoxazole and tetracycline, as well as a 99% susceptibility rate to nitrofurantoin in a subset of 18,467 isolates. Decreased *S aureus* susceptibility to levofloxacin (65%), erythromycin (47%), and clindamycin (72%) also was noted. In contrast to *S aureus*, 11,299 isolates of coagulase-negative *Staphylococcus* spp demonstrated less *in vitro* activity against trimethoprim-sulfamethoxazole and tetracycline. Statewide resistance of 13,893 isolates of *Enterococcus* spp to vancomycin was 7% in 2013 (Table 3). Susceptibility rates of subsets of 8456 isolates to penicillin and 8678 isolates to ampicillin were 89% and 93%, respectively.

Regional Differences in Antibacterial Susceptibility Profiles

A dichotomy of geographic resistance patterns was noted for *P mirabilis* and *P aeruginosa*. Decreased rates of *P mirabilis* susceptibility to ampicillin (Figure 2A), tobramycin (Figure 2B), trimethoprim-sulfamethoxazole (Figure 2C), and third-/fourth-generation cephems (Figure 2D) were observed particularly in regions 1 and/or 2. Analogous susceptibility rates were generally higher in regions 5-7, as well as region 3. In contrast, decreased susceptibility of *P aeruginosa* to piperacillin-tazobactam (Figure 3A), ceftazidime/cefepime (Figure 3B), gentamicin (Figure 3C), and ciprofloxacin (Figure 3D) was particularly noted in region 7 and, in some instances, observed in regions 3, 5, and/or 6. Northern regions of the state exhibited increased susceptibility of *P aeruginosa* to these agents.

Finally, distribution of clinically significant MRSA mirrored pockets of increased resistance in Wisconsin. Regions 1 and 7 exhibited MRSA rates of 44% and 40%, respectively, in 2013. Other regions demonstrated reduced rates, including region 3 with a rate of 27% (Figure 4A). Similarly, a significant focus of vancomycin-resistant *Enterococcus* spp was observed within region 7 (Figure 4B).

Temporal Differences in Antibacterial Susceptibility Profiles

Fifty-six of the 72 clinical entities supplying antibiogram data for 2013 provided analogous data from 2009. When comparing Gram-negative bacilli and Gram-positive cocci surveillance compilations from the 2 years at the regional level, variances of ≥5% were observed for 14.9% and 29.7% of organism/antibacterial combinations, respectively ($P < 0.0002$; Table 4).

The vast majority of instances of reduced susceptibility in 2013 profiling was observed with Gram-negative bacilli ($P < 0.0002$ versus reduced susceptibility in Gram-positive cocci). Nineteen of the 43 instances of decreased Gram-negative bacillus susceptibility were noted in *P mirabilis*. Evidence existed for the emergence of *P mirabilis* with reduced susceptibility to ciprofloxacin in regions 1 and 3 in 2013 when compared to 2009 (Table 5). A second temporal paradigm of interest is *E coli* suscepti-

bility to levofloxacin. While regions other than region 3 experienced a reduction in susceptibility from 2009 to 2013, modest improvement actually was documented in region 7.

In contrast to Gram-negative bacilli antimicrobial surveillance of 2009-2013, substantial variances in 2013 Gram-positive cocci surveillance were characterized by increased susceptibility (Table 4). Thirty-four of 40 such improvements were noted in staphylococci. In 2009, the MRSA rate reported from clinically significant isolates in region 2 was 35%. This rate ranged from 40% to 49% in the other six regions. By 2013, region 2 reported an MRSA rate of 38%, while analogous rates in four other regions demonstrated improvement, including a decline from 40% to 27% in region 3. In addition, region 7 experienced a decrease in MRSA rate from 49% to 40% (Table 5).

DISCUSSION

Limitations exist with respect to this format of surveillance. It must be assumed that laboratories are utilizing either commercial antibacterial susceptibility testing formats cleared by the Food and Drug Administration (processed per package insert guidelines) or assays that have undergone rigorous laboratory self-verification. Furthermore, it must be assumed that laboratories are assessing clinically significant isolates[4] using guidance provided by agencies such as CLSI[5-7] or the European Committee on Antimicrobial Susceptibility Testing (www.eucast.org). Moreover, on the basis of factors such as local clinician antimicrobial preference, pharmacy purchasing agreements, and commercial susceptibility testing vendor panel formats, a number of antibacterials were not common to all submitted antibiograms. In response, we used a majority approach for a given antibacterial to be considered for compilation. As a result, fewer antibacterials were included in the final compilation.

The antibiogram approach to monitor-

Figure 3. Geographic Variation in *P aeruginosa* Susceptibility to Piperacillin-Tazobactam (A), Antipseudomonad Cephems (B), Gentamicin (C), and Ciprofloxacin (D), Wisconsin 2013

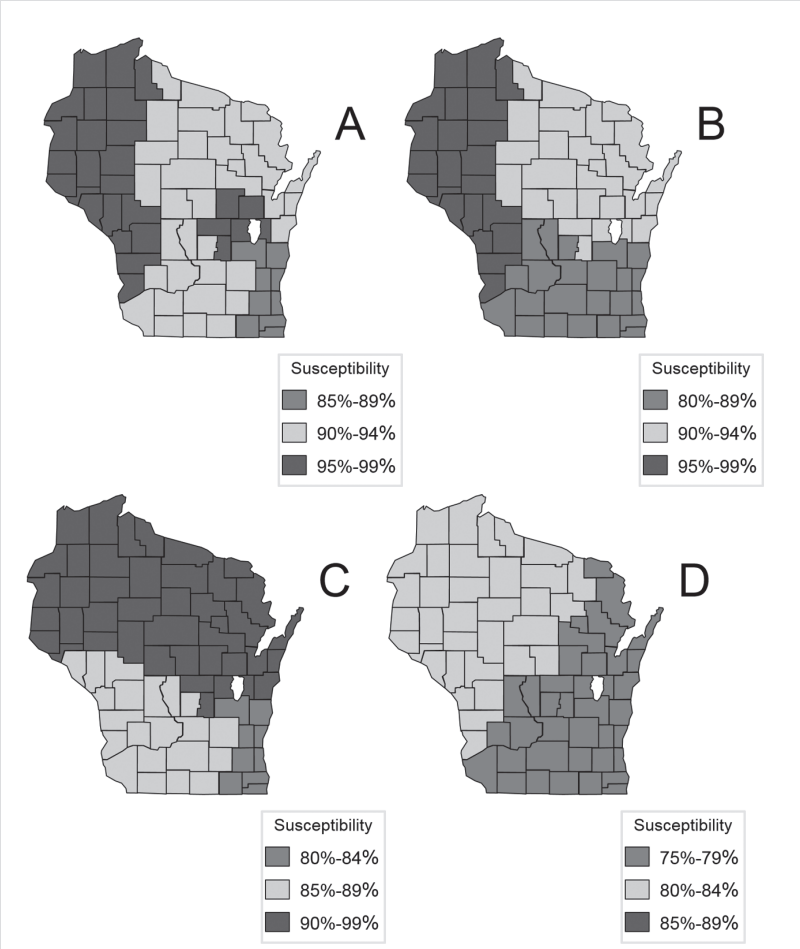


Figure 4. Geographic Variation in Distribution of Methicillin-Resistant *Staphylococcus aureus* (A) and Vancomycin-Resistant *Enterococcus* spp (B) Isolates, Wisconsin 2013

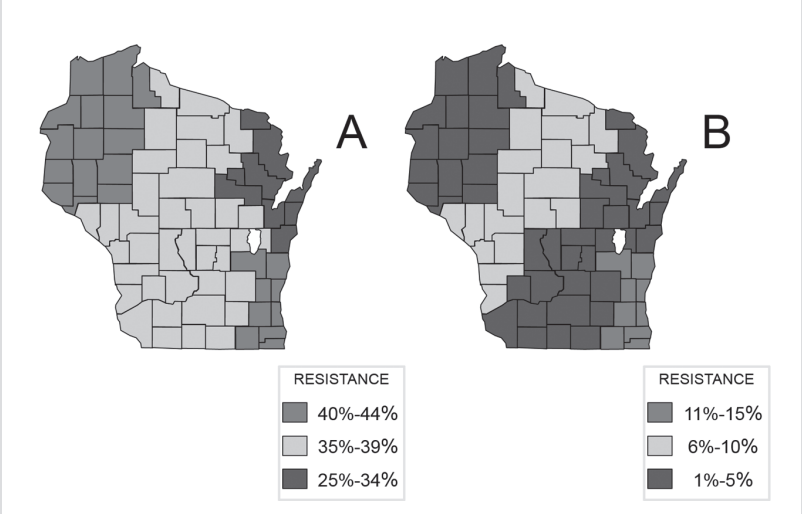


Table 4. Summary of Significant, Region-specific Variances in Gram-negative Bacilli and Gram-positive Cocci Antibacterial Susceptibility Surveillance, Wisconsin 2009-2013

Antibacterial Surveillance	Number of Organism/ Antibacterial Observations	Number of Variances[a] ≥ 5%	Number of Variances ≥ 5%	
			Reflective of Increased Susceptibility	Reflective of Decreased Susceptibility
Gram-negative bacilli	382	57 (14.9)[b]	14 (24.6)[c]	43 (75.4)[c]
Gram-positive cocci	175	52 (29.7)[b]	40 (76.9)[c]	12 (23.1)[c]

[a] Data from year 2009 used as a baseline in determination of variance.
[b] Value in parentheses represents percentage of organism/antibacterial observations.
[c] Value in parentheses represents percentage of variances ≥ 5%.

Table 5. Selected Instances of Region-Specific Temporal Changes in *E coli, P mirabilis*, and *S aureus* Antibacterial Susceptibility, Wisconsin 2005-2013

Organism	Antimicrobial	Location	Percentage Susceptible by Year 2005	2009	2013
E coli	levofloxacin	Region 1	91	80	81
		Region 3	92	85	86
		Region 7	85	78	81
		Wisconsin	90	83	82
P mirabilis	ciprofloxacin	Region 1	89	79	66
		Region 3	91	90	82
		Region 7	84	76	77
		Wisconsin	88	82	77
	trimethoprim-sulfamethoxazole	Region 1	84	84	77
		Region 3	95	91	86
		Region 7	88	82	83
		Wisconsin	89	84	83
S aureus	methicillin	Region 1	71	55	56
		Region 3	55	60	73
		Region 7	48	51	60
		Wisconsin	57	56	62

ing emerging resistance may be impacted by additional factors. The end point of the antibiogram, percentage susceptibility, does not specifically relate frank resistance or increases in rates of intermediate resistance. In certain cases, monitoring of changing minimum inhibitory concentrations for a given organism/antimicrobial combination can detect local increases in the rate of resistance before such changes can be observed in an antibiogram.[8] Antibiograms also have an inability to track emergence of resistance during a course of therapy.[9] In addition, antibacterial susceptibility testing practices can impact final antibiogram data by way of selective reporting.[10]

Another mitigating factor relates to preparation of the document itself. Individual antibiograms may be subject to deficiencies such as inclusion of duplicate isolates, reporting of misleading organism/antimicrobial combinations, insufficient n values, lack of yearly updating, and reporting of inappropriate data, such as organisms that are inherently resistant to a given antibacterial.[11-13] As one example in our 2013 compilation, the susceptibility rate of Wisconsin *S aureus* isolates to vancomycin was 99%. Due to the nature of the surveillance, we were unable to confirm true vancomycin resistance or intermediate susceptibility within this ~1% of staphylococci. A preliminary finding of vancomycin-resistant *S aureus* requires infection control notification and referral of the isolate to a public health laboratory for confirmation.[5]

To circumvent one issue relative to antibiograms from smaller facilities, only organisms with an n ≥ 30 were included in compilations. Unfortunately, as a result of this practice, data from several significant pathogens were excluded. In 2013, *Streptococcus pneumoniae* data were reported on only 32 antibiograms (44% of submitted antibiograms). Statewide *S pneumoniae* susceptibility to penicillin was 71% from 1228 isolates—largely unchanged from the 72% value reported from 1242 isolates (28 antibiograms) in 2009 (data not illustrated). *S pneumoniae* susceptibility to levofloxacin in 2013 (27 antibiograms; 840 isolates) was 98% and largely unchanged from the 99% value derived in 2009 from limited assessment of 826 isolates. With respect to chemoprophylaxis of penicillin-allergic pregnant females for beta-hemolytic *Streptococcus* group B colonization,[14] CLSI standards specify performance of both erythromycin and clindamycin susceptibility testing (with inclusion of inducible clindamycin resistance assessment), but routine reporting of only clindamycin data.[5-7] In 2013, only 21 submitted antibiograms (29% of all antibiograms) reported *Streptococcus agalactiae* susceptibility to clindamycin. The limited dataset (1801 isolates) revealed a 42% susceptibility rate—a decrease from the 71% value compiled from 15 antibiograms submitted from 2009 (868 isolates). Clearly this is an organism/antibacterial combination that requires future surveillance.

As a result of such limitations, use of the term "state antibiogram" to describe the end product of this project is not justified; "antibacterial surveillance" is more appropriate. One could further posit that the best means of performing statewide antimicrobial surveillance would be akin to surveillance programs such as CAPITAL, SENTRY, and SMART,[15-17] by which a centralized testing laboratory uses a standardized means of testing isolates sent from a number of geographic locales. Conversely, Halstead

et al[18] illustrated the value of a metropolitan antibiogram that was a compilation of 10 local antibiograms. In one instance, a 13% difference in rate of *S pneumoniae* susceptibility to penicillin was noted in the compilation when compared to a multistate summary. Moreover, Fridkin et al[19] stated that hospital antibiograms also were reflective of susceptibility patterns associated with health care-acquired infections.

Multiple health care entities within each region participated in this project. This removed bias inherent to large entities within a region and resulted in random distribution of sites within regions (Figure 1). One exception to this concept was the lack of sites (including nontertiary care facilities) within Dane County of region 5. When contemplating this uneven distribution, one must remember that participation was voluntary. Furthermore, university-based and tertiary care facilities were excluded from analysis because the study design sought to assess resistance rates as a function of geography. It was inferred that patients residing in multiple and perhaps distant regions comprised a substantial proportion of patient population at tertiary care facilities. The voluntary nature of participation in this project may provide explanation for the potential overrepresentation of less populous regions 2 and 4 in this surveillance project (Table 1).

An example of where benefits of antimicrobial stewardship programs may already be evident in some areas of Wisconsin is with respect to levofloxacin and *E coli* (Table 5). While a number of regions saw a reduction in susceptibility with this combination from 2009 to 2013, the region 7 susceptibility rate improved. When this paradigm was extended to a limited focal surveillance involving 48 antibiograms in 2005 (42,551 isolates), one can observe a trend of increasing *E coli* resistance to levofloxacin statewide and in regions 1 and 3 (Table 5). However, the trend of decreased susceptibility appears to have stabilized in region 7. Limited surveillance of *P mirabilis* beginning in 2005 (4424 isolates statewide) uncovered a secondary wave of resistance. Susceptibility rates to ciprofloxacin and trimethoprim-sulfamethoxazole decreased statewide and in regions 1 and 3 between 2005 and 2013, while region 7 susceptibility rates stabilized between 2009 and 2013. Finally, the 2005 statewide MRSA rate for 21,865 isolates was 43%. While this value decreased over the following 8 years statewide, including regions 3 and 7 (Table 5) an MRSA rate increase was experienced in region 1.

CONCLUSION

Despite limitations to antibiogram development and construction, statewide antibiogram compilation provides both an acceptable glimpse of antibacterial susceptibility patterns and a baseline for temporal comparisons. Our current investigation implicates *E coli*, *P mirabilis*, MRSA, fluoroquinolone agents, and trimethoprim-sulfamethoxazole as major factors in geographic and temporal variation of antibacterial susceptibility throughout Wisconsin. Complete datasets from the 2009 and 2013 components of this statewide antibacterial surveillance project are posted to the WSLH web portal: www.slh.wisc.edu/wcln-surveillance/wcln/wcln-resources/. In the future, the WCLN possesses sufficient infrastructure to allow for additional surveillance efforts to monitor changes in resistance patterns or to justify regional antimicrobial stewardship efforts.

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