Surveillance of Wisconsin Organisms for Trends in Antimicrobial Resistance and Epidemiology (SWOTARE): epidemiologic correlates for 2016 surveillance isolates

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Surveillance of Wisconsin Organisms for Trends in Antimicrobial Resistance and Epidemiology (SWOTARE): epidemiologic correlates for 2016 surveillance isolates

ABSTRACT

Background: The Centers for Disease Control and Prevention advocate data collection and monitoring as one facet of a comprehensive approach to combat antimicrobial resistance in the United States. However, a paucity of such data exists at the local/state level for common disease-causing organisms.

Methods: To begin to characterize epidemiologic correlates of antibacterial resistance in Wisconsin, data analyses were performed with respect to isolates in the Surveillance of Wisconsin Organisms for Trends in Antimicrobial Resistance and Epidemiology (SWOTARE) 2016 collection. In addition to submitting isolates of Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, and Streptococcus pneumoniae, participating laboratories were also requested to submit data regarding patient age, specimen source, and location of patient service.

Results: Fifty-five percent of isolates were of outpatient origin (including emergency department). In general, isolates derived from inpatients were more likely to demonstrate higher resistance rates than those from outpatient locations. Upon further stratification, isolates from emergency department encounters generally exhibited higher susceptibility rates than those from outpatient clinics. Sixty-seven percent of isolates emanated from skin and soft tissue or invasive sites. Delineation of specimen source played a minimal role in prediction of antimicrobial resistance. Older patients were more likely to generate isolates of E coli and P mirabilis exhibiting resistance to agents such as fluoroquinolones and trimethoprim-sulfamethoxazole.

Conclusions: SWOTARE facilitates epidemiologic investigations into resistance at the local/state level. Investigations are warranted to further delineate differences in isolates derived from emergency department and outpatient clinic visits. Characterizations at the demographic level could impact local empiric treatment guidelines and antimicrobial stewardship throughout Wisconsin.

The Centers for Disease Control and Prevention (CDC) have recently identified 17 groupings of bacterial and fungal organisms collectively responsible for at least two million annual illnesses and 23 000 deaths on the basis of antimicrobial resistance. CDC has additionally advocated a 4 faceted approach to address the paradigm of national antimicrobial resistance, 1 of which involves timely surveillance for the emergence of novel and unique patterns of resistance. The value of such surveillance efforts has been championed by pioneers in the field.

We have described implementation of the Surveillance of Wisconsin Organisms for Trends in Antimicrobial Resistance and Epidemiology (SWOTARE) program. In summary, a centralized microbiology laboratory assesses representative bacterial isolates using a standardized antimicrobial susceptibility testing method. These isolates are submitted by 22 clinical laboratories with widespread distribution throughout Wisconsin. With such infrastructure, we currently have capability of monitoring 3 of the CDC-targeted organism groups. Two of these, multidrug-resistant Pseudomonas aeruginosa and drug-resistant Streptococcus pneumoniae, are responsible for 51 000 healthcare-associated infections and 4 million general infections, respectively, on an annual basis. These infections further translate into resistance rates approximating 13% to 30%, with annual deaths attributable to resistant strains estimated at 440 (P aeruginosa) and 7000 (S pneumoniae). Furthermore, collected Escherichia coli can be monitored for evidence of carbapenemase and extended-spectrum β-lactamase (ESBL) production. It is estimated that these resistance mechanisms are responsible for greater than 10 000 healthcare-associated infections in the United States annually, with approximately 700 attributable deaths.

An additional component of the SWOTARE program involves submission of isolate-specific epidemiologic data from participating clinical laboratories. Such data may not be readily available in the course of surveillance endeavors strictly involving analysis of antibiotic data. Moreover, as part of the CDC-advocated surveillance approach, it is recommended that data be collected with respect to risk factors for antimicrobial resistance. This report provides introductory information relative to the epidemiology of antimicrobial resistance in Wisconsin, as generated by the 2016 SWOTARE collection.

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The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.
METHODS

SWOTARE Program

Establishment of the SWOTARE surveillance network, along with isolate submission and susceptibility testing protocols/interpretation, has been described. In summary, clinical microbiology laboratories in Ashland, Spooner, St. Croix Falls, and Eau Claire (northwest region); Marshfield, Weston, and Stevens Point (northcentral region); Manitowoc, Sturgeon Bay, and Green Bay (northeast region); Platteville, Prairie du Chien, Viroqua, and La Crosse (southwest region); Fort Atkinson, Janesville, and Madison (southcentral region); Fond du Lac, Neenah, and Appleton (Lake Winnebago region); and, West Bend and Milwaukee (southeast region) participated in the program.

Isolates and Demographic Data

Study sites were requested to collect consecutive isolates of E. coli, Proteus mirabilis, P. aeruginosa, and S. pneumoniae identified from in-house culture of clinically significant infection. Laboratories were further requested to supply limited patient demographic information, including age, sex, anatomic source, patient service location, and whether the healthcare encounter involved an intensive care unit stay. Access to protected health information for the purpose of the investigation was granted by the Marquette University Institutional Review Board. Because of the lack of direct involvement in the collection of specimens and because of the utilization of de-identified isolates from routine clinical care, the Review Board did not consider the SWOTARE program to be actively engaged in human subjects research.

Data Analysis

Genus-specific percentage susceptible, intermediate (susceptible-dose dependent for cefepime and Enterobacteriaceae combinations), and resistant values, as well as minimum inhibitory concentration (MIC) determinations (MIC₅₀ and MIC₉₀) were generated. Such analyses were applied to statewide isolates as a whole, in addition to characterizations on the basis of patient healthcare encounter location, specimen source, and patient age. Only patient service location, specimen source, and age delineations with n ≥ 25 were utilized for comparisons. The significance test of proportions determined if differences in susceptibility percentage were significant. The α level was set at .05 before the investigations commenced, and all P values are 2-tailed.

RESULTS AND EPIDEMIOLOGIC DISCUSSION

Patient Demographics and Isolate Distribution by Patient Location

One thousand eighty isolates were submitted to the program and tested in 2016. Of this total, complete demographic data were provided for 1055 (97.7%) isolates. Five hundred sixty-one (53.2%) isolates were derived from women. Mean patient age was 62.5 years, with a median of 66. Six general patient service categories (Figure 1) accounted for 94.8% of all patient isolates. As a result of the inclusion of data from long-term care facilities as inpatient data, the percentage composition of inpatient isolates was 45.4%, the largest component of which was internal medicine (25.6% of all isolates). Outpatient data consisted of outpatient clinic–derived isolates (30.0% of all isolates) and those collected from emergency departments (24.6% of all isolates).

Isolate Distribution by Specimen Source

Greater than two-thirds of specimens submitted to the SWOTARE program in 2016 were of skin and soft tissue or invasive origin (Figure 2). Invasive isolates included those derived from blood (354 isolates), cerebrospinal fluid (4), paracentesis fluid (1), hardware (1), bone (1) and bile (1). Sixteen percent of isolates were derived from urogenital (172 urine, 1 Bartholin cyst) sources. Distribution of lower respiratory tract isolates (12.6% of all isolates) included sputum (111), bronchoalveolar lavage (8), endotracheal aspiration (7), bronchial washings (6), thoracentesis fluid (3), and pleural fluid (1). Upper respiratory tract isolates included those derived from ear (18 isolates), nose (9), throat (8), eye (7), and sinus (4) specimens.

Profile by Patient Location

We compared differences in susceptibility rates for antimicrobial/organism combinations as a function of patient care location from which the isolate was derived. Table 1A demonstrates one example of inpatient isolates exhibiting an increased antimicrobial
resistance profile over that of outpatient isolates. This inpatient *P mirabilis* profile is characterized by a decreased levofloxacin percentage susceptible value, as well as an elevated MIC₉₀ value. Further subcategorization of this antimicrobial/organism paradigm is represented in Table 1B. The frank resistance rates and increased MIC₉₀ values within this profile, as well as a majority of other antimicrobial/organism profiles (data not illustrated), justify inclusion of long-term care facilities with inpatient data.

Initial insight into differences in susceptibility between isolates derived from emergency department visits (95.6% susceptibility) and those from internal medicine and outpatient clinic encounters (67.2% and 86.2%, respectively) was also observed.

On the basis of achieved n values, subsequent analysis was restricted to internal medicine, emergency department, and outpatient clinics. Greater than 61% of individual *E coli*, *P mirabilis*, *P aeruginosa*, and *S pneumoniae*/antimicrobial combinations revealed susceptibility rates that differed by less than 10% between the 3 healthcare locations (data not illustrated). Noteworthy exceptions included a cefazolin susceptibility difference of 16.1% between emergency department and internal medicine *E coli* isolates and a penicillin susceptibility difference of 22.1% between emergency department and internal medicine *S pneumoniae* isolates.

The potential influence of patient service location on empiric regimen choice is demonstrated in Table 2. For each of the 4 organisms investigated in the surveillance program, a higher proportion of antimicrobials demonstrated greater *in vitro* potency on emergency department–derived isolates when compared with outpatient clinic- and internal medicine–derived isolates. This dichotomy was especially noted with *S pneumoniae*, as 92.3% of antimicrobial/emergency department–derived isolate combinations demonstrated most *in vitro* potency when compared with internal medicine- and outpatient clinic–derived isolates (7.7% and 0%, respectively).

Studies attempting to associate increased antimicrobial resistance with patient service location have often been performed in the context of urinary tract infection. In general, healthcare-
associated urinary tract pathogens possess increased resistance rates when compared with community-acquired agents of urinary tract infection (particularly with respect to E coli resistance to fluoroquinolone agents). Examples of such data emanate from large study collections in international centers that are derived from antibiogram data from surveillance programs. From a 4-year Swiss antibiogram study, Lamoth et al reported that community-acquired strains of E coli and P aeruginosa (irrespective of specimen source) demonstrated higher susceptibility rates when compared to hospital-acquired strains. With respect to P aeruginosa, this group further implied that differences in ciprofloxacin and ceftazidime susceptibility were a function of specific inpatient unit.

Additional investigations have focused on emergency department populations. Zatorski et al compared E coli antibiograms from non-intensive care unit inpatient urine cultures with those derived from emergency department patients and found increased ceftriaxone and ciprofloxacin susceptibility rates in the latter demographic. Draper et al used an antibiogram approach to determine that emergency department–derived E coli isolates (regardless of specimen source) demonstrated increased susceptibility rates to ampicillin, levofloxacin, and trimethoprim-sulfamethoxazole when compared with hospital-wide isolates. A similar paradigm was observed with P aeruginosa and aztreonam.

Profile by Specimen Source
Differences in susceptibility rates were also compared on basis of specimen source. With respect to each organism, source-specific n values allowed comparisons among 3 specimen sources. Greater

Table 3. Frequency of Percentage Susceptibility Value Differences for Combinations of Organisms and Antimicrobial Agents Compared by Top 3 Specimen Sources, Wisconsin 2016

<table>
<thead>
<tr>
<th>Organism</th>
<th>Maximum Percentage-Susceptible Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Escherichia coli b</td>
<td>38.9</td>
</tr>
<tr>
<td>Proteus mirabilis c</td>
<td>72.2</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa d</td>
<td>55.6</td>
</tr>
<tr>
<td>Streptococcus pneumoniae e</td>
<td>33.3</td>
</tr>
</tbody>
</table>

* Individual specimen source (skin and soft tissue, invasive, urogenital, lower respiratory, upper respiratory) required 25 isolates to qualify for this analysis.
  * Top 3 specimen sources were invasive, skin and soft tissue, and urogenital.
  * Top 3 specimen sources were skin and soft tissue, urogenital, and invasive.
  * Top 3 specimen sources were skin and soft tissue, invasive, and lower respiratory.
  * Top 3 specimen sources were invasive, lower respiratory, and upper respiratory.

Table 4. MIC50 and MIC90 Distributions and Categorical Interpretations of Escherichia coli Isolate Susceptibility to A: Levofloxacin, and B: Trimethoprim-Sulfamethoxazole by Age, Wisconsin 2016

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC50</th>
<th>MIC90</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>40</td>
<td>≤0.25</td>
<td>0.5</td>
<td>92.5</td>
<td>0.0</td>
<td>7.5</td>
</tr>
<tr>
<td>40-59</td>
<td>68</td>
<td>≤0.25</td>
<td>16</td>
<td>80.9</td>
<td>0.0</td>
<td>19.1</td>
</tr>
<tr>
<td>60-79</td>
<td>159</td>
<td>≤0.25</td>
<td>32</td>
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<td>0.0</td>
<td>25.2</td>
</tr>
<tr>
<td>≥80</td>
<td>90</td>
<td>≤0.25</td>
<td>16</td>
<td>78.9</td>
<td>0.0</td>
<td>21.1</td>
</tr>
</tbody>
</table>

P = .02 for susceptibility rate of 20-39 years versus 60-79 years.
P = .06 for susceptibility rate of 20-39 years versus ≥80 years.

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC50</th>
<th>MIC90</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>40</td>
<td>≤1</td>
<td>&gt;16</td>
<td>82.5</td>
<td>17.5</td>
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</tr>
<tr>
<td>40-59</td>
<td>68</td>
<td>≤1</td>
<td>&gt;16</td>
<td>85.3</td>
<td>14.7</td>
<td>10.0</td>
</tr>
<tr>
<td>60-79</td>
<td>159</td>
<td>≤1</td>
<td>&gt;16</td>
<td>80.5</td>
<td>19.5</td>
<td>10.0</td>
</tr>
<tr>
<td>≥80</td>
<td>90</td>
<td>≤1</td>
<td>&gt;16</td>
<td>77.8</td>
<td>22.2</td>
<td>10.0</td>
</tr>
</tbody>
</table>

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration in µg/mL.
than 86% of individual *E. coli*, *P. mirabilis*, and *S. pneumoniae* antimicrobial combinations exhibited susceptibility rates that varied by <10% between specimen source (Table 3). In contrast, 22.2% of *P. aeruginosa* antimicrobial combinations involved susceptibility variation of >10% between specimen sources. This was characterized by increased meropenem and aztreonam susceptibility rates for invasive *P. aeruginosa* isolates (data not illustrated).

In essence, influence of specimen source on potential empiric regimen choice was less pronounced than that described for location of patient encounter. As one example, urogenital isolates predicted a marginally greater proportion of highly susceptible antimicrobial agents for *P. mirabilis* (50.0%) when compared with skin and soft-tissue isolates (35.7%; data not illustrated).

In essence, influence of specimen source on potential empiric regimen choice was less pronounced than that described for location of patient encounter. As one example, urogenital isolates predicted a marginally greater proportion of highly susceptible antimicrobial agents for *P. mirabilis* (50.0%) when compared with skin and soft-tissue isolates (35.7%; data not illustrated).

**Profile by Patient Age**

Finally, age-related determinants of antimicrobial resistance for each of the 4 surveillance organisms were investigated by focusing on the 2 to 3 antimicrobial agents with the lowest percentage-susceptible values, as elucidated in a previous report.3 *E. coli* isolates derived from 20- to 39-year-olds demonstrated more susceptibility to levofloxacin than those from 60- to 79-year-olds (**P** = .02; Table 4A). These isolates also trended toward greater susceptibility when compared with those from patients aged ≥ 80 years (**P** = .06).

No age-related relationships were noted with trimethoprim-sulfamethoxazole (Table 4B) and ampicillin susceptibility.

With respect to *P. mirabilis*, isolates derived from patients aged 20 to 39 years yielded increased rates of ciprofloxacin susceptibility when compared with isolates from patients aged 60 to 79 years and ≥ 80 years (**P** = .04 and **P** = .02, respectively; Table 5A). Similarly, *P. mirabilis* isolates from 20- to 39-year-old patients exhibited increased trimethoprim-sulfamethoxazole susceptibility when compared with all other age groups (**P** ≤ .04; Table 5B). No significant differences were noted when ampicillin susceptibility was stratified by patient age.

*P. aeruginosa* isolates from 40- to 59-year-old patients exhibited decreased ciprofloxacin susceptibility when compared with patients over the age of 60 years (**P** ≤ .03; Table 6A). Similarly, *P. aeruginosa*

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**Table 5.** MIC<sub>50</sub> and MIC<sub>90</sub> Distributions and Categorical Interpretations of Proteus mirabilis Isolate Susceptibility to A: Ciprofloxacin, and B: Trimethoprim-Sulfamethoxazole by Age, Wisconsin 2016

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>CLSI Breakpoints 1/2/4</th>
<th>CLSI Breakpoints 2/4</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Susceptible</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-39</td>
<td>25</td>
<td>≤0.25</td>
<td>1</td>
<td>92.0</td>
<td>0.0</td>
</tr>
<tr>
<td>40-59</td>
<td>60</td>
<td>≤0.25</td>
<td>16</td>
<td>80.0</td>
<td>1.7</td>
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<tr>
<td>60-79</td>
<td>110</td>
<td>≤0.25</td>
<td>32</td>
<td>72.7</td>
<td>3.6</td>
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<td>≥80</td>
<td>71</td>
<td>≤0.25</td>
<td>32</td>
<td>67.6</td>
<td>8.5</td>
</tr>
<tr>
<td>Wisconsin</td>
<td></td>
<td>≤0.25</td>
<td>32</td>
<td>75.6</td>
<td>4.3</td>
</tr>
</tbody>
</table>

**P** = .04 for susceptibility rate of 20-39 years versus 60-79 years.

**P** = .02 for susceptibility rate of 20-39 years versus ≥80 years.

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration in µg/mL.
isolates derived from patients aged 60 to 79 years demonstrated less susceptibility to aztreonam than isolates from patients aged ≥ 80 years (P = .03; Table 6B). No significant age delineations were determined with respect to S pneumoniae susceptibility to either penicillin (P ≥ .22; Table 7A) or erythromycin (P ≥ .18; Table 7B).

Swami and Banerjee18 used an antibiogram approach to stratify antimicrobial resistance patterns in E coli and S pneumoniae by patient age (< 18 years; 18-64 years; ≥ 65 years) at a United States institution. The authors noted that their institution-wide antibiogram underestimated resistance profiling in older patients (particularly with respect to ciprofloxacin and E coli) when compared with a specialized antibiogram devised for populations aged ≥ 65 years. In a European study, Grignon et al19 investigated E coli antimicrobial resistance in the emergency department setting in a region of France (with population of 3.6 million) with an area equivalent to the state of Maryland. Of 10 participating emergency departments, 5 were specifically cited as significant risk factors for increased fluoroquinolone resistance in uropathogenic E coli.

In discussing the current status of antimicrobial resistance in the United States, the CDC cited gaps in general knowledge that involved limited national and state capacity for the detection of emerging antimicrobial resistance trends.1 Past state-based efforts,20,21 as well as those described within the context of the 2016 SWOTARE collection, several geographic paradigms were noted.1 Grignon et al19 investigated E coli antimicrobial resistance in the emergency department setting in a region of France (with population of 3.6 million) with an area equivalent to the state of Maryland. Of 10 participating emergency departments, 5 were specifically cited as significant risk factors for increased fluoroquinolone resistance in uropathogenic E coli.

In future surveillance collections will improve the validity of antimicrobial-resistant S pneumoniae epidemiologic findings.

In addition to the demographic factors affecting antimicrobial resistance that are described in this report, one cannot discount the contribution of geographic location. In the context of the 2016 SWOTARE collection, several geographic paradigms were noted.1 Grignon et al19 investigated E coli antimicrobial resistance in the emergency department setting in a region of France (with population of 3.6 million) with an area equivalent to the state of Maryland. Of 10 participating emergency departments, 5 were specifically cited as significant risk factors for increased fluoroquinolone resistance in uropathogenic E coli.

In discussing the current status of antimicrobial resistance in the United States, the CDC cited gaps in general knowledge that involved limited national and state capacity for the detection of emerging antimicrobial resistance trends.1 Past state-based efforts,20,21 as well as those described within the context of the SWOTARE program, are therefore necessary to supplement data generated by national programs. Moreover, the SWOTARE program already possesses the infrastructure to allow for both annual assessment of resistance trending and a broadening of scope via introduction of additional organism groups into the surveillance paradigm. Boucher et al21 listed a number of pathogens (vancomycin-resistant Enterococcus faecium, methicillin-resistant Staphylococcus aureus, ESBL-producing Klebsiella spp. and E coli, carbapenemase-producing Klebsiella spp., Acinetobacter baumannii, P aeruginosa, and Enterobacter spp.) for which antimicrobial agent

### Table 6. MIC₅₀ and MIC₉₀ Distributions and Categorical Interpretations of Pseudomonas aeruginosa Isolate Susceptibility to A: Ciprofloxacin, and B: Aztreonam by Age, Wisconsin 2016

#### A

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>17</td>
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<td>94.1</td>
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<td>8</td>
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</table>

#### B

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
<th>Susceptible</th>
<th>Intermediate</th>
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<td>89.6</td>
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<tr>
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<td>16</td>
<td>81.0</td>
<td>12.3</td>
<td>6.6</td>
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</tr>
</tbody>
</table>

#### CLSI Breakpoints 1/2/4

#### CLSI Breakpoints 8/16/32

**P** = .03 for susceptibility rate of 40-59 years versus 60-79 years.

**P** = .02 for susceptibility rate of 40-59 years versus ≥80 years.

**P** = .05 for susceptibility rate of 60-79 years versus ≥80 years.

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration in µg/mL.
research and development efforts have become increasingly necessary. Before such advancements are made, close surveillance of currently available agents is essential. The SWOTARE program currently allows for statewide monitoring of 3 of the 7 aforementioned ESKAPE pathogens in Wisconsin, as well as 1 additional pathogen cited by the World Health Organization as another focus for development of alternative antimicrobial strategies.23

CONCLUSIONS

A number of approaches have been considered in the monitoring of antimicrobial resistance patterns. One advantage of a surveillance paradigm based on isolate collection, such as the SWOTARE program, is its capability of ascribing demographic information to isolates. Testing within the SWOTARE program in 2016 revealed resistance variation with respect to a number of antimicrobial/organism combinations. These differences were more relative to location of patient encounter and patient age when compared with specimen source. Year 1 of this surveillance project also revealed particular niches of potential emerging resistance that will be assessed in future seasons of isolate collection. All told, provision of these data to a broad audience may potentiate revision of local empiric therapy guidelines and contribute to antimicrobial stewardship efforts.

### Table 7. MIC₅₀ and MIC₉₀ Distributions and Categorical Interpretations of Streptococcus pneumoniae Isolate Susceptibility to A: Penicillin, and B: Erythromycin by Age, Wisconsin 2016

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
<th>Susceptible</th>
<th>Intermediate</th>
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</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>23</td>
<td>≤0.015</td>
<td>0.25</td>
<td>60.9</td>
<td>75.7</td>
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<td>72.2</td>
<td>68.2</td>
<td>27.8</td>
</tr>
<tr>
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<td>72</td>
<td>≤0.015</td>
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<td>70.3</td>
<td>31.8</td>
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#### A

**CLSI Breakpoints 0.06/0.12***

<table>
<thead>
<tr>
<th>Age, y</th>
<th>n</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>23</td>
<td>≤0.06</td>
<td>&gt;4</td>
<td>52.2</td>
<td>0.0</td>
<td>47.8</td>
</tr>
<tr>
<td>40-59</td>
<td>37</td>
<td>≤0.06</td>
<td>&gt;4</td>
<td>62.2</td>
<td>0.0</td>
<td>37.8</td>
</tr>
<tr>
<td>60-79</td>
<td>72</td>
<td>2</td>
<td>&gt;4</td>
<td>48.6</td>
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<td>51.4</td>
</tr>
<tr>
<td>≥80</td>
<td>44</td>
<td>≤0.06</td>
<td>&gt;4</td>
<td>52.3</td>
<td>0.0</td>
<td>47.7</td>
</tr>
<tr>
<td>Wisconsin</td>
<td></td>
<td>≤0.06</td>
<td>&gt;4</td>
<td>54.2</td>
<td>0.0</td>
<td>45.8</td>
</tr>
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</table>

#### B

**CLSI Breakpoints 0.25/0.5/1**

<table>
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<th>n</th>
<th>MIC₅₀</th>
<th>MIC₉₀</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
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<td>≤0.06</td>
<td>&gt;4</td>
<td>52.2</td>
<td>0.0</td>
<td>47.8</td>
</tr>
<tr>
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<td>≤0.06</td>
<td>&gt;4</td>
<td>62.2</td>
<td>0.0</td>
<td>37.8</td>
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<tr>
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<td>2</td>
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</tr>
<tr>
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<td>&gt;4</td>
<td>52.3</td>
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<td>47.7</td>
</tr>
<tr>
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<td></td>
<td>≤0.06</td>
<td>&gt;4</td>
<td>54.2</td>
<td>0.0</td>
<td>45.8</td>
</tr>
</tbody>
</table>

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration in µg/mL.

*Breakpoints for meningeal *S pneumoniae* isolates.

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REFERENCES


