Antibiotic resistance in ocular infections can affect treatment outcomes. Surveillance data on evolving antibacterial susceptibility patterns inform the treatment of such infections.

**OBJECTIVE** To assess overall antibiotic resistance profiles and trends among bacterial isolates from ocular sources collected during 10 years.

**DESIGN, SETTING, AND PARTICIPANTS** This cross-sectional study of longitudinal data from the ongoing, nationwide, prospective, laboratory-based surveillance study, the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study, included clinically relevant isolates of *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* cultured from patients with ocular infections at US centers from January 1, 2009, to December 31, 2018.

**MAIN OUTCOMES AND MEASURES** Minimum inhibitory concentrations were determined for various combinations of antibiotics and species. Odds ratios (ORs) were determined for concurrent antibiotic resistance; analysis of variance and χ² tests were used to evaluate resistance rates by patient age and geographic region; Cochran-Armitage tests identified changing antibiotic susceptibility trends over time.

**RESULTS** A total of 6091 isolates (2189 *S aureus*, 1765 CoNS, 590 *S pneumoniae*, 767 *P aeruginosa*, and 780 *H influenzae*) from 6091 patients were submitted by 88 sites. Overall, 765 *S aureus* (34.9%) and 871 CoNS (49.3%) isolates were methicillin resistant and more likely to be concurrently resistant to macrolides (azithromycin: *S aureus*: OR, 18.34 [95% CI, 13.64-24.67]; CoNS: OR, 4.59 [95% CI, 3.72-5.66]), fluoroquinolones (ciprofloxacin: *S aureus*: OR, 22.61 [95% CI, 17.96-28.47]; CoNS: OR, 9.73 [95% CI, 7.63-12.40]), and aminoglycosides (tobramycin: *S aureus*: OR, 18.29 [95% CI, 13.21-25.32]; CoNS: OR, 6.28 [95% CI, 4.61-8.56]) compared with methicillin-susceptible isolates (*P* < .001 for all). Multidrug resistance was observed among methicillin-resistant *S aureus* (577 [75.4%]) and CoNS (642 [73.7%]) isolates. Antibiotic resistance among *S pneumoniae* isolates was highest for azithromycin (214 [36.3%]), whereas *P aeruginosa* and *H influenzae* isolates showed low resistance overall. Differences in antibiotic resistance were found among isolates by patient age (*S aureus*: F = 28.07, *P* < .001; CoNS: F = 11.46, *P* < .001) and geographic region (*S aureus*: F = 8.03, *P* < .001; CoNS: F = 4.79, *P* = .003; *S pneumoniae*: F = 8.14, *P* < .001; *P aeruginosa*: F = 4.32, *P* = .005). Small changes in antibiotic resistance were noted over time (<2.5% per year), with decreases in resistance to oxacillin/methicillin (oxacillin: −2.16%; 95% CI, −3.91% to −0.41%; *P* < .001) and other antibiotics among *S aureus* isolates, a decrease in ciprofloxacin resistance among CoNS (−1.38%; 95% CI, −2.24% to −0.52%; *P* < .001), and an increase in tobramycin resistance among CoNS (0.71%; 95% CI, −0.29% to 1.71%; *P* = .03). Besifloxacin retained consistently low minimum inhibitory concentrations.

**CONCLUSIONS AND RELEVANCE** Antibiotic resistance may be prevalent among staphylococcal isolates, particularly among older patients. In this study, a few small differences in antibiotic resistance were observed by geographic region or longitudinally.

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Supplemental content

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The finding of significant antibiotic resistance among ocular pathogens in recent decades is a concern. Antibiotic resistance among ocular bacteria can lead to treatment failure and complicate the choice of antibiotic in clinical practice.

In any infection, identification of causative pathogens and determination of their antibiotic resistance profiles should ideally precede initiation of antibiotic therapy. Although cultures are performed for vision-threatening ocular infections, they are seldom performed for routine eye infections, with physicians favoring empirical therapy to avoid treatment delays associated with the time required to obtain culture and sensitivity results and/or to avoid the costs of culturing. In the absence of culture and sensitivity results, antibiotic resistance data from surveillance studies can inform the choice of initial or empirical therapy. However, regardless of how the treatment decision is made, antibiotic resistance remains an important consideration in the treatment of eye infections.

The Ocular Tracking Resistance in US Today (Ocular TRUST) study was a nationwide surveillance program conducted from 2005 to 2008 to monitor antibiotic resistance specific to common ocular pathogens. Results showed high levels of methicillin resistance among staphylococci, with a predominance of concurrent resistance to other antibiotic classes.

The Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study is a multicenter, nationwide, prospective surveillance study initiated in 2009 and designed to extend on the Ocular TRUST study in surveying antibacterial resistance among clinically relevant isolates of Staphylococcus aureus, coagulase-negative staphylococci (CoNS), Streptococcus pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae. Periodic updates and various subset analyses of ARMOR data have provided clinicians with an understanding of antibiotic resistance patterns to aid in antibiotic selection and ultimately improve patient outcomes.

To our knowledge, Ocular TRUST and ARMOR are the only prospective surveillance studies on ocular isolates, and ARMOR is the only ongoing study in the United States. Using data from ARMOR, we assessed the overall antibiotic resistance profiles and trends by age, geographic region, and over time for ocular isolates collected from January 1, 2009, to December 31, 2018.

Methods

ARMOR Study Design

This cross-sectional study used longitudinal data from the ARMOR surveillance study; the design and methods have been described previously. Community hospitals, academic or university hospitals, specialty or ocular centers, and reference laboratories in the United States were asked to provide isolates of S aureus, CoNS, S pneumoniae, P aeruginosa, and H influenzae from patients with ocular infections to a central laboratory for testing. From January 1, 2009, through December 31, 2013, up to 65 isolates, including S aureus (≤20), CoNS (≤20), S pneumoniae (≤5), P aeruginosa (≤15), and H influenzae (≤5) were requested from each site per collection year; from January 1, 2014, through December 31, 2018, a maximum of 50 (≤12 from any of the aforementioned species) were requested from each site per collection year. Sites were asked to submit isolates deemed to be clinically relevant based on their discretion; isolates could be sourced from any ocular tissue, although endophthalmitis isolates were excluded in earlier collection years (2009-2014). Site participation was inconsistent throughout all 10 years, and new sites were recruited yearly as needed. Initial ocular culture samples were not prospectively collected for ARMOR but were taken as part of routine medical care unrelated to the study and stored on site until shipment to the central laboratory. Because the study entailed laboratory research on samples already collected and there was no identifiable patient information provided with the isolates, the study was deemed to be exempt from formal institutional review board review activity per title 45 of the Code of Federal Regulations. However, the ARMOR study protocol deferred the final need for any institutional review board review activity to individual participating sites based on their own local institutional review board requirements. Institutional review board approval was not required for study conduct at any of the 88 participating ARMOR sites.

Antibiotic Susceptibility Testing

Bacterial isolates were sent via ESwab Collection/Transport Systems (Becton, Dickinson and Company) to an independent central laboratory (Eurofins Medinet [2009-2013]; International Health Management Associates Inc [2014-2018]) for species confirmation, and minimum inhibitory concentrations (MICs) were determined by broth microdilution according to Clinical and Laboratory Standards Institute (CLSI) methods with frozen antibacterial microtiter panels. The lowest drug concentrations that inhibited the growth of 90% of indicated isolates (MIC90s) were calculated. The following representative antibiotics from 10 different classes were tested as appropriate based on bacterial species: azithromycin (macrolide); clindamycin (lincosamide); cefoxitin, ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, and ofloxacin (fluoroquinolones); chloramphenicol (amphenicol); oxacillin and penicillin (beta-lactams); polymixin B (polypeptide); tetracycline (tetracycline); tobramycin (aminoglycoside); trimethoprim (dihydrofolate reductase inhibitor); and vancomycin.

Key Points

Question What are the antibiotic resistance profiles and trends among common ocular pathogens across the United States?

Findings In this cross-sectional study of more than 6000 ocular isolates of Staphylococcus aureus, coagulase-negative staphylococci, Streptococcus pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae collected between 2009 and 2018, methicillin resistance and multidrug resistance were prevalent among staphylococci. Antibiotic resistance profiles were mostly unchanged during 10 years.

Meaning These in vitro antibiotic resistance data may assist clinicians in selecting appropriate antibiotics for treatment of ocular infections.
(glycopeptide). Additional antibiotics were tested in earlier years (eg, cephradine, imipenem) but are not reported because of CLSI changes in recommended antibiotics to be used for susceptibility determinations. Some nonophthalmic antibiotics were included to allow for a comparison with reported resistance rates for nonocular isolates of the same species. When available, MICs were interpreted as indicating antibiotic susceptible, intermediate, or resistant based on the CLSI interpretive criteria in use during the collection year for that antibiotic or species combination; because no systemic formulation exists for besifloxacin, interpretive criteria are not available for this drug. Staphylococci were categorized as methicillin resistant or methicillin susceptible based on oxacillin susceptibility; the break point for oral penicillin was used to determine susceptibility of S pneumoniae to penicillin. Unless otherwise indicated, break points for ciprofloxacin were used to determine resistance to the fluoroquinolone class. Calculations for the percentage of antibiotic resistance included antibiotic-intermediate and antibiotic-resistant isolates except where noted otherwise. Multidrug resistance (MDR) was defined as resistance to at least 3 classes of antibiotics.

Statistical Analysis
Odds ratios (ORs) for resistance to each antibiotic were based on sample proportions computed directly from the data. One-way analysis of variance was used to evaluate antibiotic resistance of isolates by age of the patient and by geographic region; age analysis involved categorization of isolates by decade of life, whereas geographical analysis involved categorization of isolates based on region of origin (Midwest, Northeast, South, and West) as previously described. Because not all antibiotic classes were tested each year, the analysis of variance used means of the percentage of drug classes to which each isolate of a species or species group was resistant based on the number of antibiotic classes tested. If \( P \leq .05 \), the data provided evidence that the means were not equal. Subsequently, the Tukey honestly significant differences test was applied. Additional analyses of differences among staphylococci by methicillin resistance status were performed using \( \chi^2 \) tests followed by a multiple-comparisons test for proportions. Changes in antibiotic resistance over time were examined using a Cochran-Armitage test for linear trends in a proportion, with 2-tailed \( P \leq .05 \) values reported; weighted least squares regression analysis was conducted to estimate the magnitude of any change (ie, slope, 95% CI) over time. Statistical testing was performed using Statistix 10 (Analytical Software).

Results
Source of Isolates
A total of 6091 isolates (2189 S aureus, 1765 CoNS, 590 S pneumoniae, 767 P aeruginosa, and 780 H influenzae) were collected from 88 sites (47 community hospitals, 29 academic or university hospitals, 9 specialty or ocular centers, and 3 reference laboratories) across 41 states (2526 Midwest, 1300 Northeast, 783 South, and 1482 West). Of 6091 patients from whom isolates were obtained, 2735 (44.9%) were male, 2851 (46.8%) were female, and sex was not reported for 505 (8.3%). Patient age was known for 4988 isolates, with 1102 obtained from patients younger than 10 years. A total of 349 of 621 H influenzae isolates (56.2%) and 165 of 463 S pneumoniae isolates (35.6%) were from patients aged 0 to 9 years, whereas 313 of 1834 S aureus isolates (17.1%) came from patients with similar ages. The anatomical source (other than for ocular isolates with an unknown anatomical source) was known for 3132 isolates (51.4%) and included the conjunctiva (\( n = 1609 \)), cornea (\( n = 1288 \)), aqueous humor (\( n = 73 \)), and vitreous humor (\( n = 162 \)). Among the 460 P aeruginosa isolates from a known anatomical source, 325 (70.7%) were from corneal scrapings, and among the 328 H influenzae isolates from a known anatomical source, 287 (87.5%) were from the conjunctiva.

Cumulative Antibiotic Resistance Rates
Cumulative MIC90s and antibiotic resistance profiles for collected isolates, including those for staphylococci by methicillin-resistance phenotype, are presented by species or antibiotic combination in the Table. Of 2189 S aureus isolates, 765 (34.9%) were resistant to oxacillin/methicillin (methicillin-resistant S aureus [MRSA]). Resistance was observed to ciprofloxacin in 733 (33.5%) and to azithromycin in 1306 (59.7%) of S aureus isolates, although all were susceptible to vancomycin. Compared with methicillin-susceptible S aureus (MSSA) isolates, resistance to other antibiotics was more prevalent among MRSA isolates, with resistance greater than 70% for fluoroquinolones (not applicable for besifloxacin) and 92.9% for azithromycin. The later-generation fluoroquinolones (besifloxacin, gatifloxacin, and moxifloxacin) had lower MIC90s overall compared with the earlier ones (ciprofloxacin, levofloxacin, and ofloxacin). Besifloxacin showed the lowest MIC90s, and ciprofloxacin showed the highest.

Antibiotic resistance profiles among CoNS isolates were similar to those observed for S aureus isolates, although oxacillin/methicillin resistance was found to be higher (871 [49.3%] were methicillin-resistant CoNS). As with S aureus isolates, higher rates of resistance to other antibiotics were seen among methicillin-resistant CoNS compared with methicillin-susceptible CoNS isolates, and the later-generation fluoroquinolones demonstrated generally lower MIC90s overall against CoNS isolates.

Among S pneumoniae isolates, resistance rates were less than 10% to all antibiotics tested except for azithromycin (214 [36.3%]) and penicillin (190 [32.2%]). Rates of antibiotic resistance among P aeruginosa and H influenzae were low overall. Against P aeruginosa isolates, ciprofloxacin demonstrated the lowest MIC90s, and moxifloxacin and besifloxacin had the highest; against H influenzae, the lowest MIC90s were observed among the fluoroquinolones.

Concurrent Antibiotic Resistance and MDR
With the exception of trimethoprim, MRSA isolates were significantly more likely than MSSA isolates to be concurrently resistant to another antibacterial drug class: azithromycin (92.9 vs 41.8; OR, 18.34 [95% CI, 13.64-24.67]; \( P < .001 \)), ciprofloxacin (74.5 vs 11.4; OR, 22.61 [95% CI, 17.96-28.47]; \( P < .001 \)),
### Table. Antibiotic Resistance Profiles and MIC90s for *Staphylococcus aureus*, *CoNS*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* Isolates

| Organism, antibiotic | Isolates, No. | MIC90, μg/mL | Antibiotic resistance profile, % |
|----------------------|---------------|--------------|----------------------------------|
|                      |               |              | Susceptible | Intermediate | Resistant |
| **S. aureus**        |               |              |             |              |          |
| Besifloxacin         | All 2189 1    | NA           | NA          | NA           | NA       |
|                      | MSSA 1424 0.25| NA           | NA          | NA           | NA       |
|                      | MRSA 765 2    | NA           | NA          | NA           | NA       |
| Moxifloxacin         | All 2189 4    | 68.6         | 6.4         | 25.0         |          |
|                      | MSSA 1424 0.5 | 90.0         | 2.9         | 7.1          |          |
|                      | MRSA 765 16   | 28.8         | 12.9        | 58.3         |          |
| Gatifloxacin         | All 1989 4    | 68.2         | 2.4         | 29.4         |          |
|                      | MSSA 1302 1   | 89.2         | 1.4         | 9.4          |          |
|                      | MRSA 687 16   | 28.2         | 4.4         | 67.4         |          |
| Ciprofloxacin        | All 2189 128  | 66.5         | 1.3         | 32.2         |          |
|                      | MSSA 1424 4   | 88.6         | 1.1         | 10.4         |          |
|                      | MRSA 765 256  | 25.5         | 1.8         | 72.7         |          |
| Levofloxacin         | All 1989 16   | 67.9         | 1.6         | 30.5         |          |
|                      | MSSA 1302 2   | 89.1         | 1.0         | 9.9          |          |
|                      | MRSA 687 128  | 27.8         | 2.8         | 69.4         |          |
| Ofloxacin            | All 1989 >8   | 67.6         | 0.4         | 32.0         |          |
|                      | MSSA 1302 4   | 88.8         | 0.5         | 10.8         |          |
|                      | MRSA 687 16   | 27.5         | 0.3         | 72.2         |          |
| Azithromycin         | All 2189 >512| 40.3         | 1.1         | 58.6         |          |
|                      | MSSA 1424 >512| 58.2         | 1.6         | 40.2         |          |
|                      | MRSA 765 >512| 7.1          | 0           | 92.9         |          |
| Chloramphenicol      | All 1989 8    | 94.3         | 5.1         | 0.6          |          |
|                      | MSSA 1302 8   | 96.3         | 3.5         | 0.2          |          |
|                      | MRSA 687 8    | 90.4         | 8.3         | 1.3          |          |
| Clindamycin          | All 2189 >2   | 85.3         | 1.0         | 13.7         |          |
|                      | MSSA 1424 0.25| 93.1         | 1.1         | 5.8          |          |
|                      | MRSA 765 >2   | 71.0         | 0.8         | 28.2         |          |
| Oxacillin/methicillin| All 2189 >2   | 65.1         | 0           | 34.9         |          |
|                      | MSSA 1424 0.5 | 100          | 0           | 0            |          |
|                      | MRSA 765 >4   | 0            | 0           | 100          |          |
| Tetracycline         | All 913 0.5   | 93.9         | 0.4         | 5.7          |          |
|                      | MSSA 666 0.5  | 97.1         | 0.3         | 2.6          |          |
|                      | MRSA 247 16   | 85.0         | 0.8         | 14.2         |          |

(continued)
Table. Antibiotic Resistance Profiles and MIC90s for Staphylococcus aureus, CoNS, Streptococcus pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae isolates (continued)

| Organism, antibiotic | Isolates, No. | MIC90, μg/mL | Antibiotic resistance profile, %a |
|----------------------|---------------|--------------|----------------------------------|
|                      |               | Susceptible  | Intermediate | Resistant |
| Clindamycin          |               |              |              |           |
| All                  | 1765          | 16           | 72.4         | 5.3       | 22.3      |
| MSCoNS              | 894           | >2           | 82.2         | 7.4       | 10.4      |
| MRCoNS              | 871           | >64          | 62.3         | 3.2       | 34.4      |
| Oxacillin/ methicillin |           |              |              |           |
| All                  | 1765          | >2           | 50.7         | 0         | 49.3      |
| MSCoNS              | 894           | 0.25         | 100          | 0         | 0         |
| MRCoNS              | 871           | >2           | 0            | 0         | 100       |
| Tetracycline         |               |              |              |           |
| All                  | 671           | 16           | 87.6         | 1.3       | 11.0      |
| MSCoNS              | 341           | 2            | 90.6         | 2.6       | 6.7       |
| MRCoNS              | 330           | >16          | 84.5         | 0         | 15.5      |
| Tobramycin           |               |              |              |           |
| All                  | 1765          | 16           | 82.5         | 6.9       | 10.7      |
| MSCoNS              | 894           | 4            | 93.9         | 3.9       | 2.2       |
| MRCoNS              | 871           | 32           | 70.8         | 9.9       | 19.3      |
| Trimethoprim         |               |              |              |           |
| All                  | 1621          | >128         | 72.1         | 27.9      |           |
| MSCoNS              | 826           | 128          | 84.6         | 0         | 15.4      |
| MRCoNS              | 795           | >256         | 59.1         | 0         | 40.9      |
| Vancomycin           |               |              |              |           |
| All                  | 1765          | 2            | 100          | 0         | 0         |
| MSCoNS              | 894           | 2            | 100          | 0         | 0         |
| MRCoNS              | 871           | 2            | 100          | 0         | 0         |
| S pneumoniae         |               |              |              |           |
| Besifloxacin         | 590           | 0.06         | NA           | NA        | NA        |
| Moxifloxacin         | 590           | 0.25         | 99.8         | 0.2       | 0         |
| Gatifloxacin         | 515           | 0.25         | 99.8         | 0.2       | 0         |
| Ciprofloxacin        | 590           | 1            | NA           | NA        | NA        |
| Levofloxacin         | 515           | 1            | 99.2         | 0.6       | 0.2       |
| Azithromycin         | 590           | >128         | 63.7         | 0.3       | 35.9      |
| Chloramphenicol      | 590           | 4            | 96.9         | 0         | 3.1       |
| Penicillin           | 590           | 1            | 67.8         | 24.4      | 7.8       |
| Tetracycline         | 208           | 0.5          | 91.3         | 0         | 8.7       |
| P aeruginosa         |               |              |              |           |
| Besifloxacin         | 767           | 4            | NA           | NA        | NA        |
| Moxifloxacin         | 767           | 4            | NA           | NA        | NA        |
| Gatifloxacin         | 667           | 1            | 94.3         | 2.4       | 3.3       |
| Ciprofloxacin        | 767           | 0.5          | 92.8         | 1.4       | 5.7       |
| Levofloxacin         | 667           | 1            | 93.9         | 1.0       | 5.1       |
| Ofloxacin            | 667           | 2            | 93.1         | 1.9       | 5.0       |
| Polymyxin B          | 667           | 2            | 92.4         | 5.7       | 1.9       |
| Tobramycin           | 767           | 1            | 97.1         | 0.3       | 2.6       |

Table. Antibiotic Resistance Profiles and MIC90s for Staphylococcus aureus, CoNS, Streptococcus pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae isolates (continued)

| Organism, antibiotic | Isolates, No. | MIC90, μg/mL | Antibiotic resistance profile, %a |
|----------------------|---------------|--------------|----------------------------------|
|                      |               | Susceptible  | Intermediate | Resistant |
| H influenzae         |               |              |              |           |
| Besifloxacin         | 780           | 0.03         | NA           | NA        | NA        |
| Moxifloxacin         | 780           | 0.03         | 99.9         | 0         | 0.1       |
| Gatifloxacin         | 707           | 0.015        | 99.9         | 0         | 0.1       |
| Ciprofloxacin        | 780           | 0.015        | 99.9         | 0         | 0.1       |
| Levofloxacin         | 707           | 0.03         | 99.9         | 0         | 0.1       |
| Ofloxacin            | 707           | 0.03         | 99.9         | 0         | 0.1       |
| Azithromycin         | 780           | 2            | 99.6         | 0         | 0.4       |
| Chloramphenicol      | 780           | 1            | 96.9         | 0         | 0.4       |
| Tetracycline         | 354           | 0.5          | 98.6         | 0         | 1.4       |

Abbreviations: CoNS, coagulase-negative staphylococci; MIC90, minimum inhibitory concentration that inhibits the growth of 90% of isolated isolates; MRCoNS, methicillin-resistant CoNS; MRSA, methicillin-resistant S aureus; MSCoNS, methicillin-susceptible CoNS; MSSA, methicillin-susceptible S aureus; NA, Clinical and Laboratory Standards Institute interpretive breakpoint currently not available or applicable.

a Percent susceptible, intermediate, and resistant may not add to 100 because of rounding.

b The 1765 CoNS isolates included Staphylococcus arlettae (1), Staphylococcus auricularis (2), Staphylococcus capitis (79), Staphylococcus caprae (14), Staphylococcus cohnii (3), Staphylococcus condimenti (1), Staphylococcus epidermidis (1349), Staphylococcus equorum (1), Staphylococcus hominis (96), Staphylococcus lugdunensis (31), Staphylococcus pasteuri (11), Staphylococcus pettenkoferi (9), Staphylococcus saprophyticus (3), Staphylococcus schleiferi (2), Staphylococcus simulans (8), Staphylococcus warneri (66) Staphylococcus xylosus (1), and unspeciated CoNS (55).

clindamycin (29.0 vs 7.0; OR, 5.47 [95% CI, 4.23-7.08]; P < .001), tetracycline (38.4 vs 3.3; OR, 18.29 [95% CI, 13.21-25.32]; P < .001), chloramphenicol (84.6 vs 39.3; OR, 2.78 [95% CI, 1.89-4.08]; P < .001), and tobramycin (15.0 vs 2.9; OR, 6.00 [95% CI, 3.38-10.66]; P < .001) (Figure 1A). Similarly, with the exception of chloramphenicol, methicillin-resistant CoNS isolates were more likely to be concurrently resistant to another antibacterial drug class compared with methicillin-susceptible CoNS isolates: azithromycin (78.6 vs 44.5; OR, 4.59 [95% CI, 3.72-5.66]; P < .001), ciprofloxacin (56.9 vs 12.0; OR, 9.73 [95% CI, 7.63-12.40]; P < .001), clindamycin (37.7 vs 17.8; OR, 2.79 [95% CI, 2.24-3.48]; P < .001), tetracycline (29.2 vs 6.2; OR, 6.28 [95% CI, 4.61-8.56]; P < .001), trimethoprim (41.0 vs 15.4; OR, 3.83 [95% CI, 3.02-4.84]; P < .001), and tetracycline (15.5 vs 9.4; OR, 1.77 [95% CI, 1.10-2.83]; P = .02) (Figure 1B). Figure 1C and D summarize the percentage of MDR among staphylococcal isolates. The rate of MDR among all S aureus isolates was 30.1% and all CoNS isolates was 41.2%, whereas the rate among MRSA isolates was 75.4% and among methicillin-resistant CoNS isolates was 73.7%.

Antibiotic Resistance Rates by Patient Age or Geographic Region

Analysis of variance of the mean percentage of resistance by patient age (categorized by decade of life) showed differences among S aureus (F = 28.07, P < .001) (Figure 2A), CoNS
(F = 11.46, P < .001) (Figure 2B), and S pneumoniae isolates (F = 2.08, P = .03) but not among P aeruginosa and H influenzae isolates. Pairwise differences were found for S aureus isolates from younger patients compared with older patients, reflecting an increase in antibiotic resistance with patient age; similar results were obtained for CoNS isolates. For both S aureus and CoNS isolates, oxacillin/methicillin resistance also differed by patient age and paralleled that of mean percentage of resistance, again with higher methicillin resistance among isolates from older patients and significant pairwise differences across the decades (Figure 2). No significant pairwise differences were found for S pneumoniae isolates.

Analysis of variance showed small differences in the percentage of resistance by geographic region for S aureus (F = 8.03, P < .001), CoNS (F = 4.79, P = .003), S pneumoniae (F = 8.14, P < .001), and P aeruginosa isolates (F = 4.32, P = .005) (Figure 3). Compared with other regions, mean percentage of antibiotic resistance was significantly lower in the West for S aureus isolates and highest in the South for CoNS isolates. The mean percentage of resistance among S pneumoniae isolates was higher in the Midwest than in the Northeast and West, whereas for P aeruginosa isolates, antibiotic resistance in the Midwest and South was higher compared with the West. Oxacillin/methicillin resistance in S aureus isolates paralleled that for the mean percentage of resistance, with significant pairwise differences between the West and both the South and the Midwest. Among CoNS isolates, pairwise differences were observed between the Midwest and both the West and the Northeast.
Antibiotic Resistance Rates Over Time

Figure 4 shows antibiotic resistance rates by year during the study period. Oxacillin/methicillin resistance decreased slightly among \textit{S aureus} isolates but did not change among CoNS isolates. Small decreases over time were also observed in resistance to azithromycin, ciprofloxacin, chloramphenicol, and tobramycin among \textit{S aureus} isolates and in ciprofloxacin among CoNS isolates. The mean changes per year in percent of antibiotic resistance were $-2.16\%$ (95% CI, $-3.91\%$ to $-0.41\%$; $P < .001$) for oxacillin/methicillin, $-1.44\%$ (95% CI, $-2.35\%$ to $-0.52\%$; $P < .001$) for azithromycin, $-2.24\%$ (95% CI, $-3.59\%$ to $-0.89\%$; $P < .001$) for ciprofloxacin, $-0.54\%$ (95% CI, $-1.28\%$ to $0.21\%$; $P = .005$) for chloramphenicol, $-1.84\%$ (95% CI, $-2.53\%$ to $-1.14\%$; $P < .001$) for tobramycin among \textit{S aureus} isolates, and $-1.38\%$ (95% CI, $-2.24\%$ to $-0.52\%$; $P < .001$) for ciprofloxacin among CoNS isolates. A small increase over time was noted in CoNS resistance to tobramycin, with a mean change in percent resistance per year of $0.71\%$ (95% CI, $-0.29\%$ to $1.71\%$; $P = .03$). Among MRSA isolates, there was a decrease in resistance to tobramycin (mean change, $-2.53\%$; 95% CI, $-3.91\%$ to $-1.14\%$; $P < .001$), whereas methicillin-resistant CoNS isolates showed an increase in resistance to tobramycin (mean change, $1.85\%$; 95% CI, $0.19$ to $3.50\%$; $P < .001$). No changes in antibiotic resistance were observed among \textit{P aeruginosa} and 3 \textit{S pneumoniae} isolates (eFigure 1 in the Supplement).

Discussion

The first analysis of ARMOR study data, based on ocular isolates collected in its inaugural year, showed high rates of methicillin resistance and MDR among \textit{S aureus} and CoNS isolates.\textsuperscript{19} Analyses in subsequent years suggested that rates of MRSA could be declining; however, MDR, especially among methicillin-resistant staphylococci, remained high.\textsuperscript{21-23}

The present report expands on previous ARMOR study reports and describes antibiotic resistance profiles for the current cumulative data set of more than 6000 clinical isolates collected during 10 years. Overall, 1 in 3 \textit{S aureus} isolates and 1 in 2 CoNS isolates were resistant to methicillin and approximately 3 in 4 methicillin-resistant staphylococcal isolates were MDR. Concurrent antibiotic resistance was higher among methicillin-resistant compared with methicillin-susceptible staphylococcal isolates, with MRSA isolates being 3 to 23 times more likely to be resistant to other commonly used antibiotics except trimethoprim and with methicillin-resistant CoNS isolates being 2 to 10 times more likely to be resistant to other antibiotics. However, susceptibility to vancomycin remained high for all species. In contrast with staphylococcal isolates, low resistance was observed among \textit{S pneumoniae}, \textit{P aeruginosa}, and \textit{H influenzae} isolates, although 1 in \textit{S pneumoniae} isolates
were resistant to azithromycin and penicillin. Overall, these findings align with previous ARMOR reports and retrospective reviews of ocular isolates from single US clinical centers. Differences in MIC90s were found within the fluoroquinolone class of antibiotics. Among \textit{S. aureus} and CoNS isolates overall and by methicillin resistance phenotype, MIC90s were generally lower for the later-generation fluoroquinolones compared with the older ones, with besifloxacin demonstrating the lowest MIC90 against \textit{S. pneumoniae}, whereas ciprofloxacin had the lowest MIC90 against \textit{P. aeruginosa}. Older fluoroquinolones may have acquired increased in vitro resistance because of longer systemic use; resistance against older fluoroquinolones may result from a single mutation in DNA gyrase or DNA topoisomerase IV, whereas resistance against later-generation fluoroquinolones requires mutations in both enzymes. The MIC90s reported here for besifloxacin are similar to those obtained during clinical trials of besifloxacin treatment for bacterial conjunctivitis conducted from 2004 through 2007 and suggest negligible resistance development to this fluoroquinolone to date. These findings are notable given reporting in ocular infections—albeit limited, to date, to bacterial keratitis—of a correlation between low fluoroquinolone MICs and improved treatment outcomes, together with the established understanding in systemic infections that antibiotics with lower MICs are associated with higher rates of treatment response than those with higher MICs. Higher rates of mean percentage of resistance and methicillin resistance were seen among staphylococcal isolates obtained from older patients, consistent with previous reporting. There was insufficient evidence to conclude that regions had different mean resistance percentages for the Midwest, Northeast, and South in \textit{A}, the Midwest, Northeast, and West in \textit{B}, the Midwest and South and the Northeast, South, and West in \textit{C}; and the Midwest, Northeast and South and the Northeast and West in \textit{D}. Error bars indicate standard error of the mean.

\textbf{Figure 3. Mean Antibiotic Resistance and Methicillin Resistance Among Isolates by Geographic Region}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{Mean Antibiotic Resistance and Methicillin Resistance Among Isolates by Geographic Region}
\end{figure}

\textit{A}, \textit{Staphylococcus aureus}:

\begin{itemize}
  \item \textit{Mean antibiotic resistance}
  \item \textit{Oxacillin/methicillin resistance}
\end{itemize}

\textit{B}, \textit{Coagulase-negative staphylococci}:

\textit{C}, \textit{Streptococcus pneumoniae}:

\textit{D}, \textit{Pseudomonas aeruginosa}:

\[ P \text{ values were calculated using analysis of variance (ANOVA) for mean resistance and the } \chi^2 \text{ test for oxacillin/methicillin resistance.} \]

\begin{itemize}
  \item \textit{A}, \textit{P} < .001 by ANOVA and \( \chi^2 \) test.
  \item \textit{B}, \textit{P} = .003 by ANOVA and \( P < .001 \) by \( \chi^2 \) test.
  \item \textit{C}, \textit{P} < .001 by ANOVA.
  \item \textit{D}, \textit{P} = .005 by ANOVA. \text{There was insufficient evidence to conclude that regions had different mean resistance percentages for the Midwest, Northeast, and South in \textit{A}, the Midwest, Northeast, and West in \textit{B}, the Midwest and South and the Northeast, South, and West in \textit{C}; and the Midwest, Northeast and South and the Northeast and West in \textit{D}. Error bars indicate standard error of the mean.} \end{itemize}
cations for older patients presenting with ocular infections and/or undergoing ocular surgery. For example, dropless cataract surgery may need reconsideration in this age group because it is unclear whether intracocular moxifloxacin levels are maintained above the MIC sufficiently long enough to fully eradicate any antibiotic-resistant *Staphylococcus* that may breach the surgical wound; in this regard, there have been reports of endophthalmitis after dropless cataract surgery with moxifloxacin. Of importance, of methicillin-resistant *Staphylococcus* sourced from vitreous or aqueous humor in this study, 91% of MRSA isolates and 71% of methicillin-resistant *CoNS* isolates had concurrent resistance to moxifloxacin (Appendix, eFigure 2, and eFigure 3 in the Supplement). An increasing prevalence of resistance to antibiotics, especially fluoroquinolones, with patient age has also been reported by other researchers. In contrast to older patients, antibiotic resistance findings for pediatric patients were lower. However, even in this age group, the mean percentage of antibiotic resistance, including methicillin resistance among staphylococcal isolates, was notable (Figure 2) and should be considered in the context of an increasing recognition of the polybacterial nature of conjunctivitis and keratitis infections.

Small differences were found in antibiotic resistance by geographic region for each species, with higher mean percentages of resistance (and methicillin resistance among staphylococcal isolates) in the South and/or Midwest and lower rates in the West. The findings for *S aureus* isolates are consistent with previous ARMOR reporting and results from Blanco and colleagues, who observed higher rates of MRSA infection in intensive care units in the southern region of the United States. Small changes, mostly decreases, were found in antibiotic resistance over time and likely reflect improved antibiotic stewardship. The small decrease in methicillin resistance suggested in earlier ARMOR reports was supported for the 10-year study period, although no such change was seen among *CoNS* isolates. Not observed before was the increase in *CoNS* resistance to tobramycin, whereas a previous increase to trimethoprim among *CoNS* isolates and previous decreases to ciprofloxacin and tobramycin among *P aeruginosa* isolates were not confirmed. Although an approximately 2-fold increase in resistance to azithromycin over time was observed among *S pneumoniae* isolates in the 7-year analysis, no changes in resistance over time to azithromycin, penicillin, moxifloxacin, chloramphenicol, or tetracycline among *S pneumoniae* isolates were evident over the extended 10-year time frame.

In addition, antibiotic resistance trends among ocular isolates were similar when evaluated by anatomical source (eg, conjunctiva, cornea, and intraocular) (Appendix and eFigures 4-7 in the Supplement). In parallel with this finding, an-
tibiotic resistance trends in the 10-year ARMOR data set were also similar to those reported for nonocular isolates from systemic infections in both US and global surveillance studies, such as Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE),58,71,72 Linezolid Experience and Accurate Determination of Resistance (LEADER),73,74 Tigecycline Evaluation and Surveillance Trial (TEST),75,76 and the SENTRY Antimicrobial Surveillance Program.77-79 For instance, recent patterns in systemic infections.

In our study. These findings suggest that ARMOR study re-in the last years (2015-2016)78; however, ciprofloxacin resistance than 65 000 accuracy of the data analysis.

had full access to all the data in the study and take

responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

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Conflict of Interest Disclosures: Dr Asbell reported serving as a consultant and receiving personal fees from Alcon, Kao, Medscape, Perrigo, Santen, ScientiaCME, Senju, and Shire and serving on advisory boards for Allikos, Allergan, Bausch + Lomb (a division of Bausch Health US, LLC), Dompé, Kala, Novalix, Novartis, Regeneron Pharmaceuticals, and Sun Pharmaceuticals outside the submitted work. Dr Sanfilippo reported being an employee of Bausch + Lomb (a division of Bausch Health US, LLC). Dr Sahm reported being an employee of International Health Management Associates Inc. Dr DeCory reported being an employee of Bausch + Lomb (a division of Bausch Health US, LLC).

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Asbell PA, Colby KA, Deng S, et al. Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates. Am J Ophthalmol. 2008;145(6):951-958. doi:10.1016/j.ajo.2008.01.025

Blanco C, Núñez MX. Antibiotic susceptibility of staphylococcal isolates from patients with chronic conjunctivitis: including associated factors and clinical evaluation. J Ocul Pharmacol Ther. 2013;29(9):803-808. doi:10.1089/jop.2013.0040

Amato M, Peshing S, Wallick M, Tanaka S. Trends in ophthalmic manifestations of methicillin-resistant Staphylococcus aureus (MRSA) in a northern California pediatric population. J AAPOS. 2013;17(3):243-247. doi:10.1016/j.jaapos.2012.12.151

Chatterjee S, Agrawal D. Multi-drug-resistant Pseudomonas aeruginosa keratitis and its effective treatment with topical colistimethate. Indian J Ophthalmol. 2008;56(3):181-183. doi:10.1016/j.ijjo.2008.03.008

Trends in Antibiotic Resistance Among Ocular Microorganisms in the United States From 2009 to 2018

The findings suggest that methicillin resistance and MDR is prevalent among ocular S aureus and CoNS isolates in the United States and should be considered when treating staphylococcal ocular infections, especially in older patients. The small decreases in antibiotic resistance among S aureus isolates are encouraging but require further monitoring.
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Ophthal. 2016;6(4):153-157, doi:10.4103/0301-4738.179721

10. Garg P, Sharma S, Rao GN. Ciprofloxacin-resistant Pseudomonas keratitis. Ophthalmology. 1999;106(7):1319-1323. doi:10.1016/S0161-6420(99)00714-4

11. Mohshir M, Mirzaal G, Feiz V, Kang PC. Fourth-generation fluoroquinolone-resistant bacterial keratitis after refractive surgery. J Cataract Refract Surg. 2006;32(3):515-518. doi:10.1016/j.jcrs.2005.12.108

12. Segreti J, Jones RN, Bertino JS Jr. Challenges in assessing microbial susceptibility and predicting clinical response to newer-generation fluoroquinolones. J Ocul Pharmacol Ther. 2012;28(1):3-11. doi:10.1089/jop.2011.0072

13. Wilhelms K, Abshire RL, Schlech BA. Influence of fluoroquinolone susceptibility on the therapeutic response of fluoroquinolone-treated bacterial keratitis. Arch Ophthalmol. 2003;121(9):1229-1233. doi:10.1001/archopht.121.9.12229

14. Goff DA, Jankowski C, Jenover CF. Using rapid diagnostic tests to optimize antimicrobial selection in antimicrobial stewardship programs. Pharmacotherapy. 2012;32(8):677-687. doi:10.1002/phar.1193

15. American Academy of Ophthalmology. Bacterial keratitis preferred practice pattern-2018. https://www.aao.org/preferred-practice-pattern/bacterial-keratitis-ppp-2018. Published November 2018. Accessed March 5, 2019.

16. American Academy of Ophthalmology. Conjunctivitis preferred practice pattern-2018. https://www.aao.org/preferred-practice-pattern/conjunctivitis-ppp-2018. Published November 2018. Accessed March 5, 2019.

17. Asbell PA, Sahm DF. Longitudinal nationwide antimicrobial susceptibility surveillance in ocular isolates: results from Ocular TRUST 2. Presented at: American Society of Cataract and Refractive Surgery Annual Meeting; April 28, 2008; San Diego, CA.

18. Asbell PA, Sahm DF, Sheddien A. Ocular TRUST 3: ongoing longitudinal surveillance of antimicrobial susceptibility in ocular isolates. Presented at: American Society of Cataract and Refractive Surgery Annual Meeting; April 7, 2009; San Francisco, CA.

19. Haas W, Pillar CM, Torres M, Morris TW. Sahm DF. Monitoring antibiotic resistance in ocular microorganisms: results from the Antibiotic Resistance Monitoring in Ocular microorganisms (ARMOR) Surveillance Study. Am J Ophthalmol. 2011;152(4):567.e3-574.e3. doi:10.1016/j.ajo.2011.03.010

20. Asbell PA, Pandit RT, Sanfilippo CM. Antibiotic resistance rates by geographic region among ocular pathogens collected during the ARMOR Surveillance Study. Ophthal. Ther. 2018;7(2):417-429. doi:10.3402/oht.v7i2.18441

21. Asbell PA, Sanfilippo CM, Pillar CM, DeCory HH, Sahm DF, Morris TW. Antibiotic resistance among ocular pathogens in the United States: five-year results from the Antibiotic Resistance Monitoring in Ocular microorganisms (ARMOR) Surveillance Study. JAMA Ophthalmol. 2015;133(12):1445-1454. doi:10.1001/jamaophthalmology.2015.3888

22. Asbell PA, Sanfilippo CM. Antibiotic resistance trends among ocular pathogens in the US—cumulative results from the Antibiotic Resistance Monitoring in Ocular microorganisms (ARMOR) Surveillance Study. US Ophthalmol Rev. 2017;10(1):35-38. doi:10.17925/USORT.2017.10.01.35

23. Thomas RK, Melton R, Asbell PA. Antibiotic resistance among ocular pathogens: current trends from the ARMOR Surveillance Study (2009-2016). Clin Optom (Auckl). 2019;11:15-26. doi:10.2147/OPTO.S189115

24. Alter SJ, Sanfilippo CM, Asbell PA, DeCory HH. Antibiotic resistance among pediatric-sourced ocular pathogens: 8-year findings from the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. J Cataract Refract Surg. 2015;41(2):1841-1843. doi:10.1016/j.jcrs.2015.11.008

25. Asbell PA, Mah FS, Sanfilippo CM, DeCory HH. Antibiotic susceptibility of bacterial pathogens isolated from the aqueous and vireous humor in the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. J Infect. 2015;68(10):e510-518. doi:10.1097/INF.00000000000002206

26. Asbell PA, DeCory HH. Antibiotic resistance among bacterial conjunctival pathogens collected in the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. PLoS One. 2018;13(10):e0205814. doi:10.1371/journal.pone.0205814

27. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard. 8th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2009. CLSI document M07-A8.

28. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard. 9th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI document M07-A9.

29. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard. 10th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2015. CLSI document M07-A10.

30. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard. 11th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. CLSI document M07-A11.

31. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 19th Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2009. CLSI document M100-S19.

32. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 20th Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI document M100-S20.

33. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 21st Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2011. CLSI document M100-S21.

34. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 22nd Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI document M100-S22.

35. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 23rd Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2013. CLSI document M100-S23.

36. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 24th Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI document M100-S24.

37. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 25th Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2016. CLSI document M100-S26.

38. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: 26th Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. CLSI document M100-S28.

39. Tukey JW. Comparing individual means in the analysis of variance. Biometrics. 1949;5(2):99-114. doi:10.2307/3001913

40. Armitage P. Tests for linear trends in proportions and frequencies. Biometrics. 1955;11(3):375-386. doi:10.2307/3001775

41. Truong DT, Bui MT, Memon P, Cavanagh HD. Microbial keratitis at an urban public hospital: a 10-year update. J Clin Exp Ophthalmol. 2015;6(6):498. doi:10.4172/2155-9570.1000498

42. Jin H, Parker WT, Law NW, et al. Evolving risk factors and antibiotic sensitivity patterns for microbial keratitis at a large county hospital. Br J Ophthalmol. 2017;101(11):1483-1487. doi:10.1136/bjophthalmol-2016-310026

43. Oydanich M, Dingle TC, Hamula CL, Ghisa C, Asbell P. Retrospective report of antimicrobial susceptibility observed in bacterial pathogens isolated from ocular samples at Mount Sinai Hospital, 2010 to 2015. Antimicrob Resist Infect Control. 2017;6:29. doi:10.1186/s13756-017-0185-0

44. Peng MY, Cavallaro V, McLeod SD, Lietman TM, Rose-Nussbaumer J. Bacterial keratitis: isolated organisms and antibiotic resistance patterns in San Francisco, CA. Cornea. 2018;37(1):84-87. doi:10.1097/ICO.0000000000001417

45. Fintelmann RE, Hoskins EN, Lietman TM, et al. Topical fluoroquinolone use as a risk factor for in vitro fluoroquinolone resistance in ocular cultures.
E12 JAMA Ophthalmology Published online April 9, 2020 jamaophthalmology.com

Arch Ophthalmol. 2011;129(4):399-402. doi:10.1001/archophthalmol.2011.45

48. Hooper DC. Mechanisms of action and resistance of older and newer fluoroquinolones. Clin Infect Dis. 2000;31(suppl 2):S24-S28. doi:10.1086/314056

49. Kowalski RP. Is antibiotic resistance a problem in the treatment of ophthalmic infections? Expert Rev Ophthalmol. 2013;8(2):119-126. doi:10.1586/eop.13.7

50. Chen A, Praja A, Sinivasan M, et al. Does in vitro susceptibility predict clinical outcome in bacterial keratitis? Am J Ophthalmol. 2008;145(3):409-412. doi:10.1016/j.ajo.2007.11.004

51. Kaye S, Tuft S, Neal T, et al. Bacterial susceptibility to topical antimicrobials and clinical outcome in bacterial keratitis. Invest Ophthalmol Vis Sci. 2010;51(1):362-368. doi:10.1167/iovs.09-3933

52. Lalitha P, Sinivasan M, Manikandan P, et al. Relationship of in vitro susceptibility to moxifloxacin and in vivo clinical outcome in bacterial keratitis. Clin Infect Dis. 2012;54(10):1381-1387. doi:10.1093/ciidi/cis189

53. Doern GV, Brecher SM. The clinical predictive value (or lack thereof) of the results of in vitro antimicrobial susceptibility tests. J Clin Microbiol. 2011;49(9)(suppl):S11-S14. doi:10.1128/JCM.00580-11

54. Chiquet C, Maurin M, Altayrac J, et al. Correlation between clinical data and antibiotic resistance in coagulase-negative Staphylococcus species isolated from 68 patients with acute post-cataract endophthalmitis. Clin Microbiol Infect. 2015;21(6):592.e1-592.e8. doi:10.1016/j.cmi.2015.06.017

55. Olson R, Donnenfeld E, Bucci FA Jr, et al. Methicillin resistance of Staphylococcus aureus among healthcare and nonhealthcare workers in northeastern Ohio. J Med Microbiol. 2013;62(1):1782-1789. doi:10.1099/jmm.0.000635

56. Blaoude JM, Sanfilippo CM, Deyro HH. Incidence of polybacterial infections in three bacterial conjunctival studies and outcomes with besifloxacin ophthalmic suspension 0.6%. Invest Ophthalmol Vis Sci. 2019;60(9):245.

57. Aoki R, Fukuda K, Ogawa M, et al. Identification of causative pathogens in eyes with bacterial conjunctivitis by bacterial cell count and microbiota analysis. Ophthalmol. 2013;120(4):668-676. doi:10.1016/j.ophtha.2012.10.001

58. Tuft S. Polymicrobial infection and the eye. Br J Ophthalmol. 2006;90(3):257-258. doi:10.1136/bjo.2005.084295

59. Bianco N, Perencevich E, Li SS, et al; CDC National Healthcare Surveillance System (NHSS) Team. Epidemiology and surveillance of antimicrobial-resistant bloodstream infections caused by methicillin-resistant Staphylococcus aureus in the United States from the LEADER Surveillance Program, 2010 to 2016. Open Forum Infect Dis. 2019;6(suppl 1):547-553. doi:10.1093/ofid/ofy343

60. Tuft S. Dropless cataract surgery: an overview. Liegner JT. Dropless cataract surgery: an overview. Arch Ophthalmol. 2011;129(4):399-402. doi:10.1001/archophthalmol.2011.45

61. Sader HS, Mendes RE, Streit JM, Flamm RK. Antimicrobial susceptibility trends among Staphylococcus aureus isolates from US hospitals: results from 7 years of the Ceftaroline (AWARE) Surveillance Program, 2010 to 2016. Antimicrob Agents Chemother. 2018;62(2):e01555-17. doi:10.1128/AAC.01555-17

62. Sader HS, Mendes RE, Streit JM, Flamm RK. Five-year summary of in vitro activity and resistance mechanisms of linezolid against clinically important gram-positive cocci in the United States from the LEADER Surveillance Program (2011 to 2015). Antimicrob Agents Chemother. 2016;61(7):e00609-e00617. doi:10.1128/AAC.00609-17

63. Zhang Z, Chen M, Yu Y, Pan S, Liu Y. Antimicrobial susceptibility among gram-positive and gram-negative blood-borne pathogens collected between 2012-2016 as part of the Tigecycline Evaluation and Surveillance Trial. Antimicrob Resist Test Infect Control. 2018;7;152. doi:10.1186/s13756-018-0441-y

64. Giammanco A, Cala C, Fasciana T, Dzwicky MJ. Global assessment of the activity of Tigecycline against multidrug-resistant gram-negative pathogens between 2004 and 2014 as part of the Tigecycline Evaluation and Surveillance Trial. mSphere. 2017;2(1):e00310-e00316. doi:10.1128/mSphere.00310-16

65. Diekema DJ, Pfaller MA, Shortridge D, Zervos M, Jones RN. Twenty-year trends in antimicrobial susceptibilities among Staphylococcus aureus from the SENTRY Antimicrobial Surveillance Program. Open Forum Infect Dis. 2019;6(suppl 1):547-553. doi:10.1093/ofid/ofy270

66. Sader HS, Mendes RE, Li J, Denys G, Flamm RK, Jones RN. Antimicrobial susceptibility of Streptococcus pneumoniae from North America, Europe, Latin America, and the Asia-Pacific Region: results from 20 years of the SENTRY Antimicrobial Surveillance Program (1997-2016). Open Forum Infect Dis. 2019;6(suppl 1):514-523. doi:10.1093/ofid/ofd263

67. Shortridge D, Gales AC, Streit JM, Huband MD, Tsakris A, Jones RN. Geographic and temporal patterns of antimicrobial resistance in Pseudomonas aeruginosa over 20 years in the SENTRY Antimicrobial Surveillance Program, 1997-2016. Open Forum Infect Dis. 2019;6(suppl 1):563-568. doi:10.1093/ofid/ofd343