# Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surveillance Report 2008

Oregon Active Bacterial Core Surveillance (ABCs)
Office of Disease Prevention & Epidemiology
Oregon Department of Human Services
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## Background

Active Bacterial Core surveillance (ABCs) is a core component of the Emerging Infections Program (EIP) Network sponsored by the Centers for Disease Control and Prevention (CDC). The purpose of the ABCs program is to determine the incidence and epidemiologic characteristics of invasive disease due to *Haemophilus influenzae*, *Neisseria meningitidis*, group A *Streptococcus* (GAS), group B *Streptococcus* (GBS), *Streptococcus pneumoniae*, and methicillin-resistant *Staphylococcus aureus* (MRSA). The entire EIP Network represents over 38 million persons in 10 surveillance areas around the United States. More information on the EIP/ABCs Network is found at: http://www.cdc.gov/abcs/index.html.

In Oregon, the surveillance area for MRSA comprises the tri-county (Clackamas, Multnomah, and Washington) Portland metropolitan area with a 2008 estimated population of 1,614,465. More information on the Oregon ABCs program is found at: http://oregon.gov/DHS/ph/acd/abc.shtml.

## Methods

An invasive MRSA infection* is defined as the isolation of MRSA from a normally sterile body site in a tri-county resident. Tri-county hospital laboratories submit MRSA isolates to the Oregon State Public Health Laboratory (OSPHL) for identification. The OSPHL forwards a subset of these isolates to a CDC laboratory for further characterization and antimicrobial susceptibility testing. Additional cases are identified through regular laboratory record reviews. Health record reviews of each case allow standardized reports of demographic characteristics, clinical syndrome manifestations, underlying conditions and diseases, healthcare-associated risk factors, and illness outcome.

Cases are classified based on the presence of established healthcare risk factors and time of culture collection in relation to hospital admission. Healthcare-onset (HO-) MRSA infections are those in which the initial culture was collected >48 hours after hospital admission; healthcare-associated, community-onset (HACO-) MRSA cases are those in which the initial culture was collected ≤48 hours after hospital admission or evaluation and the medical chart indicates one or more of the following risk factors: previous MRSA colonization or infection, presence of an invasive device or catheter at the time of admission or evaluation, or hospitalization, surgery, dialysis, or resident of a long-term care facility (LTCF) within the year preceding the index culture date; and community-associated (CA-) MRSA cases are those in which the initial culture was collected ≤48 hours after hospital admission or evaluation and none of the above risk factors are noted in the medical record.

Additional technical information on surveillance methodology, including data elements collected, healthcare risk factors, clinical manifestations, and underlying diseases and conditions can be found at the EIP/ABCs Network website listed above.

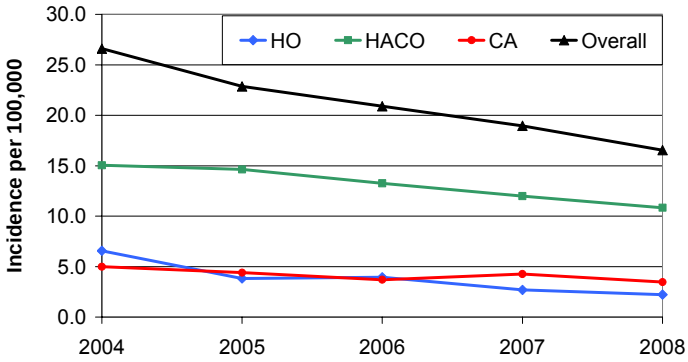
* MRSA *infection* is the invasion of bacteria in the tissues of the host leading to clinical signs and symptoms of illness or infection whereas *colonization* refers to the presence of bacteria but without tissue damage and signs of illness or infection. Colonized patients are also known as asymptomatic carriers.

## Surveillance Results

*Descriptive Epidemiology*

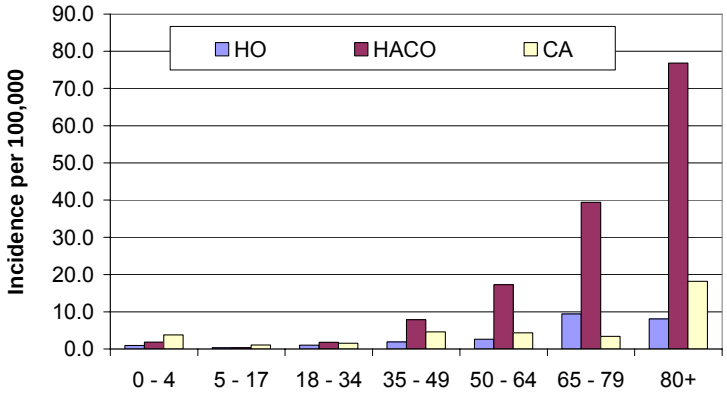
In 2008, we identified 267 cases of invasive MRSA disease for an overall incidence of 16.5/100,000 persons (Figure 1). Of these, 31 (12%) were recurrent cases, reported in those with a previous invasive MRSA infection. Since surveillance began in 2004, when 405 cases were reported (26.6/100,000), the incidence of invasive MRSA disease has decreased 38 percent. The mean and median ages of cases reported in 2008 were 59 and 60 years, respectively (range: 0-96 years). Fifty-five percent of all reported cases were male; of the 46 percent of cases for which race was reported, 86 percent were white, 9 percent were black, and 5 percent were of another race. The highest incidence of invasive MRSA disease occurred among residents of Multnomah county (22.3/100,000); followed by residents in Clackamas (16.2/100,000) and Washington (8.8/100,000) counties. Forty-one cases were fatal, for mortality and case fatality rates of 2.5/100,000 and 15 percent, respectively. The case fatality rate has not changed since 2004. The mean and median ages of death due to invasive MRSA infection were equivalent at 70 years, with a range of 23 to 95 years. Risk of death was associated with increasing age (p=0.0003). Among those who died, 68 percent were 65 and older, and 90 percent were 50 and older; one death (2%) occurred among those younger than 35 years of age.

**Figure 1: Incidence of Invasive MRSA Cases, by Infection Type, 2004-2008.**




Of the 267 total cases reported, 36 (13%) were HO (2.2/100,000); 175 (66%) were HACO (10.8/100,000); and 56 (21%) were CA (3.5/100,000). Since 2004, the incidence of HO has decreased 66 percent, that of HACO has decreased 28 percent and that of CA has decreased 31 percent (Figure 1). HO cases have comprised a *decreasing* proportion of all MRSA cases, from 25 percent in 2004 to 13 percent in 2008 (test for trend, p=0.0001), while HACO cases have comprised an *increasing* proportion of all MRSA cases, from 57 percent in 2004 to 66 percent in 2008 (p=0.0298). The proportion of CA cases did not change significantly over time.

**Figure 2: Incidence of Invasive MRSA, by Infection Type and Age, 2008.**




Epidemiologic classification of cases as HO, CA, or HACO-MRSA was associated with age (Figure 2). The mean and median ages for CA (48 and 49, respectively) were significantly lower than those seen for HACO (63 for each) (p<0.0001), but not for HO (56 and 60, respectively). Classification was not associated with sex or race. Mortality was highest among HACO cases (1.5/100,000), followed by HO (0.7/100,000) and CA (0.3/100,000); case fatality was highest among HO (33%), followed by HACO (14%) and CA (9% each). However, after adjusting for age, the

odds of death were 1.6 times *lower* (Odds Ratio [OR] 1.6; 95% Confidence Interval [CI] 1.0, 2.5]) for HACO cases than CA cases, and almost two times *higher* (OR 1.8; 95% CI [1.2, 2.9]) for HO cases than CA cases.

*Clinical Manifestations*

The most common clinical manifestations of invasive MRSA infections reported in 2008 are displayed in Table 1. The profiles for these syndromes are not significantly different from those reported during 2004-2007 with the exception of arthritis and endocarditis ($p<0.0001$ for both syndromes). Cases with healthcare-associated risk factors (including HO and HACO) were more likely to manifest as bacteremia (OR 2.2; CI 1.0, 4.5) than CA cases, while CA cases were more likely to manifest as an abscess from a normally sterile site (OR 2.2; CI 1.1, 4.8) and cellulitis (OR 2.4; CI 1.1, 4.9) than HO and HACO cases. Other syndromes were reported similarly across infection types. Compared with other clinical manifestations, a fatal outcome was almost three times more likely with pneumonia (CI 1.2, 5.7). This effect was independent of age and infection type.

**Table 1: Common Clinical Manifestations of Invasive MRSA Cases, by Infection Type, 2008.**[†]

| | HO N (%) | HACO N (%) | CA N (%) | Total N (%) |
|---|---|---|---|---|
| Bacteremia | 31 (86) | 154 (88) | 43 (77) | 228 (85) |
| Pneumonia* | 11 (31) | 26 (15) | 10 (18) | 47(18) |
| Cellulitis | 3 (8) | 23 (13) | 14 (25) | 40 (15) |
| Abscess | 2 (6) | 23 (13) | 13 (23) | 38 (14) |
| Osteomyelitis | 3 (8) | 18 (10) | 5 (9) | 26 (10) |
| Urinary Tract Infection | 0 (0) | 13 (7) | 3 (5) | 16 (6) |
| Bursitis | 0 (0) | 7 (4) | 4 (7) | 11 (4) |
| Arthritis | 3 (8) | 4 (2) | 3 (5) | 10 (4) |
| Empyema | 1 (3) | 2 (1) | 6 (11) | 9 (3) |
| Endocarditis | 0 (0) | 4 (2) | 2 (4) | 6 (2) |
| Peritonitis | 2 (6) | 2 (1) | 1 (2) | 5 (2) |
| Meningitis | 0 (0) | 2 (1) | 1 (2) | 3 (1) |
| None | 4 (11) | 5 (3) | 6 (11) | 15 (6) |

[†] Some cases report more than 1 syndrome.

* Only those cases of pneumonia with a sterile site isolate are included. Sputum or endotracheal aspirates are not considered sterile sites.

*Underlying Conditions*

Almost all (94%) invasive MRSA cases were in individuals reporting one or more underlying diseases or conditions (Table 2). Cases with healthcare-associated risk factors (including HO and HACO) were more likely to report diabetes (OR 2.8; CI 1.4, 5.7), renal failure (OR 5.4; CI 1.9, 15.6), cardiovascular disease or congestive heart failure (CVD/CHF) (OR 5.7; CI 2.2, 15.0), COPD (OR 4.1; CI 1.4, 12.0), solid organ malignancy (OR 8.8; CI 1.2, 65.8), and stroke (OR 9.1; CI 1.2, 68.4) than CA cases.

**Table 2: Common Underlying Conditions Reported Among Invasive MRSA Cases, by Infection Type, 2008.**[†]

| | HO N (%) | HACO N (%) | CA N (%) | Total N (%) |
|---|---|---|---|---|
| Diabetes | 9 (25) | 83 (47) | 12 (21) | 104 (39) |
| CVD/CHF | 10 (28) | 66 (38) | 5 (9) | 81 (30) |
| Renal Failure | 4 (11) | 58 (33) | 4 (7) | 66 (25) |
| COPD | 9 (25) | 42 (24) | 4 (7) | 55 (21) |
| Smoking | 5 (14) | 34 (19) | 16 (29) | 55 (21) |
| Immunosuppressive Therapy | 8 (22) | 35 (20) | 5 (9) | 48 (18) |
| Obesity | 5 (14) | 30 (17) | 8 (14) | 43 (16) |
| Stroke | 4 (11) | 26 (15) | 1 (2) | 31 (12) |
| Solid Organ Malignancy | 3 (8) | 26 (15) | 1 (2) | 30 (11) |
| Asthma | 4 (11) | 17 (10) | 5 (9) | 26 (10) |
| Alcohol Abuse | 5 (14) | 12 (7) | 6 (11) | 23 (9) |
| IVDU | 0 (0) | 9 (5) | 8 (14) | 17 (6) |
| None | 4 (11) | 5 (3) | 6 (11) | 15 (6) |

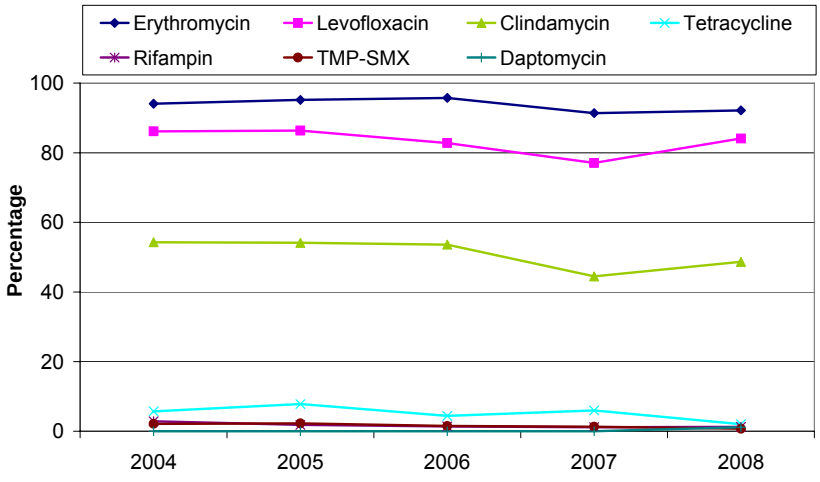
[†] Some cases report more than 1 condition. Not all conditions shown.

After controlling for age and infection type, only cardiovascular disease (or congestive heart failure) and immunosuppressive therapy were significantly associated with a fatal outcome ([adjusted OR 2.4; CI 1.1, 5.2] and [adjusted OR 2.5; CI 1.1, 5.8], respectively).

*Antibiotic Susceptibilities*

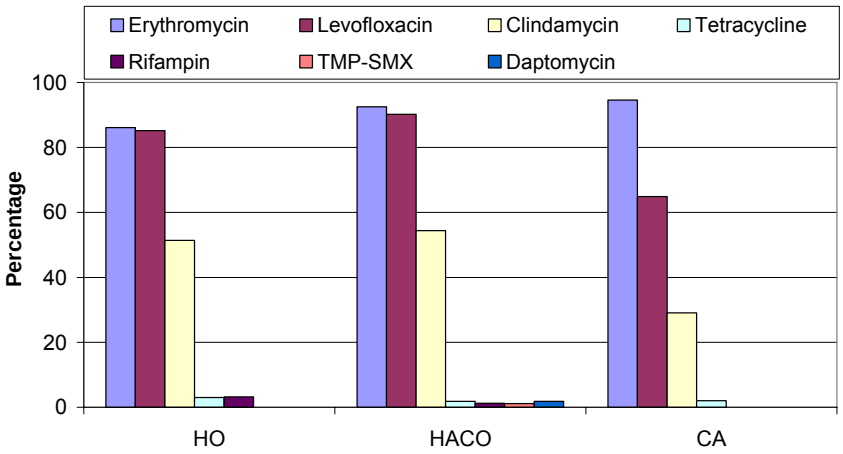
By definition, all MRSA isolates are resistant to β-lactam antibiotics, including penicillin and methicillin. Additionally, among isolates tested, a proportion displayed decreased susceptibility (intermediate or full resistance) to several commonly assayed antibiotics in 2008, including: erythromycin (92%, n=267), levofloxacin (84%, n=176), clindamycin (49%, n=261), tetracycline (2%, n=245), rifampin (1%, n=238), daptomycin (1%, n=171) and trimethoprim-sulfa (1%, n=266). Since 2004, the percentages of invasive MRSA isolates with decreased susceptibility to these select antibiotics have remained relatively stable (Figure 3). No isolates during this time period have displayed decreased susceptibility to linezolid or vancomycin. Resistance to antibiotics was not associated with a fatal disease outcome.

**Figure 3: Percentage of Invasive MRSA Isolates with Decreased Susceptibility (Intermediate or Full Resistance) to Select Antibiotics, 2004-2008.**




In 2008, HO and HACO cases, combined, were three times more likely to display decreased susceptibility (intermediate or full resistance) to clindamycin (95% CI 1.5, 5.4) and four times more likely to display decreased susceptibility to levofloxacin (95% CI 1.9, 10.6) than community-associated cases (Figure 4). Other differences were not statistically significant or were unable to be tested due to insufficient sample size.

**Figure 4: Percentage of Invasive MRSA Isolates with Decreased Susceptibility (Intermediate or Full Resistance) to Select Antibiotics, by Infection Type, 2008.**

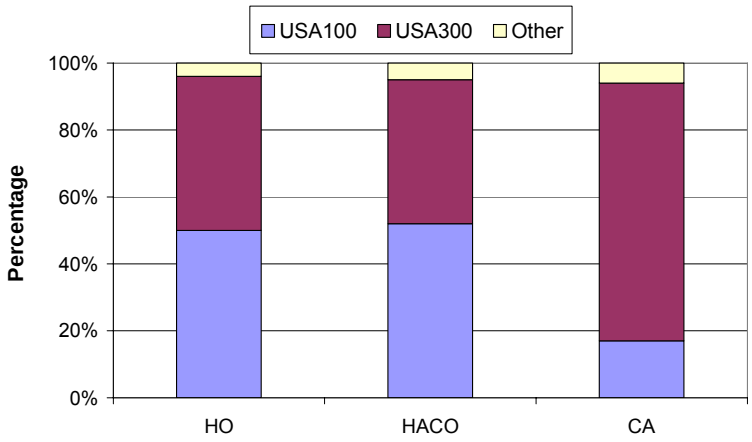


*Strain Typing*

Strain typing, by pulsed-field gel electrophoresis (PFGE), was completed for a subset of invasive MRSA cases (184/267 (69%)). PFGE results were available for over 90 percent of these available isolates (169/184). Of the 169 isolates, 75 (44%) were USA100, 86 (51%) were USA300, and eight (5%) were other types (i.e. USA200, 500, 800, 900, 1000)**.**

Figure 5 displays the percentage of cases of isolates determined to be USA100, USA300, other strain type, by epidemiologically classified infection type.

**Figure 5: Percentage of Isolates Typed as USA100, USA300, and Other, by Infection Type, 2008.**




Among cases for which PFGE results were available, bacteremia was by far the most common clinical manifestation among those with USA100 and USA300 (93% and 97%, respectively). All other clinical syndromes were present in fewer than 25 percent of these cases. Among cases with USA100, diabetes (50%), cardiovascular disease (51%), and renal failure (37%) were the most common underlying conditions. Among those with USA300 type, diabetes (34%),smoking (26%), and cardiovascular disease (24%) were the most common underlying conditions.

*Expanded HACO Analysis*

The distribution of healthcare risk factors among HACO cases is shown in Table 3. Since 2004, the proportion of cases having been hospitalized or having surgery during the year prior to the date of MRSA culture significantly increased, while the proportion of cases having a central venous catheter in place at the time of culture or a previously documented MRSA infection significantly decreased ($p<0.01$ for each). Among HACO cases in 2008, 38 (22%) had one healthcare risk factor; 58 (33%) had two; 52 (30%) had three; 18 (10%) had four; 9 (5%) had five; and none had all six risk factors. The proportion of cases with multiple reported risk factors has remained stable since 2004.

**Table 3: Distribution of Healthcare Risk Factors among HACO Cases, 2004-2008.**

| Risk Factor | Overall N (%) |
|---|---|
| Dialysis[1] | 213 (21) |
| Central Venous Catheter[2] | 222 (22) |
| LTCF Residence[1] | 385 (37) |
| Prior Surgery[1] | 634 (62) |
| Hospitalization[1] | 837 (81) |
| Previous MRSA[3] | 357 (35) |

[1] Within year before date of culture
[2] In place at time of culture
[3] Ever documented infection or colonization

Dialysis, a central venous catheter (CVC) in place at the time of culture, and residence in a long-term care facility (LTCF) within the year before the date of culture, were associated with bacteremia independent of age (Table 4). Surgery was associated with abscesses from a normally sterile site and osteomyelitis. Also, the presence of multiple risk factors was significantly associated with bacteremia (OR 1.4; CI 1.2, 1.7).

**Table 4: Adjusted Odds Ratios of Positive and Significant Associations between Healthcare Risk Factors and Clinical Manifestations of HACO Disease, 2004-2008.[1]**

| | Dialysis | CVC | LTCF | Surgery |
|---|---|---|---|---|
| Bacteremia | 5.2 (1.8, 14.8) | 6.8 (2.4, 19.6) | 2.5 (1.5, 4.1) | |
| Abscess | | | | 2.6 (1.5, 4.5) |
| Osteomyelitis | | | | 1.8 (1.1, 3.0) |

[1]Adjusted for age, with hospitalization within year prior to culture date as the referent group; those with previous documented MRSA colonization or infection only were excluded.

## Discussion

Five full years of surveillance have allowed for a better characterization of the epidemiology of invasive MRSA disease in the Portland tri-county metropolitan area. Over this time, the incidence of invasive MRSA disease has decreased substantially, with the greatest decrease seen among HO cases. With the exception of invasive disease due to *N. meningitidis*, which has been decreasing nationally over the past several years, the stable incidence rates of other pathogens under surveillance through ABCs support a true decreasing incidence of invasive MRSA disease. The reasons for this decrease are currently unknown and will be the subject of further investigation through the ABCs program.

Results from 2008 are consistent with previous years, in that invasive MRSA disease manifests largely in those with an underlying condition or behavior that is directly related to their infection. Almost all cases in those with healthcare-defining risk factors were in those with underlying chronic diseases, such as diabetes, cardiovascular disease, renal failure, etc., that require frequent encounters with the health care system and/or invasive medical procedures. That HO and HACO cases generally increase with age and occur primarily among those 65 and older reflect the increasing prevalence of these diseases among the elderly population.

Looking at disease manifestation along with underlying conditions, several patterns emerge. For example, bacteremia commonly occurs in those with systemic conditions, such as diabetes and cardiovascular disease, which involve direct introduction of the bacteria into the blood stream through medical interventions. While type of surgery is not collected on the form, it is likely that localized joint and bone infections in the area of surgery occur after orthopedic surgeries in those areas.

The more frequent susceptibility of CA-MRSA isolates to clindamycin is consistent with the fact that a greater proportion of these are USA300 PFGE type, which usually carries fewer resistance genes than healthcare associated PFGE types. Clindamycin is not generally used as primary therapy for invasive MRSA disease. Intermediate or full resistance to vancomycin has not been detected among invasive MRSA isolates in Oregon, based on accepted breakpoint minimum inhibitory concentration (MIC) values. There are numerous reports in the medical literature of possible decreasing effectiveness of vancomycin due to small but significant

increases in resistance of MRSA to this drug, reflected in slowly rising MIC values. However, since methods for determining MICs may vary between laboratories, and isolates are generally reported as either “susceptible” or not, the extent vancomycin MICs have been increasing over time among MRSA isolates in Oregon is unclear. Additional characterization of the MRSA isolates is required to answer this question.

The use of molecular strain type information has demonstrated an increase in the traditional ‘community-associated’ USA300 strain among cases classified epidemiologically as healthcare-associated. This finding raises two possibilities: USA300 could increasingly be transmitted within the healthcare setting – at least among those with traditional healthcare risk factors – an observation supported in recently-published literature; or cases may be misclassified as healthcare-associated, due to the presence of the established ‘risk factors’, when they were actually acquired in the community.[1,2] Although both factors likely play some role, further investigation will be needed to better understand MRSA infection and invasive disease in the healthcare and community settings.

## References


1. Popovich KJ, Weinstein RA, Bota B. Are community-associated Methicillin-Resistant *Staphylococcus aureus* (MRSA) strains replacing traditional nosocomial MRSA strains? *Clin Infect Dis*. 2008;46:787-94.
2. Boyce JM. Community-associated Methicillin-Resistant *Staphylococcus aureus* as a cause of health care-associated infection. *Clin Infect Dis*. 2008;46:795-8.