Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surveillance Report 2007

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 ABCs 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), and methicillin-resistant *Staphylococcus aureus* (MRSA). The entire EIP Network represents 39.5 million persons in 10 surveillance areas around the United States. More information on the EIP/ABCs Network is found at: http://www.cdc.gov/ncidod/dbmd/abcs.

In Oregon, the surveillance area for MRSA comprises the Tri-County (Clackamas, Multnomah, and Washington) Portland metropolitan area with a 2007 estimated population of 1,596,370. 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 for strain typing (i.e. USA100, USA300, etc.) and forwarding 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 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.

Surveillance Results

Descriptive Epidemiology

In 2007, we identified 300 cases of invasive MRSA disease for an overall incidence of 18.8/100,000 persons (Figure 1). Of these, 30 (10%) were recurrent cases, reported in those with a previous invasive MRSA infection. Since surveillance began in 2004, when 404 cases were reported (26.5/100,000), the incidence of invasive MRSA disease has decreased 29%. The mean and median ages of cases reported in 2007 were equivalent at 57 years (range: 0-96 years). Fifty-eight percent of all reported cases were male; of the 64% of cases for which race was reported, 88% were white, 9% were black, and 3% were of another race. The highest incidence of invasive MRSA disease occurred among residents of Multnomah County (25/100,000); followed by residents in Clackamas (14/100,000) and Washington (13/100,000) Counties. Thirty-eight cases were fatal, for mortality and case fatality rates of 2.4/100,000 and 13%, respectively. The case fatality rate has not changed since 2004. The mean and median ages of death due to invasive MRSA infection were 67 and 72 years, respectively, with a range of 0 to 96 years. However, fatal outcome was not distributed uniformly across the age spectrum: whereas two deaths (5%) were reported among those younger than 35 years of age (case fatality rate, 5%), 31 (82%) were reported in those 50 and older and 23 (61%) were reported in those 65 and older, among whom the case fatality rate was 20%. Consequently, increasing age was associated with a fatal outcome from invasive MRSA infection (p=0.0027).

Figure 1: Incidence of Invasive MRSA Cases, by Infection Type, 2004-2007.

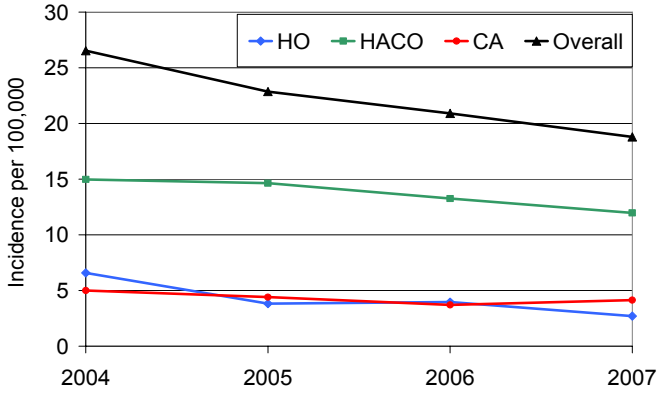
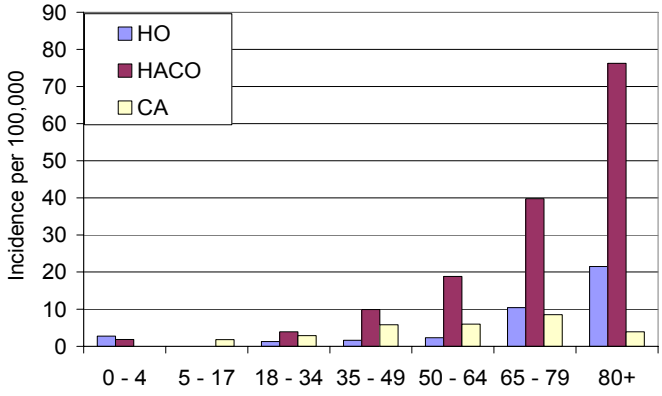


Figure 2: Incidence of Invasive MRSA, by Infection Type and Age, 2007.



Of the 300 total cases reported, 43 (14%) were HO (2.7/100,000); 191 (64%) were HACO (12.0/100,000); and 66 (19%) were CA (4.1/100,000). Since 2004, the incidence of HO has decreased 59%, that of HACO has decreased 20% and that of CA has decreased 17% (Figure 1). HO cases have comprised a decreasing proportion of all MRSA cases, from 25% in 2004 to 14% in 2007 (test for trend, p=0.0016), while the proportion of the other infection types did not change significantly. Although race and sex did not differ significantly by infection type, such a difference, by age, was seen (Figure 2). The mean and median ages for CA (47 for each) were significantly lower than those seen for HO (57 and 65, respectively) or HACO (60 for each) (p<0.0001). Mortality was highest among HACO cases (1.5/100,000), followed by HO (0.6/100,000) and CA (0.3/100,000); case fatality was highest among HO (23%), followed by HACO (13%) and CA (6% each). However, after adjusting for age, the odds of death were almost two times lower (Odds Ratio [OR] 1.8; 95% Confidence Interval [CI] 1.1, 2.9]) for HACO cases than CA cases; the odds of death for HO cases was not significantly different than those for CA cases.

Clinical Manifestations

The most common clinical manifestations of invasive MRSA infections reported in 2007 are provided in Table 1. This profile is not significantly different from cases reported during 2004-2006. Cases with healthcare-associated risk factors (including HO and HACO) were more likely to manifest as bacteremia (OR 2.5; CI 1.3, 4.7) than CA cases, while CA cases were more likely to manifest as sterile abscess (OR 2.0; CI 1.0, 3.8), cellulitis (OR 2.2; CI 1.1, 4.3), bursitis (OR 14.1; CI 4.4, 45.0), and endocarditis (OR 6.5; CI 2.4, 17.5) than HO and HACO cases. Pneumonia and empyema were reported similarly across infection types. Compared with other clinical manifestations, a fatal outcome was ten times more likely with bacteremia (CI 1.3, 75.0) and three times more likely with pneumonia (CI 1.2, 5.6). This effect was independent of age and infection type.

Table 1: Common clinical manifestations of invasive MRSA cases, by infection type, 2007.[†]

	HO	HACO	CA	Total
Bacteremia	36 (84)	165 (86)	47 (71)	248 (83)
Pneumonia	10 (23)	29 (15)	17 (26)	56 (19)
Sterile Abscess	4 (9)	31 (16)	17 (26)	52 (17)
Cellulitis	1 (2)	27 (14)	15 (23)	43 (14)
Bursitis	1 (2)	3 (2)	13 (20)	17 (6)
Endocarditis	0 (0)	7 (4)	11 (17)	18 (6)
Empyema	5 (12)	4 (2)	3 (5)	12 (4)
Osteomyelitis	1 (2)	20 (10)	9 (9)	27 (9)

[†] Reported in at least 10% of cases of at least one infection type. Some cases report more than 1 syndrome. Not all syndromes shown.

Underlying Conditions

Almost all (95%) of 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 3.0; CI 1.6, 5.9); renal failure (OR 11.5; CI 2.7, 48.5); cardiovascular disease or congestive heart failure (CVD/CHF) (OR 6.6; CI 2.5, 17.0); solid organ malignancy (OR 6.8; CI 1.6, 28.9), and stroke (OR 10.3; CI 1.4, 76.8) than CA cases, while CA cases were more likely to report intravenous drug use (IVDU) (OR 3.6; CI 1.8, 7.3) and were more likely not to have any underlying condition reported (OR 4.5; CI 1.6, 13.0) than HO and HACO cases. After controlling for age and infection type, only immunosuppressive therapy was significantly associated with a fatal outcome (adjusted OR 2.5; CI 1.1, 5.7).

Table 2: Common underlying conditions reported among invasive MRSA cases, by infection type, 2007[†]

	HO N (%)	HACO N (%)	CA N (%)	Total N (%)
Diabetes	10 (23)	90 (47)	13 (20)	113 (38)
Smoking	11 (26)	58 (30)	26 (39)	95 (32)
Renal Failure	7 (16)	55 (29)	2 (3)	64 (21)
CVD/CHF	12 (28)	70 (37)	5 (8)	87 (29)
IVDU	0 (0)	22 (12)	18 (27)	40 (13)
Immunosuppressive Therapy	10 (23)	28 (15)	5 (8)	43 (14)
COPD	8 (19)	31 (16)	6 (9)	45 (15)
Solid Organ Malignancy	7 (16)	34 (18)	2 (3)	43 (14)
Obesity	7 (16)	30 (16)	5 (8)	42 (14)
Stroke	3 (7)	29 (15)	1 (2)	33 (11)
Alcohol Abuse	6 (14)	18 (9)	4 (6)	28 (9)
None	3 (7)	4 (2)	8 (12)	15 (5)

[†] Some cases report >1 condition; not all conditions shown.

In 2007, cases reported with presence of commonly-reported underlying conditions were associated with the clinical manifestation of invasive MRSA disease, as shown in Table 3.

Table 3: Associations between common underlying conditions and clinical manifestation of invasive MRSA disease, 2007[†].

	Bacteremia	Pneumonia	Osteo.	Abscess	Endocarditis
Diabetes	4.0 (1.8, 8.9)		2.2 (1.0, 5.0)		
Renal Failure	2.9 (1.1, 7.7)				
IVDU			2.5 (1.0, 6.5)	4.1 (2.0, 8.6)	6.3 (2.3, 17.0)
Immuno. Therapy		2.5 (1.2, 5.1)			
Stroke	7.6 (1.0, 56.6)				

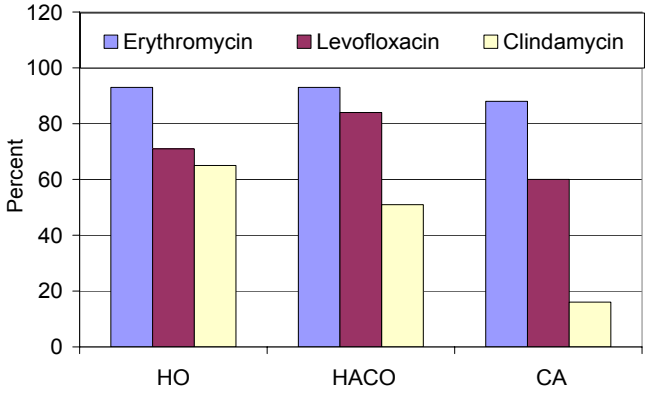
[†]The upper value is the univariate odds ratio between the respective underlying condition and clinical manifestation; the lower number, in parenthesis, is the 95% confidence interval. Only positive, significant associations are shown.

Antibiotic Susceptibilities

By definition, all MRSA isolates are resistant to β-lactam antibiotics, including penicillin and methicillin. Additionally, a proportion of isolates displayed decreased susceptibility (intermediate or full resistance) to several commonly assayed antibiotics in 2007, including: erythromycin (92%), levofloxacin (77%), clindamycin (45%), tetracycline (6%), and trimethoprim-sulfa and rifampin (1% each). No isolates displayed decreased susceptibility to vancomycin. The proportion of isolates with decreased susceptibility to these antibiotics has not changed since 2004 and decreased susceptibility to antibiotics was not associated with a fatal disease outcome.

In 2007, HO and HACO cases, combined, were three times more likely (95% CI 1.2, 7.6) to display decreased susceptibility to levofloxacin and six times more likely to display decreased susceptibility to clindamycin (95% CI 2.9, 12.2) than community-associated cases (Figure 3). Although a greater proportion of HO and HACO cases also displayed decreased susceptibility to erythromycin, this difference was not statistically significant.

Figure 3: Percentage of invasive MRSA isolates with intermediate or full resistance to select antibiotics, by infection type, 2007.



Strain Typing

Strain typing, by pulsed-field gel electrophoresis (PFGE), was completed for a subset of invasive MRSA cases and PFGE results are available for 145/300 (48%) cases reported in 2007, with no difference in the proportion of cases with isolate PFGE results, by infection type (p=0.41).

Of the 145 isolates, 52 (36%) of isolates were USA100, 87 (60%) were USA300, and 6 (4%) were another type. The proportion of isolates identified as USA100 has decreased 36% since 2005, from 27% to 17% in 2007 (p=0.004). Of the 139 isolates determined to be either USA100

(37%) or USA300 (63%), there was no difference between the strains in the proportion of cases with a fatal outcome.

Figure 4: Percentage of isolates typed as USA100 and USA300, by infection type, 2007.

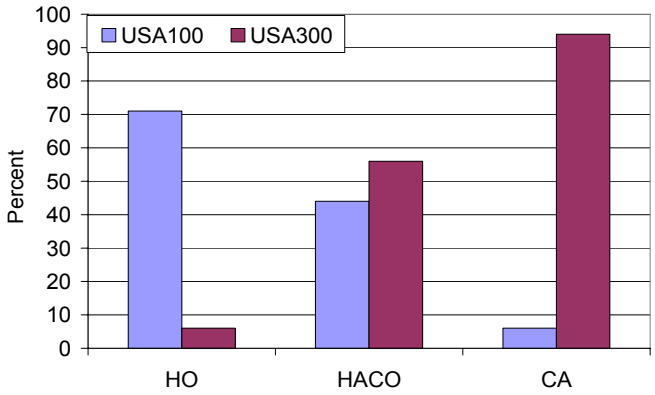


Figure 4 displays the percentage of cases of isolates determined to be USA100 or USA300, by epidemiologically classified infection type. For the first time, in 2007, a greater proportion of HACO cases were USA300 than USA100. Strain type is significantly associated with age ($p<0.0001$), with the mean and median ages of cases due to USA100 (69 and 74 years, respectively) higher than those due to USA300 (48 and 49, respectively). This significant association between age and strain type was independent of the effect of infection type.

Among cases for which isolate PFGE results were available, USA100 comprised 63% of urinary tract infections, 40% of cellulitis cases, 38% of bacteremia cases, 33% of osteomyelitis cases, 32% of cases presenting as pneumonia, 31% of endocarditis cases, 22% of arthritis cases, and 17% of internal abscesses. None of these clinical manifestations, however, were significantly associated with strain type. Strain type did significantly ($p<0.05$) differ by underlying condition: USA100 was identified in a higher proportion of cases with immunsuppressive therapy (79%), renal insufficiency (66%), cardiovascular disease (63%), COPD (63%), and stroke (65%); USA300 was identified in a higher proportion of cases with IVDU (95%) and smoking (80%). While cases with no reported underlying conditions also had a higher proportion of USA300 isolates (88%), the association was not significant, likely due to a small sample size.

Decreased susceptibility to levofloxacin was found among all USA100 strains and 68% of USA300 strains, while decreased susceptibility to clindamycin was found among 84% of USA100 strains and 9% of USA300 strains; both differences are significant at $p\leq0.0002$. No other differences in decreased susceptibility to antibiotics were seen by strain type.

Expanded HACO Analysis

The distribution of healthcare risk factors among HACO cases is shown in Table 4. Since 2004, the proportion of cases having been hospitalized and having surgery during the year prior to the date of MRSA culture significantly increased, while the proportion of cases having had dialysis significantly decreased ($p<0.03$ for each). Among HACO cases, 36 (19%) had one healthcare risk factor; 67 (35%) had two; 47 (25%) had three; 30 (16%) had four; 10 (5%) had five; and 1 (1%) had all six. The proportion of cases with multiple reported risk factors has remained stable since 2004.

Table 4: Distribution of healthcare risk factors among HACO cases, 2004-2007.

Risk Factor	Overall N (%)
Dialysis[1]	174 (20)
Central Venous Catheter[2]	207 (24)
LTCF Residence[1]	324 (38)
Prior Surgery[1]	510 (60)
Hospitalization[1]	686 (80)
Previous MRSA[3]	320 (37)

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

Independent of age, dialysis and residence in a long-term care facility (LTCF) within the year before the date of culture and a central venous

Table 5: Adjusted odds ratios of significant, positive associations between healthcare risk factors and clinical manifestations and isolate strain type of HACO disease, 2004-2007.[1]

	Dialysis	CVC	LTCF	Surgery
Bacteremia	7.3 (1.7, 32.4)	5.9 (2.0, 17.2)	2.1 (1.3, 3.5)	
Abscess				3.2 (1.6, 6.3)
Osteomyelitis				1.7 (1.0, 3.0)
USA100		2.2 (1.3, 3.8)	2.2 (1.5, 3.3)	

[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.

catheter (CVC) in place at the time of culture were independently associated with bacteremia; the latter two risk factors were also associated with USA100 isolate strain type (Table 5). Surgery was associated with sterile abscess and osteomyelitis; and USA100 isolate strain type was associated with having a CVC in place at the time of culture and LTCF residence within a year before the date of culture. The presence of multiple risk factors also a factor: the presence of each additional risk factor was significantly associated with bacteremia (OR 1.4; CI 1.1, 1.6) and USA100 isolate strain type (OR 1.2; CI 1.1, 1.4).

Discussion

Four 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 decreases seen among HO and HACO cases. With the exception of invasive disease due to *N. meningitidis*, which has been decreasing nationally over the past several years, that the incidence rates of other pathogens under surveillance through ABCs have not shown similar decreases supports 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 2007 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 renal failure, diabetes, cardiovascular disease, etc., that require frequent encounters with the health care system and/or invasive medical procedures. That HO and HACO cases increase with age and occur primarily among those 65 and older reflect the increasing prevalence of these diseases among this population. Among CA cases, IVDU is the primary risk factor for invasive MRSA disease. Based on unpublished estimates of the number of persons who inject drugs in the Portland area, the risk of invasive MRSA disease in this population is 1 in 300 to 1 in 2,600. In contrast, the risk of invasive MRSA disease among those in the general population who do not inject drugs is extremely low, estimated at 1 in 35,000. Looking at disease manifestation along with underlying conditions, several patterns emerge. For instance, bacteremia commonly occurs in those with systemic conditions, such as diabetes and renal failure, which involve direct introduction of the bacteria into the blood stream through medical interventions (i.e. dialysis); 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; and injection drug use leads to the observed localized invasive infections.

Several interesting points are noted in our results, with respect to antibiotic use for treatment of invasive MRSA disease. First, while strains causing CA disease display, in general, a higher sensitivity to antibiotics than do strains causing HO and HACO disease, over half of all CA strains are resistant to quinolones. Consequently, quinolones may not be an effective empiric treatment for invasive MRSA. Second, an increasing use of more effective antibiotics against invasive MRSA disease (i.e. daptomycin) would be expected to reduce its case fatality rate. That this is not supported by our surveillance results may require further research into current therapeutic practices. Third, while intermediate or full resistance to vancomycin has not been detected among invasive MRSA isolates in Oregon, based on accepted breakpoint values, the extent to which reduced susceptibility to this drug is reflected in increased minimum inhibitory concentrations has not been fully ascertained and may require additional characterization.

The addition of molecular strain type information has demonstrated an increase in the traditional 'community-associated,' USA300 strain among cases classified epidemiologically as healthcare-associated, raising 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 work (such as the expanded HACO analysis presented for the first time in this report) will be needed to better refine our understanding of 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.