Treating CA-MRSA Infections: A Review of Antibiotic Therapy Selection and Patient Treatment Outcomes at a VA Institution

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A retrospective chart review evaluated the antibiotic susceptibility profiles of community-acquired methicillin-resistant *Staphylococcus aureus* isolates at the Southern Arizona VA Health Care System.

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections traditionally have been associated with the hospital setting. Recently, however, an increasing number of patients are acquiring MRSA in the community setting, hence the term "community-acquired MRSA (CA-MRSA)." Between 2001 and 2004, the prevalence of MRSA among patients with skin and soft tissue infections (SSTIs) at a Los Angeles institution increased from 29% to 64%.[1] Although CA-MRSA infections usually present as SSTIs, the incidence of invasive CA-MRSA infections is increasing. A recent study estimated this incidence to be about 14% of all CA-MRSA infections.[2]

The rate of MRSA colonization in the general population is estimated to be between 0.2% and 2.8%.[3] Nasal swab cultures are obtained from all patients admitted to the Southern Arizona VA Health Care System (SAVAHCS)—a practice that began in 2006, prior to our study period.

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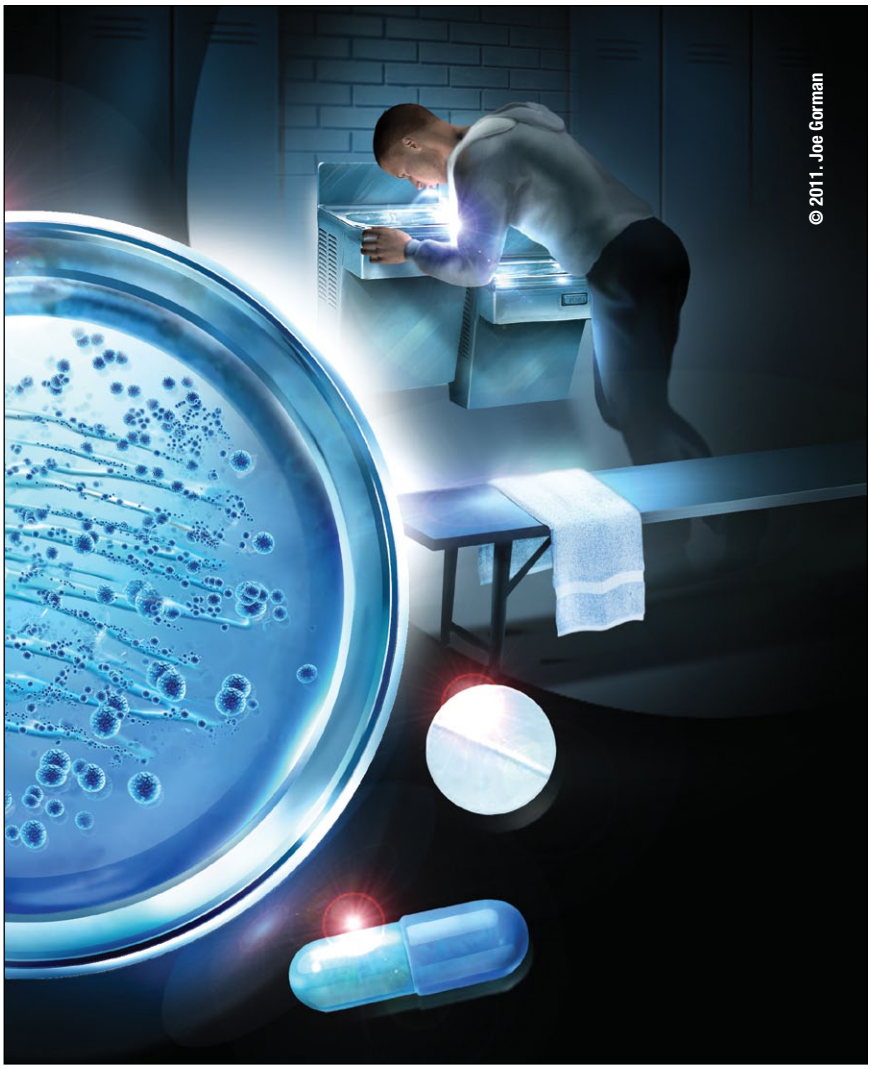
CA-MRSA accounts for more than 50% of the *Staphylococcus aureus* isolates in SSTIs.[4] Risk factors for CA-MRSA include skin trauma, incarceration, sharing equipment that has not been cleaned or laundered between users, and physical contact with others who have MRSA colonization or infection. Many patients who have CA-MRSA have no risk factors. Common pharmacologic treatment for SSTIs has been beta-lactam antibiotics; however, CA-MRSA isolates are resistant to these agents.[5] Studies by Moran and colleagues[6] and Ruhe and colleagues[7] have shown that a large number of patients—57% and 41%, respectively—were prescribed an empiric antibiotic for CA-MRSA to which the isolate was resistant.

Most localized SSTIs can be managed with simple incision and drainage (I&D) and do not require antibiotic treatment. Per the 2005 Practice Guidelines for Management of SSTIs, antibiotic therapy may be indicated in SSTIs if the infection is larger than 5 cm in size or if a patient has signs of a systemic infection (temperature > 101°F or pulse rate > 100 beats/min).[5] CA-MRSA strains generally are sensitive to trimethoprim/sulfamethoxazole (TMP/SMX), tetracyclines, and clindamycin.[8] These agents usually are considered first-line pharmacologic therapy for CA-MRSA if antibiotics are warranted. Clindamycin has been shown to be effective against CA-MRSA, but inducible resistance is possible. A key indicator for inducible clindamycin resistance is when the MRSA isolate is susceptible to clindamycin but resistant to erythromycin on initial testing.[9]

Current antibiograms at the SAVAHCS do not include antibiotic susceptibility profiles for CA-MRSA to assist providers in choosing appropriate empiric antibiotic therapy. Given the lack of clear-cut guidelines for pharmacologically treating patients who present with CA-MRSA at the time of our study, we conducted a retrospective chart review of the antibiotic therapy selected for patients during a 1-year period at our institution.

Our primary study objectives included evaluating antibiotic susceptibility profiles of CA-MRSA isolates, determining if the prescribed antibiotic therapy was appropriate based on the duration of treatment and correla-

tion with microbiology results, and evaluating the treatment outcomes of patients. Our secondary objectives included assessing nasal swab results to determine an association between MRSA colonization and active infections. We also sought to determine the need for provider education regarding susceptibility profiles for CA-MRSA at the SAVAHCS and treatment outcomes of CA-MRSA infections.



METHODS

We conducted our retrospective study at the SAVAHCS with approval from the investigational review board at the University of Arizona and the Research and Development Committee at the SAVAHCS, both in Tucson, Arizona. The SAVAHCS is a 250-bed, tertiary-care, academic hospital with several associated ambulatory care clinics. Patients with an *International Classification of Diseases, Ninth Revision (ICD-9)* code for MRSA between October 1, 2006, and October 1, 2007, were screened for inclusion. We used an electronic chart to extract information relating to the CA-MRSA infection.

Patients were included if a diagnosis of MRSA was made in the outpatient setting, as noted by primary care providers or emergency department providers, or by a culture that tested positive for MRSA within 48 hours after hospital admission, as these met the definition of CA-MRSA. Patients were excluded if they were younger than age 18 years or older than age 90 years at the time of diagnosis or if they had any risk factors for hospital-acquired MRSA. These risk factors included having been hospitalized or admitted to a long-term care facility, or having received dialysis or surgery within a year of diagnosis; having an indwelling catheter or medical device that passed through the skin into the body at the time of culture; or having ever had a medical history of MRSA infection or colonization.

An appropriate duration of therapy for most CA-MRSA infections is 7 to 14 days. Treatment failure was defined as documented worsening signs of infection (including erythema, edema, tenderness, purulent drainage, increase in white blood cell count, or temperature > 100.4°F) at least 2 days after initial treatment, performance of an additional I&D procedure, need for subsequent hospital admission, or persistence of MRSA-positive microbiology culture from the original site of infection after completion of antibiotic therapy. Successful outcomes were defined as resolution of signs or symptoms of infection. If patients did not have a documented treatment failure in their chart, a successful outcome was assumed.

To achieve the goals of our secondary objectives, we assessed available nasal swab cultures for patients included in our study.

RESULTS

A total of 213 patients were identified as having an *ICD-9* code for MRSA in their medical chart; of these, 40 pa-

tients with 41 episodes of CA-MRSA were included in the study. (Two separate SSTIs were concurrently diagnosed in 1 patient. Both infections were included in this study, and cultures revealed that the 2 infections had different microbiology susceptibility profiles.) Figure 1 summarizes the disposition of study patients and reasons for exclusion. The mean age of the patients included was 59 years (range, 30 to 90 years), and 95% were men. Most (90%) of the infections were SSTIs (abscess, n = 16; furuncle, n = 10; cellulitis, n = 5; other, n = 6), while the other 10% were invasive infections (urinary tract infection [UTI], n = 2; pneumonia, n = 1; and bacteremia, n = 1). Most infections (n = 27; 67.5%) were diagnosed in the outpatient setting, whereas, 13 infections (32.5%) were diagnosed within 48 hours after patients' hospital admission.

Beta-lactams were the most common empiric antibiotic prescribed for CA-MRSA infections (Figure 2), with cephalexin being the most commonly prescribed. Two patients (5%) were not prescribed antibiotic therapy as initial treatment. Fourteen patients (39%) with SSTIs received I&D as sole initial treatment or in combination with antibiotics.

Four patients had microbiology cultures drawn at non-VA hospitals, as such, their susceptibility profiles were not available in the electronic chart; however, these patients did receive their antibiotic therapy from the SAVAHCS. Microbiology cultures from the site of infection were available for 37 of the 41 episodes of CA-MRSA. MRSA susceptibilities were as follows: All isolates were susceptible to TMP/SMX (37 of 37), gentamicin (37 of 37), vancomycin (37 of 37), and nitrofurantoin (2 of 2); 77% were susceptible to clindamycin (27 of 35); 19% were susceptible to fluoroquinolones (7 of 37); and 8.5% were susceptible to erythromycin (3 of 35). Nitrofurantoin was included only in the susceptibility profiles of the 2 patients who had UTIs.

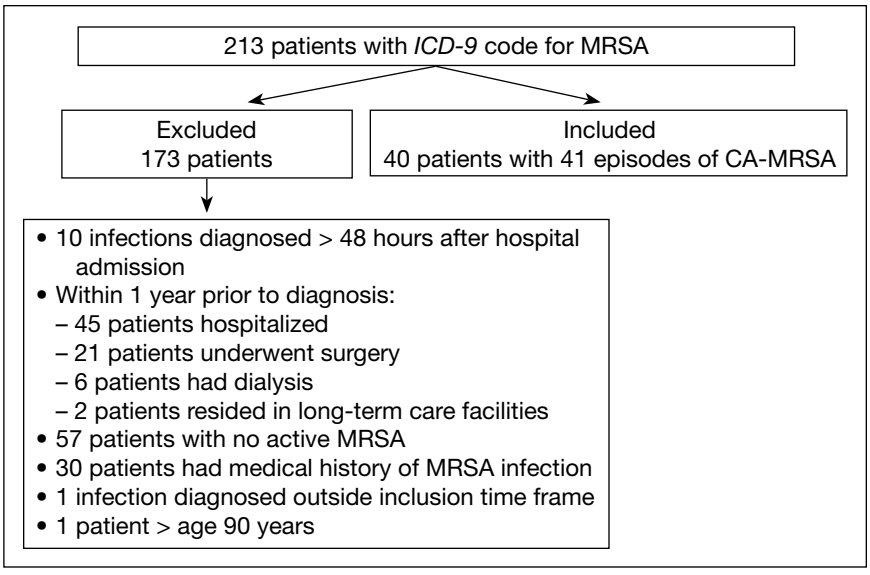


Figure 1. Inclusion and exclusion criteria for study patients. CA-MRSA = community-acquired methicillin-resistant *Staphylococcus aureus; ICD-9 = International Classification of Diseases, Ninth Revision*; MRSA = methicillin-resistant *Staphylococcus aureus*.

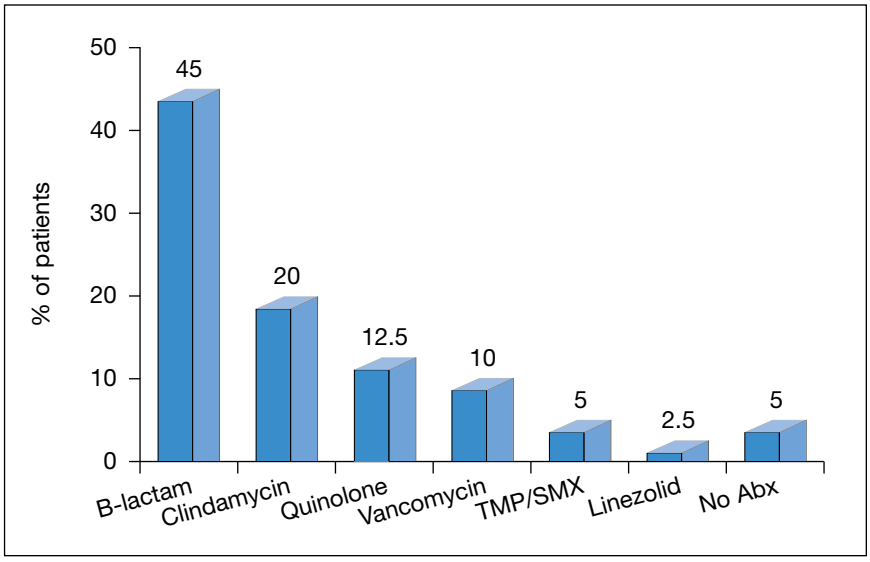


Figure 2. Empiric antibiotic therapy. Abx = antibiotic; B-lactam = beta-lactam; TMP/SMX = trimethoprim/sulfamethoxazole.

After microbiology results became available, 47% of patients had their antibiotic therapy tailored to correlate with microbiology results. This change allowed for 70% of all patients being treated to receive an antibiotic to which their isolate was susceptible. Figure 3 shows the tailored therapies. Five percent of patients (n = 2) re-

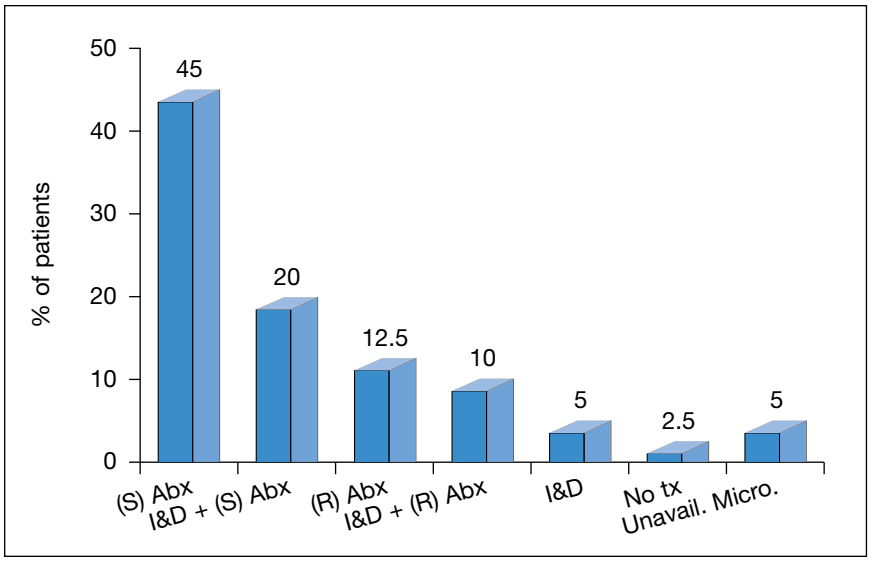


Figure 3. Tailored therapy. Abx = antibiotic; I&D = incision and drainage; (R) = resistant; (S) = susceptible; tx = treatment; Unavail. Micro. = unavailable microbiology results.

ceived no antibiotic therapy for their infection.

The usual duration of antibiotic therapy for CA-MRSA infections is between 7 and 14 days. Seventy percent of patients (n = 28) received antibiotics for an appropriate duration. Three patients received antibiotics for less than 7 days, 5 patients received antibiotics for more than 14 days, and 2 patients received antibiotics for an unknown period of time, as these patients did not have their antibiotic prescription filled at the VA. Variations in treatment duration were due to provider preference when prescribing antibiotics.

Treatment outcomes were assessed with the treatment used, and successful outcomes and treatment failures are depicted in Figure 4. A total of 29 patients (72.5%) had successful outcomes. Five patients (12.5%) had a successful outcome while being treated with an antibiotic to which their MRSA isolate was resistant. Two patients did not receive antibiotic therapy and both had successful outcomes. Eleven patients (27.5%) had treatment failures. Nine of these 11 patients received antibiotics to which their MRSA isolate was susceptible; 5 of which were treated with clindamycin. All of those isolates were clindamycin susceptible and erythromycin resistant in the initial susceptibility profile. The other 4 patients were treated with TMP/SMX (n = 2) and intravenous (IV) vancomycin (n = 2). All patients who had treatment failures with susceptible antibiotics were treated for an appropriate duration.

Patients whose infections were diagnosed in the inpatient setting (32.5%) had nasal swab cultures performed. Of those patients, 54% were negative for nasal colonization.

DISCUSSION

This study showed that CA-MRSA isolates were resistant to the prescribed empiric antibiotic in most patients, which is consistent with the results found by Moran and colleagues.[6] This finding suggests a need to reconsider empiric antibiotic choices when CA-MRSA is suspected. This study also showed the percentage of isolates that were susceptible to commonly prescribed antibiotics for CA-MRSA, with 100% of the isolates susceptible to TMP/SMX and 77% susceptible to clindamycin. These findings can be used to educate providers about susceptibility patterns of CA-MRSA at the SAVAHCS and can assist them in choosing antibiotic therapy. If a patient is an appropriate candidate for treatment with TMP/SMX, it should be considered as first-line therapy over clindamycin because of TMP/SMX's higher susceptibility rate.

The duration of antibiotic therapy was appropriate in 70% of patients included in the study. This finding suggests that providers may need to be educated about the usual duration of treatment for CA-MRSA infections.

Seven patients (17.5%) had successful outcomes with no treatment, with I&D alone, or with an antibiotic to which their CA-MRSA isolate was resistant. These outcomes reveal that antibiotic therapy may not be necessary for all CA-MRSA infections. Treatment failures were more prevalent in patients who were prescribed an antibiotic to which their CA-MRSA isolate was susceptible as opposed to resistant. This could be the result of induced clindamycin resistance, because 5 of 9 patients who had treatment failures were treated with clindamycin and were susceptible to clindamycin on initial microbiology susceptibilities but resistant to erythromycin, as demonstrated by Siberry and colleagues.[9] Inducible resistance should be considered as a possibility prior to prescribing clindamycin, especially if the MRSA isolate is clindamycin susceptible and erythromycin resistant on the initial microbiology susceptibility profile. This may be another reason to consider TMP/SMX over clindamycin for the treatment of CA-MRSA.

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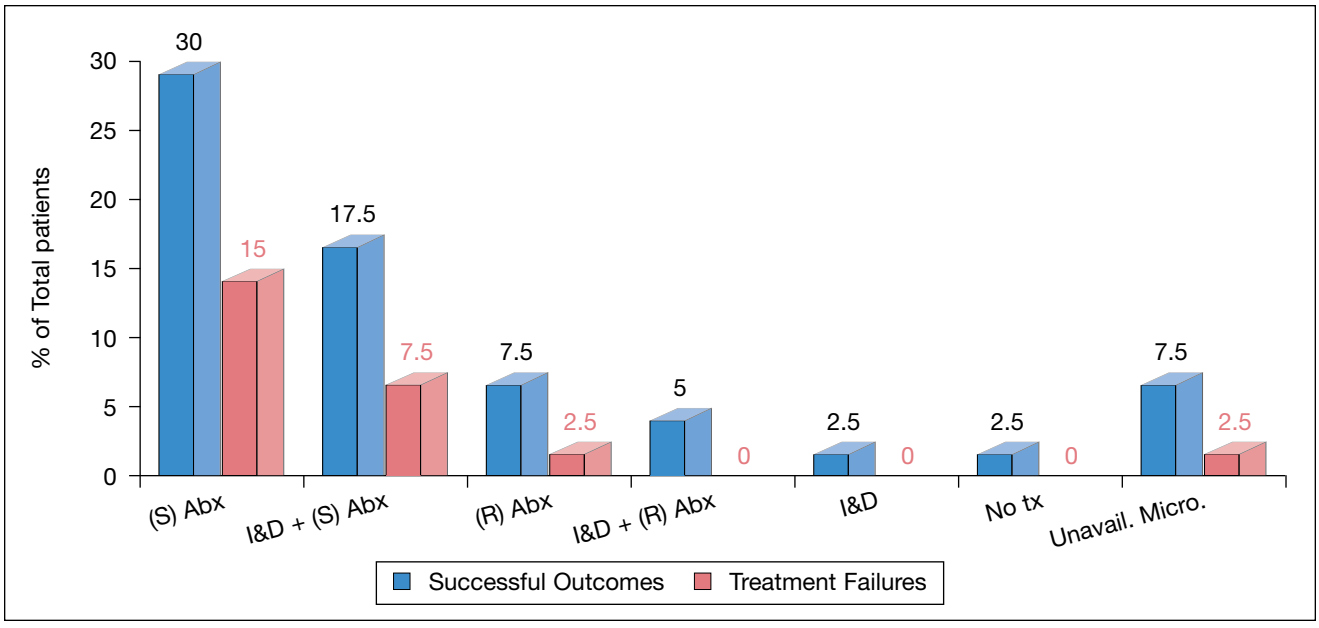

Figure 4. Treatment outcomes. Abx = antibiotic; I&D = incision and drainage; (R) = resistant; (S) = susceptible; tx = treatment; Unavail. Micro. = unavailable microbiology results.

Poor adherence to antibiotics may have been a reason for treatment failures in the outpatient setting. As this was a retrospective chart review, only the intended duration of the antibiotic could be assessed, not each patient's adherence. A possible reason for treatment failure in patients who received TMP/SMX could be the dose that was used (1 double-strength tablet twice daily). One reference recommends a dose of up to 2 double-strength tablets twice daily for SSTIs caused by CA-MRSA.[5] The 2 patients who had treatment failures on IV vancomycin likely had more severe infections. One of these patients required a longer course (4 weeks total) of vancomycin, and the other required an additional I&D before treatment was successful.

Forty-six percent of patients who had a nasal swab culture performed tested positive for colonization, which is higher than the estimated colonization rate (0.2% to 2.8%) for the general population.[3] However, because of the small percentage of patients who had nasal swab cultures obtained in this study, a clear association cannot be made between having an active CA-MRSA infection and being colonized with MRSA.

Study limitations

Limitations to this study include the retrospective design and small sample size. Also, an electronic chart was used to extract all data and the documentation in the chart may not have been complete or accurate. For example, patients who were included may have had risk factors for hospital-acquired MRSA that were not documented. Adherence to antibiotics also was not evaluated, and nonadherence could have contributed to treatment failures. Furthermore, patients were not observed for a uniform duration of time. There may have been treatment failures after the last documented follow-up, or patients may have gone to non-VA hospitals or clinics for follow-up. Patients who had no documented follow-up were assumed to have had successful outcomes with their initial treatment.

CONCLUSION

Our retrospective chart review showed that antibiotic therapy may not be necessary for all CA-MRSA infections. If antibiotics are warranted, empiric therapy should include an antibiotic that has a high susceptibility rate, such as TMP/SMX, as found in our study's results. The clindamycin failure rate may have been due to inducible resistance, and this should be considered prior to prescribing clindamycin. In our study, no clear association was found between having an active MRSA infection and MRSA nasal colonization. Our study was used to educate providers regarding the susceptibility patterns and treatment outcomes for CA-MRSA, and also was used, in part, to help develop guidelines to restrict the use of clindamycin for SSTIs at the SAVAHCS.

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REFERENCES

1. Moran GJ, Amii RN, Abrahamian FM, Talan DA. Methicillin-resistant *Staphylococcus aureus* in community-acquired skin infections. *Emerg Infect Dis.* 2005;11(6):928–930.
2. Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *JAMA.* 2007;298(15):1763–1771.
3. Frazee BW, Lynn J, Charlebois ED, Lambert L, Lowery D, Perdreau-Remington F. High prevalence of methicillin-resistant *Staphylococcus aureus* in emergency department skin and soft tissue infections. *Ann Emerg Med.* 2005;45(3):311–320.
4. King MD, Humphrey BJ, Wang YF, et al. Emergence of community-acquired methicillin-resistant *Staphylococcus aureus* USA 300 clone as the predominant cause of skin and soft-tissue infections. *Ann Intern Med.* 2006;144(5):309–317.
5. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. *Clin Infect Dis.* 2005;41(10):1373–1406.
6. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med.* 2006;355(7):666–674.
7. Ruhe JJ, Smith N, Bradsher RW, Menon A. Community-onset methicillin-resistant *Staphylococcus aureus* skin and soft-tissue infections: impact of antimicrobial therapy on outcome. *Clin Infect Dis.* 2007;44(6):777–784.
8. MRSA Infections. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/mrsa/treatment/. Updated August 9, 2010. Accessed January 14, 2011.
9. Siberry GK, Tekle T, Carroll K, Dick J. Failure of clindamycin treatment of methicillin-resistant *Staphylococcus aureus* expressing inducible clindamycin resistance in vitro. *Clin Infect Dis.* 2003;37(9):1257–1260.

EDITORIAL

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increasingly the case, it may not be a good use at all of society's finite health care dollars to spend a large amount of money screening for a disease that only a few actually have. The cost per discovered case may turn out to be unacceptably high.

It might sound cruel to ignore the tremendous benefits that a handful of "lucky" patients may experience if they undergo expensive screening and are found to have a disease which can be favorably modified by early treatment. But isn't it equally cruel, if not more cruel, to ask society to shell out large amounts of money that will mostly be wasted in confirming that most of the patients screened do not have the disease and were at no long-term risk to start with? Screening, it appears, may not be the panacea that the well-meaning but numerically challenged would like us to believe it is. ●

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