INTERNATIONAL SOCIETY ISMR OF MICROBIAL RESISTANCE

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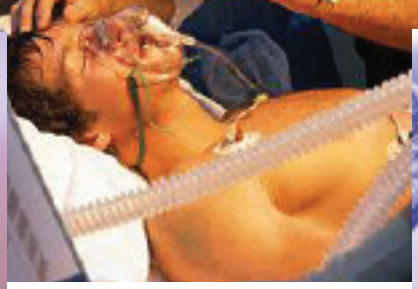
Burden of Methicillin-resistant *Staphylococcus aureus* on Healthcare Cost and Resource Utilization

CME Opportunity
From the 2006 MRSA
Education Summit



Impact of MRSA on Outcomes

How the Burden of Infectious Disease Is Measured

Cost and Resource Burden of MRSA Infections

Supported by an unrestricted educational grant from Pfizer Inc.

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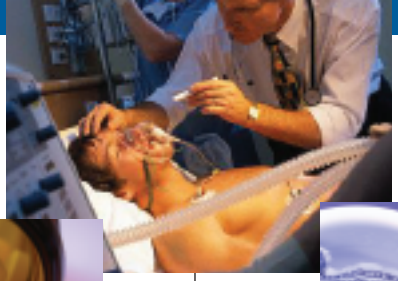

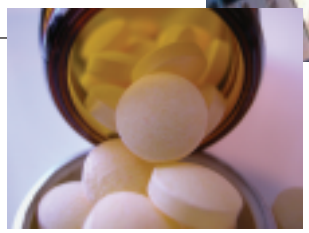

CME Opportunity
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Burden of Methicillin-resistant *Staphylococcus aureus* on Healthcare Cost and Resource Utilization

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Needs Statement

Since antimicrobial agents were first developed, microorganisms have been acquiring resistance to them. In the case of *Staphylococcus aureus*, resistance to methicillin, called methicillin-resistant *Staphylococcus aureus*, or MRSA, was first reported in 1961, shortly after semisynthetic penicillins were introduced.[1] Paradoxically, MRSA was considered to be rare and of doubtful clinical significance at that time.[2] This monograph will explore the epidemiology of MRSA and how it has evolved to become a major public health concern.

Accreditation Statements

Physician: This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the University of Kentucky College of Medicine and the International Society of Microbial Resistance. The University of Kentucky College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The University of Kentucky College of Medicine designates this educational activity for a maximum of *1.0 AMA PRA Category 1 Credit™*. Physicians should claim only credit commensurate with the extent of their participation in the activity.

The University of Kentucky Colleges of Pharmacy and Medicine present this activity for educational purposes only. Participants are expected to utilize their own expertise and judgment while engaged in the practice of medicine. The content of the presentations is provided solely by presenters who have been selected because of recognized expertise in their field.

Pharmacy:

The University of Kentucky College of Pharmacy is approved by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education.

This activity has been assigned ACPE #022-999-06-005-H04 and will award 1.0 contact hour (0.1 CEUs) of continuing pharmacy education credit in states that recognize ACPE providers. Statements of credit will indicate hours and CEUs based on successful completion of a posttest (score 70% or higher). The college complies with the Criteria for Quality for continuing education programming.

Learning Objectives

At the completion of this activity, participants should be able to:

1) Understand the impact of MRSA infection on the cost of healthcare and utilization of resources, and the components that drive the burden of MRSA infection.

2) Discuss the economic implications of various alternatives for treating MRSA.

3) Identify scenarios in which novel antimicrobial options may be cost-effective despite initially higher pharmacy acquisition costs.

Target Audience

This educational program is intended for physicians, pharmacists, and other healthcare professionals who manage the care of patients with MRSA infections or who are at risk for MRSA infections.

Disclosure of Financial Interest

All faculty members participating in continuing medical education programs sponsored by the University of Kentucky Colleges of Pharmacy and Medicine Continuing Education Office are expected to disclose any real or perceived conflict of interest related to the content of their presentations. Faculty disclosures are listed above.

Estimated Time of Completion

This activity should take approximately 1.0 hour to complete.

Method of Participation

There are no fees for participating in and receiving credit for this activity. The participant should: read the objectives and monograph; answer the multiple-choice posttest; and complete the answer sheet with registration and evaluation and mail to: Attn: Distance Education, Continuing Education Office, Colleges of Pharmacy and Medicine, University of Kentucky, 1 Quality St, 6th Floor, Lexington, KY 40507-1428 or fax to (859) 323-2920. Certificates will be mailed to participants in approximately 4 weeks after receipt of the mailed or faxed submissions. This credit is valid through July 17, 2007.

Support Statement

This activity is supported by an unrestricted educational grant from Pfizer Inc.

Joint Sponsorship Statement

Jointly sponsored by the University of Kentucky Colleges of Pharmacy and Medicine and the International Society of Microbial Resistance.

Burden of Methicillin-resistant *Staphylococcus aureus* on Healthcare Cost and Resource Utilization

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Introduction

Since antimicrobial agents were first developed, microorganisms have been acquiring resistance to them. In the case of *Staphylococcus aureus*, resistance to methicillin, called methicillin-resistant *Staphylococcus aureus*, or MRSA, was first reported in 1961, shortly after semisynthetic penicillins were introduced.[1] Paradoxically, MRSA was considered to be rare and of doubtful clinical significance at that time.[2] This monograph will explore the epidemiology of MRSA and how it has evolved to become a major public health concern. This monograph will also explore the impact of MRSA infection on the cost of healthcare and utilization of resources, and the components that drive the burden of MRSA infection. Additionally, we will discuss the economic implications of various alternatives for treating MRSA, and provide scenarios in which novel antimicrobial options may be cost-effective despite initially higher pharmacy acquisition costs.

Evolving Epidemiology of MRSA

Isolates of MRSA were initially recovered in hospitals; the first isolate was detected at a hospital in the United Kingdom.[1] Within a few years, MRSA was found in other European countries, Japan, and Australia,[3] and the first isolate in the United States was discovered at Boston City Hospital.[4] By the late 1980s, MRSA had become endemic in many hospitals, according to results from large surveillance studies such as the National Nosocomial Infections Surveillance (NNIS)[5] conducted by the Centers for Disease Control and Prevention (CDC). In the United States hospitals, the proportion of *S aureus* isolated that was resistant to methicillin rose from 2.4% in 1975 to 29% in 1991[6]; the proportion of MRSA continued to increase during the next decade and rose by approximately 3% per year in intensive care units (ICUs) between 1992 and 2003.[7] The mean was 59.5% in ICUs in 2003, reflecting an 11% overall increase, compared with the time period from 1998 through 2002.[5] In a surveillance study conducted from 2000 through 2002,[8] the proportion of MRSA was also high, but variable, in ICUs in other industrialized countries, ranging from 21% in Germany to 59% in Italy, but only 20% in Canada.

Recent results from inpatient isolates confirm that the highest proportion of MRSA occurs in ICUs, but MRSA is also prevalent in other areas of the hospital. The pooled mean was 53% in ICUs, 46% in non-ICUs, and 31% in outpatient areas, according to NNIS data collected from 1998 through 2004.[5] In 2005, MRSA rates rose to 59% in ICUs, 55% in non-ICUs, and 48% in outpatient areas, according to The Surveillance Network-USA.[9]

MRSA causes infections in patients of all ages throughout the United States, as demonstrated by an NNIS analysis of hospitalizations from 1999 to 2000.[10] The estimated annual occurrence of MRSA infection was 125,969, accounting for 43.2% of *S aureus* infections and 3.95 of every 1000 discharges. Between 1999 and 2000, MRSA accounted for 13.1 of every 1000 discharges for children aged 14 years and younger, and progressively increased with age ($P<.05$) to 63.3 of every 1000 discharges for patients aged 65 or older. Regionally, MRSA-related hospitalizations were highest in the US South, 4.45 for every 1000 discharges; followed by the Midwest (3.94/1000), the Northeast (3.52/1000), and the West (2.84/1000). MRSA can cause many types of infections; the most common are bloodstream infections (25% of *S aureus*) and pneumonia (24%), and the remaining 51% of MRSA infections are wound and other postoperative infections, cellulitis or abscess, implanted device or graft infections, and urinary tract infections.[9,10]

The most recent epidemiologic change is the rapid emergence of MRSA in the community since the late 1990s.[3,11,12] Unlike previous antibiotic resistance organisms that are first detected in the hospital prior to the community setting, the strains responsible for community-acquired MRSA (CA-MRSA) infection appear to have arisen from non-healthcare sources, and display characteristics that distinguish them from strains associated with healthcare-associated (HA-MRSA) infections by producing cytotoxins that cause tissue necrosis and leukocyte destruction,[13] as well as a host of virulence factors that may convey pathogenic advantages.[14] At first, CA-MRSA infections were limited to selected populations, such as children, Alaskan Natives, Native Americans, Pacific Islanders, prisoners, military personnel, and members of athletic teams.[13] However, CA-MRSA infections have become common in the general population, necessitating changes to the therapeutic approach, such as culturing skin lesions to determine whether MRSA is present.[3,11,12]

Impact of MRSA on Outcome

The impact of MRSA on the cost of healthcare and on resource utilization depends on the outcome

being measured, the perspective taken from which one evaluates costs, the reference group employed for the comparison, and efforts made to control other potential confounding factors.[15-17] Mortality is an example of an outcome that appears to be straightforward, but can be measured in different ways, eg, as deaths that occur during hospitalization that are attributable to infection, or as all-cause mortality up to a predefined time after hospital discharge. The differences in these 2 measures of mortality can impact conclusions drawn from clinical and economic studies. Morbidity is another outcome that can be measured in different ways, such as length of hospitalization, need for care in an ICU, need for surgery or other intervention, patient activity level at discharge, or patient functional status.[15-17]

Outcomes also differ depending on perspective, as is often the case in cost analysis. The central question in any cost analysis is: cost to whom? The issue of perspective is a key component in all economic analyses, which are often performed from the perspective of hospitals or third-party payers. It is also important to consider the constraints of a given economic analysis and consider alternative perspectives. For example, an intervention may appear to be cost-effective or even cost-saving to an institution because it shifts costs to a third-party payer. For the payer, however, the same intervention that is attractive to an institution may be less than optimal from an overall disease management perspective. Furthermore, these 2 perspectives do not account for the perspective of the patient, which includes the burden of requiring care in an isolation room, lost time from work and family due to prolonged hospitalization, recovery period, and long-term consequences of MRSA infection. To address the patient perspective, formal recommendations for the conduct of cost-effectiveness analyses encourage adoption of a societal perspective. Utilization of a common societal perspective can also facilitate comparisons across alternatives. In critical care and infectious disease outcomes research, however, a societal perspective poses specific challenges; as one review notes, "The societal perspective forces consideration of outcomes and costs not usually considered in critical care studies and a time horizon longer than most critical care studies."

Another factor that influences the impact of MRSA is the choice of patients who serve as a reference or control group for the purpose of a comparative analysis. For example, MRSA-infected patients can be compared with patients who are infected with methicillin-susceptible *S aureus* (MSSA),[18] those who are colonized with MRSA, or those who are not infected. Underlying severity of illness, comorbidities, and length of hospitalization before onset of infection also serve as confounding factors.[15,16]

Mortality

The impact of MRSA infection on mortality has been studied primarily in patients with bacteremia.[16] Initial studies yielded conflicting results, prompting a debate over whether MRSA truly increases mortality or whether patients with MRSA infections are more likely to die because of underlying comorbidities and severity of illness. Two recent meta-analyses provide evidence of increased mortality in patients with MRSA infection relative to those with MSSA infection. Whitby and colleagues[19] pooled data from 9 studies comprising a total of more than 2000 patients. MRSA infection was associated with approximately a twofold increased risk of mortality, regardless of whether risk was calculated by the fixed-effect method (relative risk [RR], 2.12) or the random-effect method (RR, 2.03; P<.001 for both methods). Cosgrove and colleagues[20] pooled data from 31 studies describing a total of nearly 4000 patients. As with the Whitby meta-analysis, MRSA infection was associated with approximately a twofold increased risk of mortality (pooled, unadjusted odds ratio [OR], 1.93; P<.001). To counterbalance heterogeneity among studies, Cosgrove and colleagues[20] performed subgroup analyses, including a group that only contained studies that controlled for disease severity, and found that the increased mortality rate persisted after adjusting for comorbidities or severity of illness. In all of these subgroup analyses, the odds ratio between MRSA and death consistently remained at 1.56 to 2.2, and association between MRSA and mortality persisted even when adjustments were made for severity of illness. Based on their findings, the authors cited type II error as the primary reason for heterogeneity among results of previous *S aureus* bacteremia outcomes studies.*

MRSA infection is also associated with increased mortality in patients with other types of infection. Engemann and colleagues[18] performed a cohort study of nearly 500 hospitalized patients who had surgical site infections. MRSA infection was associated with a 12-fold increase in 90-day mortality risk relative to no infection (OR, 12.3; P<.001) and fourfold increased risk relative to MSSA infection (OR, 3.6; P<.001); the latter remained significant after adjusting for age, severity of illness, and long duration of surgery (adjusted OR, 3.4; P=.003), similar to the findings of Cosgrove[20] in bacteremia. Metkontso-Dessap and colleagues[21] analyzed 41 hospitalized patients who had poststernotomy mediastinitis due to *S aureus;* MRSA infection was associated with a fivefold increased risk of mortality relative to MSSA infection and was the only independent risk factor for overall mortality (OR, 4.6; P=.04).

Morbidity in the Hospital

Findings from recently published studies comprising at least 100 patients confirm that MRSA infection is associated with increased morbidity relative to MSSA infection (Table).[18,22-25] Data from different studies are highly variable partly because of differences in patient populations and study design; for example, the longest duration of stay occurred in patients who were in ICUs and who had ventilator-associated pneumonia.[25] The highest economic burden occurred when charges to patients were used

**Errors in the statistical analysis of data can be broadly divided into 2 categories. Type I errors occur when there is no real difference between groups, but the analysis indicates that a difference exists. A type II error is the failure to detect a significant difference when one really does exist. Both error types have their origins in the design of the statistical analysis used for a given study and/or the characteristics of the study population being analyzed.*

Table. Impact of MRSA Infection on Morbidity as Measured by Mean Length of Stay and Hospital Cost, Odds Ratio, and Attributable Morbidity

Reference	Number of Patients With MRSA/MSSA Infection	MRSA vs MSSA (P value) LOS (days)	Cost ($)
Cosgrove 2005[22]	96/252 Bacteremia	9 vs 7 (.045)* OR, 1.29 (.016)† Attributable LOS, 2.2	14,655 vs 10,655 (.008)* OR, 1.36 (.017)† Attributable cost, 3836
Engemann 2003[18]	127/173 Surgical site infection	22 vs 13 (.001) OR, 1.2 (.11)† Attributable LOS, 2.6	118,415 vs 73,165 (.001)‡ OR, 1.19 (.03)† Attributable charge, 13,901
Lodise 2005[23]	170/183 Bacteremia	19.1 vs 14.2 (.005)† OR, 1.4 (.003)†	21,577 vs 11,688 (.001)† Not available
Reed 2005[24]	54/89 Hemodialysis bacteremia	16.6 vs 9.3 (.0001) Not available (.0001)†	28,297 vs 16,066 (.0001) 21,251 vs 13,978 (.012)†
Shorr 2006[25]	38/69 VAP	33 vs 22 (.047)*	Not available

MRSA = methicillin-resistant *Staphylococcus aureus*; LOS = length of stay; OR = odds ratio; MSSA = methicillin-susceptible *S aureus*; VAP = ventilator-associated pneumonia. *Median instead of mean. †Adjusted for confounding factors. ‡Charge to patient instead of cost to hospital.

instead of costs incurred by hospitals and when readmissions (of interest to payers) were included in the calculation of economic burden.[18] Although these differences preclude direct comparison of data from different studies, the findings consistently indicate that MRSA is associated with increases in both the length of hospital stay and cost of hospitalization, typically on a magnitude of 1.2- to 2-fold increase in morbidity and costs.[15] Furthermore, the increases in both types of morbidity were usually statistically significant and usually correlated. The only nonsignificant value was the odds ratio for increased length of stay, calculated after adjusting for confounding factors in the analysis by Engemann and colleagues.[18] The authors hypothesized that this unexpected finding was due to the longer duration of stay in the ICU among patients with MRSA infection, which costs more than staying in the ward and therefore could have increased the overall cost without increasing the duration of hospitalization.

Of particular interest is total cost attributable to treating a patient with MRSA infection relative to treating a patient with MSSA infection, especially after performing multivariate analysis to adjust for confounding factors. Cosgrove and colleagues[22] reported that MRSA bacteremia had a mean attributable hospital charge of $6916 and hospital cost of $3836. These charges were based on total hospital charges in the hospital's billing system that were incurred from the time of onset of MRSA infection to the end of hospitalization. Hospital costs were estimated by adjusting charges using the overall Medicare cost-to-charge ratio for the institution. Engemann and colleagues[18] reported that MRSA surgical site infection had a mean attributable hospital charge of $13,901, and did not report hospital cost; these charges included readmissions.

Morbidity in the Community

CA-MRSA infection also appears to be associated with increased morbidity, but few dedicated studies have been conducted. Purcell and colleagues[26] estimated the economic burden on a pediatric health plan during a 3-year epidemic of CA-MRSA infections, which usually manifested as cellulitis or abscess. Total health plan expenses for cellulitis or abscess doubled (from 1.7% to 3.3%; P<.001), and per member per month expenses for these 2 types of infection increased (from $0.74 to $1.19; P<.001). In contrast, total per member per month expenses for all diagnoses decreased during the same 3-year period (from $43.11 to $35.54; P<.001). The authors did not determine the microbiologic etiology of cellulitis or abscess; however, it is reasonable to assume that CA-MRSA infection was associated with a significant increase in the overall cost of healthcare from the perspectives of both the provider and the patient.

Distribution of Attributable Costs

Methods for calculating cost merit further consideration and a definition of terms. *Total cost* comprises both direct and indirect cost. *Direct cost* refers to that which is directly related to providing patient care and that can be attributed to a particular product or service. Direct cost has 2 components. The first, *fixed direct cost*, does not vary with the volume of patient activity—an example is building overhead. The second component, *variable direct cost*, varies directly and proportionately with volume—examples include drugs and other supplies. Nursing staff and other professional personnel are essential resources to hospitals and often in short supply; the cost of this resource is an example of a direct cost, which can be fixed if the staff receives annual salaries that do not vary with the number of services provided, or can be variable if employment varies with the hospital census. For full-time staff, time allocated to delivery of a specific intervention (drug delivery and monitoring) can be difficult to quantify, but has implications for institution resource utilization. *Indirect cost* refers to that not directly related to patient care—examples include housekeeping, medical records, and other administrative services.

A series of 3 studies provide insight regarding the distribution of attributable costs to MRSA infection.

Lodise and colleagues[23] reported that MRSA bacteremia was associated with increases in all 3 components of hospital costs relative to MSSA bacteremia. Specifically, the mean costs for MRSA infection vs MSSA infection, in descending order of cost, were as follows:

- Variable direct costs including nursing staff: $9358.37 vs $4497.80 (P<.001)
- Fixed indirect costs: $9300.37 vs $4862.95 (P<.001)
- Fixed direct costs: $3874.36 vs $1781.96 (P<.001)

Based on the above information, MRSA bacteremia was associated with a twofold increase for all of the components.[23]

Kim and colleagues[27] determined the impact of MRSA infection (n=20) and colonization (n=79) on healthcare cost and resource utilization in Canadian hospitals. MRSA infection was associated with 14 additional days and an additional hospital cost of $14,360 per infection in Canadian dollars in the late 1990s. Most of these attributable costs were due to per diem and included the collective costs of nursing care, housekeeping, laundry, and pharmacy. Only 4% was due to the cost of antimicrobial therapy; 1% was due to the cost of microbiological testing. The authors also calculated the cost of isolation or barrier precautions for patients with MRSA colonization based on previous observations, including the costs of gowns, gloves, and 1 minute of nursing time, each multiplied by an average of 60 contacts per day of isolation. The hospital costs were $1363 for each patient in isolation and $109,813 for MRSA surveillance, resulting in total annual costs of approximately $250,000 for patients who were infected or colonized with MRSA.[27]

Plowman and colleagues[28] further subdivided the economic burden and estimated the attributable cost of nosocomial infections in approximately 4000 adults hospitalized in England (Figure). Although the authors did not focus on MRSA infection per se, it is reasonable to assume that MRSA infections were prevalent in this large analysis. The exact costs have increased since the data were collected in the mid-1990s, but it is assumed that the distribution of those costs has not changed substantially. As expected, the highest cost, accounting for 52% of additional cost of nosocomial infection relative to no infection, was the direct cost for nurses and other healthcare professionals. The next highest cost, accounting for 33%, was hospital overhead, capital charges, and directorate management. The direct variable cost of treatment accounted for only 15% of additional costs, such as drug therapy, other consumables, tests, surgical interventions, and endoscopy and radiology. Surprisingly, (but consistent with the previous study),[27] antimicrobial therapy accounted for only 2% of the attributable cost of nosocomial infection in this large analysis.[28]

In summary, MRSA clearly adversely affects both morbidity and mortality. Additionally, the impact of MRSA can be seen in both hospitalized patients and outpatients. Given the continuing increase in the spread of MRSA and the evolution of community-associated strains of MRSA, this pathogen is likely to remain a major treatment challenge for clinicians.

Drivers of Cost

Inadequate or Delayed Antimicrobial Treatment

Findings from recent studies provide insight about what factors drive the economic burden of MRSA relative to infections with MSSA. Kollef and colleagues[29] were among the first to describe the impact of inadequate antimicrobial treatment, defined as failure to provide an antimicrobial active against the culprit pathogen based on the results of in vitro sensitivity testing. They prospectively followed a cohort comprised of 2000 critically ill patients who were consecutively admitted to the ICU, including 655 patients who had a variety of infections. Inadequate antimicrobial treatment was associated with a fourfold increase in hospital mortality (RR, 4.3; P<.001), and with a twofold increase in infection-related mortality (RR, 2.4; P<.001). Furthermore, inadequate antimicrobial treatment was the most important independent determinant of hospital mortality for the entire patient cohort in a logistic regression analysis (adjusted OR, 4.3; P<.001).[29] Others have reported similar findings that confirm the deleterious effects of initially inadequate antimicrobial treatment in patients with bacteremia.[30,31]

Moreover, delaying antimicrobial treatment is associated with increased mortality and morbidity in patients with staphylococcal bacteremia. Lodise and colleagues[32] evaluated 167 consecutive episodes of *S aureus* bacteremia during a 2-year period. Use of classification and regression tree analysis (CART) revealed that the mortality breakpoint between early and delayed treatment was 45 hours. After controlling for severity of illness and other risk factors, delayed treatment was an independent predictor of infection-related mortality (OR, 3.8; P=.01) and was associated with a longer duration of hospitalization (adjusted mean, 20.2 days vs 14.3 days; P=.05). Furthermore, MRSA infection was the most significant predictor of delayed treatment as determined by both univariate analysis (P<.001) and logistic regression analysis (OR, 8.3; 95% confidence interval [CI], 2.6-16.8).[32] Others have also reported that inappropriate or delayed antimicrobial treatment is an independent predictor of infection-related,[33,34] but not all-cause,[35] mortality. These findings may explain some of the differing results noted in various analyses designed to evaluate the impact of MRSA on morbidity and mortality. Many authors of the previously described studies[15,18,19,22] did not consider inappropriate or delayed antimicrobial treatment when they adjusted for potential confounding factors.

In contrast, appropriate initial antimicrobial treatment was one of the prospectively defined inclusion criteria in the analysis by Combes and colleagues.[36] In their cohort of 171 patients with ventilator-associated pneumonia due to either MSSA or to MRSA, all subjects received initially appropriate antimicrobial treatment. For those with MRSA, this was defined as use of high-dose vancomycin (15 mg/kg, dosed to a trough of 15-20 mcg/mL). No linezolid was used in this evaluation. As one might predict, MRSA infection was associated with an increased crude mortality at 28 days; specifically, those with MRSA were nearly 3 times more likely

to die when compared with those with MSSA pneumonia (OR, 2.6; P=.001). However, in the Combes multivariate analysis, MRSA infection was not a significant predictor of death (OR, 1.7; P=.22).[36] Despite these observations, a subsequent analysis[25] of the same cohort focused on morbidity. This analysis was limited to the 107 patients who survived beyond the stay in the ICU, in order to eliminate confounding due to the timing of death in the ICU. Those suffering from MRSA infection spent 11 additional days in the ICU (P=.047; Table). Controlling for multiple confounders including severity of illness and chronic health state revealed that MRSA (relative to MSSA) doubled the need for continued ICU stay (hazard ratio [HR], 2.1; P=.03).[25]

Collectively, these findings suggest that appropriate antimicrobial treatment can minimize the attributable mortality of MRSA, but the morbidity problem persists when vancomycin is chosen as the antimicrobial agent. Vancomycin became available more than 50 years ago but rapidly fell out of favor as other antimicrobial agents were deemed to be more effective and less toxic.[37] As gram-positive cocci developed resistance to other antimicrobial agents, vancomycin regained popularity and became the standard treatment for patients with MRSA infection. More recently, the role of vancomycin has again been questioned in the treatment of MRSA infection because of antimicrobial, pharmacokinetic, and clinical considerations. First, vancomycin may be less rapidly bactericidal than semisynthetic penicillins for the treatment of severe *S aureus* infection.[38,39] Second, vancomycin concentrations in lung tissue[40] and pulmonary lining fluid[41] are low relative to plasma concentrations. In a vancomycin lung penetration study, the lung tissue:serum concentration ratio ranged from 0.24 (at 1 hour) to 0.41 (at 12 hours), after 1 g of vancomycin was infused over 30 minutes. Of more concern was the fact that nearly half the patients whose samples were measured 12 hours postdose had undetectable levels of vancomycin in lung tissue.

In epithelial lining fluid (ELF), the vancomycin blood-to-ELF ratio of drug penetration was 6:1. Third, vancomycin was associated with lower clinical cure and survival rates than was linezolid in a retrospective analysis[42] of 2 randomized studies of patients with ventilator-associated pneumonia due to MRSA. A prospective randomized trial of linezolid vs vancomycin for ventilator-associated pneumonia is currently under way to validate the findings of this subset analysis. Vancomycin was also found to have significantly lower rates of clinical and microbiologic success rates for MRSA surgical site infections and complicated skin and soft tissue infections in prospective, open-label, comparator-controlled, multicenter studies that included patients with suspected or proven MRSA complicated skin and soft tissue infections and surgical site infections.[43,44]

Another aspect of vancomycin use is the need for intravenous administration, which can increase economic burden by prolonging the duration of hospitalization or by necessitating special arrangements for administration in the outpatient setting. Although drug administration costs less in an outpatient setting than in an inpatient setting, administering vancomycin to outpatients remains expensive because of resource utilization and the costs of drugs and supplies.[45] Tice and colleagues[45] reported that, in addition to the cost, outpatient administration of vancomycin was associated with other problems such as the inconvenience of twice-daily administration, pharmacokinetic monitoring, and adverse events in 11% of patients. Furthermore, they reported that the cost of drug acquisition, nursing time, supplies for outpatient IV vancomycin therapy, IV line placement and replacement, management costs, and laboratory costs were quite high and substantially greater than the average daily reimbursement of approximately $300 estimated from 4 different healthcare payers.

Four antimicrobial agents provide alternatives to vancomycin with effective activity against MRSA: quinupristin/dalfopristin, daptomycin, tigecycline, and linezolid. Like vancomycin, quinupristin/dalfopristin, tigecycline, and daptomycin must be administered parenterally. Unlike vancomycin, linezolid has 100% bioavailability[46] and is therefore suitable for oral administration.

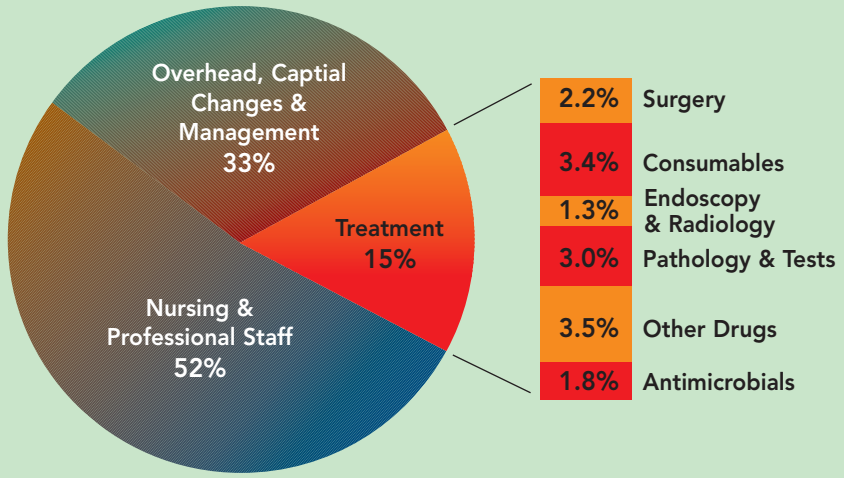
Economic Impact of New Agents With MRSA Activity

To date, the only newly approved agent with MRSA activity and demonstrated economic advantage over vancomycin is linezolid.

The economic benefits of linezolid are attributable to improved clinical outcomes[47,48] and to savings associated with the switch from intravenous to oral administration.[48-51] In general, intravenous therapy is more expensive than oral therapy given the indirect cost related to the preparation of intravenous agents and their administration to the patient, irrespective of whether they are treated in the hospital or at home. These higher administration costs have recently been shown to offset the greater acquisition cost of linezolid relative to vancomycin. Benefits have been demonstrated in 5 studies of patients with different types of infections, including ventilator-associated pneumonia (Shorr),[47] suspected methicillin-resistant staphylococcal infections (Parodi),[51] skin and soft tissue infection (Sharpe, Itani),[48,49] and infections treated in outpatient settings (McKinnon).[50] Two of the studies were based on hypothetical modeling[47,51]; the others were based on participants in randomized studies[48,49] and a very large group of outpatients.[50]

Shorr and colleagues[47] used decision model analysis and took a societal perspective to estimate the incremental cost-effectiveness of linezolid treatment relative to vancomycin treatment, in a hypothetical cohort of 1000 patients with ventilator-associated pneumonia. Assumptions were based on a previous analysis[42] demonstrating that linezolid was an independent predictor of clinical cure and survival for all patients with ventilator-associated pneumonia, as well as for the subsets with documented staphylococcal infection or with MRSA infection. In the economic analysis,[47] incremental costs included the higher direct cost of linezolid, together with the higher cost for survivors during hospitalization and after discharge. The incremental cost-effectiveness

Figure. Distribution of additional healthcare costs incurred by infected patients relative to uninfected patients.[28]



Adapted from Plowman R, et al. *J Hosp Infect.* 2001;47:198-209.

of linezolid was approximately $30,000 per quality-adjusted life-year, which compared favorably with the accepted standard of $100,000.[52] This also compared favorably to a number of other interventions routinely undertaken in the ICU.

Parodi and colleagues[51] estimated the potential savings associated with early switch from intravenous vancomycin to oral linezolid treatment for suspected methicillin-resistant staphylococcal infections, a switch that would result in earlier discharge from the hospital. They considered the direct variable costs of drug acquisition and specialty-based hospital bed costs, which ranged from approximately $1000 per patient for the rehabilitation or transitional care unit to $2500 per patient for the ICU at the Veterans Administration Greater Los Angeles System. Switching from intravenous vancomycin to oral linezolid, it was determined, would yield an estimated mean decrease in the duration of hospitalization of 3.3 days and a mean savings of $3478 per treatment episode.[51]

Sharpe and colleagues[48] documented clinical and economic benefits in 60 patients with complicated MRSA infections of the skin and soft tissue who were randomly assigned to receive treatment with intravenous vancomycin or oral linezolid. Linezolid was associated with higher clinical cure or improvement rates vs vancomycin (97% vs 43%; P<.02) and fewer amputations of lower extremities (0 vs 7; P=.01). The duration of hospitalization was 3 days shorter in the linezolid group (P=.003), resulting in an average savings of $6438 in total hospital charges to the patient. Linezolid also had a lower median outpatient charge than did vancomycin ($103 vs $200; P<.001).

Itani and colleagues[49] analyzed the outcomes in a multinational study of 1200 patients who had complicated skin and soft tissue infections and who were randomly assigned to receive treatment with vancomycin or linezolid. This was a prospective trial unlike several earlier analyses of the impact of linezolid on length of stay in the hospital. This study was powered specifically to be able to detect an effect on duration of hospitalization. In this trial, vancomycin was administered intravenously and, if the pathogen was MSSA, switched to a semisynthetic penicillin. Linezolid could be initiated as oral therapy or switched from intravenous to oral therapy. Linezolid treatment was associated with clinical outcomes that were at least equivalent to those of vancomycin treatment; additionally, significantly higher clinical response rates (88.6% vs 66.9%; P<.001) were noted in the subset of patients with MRSA infections.[43] In the economic analysis,[49] linezolid treatment was associated with a shorter mean duration of hospitalization in the intent-to-treat analysis relative to vancomycin treatment (mean, 7.4 vs 9.8 days; P<.0001) and in the subset with MRSA infection (mean, 8.1 vs 10.7 days; P=.003). Although it was not possible to quantify the exact economic benefits in this large study,[49] findings from previous studies[25,48,51] indicate that reducing the duration of hospitalization by 2 days will yield substantial savings in healthcare cost and resource utilization.

McKinnon and colleagues[50] studied patients treated with intravenous vancomycin or oral linezolid in an outpatient setting during a 2-year period. Approximately 2000 patients were matched for variables such as demographic characteristics, comorbidities, and payer and plan type. Oral linezolid treatment was associated with less resource utilization as measured by duration of hospitalization (mean, 1.7 vs 2.2 days; P=.02), physician office visits (P<.0001), laboratory and diagnostic tests (P<.0001), and other outpatient services (P<.0001). In contrast, patients treated with intravenous vancomycin were more likely to require hospitalization (OR, 1.3; 95% CI, 1.1-1.6) and to visit the emergency department (OR, 1.5; 95% CI, 1.2-2.0). These differences more than offset the higher acquisition cost of linezolid ($1485 vs $333), resulting in a lower total healthcare cost for outpatients treated with oral linezolid (mean, $8922 vs $13,552; P<.0001).[50]

Conclusions

MRSA infection places a substantial burden on healthcare cost and resource utilization. Outcomes studies confirm that the attributable cost of MRSA infection is substantial, albeit variable, and statistically significant, relative to MSSA infection; this is evident in both inpatient and outpatient settings and across a range of infection types. Although antimicrobial treatment costs comprise a small percentage of total healthcare costs, prompt initiation of an appropriate

agent can reduce the overall cost of healthcare. Experience with MRSA also indicates that, in certain instances, novel interventions may prove economically attractive, despite their acquisition costs, because of their effect on length of stay and secondary drug administration charges. Additional studies are needed to document the benefit of newer antimicrobial agents and other innovative interventions on healthcare cost and resource utilization.

References

1. Lowy FD. *Staphylococcus aureus* infections. *N Engl J Med.* 1998;339:520-532.
2. Barber M. Methicillin-resistant staphylococci. *J Clin Pathol.* 1961;14: 385-393.
3. Boyce JM, Cookson B, Christiansen K, et al. Methicillin-resistant *Staphylococcus aureus*. *Lancet Infect Dis.* 2005;5:653-663.
4. Barrett FF, Casey JI, Finland M. Infections and antibiotic use among patients at Boston City Hospital, February, 1967. *N Engl J Med.* 1968;278:5-9.
5. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control.* 2004;32:470-485.
6. Panlilio AL, Culver DH, Gaynes RP, et al. Methicillin-resistant Staphylococcus aureus in U.S. hospitals, 1975-1991. *Infect Control Hosp Epidemiol.* 1992;13:582-586.
7. Klevens RM, Edwards JR, Tenover FC, McDonald LC, Horan T, Gaynes R. Changes in the epidemiology of methicillin-resistant *Staphylococcus aureus* in intensive care units in US hospitals, 1992-2003. *Clin Infect Dis.* 2006;42:389-391.
8. Jones ME, Draghi DC, Thornsberry C, Karlowsky JA, Sahm DF, Wenzel RP. Emerging resistance among bacterial pathogens in the intensive care unit-a European and North American Surveillance study (2000-2002). *Ann Clin Microbiol Antimicrob.* 2004;3:14.
9. Styers D, Sheehan DJ, Hogan P, Sahm DF. Laboratory-based surveillance of current antimicrobial resistance patterns and trends among *Staphylococcus aureus*: 2005 status in the United States. *Ann Clin Microbiol Antimicrob.* 2006;5:2.
10. Kuehnert MJ, Hill HA, Kupronis BA, Tokars JI, Solomon SL, Jernigan DB. Methicillin-resistant-*Staphylococcus aureus* hospitalizations, United States. *Emerg Infect Dis.* 2005;11:868-872.
11. Fridkin SK, Hageman JC, Morrison M, et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *N Engl J Med.* 2005;352:1436-1444.
12. Moellering RC Jr. The growing menace of community-acquired methicillin-resistant *Staphylococcus aureus*. *Ann Intern Med.* 2006;144:368-370.
13. Weber JT. Community-associated methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis.* 2005;41(suppl 4):S269-S272.
14. Zetola N, Francis J, Nuermberger E, Bishai W. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging threat. *Lancet Infect Dis.* 2005;5:275-286.
15. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis.* 2003;36:1433-1437.
16. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis.* 2006;42(suppl 2):S82-S89.
17. Nathwani D. Impact of methicillin-resistant *Staphylococcus aureus* infections on key health economic outcomes: does reducing the length of hospital stay matter? *J Antimicrob Chemother.* 2003;51(suppl 2):ii37-ii44.
18. Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis.* 2003;36:592-598.
19. Whitby M, McLaws ML, Berry G. Risk of death from methicillin-resistant *Staphylococcus aureus* bacteraemia: a meta-analysis. *Med J Aust.* 2001;175:264-267.
20. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis.* 2003;36:53-59.
21. Mekontso-Dessap A, Kirsch M, Brun-Buisson C, Loisance D. Poststernotomy mediastinitis due to *Staphylococcus aureus*: comparison of methicillin-resistant and methicillin-susceptible cases. *Clin Infect Dis.* 2001;32:877-883.
22. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol.* 2005;26:166-174.
23. Lodise TP, McKinnon PS. Clinical and economic impact of methicillin resistance in patients with *Staphylococcus aureus* bacteremia. *Diagn Microbiol Infect Dis.* 2005;52:113-122.
24. Reed SD, Friedman JY, Engemann JJ, et al. Costs and outcomes among hemodialysis-dependent patients with methicillin-resistant or methicillin-susceptible *Staphylococcus aureus* bacteremia. *Infect Control Hosp Epidemiol.* 2005;26:175-183.
25. Shorr AF, Combes A, Kollef MH, Chastre J. Methicillin-resistant *Staphylococcus aureus* prolongs intensive care unit stay in ventilator-associated pneumonia, despite initially appropriate antibiotic therapy. *Crit Care Med.* 2006;34:700-706.
26. Purcell K, Fergie J, Peterson MD. Economic impact of the community-acquired methicillin-resistant *Staphylococcus aureus* epidemic on the Driscoll Children's Health Plan. *Pediatr Infect Dis J.* 2006;25:178-180.
27. Kim T, Oh PI, Simor AE. The economic impact of methicillin-resistant *Staphylococcus aureus* in Canadian hospitals. *Infect Control Hosp Epidemiol.* 2001;22:99-104.
28. Plowman R, Graves N, Griffin MA, et al. The rate and cost of hospital-acquired infections occurring in patients admitted to selected specialties of a district general hospital in England and the national burden imposed. *J Hosp Infect.* 2001;47:198-209.
29. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. *Chest.* 1999;115:462-474.
30. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest.* 2000;118:146-155.
31. Leibovici L, Shraga I, Drucker M, Konigsberger H, Samra Z, Pitlik SD. The benefit of appropriate empirical antibiotic treatment in patients with bloodstream infection. *J Intern Med.* 1998;244:379-386.
32. Lodise TP, McKinnon PS, Swiderski L, Rybak MJ. Outcomes analysis of delayed antibiotic treatment for hospital-acquired *Staphylococcus aureus* bacteremia. *Clin Infect Dis.* 2003;36:1418-1423.
33. Romero-Vivas J, Rubio M, Fernandez C, Picazo JJ. Mortality associated with nosocomial bacteremia due to methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis.* 1995;21:1417-1423.
34. Soriano A, Martinez JA, Mensa J, et al. Pathogenic significance of methicillin resistance for patients with *Staphylococcus aureus* bacteremia. *Clin Infect Dis.* 2000;30:368-373.
35. Roghmann MC. Predicting methicillin resistance and the effect of inadequate empiric therapy on survival in patients with *Staphylococcus aureus* bacteremia. *Arch Intern Med.* 2000;160:1001-1004.
36. Combes A, Luyt CE, Fagon JY, et al. Impact of methicillin resistance on outcome of *Staphylococcus aureus* ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 2004;170:786-792.
37. Levine DP. Vancomycin: a history. *Clin Infect Dis.* 2006;42(Suppl 1): S5-S12.
38. Levine DP, Fromm BS, Reddy BR. Slow response to vancomycin or vancomycin plus rifampin in methicillin-resistant *Staphylococcus aureus* endocarditis. *Ann Intern Med.* 1991;115:674-680.
39. Small PM, Chambers HF. Vancomycin for *Staphylococcus aureus* endocarditis in intravenous drug users. *Antimicrob Agents Chemother.* 1990;34:1227-1231.
40. Cruciani M, Gatti G, Lazzarini L, et al. Penetration of vancomycin into human lung tissue. *J Antimicrob Chemother.* 1996;38:865-869.
41. Lamer C, de Beco V, Soler P, et al. Analysis of vancomycin entry into pulmonary lining fluid by bronchoalveolar lavage in critically ill patients. *Antimicrob Agents Chemother.* 1993;37:281-286.
42. Kollef MH, Rello J, Cammarata SK, Croos-Dabrera RV, Wunderink RG. Clinical cure and survival in Gram-positive ventilator-associated pneumonia: retrospective analysis of two double-blind studies comparing linezolid with vancomycin. *Intensive Care Med.* 2004;30:388-394.
43. Weigelt J, Itani K, Stevens D, Lau W, Dryden M, Knirsch C. Linezolid versus vancomycin in treatment of complicated skin and soft tissue infections. *Antimicrob Agents Chemother.* 2005;49:2260-2266.
44. Weigelt J, Kaafarani H, Itani K, Swanson R. Linezolid eradicates MRSA better than vancomycin from surgical site infections. *Am J Surg.* 2004;188:760-766.
45. Tice AD, Hoaglund PA, Nolet B, McKinnon PS, Mozaffari E. Cost perspectives for outpatient intravenous antimicrobial therapy. *Pharmacotherapy.* 2002;22(2 Pt 2):63S-70S.
46. Stalker DJ, Jungbluth GL. Clinical pharmacokinetics of linezolid, a novel oxazolidinone antibacterial. *Clin Pharmacokinet.* 2003;42:1129-1140.
47. Shorr AF, Susla GM, Kollef MH. Linezolid for treatment of ventilator-associated pneumonia: a cost-effective alternative to vancomycin. *Crit Care Med.* 2004;32:137-143.
48. Sharpe JN, Shively EH, Polk HC Jr. Clinical and economic outcomes of oral linezolid versus intravenous vancomycin in the treatment of MRSA-complicated, lower-extremity skin and soft-tissue infections caused by methicillin-resistant *Staphylococcus aureus*. *Am J Surg.* 2005;189: 425-428.
49. Itani KM, Weigelt J, Li JZ, Duttagupta S. Linezolid reduces length of stay and duration of intravenous treatment compared with vancomycin for complicated skin and soft tissue infections due to suspected or proven methicillin-resistant *Staphylococcus aureus* (MRSA). *Int J Antimicrob Agents.* 2005;26:442-448.
50. McKinnon P, Carter C, Girase P, Liu L, Carmelli Y. Impact of oral linezolid vs. IV vancomycin on resource utilization and cost in the outpatient setting. Presented at: Infectious Diseases Society of America; October 5-9, 2005 [poster]; San Francisco, Calif.
51. Parodi S, Rhew DC, Goetz MB. Early switch and early discharge opportunities in intravenous vancomycin treatment of suspected methicillin-resistant staphylococcal species infections. *J Manag Care Pharm.* 2003;9:317-326.
52. Understanding costs and cost-effectiveness in critical care: report from the second American Thoracic Society workshop on outcomes research. *Am J Respir Crit Care Med.* 2002;165:540-550.

CE Posttest

Select the single-letter response that best answers the question or completes the sentence.

1) Both direct and indirect costs are taken into account when conducting pharmacoeconomic studies. The cost of hospital staff (nurses, pharmacists, etc) is considered:
a. Fixed direct costs
b. Variable direct costs
c. Indirect costs
d. Fixed or variable direct costs, depending on full-time vs part-time employment status
e. Fixed or variable costs, depending on the level of benefits the employee receives

2) In the meta-analysis of 31 studies on MRSA infections by Cosgrove and colleagues, MRSA infections were associated with:
a. An approximate twofold increase in mortality for the main group, which was also seen in subgroup analysis that adjusted for comorbidities and severity of disease
b. An approximate twofold increase in mortality for the main group, but no differences in the subgroup analysis that adjusted for comorbidities and severity of disease
c. No effect on mortality in the main group analysis, but an approximate twofold increase in subgroup analysis for comorbidities or disease severity

3) In the cost analysis by Lodise and colleagues that compared MRSA and MSSA infections in a hospital setting, higher cost for MRSA infection was observed for the:
a. Variable direct costs
b. Fixed direct costs
c. Indirect costs
d. Variable and fixed direct costs, but not the indirect costs
e. All 3 cost groups

4) In the ICU-based study by Kollef, as well as hospital-wide studies by Lodise et al, delayed administration of appropriate antibiotics is associated with:
a. Higher mortality in the ICU patients but not in other hospitalized patients
b. Higher mortality in both the ICU and hospital population
c. No impact on mortality, but significant increases in morbidity

5) True or False: In a decision-model economic analysis, Shorr et al incorporated clinical trial data to show that linezolid is a cost-effective therapy for VAP.

6) In a prospective study of appropriate initial antibiotic treatment Combes et al observed that ventilator-associated pneumonia (VAP), due to MRSA was associated with:
a. A 3-day longer ICU stay compared with MSSA VAP
b. A 5-day longer ICU stay compared with MSSA VAP
c. A 7-day longer ICU stay compared with MSSA VAP
d. An 11-day longer ICU stay compared with MSSA VAP
e. No difference in ICU stay

7) True or False: In the study by Tice et al, the total cost estimates for outpatient vancomycin therapy included: drug acquisition cost, IV supplies, nursing time, cost of IV line placement and replacement, and management costs.

8) In the 2-year cost comparison of IV vancomycin and PO linezolid by McKinnon et al, IV vancomycin was associated with:
a. Greater resource utilization compared with linezolid
b. Lower overall cost compared with linezolid
c. Fewer visits to the emergency department compared with linezolid
d. Less use of laboratory and diagnostic testing compared with linezolid
e. None of the above

Burden of Methicillin-resistant *Staphylococcus aureus* on Healthcare Cost and Resource Utilization

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Posttest Answers (circle the correct answer)

1.	a	b	c	d	e
2.	a	b	c		
3.	a	b	c	d	e
4.	a	b	c		
5.	True	False			
6.	a	b	c	d	e
7.	True	False			
8.	a	b	c	d	e

Evaluation	Poor		Satisfactory		Excellent
1. Extent to which the objectives were achieved:	1	2	3	4	5
2. Potential impact on your practice:	1	2	3	4	5
3. Detail of information presented:	1	2	3	4	5
4. Extent to which commercial bias appeared:	1	2	3	4	5

5. Suggestions for future CE topics:

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Burden of Methicillin-resistant *Staphylococcus aureus* on Healthcare Cost and Resource Utilization

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