Comparing the Use of Intravenous Antibiotics Under the Medical Benefit With the Use of Oral Antibiotics Under the Pharmacy Benefit in Treating Skin and Soft Tissue Infections

Patients treated with oral linezolid, covered under the pharmacy benefit, had lower re-hospitalizations and emergency room visits than patients treated with vancomycin or daptomycin, covered under the medical benefit


ABSTRACT
Purpose
To assess differences in the simultaneous management of pharmacy and medical benefits by analyzing the health care utilization and costs associated with managed care patients who received oral linezolid as a pharmacy benefit or intravenous (IV) daptomycin or IV vancomycin as medical benefits for skin and soft tissue infections (SSTIs).

Methodology
The first medical or pharmacy claim from 03/01/2007 to 03/01/2010 was defined as the index date. Patients 18–64 years of age, with an inpatient SSTI diagnosis and ≥1 target antibiotic claim(s), were included. Follow-up was 45 days; hospitalizations, emergency room (ER) visits, outpatient medical services, prescription fills, and total health care costs were compared for the treatments using univariate generalized linear modeling (GLM) analyses. Total health care costs were compared with GLM multivariate analyses adjusting for baseline covariate values.

Results
Of the 8,905 patients included, 2,123 received linezolid, 5,503 vancomycin, and 1,279 daptomycin therapy; 14.4% of linezolid, 37.7% of vancomycin, and 22.8% of daptomycin patients were re-hospitalized (p<0.001). A smaller proportion of linezolid patients (8.6%) required emergency services, versus 11.6% of vancomycin and 10.8% of daptomycin patients (p<0.001).

Multivariate analyses showed vancomycin costs to be significantly lower than daptomycin costs, $5,425 (95% CI, $1,535 to $9,315), and a significantly higher mean cost difference for vancomycin, $11,182 (95% CI, $6,255 to $16,108), and daptomycin, $16,607 (95% CI, $9,426 to $23,788), versus linezolid.

Conclusion
Patients treated with oral linezolid had fewer re-hospitalizations and emergency room visits and lower total costs compared with patients who received vancomycin or daptomycin therapy, suggesting that oral linezolid, which is covered under members’ pharmacy benefits, may be more cost-effective than the two intravenous treatments for SSTIs.

INTRODUCTION
Pharmacy and medical benefit coverage constitute distinct and separate components of health plans and are governed by different payment methods and pricing guidelines (McDonald 2008). They are typically managed by separate policies, procedures, and personnel. As a result, challenges abound in the management of medication classes covered under these two benefits types. Antibiotics prescribed for the treatment of methicillin-resistant Staphylococcus aureus (MRSA) are an important case in point.

Three of the most commonly used agents to treat MRSA infections are linezolid, vancomycin, and daptomycin. Intravenous (IV) vancomycin was once considered the standard treatment for S. aureus worldwide (Li 2003) and the first-line treatment against MRSA because other antibiotics were ineffective against resistant S. aureus (Jones 2003, Stevens 2005). More recently, daptomycin and linezolid have provided alterna-
atives to vancomycin for MRSA. Daptomycin, which is effective against gram-positive organisms, including vancomycin-resistant pathogens, has also been approved to treat SSTIs, including MRSA-complicated forms (Bliziotis 2011, Crompton 2010). Linezolid has shown activity against antibiotic-susceptible and antibiotic-resistant gram-positive bacteria but is typically reserved for MRSA or vancomycin-resistant enterococcal infections (Ballow 2002, Mutnick 2002). Its 100% bioavailability permits sequential IV-to-oral administration without the necessity to change drug or adjust dosage. International usage data suggest that this practical advantage shortens expensive hospital stays, which can offset the lower acquisition cost of vancomycin (Grau 2008, Plosker 2005). This difference in the mode of administration has implications for how the drug is made available to patients and profoundly influences how it is covered for patients and how its costs are paid to providers.

Oral prescription treatments (such as oral linezolid), generally dispensed by pharmacists, are covered under pharmacy benefits, which are managed under drug formularies controlled by Pharmacy & Therapeutics (P&T) Committees. Drugs administered by physicians, nurses, and other clinical personnel, including IV vancomycin and IV daptomycin, are typically covered under medical benefits. The administration costs for intravenous therapy that accompany medical coverage, such as physician visits, infusion services, and other related procedures, may be greater than those of orally administered drugs, which are typically taken in the home setting with minimal supervision by clinicians. These costs may not always be taken into account in pharmacoeconomic and medical decision making (McKinnon 2007).

As a result of coverage differences, a P&T committee may not take the alternative IV treatments, vancomycin and daptomycin, into account if linezolid is seen as the preferred or nonpreferred agent. Also, if pharmacy benefit managers have little to no control or influence over the medical benefit, or the ability to alter physician prescribing patterns, drug acquisition costs are likely to be important in the decision, especially when the safety and efficacy of the agents are not substantially different. In this situation, the drug acquisition cost of vancomycin is significantly less than that of linezolid and daptomycin for the treatment of SSTI.

Several studies have suggested that linezolid and daptomycin treatments produce better clinical (Arbeit 2004, Itani 2005, Itani 2009, Mulin 2006, Sharpe 2005, Weigelt 2005) and economic outcomes (Davis 2007, McKinnon 2007) versus vancomycin among patients with SSTIs. One recent economic analysis used longitudinal claims data from 80 health plans, propensity score-matched patients treated with linezolid, and controls treated with vancomycin; 1,048 matched pairs were identified. Overall, linezolid patients had significantly lower resource utilization; laboratory, diagnostic, and pharmacy claims; ER visits; and hospitalizations versus patients on vancomycin. Mean total adjusted costs were 60% ($4,707) less for patients who received linezolid therapy compared to vancomycin ($8,401 versus $13,108, p<0.001) (McKinnon 2007). As of now, however, linezolid, vancomycin, and daptomycin have never been compared in the same study within a common managed care population.

In the course of this study, oral linezolid treatments were covered under pharmacy benefits, while IV vancomycin and IV daptomycin were covered as medical benefits. The objective was to assess differences in the simultaneous management of pharmacy and medical benefits by analyzing the health care utilization and costs associated with three large groups of managed care patients who received oral linezolid as a pharmacy benefit or IV daptomycin or IV vancomycin as medical benefits for skin and soft tissue infections.

METHODS

Study data

This study utilized administrative claims data from the HealthCore Integrated Research Database (HIRD), which includes medical and pharmacy claims data from 14 commercial health care plans in the northeastern, southeastern, mid-Atlantic, midwestern, and western regions of the United States (U.S.). All data in this nonexperimental, retrospective study were handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Patient confidentiality and anonymity were safeguarded throughout. Since this was a retrospective, observational study, and researchers only had access to a limited study database with masked patient identifiers, Institutional Review Board approval was not required.

Inclusion/exclusion criteria

Included subjects were required to have at least one medical or pharmacy claim for linezolid, daptomycin, or vancomycin between 03/01/2007 and 03/31/2010; the service date of the first occurrence was labeled the index date. Also, subjects were required to have an inpatient hospitalization that included either a diagnosis of complicated SSTI or uncomplicated SSTI within 30 days prior to the index date. SSTI diagnosis codes were pre-specified (Appendices). Subjects were required to be ≥18 and ≤64 years old by their index date. Excluded from the study were subjects receiving any combination of the study antibiotics on the index date or with a diagnosis of osteomyelitis or endocarditis.
Outcome measures
This study used a 45-day follow-up period, and all patients were followed for the entire duration; all of them maintained their health plan eligibility. The selection of a 45-day follow-up period is consistent with several preceding studies, including Kollef et al and Wunderink et al, both of which followed Gram-positive pneumonia patients up to 28 days after the end of therapy (Kollef 2004, Wunderink 2003, Wunderink 2008), and Wunderink et al, which followed nosocomial pneumonia patients up to 21 days after the end of treatment in a multicenter comparison of linezolid and vancomycin (Wunderink 2003). Outcome measures in our study included utilization and costs of health care resources, such as emergency room visits, hospital readmissions, physician office visits, and other outpatient services, including, but not limited to, antibiotic infusions, skilled nursing services, laboratory services, and antibiotic medications. All cost calculations included both health plan and member portions.

Statistical analysis
To assess comparability of the linezolid, vancomycin, and daptomycin cohorts at baseline, chi-square tests were conducted for categorical variables and analyses of variance (ANOVAs) were used for quantitative variables. For outcome comparisons, a general linear model (GLM) with a Poisson distribution and log link was used for unadjusted means for utilization variables and a univariate GLM with gamma distribution and log link was used to compare unadjusted mean health care component and total costs among the three groups. The covariate adjusted analysis for total cost associated with treatment was conducted using a GLM with a gamma distribution and log link function. The analyses controlled for age, gender, geographic region, presence of cancer, organ transplant, primary immunodeficiency disorder, diabetes mellitus, chronic kidney disease, the calculated Deyo-Charlson Comorbidity Index (DCI) (Deyo 1992), sepsis, and pre-index total allowed cost of care to evaluate mean differences among the groups. The DCI comprises 17 diagnoses based on ICD-9-CM codes, each with a designated weight of 1 to 6. The final score is the sum of weighted values of the comorbidities, and higher scores indicate greater comorbidity burden. Statistical analyses were conducted with STATA 11.0 software. Alpha was set at 0.05 for each test.

RESULTS
Sample derivation
A total of 8,905 patients met age requirements, were hospitalized with an SSTI diagnosis (99% had complicated SSTI, with no differences between treatment groups) within 30 days prior to their first outpatient antibiotic claim, and received one of the antibiotics of interest — linezolid (n=2,123), vancomycin (n=5,503), or daptomycin (n=1,279) therapy — and were included in the final study sample (Figure 1).

Baseline clinical and demographic characteristics
The mean (SD) age of the linezolid patients was 46.0 (11.8) years; vanco-
mycin, 47.9 (11.5) years; and daptomycin, 47.6 (11.4) years ($p<0.0001$).

There were significantly more patients in the 46–55 and 56–64 years age range versus younger patients (18–35 and 36–45 years) in all three cohorts.

Males outnumbered females across all cohorts, totaling 55.0% of the linezolid, 54.6% of the vancomycin, and 53.4% of the daptomycin groups.

Along with other clinical and demographic attributes shown in Table 1, there were significant differences in the mean (SD) Deyo-Charlson Comorbidity Index scores of the three cohorts: 1.7 (2.5) for linezolid patients, 2.1 (2.8) for vancomycin patients, and 1.8 (2.7) for daptomycin patients ($p<0.0001$).

In addition, significant differences were reported for cancer and other malignancies: 27.1%, 32.3%, and 33.4% in the linezolid, vancomycin, and daptomycin cohorts, respectively, at baseline ($p<0.0001$).

### Health care utilization

During the 45 day follow-up period, there were significant differences among the linezolid, vancomycin, and daptomycin cohorts for both inpatient hospitalizations and emergency room visits, as shown in Figure 2. In the study period, inpatient services were used by 14.4% of the linezolid patients, 37.7% of the vancomycin patients, and 22.8% of those treated with daptomycin ($p<0.0001$). Regression analysis demonstrated that patients treated with vancomycin had significantly more inpatient hospitalizations (0.26) compared with patients treated with linezolid (95% CI, 0.22 to 0.30). Daptomycin patients were also associated with significantly more hospitalizations (0.15) compared with daptomycin patients (95% CI, 0.10 to 0.20). The relative risk of vancomycin-treated patients being re-hospitalized compared to linezolid-treated patients was 2.61 (95% CI, 2.38 to 2.88), and the risk difference was 0.233 (0.210, 0.256), or 23.3 per hundred patients treated with each drug. The relative risk of daptomycin versus linezolid patients being re-hospitalized was 1.58 (1.37, 1.83), and the risk difference was 0.084 (0.058, 0.110), or 8.4 per hundred. Vancomycin-treated patients had a higher relative risk of re-hospitalization than daptomycin-treated patients (1.65; 95% CI, 1.50 to 1.82), and the risk difference was 0.148 (0.120, 0.177), or 14.8 per hundred.

Significantly fewer (9.1%) linezolid patients required subsequent infection-related inpatient services, versus 31.3% of the vancomycin patients and 17.1% of the daptomycin patients ($p<0.0001$). Vancomycin patients had 0.23 more infection-related hospitalizations than linezolid patients (95% CI, 0.20 to 0.26), and daptomycin patients experienced 0.1 more infection-related inpatient admissions than

### Table 1

<table>
<thead>
<tr>
<th>Patient demographic characteristics by cohorts</th>
<th>Oral linezolid N = 2,123</th>
<th>IV vancomycin N = 5,503</th>
<th>IV daptomycin N = 1,279</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>46.0 (11.8)</td>
<td>47.9 (11.5)</td>
<td>47.6 (11.4)</td>
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</tr>
<tr>
<td>Gender</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Male</td>
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<td>3,004</td>
<td>683</td>
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</tr>
<tr>
<td>Female</td>
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</tr>
<tr>
<td>Region</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>402</td>
<td>870</td>
<td>81</td>
<td>0.001</td>
</tr>
<tr>
<td>South</td>
<td>852</td>
<td>1,637</td>
<td>400</td>
<td>0.313</td>
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<tr>
<td>Midwest</td>
<td>540</td>
<td>1,567</td>
<td>360</td>
<td>0.281</td>
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<tr>
<td>West</td>
<td>329</td>
<td>1,429</td>
<td>438</td>
<td>0.012</td>
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<tr>
<td>Comorbidities</td>
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<td></td>
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<tr>
<td>Cancer</td>
<td>575</td>
<td>1,778</td>
<td>427</td>
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<tr>
<td>Organ transplant</td>
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<td>2,134</td>
<td>481</td>
<td>0.288</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>531</td>
<td>1,492</td>
<td>301</td>
<td>0.014</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>67</td>
<td>211</td>
<td>29</td>
<td>0.015</td>
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<tr>
<td>Deyo-Charlson Comorbidity Index (DCI)</td>
<td></td>
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<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.7 (2.5)</td>
<td>2.1 (2.8)</td>
<td>1.8 (2.7)</td>
<td></td>
</tr>
</tbody>
</table>

SD = Standard Deviation
linezolid patients (95% CI, 0.05 to 0.13). There was also a significant difference between vancomycin-treated patients and daptomycin-treated patients (mean difference = 0.14; 95% CI, 0.10 to 0.18).

There were significant differences in the total use of emergency room services by the three cohorts. A smaller proportion of linezolid patients (8.6%) required any ER services, versus 11.6% of the vancomycin patients and 10.8% of the daptomycin patients (p<0.001). Vancomycin patients used significantly more ER services than patients treated with linezolid (mean difference = 0.045; 95% CI, 0.02 to 0.07). There were no significant differences in the amount of infection-related ER services used by daptomycin patients and linezolid patients (mean difference = 0.029; 95% CI, -0.02 to 0.6) or between vancomycin and daptomycin cohorts (mean difference = 0.015; 95% CI, -0.01 to 0.05). There was no significant main effect for infection-related ER services (p = 0.831).

**Costs**

Table 2 provides a breakdown of mean (±SD) and median costs for antibiotics, inpatient and ER services, outpatient and total costs, as well as adjusted mean cost for patients in each of the three cohorts.

**Antibiotics**

Medication acquisition costs were significantly different among cohorts. The mean (SD) cost of linezolid was $1,686 ($4,581) compared to $519 ($1,978) for vancomycin and $3,478 ($3,867) for daptomycin (p=0.0001). The results showed that medication costs for linezolid were significantly higher than for vancomycin (mean difference = $1,167; 95% CI, $1,062 to $1,272; p<0.0001) and significantly lower than for daptomycin (mean difference = $1,792; 95% CI, $1,499 to $2,084; p<0.0001). The mean daptomycin medication costs were significantly higher than those for vancomycin (mean difference = $2,959; 95% CI, $2,684 to $3,233; p<0.0001).

**Inpatient and ER**

There were significant differences in the mean costs for inpatient and ER services among the cohorts. Mean (SD) cost for the linezolid patients was $6,650 ($48,866), whereas for the vancomycin group it was $15,138 ($54,224) and for the daptomycin cohort it was $12,950 ($49,048), p<0.0001. Cost differences showed that patients on vancomycin had significantly greater mean inpatient plus ER health care costs compared with those on linezolid (mean difference = $8,488; 95% CI, $6,632 to $10,345). Daptomycin costs were also significantly greater than those for linezolid (mean difference = $6,300; 95% CI, $3,405 to $9,195). No significant difference was observed in the combined mean inpatient and ER costs for IV vancomycin and IV daptomycin (mean difference = $2,188; 95% CI, -$889 to $5,275).

**Outpatient**

Outpatient health care costs were incurred for provider evaluation and management, laboratory and nursing services, home health care, medical equipment, and infusions. There was a significant main effect for outpatient costs (p<0.0001). There was a significantly greater mean outpatient cost for vancomycin patients compared with those treated with linezolid (mean difference = $3,048; 95% CI, $2,701 to $3,395). Daptomycin patients also had significantly greater mean outpatient costs versus linezolid patients (mean difference = $5,998; 95% CI, $5,086 to $6,910). Mean outpatient costs were significantly higher for daptomycin versus vancomycin patients (mean difference = $2,950; 95% CI, $2,018 to $3,882). As shown in Figure 3, linezolid patients had lower costs for laboratory, nursing, medical equipment, and infusions provided on an outpatient basis. Provider evaluation and management costs were significantly less for both linezolid and vancomycin than for daptomycin. Lower costs were also reported for linezolid patients in all outpatient categories compared with patients treated with daptomycin.
DISCUSSION

Because this analysis compares the effect of different antibiotic agents on health care utilization and costs, the actual outcomes are heavily influenced by an important administrative consideration: how to manage policies for therapeutic classes in which some medications are covered by pharmacy benefits and others by medical benefits. The principal goals in the treatment of bacterial SSTI infections are to relieve patient symptoms and eliminate infectious pathogens as rapidly as possible. Success in both goals results in reduced re-hospitalizations, less utilization of emergency and other outpatient services, and overall cost curtailment (Mullins 2011). The decision about what agents will be available to target those goals for patients in any given situation, however, rests heavily on whether a patient’s pharmacy benefits, required not these policies can affect physician prescribing patterns.

In the post-index period of this study, patients treated with linezolid, which was supplied under members’ pharmacy benefits, required significantly fewer total and infection-related re-hospitalizations and total ER services compared to patients treated with vancomycin and daptomycin, both supplied under medical benefits. Infection-related ER services were not significantly different among the treatment groups. Mean inpatient, ER, and outpatient costs were significantly lower for patients treated with linezolid compared with the other two agents, as were both the unadjusted and adjusted total costs. The mean drug costs were significantly higher for linezolid, a newer branded antibiotic, compared to vancomycin, which has been in use for some time and is available in generic formulations. On the other hand, the mean costs attributable to linezolid were significantly less than those for daptomycin, another newer branded antibiotic. Compared with vancomycin, the higher drug cost of linezolid was offset by higher inpatient and outpatient expenditures associated with vancomycin therapy, relative to the significantly lower mean total costs for linezolid patients. As an effect of lower utilization rates, the mean costs attributable to linezolid-treated patients for laboratory services, provider evaluation and management, nursing, the use of medical equipment, and infusion services were significantly less than those for both vancomycin and daptomycin patients.

**TABLE 2**  
Summarized health care cost by cohorts

<table>
<thead>
<tr>
<th>Antibiotic costs (Mean ± SD)</th>
<th>Oral linezolid N = 2123</th>
<th>IV vancomycin N = 5503</th>
<th>IV daptomycin N = 1279</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient and ER costs</td>
<td>$1,686 ± $4,581</td>
<td>$519 ± $1,978</td>
<td>$3,478 ± $3,867</td>
<td>.0001</td>
</tr>
<tr>
<td>Outpatient costs</td>
<td>$6,650 ± $48,866</td>
<td>$15,138 ± $48,866</td>
<td>$12,950 ± $49,048</td>
<td>.0001</td>
</tr>
<tr>
<td>Unadjusted total cost</td>
<td>$2,532 ± $7,525</td>
<td>$5,580 ± $9,997</td>
<td>$8,529 ± $10,068</td>
<td>.0001</td>
</tr>
</tbody>
</table>

**Adjusted total cost**

- Adjusted mean costs: $11,328, $22,510, $27,935, p < .0001
- 95% confidence interval: $7,716–$14,940, $15,652–$29,368, $19,207–$36,664

*Analysis conducted with the General Linear Model (GLM) approach with gamma distribution and log link function controlling age, gender, geographic region, cancer, organ transplant, primary immunodeficiency disorder, diabetes mellitus, chronic kidney disease, the DCL, sepsis, and pre-index total allowed cost of care. Because of the very small number of patients with HIV, this variable could not be included in the model.

SD = Standard Deviation
These findings are consistent with those of recent studies that compared the agents of interest in this study for the treatment of MRSA infections in patients with SSTIs (Mullins 2011, Itani 2005, Itani 2009, Itani 2011, Mullins 2006, Sharpe 2005, Weigelt 2005). Weigelt et al showed that while safety and side effect profiles were similar, linezolid was well tolerated and superior to vancomycin for complicated SSTIs with MRSA (Weigelt 2005). Sharpe et al found that linezolid treatment was associated with significantly better clinical outcomes and improvement and was associated with a three-day shorter median inpatient stay and reduced outpatient costs versus vancomycin (Sharpe 2005). Itani et al reported that linezolid-treated patients had significantly shorter inpatient stays, shorter durations of antibiotic treatments, and greater discharge rates (Itani 2005). Mullins et al reported significantly lower re-hospitalization rates for linezolid- versus vancomycin-treated patients (26.1% vs. 33.4%, \( p < 0.0001 \)).

The skin infections segment of the Mullins et al study demonstrated that linezolid-treated patients had lower risk of readmission (27.3%) compared with vancomycin patients (Mullins 2006). In this study, we found similar and stronger associations between linezolid and lower hospital readmission rates. The readmission rate for linezolid was 14.4%, compared to 37.7% for vancomycin and 22.8% for daptomycin (\( p = 0.0001 \)).

An economic analysis used longitudinal claims data from 80 health plans, propensity score-matched patients treated with linezolid, and controls treated with vancomycin; 1,048 matched pairs were identified. Overall, linezolid patients had significantly lower resource utilization; laboratory, diagnostic, and pharmacy claims; ER visits; and hospitalizations versus patients on linezolid. Mean total adjusted costs were 60% ($4,707) less for patients who received linezolid therapy compared to vancomycin ($8,401 versus $13,108, \( p < 0.001 \)) (McKinnon, 2007). In another evaluation, Davis et al showed that although daptomycin was associated with higher drug costs for SSTIs at a level-one trauma center, median hospitalization costs were significantly less for daptomycin patients versus vancomycin patients ($5,027 versus $7,816, respectively) (Davis 2007).

Supported by the results of the foregoing studies, it would seem reasonable to imply from our findings that linezolid could be a suitable addition to managed care formularies and could even become the first-line therapy for SSTIs. Such implications must be approached with caution, however, and only after a thorough analysis of several associated and intervening factors. One is the emergence of resistance to linezolid, which has been confirmed in reports in the United States and various other parts of the world (Endimiani 2011, Gaynes 2005, Peeters 2005). With such potential resistance, it would appear prudent from a public health perspective to reserve agents like linezolid for predefined clinical scenarios, limit their exposure, and preserve their effectiveness against MRSA organisms.

It is noteworthy that the three cohorts in this study had differing comorbidity profiles at baseline. For example, cancer rates were lowest in the linezolid-treated group versus the other two, and the DCI scores indicated that linezolid patients had a lower comorbidity burden overall, which could have affected both resource utilization and costs. With respect to hospitalizations, however, one of the costliest categories in this analysis, all patient admissions included in the study were required to have an infection code. So while it was not possible to ascertain the primary reason of an individual hospitalization from our data, there was no doubt that each admission had a definite infection diagnosis code and was infection-related.

While acknowledging the baseline differences and the challenges inherent in managing different ben-
eft types, we thought it would be instructive to evaluate the cost effects of switching patients from the two IV agents to oral linezolid. The potential adjusted savings likely for switching to linezolid from vancomycin ranged from $6,255 to $16,108 per patient. Switching from daptomycin to linezolid would result in savings of $9,426 to $23,788 per patient. On the basis of annual estimates of vancomycin and daptomycin usage from this population, switching just 10% of the subjects to linezolid could result in millions of dollars in savings.

Overall, this analysis suggests that a paradigm shift is needed to appropriately assess the cost of therapy. The shift should be away from an analytic focus limited to just the acquisition cost of a medication and must evolve to consider the inclusion of the incremental cost of supportive services, supplies, and administration into a total cost of care for a day of therapy. This analysis also demonstrates that the downstream medical consequences resulting from the tolerability and effectiveness of an intervention can dramatically influence the episode total cost of care. Comparative effectiveness research that reflects actual utilization patterns and costs of care can facilitate alignment of economic incentives for physicians, health plans, and consumers with optimal clinical outcomes. The recognition that optimal clinical outcomes (i.e., lower inpatient readmission and emergency room utilization) associated with the lowest total cost of care have yielded the highest value of health care can facilitate payment innovation and policy development to reward mutually aligned goals.

LIMITATIONS
Claims data are an excellent starting point for retrospective studies, which generate important post-marketing information on products devoid of the strictures imposed on randomized clinical trials. Still, administrative claims data are subject to important setbacks. Claims data are subject to incompleteness, unreliable clinical coding, and the omission of unobservable factors that may influence outcomes. Data on infection severity and concomitant conditions are lacking in this study; thorough reviews of medical records are required to identify such information. An important limitation in this study was the unavailability of dosing information and treatment strategies for three antibiotic agents and the patient cohorts. Bounthavong et al demonstrated that dosing regimens and treatment strategies have important implications for patient outcomes and affect the major cost areas (Bounthavong 2009).

CONCLUSION
Patients treated with oral linezolid had fewer re-hospitalizations

APPENDICES

APPENDIX 1
Study drugs and codes

<table>
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<th>Cohort</th>
<th>Drug</th>
<th>HCPCS</th>
<th>GPI</th>
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<td>1</td>
<td>Oral linezolid</td>
<td>NA</td>
<td>16230040000330 (Tablets)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>16230040001920 (Oral Suspension)</td>
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<tr>
<td>2</td>
<td>IV vancomycin</td>
<td>J3370</td>
<td>16000060* (Except the following: Tablets: 16000060100110 &amp; 16000060100120; Oral Solutions: 16000060102150 &amp; 16000060102160, and Powder: 16000060102900)</td>
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<tr>
<td>3</td>
<td>IV daptomycin</td>
<td>J0878</td>
<td>16270030002140</td>
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</tbody>
</table>

*Each drug has a GPI code consisting of 14 digits. The first 8 digits identify what the drug is. The asterisk represents the other 6 digits and are not needed.

APPENDIX 2
Diagnostic codes

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>ICD-9 codes</th>
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<td>Any SSTI episodes</td>
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<tr>
<td>Complicated SSTI</td>
<td></td>
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<tr>
<td>Infection due to device or graft</td>
<td>996.6x</td>
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<tr>
<td>Surgical site infection</td>
<td>998.5x, 999.3x</td>
</tr>
<tr>
<td>Nonhealing surgical wound</td>
<td>998.83</td>
</tr>
<tr>
<td>Decubitis ulcer</td>
<td>707.x</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue infections</td>
<td>686.x</td>
</tr>
<tr>
<td>Cellulitis, erysipelas and folliculitis in patient setting</td>
<td>See codes below</td>
</tr>
<tr>
<td>Uncomplicated SSTI</td>
<td></td>
</tr>
<tr>
<td>Carbuncle and furuncle</td>
<td>680.x</td>
</tr>
<tr>
<td>Cellulitis and abscess (exclude if occurs INP)</td>
<td>681.x-682.x</td>
</tr>
<tr>
<td>Erysipelas (exclude if occurs INP)</td>
<td>035.x</td>
</tr>
<tr>
<td>Impetigo</td>
<td>684.x</td>
</tr>
<tr>
<td>Mastitis</td>
<td>611.0x, 771.5x</td>
</tr>
<tr>
<td>Folliculitis (exclude if occurs INP)</td>
<td>704.8x</td>
</tr>
</tbody>
</table>
and emergency room visits and lower total costs compared with patients who received vancomycin or daptomycin therapy, suggesting that oral linezolid, which was covered under members’ pharmacy benefits, may be more cost-effective than the two intravenous treatments, which were covered under medical benefits, for SSTIs.

REFERENCES


McDonald RC. Managing the intersection of medical and pharmacy benefits. J Manag Care Pharm. 2008;14:S7–11.


