HHS Public Access

Author manuscript

Infect Control Hosp Epidemiol. Author manuscript; available in PMC 2019 April 29.

Published in final edited form as:

Infect Control Hosp Epidemiol. 2014 October ; 35(10): 1229–1235. doi:10.1086/678066.

Economic Impact of Redundant Antimicrobial Therapy in US Hospitals

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Abstract

BACKGROUND.—Overutilization of antimicrobial therapy places patients at risk for harm and contributes to antimicrobial resistance and escalating healthcare costs. Focusing on redundant or duplicate antimicrobial therapy is 1 recommended strategy to reduce overutilization and its attendant effects on patient safety and hospital costs.

OBJECTIVE.—This study explored the incidence and economic impact of potentially redundant antimicrobial therapy.

METHODS.—We conducted a retrospective analysis of inpatient administrative data drawn from 505 nonfederal US hospitals. All hospitalized patients discharged between January 1, 2008, and December 31, 2011, were eligible for study inclusion. Potentially redundant antimicrobial therapy was identified from pharmacy records and was defined as patients receiving treatment with overlapping antibiotic spectra for 2 or more consecutive days.

RESULTS.—We found evidence of potentially inappropriate, redundant antimicrobial coverage for 23 different antimicrobial combinations in 394 of the 505 (78%) hospitals, representing a total of 32,507 cases. High-frequency redundancies were observed in 3 antianaerobic regimens, accounting for 22,701 (70%) of the cases. Of these, metronidazole and piperacillin-tazobactam accounted for 53% (n = 17,326) of all potentially redundant cases. Days of redundant therapy totaled 148,589, representing greater than $12 million in potentially avoidable healthcare costs.

CONCLUSIONS.—Our study suggests that there may be pervasive use of redundant antimicrobial therapy within US hospitals. Appropriate use of antimicrobials may reduce the risk of harm to patients and lower healthcare costs.

Overuse and inappropriate use of antimicrobials is a major public health issue and contributes to patient harm, antimicrobial resistance, and unnecessary healthcare costs.[1–3] It has been recognized for several decades that of patients receiving antimicrobial therapy, up to half receive unnecessary or inappropriate therapy, including redundant therapy.[4–6]

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Focusing on redundant or duplicate antimicrobial therapy is 1 recommended strategy to reduce overutilization and its attendant effects on patient safety and hospital costs.[5,7]

Examination of treatment pathways shows that some clinicians will administer antibiotics with overlapping spectra as empiric therapy to reduce the chances that the infecting organism will be resistant to the regimen. However, aside from this use, there are very few clinical indications for using antibiotics with overlapping spectra. Additionally, overprescribing or redundant coverage can result from systemic and/or individual practitioner factors, including prescribing errors arising from the lack of knowledge of the patient's antibiotic regimen, suboptimal care coordination, or difficulties in accessing current pharmacy records. Similarly, a lack of knowledge of the antimicrobial spectra, intentional prescribing errors (eg, antibiotic combinations prescribed with intended overlap but for which there was no clinical indication), or the desire to meet patient expectations may lead to inappropriate use.[8,9]

This study explored the incidence and economic impact of potentially redundant antimicrobial therapy, including dual antianaerobic agents, dual β-lactams, and dual treatment with agents active against resistant gram-positive infections (anti–methicillin-resistant *Staphylococcus aureus* [MRSA] agents). Because these combinations of antibiotics with redundant spectrum are so rarely clinically indicated, they could represent an early opportunity to improve antibiotic use and reduce the potential for patient harm and healthcare waste.

METHODS

Study Design

We conducted a retrospective analysis of hospital administrative data for acute care inpatients. Data were provided by Premier. The Premier database constitutes the nation's largest outcomes database developed for quality and safety improvement and includes approximately 1 in 4 (26%) US hospital discharges, 2.5 million real-time daily clinical transactions, and nearly $50 billion in annual purchasing data.

All patient records used in this study were de-identified in compliance with the Health Insurance Portability and Accountability Act of 1996. All statistical analyses were performed using SAS (ver. 9.2; SAS Institute).

Definitions

For study inclusion, patients had to be hospital inpatients discharged between January 1, 2008, and December 31, 2011, and have *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes and pharmacy records.

All pharmacy data for each patient included in the study sample were examined for antibiotic usage. Because drugs were coded as either generic and/or brand name and a variety of spellings were used, we used both the drug name(s) and billing codes to identify potential usage of 23 combinations representing 3 categories: (1) antianaerobics, (2) anti-MRSA, and (3) dual β-lactams. These combinations are listed in Table 1.

In accord with similar studies of redundant antimicrobial coverage, we defined redundant antimicrobial usage as the administration of 2 agents that provide coverage for the same organism(s) for at least 2 consecutive days during the same hospitalization.[10] The standard measure of days of therapy was amended to days of combination antimicrobial therapy, on the basis of the metric proposed by Polk et al.[11] Multiple instances of dual therapy in the same patient were counted only once, and if a patient received several courses of dual antibiotic therapy, then the total days of combination antimicrobial therapy was the summation ofall dual therapy days, regardless of whether there was a break in therapy.

Because *Clostridium difficile* infections (CDIs) should be treated with either oral metronidazole or oral vancomycin, we limited our analysis to intravenously administered agents to exclude patients who might have received an intravenous agent to treat 1 infection along with oral metronidazole or vancomycin to treat CDI. We did include cases where patients were receiving oral and intravenous metronidazole or oral and intravenous vancomycin along with another intravenous agent with antianaerobic or anti-MRSA activity.

In keeping with the protocol suggested by Huttner et al,[10] we excluded patients with cholecystitis (ICD-9-CM code 575.0) and cholangitis (ICD-9-CM code 576.1). Although contradictory evidence exists,[12] some studies have concluded that these patients represent potentially appropriate cases for dual therapy.[13–16]

Diagnoses and Testing for MRSA and CDI

We searched for ICD-9-CM codes for CDI and MRSA and designated these patients as uncoded (ie, had no recorded diagnosis code for CDI or MRSA), coded for CDI, or coded for MRSA. The ICD-9-CM code searched for CDI was 008.45, whereas the ICD-9-CM codes searched for MRSA included 038.12, 041.12, and V09.0.

Because several studies of CDI have found only low to moderate correlation between ICD-9-CM codes and microbiology results,[17–20] we conducted an additional test to determine whether patients receiving dual therapy also had a test for CDI and/or MRSA. Our hypothesis was that in some cases, practitioners may have assumed the presence of CDI or MRSA on the basis of related symptoms and commenced aggressive therapy before laboratory results were available. We searched patient billing data for tests for CDI and MRSA, using variations on the name of specific tests (eg, “c diff,” “c difficile,” “clostridium diff toxin,” “MRSA,” “methicillin resist”) as well as common procedure terminology codes. Combined, this search captured all CDI- or MRSA-related tests whether culture or toxin (CDI) or nasal swab, tissue sample, or blood or bodily fluid culture (MRSA) for which a test was billed. While MRSA tests performed for surveillance are not eligible for Medicare reimbursement and might not have been recorded, we assumed that if a test was positive, the hospital would have included the test findings (and thus bill for the test) as justification for treatment costs.

Costs and Resource Consumption

We calculated potentially avoidable days of combination antimicrobial therapy and costs on the basis of administrative and pharmacy billing data for each of the drug combinations listed in Table 1. The data were examined for patterns of drug administration where 2

redundant therapies were administered concomitantly for at least 2 consecutive service days. In order to standardize drug cost across hospitals, we calculated the median acquisition cost for each drug at the commonly used dosage for adult patients.

Excess cost for the antianaerobic drug combinations was determined by setting the least expensive and narrower-spectrum drug (ie, metronidazole) as the primary agent and the more expensive and wider-spectrum drug as redundant. Because there were large variations in drug pricing for the anti-MRSA and dual β-lactam combinations, excess cost was determined by setting each drug, in turn, as the redundant agent. For example, if the median cost for vancomycin (1 g every 12 hours) was $10.38 per dose day and the median cost for linezolid (600 mg every 12 hours) was $163.24 per dose day, then the excess cost for this combination was $163.24 per patient for each day of combination antimicrobial therapy when linezolid was considered redundant and $10.38 when vancomycin was considered redundant.

Total redundancy cost (potential cost avoidance) was calculated by summing the total cost of the highest-priced drug for each of the redundant combinations where total cases were 100 or more. While focusing on the most common combinations produced a lower cost estimate, it also reduced between-hospital variability and aligned the results with the National Quality Forum's recommendations for quality measurement (ie, high impact, feasible, useful).[21]

RESULTS

From January 1, 2008, through December 31, 2011, of a total of 505 acute care hospitals in the study cohort, 394 (78%) had evidence of 1 or more of the 23 combinations of potentially redundant antimicrobial coverage listed in Table 1. Analysis of individual cases showed a total of 32,507 cases in the study sample of patients who received at least 2 consecutive service days of 1 or more of the redundant antimicrobial combinations (Table 1). Mean days of combination antimicrobial therapy ranged from 3 to 6 days of administration.

Combinations with multiple intravenous antianaerobics were most common, with the greatest utilization being the intravenous metronidazole and piperacillin-tazobactam combination (n = 17,326, or 53% of sample). For the anti-MRSA treatments, the vancomycin and linezolid combination accounted for 5% of total patients (n = 1,611), while the vancomycin and daptomycin combination accounted for 3% (n = 987).

Similar to the highest-frequency antianaerobic combination, the dual β-lactam combinations (1% or more) included piperacillin-tazobactam. These dual β-lactam combinations accounted for 5 percent of all patients receiving dual therapies.

Data Trends

The frequency of redundant antimicrobial combinations by year (2008–2011) is shown in Table 2. With few exceptions, the unadjusted data trended higher each year. Overall, the metronidazole and piperacillin-tazobactam combination accounted for the majority of the growth in redundant combination use. Of note is the decrease in the metronidazole and ampicillin-sulbactam combination from 2008 to 2011. Adjusting for patient volume (rate per

1,000 patients), total usage per year showed a slight but significant decrease (Kruskal-Wallis test, $P = .042$).

ICD-9-CM Codes and Sensitivity Analyses

Examination of the 26,544 cases of redundant intravenous metronidazole use showed that only 5% of the cases ($n = 1,322$) had a recorded ICD-9-CM code for CDI (Table 1). Similarly, of the 2,917 cases of redundant usage for anti-MRSA agents, only 1,281 (44%) had a corresponding ICD-9-CM code for MRSA.

Review of patient billing data to determine whether patients receiving dual therapy had a recorded test for CDI or MRSA showed that out of the 26,544 patients receiving an antianaerobic combination, only 8,915 (34%) had a recorded test for CDI. Likewise, of the 2,917 patients receiving an anti-MRSA combination, 36% ($n = 1,044$) had a recorded test for MRSA. Overall, of the 32,507 patients receiving any of the 23 dual therapy combinations, only 18,939 (58%) had tests for either CDI or MRSA.

Cost Estimates

Using the median acquisition cost for metronidazole as the baseline (primary treatment), the total cost for the 6 redundant antianaerobe regimens exceeded $9.9 million (Table 3). Similarly, for the 2 anti-MRSA regimens, if vancomycin was set as the baseline (primary treatment), the potential cost savings from eliminating redundancy was daptomycin ($855,228) and linezolid ($1,072,487). If daptomycin was set as the baseline (primary treatment), the cost avoidance from using linezolid was $335,948. Summation of the 17 most common redundant combinations (setting the highest-cost drug as redundant) exceeded $12 million in potential cost avoidance.

DISCUSSION

We examined the incidence of several potentially redundant antimicrobial combinations within a large, representative sample of nonfederal, acute care hospitals in the United States. We found evidence to suggest the existence of costly and potentially avoidable patterns of redundant antimicrobial use. Of note was the frequency of use of intravenous metronidazole in combination with another antimicrobial agent with anaerobic activity. Three of the metronidazole combinations and 1 combination in particular—metronidazole and piperacillin-tazobactam—accounted for greater than 70% of potential redundant usage. In addition, analysis of the data by year showed that despite recommendations to the contrary, [22] hospitals in the sample continued at roughly the same rate of potentially redundant or duplicate antimicrobial usage from 2008 to 2011. An exception to this was the decrease in the metronidazole and ampicillin-sulbactam combination. As the Surgical Infection Society and Infectious Disease Society of America's 2010 guidelines alerted practitioners of the growing resistance of *Escherichia coli* to ampicillin-sulbactam,[14] this decrease was expected and validates the power of the study to detect known variations in clinical practice.

Although there may be rare instances where the combinations we examined were appropriate, we believe that the vast majority of these cases represent avoidable duplication. There is no evidence to support the routine use of any of the combinations we analyzed.

Treatment guidelines do not recommend the combination of multiple agents with antianaerobic or anti-MRSA activity, and these combinations accounted for greater than 90% of the cases we found. Likewise, the use of dual β-lactams is not recommended and may be detrimental.[23] Because oral metronidazole is recommended for the treatment of CDI,[24] its use in combination with other mtianaerobic agents could be appropriate; hence, combinations that included oral metronidazole were excluded from our analysis. Intravenous metronidazole is not recommended for the treatment of CDI except in cases of severely ill patients with ileus;[25] hence, the combination of metronidazole with mother antianaerobic agent would be considered inappropriate in most instances, even in patients with CDI.

We searched for the presence of an ICD-9-CM code indicating CDI among patients receiving multiple antianaerobic agents and found that the vast majority (95%) had no ICD-9-CM diagnosis code of CDI. Further, in the majority of cases, he hospital billing data did not contain a billing code indicating that a CDI (34%) or MRSA (36%) test had been performed with the drug combinations typically used for those infections. Regardless of the potential for some cases where ICD-9-CM or billing codes may have been missing for patients with confirmed cases of CDI and/or MRSA, there are currently no recommendations for the use of either metronidazole or vancomycin for prophylaxis against CDI during the administration of other antibiotics. Multiple studies have indicated that prolonged metronidazole exposure is associated with peripheral neuropathy, and the use of multiple antibiotics compared with single antibiotics is associated with an overall increased risk of subsequent CDI.[22,26,27]

If we consider the median drug acquisition cost for the 124,928 days of metronidazole administration as the baseline therapy, the cost of redundant treatment exceeds $9.9 million. The total potential cost savings in drug costs alone from reducing the 17 most frequent redundant antimicrobial combinations to monotherapy (setting the highest-cost drug as redundant) exceeded $12.9 million for the 398 hospitals for years 2008–2011. If our findings for the hospital sample were indicative of community hospital practice throughout the United States,[28] then the potential cost savings from eliminating redundant antimicrobial therapy during the same time frame could exceed $163 million, or almost 2% of the total expenses for all US hospitals for 2012.[29] Because these estimates do not include the lower incidence combinations (ie, those less than 100 cases) and associated non-drug-related supply and labor costs for the pharmacy and nursing departments, hospital operations, and the cost of potential complications, the total cost savings could be substantially higher.

In addition to excess costs, these unnecessary antibiotic combinations increase the risk of adverse drug events.[30] Each agent has a risk of side effects, and combinations increase those risks as well as the risks for drug-drug interactions, such as the potential drug antagonism with vancomycin and linezolid.[31,32] Further, the combinations identified in this study were all intravenous agents that can pose unnecessary exposure to injectable medications and the risks that come with those exposures (eg, bloodstream infections). Looking just at combinations with metronidazole, this constitutes at a minimum 124,928 days of needless administration of an injectable medication. In a recent investigation of the economic burden of preventable adverse drug events, anti-infectives were the second-highest risk-prone category of injectable medications by volume.[33]

Antimicrobial stewardship is an effective strategy in reducing overutilization and redundant therapy, antimicrobial resistance, patient harm, and wasteful spending.[3,34,35] Improving the use of antibiotics has been identified as a critical need to address the combination of rising rates of antimicrobial resistance, a rapidly dwindling effective antimicrobial armamentarium, and increasing financial pressures.[3,36] A combined policy statement from 3 professional societies (Society for Healthcare Epidemiology of America, Infectious Diseases Society of America, and Pediatric Infectious Diseases Society) declared that all healthcare institutions have a fiduciary responsibility to practice in a manner consistent with antimicrobial stewardship and in a manner that promotes both patient safety and good public health.[1] Eliminating unnecessarily duplicative antibiotic therapy is a simple stewardship intervention that can be implemented in all facilities. Our findings demonstrate that doing so may provide cost savings and could simultaneously improve patient outcomes.

Our study had several limitations. First, the challenges inherent in the use of hospital administrative databases for drug utilization studies are well known.[37] Despite the evidence of low to moderate correspondence between microbiology results and ICD-9-CM codes, using ICD-9-CM diagnosis codes to identify cases of CDI and MRSA may have underestimated the number of patients with these diagnoses.[38] Second, because we included only cases with 2 or more service days of dual antimicrobial usage, the costs associated with the redundant combinations may represent a conservative estimate. Third, because of the variability in hospital operating costs and contract pricing for generic drugs versus nongeneric drugs, we opted to use the median acquisition cost for each drug at the standard dosing for adults. While this allowed for simplifying the analyses,[39] the use of the median acquisition cost may have contributed to a lower estimate of the potential cost savings, since numerous studies have noted the high variability in provider charges.[40] Fourth, our study of drug usage was limited to Premier facilities and for whom pharmacy data were available. The use of other potentially redundant antimicrobial combinations within the larger population of US hospitals maybe greater. Finally, though guidelines indicate that the vast majority of the combinations we assessed were unnecessary, we did not have clinical information on the cases to exclude the potentially small number of justifiable combinations. Therefore, while our results are applicable to the hospitals included in the study, they may not be applicable to all US hospitals in general.

Our findings suggest that significant impact can be obtained by focusing on a limited number of combinations that accounted for more than 70% of the unnecessary combinations in our study. On the basis of our findings of metronidazole used with piperacillin-tazobactam as the most common inappropriate or redundant combination, this single combination should be considered a possible initial target for antimicrobial stewardship programs. One successful approach that has been recommended is for healthcare organizations to develop a list of “never” combinations of antibiotics or redundant combinations (eg, 2 anaerobic agents used concurrently absent clinical indication) and provide alerts to providers when these combinations are ordered.[35] We believe all facilities should consider, where possible, implementing these simple antibiotic stewardship practices, which will not only save money but also likely improve patient outcomes at the same time.

ACKNOWLEDGMENTS

Potential conflicts of interest. L.S., T.J.L., G.P., and D.N. report that they are employees of Premier, a for-profit corporation. A.S. reports that he is an employee of the Centers for Disease Control and Prevention and received no compensation for his participation in this research. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

The findings and conclusions of this report are those of the authors and may not represent the views of the Centers for Disease Control and Prevention.

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TABLE 1.

Frequency of Redundant Antimicrobial Therapies, Mean Dosing Days, and Coded Presence of *Clostridium difficile* Infection (CDI) and Methicillin-Resistant *Staphylococcus aureus* (MRSA) by Drug Category and Specific Combinations, 2008–2011 (n = 32,507)

	ICD-9-CM code			Recorded test		Patients[a]		Dose days	
Combination	**Uncoded**	**CDI**	**MRSA**	**CDI**	**MRSA**	**Total**	**%**	**Total**	**Mean (SD)**
Antianaerobics									
Metronidazole and doripenem	899	147	89	602	464	1,103	3	5,865	5.32 (4.00)
Metronidazole and imipenem	1,156	165	80	644	340	1,370	4	7,576	5.53 (3.85)
Metronidazole and meropenem	1,123	178	90	713	410	1,370	4	7,528	5.49 (3.98)
Metronidazole and ertapenem	2,051	82	38	620	396	2,167	7	9,397	4.34 (2.67)
Metronidazole and ampicillin-sulbactam	3,109	60	42	652	496	3,208	10	12,544	3.91 (2.39)
Metronidazole and piperacillin-tazobactam	16,276	690	445	5,684	3,393	17,326	53	82,018	4.73 (2.99)
Anti-MRSA									
Daptomycin and linezolid	89	24	223	166	120	319	<1	2,058	6.45 (5.92)
Vancomycin and daptomycin	452	163	435	441	338	987	3	4,705	4.77 (4.52)
Vancomycin and linezolid	731	348	623	840	586	1,611	5	6,570	4.08 (3.57)
Dual β-lactams									
Cefepime and doripenem	57	7	14	30	40	77	<1	321	4.17 (3.38)
Cefepime and ertapenem	36	2	3	15	18	41	<1	142	3.46 (2.06)
Cefepime and imipenem	60	6	2	31	23	68	<1	284	4.18 (2.72)
Cefepime and meropenem	104	8	10	49	44	121	<1	532	4.40 (4.31)
Cefepime and piperacillin-tazobactam	358	22	40	165	159	415	1	1,493	3.60 (2.70)
Ceftriaxone and doripenem	82	7	10	36	45	98	<1	392	4.00 (4.41)
Ceftriaxone and ertapenem	93	1	5	25	28	99	<1	326	3.29 (2.39)
Ceftriaxone and imipenem	72	1	10	24	26	83	<1	265	3.19 (1.84)
Ceftriaxone and meropenem	111	5	8	36	41	122	<1	406	3.33 (2.70)
Ceftriaxone and piperacillin-tazobactam	1,018	30	90	333	329	1,135	3	3,464	3.05 (1.90)
Piperacillin-tazobactam and doripenem	121	9	18	70	70	147	<1	529	3.60 (2.92)
Piperacillin-tazobactam and ertapenem	242	5	8	69	55	255	<1	786	3.08 (1.85)
Piperacillin-tazobactam and imipenem	169	6	13	65	65	188	<1	667	3.55 (2.46)
Piperacillin-tazobactam and meropenem	164	16	19	83	60	197	<1	721	3.66 (3.92)

NOTE. ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification;* SD, standard deviation.

[a]Totals may differ from the summation of the columns because some patients had diagnoses of both CDI and MRSA.

TABLE 2.

Frequency of Redundant Antimicrobial Therapies by Year, 2008–2011 (n = 32,507)

Combination	2008	2009	2010	2011
Antianaerobics				
Metronidazole and piperacillin-tazobactam	3,047	3,475	4,144	4,518
Metronidazole and imipenem	405	329	264	259
Metronidazole and meropenem	256	285	272	309
Metronidazole and doripenem	45	164	356	412
Metronidazole and ertapenem	346	432	473	612
Metronidazole and ampicillin-sulbactam	780	760	683	686
Anti-MRSA				
Vancomycin and linezolid	295	368	359	419
Vancomycin and daptomycin	163	220	209	271
Daptomycin and linezolid	37	90	72	87
Dual β-lactams				
Ceftriaxone and piperacillin-tazobactam	174	243	292	281
Cefepime and piperacillin-tazobactam	72	92	98	111
Piperacillin-tazobactam and ertapenem	43	64	60	58
Piperacillin-tazobactam and imipenem	53	51	37	36
Piperacillin-tazobactam and meropenem	31	46	48	39
Piperacillin-tazobactam and doripenem	10	21	44	57
Cefepime and meropenem	24	26	25	32
Ceftriaxone and meropenem	20	20	35	19
Ceftriaxone and doripenem	4	18	28	39
Ceftriaxone and ertapenem	12	24	24	25
Cefepime and doripenem	5	12	24	32
Ceftriaxone and imipenem	23	19	18	15
Cefepime and imipenem	17	10	17	18
Cefepime and ertapenem	9	4	12	13
Total usage[a]	5,630	6,409	7,200	7,917
Total discharges	5,112,915	5,631,682	6,769,840	7,903,926

Combination	2008	2009	2010	2011
Adjusted rate per 1,000 patients[b]	1.10	1.14	1.06	1.00

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Totals may differ because of patients receiving more than 1 combination therapy during their hospitalization.

[b] Kruskal-Wallis test, $P = .042$.

TABLE 3.

Median Drug Cost and Estimated Excess Cost for Redundant Antimicrobial Therapies, 2008–2011

			Median cost per day, $		Excess redundancy cost, $	
Drug 1	**Drug 2**	**Dose days**	**Drug 1**	**Drug 2**	**Drug 1**	**Drug 2**
Metronidazole	Doripenem	5,865	2.84	114.99	16,657	674,416
Metronidazole	Imipenem	7,576	2.84	27.93	21,516	210,257
Metronidazole	Meropenem	7,528	2.84	87.66	21,380	659,904
Metronidazole	Ertapenem	9,397	2.84	60.13	26,687	565,042
Metronidazole	Ampicillin-sulbactam	12,544	2.84	27.64	35,625	346,716
Metronidazole	Piperacillin-tazobactam	82,018	2.84	90.84	232,931	7,450,515
Daptomycin	Linezolid	2,058	181.77	163.24	374,083	335,948
Vancomycin	Daptomycin	4,705	10.38	181.77	48,838	855,228
Vancomycin	Linezolid	6,570	10.38	163.24	68,197	1,072,487
Cefepime	Meroperem	532	23.12	87.66	12,300	46,635
Cefepime	Piperacillin-tazobactam	1,493	23.12	90.84	34,518	135,624
Ceftriaxone	Meroperem	406	12.88	87.66	5,229	35,590
Ceftriaxone	Piperacillin-tazobactam	3,464	12.88	90.84	44,616	314,670
Piperacillin-tazobactam	Doripenem	529	90.84	114.99	48,054	60,830
Piperacillin-tazobactam	Ertapenem	786	90.84	60.13	71,400	47,263
Piperacillin-tazobactam	Imipenem	667	90.84	27.93	60,590	18,629
Piperacillin-tazobactam	Meropenem	721	90.84	87.66	65,496	63,203

NOTE. Cost per day is the median acquisition cost for the drug at the commonly administered dosage and frequency in adult patients. Drug costs are shown for combinations with 100 or more cases.