

# Comparing the Cost of Administering and Monitoring Vancomycin and Daptomycin Through a Home Infusion Pharmacy

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## ABSTRACT

### Introduction

This study evaluates the cost differences between administering and monitoring vancomycin and daptomycin in a home infusion pharmacy (HIP) setting. Both antibiotics are widely used for treating methicillin-resistant *Staphylococcus aureus* (MRSA) and other gram-positive infections in outpatient parenteral antibiotic therapy (OPAT), but vancomycin requires more intensive therapeutic monitoring than daptomycin. The study aims to quantify pharmacist time spent monitoring patients, lab costs, and overall drug administration costs associated with each therapy in a HIP serving 16 medical centers in Northern California.

### Methods

Using a retrospective chart review of 113 patients who received either vancomycin or daptomycin between August and December 2022, the study compares pharmacist time spent, drug and administration device costs, and laboratory costs for each therapy.

### Results

Results show that while pharmacist time spent per note was similar for both antibiotics, vancomycin patients required significantly more notes per therapy day, resulting in higher monitoring costs. The average daily pharmacist time and associated costs for vancomycin were significantly higher than for daptomycin (\$37.99 vs. \$22.60 per day). Additionally, vancomycin required more frequent and expensive lab tests, leading to higher laboratory costs (\$14.01 vs. \$5.24 per day).

### Discussion

The overall cost per therapy day for vancomycin was significantly higher than for daptomycin (\$84.56 vs. \$59.75), largely due to increased pharmacist time and lab costs, despite the similar cost of drug and administration devices. The study highlights the potential cost savings of using daptomycin over vancomycin in a home infusion setting, particularly for uncomplicated infections. However, limitations include the exclusion of complex clinical scenarios and the potential variation in costs across different health care systems.

### Conclusions

These findings suggest that daptomycin may be a more cost-effective alternative to vancomycin for home-based therapy, prompting further evaluation of clinical practices and resource allocation in HIP services.

**Keywords:** vancomycin, daptomycin, home infusion pharmacy, cost

## INTRODUCTION

Vancomycin and daptomycin are intravenous antibiotics used in outpatient parenteral antibiotic therapy (OPAT) for treatment of complicated infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and other gram-positive organisms.<sup>1</sup> Daptomycin is established as being noninferior to vancomycin for treatment of serious MRSA infections, and patients with bloodstream infections due to MRSA have better outcomes when switched from vancomycin to daptomycin within 3 days of initial receipt of vancomycin.<sup>2-6</sup> Vancomycin has been more widely prescribed than daptomycin for reasons that include reliable activity, low cost, lack of resistance despite long-standing use, and good organ penetration.<sup>4,7,8</sup> Except during certain drug shortages, the cost of vancomycin has historically been considerably less than daptomycin. Before the generic version of daptomycin was released in 2016, the average wholesale price (AWP) of daptomycin was \$535 per 500 mg compared to vancomycin's AWP of \$7.70 per 1 gram.<sup>9</sup> After the generic form of daptomycin was released, the AWP decreased to \$72 per 500 mg.<sup>10,11</sup> In addition, as pharmacist-driven vancomycin therapeutic monitoring programs are associated with improved monitoring, dosing, and patient outcomes, the responsibility of vancomycin dosing and monitoring has largely transitioned to pharmacists and has become safer to prescribe.<sup>12-14</sup>

Home infusion pharmacy (HIP) utilization has become increasingly popular as home infusion services reduce patient burden and cost for hospitals and ambulatory infusion centers. While home-based OPAT can significantly increase cost savings, it comes with its own challenges; the patient and/or caregivers need to be able to understand and follow the OPAT plan, communication with the patient at home about laboratory monitoring and dose changes may be more difficult, and the incidence of adverse events to antimicrobials may increase with longer therapy duration.<sup>15-17</sup> Unlike daptomycin, vancomycin often requires ongoing dose adjustments, frequent labs, and timely communication with the patient or caregivers to ensure proper therapeutic range and to prevent adverse events when vancomycin levels are supra- or sub-therapeutic. Vancomycin can be cumbersome for patients to administer at home, often requiring 2 or 3 daily infusions, with each infusion taking at least 60-90 minutes. Daptomycin is less disruptive, requiring 1 dose every 24-48 hours as IV push. According to patient satisfaction surveys among

home infusion patients, daptomycin patients were more satisfied (100% responding  $\geq$  8/10 satisfaction) than vancomycin patients (67% responding  $\geq$  8/10 satisfaction).<sup>18</sup> Unsurprisingly, patients who received vancomycin reported that it interfered with their daily routine. Therefore, when a patient who is prescribed vancomycin in the hospital is ready to be discharged to home, HIP pharmacists may ask the managing clinician to consider transitioning the patient's therapy from vancomycin to daptomycin. In the inpatient setting, daptomycin restrictions are often set in place by antimicrobial stewardship programs due to concerns about off-label use, the need for increased dosage in patients with invasive or serious infections with gram-positive organisms, and the contraindication for daptomycin use in patient with pneumonia, and because of these restrictions, physicians may be hesitant to prescribe daptomycin.

The cost of daptomycin has continued to decrease as more manufacturers produce this drug, and as of June 2024, the AWP cost of daptomycin is \$29.08 per 500 mg.<sup>19</sup> The availability of generic daptomycin raises the question of whether daptomycin is a cost-effective option in comparison to vancomycin for home infusion pharmacies when considering lab and labor-associated costs, and drug acquisition in the outpatient setting. To answer this question, we assessed and compared the cost of administering and monitoring intravenous vancomycin and daptomycin through a HIP serving 16 medical centers in Northern California. We specifically aimed to quantify the following: 1) pharmacist time spent monitoring and communicating with patients receiving either of these 2 antibiotics, 2) lab and lab-associated labor costs, and 3) cost of drug and administration devices. To our knowledge, there are no published studies that have compared the cost of administering and monitoring these antibiotics through a HIP. This information will help HIP pharmacists and physicians develop cost reduction strategies for treating patients with gram-positive infections at home.

## METHODS

### Setting

This was a study within a large multi-center membership-based, prepaid, direct health care system located in California, Colorado, the District of Columbia, Georgia, Hawaii, Maryland, Oregon, Virginia, and Washington. Nationally, the health care system has 12.5 million members, with Northern California (NC), providing care and coverage to 4.4 million members.

NC members needing home infusion therapy receive services from 2 regional HIPs located in Berkeley and Sacramento. Therapies provided by these HIPs include intravenous antimicrobials, parenteral nutrition (PN), patient-controlled analgesia (PCA), hydration, and miscellaneous therapies (e.g., subcutaneous immune globulin, deferoxamine, sodium thiosulfate). Patients are referred to HIP from the outpatient setting when diagnosed with a condition needing infusion therapy at home or from the inpatient or skilled nursing setting at the time of discharge. Berkeley HIP collaborates with 16 NC medical centers with a catchment population of approximately 3.1 million members. In 2023, the average daily census of Berkeley HIP was 167 patients.

### Design and Participants

This was a retrospective chart review of patients who received services from Berkeley HIP for treatment with vancomycin or daptomycin at home. Patients were identified based on the following inclusion criteria: 1)  $\geq 18$  years of age; 2) prescribed either vancomycin or daptomycin for  $\geq 7$  days; and 3) admitted to HIP between August 1 – December 27, 2022. Exclusion criteria were: 1) an absolute neutrophil count  $< 1000$  cells/mm<sup>3</sup> at the time of HIP intake; 2) a baseline serum creatinine  $\geq 2$  mg/dL; 3) having received an intravenous aminoglycoside within 7 days before or 30 days after hospital discharge; or 4) having transitioned from vancomycin to daptomycin or vice versa during the study period.

### Data Collection

The list of patients was generated from the HIP weekly intake log. All data were obtained from Epic (Epic Systems Corporation), the electronic health record software used by the NC site. A standardized data collection tool was used to collect the following information: demographics (sex, age, documented race and calculated body mass index (BMI)); baseline serum creatinine and creatinine clearance, documented penicillin or cephalosporin allergy if applicable, comorbidities (heart failure, diabetes, dementia), date of hospital discharge, receipt of potentially nephrotoxic agents (angiotensin converting enzyme inhibitors, angiotensin receptor blockers, furosemide), receipt of vancomycin or daptomycin, receipt of other antimicrobials, presence of MRSA in blood or body fluid cultures, diagnosis, total days of vancomycin or daptomycin therapy while on HIP service, total number of pharmacists' clinical notes, total number of pharmacists' minutes (method described later), and

quantity of per protocol labs drawn over the course of therapy. The NC health system Institutional Review Board determined this project to be exempt under the Federal Regulations (45 CFR 46.104).

### Cost Determination

#### *Cost of Clinical Monitoring by Pharmacists*

The number of minutes HIP pharmacists spent in clinical documentation was used as a surrogate marker for time spent in clinical monitoring. For each patient, we counted the number of notes written by HIP pharmacists from HIP intake to discharge. When writing a note, the general pharmacist workflow is to open the note, review the chart, check that the prescribed medication is dosed appropriately and calculate any needed dose adjustments, call the patient, document the encounter, and then close the note. The time spent in each note was calculated by subtracting the time the note was opened from the time the note was filed. To account for notes left open overnight, the pharmacist time for these notes was approximated using the average time from all other notes for that particular patient.

#### *Cost of Antibiotics and Administration Devices*

Records of all compounded and delivered doses of each patient's therapy were obtained from HIP's billing software (Ascend Medication Management, Lenexa, KS). Antibiotic and administration device costs were obtained by identifying the cost billed to the patient's insurance plan. Two different administration devices were used depending on therapy and dose. Vancomycin was administered via an elastomeric device for all doses. Doses of daptomycin  $\leq 600$  mg were administered via syringes by intravenous push and doses  $> 600$  mg were administered via an elastomeric device. Total drug and administration device cost billed to the patient's insurance was the sum of the cost for antibiotics, administration devices, and drug compounding fee.

#### *Lab Costs*

This HIP has protocols for ordering safety monitoring labs for each therapy. Vancomycin requires a weekly complete blood count with differential, creatinine, and vancomycin level. Daptomycin requires a weekly complete blood count with differential, creatinine, alanine transaminase (ALT), and creatinine phosphokinase (CPK). Providers may request that additional labs be added to the weekly safety labs monitored by HIP pharmacists (e.g., C-reactive protein). Additional monitoring labs are ordered

as needed (e.g., a vancomycin level may need to be checked more than once weekly to ensure correct dosing if levels are not as expected). The NC regional home infusion pharmacies implemented area under the curve (AUC)-guided dosing and monitoring of vancomycin in September 2022. Prior to this, the trough-based method was used. An internal review found that there was no significant difference in the number of pharmacist interventions using these 2 dosing and monitoring methods.

Data for laboratory costs was extracted directly from the multi-center health system Cost Management Information System (CMIS), which included the total costs applied in the provision of the following laboratory services: 1) per protocol weekly labs and any additional protocol labs ordered by a pharmacist when increased monitoring was indicated; 2) phlebotomist labor performing blood draws; and 3) transport to lab for processing. The total lab cost includes variable direct costs (expenses of the servicing department that are directly applied in the provision of the service, such as support staff labor and medical supplies), fixed direct costs (expenses of the servicing department that are not directly applied in the provision of service, such as administration time or non-medical supplies) and fixed indirect costs (allocated facility and administration overhead and support services and patient care costs that cannot be captured by utilization, such as health education).

### Statistical Analysis

Categorical variables were evaluated by chi-square test or Fisher's exact test. Continuous variables were evaluated by unpaired t-test or ANOVA. Mann-Whitney U test was used to calculate *p*-values between median values. Values are expressed as a mean for continuous variables and as a number (percentage of the group from which they were derived) for categorical variables. *P*-values <0.05 were considered statistically significant. Statistical analyses were performed using GraphPad Prism Software version 9.5.1 (GraphPad Software, Boston, MA). No formal power calculation was determined *a priori*; a convenience sample of all eligible patients was included.

## RESULTS

### Study population

One hundred sixty-four patients were referred to the HIP for vancomycin or daptomycin therapy at home during the study period. We identified 57 vancomycin patients and 56 daptomycin patients

who met inclusion criteria. There were no significant demographic differences between the 2 groups (Table 1).

### Pharmacist time and cost

There was no significant difference in the average amount of time pharmacists spent writing a single note for a patient prescribed vancomycin or daptomycin (25.6 vs. 23.8 minutes, *p* = 0.52). Pharmacists wrote approximately twice as many notes per therapy day for patients prescribed vancomycin compared to daptomycin (1.04 vs. 0.58 notes per therapy day, *p* < 0.05), which resulted in more time each day of therapy spent monitoring patients receiving vancomycin compared to daptomycin (24.9 vs. 14.5 minutes, *p* < 0.05). The average cost of pharmacist time per therapy day was significantly higher for patients receiving vancomycin compared to daptomycin (\$37.99 vs. \$22.60, *p* < 0.05).

### Drug and administration device cost

The average drug and administration device combined cost per therapy day for vancomycin and daptomycin was similar (\$32.56 vs. \$31.91, *p* = 0.83).

### Laboratory cost

The average laboratory cost per therapy day for patients receiving vancomycin was significantly higher compared to patients receiving daptomycin (\$14.01 vs. \$5.24, *p* < 0.05).

### Total cost

The average total cost per therapy day for patients receiving vancomycin was significantly higher compared to patients receiving daptomycin (\$84.56 vs. \$59.75, *p* < 0.05). These costs include the cost of pharmacist time, drug and administration device cost, and laboratory cost (Table 2).

## DISCUSSION

This study shows that the overall cost of vancomycin administration and monitoring through a HIP is significantly higher than daptomycin due to 2 factors, pharmacist time spent in monitoring and lab costs. The average cost of drug and administration device combined per therapy day is similar between vancomycin and daptomycin.

Although this study shows that daptomycin is a cost-effective option for HIP in uncomplicated MRSA treatment, there were some limitations. We excluded patients who were transitioned from vancomycin to daptomycin or vice versa to exclude patients

TABLE 1 | Demographic and Clinical Characteristics of Patients Prescribed Vancomycin and Daptomycin

Characteristic	Vancomycin (n = 57)	Daptomycin (n = 56)	p-value
Male (%)	31 (54.39)	36 (64.29)	0.36
White race (%)	44 (77.19)	38 (67.86)	0.27
Median Age [IQR Range]	66 [74.5 – 55]	61 [72.5 – 50.3]	0.13
BMI (kg/m <sup>2</sup> ) (%)			
< 25	24 (42.10)	16 (28.57)	0.13
25 - < 30	13 (22.80)	19 (33.93)	0.19
≥ 30	20 (35.09)	21 (37.50)	0.79
β-Lactam allergy (%)	17 (29.82)	15 (26.79)	0.72
Congestive heart failure (%)	11 (19.30)	9 (16.07)	0.65
Diabetes (%)	22 (38.60)	24 (42.86)	0.64
ACE-inhibitor or ARB (%)	21 (36.80)	19 (33.93)	0.75
Furosemide (%)	12 (21.05)	11 (19.64)	0.85
Receipt of another antibiotic (%)	25 (43.86)	33 (58.93)	0.11
Diagnosis (%)			
Bacteremia	13 (22.81)	9 (16.07)	0.37
Osteomyelitis or PJI	25 (43.86)	32 (57.14)	0.16
Endocarditis	3 (5.26)	3 (5.36)	> 0.99
Other infections (skin/soft tissue, surgical site, intra-abdominal, meningitis, pneumonia, pyelonephritis, sinusitis)	11 (19.30)	12 (21.43)	0.78
MRSA in culture (%)	15 (26.32)	20 (35.71)	0.28
Baseline CrCl (mL/min) (%)			
0 - < 30	1 (1.75)	1 (1.79)	> 0.99
30 - 50	10 (17.54)	10 (17.86)	0.97
> 50	45 (78.95)	45 (80.36)	0.85
Median Outpatient DOT [IQR Range]	28 [38 – 11.5]	34 [41.3 – 22]	0.06

Data presented as number (%), median [interquartile range].

Mann Whitney test was used to calculate p-values between median values. For categories written as number (%), p-value was calculated using Pearson's Chi-square calculator for 2 x 2 contingency table.

TABLE 2 | Comparison of Costs of Administering and Monitoring Vancomycin and Daptomycin

	Vancomycin	Daptomycin	p-value
Pharmacist time (minutes)	24.9	14.5	p < 0.05
Pharmacist cost	\$37.99	\$22.60	p < 0.05
Drug and administration device cost	\$32.56	\$31.91	p = 0.83
Laboratory cost	\$14.01	\$5.24	p < 0.05
Total cost	\$84.56	\$59.75	p < 0.05

who may have developed a drug-related adverse event to one of the medications, which would in turn require increased pharmacist monitoring and labs. The study did not calculate the relative costs of monitoring and administering vancomycin and daptomycin for complicated clinical scenarios and with medication switching. The cost of normal saline flushes was excluded from the overall cost analysis of drug and administration devices since the number of flushes depended not only on the frequency of drug administration, but also factors unrelated to vancomycin administration, such as whether the line was being used to administer other drugs, line type, and number of lumens. The cost of courier services for home therapy was also excluded, which are billed to the referring medical center, home health nursing visits, and infusion center services. Pharmacy and lab costs are specific to the NC health system site and may not be generalizable to other health care organizations.

The higher lab cost associated with vancomycin monitoring is due to the cost of obtaining vancomycin levels. Within the NC site, the cost of a vancomycin level is approximately 3.5 times the combined cost of ALT and CPK levels. In addition, vancomycin levels are usually obtained more than once weekly if the vancomycin dose is adjusted, if the patient is new to service with HIP, or if the patient has unstable renal function.

The exact time a HIP pharmacist spends on clinical monitoring is difficult to capture. The intake process requires interactions with several different teams. For patients referred from the hospital, the intake assessment includes multiple interactions with the inpatient team, the inpatient pharmacy, the recuperative skills nurse who is teaching the patient to administer the drug, and the patient. For outpatient referrals, the intake assessment includes interactions with the referring physician and the adult infusion center where the patient has a line placed, receives the first dose of the drug, and is taught how to self-administer the drug. If the patient is receiving home health nursing services, intake assessment also includes communicating with the home health agency.

Time spent communicating with home health nurses after the intake process is often not captured. The ongoing monitoring process includes reviewing labs, contacting the patient for regularly scheduled check ins, communicating with home health nursing services

and infusion center nurses, contacting the overseeing physician with any issues, and addressing problems as they arise. For this study's purposes, we used time spent documenting the above as a surrogate for actual time spent on patient intake and monitoring. This may not be an exact reflection of actual time, as a pharmacist may forget to close an encounter or pause documenting to perform other duties but leave the note open. Berkeley HIP does not have a standardized workflow for opening and closing notes.

That vancomycin dosing and monitoring requires significantly more time than daptomycin should be relevant to any HIP. In 2022, this HIP had an average of 70 vancomycin patients per quarter. In September 2023, as a result of this study, we began education to NC infectious diseases physicians on the differences between vancomycin and daptomycin costs in terms of pharmacist time and lab and lab-associated labor; we recommended that daptomycin be considered upon discharge home instead of vancomycin if clinically appropriate. Monitoring vancomycin levels requires extensive resources apart from the time and cost included in this study, and daptomycin may offer a safe and less costly alternative overall.

In the last quarter of 2023, the number of patients prescribed vancomycin through HIP fell to 41. As home infusion options continue to grow, stewardship of pharmacists' time will become increasingly important. Any therapy which requires intensive dosing and monitoring should be relevant to other aspects of any health care organization, as time associated with monitoring also affects patients and the medical staff involved with obtaining and monitoring labs, including lab personnel, home health nurses, infusion center staff, and prescribers. More studies are needed to evaluate the full costs associated with therapy requiring more intensive monitoring and not just dependent on medication cost alone.

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