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# Evaluation of pharmacist time dedicated to vancomycin dosing in adult patients using a 24-hour AUC nomogram or trough monitoring approach: A time motion study

Supplementary material is available with the full text of this article at *AJHP* online.

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**Purpose:** Evidence-based guideline recommendations for vancomycin dosing recently shifted from a trough-based strategy to an area under the curve (AUC) approach. While several AUC dosing methods exist, the optimal approach has not been determined. Literature characterizing time requirements for various vancomycin dosing strategies remains limited.

**Methods:** A time and motion study was conducted to measure the time spent by clinical pharmacists dosing vancomycin using an AUC nomogram. Pharmacists who dosed and monitored vancomycin for adult patients on the general medical ward (GMW) or intensive care unit (ICU) of a large academic medical center consented to study participation. Vulnerable patients and vancomycin orders for surgical infection prophylaxis were excluded. The primary outcome was the median amount of time clinical pharmacists dedicated to vancomycin-related clinical activities during an 8-hour weekday shift. Secondary outcomes included the proportion of patients prescribed vancomycin at the beginning of each shift and factors contributing to greater than average time spent on vancomycin-related responsibilities.

**Results:** Seven clinical pharmacists collected data on 178 vancomycin orders. The estimated amount of time a clinical pharmacist spent on daily vancomycin responsibilities averaged 10.45 minutes (interquartile range [IQR], 6.94-15.8 minutes). The overall median time requirement per vancomycin assessment was 3.45 minutes (IQR, 1.95-6.7 minutes). The only factor independently associated with prolonged dosing time was follow-up dosing from a previous day.

**Conclusion:** The study elucidated time requirements associated with an AUC nomogram–based vancomycin dosing approach. This data could be used to compare time requirements associated with other existing vancomycin dosing strategies, which may help healthcare systems determine the optimal AUC dosing method for their specific practice model.

**Keywords:** area under curve, methicillin-resistant *Staphylococcus aureus*, pharmacists, pharmacokinetics, time and motion studies, vancomycin

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Vancomycin is a glycopeptide antibiotic used to treat gram-positive bacterial infections, most notably methicillin-resistant *Staphylococcus aureus* (MRSA). It is a commonly used antibiotic within the hospital setting and has been linked to increased rates of bacterial resistance.[1,2] The current vancomycin dosing and monitoring guidelines recommend an area under the curve (AUC)–based monitoring approach over the traditional trough strategy, with a goal target AUC of 400 to 600 mg/L · h.[3] This target range, when compared with traditional trough goals of 15 to 20 mg/L, provides equivalent

efficacy with a reduced nephrotoxicity risk.[3] Moreover, evidence suggests traditional trough goals of 15 to 20 mg/L are not associated with improved patient outcomes.[3-5]

Despite the benefits of AUC dosing strategy for MRSA infections, vancomycin dosing and monitoring can be a significant time commitment for pharmacists.[6-8] Vancomycin is often prescribed for nonestablished MRSA infections and is used inappropriately in patients without an indication for MRSA coverage.[1,2,9] Therefore, optimizing vancomycin dosing workflow can improve pharmacist efficiency and allow for additional patient care activities. Current AUC dosing strategies include a 2-point pharmacokinetic trapezoidal method, Bayesian software, and a nomogram-based approach.[3]

Ensuring appropriate vancomycin utilization and dose optimization in practice, however, can contribute to greater time, financial, and workload requirements. A large academic medical center underwent a change in its vancomycin dosing protocol on August 1, 2019, shifting from a trough strategy to a population-based pharmacokinetic nomogram approach correlating vancomycin dose (in mg/kg) and trough level to expected AUC.[10] The purpose of the study described here was to assess the amount of time that a clinical pharmacist dedicates to vancomycin-related clinical activities during an 8-hour weekday shift while using an AUC nomogram approach.

## KEY POINTS

- An area under the curve (AUC) approach is recommended for vancomycin monitoring, but the optimal method in terms of workflow efficiency is unknown.
- A time-motion study showed that pharmacists using an AUC nomogram–based vancomycin dosing guideline each spent approximately 10 minutes on vancomycin dosing and monitoring per day.
- Overall, there was low utilization of the AUC nomogram, primarily due to a low prevalence of both documented MRSA infections and acute kidney injury.

## Methods

This was an institutional review board–approved time and motion study performed at an 877-bed academic medical center located in Detroit, MI, between December 2019 and March 2020. Since time and motion studies collect quantitative data regarding the duration and movements of a specific task, they're often utilized to optimize workflow efficiency.[11] At the study institution, physicians and advanced practice providers prescribe vancomycin. Decentralized clinical pharmacists provide direct patient care on the general medical wards (GMWs) and intensive care units (ICUs). Pharmacists assess appropriateness of vancomycin therapy and are delegated authority for vancomycin dosing, monitoring, and documentation of therapy in the electronic medical record (EMR) based on an institutional clinical practice guideline. Pharmacists place a pharmacokinetic consultation note in the EMR for vancomycin therapy initiation, dose adjustment(s), level assessment(s), and therapy discontinuation.

A modified Matzke dosing nomogram was used to select the initial maintenance dose according to actual body weight and creatinine clearance (eTables 1 and 2).[12] A maximum dose of 2 g intravenously every 8 hours was utilized. AUC nomogram–based monitoring is used for empiric treatment of serious infections in which MRSA is a possible pathogen or for culture-confirmed MRSA infections. The nomogram was adapted from a population based pharmacokinetic study by Lewis et al[10] (eFigure 1). MRSA risk factors include treatment with antibiotics within 90 days, hospitalization within 90 days, history of MRSA infection, immunocompromising conditions, severe and/or purulent wound infections, and history of injection drug use. Examples of serious MRSA infections include culture-confirmed or suspected MRSA pneumonia, MRSA bacteremia, and MRSA endocarditis.

In patients with gram-positive central nervous system (CNS) infections, a trough goal of 15 to 20 μg/mL is targeted along with an AUC goal of less than 700 mg/L · h to mitigate nephrotoxicity risk. Higher trough goals are used in these patients to ensure adequate vancomycin concentrations within the CNS. Trough-based monitoring targeting a goal of 8 to 15 μg/mL and linear kinetics are used for other scenarios, which include non-MRSA gram-positive infections, and for suspected or confirmed MRSA infections without bacteremia or pneumonia (ie, skin infection and urinary tract infection).

If acute kidney injury (AKI) is present, vancomycin therapy is dosed using intermittent doses, with random sampling of vancomyin levels, for all infection scenarios. For purposes of our study, AKI was defined as a serum creatinine increase of 0.3 mg/dL or 30% (whichever was greater) or urine output less than 0.5 mL/kg/h for 6 hours or more. Renal function was considered to be at baseline if the patient's current serum creatinine values were near a known baseline level, if available. Stable renal function was defined as toleration of a scheduled vancomycin regimen without either AKI or requirement of renal replacement therapy. Once a vancomycin level is obtained based on the dosing scenario described above, the institutional vancomycin guideline recommends a trough or AUC monitoring approach based upon infection source(s), renal function status, whether or not empiric MRSA risk factors are present, and whether or not an MRSA infection is confirmed by culture.

Pharmacists were eligible for study inclusion if they had completed a minimum of 1 year of practice after their terminal postgraduate year (PGY) training,

practiced on a GMW or ICU at the study institution during a weekday dayshift (7:00 AM-3:30 PM), and provided consent for study participation. Pharmacists recorded the time requirements to complete vancomycin orders that took place during a weekday, day shift. Vancomycin orders not included in the study results were those for patients who were pregnant, were incarcerated, received vancomycin for surgical infection prophylaxis, orders placed outside of a weekday dayshift, orders completed by pharmacy trainees, and orders placed in the emergency room, labor and delivery unit, or operating room.

The primary outcome was the median time that a study pharmacist spent on vancomycin-related clinical activities on an 8-hour weekday shift while using the updated institutional AUC nomogram approach. This was calculated by measuring the total time spent on vancomycin-related clinical activities per study day per pharmacist. All individual pharmacist study days involving time spent on vancomycin-related activities were then added together and divided by the total pharmacist study days. Study days with no qualifying vancomycin orders were excluded from the primary outcome. Secondary outcomes included the proportion of vancomycin-treated patients at the beginning and end of each clinical shift, study pharmacists' median daily patient census, and factors that contributed to greater than average time spent on vancomycin responsibilities. Each vancomycin consultation was classified as new start therapy or follow-up on an existing order. All endpoints were compared between GMW and ICU patients. Documented resistant infections were defined as those for which microbiological culture data were positive for either MRSA or a vancomycin-resistant enterococcus. Chronic kidney disease (CKD) was defined as a creatinine clearance of ≤60 mL/min without evidence of AKI.

At study initiation, the study pharmacists underwent training to standardize the data collection method. Study pharmacists self-timed and self-captured their own daily vancomycin order time requirements using standardized stopwatches on cellphones. Standardization of the cellphone stopwatches was performed by the primary investigator to ensure more reliable outcomes.[11] The primary investigator standardized the stopwatches by comparing each of the study pharmacists' phones with a control device to ensure the phones all accurately recorded time. From that moment, each of the study pharmacists self-timed themselves. The time data captured included time required for vancomycin dosing, monitoring of therapy, medical record review, and additional responsibilities associated with vancomycin orders. Additional vancomycin-related responsibilities included time required to speak with a provider or other staff regarding vancomycin clarification and/or recommendations. Each pharmacist initiated their stopwatch upon entering a patient chart and reviewing the vancomycin order. After timer initiation, each pharmacist hid the stopwatch screen by turning their phone over. Upon order completion, pharmacists returned their phones to face-up position, stopped the timer, and documented the time requirement in a standardized data collection form. Interruptions and time spent on unrelated activities were excluded by pausing the timer during these situations.

Prior to the active data collection phase, a 7-day data washout period took place for each study pharmacist. Washout period data were excluded from the study. All vancomycin orders included in the results were randomized and equally distributed amongst participating pharmacists until there were no additional orders remaining. To validate the accuracy of the stopwatch method, EMR consult note times were used as time surrogate markers. Time notations for generating and finalizing a note were abstracted specifically for new and preexisting vancomycin orders that required a vancomycin level assessment. These note completion times were compared with pharmacist self-timed data. The primary investigator trained the study pharmacists to integrate the consult note process into the self-timing methodology.

Study pharmacists were responsible for collecting data on vancomycin dosing weight, dosing strategy used, therapeutic target, volume of distribution assessment, day of therapy, and ordering of vancomycin levels. The primary investigator was responsible for collecting all baseline patient and infection characteristics, in addition to AUC utilization rate.

Continuous data were analyzed using measures of central tendency depending on whether the data were parametric or nonparametric. Categorical data were described using a chi-square test, while all continuous data were described using a 2-sample *t* test. A bivariate regression analysis was performed to determine factors which contributed to prolonged vancomycin dosing time. A multivariable analysis was performed to determine factors that contributed to prolonged dosing time, which was defined by comparing the time requirements of the 75th percentile and the top quartile. Variables were considered for inclusion in the regression model based on a significance level of $P < 0.2$ in bivariate analysis and on clinical rationale. No formal power calculation was performed, but a conveyance sample of a 1-month time period for each included pharmacist was used. Statistical significance was defined as a $P$ value of <0.05. Data analysis was performed using SPSS Statistics for Windows, Version 25 (IBM Corporation, Armonk, NY).

## Results

Seven clinical pharmacists provided consent and were included in the study (4 GMW and 3 ICU pharmacists). There were 2 male and 5 female pharmacists. All the included pharmacists were PGY1 residency trained and Board of Pharmacy Specialties certified. Three pharmacists were also PGY2 residency trained. The median time in practice post residency was 4 years (range, 2-8 years). The median daily

patient workload for a clinical pharmacist was 34.5 (interquartile range [IQR], 19-43) patients. GMW pharmacists' daily patient census was significantly greater than ICU pharmacists' (42.5 [IQR, 39-48] vs 18 [IQR, 18-20], $P < 0.05$). Additional pharmacist vancomycin consult/workload characteristics are represented in Table 1. Overall,

**Table 1.** Vancomycin Order Characteristics[a]

| | GMW orders | ICU orders | Overall | *P* value |
|---|---|---|---|---|
| **Workload characteristics** | **n = 48** | **n = 38** | **n = 86** | |
| Vancomycin orders at beginning of shift, median (IQR)[b] | 2.5 (1-4) | 4 (3-5) | 3 (1.25-4.75) | 0.026 |
| Patients at beginning of shift, median (IQR)[b] | 42.5 (39-48) | 18 (18-20) | 34.5 (19-43) | <0.001 |
| Vancomycin orders at end of shift, median (IQR)[b] | 2 (1-4) | 3.5(2-4) | 3 (1-4) | 0.022 |
| Patients at end of shift, median (IQR)[b] | 42 (37-46) | 18 (18-20) | 35 (19-42) | <0.001 |
| **Dosing strategy, No. (%)** | **n = 85** | **n = 93** | **n = 178** | |
| New initiation of vancomycin | 11 (12.9) | 10 (10.8) | 21 (11.8) | 0.651 |
| Nomogram | 5 (5.9) | 1 (1.1) | 6 (3.4) | 0.105 |
| Dose per levels | 2 (2.4) | 3 (3.2) | 5 (2.8) | >0.999 |
| Intermittent hemodialysis | 3 (3.5) | 3 (3.2) | 6 (3.4) | >0.999 |
| Previous PK/kinetics used[c] | 1 (1.2) | 2 (2.2) | 3 (1.7) | >0.999 |
| Therapy discontinued | 0 (0) | 1 (1.1) | 1 (0.6) | >0.999 |
| Follow-up day of therapy | 74(87.1) | 83 (89.2) | 157 (88.2) | 0.651 |
| **Order characteristics, No. (%)** | **n = 25** | **n = 36** | **n = 61** | |
| Vancomycin level within therapeutic range | 11 (44) | 22 (61.1) | 33 (54.1) | 0.187 |
| AUC utilization rate | 3 (12) | 5 (13.9) | 8 (13.1) | 0.723 |
| **Infection source, No. (%)** | **n = 85** | **n = 93** | **n = 178** | |
| Respiratory[b] | 14 (16.5) | 70 (75.3) | 84 (47.2) | <0.001 |
| SSTI[a] | 34 (40) | 11 (11.8) | 45 (25.3) | <0.001 |
| Other[d] | 18 (21.2) | 13 (14) | 31 (17.4) | 0.206 |
| Intraabdominal | 18 (21.2) | 13 (14) | 31 (17.4) | 0.206 |
| Bacteremia and/or endocarditis | 14 (16.5) | 15(16.1) | 29 (16.3) | 0.951 |
| GU | 5 (5.9) | 13 (14) | 18 (10.1) | 0.074 |
| Bone and joint[b] | 15 (17.6) | 2 (2.2) | 17 (9.6) | <0.001 |
| CNS | 0 (0) | 5 (5.4) | 5 (2.8) | 0.060 |
| **Resistance attributes, No. (%)** | **n = 85** | **n = 93** | **n = 178** | |
| Documented resistant infection[e] | 11 (12.9) | 14 (15.1) | 25 (14) | 0.685 |
| Documented resistant infection[e] | 11 (12.9) | 14 (15.1) | 25 (14) | 0.685 |
| MRSA risk factor[f] | 75 (88.2) | 81 (87.1) | 156 (87.6) | 0.818 |
| Enterococcus risk factor[g] | 29 (34.1) | 32 (34.4) | 61 (34.3) | 0.967 |

Abbreviations: AUC, area under the curve; CNS, central nervous system; GMW, general medical ward; GU, genitourinary; ICU, intensive care unit; OSH, outside hospital; PK, pharmacokinetics SSTI, skin and soft tissue infection.
[a]Values for n are number of vancomycin orders/consults.
[b]Statistically significant difference ($P < 0.05$) for comparison of GMW vs ICU.
[c]Use of a regimen previously used to attain therapeutic levels. This dosing did not necessarily follow the nomogram empiric recommendations.
[d]Unknown infectious source or fever of unknown origin.
[e]Documented microbiological culture data positive for either MRSA or vancomycin-resistant enterococcus.
[f]Antibiotic therapy within 90 days, inpatient hospitalization within 90 days, history of MRSA infection, immunocompromising conditions, severe and/or purulent wound infections, and history of injection drug use.
[g]Previous enterococcal infection, benign prostatic hyperplasia in men with urinary tract infection, structural abnormalities of the urinary tract, or immunosuppressive agent use.

8.7% of patients cared for by the study pharmacists during the study period had an active vancomycin order.

A total of 178 vancomycin orders were included in the study. Four pharmacists contributed 28 vancomycin orders each, while the remaining 3 pharmacists contributed 21, 18, and 3 orders, respectively. Of the 178 orders, 85 were for GMW patients and 93 were for ICU patients. The difference in the mean ages of GMW and ICU patients was statistically significant (63 [13] years vs 60 [13] years, $P = 0.005$). Compared with ICU patients, GMW patients had a higher proportion of male patients (61.2% vs 43%, $P = 0.015$) and a higher incidence of stable renal function at baseline (68.2% vs 41.9%). Additional baseline patient characteristics, infection characteristics, and resistance attributes can be found in Table 2. The incidence of both AKI and intermittent hemodialysis was greater in ICU patients. Most vancomycin orders evaluated by pharmacists were follow-ups on existing orders, in both the GMW and ICU settings (57.6% and 89.2% of orders, respectively). Respiratory infections were the predominant indication for vancomycin use in the ICU (74.2% of orders), while skin and soft tissue infections (SSTIs) were the most common indication in the GMW (41.2%). There was no significant difference in the incidence of MRSA risk factors between the GMW and ICU cohorts (88.2% vs 87.1%, $P = 0.818$), with low rates of documented MRSA positive cultures in both groups (10.6% and 11.8%, respectively).

For the primary outcome, the median pharmacist time dedicated to vancomycin-related clinical activities per weekday clinical day shift was 10.45 minutes (IQR, 6.94-15.8 minutes). There was a minimal difference in median time requirement between the GMW (11.0 [IQR, 6.74-15.30] minutes) and ICU (9.40 [IQR, 6.98-15.92] minutes) pharmacists. The overall median time requirement per vancomycin assessment was 3.45 minutes (IQR, 1.95-6.7 minutes). There were no significant differences in median time requirements documented by the GMW and ICU pharmacists (3.45 minutes [IQR, 1.l94-7.76 minutes] vs 3.53 minutes [IQR, 2.02-6-21 minutes], $P = 0.811$). Vancomycin consults that included AUC-based monitoring required a greater amount of time per patient (median, 6.2 minutes [IQR, 3.24-9.55 minutes] vs 3.48 minutes [IQR, 1.95-6.83 minutes]; $P = 0.162$). Additional findings are represented in Figure 1. Analysis of EMR consult note validation times revealed no significant differences from self-recorded times. For patients prescribed vancomycin for whom an EMR note was placed, the GMW pharmacists' self-timing resulted in a median validation time of 8.1 minutes (IQR, 6.3-10.1 minutes), while the note time stamps indicated a median of 7 minutes (IQR, 6-9 minutes). Within the ICU pharmacist group, self-timing resulted in a median of 5.7 minutes (IQR, 3.8-8.2 minutes), while note time stamps showed a median of 5 minutes (IQR, 4-8 minutes).

While many characteristics were tested in the bivariate analysis, only follow-up dosing orders were significantly correlated with prolonged dosing time ($P = 0.002$). Variables included in the multivariable regression analysis were dosing strategy, new versus continued therapy, infection source, and hospital location. After adjustment for AUC dosing and patients with other infections, follow-up dosing was an independent predictor of prolonged dosing time ($P = 0.002$).

## Discussion

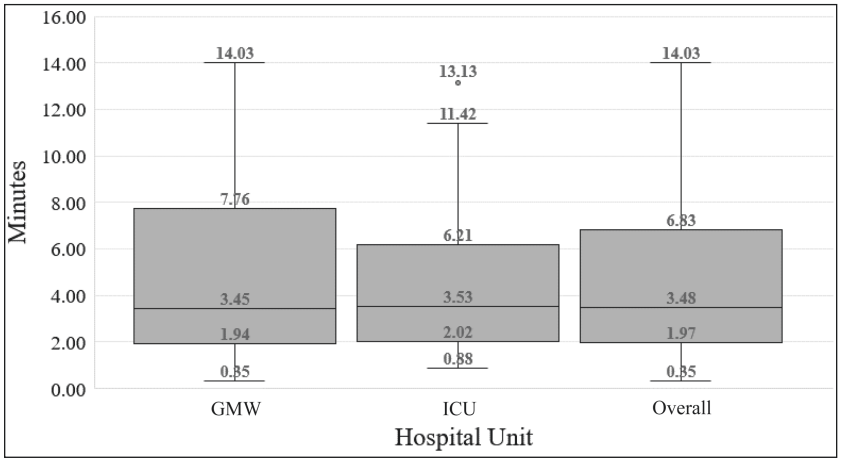
While previously published studies aimed to better understand the benefits of an AUC dosing strategy versus a trough strategy, time assessments

**Table 2.** Patient Characteristics

| Characteristic[a] | GMW orders (n = 85) | ICU orders (n = 93) | Overall (n = 178) | *P* value |
|---|---|---|---|---|
| Age, median (IQR), y | 63 (51-70) | 60 (49.5-68.5) | 62 (51-69) | 0.130 |
| Male, No. (%)[b] | 52 (61.2) | 40 (43) | 92 (51.7) | |
| Actual body weight, median (IQR), kg | 83.5 (69.65-102.7) | 72.6 (60.25-99.2) | 79.9 (63.8-100) | 0.109 |
| Renal function, No. (%) | | | | |
| Stable at baseline[b] | 58 (68.2) | 37 (39.8) | 95 (53.4) | <0.001 |
| AKI[b] | 11 (12.9) | 34 (36.6) | 45 (25.3) | <0.001 |
| CKD[c] | 0 (0) | 2 (2.2) | 2 (1.1) | 0.498 |
| CRRT | 0 (0) | 2 (2.2) | 2 (1.1) | 0.498 |
| iHD | 13 (15.3) | 18 (19.4) | 31 (17.4) | 0.476 |
| PD | 3 (3.5) | 0 (0) | 3 (1.7) | 0.107 |

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; GMW, general medical ward; iHD, intermittent hemodialysis; ICU, intensive care unit; PD, peritoneal dialysis.
[a]Data for No. (%) are for number (percentage) of patients or orders.
[b]Statistically significant difference for comparison of GMW vs ICU ($P < 0.05$).
[c]Creatinine clearance of ≤60 mL/min without evidence of acute injury.

**Figure 1.** Average time requirements per vancomycin order. Outlier time values in the intensive care unit (ICU) included values of 24.41, 15.56, and 14.88 minutes. GMW indicates general medical ward.




were often underrepresented.[3,6] This study was performed to improve understanding in this area. A clinical pharmacist at the study institution spent a median time of 10.45 minutes per day on vancomycin orders during an 8-hour weekday shift. When extrapolated to a 40-hour weekday dayshift work schedule over 52 weeks, these results indicate that pharmacists using the described AUC nomogram strategy would each spend approximately 45 hours on vancomycin-related clinical activities yearly. There were low rates of AUC monitoring in both the GMW and ICU settings (12% and 13.9%, respectively), likely due to the low prevalence of confirmed serious MRSA infections and high rates of AKI observed in the study population. There was likely an underestimation of daily vancomycin time responsibilities, which we believe was primarily due to excluding afternoon/midnight/weekend orders, vancomycin ordering for perioperative prophylaxis, and processing of vancomycin orders by trainees.

The aforementioned consensus guidelines[3] give preference to a 2-point pharmacokinetic trapezoidal model or Bayesian software approaches to vancomycin AUC monitoring. This is because the AUC nomogram approach is not patient specific. However, there has never been a direct comparison of the available strategies. There are a limited number of published studies that assess the time involved with vancomycin dosing and safety monitoring.[6] It is unclear if the precision of a Bayesian model AUC estimate correlates with improved outcomes compared to other, less labor-intensive approaches to achieving lower overall vancomycin doses. A prospective study showed cost savings with the Bayesian software approach.[13] The software, however, was possibly unaffordable for smaller institutions that had lower vancomycin use.[14] Advantages of the Bayesian software include adaptive, fast predictions; moreover, it doesn't require that a patient be at steady state for assessment, unlike trapezoidal model and other first-order equation–based models.[15,16] Because the trapezoidal model uses 2 steady-state vancomycin plasma levels and calculates pharmacokinetic parameters on the basis of those static variables, it can be impractical in some settings.[13] Examples may include institutions with a limited number of laboratory sample runs per day, with limited phlebotomy and laboratory staffing, or where there are delays in properly obtaining both levels. Acute physiologic changes can also be difficult to account for with this method, and AUC values may be underestimated relative to Bayesian estimates.[15,16]

The time requirements demonstrated in this study, with use of the AUC nomogram method described, are arguably noninvasive in terms of pharmacists' overall daily responsibilities; thus, the method could be considered an efficient approach to vancomycin dosing. It is worth noting that when AUC monitoring was required, the median time spent per patient nearly doubled (from 3.48 to 6.2 minutes). While vancomycin is often prescribed for nonestablished MRSA infections, time contribution towards unnecessary vancomycin therapy was minimal, with only approximately 11% of patients having a documented serious MRSA infection. This additional time allows for pharmacists to focus on other patient-focused interventions, which include antimicrobial stewardship, transitions of care, patient education, and other clinical responsibilities.

There were several limitations to this study. Self-reporting and measurement bias may have occurred, because each pharmacist recorded their own findings. This method is commonplace in time and motion studies.[17,18] To mitigate these forms of bias in the study, all stopwatch processes and devices were standardized, standardized training took place prior to data collection, a 7-day washout phase was included to allow study pharmacists to become proficient in the time and motion methods, and clinical chart note times were used as surrogate time markers.[11] Note times were not significantly different from study pharmacists' self-timing values, and the numbers of observations and studied individuals in the study were higher than those documented in previous healthcare time and motion studies.[10,17,18] Patient outcomes, including efficacy and safety, were not evaluated in the study.

## Conclusion

To the authors' knowledge, this study represents the first assessment of a population-based AUC nomogram approach to determining the

time dedicated to vancomycin-related clinical services. Clinical pharmacists spent approximately 10 minutes per day performing activities related to vancomycin dosing. Future research is needed to evaluate the time and financial requirements of various AUC-based vancomycin dosing strategies.

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## Disclosures

The authors have declared no potential conflicts of interest.

## Previous affiliations

At the time of writing, Dr. Chung was affiliated with Department of Pharmacy, Henry Ford Hospital, Detroit, MI.

## References

1. Balkhy HH, El-Saed A, Alshamrani MM, et al. Ten-year resistance trends in pathogens causing healthcare-associated infections; reflection of infection control interventions at a multi-hospital healthcare system in Saudi Arabia, 2007-2016. *Antimicrob Resist Infect Control*. 2020;9(1):21.
2. Applebaum PC. The emergence of vancomycin-intermediate and vancomycin-resistant *Staphylococcus aureus*. *Clin Microbiol Infect*. 2006;12(suppl 1):16-23.
3. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: a revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health-Syst Pharm*. 2020;77(11):835-864.
4. van Hal SJ, Paterson DL, Lodise TP. Systematic review and meta-analysis of vancomycin-induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. *Antimicrob Agents Chemother*. 2013;57(2):734-744.
5. Prybylski JP. Vancomycin trough concentration as a predictor of clinical outcomes in patients with *Staphylococcus aureus* bacteremia: a meta-analysis of observational studies. *Pharmacotherapy*. 2015;35(10):889-898.
6. Jeffres MN. The whole price of vancomycin: toxicities, troughs, and time. *Drugs*. 2017;77:1143-1154.
7. Momattin H, Zogheib M, Homoud A, et al. Safety and outcome of pharmacy-led vancomycin dosing and monitoring. *Chemotherapy*. 2016;61(1):3-7.
8. Schulz LT, Dilworth TJ, Rose WE. Pragmatic application of AUC-based monitoring recommendations from the 2020 vancomycin consensus guidelines. *Am J Health-Syst Pharm*. 2021;78(15):1363-1364.
9. Atrash S, Lusardi KT, Rico JC, et al. A quality improvement project to decrease overuse of vancomycin in an inpatient hematology/oncology service. *J Clin Oncol*. 2016;34:(15 suppl):e18167.
10. Lewis P. Vancomycin area under the curve simplified. *Ther Drug Monit*. 2018;40(3):377-380.
11. Lopetegui M, Yen PY, Lai A, et al. Time motion studies in healthcare: what are we talking about? *J Biomed Inform*. 2014;0:292-299.
12. Matzke GR, McGory RW, Halstenson CE, et al. Pharmacokinetics of vancomycin in patients with various degrees of renal function. *Antimicrob Agents Chemother*. 1984;25:433-437.
13. DeRyke CA, Alexander DP. Optimizing vancomycin dosing through pharmacodynamic assessment targeting area under the concentration-time curve/minimum inhibitory concentration. *Hosp Pharm*. 2009;44(9):751-765.
14. Neely MN, Kato L, Youn G, et al. Prospective trial on the use of trough concentration versus area under the curve to determine therapeutic vancomycin dosing. *Antimicrob Agents Chemother*. 2018;62(2):pii:e02042-17.
15. Turner RB, Kojiro K, Shephard EA, et al. Review and validation of Bayesian dose-optimizing software and equations for calculation of vancomycin area under the curve in critically ill patients. *Pharmacotherapy*. 2018;38(12):1174-1183.
16. Pai MP, Neely M, Rodvold KA, et al. Innovative approaches to optimizing the delivery of vancomycin in individual patients. *Adv Drug Deliv Rev*. 2014;77:50-57.
17. Hendrich A, Chow MP, Kaczynski BA, et al. A 36-hospital time and motion study: how do medical-surgical nurses spend their time. *Perm J*. 2008;12(3):25-34.
18. Hollingworth W, Devine EB, Hansen RN, et al. The impact of e-prescribing on prescriber and staff time in ambulatory care clinics: a time–motion study. *J Am Med Inform Assoc*. 2007;14(6):722-730.