CONCISE COMMUNICATION

A Simple Microsoft Excel Method to Predict Antibiotic Outbreaks and Underutilization

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Benchmarking strategies are needed to promote the appropriate use of antibiotics. We have adapted a simple regressive method in Microsoft Excel that is easily implementable and creates predictive indices. This method trends consumption over time and can identify periods of over- and underuse at the hospital level.

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The emergence of antibiotic-resistant bacteria is an increasingly serious threat to global public health.[1] Infections caused by these organisms are associated with a significant clinical and financial burden worldwide and are responsible for at least 2 million illnesses and 23,000 attributable deaths annually in the United States alone.[2] Moreover, the Centers for Diseases Control and Prevention (CDC) estimates that up to 50% of antibiotic prescriptions in the United States are unnecessary.[2]

As a result of inappropriate overuse, various calls to action for antimicrobial stewardship have been sounded. While a need to curtail inappropriate use through stewardship exists, defining this in the hospital setting can be difficult and requires standardization.[3,4] One mechanism aimed at benchmarking consumption and evaluating national trends is the CDC Antibiotic Use and Resistance (AUR) module for reporting data to the National Healthcare Safety Network (NHSN). We recently described a methodology to identify potential "antibiotic outbreaks" and periods of underutilization using data compiled by the NHSN AU method. Antibiotic use (ie, consumption) was measured in days of therapy (DOT), which was standardized to days present (DP) in the hospital (ie, DOT/1,000 DP). Over- and under-utilization was defined as a monthly rate of use outside the trend-adjusted prediction window.[5] One barrier to implementing our previous methodology is the requirement for users to have technical statistical software (eg, Stata, StataCorp LP, College Station, TX) and statistical expertise. In this manuscript, we translate our methodology into a "plug and play strategy" using Microsoft Excel. By using well-known and readily available software, most hospital users should be able to employ these strategies. This method is easy to implement in any hospital that generates longitudinal antimicrobial utilization data, including those who participate in the NHSN AUR module.

For method illustration, data were obtained from Northwestern Memorial Hospital, an 897-bed, tertiary-care, academic medical center in Chicago, Illinois. Data regarding intravenous administration of piperacillin-tazobactam were extracted from our medical intensive care unit (MICU) monthly from January 1, 2012, to December 31, 2015. Antibiotic consumption was calculated as antimicrobial days (AD) per 1,000 DP in the ICU and compiled according to the NHSN AU methodology.[6] Antimicrobial days and DP facility wide were extracted from the electronic medication record (eMAR) and tallied. Microsoft Excel (2016) standard formulae were used for all calculations, and priority for formulae/code was based on compatibility with older Microsoft Excel versions. A database is supplied as Supplementary Material with formulae for each calculated text box. Interested readers can transfer their own data and generate similar graphics and predictions.

Our data were extracted from the NHSN portal as follows. The "Analysis" portal within the Patient Safety component was accessed, and the "Output options" section was selected. From this portal, the Antimicrobial Use and Resistance module was chosen and directed to Antimicrobial Use data. Using the "CDC defined output," "Line Listing-All Submitted AU Data by Location" was downloaded (although whole-hospital [FACWIDEIN] is also an option). By modifying the output to comma-separated-value format (*.csv), the data were immediately available in Microsoft Excel. Date data (ie, month of use) are defined in the NHSN data as "summaryYM." Numerator data (ie, consumption) were obtained from "IV_Count." Denominator data (ie, days present) were obtained from "numDaysPresent." After sorting for location and antibiotic of choice, sequential months were enumerated. Consumption data were then standardized as DOT/1,000 DP in the adjacent column for each corresponding month using the formula (= cell defining "IV_Count"/cell defining "numDaysPresent" *1,000; see Supplementary Material).

Because NHSN data are not universally available to all institutions, any antibiotic consumption data following a similar format (eg, DOT/1,000 DP) can be modeled using the file available in the Supplementary Material. That is, this document only requires that users insert institution-specific consumption data standardized to 1,000 DP. Formulae are included in the Supplementary Material, and derivations are detailed in Table 1.

To investigate antibiotic outbreak thresholds and periods of underutilization, prediction intervals were defined for each individual time period.[5] In this case, an 80% prediction interval was arbitrarily chosen to define potential antibiotic outbreaks; however, percentages can be set to any threshold at the discretion of each institution. We propose that this value has greater utility than the more generally reported 95% confidence interval for the mean, which predicts the

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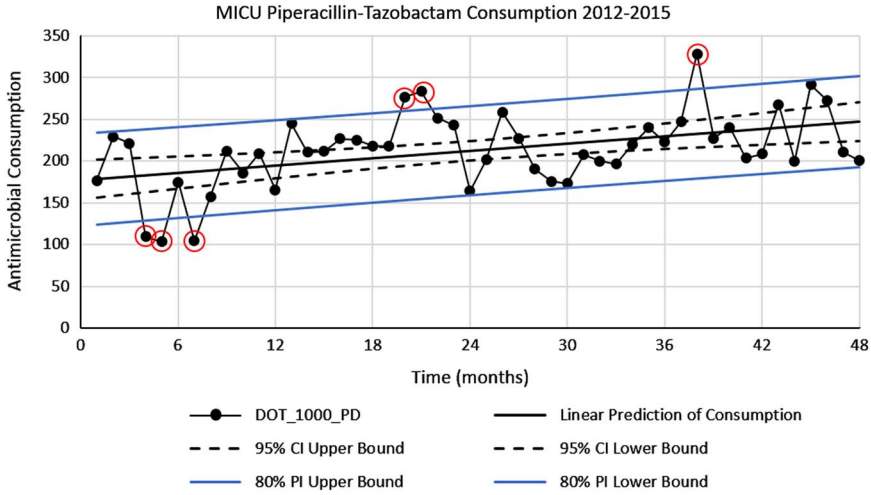

FIGURE 1. Linear regression of piperacillin-tazobactam consumption (DOT/1000 PD) in the medical intensive care unit as the *y*-axis from the period from January 2012 to December 2015 as sequential months from 1 to 48 (*x*-axis). Dashed lines represent upper and lower bounds of the 95% confidence interval. Solid lines represent upper and lower bounds of the 80% prediction interval. The latter is suggested to predict periods of potential under- and overuse.

TABLE 1. Derivations of Equation From the Supplemental Material[a]

Equation Set 1		
1.1[b]	Linear prediction value obtained from regression	$\hat{y}$ = *FORECAST(month,antibiotic_DOT_1000_PD,T)*
1.2[c]	Standard error of the mean for the given month	*SEM = steyx_drug*SQRT(1/COUNT(Analysis_period) + ((month-AVERAGE ($Months_{Total}$))^2/devsq_ Analysis_period))*
1.3	Standard error of the predicted *y* value for each *x* in the regression	*steyx_drug = STEYX(antibiotic_DOT_1000_PD, Analysis_period)*
1.4	Standard deviation for the given month	*devsq_ Analysis_period = DEVSQ(Analysis_period)*
1.5[d,e]	Upper bound 95% confidence interval	*95% CI_UB =* $\hat{y}$ *+ TINV(0.05,COUNT(Analysis_period)-2)*SEM at that month*
1.6	Lower bound 95% confidence interval	*95% CI_LB =* $\hat{y}$ *- TINV(0.05,COUNT(Analysis_period)-2)* SEM at that month*
Equation Set 2		
2.1	Standard error of prediction	*SE of Prediction = steyx_drug*SQRT(1 + (1/COUNT(analysis_period)) + ((month-AVERAGE(analysis_period))^2/devsq_analysis_period))*
2.2	Upper bound 80% prediction interval	*80% PI_UB =* $\hat{y}$ *+ TINV(0.2,COUNT(analysis_period)-2)* SE of Prediction*
2.3	Lower bound 80% prediction interval	*80% PI_LB =* $\hat{y}$ *- TINV(0.2,COUNT(analysis_period)-2)* SE of Prediction*

NOTE. DOT, days of therapy; PD, patient days; T, time; SEM, standard error of the mean; SQRT, square root; DEVSQ, squared deviation of the sample mean; TINV, inverse of the two-tailed Student *t* distribution; PI_UB; upper bound 80% prediction interval PI_LB, lower bound 80% prediction interval; SE, standard error.

[a]Equation set 1 includes the formulae needed to construct a simple linear regression model using the FORECAST function with DOT/1,000 DP as the dependent variable and time as the independent variable. This calculates mean linear predictions for consumption data across ordered time months, with variability quantified as standard error of the mean (SEM) and attendant 95% confidence intervals at each time point. Equation set 2 includes the formulae needed to calculate standard errors of predictions and attendant 80% prediction intervals at each time point.

[b]Month is a single numeric value when months are numbered sequentially.

[c]Analysis_period is the total time of analysis.

[d]TINV is the 2-tailed inverse of the Student *t* distribution: the first number following TINV is the probability associated with the 2-tailed Student *t* distribution and the second number following it is the degrees of freedom.

[e]The COUNT -2 function is used to determine the needed degrees of freedom.

confidence interval for the mean (rather than any individual single prediction).[7] Values above or below the prediction interval serve as a decision support tool for the investigation of antibiotic over- or underuse. Upper and lower bounds of these predictive intervals were calculated using standard errors of predictions (see Table 1, equation set 2).[8,9]

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One application of this method may be to identify a hospital's or unit's adherence to antimicrobial stewardship policies over time and to provide trigger points for further ASP review. Trigger points would be those that were above (ie, potential overutilization due to inappropriate use) or below (ie, potential underutilization due to overly aggressive policy application) the prediction interval. In Figure 1, these trigger points are circled (ie, 3 below and 3 above the prediction interval). The stewardship team can conduct a drug utilization review for the antibiotic in question, focusing on the period surrounding the trigger point and determining whether use during the identified period was appropriate or inappropriate. Another application would be to test whether newly implemented stewardship strategies resulted in a departure from the previous linear trend (ie, Does consumption decrease beyond a certain prediction interval post implementation of stewardship strategy?). To measure impact, using the supplemental file, one would input the previous data that defined the past trend and would then omit data for the period that defined the intervention. The supplementary file is set up to automatically predict future trends. The investigator can utilize these calculations to determine whether the intervention resulted in a departure from the predicted trend.

We have adapted a methodology to identify potential antibiotic outbreaks using a widely available program, Microsoft Excel. This method can be easily implemented in individual institutions using NHSN or other similarly collected antibiotic consumption data. Variation of site-specific antimicrobial consumption and internal trends in antimicrobial use can then be identified. Determining such trends is highly relevant for individual institutions and may provide antimicrobial stewardship programs a stable method for comparing antimicrobial consumption over time for conserved patient mixes (eg, their own hospital). We believe this method has a variety of applications including quality assessment of stewardship protocols, formulary changes, or drug shortages.

It is important to understand several caveats when applying this methodology. As with most mathematic models, predictions have inherent uncertainty. Thus, we advise caution when interpreting these data to avoid any overconfidence or confirmation bias. In addition, this method assumes linearity of predicted consumption values and homoscedasticity of errors. These assumptions can be easily confirmed or refuted through visual inspection, where predictions around the line at zero should have roughly equal numbers of residuals above and below zero. Once these assumptions are verified, this model can be applied as a practical screening tool to identify institution-specific utilization trends and consumption triggers for further investigation.

SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2017.72

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