# A Long-term Forecast of MRSA Daily Burden Using Logistic Modeling

BRADFORD D ALLEN, ROCCO J PERLA

**OBJECTIVE:** This article presents a logistic model that describes the mean number of unique methicillin-resistant *Staphylococcus aureus* (MRSA) isolates collected daily at a 150-bed community hospital in central Massachusetts. The model is used to derive a long-term forecast of the mean MRSA isolate frequency.

**METHODS:** The mean number of MRSA isolates collected daily was found for each quarter from the first quarter of 1996 to the first quarter of 2008. A logistic model was fit to the data and then extrapolated to obtain a long-term forecast.

**SETTING:** Data was collected at a one-hundred-fifty bed community hospital in central Massachusetts.

**RESULTS:** The coefficient of determination indicates that 87% of the variation in transformed data is explained by the model. The extrapolated logistic model prediction is that the mean number of MRSA isolates collected daily approaches 1.42 MRSA isolates per day.

**CONCLUSION:** Logistic modeling of empirical data using modest mathematical assumptions is an effective way to understand, visualize, and forecast MRSA daily frequencies over time. The advantage for laboratorians and epidemiologists is that logistic models provide reliable trending and long-term prediction ability of multi-drug resistant organism frequencies. Moreover, as additional data is obtained, the logistic model assumptions can be checked, the model updated, and forecasts improved.

**ABBREVIATIONS:** MRSA = methicillin-resistant *Staphylococcus aureus*.

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**INDEX TERMS:** infection control; logistic model; microbiology; MRSA; Poisson distribution.

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This article presents a long-term forecast of the mean daily frequencies of unique methicillin-resistant *Staphylococcus aureus* (MRSA) isolates. The forecast is found by extrapolating a logistic model that is derived from MRSA isolate data collected daily at a 150-bed community hospital in central Massachusetts from the first quarter of 1996 through the first quarter of 2008. The logistic model used to generate the forecast was first described by the Dutch mathematical biologist PF Verhulst[1] in 1838 and later by R Perl[2] in 1920. The model has good predictive ability provided its moderate assumptions remain approximately true. In addition to providing a reasonable forecast of MRSA burden, the research presented here shows the value of using historical laboratory data to describe important laboratory processes and identify trends. In another article appearing in this journal, we present theoretical and empirical support for a Poisson distribution model of MRSA isolates collected daily at the same central Massachusetts hospital.[3] The Poisson probability model provides a reliable way to recognize when unusually high numbers of MRSA isolates may signal

MRSA outbreaks. If the Poisson model of MRSA isolates is combined with the logistic model presented here, then the forecast may be seen as a prediction of the long-term mean of Poisson-distributed MRSA isolates collected daily. The prediction is based on over twelve years of data collected at the same Massachusetts hospital. If the models are treated separately, as is done in the two articles appearing in this issue, the Poisson model provides a statistical warning system that signals when high MRSA frequencies may signal an outbreak. Alternatively, the logistic model provides a deterministic trend and long-term forecast of MRSA daily burden. Moreover, these models could be used to monitor and analyze other multi-drug-resistant organism frequencies over time.

## MATERIALS AND METHODS

Laboratory records of MRSA isolates recovered daily from the first quarter of 1996 through the first quarter of 2008 were collected using the Vitek DataTrac Logbook Report program (bioMerieux, Durham NC) following the "first isolate rule" (i.e., one patient isolate per year) and following Clinical and Laboratory Standards Institute guidelines for the analysis of susceptibility data.[4] The data include all clinical isolates (inpatients and outpatients), with duplicate patient isolates, surveillance cultures, and screens omitted from the analysis. The actual specimen collection date (not the date reported to infection control) was used to organize the data because the date of collection provides a reasonable and standard estimate of frequency across time. The mean number of MRSA isolates collected daily was found for each quarter over a 12.25 year time interval. The means were smoothed using a four-quarter moving average and *changes* in the mean number of MRSA isolates from one quarter to the next were found.

## RESULTS

A plot of the mean number of MRSA isolates collected daily for each quarter is shown in Figure 1. After the MRSA means were smoothed using a four-quarter moving average and *changes* in the means were found, the changes were plotted in terms of the size of the means. Figure 2 shows the relationship between changes in the mean number of MRSA isolates collected daily and the actual mean number of isolates. The plot shows that as the mean number of isolates increases, the change in the number of isolates collected daily increases at first but then declines. It can be seen from Figure 2 that the change in the number of isolates per day from quarter to quarter reaches a maximum of 0.09 isolates when the mean number of isolates per day is 0.68. This observed maximum occurs in the 40$^{th}$ quarter and we expect that the true maximum, $M$, also occurs around this time.

If the *change* in the mean number of MRSA isolates collected daily from quarter to quarter continues its decline toward zero, then growth in the mean number of MRSA isolates collected daily will begin to level off, and over the long-term, remain at a stable level close to the value $M$. Drug-resistant organisms frequently persist in environments at stable levels as the organisms become more established.[5] Stable organism levels imply that *changes* in the levels have declined to zero. Figure 2 shows a pattern where the rate of change is beginning to decline. Such a pattern would occur if the change in

**Figure 1.** Mean MRSA daily isolates by quarter from 1996 to 2008

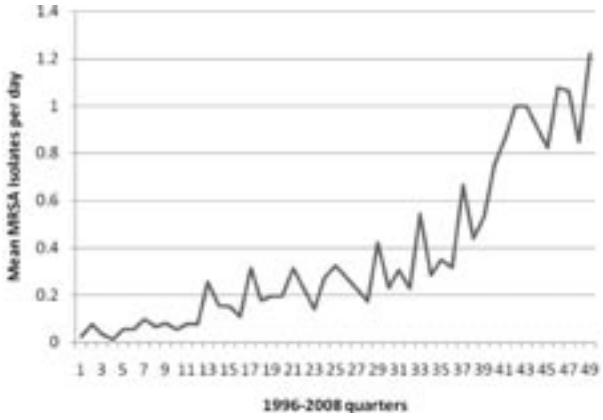
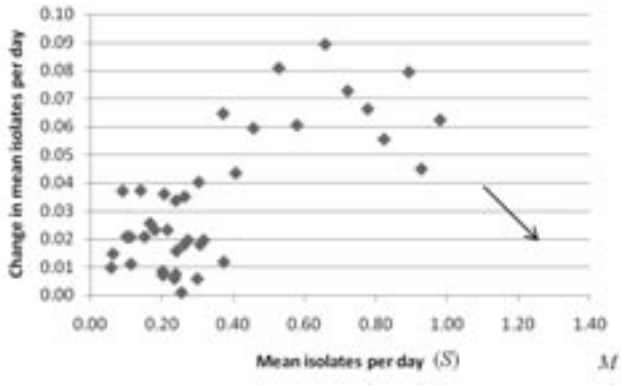


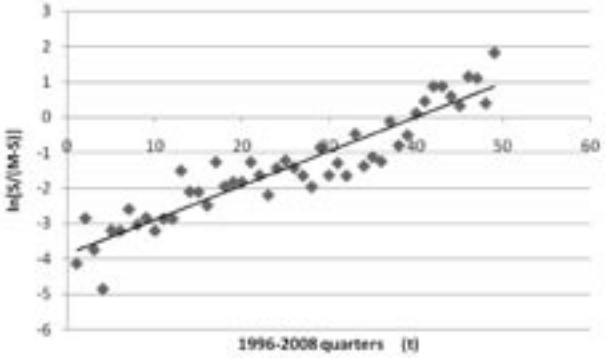

**Figure 2.** Change in mean MRSA isolates per day by mean MRSA isolates (data smoothed with a four-quarter moving average)



the number of isolates collected daily and the actual number of isolates collected daily are proportional, but the rate of proportionality is declining. If the change in the number of isolates approaches zero as the actual number of isolates approaches $M$, then as Figure 2 suggests, the change in the mean number of isolates can be approximated with a quadratic function. If we let $S$ represent the mean number of MRSA isolates collected daily and let $M$ represent the point at which the rate of change reaches zero, we can express the *change* in the mean number of isolates in terms of the actual mean number of isolates using a quadratic equation with zeros at $S$=0 and $S$= $M$ . That is:

$$\frac{dS}{dt} = r(M - S)S \qquad (1)$$

**Figure 3.** Transformed data by quarter with a linear model generated from the rate of change in the mean number of MRSA isolates




where $r$ >0 is a constant that reflects the maximum possible rate of change in the mean number of isolates. Using separation of variables and partial fractions, we find that:

$$\ln[S/(M - S)] = rMt + C \qquad (2)$$

The right-hand-side of Equation 2 shows that $\ln[S/(M-S)]$ is linear in terms of $t$, where $t$ is the number of quarters starting from the first quarter of 1996. Using Figure 2, we estimate that $M \approx 1.4$. To test this model further, we use the actual data values plotted in Figure 1 for values of $S$ and plot $\ln[S/(M-S)]$ in terms of $t$ from 1996 to 2008. If the model is good, the resulting plot will be linear in terms of $t$. Figure 3 is a plot of the transformed data $\ln[S/(M-S)]$ in terms of $t$. To get the best linear relationship, the value of $M$ was adjusted to $M$ =1.42. The resulting coefficient of determination for the linear model reveals that 87% of the variation in the transformed data is explained by the linear model. Solving Equation 2 for $S$ gives a logistic model whose graph is shown in Figure 4.

To see the long-term trend of the mean number of MRSA isolates collected daily, the logistic model is extended several more years in Figure 5. The logistic model shows that the mean number of MRSA isolates collected daily approaches a stable long-term level of $M$ =1.42 MRSA isolates per day.

## DISCUSSION

Clinical laboratory scientists, researchers, microbiologists, and epidemiologists would benefit from using MRSA daily frequency data and logistic modeling to make informed decisions about MRSA trends. For example, the logistic model can be used to predict MRSA frequencies well before

**Figure 4.** Mean MRSA daily isolates by quarter with the logistic model

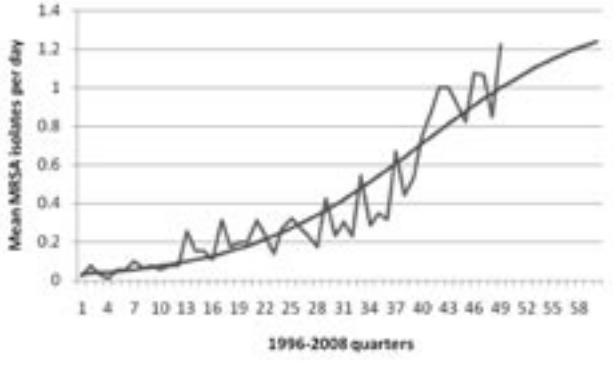
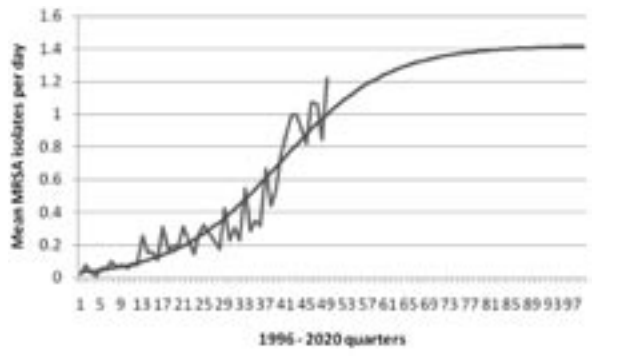



**Figure 5.** Mean MRSA daily isolates by quarter with the long-term logistic model



the long-term frequency is reached. Researchers should be aware, however, that growth in a restrictive environment can approach a stable level in different ways. As our data begins to show, the number of isolates can level off by means of a gradual decrease in the rate of change. Alternatively, the mean isolate frequency can move past a long-term level but might then decrease in a smooth or an oscillatory way. Long-term stability also occurs if isolate frequency exceeds a potential long-term stable level but by doing so, new restrictions on growth and transmission that reduce the long-term frequency are generated. For example, an outbreak could focus intense and persistent infection control measures that result in a long-term endemic state at a lower level than had the outbreak not occurred.

Logistic growth models can give insights into claims by researchers and infection control professionals where significant treatment or intervention effects were observed on experimental or observational studies or in reports from the field. Limitations to growth in the environments of drug-resistant organisms may lead some to incorrectly attribute a reduction in MRSA growth and transmission to an intervention program or initiative when the reduction may be nothing more than a reflection of the natural evolution of the organisms as described by the logistic model. At a minimum, the effectiveness of reduction efforts directed at MRSA and other multi-drug resistant organisms (MDROs) needs to be measured and assessed in the context of the natural evolution of these organisms. Clinical laboratory scientists, epidemiologists, healthcare quality professionals, and manufactures of susceptibility testing systems should recognize the importance of using time-series data and logistic modeling to develop trending and forecasting models for MDROs.

*Clin Lab Sci encourages readers to respond with thoughts, questions, or comments regarding this article. Email responses to david.mcglasson@lackland.af.mil. In the subject line, please type "CLIN LAB SCI 22(1) RR ALLEN". Selected responses will appear in the Dialogue and Discussion section in a future issue. Responses may be edited for length and clarity. We look forward to hearing from you.*

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