Epidemiologic and Economic Effect of Methicillin-Resistant *Staphylococcus aureus* in Obstetrics

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**OBJECTIVE:** To quantify the epidemiologic and economic burden of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the obstetric population, identify main factors influencing the magnitude of disease, and evaluate the cost-effectiveness of MRSA screening and decolonization.

**METHODS:** A cost-effectiveness decision analytic model was constructed for estimations from both the societal and third party–payer perspectives. Probabilities were derived from prior studies when available. Cost data came from the Healthcare Cost and Utilization Project, medication wholesale prices, and the Centers for Medicare & Medicaid Services. Sensitivity analysis was conducted to assess the effect of variables across a range of values.

**RESULTS:** Approximately 14,294 pregnant or postpartum women experience an invasive MRSA infection in the United States annually. The majority of invasive MRSA infections are mastitis (n=8,880). The annual economic effect of MRSA infections is projected to be approximately $8.7 million and approximately $8.0 million from the societal and payer perspectives, respectively. Sensitivity analyses demonstrate that the prevalence of MRSA, incidence of mastitis, and rate of cesarean deliveries were key driving factors for the estimations.

**CONCLUSION:** Methicillin-resistant *S aureus* is an important emerging pathogen responsible for a modest burden of puerperal infections and associated costs. Universal screening and decolonization efforts do not currently seem to be cost-effective.

*(Obstet Gynecol 2009;113:983–91)*

**LEVEL OF EVIDENCE:** III

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*Supported in part by the National Institutes of Health (NIH) National Institute of General Medical Sciences (NIGMS) Models of Infectious Disease Agent Study (MIDAS) research network.*


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*Financial Disclosure* The authors did not report any potential conflicts of interest.

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ISSN: 0029-7844/09

VOL. 113, NO. 5, MAY 2009

**OBSTETRICS & GYNECOLOGY** 983
Klevens et al. recently published a national approximation of the burden of MRSA infections among the general population, estimating that 94,360 invasive MRSA infections (31.8 per 100,000 persons) occurred in the United States in 2005. Published national estimates of the burden of MRSA and/or the cost-effectiveness of screening for MRSA colonization among pregnant women cannot be located. The goals of the current investigation were to use modeling methods to estimate among the United States pregnant population 1) the

Fig. 1. Model structure. A. Methicillin-resistant *Staphylococcus aureus* screening and decolonization base model. B. Outcomes main model. MRSA, methicillin-resistant *Staphylococcus aureus*. (continued)

epidemiologic effect of MRSA, 2) the economic burden of MRSA, and 3) the cost-effectiveness of universal screening and attempted decolonization for MRSA. Our hypothesis is that MRSA infections are responsible for a sizable epidemiologic and economic burden among the obstetric population.

MATERIALS AND METHODS

To estimate the burden of MRSA on the pregnant population in the United States we used TreeAge Pro Suite with Excel 2008 (TreeAge Software, Williams-town, MA) to develop a Monte Carlo simulation model. The model simulated a woman going through pregnancy, experiencing a live birth, and the first year after birth. Specific obstetric infectious events were included, and costs were assigned to each event. The base-case scenario assumed the societal perspective, which accounts for both direct (all costs associated with treatment) and indirect costs (productivity losses such as time in the hospital or time off of work). The third-party-payer perspective considers only the direct costs of illness.

The cost-effectiveness of universal surveillance for MRSA with subsequent efforts aimed at decolonization for those found to be colonized was also evaluated. This was done using a cost-effectiveness model that assumed the costs of universal screening on every pregnant woman and then used ranges of effectiveness of decolonization (0.0% effective through 90% effective) with its associated costs. Screening included performing cultures and susceptibility testing on positive isolates on every pregnant woman plus use of an effective decolonization regimen tested in the nonpregnant population (no such regimen has been published in pregnancy). This regimen includes use of both systemic and topical antimicrobials in addition to washing with antibacterial soap. After screening, all women then entered the model with the base assumption that the decolonization was 0.0% effective, with subsequently increasing increments of effectiveness. Simulated patients were then run through the model to obtain costs and effectiveness (in quality-adjusted life years) distributions for each strategy. Subsequently, incremental
cost-effectiveness ratios for each level of effectiveness for the screening and decolonization strategy were calculated and then compared with baseline (ie, no surveillance and/or decolonization procedures).

Figure 1A–C demonstrates the general structure of the simulation model. Every pregnant woman who enters the model has a baseline probability distribution of being colonized with MRSA but then subsequently has decreasing rates of colonization that are dependent on increasing effectiveness of the decolonization regimen. The woman then has a probability distribution of undergoing a cesarean delivery. Those who undergo a cesarean delivery may develop a wound infection, which leads to different series of events depending on the severity and extent of infection. Mild cases require only outpatient antibiotic treatment. More severe cases may involve inpatient stays and operating room wound debridement. After any type of delivery, a woman also has a probability of breast-feeding. Women who breastfeed have a chance of developing lactation mastitis. Mastitis can range in severity from mild, requiring outpatient antibiotics, to severe, which may necessitate incision and drainage of an abscess. These two infectious processes were chosen given their significant prevalence in the obstetric population and recognized causative contribution of *S. aureus* when compared with other infectious outcomes not included in the model.

When available, published literature was used to determine the probability estimations used in the model. In the absence of published data the model assumed that cases of mastitis and wound infection that developed in MRSA-colonized women were, in fact, caused by MRSA. In addition, the base model assumed a 48-hour lag time between the initiation of empiric antibiotics and the switch to MRSA-specific antimicrobial therapy. Specifically, a patient with a MRSA infection would remain on empiric antibiotics that would not be predicted to provide adequate MRSA coverage for 48 hours before either the recovery of MRSA from the site of infection or failure to clinically respond. The antibiotics used for the cost estimations in these situations were cephalexin for outpatient treatment of both wound and breast infections, and intravenous ampicillin-sulbactam for these same infections treated as an inpatient. After the initial 48 hours of therapy the patient would be changed to an antibiotic providing adequate MRSA coverage. The model assumed vancomycin as the first-line agent for MRSA infection in the inpatient setting and trimethoprim-sulfamethoxazole in the outpatient setting. Finally, the chosen length of antibiotic therapy was 7 days for wound infections and 10 days for breast infections.

Table 1 lists the various probability inputs for the model, including the distribution parameters and the data sources for each variable. When possible, probability estimates used in the model were derived from the published literature. Probability estimates not available in the literature were based on ranges from our own institution’s reproductive infectious diseases service experience. Magee-Womens Hospital is a university-based large academic women’s hospital that performs approximately 10,000 deliveries per year. The estimates generated from local hospital data include the probability of hospitalization for breast infections, the probability of having an incision and drainage procedure performed for a breast abscess, the probability of having the procedure performed in an operating suite, and the probability of requiring home health care services. Cost estimates were derived largely from Centers for Medicare & Medicaid Services and Healthcare Cost and Utilization Project published data and are presented in Table 2. For costs not available from these sources, estimates from Magee-Womens Hospital of the University of Pittsburgh Medical Center were used. All costs were in 2008 U.S. dollars. For costs available only from previous years, a 5% rate inflated costs to 2008 values. Applic-
ing a standard cost-to-charge ratio conversion factor of 0.482/0.135 converted medical charges to costs.\textsuperscript{41}

We simulated a year of pregnancies and live births. Using the number of live births in the United States and the seasonal distribution, simulated pregnant women (average age of 27.4 years) were sent one-by-one through the model, starting from January 1, 2007, and concluding December 31, 2007. During each simulation run, the model drew parameter values from each input’s distribution. The probability distributions were independent of each other (eg, the probability of mastitis is not dependent on whether the patient previously developed a wound infection). Where possible, we used triangular distributions. The base value of life expectancy of each pregnant woman in the model was calculated as 46.72 quality-adjusted life years based on age-related mortality data and conversion of years into quality-adjusted life years.\textsuperscript{42,43}

The effect of a MRSA infection in the puerperal period was designated as a decrement in quality of life for that specific year of the infection of 0.35 quality-adjusted life years.\textsuperscript{32,41} The value for incremental cost-effectiveness ratio used in this analysis that denotes a cost-effective strategy is $50,000.00 per quality-adjusted life year based on usual convention and published literature.\textsuperscript{44}

Performing probabilistic (Monte Carlo) sensitivity analyses involved simultaneously drawing all parameters from probability distributions to account for the natural stochasticity of the subsequent outcomes. We also examined the effects of varying different parameter values individually throughout the ranges listed in Table 1 for each variable.

RESULTS

The model produced the following estimations of national burden of MRSA-associated obstetric infectious morbidity: 8,880±184 cases of mastitis and 5,414±144 cases of wound infection without any surveillance measures (total cases 14,294). This total number of MRSA-associated infectious cases (N 14,294) translates into approximately 357.4/5 per 100,000 pregnancies that result in a live birth. Additional attributable morbidity from the mastitis-associated cases are that approximately 157/25 women would require hospitalization and 29/11 of these women would develop a breast abscesses caused by MRSA.

The number of national hospitalizations from wound infection was 105/20. Overall, 477/43 women will require home care services related to MRSA-attributable wound infections.

From a societal perspective, economic modeling estimates that on a national scale MRSA-associated infectious morbidity currently generates $8,747,009±267,867 of costs, including all outcomes considered in?

\begin{table}[h]
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\begin{tabular}{|l|c|c|c|l|}
\hline
\textbf{Costs*} & \textbf{Base} & \textbf{Minimum} & \textbf{Maximum} & \textbf{Reference} \\
\hline
Hospitalization due to wound infection after cesarean delivery & 5,069.60 & 3,651.95 & 6,487.26 & 37 \\
Open wound incision in office & 30.97 & 22.31 & 39.64 & 37 \\
Open wound incision in operating room & 324.91 & 234.05 & 415.77 & 37 \\
Breast ultrasonography & 38.19 & 27.51 & 48.87 & 37 \\
Hospitalization due to mastitis & 2,620.44 & 1,887.66 & 3,353.22 & 38 \\
Incision and drainage of breast abscess & 176.77 & 127.34 & 226.21 & 37 \\
Culture and susceptibility testing & 9.59 & 7.20 & 12.00 & †
Decolonization regimen & 103.95 & 77.97 & 124.94 & 39 \\
Breast abscess needle aspiration & 47.65 & 34.33 & 60.98 & 37 \\
TMP-SMX DS antibiotic treatment per d & 4.81 & 4.13 & 4.85 & 39 \\
\text{Cephalexin 500 mg antibiotic treatment per day} & 13.74 & 11.59 & 18.00 & 39 \\
\text{Intravenous infusion, first h} & 32.85 & 23.66 & 42.03 & 37 \\
\text{Intravenous infusion per h, after first h} & 10.67 & 7.68 & 13.65 & 37 \\
Ampicillin-sulbactam intravenous antibiotic treatment per day & 73.02 & 71.06 & 74.98 & 39 \\
\text{Vancomycin intravenous antibiotic treatment per day} & 17.14 & 15.50 & 40.70 & 39 \\
\text{Home health care supplies per wk} & 87.50 & 65.63 & 109.38 & ‡ \\
\text{Home health care visitation} & 1,042.50 & 772.50 & 1,362.50 & ‡ \\
\text{Average wage per h} & 17.97 & 13.48 & 22.46 & 40 \\
\hline
\end{tabular}
\caption{Costs Used in the Model}
\textsuperscript{*} All costs are in United States dollars.
\textsuperscript{†} Estimates derived from local laboratory.
\textsuperscript{‡} Estimates derived from local home health care agency affiliated with University of Pittsburgh Medical Center.
\end{table}
the model but not including any costs related to surveillance practices. From a payer perspective, the total economic burden of MRSA is $8,037,789 ± 237,346. The average additional cost per case of MRSA infection is $611.68. Although patient hospitalization that subsequently requires operative room drainage procedures is an overall rare occurrence, these cases engender the highest cost per case.

The results of the multidimensional sensitivity analysis demonstrate that the estimates produced in this model are most sensitive to rates of cesarean delivery (which varied costs from a societal perspective by ±$278, 614), rates of mastitis (which varied costs from a societal perspective by ±$271, 879), and the prevalence of MRSA in the obstetric population (which varied costs from a societal perspective by ±$259, 068). Results from a payer perspective were comparable, with smaller effects on costs (±$216,632 for rates of cesarean delivery, ±$244,695 for rates of mastitis, and ±$219,975 for MRSA colonization rates). Variables that had minimal overall effect in the model on the estimates of rates of disease or costs in this population include rates of hospitalization for wound infection or mastitis-related conditions, costs of antibiotics, costs of home care, and need for operating room drainage procedures.

The results for the analysis, including universal surveillance for MRSA among the entire pregnant population with subsequent attempts to decolonize women with MRSA, are demonstrated in Table 3. None of the incremental cost-effectiveness ratios approximate the benchmark of $50,000.00 per quality-adjusted life year gained, regardless of the assumed success of surveillance and decolonization.

**DISCUSSION**

This model suggests that currently, MRSA accounts for a modest burden of infectious morbidity and costs among the obstetric population in addition to those caused by methicillin-susceptible *S. aureus* and other perinatal pathogens. Despite this calculated burden, it does not seem from this investigation that universal screening of the entire pregnant population for MRSA colonization with subsequent attempts to decolonize women is a cost-effective strategy. The estimates of burden of disease in this model are most sensitive to rates of cesarean delivery, mastitis, and MRSA colonization. It is therefore likely that the projected attributable morbidity and costs are likely to increase in the future, given the increasing rate of cesarean delivery, increasing rates of adoption of lactation, and the increasing rates of MRSA-associated infections being reported in the literature.21,24,29,33

The standardized rate of 357.4 invasive MRSA obstetric infections per 100,000 live births is significantly higher than the rate estimated by Klevens et al of 31.8 per 100,000 persons in the general population.21 Some comparisons from the vaccine preventable disease surveillance estimates provide perspective. These include annual rates of meningococcal disease among children aged 2–19 years (0.68–3.9 per 100,000), annual hepatitis B rates in both the postvaccine and prevaccine era, respectively (2.5 and 11.6 per 100,000 persons), and annual influenza-related hospitalizations in adults (190–560 per 100,000).45

A key component of the model is the estimation of MRSA colonization in the obstetric population that comes from two sources. Available literature suggested a rate of 0.5–2.0%, and local hospital quality control surveillance estimations among admissions to the high-risk obstetric service produced a range of 1–7%.19,20 An important contribution made by predictive modeling is that key areas for further research are identified. From this model, it is apparent that robust longitudinal data on the prevalence of MRSA colonization and any associated subsequent infectious morbidity among pregnant women is needed to appreciate the full scope of the problem.

The costs attributable to MRSA infections in this model are sizable (in excess of 8 million dollars) and are likely to increase over time. Others have demonstrated that infections associated with antibiotic-resistant bacteria, including MRSA, lead to increases in costs of care.46,47 An approach that has been demonstrated to be cost-effective in hospitals to decrease infections from drug-resistant pathogens is active surveillance followed by contact isolation of those colonized and/or infected.48,49

The current investigation did evaluate the cost-effectiveness of universal screening for MRSA colonization among all U.S. pregnant women plus the costs of attempting decolonization of those found to be colonized. Our findings of a lack of cost-effectiveness are not surprising given the high costs of

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<th>Rates of Successful Decolonization (%)</th>
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ICER, incremental cost-effectiveness ratio.
universal surveillance with decolonization and moderate rates of disease noted herein (with no attributable mortality). Future investigations of targeted surveillance in specific pregnant populations at higher risk for MRSA colonization or among those at higher risk for surgical site infectious morbidity (planned cesarean delivery) may prove cost-effective. This investigation does not address the cost-effectiveness of surveillance plus contact isolation, and thus, no conclusions about that practice can be made.

It is important to note that the projections generated by this model are likely underestimates of the overall burden of MRSA in obstetrics. This is primarily due to the fact that only two specific infectious outcomes were included: cesarean wound infections and lactation-associated breast infections. These two clinical entities were chosen because published reports demonstrate that S. aureus is a major pathogen in these two outcomes. Other potential burdensome infections of perinatal importance such as chorioamnionitis and/or postpartum endometritis were not included due to the lack of formal reports documenting MRSA as a direct cause of these intrauterine infections. In addition, a recent investigation by Thurman et al (including pregnant women) documents a high rate of vulvar abscesses attributable to MRSA, thus highlighting the overall increasing burden.

A few limitations to this investigation based on some of the model assumptions warrant consideration. First and foremost, in lieu of clear data in the obstetric literature regarding actual case rates of MRSA infections, the model assumed that MRSA colonization was an accurate surrogate for infectious cases. This is a reasonable assumption, given that nasal colonization with methicillin-susceptible S. aureus has been demonstrated to be a predisposing factor for increased risk from infectious morbidity in other patient populations, including surgical patients.

This assumption, however, does not allow for de novo infections to occur in uncolonized or newly colonized patients, potentially underestimating the full burden of disease. It was assumed that, when patients were managed with antibiotics, the agents were chosen empirically for 48 hours and then were changed to antibiotics that have activity against MRSA. In addition, our treatment courses of 7 days of antibiotics for wound infections and 10 days for breast infections may also not be completely standardized at all institutions. Although this may not accurately depict the exact sequence or length of therapy for all cases, neither of these variables were identified in the sensitivity analysis as key factors and are thus of little consequence for the overall economic estimates. A further recognized limitation is that the model assumed that every patient diagnosed with a breast abscess was hospitalized, which may not completely represent standard practice for all providers. Last, due to the lack of national data on various outcomes and costs, local estimates from Magee-Womens Hospital were used and may not perfectly reflect national estimates. More robust data available in the literature would have improved the precision of our estimates.

Methicillin-resistant S. aureus is currently estimated to produce a modest burden of disease and health care costs among obstetric patients. Currently, it does not seem to be cost-effective to screen the entire pregnant population and attempt to decolonize those that are colonized. The rates of morbidity and costs attributable to MRSA are, however, likely to increase, thus continued surveillance and ongoing efforts aimed at control of this emerging pathogen among this patient population seem warranted.

REFERENCES


