Successful Veterans Affairs Initiative to Prevent Methicillin-Resistant *Staphylococcus aureus* Infections Revisited

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In 2011 Jain et al reported a 62% reduction of healthcare-associated methicillin-resistant *Staphylococcus aureus* infections that resulted from an intervention bundle. Here we present a mathematical model and prove, using parameters from the study by Jain et al, that the universal screen and isolate strategy can have contributed only marginally to the reduction in infections.

Infections caused by antibiotic-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), frequently occur in hospitalized patients and are associated with increased disease burden and worse patient outcome [1]. Curtailing nosocomial transmission of MRSA to prevent hospital-acquired MRSA infections is an important goal of hospital infection prevention. The application of barrier precautions for patients infected or colonized with MRSA has been effective in several countries with low-endemicity MRSA levels [2], yet implementation of universal MRSA screening and isolation of identified carriers has remained controversial in countries with high-endemicity MRSA-levels, primarily because several studies have shown reductions in MRSA infections [3,4] while others have not [5,6]. Recently, implementation of a MRSA bundle in 153 hospitals was associated with a 62% reduction in rates of healthcare-associated MRSA infections [7]. Like all quasi-experimental studies, controlling for confounding variables is difficult and causality between interventions and observed changes cannot be automatically assumed [8]. The bundle, which was fully implemented in October 2007 and observed until June 2010, comprised 3 interventions: (1) universal nasal MRSA surveillance of admitted and transferred patients followed by contact precautions for colonized patients, (2) improved adherence to hand hygiene protocols, and (3) an institutional culture change whereby everyone with patient contact is responsible for infection control. The first 2 interventions aim to reduce the number of transmission events. Indeed, Jain et al observed a 17% reduction in MRSA acquisition events in intensive care units (ICUs) and a 21% reduction in non-ICUs (from 3.02 and 2.54 per 1000 patient-days in October 2007 to 2.50 and 2.00 per 1000 patient-days in June 2010, respectively). With a constant colonization prevalence of MRSA of 13.6% at admission [7], the decline in point prevalence of MRSA should be relatively less than the decline in acquisition rates. One would expect the incidence of MRSA infections to decrease more or less proportionally to the decrease in the point prevalence of MRSA colonization. However, Jain et al observed incidence reductions as high as 62% (1.64 to 0.62 per 1000 patient-days from October 2007 to June 2010) in ICUs and 45% (0.47 to 0.26 per 1000 patient-days) in non-ICUs. During this program 1 712 537 surveillance-screening tests were obtained and other significant financial efforts—eg, manpower to obtain, transport, and perform tests, and to communicate results—are likely to have been used. Here we assess the extent to which prevention of MRSA transmission, through either better hand hygiene or barrier precautions, contributed to the observed reduction in MRSA infections.

**METHODS AND RESULTS**

We consider 2 simple models for the dynamics of MRSA colonization (see Supplementary Material for details on model choice). In both models there is a constant probability, \( α = 0.136 \), that an admitted patient is colonized with MRSA [7]. Independent of colonization status, patients have a median length of stay (LOS) of 3.0 days [6], which, for simplicity, we assume to be exponentially distributed (see Supplementary Material for 9 other distributions). In model 1, we
ascribe the reductions in MRSA carriage acquisition rates after bundle implementation fully to improved hand hygiene without effects of barrier precautions. Bundle implementation reduces the transmission parameter from $\beta$ to $\beta_1$. In model 2, we ascribe the reductions in MRSA carriage acquisition rates fully to contact precautions without improvement in hand hygiene if contact precautions are absent (see Supplementary Material for modeling details).

Although the point prevalence of MRSA colonization was not directly reported, patients were screened at admission and at discharge. Based on reported numbers of MRSA acquisitions per 1000 patient-days ($T$) in ICUs and non-ICUs, we can estimate the point prevalence ($P$) according to: $P = \alpha + T \cdot \text{loss}/1000$, with $\text{loss}$ the average LOS (1.44 times the median LOS for exponential distributions). If MRSA dynamics were stable before bundle implementation, estimated MRSA transmission parameters at the start of interventions are $\beta = 0.024$ for ICUs and $\beta = 0.020$ for non-ICUs. This corresponds to reproduction numbers per hospital admission ($R_A = \beta \cdot <\text{loss}>$) of 0.10 in ICUs and 0.09 in non-ICUs. After bundle implementation, MRSA dynamics are expected to change, but we can assume that the equilibrium is reached when the observation period ends after 33 months (see Supplementary Material). With this assumption and model 1, we obtain $\beta_1 = 0.84 \cdot \beta$ for ICUs and $\beta_1 = 0.80 \cdot \beta$ for non-ICUs; a 16% hand hygiene efficacy improvement in ICUs and a 20% improvement in non-ICUs. Other distributions for the LOS gave similar results (see Supplementary Material).

In the second scenario, the MRSA transmission parameter $\beta$ is reduced to $\beta_1$ only for isolated patients; bundle implementation does not affect spread by unisolated colonized patients. If MRSA colonization is detected only by means of admission and discharge screening and not by means of clinical cultures or during transfer between wards, colonized patients will face contact precautions either during their entire hospital stay or not at all. Although unrealistic, this assumption maximizes the estimated isolation efficacy. Of admitted patients, 96% [7] were screened. Assuming 100% sensitivity of screening tests, instantaneous availability of test results, and immediate treatment with barrier precautions for detected carriers, we find that $\beta_1 = 0.82 \cdot \beta$ in ICUs and $\beta_1 = 0.78 \cdot \beta$ in non-ICUs, for an isolation efficacy of 18% and 22%, respectively. With test sensitivity of 93% and a 1-day delay before installation of barrier precautions, estimated isolation efficacy increases to 24% in ICUs and 29% in non-ICUs.

Assuming a constant daily risk ($k$) for colonized patients to develop an infection, we can calculate this risk based on numbers of healthcare-associated infections, as reported by Jain et al [7]. Independent of model choice, the daily infection risk needs to decrease by 64% in ICUs and by 44% in non-ICUs to explain the observations. Based on estimates obtained for efficacy of the intervention on transmission prevention and daily infection risk, we can predict how healthcare-associated infection rates would decline if the intervention affected either only the parameter $k$ or only the transmission parameter. We conclude (see Supplementary Material) that in ICUs 1%–4% of the reduction in infection rate is attributable to prevention of acquisition of colonization. In non-ICUs, this range is 3%–6%. Even if patients who became colonized during their stay had a 10 times higher daily infection risk compared with patients already colonized at admission, only 6%–15% of the reduction in infection rates in ICUs and 17%–26% in non-ICUs (see Figure 1) is attributable to transmission prevention. If, in addition to this high daily infection risk after acquisition, acquisition was 20% less effectively detected before bundle implementation than after it, 16%–33% of the reduction in infections in ICUs and 36%–50% in non-ICUs would be attributable to transmission prevention measures.

**DISCUSSION**

Only a small fraction of the phenomenal effects on MRSA infection rates described by Jain et al can result from interventions aimed at transmission prevention, simply because transmission rates before bundle implementation were already low and most patients with MRSA colonization were already colonized at admission. Unless barrier precautions reduce the daily infection risk for colonized patients, admission screening and isolation could not have caused the observed reduction in
infections. We therefore hypothesize that other practices have changed, eg, better management of intravascular lines. This is supported by concurrent reduction in infections caused by vancomycin-resistant enterococci and *Clostridium difficile*, as reported voluntarily by some participating hospitals.

We deliberately determined the maximum possible effects of both interventions by excluding any effect of the other intervention and no identification of MRSA carriage after admission screening. Including these possibilities would reduce the estimated efficacy of each intervention. The efficacy of patient isolation on MRSA transmission prevention has not been determined frequently. The other best estimate (25%) was also obtained in US hospitals [9] and coincides with our estimate. The calculated reproduction number per hospital admission ($R_A$) was much lower than previous estimates of $R_A$ values for MRSA. Ranges of 0.1–0.6 in 8 ICUs in the United States [9] and 0.68–0.93 in The Netherlands [10] were reported, and modeling studies suggest that $R_A$ should be in the range of 0.5–1 [11, 12]. The combination of low nosocomial transmission rates and the 13.6% admission MRSA prevalence implies either that patients have had multiple previous hospital admissions or that MRSA was acquired outside hospitals. Unfortunately, no information is available on patient transfers from other hospitals or long-term care facilities or on community-acquired MRSA proportions.

Naturally, our analyses can provide only crude estimates, because we considered aggregated data from 153 hospitals. Therefore, some individual hospitals may have had higher efficacy levels of transmission interruption measures. Furthermore, most hospitals started implementation in the months before the baseline measurement was taken in October 2007. However, incidences of healthcare-associated MRSA infections started to decline only in April 2008 in ICUs and even later in non-ICUs. Therefore, reductions in transmission before October 2007, if present, were not associated with fewer healthcare-associated MRSA infections.

Furthermore, in the cluster-randomized trial by Huskins et al [6], admission screening followed by barrier precaution did not prevent MRSA colonization or infection. These and our findings have important implications for translating the results of Jain et al into practice guidelines. The low efficacy of both measures aimed at interrupting MRSA transmission should be balanced with universal screening costs. Therefore, policy makers should be reluctant to recommend adaptation of universal screening and patient isolation of MRSA carriers. However, more cluster-randomized trials are needed to determine the key factors for isolation success or failure.

**Supplementary Data**

Supplementary materials are available at *Clinical Infectious Diseases* online (http://www.oxfordjournals.org/our_journals/cid/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyrighted. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

**Notes**

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