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Choosing between methods to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in Intensive Care Units

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of infections, annually accounting for over 62,000 invasive healthcare-associated infections in the U.S.¹ In this issue of Critical Care Medicine, Ziakas et al.² present a decision analysis estimating costs related to MRSA prevention methods examined in the REDUCE MRSA trial.³ The REDUCE MRSA cluster trial randomized 74 intensive care units (ICUs) in 43 hospitals to either: *active surveillance culturing (ASC) with isolation* of patients found to be positive, *ASC with targeted decolonization* of those found to be positive or *universal decolonization* of all patients without ASC. Decolonization was performed with daily chlorhexidine bathing and intranasal mupirocin antibiotic. The REDUCE MRSA trial found universal decolonization was the most effective strategy, reducing MRSA clinical cultures and all cause bacteremia, the biggest effect being on skin commensals.³ A similar ICU randomized cluster trial of chlorhexidine bathing *without* mupirocin found a 23% decrease in MRSA or vancomycin-resistant *Enterococcus* (VRE) colonization by screening cultures and a decrease in bacteremia, with the biggest effect on skin commensals again.⁴ Finally, a cluster trial of universal use of gown and glove use without ASC in all ICU patients (that I helped conduct) found a 40% decrease in MRSA colonization by screening cultures.⁵ How should an ICU allocate limited resources between these and the other methods of infection control (hand hygiene, environmental cleaning, healthcare-associated infection prevention bundles etc.)?

It is from this perspective that one reads the decision analysis by Ziakas and colleagues modeling the expected financial costs associated with adoption of the different interventions of the REDUCE MRSA trial.² Notably, there is no assessment of the standard Centers for Disease Control and Prevention (CDC) recommended practice of Contact Precautions for patients with MRSA or VRE identified by clinical cultures (and not ASC). As with any model, there are many assumptions, terms and data rich tables that induce heavy eyelids in clinicians. To understand the model, it is key to focus on the assumptions. These include: 1) 9% admission prevalence for MRSA, which lower than in many regions and 2) costs associated with identifying MRSA by ASC, they choose the less expensive culture vs.

polymerase chain reaction (PCR) test (\$75 vs. \$311, per authors). The most important assumption is the estimated effect of MRSA clinical cultures on length of stay. Estimates were based on a study finding a 0.3-1.2 day increased length of stay with the more rigorous definition of MRSA infection and not MRSA clinical cultures.⁶ These assumptions lead to the conclusion that the more effective strategy for MRSA clinical culture reduction is also more cost-effective. Universal decolonization was less expensive, saving \$189 per patient over ASC with Contact Precautions and \$172 over ASC with targeted decolonization. Given chlorhexidine and mupirocin is generally less expensive than gowns, gloves and admission MRSA screening, this has face validity.

Recently the investigators who performed the REDUCE MRSA trial published a decision analysis of their trial that included costs of each intervention and instead of examining the impact of MRSA clinical cultures, looked at the impact of overall bacteremia.⁷ This makes an interesting comparison to the decision analysis by Ziakas et al. focused on MRSA clinical cultures.² Huang et al. estimate a per patient savings of \$171 over ASC with Contact Precautions and \$100 over ASC with targeted decolonization. The assumptions of the models were similar, beyond the assumption by Huang et al that each bacteremia resulted in a 3.3 longer length of stay based on an administrative study for any infection, which may not be the case for bacteremias with skin commensals.⁸ Both studies found a small cost benefit from universal decolonization over ASC without considering clinical outcomes. Using possible overestimates of the clinical impact of MRSA clinical cultures or bacteremia studies report a larger savings.

Although these dollar estimates will likely be helpful to the ICU director or hospital epidemiologist making a business case for changing to universal decolonization, they are a small part of the decision whether to implement each intervention. This decision is primarily based on effectiveness of the intervention, concern for potential negatives of the intervention and least measured but possibly most important, the amount of staff effort required for the intervention. Clinical staff are burdened by a diversity of tasks and many competing safety initiatives in addition to patient care. Use of gowns and gloves impacts all aspects of clinical care resulting in fewer healthcare worker visits and possible unintended consequences.^{9,10} ASC testing for MRSA requires a process to obtain a sample, test in the lab, feedback results and appropriately identify patient as requiring an intervention. Universal decolonization, on the other hand, is relatively simple. Once a day bathing of patients is completed with chlorhexidine instead of soap and water. Mupirocin application to nares twice a day by a nurse requires more effort but has been considered by many to be unimportant to the effect observed in REDUCE MRSA.¹¹

Possibly as a result of the ease of intervention, when the REDUCE MRSA trial was published in 2013, chlorhexidine bathing was already commonly used in the U.S. A survey of the Society for Healthcare Epidemiology of America (SHEA) Research Network identified 72% of hospitals were using chlorhexidine bathing in at least one unit and 45% of hospitals expected an increase in use of chlorhexidine in 2014 (Unpublished data).

With widespread chlorhexidine use, concern exists for the emergence of chlorhexidine resistant bacteria. Although qac mutations provide some tolerance to chlorhexidine, no

meaningful clinical impact has been identified.¹²Mupirocin resistance, on the other hand, is clearly associated with increasing mupirocin use.¹³

In summary, this manuscript can help those already inclined by effectiveness data and ease of use to implement chlorhexidine bathing. It provides further support away from active surveillance culturing as being neither effective or cost-effective. Hopefully, by making a business case in the language of administrators, the article by Ziakas et al. will make it easier to provide the best care for patients.

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