

A Perspective on How the United States Fell behind Northern Europe in the Battle against Methicillin-Resistant *Staphylococcus aureus*

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The United States is falling behind Northern Europe in the control of multiple-drug-resistant organisms (MDROs) (1). According to the Center for Disease Dynamics, Economics & Policy, Northern Europe has less than 5% of its staphylococcal cultures positive for MRSA, whereas the United States has over 50%. Only Israel and Malta were the percentages found to be higher (1). At the heart of this issue may be the policy on active detection (surveillance) and isolation (ADI).

It has been just over 10 years since the 2003 SHEA (Society for Healthcare Epidemiology of America)-HICPAC (Healthcare Infection Control Practices Advisory Committee, Centers for Disease Control and Prevention [CDC]) report recommended surveillance as an integral part of efforts to control the looming methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* epidemic (2). Health care policy in the United States underwent an abrupt change, deviating from Northern Europe and no longer considering ADI essential for controlling the epidemic of MDROs.

In 2006, HICPAC stated that active surveillance can be considered in some settings where other measures are not working but that more research was needed to determine where it would be most beneficial. As part of its justification for this deviation, a review by Cooper et al. (3), a study in England that focused primarily on the methodological weakness in studies recommending isolation protocols, was referenced. This study did not specifically address the issue of active surveillance. However, Cooper et al. found little evidence that isolation measures fail to work and recommenced continuing current practices. In a 2004 editorial, Andreas Voss, from the Netherlands, supported the conclusions of Cooper et al. and stated that isolation measures can “substantially reduce the transmission of MRSA” (4).

In the United States, the concern regarding legislative mandates grew. In March 2007, a SHEA and APIC (Association for Professionals in Infection Control and Epidemiology) position paper referenced the legislative effort in Maryland and stated that the organizations did not support legislative mandates for active-surveillance cultures (5). Two of the report's coauthors, S. S. Huang and W. C. Huskins, will become lead authors of recent major antisurveillance reports published in the New England Journal of Medicine (NEJM).

Despite the growing antisurveillance and -isolation sentiment in the United States, on 6 February 2007, the Veterans Administration (VA) hospital in Pittsburgh, PA, reported reductions in MRSA infections in surgical units by 70% from using a bundle of hand hygiene, surveillance, and full contact precautions (i.e., isolation) (6). A week later, Undersecretary for Health Michael Kussman mandated the enactment of this protocol throughout the VA System.

The United States Congress became involved, and a hearing on

health care-associated infections was convened on 16 April 2008 (7). However, shortly before this hearing, two studies with seemingly opposite results were published, a JAMA Swiss study refuting surveillance (8) and a Northwestern MRSA study supporting surveillance (9).

The methodology of the JAMA Swiss study was apparently not analyzed in detail, since prior to surgery over half of the known MRSA carriers were not given antibiotics effective against MRSA and because of delays and emergency intervention, 31% of the carriers were identified as MRSA carriers only after surgery (8). An accompanying editorial by Diekema and Climo stated that despite legislative mandates that have been approved or introduced in Illinois, Maryland, New Jersey, and Pennsylvania, broad-based application of surveillance for MRSA carriers remains controversial (10).

Because of the conflicting nature of the JAMA Swiss and Northwestern MRSA studies, during a congressional hearing, Representative Henry Waxman concluded that no recommendations could be made regarding surveillance (7; email from E. F. Letter, 2 February 2012 [<http://www.healthwatchusa.org/publications/2012-Documents/20120202-Waxman-HAI-Hearing.pdf>]). In October 2008, SHEA-HIPAC echoed this sentiment, referencing these conflicting studies as the reason why recommendations cannot be made regarding the use of surveillance to prevent MRSA infections (11).

To settle this debate and bolster evidence supporting ADI, patient activists were anxiously awaiting the national results of the VA MRSA surveillance initiative, but over 3 years had passed. Health Watch USA then requested a congressional inquiry through one of U.S. Senator Mitch McConnell's field representatives, who nearly died from a postsurgical MRSA infection. The results of the inquiry confirmed the initial VA report issued 3 years earlier and found a 76% decline in MRSA infections in the intensive care unit (ICU) setting and a 28% decline in the non-ICU setting (12).

On 15 April 2011, the VA study was published in the NEJM (13) but similar to what happened prior to the congressional hearing, a competing study, STAR*ICU, authored by W. C. Huskins et al. (14), was published alongside the VA study. The authors of the

Published ahead of print 7 October 2013

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doi:10.1128/AAC.01839-13

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STAR*ICU study did not observe a significant effect of their MRSA surveillance and isolation protocol.

Analogous to the JAMA Swiss study, the STAR*ICU study appeared to have significant methodological problems. In the surveillance arm, cultures were performed but it took 5 days to receive the results. Furthermore, in the majority of patient days, patients in the intervention group did not receive effective intervention (14, 15). An accompanying NEJM editorial, (16) stated that these two studies “underscore the importance of carefully evaluating the effect of existing state mandates to perform surveillance testing.” A myriad of studies and reports (15), including one governmental blog (17), followed that used the STAR*ICU and JAMA Swiss studies as justification for not recommending expanded and uniform use of active surveillance testing.

However, studies have shown that MRSA carriers have a greater risk of infection and also increase the risk of infection in other patients (18, 19, 20). Nevertheless, many facilities adopted the use of surveillance, as evidenced by a 2012 report that found that 59% of surveyed hospitals screen for MRSA in ICUs (21). Recently, the CDC has also recommended surveillance as a key component of efforts to control carbapenem-resistant members of the family *Enterobacteriaceae* and HIV. The U.S. Preventive Services Task Force also recommended universal screening for hepatitis C for all adults born in the years 1945 through 1965, despite finding no direct evidence that this intervention will reduce morbidity or mortality (22). The rationale given was that many adults are unaware that they are carrying the hepatitis C virus and medicine has the ability to detect and treat this pathogen.

In an attempt to synthesize the results of MRSA surveillance, the Agency for Healthcare Research and Quality (AHRQ) undertook a comprehensive review of the literature (23). Only two articles, the JAMA Swiss and STAR*ICU articles, were cited as not observing a decrease in MRSA infection or acquisition associated with surveillance. The methodology in both studies was rated “good.” The methodological problems in these two studies were outlined in comments on the draft report by 19 consumer advocates (24), but the advice apparently went unheeded. It should also be noted that two of the eight peer reviewers of this report were W. Charles Huskins, the lead author of the STAR*ICU study, and Daniel Diekema, the lead author of the editorial published alongside the JAMA Swiss study.

In contradistinction, the AHRQ report found 41 other studies that observed a decrease in MRSA infection and acquisition associated with surveillance. Thirty-three of these studies had statistically significant findings; however, only 2 of the 41 studies were rated “good” and the rest were designated as “poor” or “studies not controlling for confounding and/or secular trends.”

The AHRQ report concluded that there was low strength of evidence regarding universal screening and “insufficient evidence” to make recommendations in other settings. It was also concluded that the study could not support or refute legislative mandates. One can argue that the strength of evidence in support of MRSA screening is just as strong as, if not stronger than, the evidence for hepatitis C virus screening.

As an alternative to screening, the REDUCE-MRSA trial was published in the NEJM by Susan Huang et al. (25). In the ICU setting, that study investigated the efficacy of universal and daily use of chlorhexidine and mupirocin for controlling infections. Compared to controls, MRSA bloodstream infections showed a

statistically nonsignificant decrease. The study did not evaluate ADI versus no intervention. According to www.clinicaltrials.gov, 6 months after the study completion date, the registry’s records for the study were updated by adding a measure for all-pathogen bloodstream infections and eliminating the measures for central-line-associated bloodstream infections and MRSA urinary cultures. The all-pathogen bloodstream infection (primarily skin commensal organisms) and nosocomial MRSA clinical culture measures showed a statistically significant improvement over the control. Huang et al. also stated that the results of the REDUCE-MRSA study had implications regarding legislative mandates and referenced the 2007 SHEA-APIC position paper on legislative mandates for control of MDROs (5, 25).

A critical caveat in the adoption of the REDUCE-MRSA protocols over ADI with or without targeted decolonization is that antimicrobial overuse is recognized as a major cause of the MDRO epidemic. Although what constitutes resistance to chlorhexidine has not been defined (26), reduced susceptibility has been observed in MRSA (26). It has also been postulated that chlorhexidine use may have produced a selective advantage to the extremely drug-resistant epidemic strain of *Klebsiella pneumoniae* (27). Resistance to mupirocin is also a concern, as evidenced by a paper Susan Huang coauthored, which reported that up to one-third of MRSA isolates in some nursing homes are resistant to mupirocin, a key component of the REDUCE-MRSA decolonization bundle (28).

Similar to the JAMA Swiss and STAR*ICU studies, an editorial accompanying the REDUCE-MRSA study report called for the repeal of patient safety legislation mandating surveillance (29). In contradistinction, on the basis of the strength of the literature, one could argue that legislative mandates should be expanded from ICU to facility-wide surveillance (9, 13). This position is further supported by a recent multicenter study coauthored by Stephan Harbarth (the JAMA Swiss study’s lead author) that found screening coupled with contact precautions and decolonization to be effective in preventing MRSA infections in surgical wards (30).

The CDC has estimated that there were over 80,000 MRSA infections in 2011, causing over 11,000 associated deaths (31). On the basis of the percentage of MRSA isolates found in *S. aureus* cultures, one can also argue that if the effectiveness of the United States’ confrontation of the MRSA epidemic were equal to that of Northern Europe, over 85% of the MRSA infections might have been prevented.

Given the evidence, it is unclear why the U.S. health care industry has not embraced ADI as an integral part of infection control. Some patient advocates believe that one of the reasons is to prevent the passage of legislative mandates. If this is the case, the best way to prevent legislative mandates is by having a quality health care system that adopts and implements standards of care based upon the best evidence available. In view of the severity of the MDRO epidemic in the United States, a reevaluation of the setting of standards of care for the expanded and uniform use of active MRSA surveillance testing should be undertaken.

ACKNOWLEDGMENT

We have no conflict of interest regarding this Commentary.

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