

## COMMENTARY

## Approaches for Preventing Healthcare-Associated Infections: Go Long or Go Wide?

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In this issue, the continuing “A Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals: 2014 Updates” series presents updated recommendations for preventing central line-associated bloodstream infections<sup>1</sup> and preventing transmission and infection due to methicillin-resistant *Staphylococcus aureus*.<sup>2</sup> During revision of these articles, several reviewers raised a critical question: What is the relative effectiveness (and cost-effectiveness) of vertical versus horizontal approaches to infection prevention? As multidrug-resistant organisms such as extended-spectrum  $\beta$ -lactamase-producing and carbapenem-resistant Enterobacteriaceae emerge and spread, it will become increasingly important to understand the relative benefits and costs of pathogen-specific screening and intervention strategies compared with reliable application of more “generic” methods to mitigate transmission and infection.

Over the last decade, the general approaches to healthcare-associated infection (HAI) prevention have taken two conceptually different paths: (1) vertical approaches that aim to reduce colonization, infection, and transmission of specific pathogens, largely through use of active surveillance testing (AST) to identify carriers, followed by implementation of measures aimed at preventing transmission from carriers to other patients, and (2) horizontal approaches that aim to reduce the risk of infections due to a broad array of pathogens through implementation of standardized practices that do not depend on patient-specific conditions. Examples of horizontal infection prevention strategies include minimizing the unnecessary use of invasive medical devices, enhancing hand hygiene, improving environmental cleaning, and promoting antimicrobial stewardship (Table 1).<sup>3</sup> Although vertical and horizontal approaches are not mutually exclusive and are often intermixed, some experts believe that the horizontal approach under usual endemic situations may offer the best overall value given the diversity of microorganisms that can

cause HAIs and the constrained resources available for infection prevention efforts. When informed by local knowledge of microbial epidemiology and ecology and supported by a strong quality improvement program, this strategy allows healthcare facilities to focus on approaches that target all rather than selected organisms in the absence of an organism-specific epidemic.

In addition to comparing the strength of evidence supporting each approach, it is also important to take into account financial costs and potential consequences associated with various infection prevention strategies, including the impact on hospital personnel effort and on aspects of patient care; for example, placing patients on isolation precautions may lead to fewer healthcare provider visits.<sup>4,6</sup> These comparisons are difficult to make because of conflicting study results, at least partly reflecting the heterogeneity of study designs and settings (ie, where the prevalence of the target pathogen ranges from rare to endemic to epidemic) and the paucity of high-quality cost-effectiveness analyses that are needed to estimate the economic impact of specific HAI prevention interventions.

### VERTICAL APPROACHES TO PREVENT HAIs

Vertical approaches utilize activities that are directed at a single pathogen or specific groups of pathogens and are often based on the results of AST. The rationale for AST is that multidrug-resistant organisms (MDROs) such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), multidrug-resistant (MDR) gram-negative organisms, and *Clostridium difficile* share several epidemiological features: colonization can precede infection, transmission can occur by direct patient contact or indirect contact with contaminated equipment or environmental surfaces, the number of asymptomatic “source” patients greatly exceeds

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TABLE 1. Preventing Healthcare-Associated Infections: Examples of Vertical and Horizontal Approaches

<p><b>Vertical approaches</b> reduce risk of infections due to specific pathogens:</p> <ul style="list-style-type: none"> <li>• Active surveillance testing to identify asymptomatic carriers</li> <li>• Contact precautions for patients colonized or infected with specific organisms</li> <li>• Decolonization of patients colonized or infected with specific organisms</li> </ul> <p><b>Horizontal approaches</b> reduce risk of a broad range of infections and are not pathogen specific:</p> <ul style="list-style-type: none"> <li>• Standard precautions (eg, hand hygiene)</li> <li>• Universal use of gloves or gloves and gowns</li> <li>• Universal decolonization (eg, chlorhexidine gluconate bathing)</li> <li>• Antimicrobial stewardship</li> <li>• Environmental cleaning and disinfection</li> </ul>
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SOURCE. Modified from Wenzel and Edmond.<sup>3</sup>

the number of infected patients, and asymptomatic carriers can serve as the reservoir for spread to other patients. AST is used to identify patients who are carriers of these target pathogens so that these patients can be isolated from non-carriers and, in some situations, can undergo decolonization in order to eradicate pathogen carriage.

This approach has been most intensely studied for prevention of MRSA transmission and infection. More than 100 observational studies have evaluated the use of MRSA AST to target MRSA carriers for contact precautions, with or without supplemental decolonization. The effectiveness of AST in preventing MRSA transmission and infection continues to be controversial, and studies on this topic have yielded varying conclusions. The Dutch national strategy for MRSA prevention and control is based on a very proactive and aggressive approach called “search and destroy,” aimed at identifying all hospitalized MRSA carriers.<sup>7</sup> This process requires AST of persons with epidemiologic links to MRSA carriers (eg, other patients hospitalized in geographic proximity, healthcare providers, family members) as well as isolation of MRSA carriers and cohorting of staff who care for MRSA carriers. However, critics point out that aggressive strategies such as these may only be cost effective in parts of the world with very low MRSA prevalence. Jain et al<sup>8</sup> described a nationwide intervention in Veterans Affairs acute care hospitals that included MRSA AST and contact precautions for MRSA carriers, improved compliance with hand hygiene, and an institutional culture change that was temporally associated with a large decline in infections caused by MRSA as well as other pathogens. In contrast, in a concurrently published study, Huskins et al<sup>9</sup> described a multicenter cluster-randomized, controlled trial in intensive care units (ICUs) that demonstrated that an intervention involving MRSA AST plus universal gloving until a patient’s colonization status was known to be negative did not impact rates of MRSA colonization or infection. A recent review of MRSA screening strategies concluded that the overall quality of evidence to support the use of AST to prevent healthcare-associated MRSA infections was low.<sup>10</sup>

The data assessing the utility of AST for preventing MDR gram-negative bacilli transmission and infection are even more controversial, and supporting evidence is largely based

on studies in which AST and a number of additional control measures are simultaneously implemented to control carbapenem-resistant Enterobacteriaceae (CRE) transmission in hospital and regional outbreak settings.<sup>11–16</sup> AST is recommended by the Centers for Disease Control and Prevention as a strategy to control CRE transmission.<sup>17</sup>

#### HORIZONTAL APPROACHES TO PREVENT HAIs

Hand hygiene is acknowledged as one of the most important horizontal strategies for preventing HAIs. Despite this, published rates of hand hygiene adherence average about 40%.<sup>18</sup> There are dramatic examples of the impact of hand hygiene improvements on the risk of infections associated with resistant organisms. Jarlier and colleagues demonstrated that a 35% decrease in MRSA infections in French ICUs correlated with an increase in hand hygiene.<sup>19</sup> In addition, some studies have suggested that universal gloving can also reduce transmission of MDROs by preventing contamination of the hands of healthcare personnel,<sup>20</sup> and universal gloving has been associated with significant reductions in all-cause bacteremia and central line-associated bloodstream infections in acute pediatric units during respiratory syncytial virus season.<sup>21</sup> The impact of universal gowning and gloving remains controversial. A recently published cluster-randomized trial involving 20 adult ICUs assigned to either routine use of contact precautions for patients with known pathogen carriage or use of gowns and gloves for all patient contacts concluded that universal gowning and gloving did not result in a significant difference in the primary study outcome of MRSA or VRE acquisition but was associated with a lower risk of MRSA acquisition alone.<sup>22</sup> The investigators found that use of gloves and gowns was associated with fewer healthcare personnel visits but improved hand hygiene compliance in both control and intervention ICUs, and no difference in the risk of adverse events was noted between control and intervention patients. Because of the associated expense and healthcare personnel time required for universal usage of gloves and gowns, this strategy is unlikely to be feasible outside of the ICU setting.

Decolonization of all patients in high-risk settings using topical chlorhexidine gluconate (CHG) is another horizontal strategy that has received increased attention. CHG bathing has been shown to decrease the bioburden of microorganisms on the patient, the environment, and the hands of healthcare personnel.<sup>23</sup> During 2013, four randomized cluster trials were published evaluating the effectiveness of CHG bathing in preventing HAIs among ICU patients. Climo et al<sup>24</sup> performed a cluster-crossover study and found that daily CHG bathing of adult ICU patients significantly reduced their risks for developing hospital-acquired bloodstream infections, including central line-associated bloodstream infection, and acquiring VRE. Using a similar study design, Milstone et al<sup>25</sup> reported that CHG bathing was associated with a significant reduction in bloodstream infections among pediatric ICU patients compared to standard bathing. Two additional studies included a comparison of horizontal and vertical approaches. Huang et al<sup>26</sup> compared three approaches to MRSA prevention among patients in 74 adult ICUs (the REDUCE MRSA study). Vertical approaches consisting of AST with and without targeted decolonization of MRSA carriers with CHG bathing and intranasal mupirocin were compared to a more horizontal approach involving universal decolonization of all ICU patients regardless of MRSA status. The investigators found that universal decolonization of all ICU patients was associated with the largest reduction in all-cause bloodstream infection (44%) and MRSA clinical culture rates (37%). Finally, Derde et al<sup>27</sup> demonstrated that improved hand hygiene plus universal CHG bathing reduced acquisition of MDROs including MRSA and showed that in a setting where high levels of adherence to hand hygiene and CHG bathing were sustained, the addition of AST (either rapid or conventional testing) and isolation of carriers did not further reduce MDRO acquisition rates. These four recent studies add to growing evidence that in endemic settings, vertical strategies that involve AST and isolation may not be as effective as more horizontal approaches utilizing hand hygiene and universal decolonization using CHG bathing with or without intranasal mupirocin. It should be noted that although these studies evaluate interventions applied to all patients in high-risk settings (ie, ICUs), the use of intranasal mupirocin specifically targets *Staphylococcus aureus*, one out of many potential pathogens.

Decolonization using CHG bathing to prevent CRE transmission and infection has been utilized along with other infection control strategies in outbreak settings.<sup>14,15,28</sup>

Selective digestive tract decontamination (SDD) is a horizontal strategy aimed at eradicating carriage of pathogens to prevent subsequent respiratory tract infections. SDD typically consists of topical application of antimicrobial agents (eg, polymyxin, tobramycin, and amphotericin) in the oropharynx and into the gastrointestinal tract through a nasogastric tube. Some SDD regimens also include an initial course of parenteral antimicrobials (eg, cefotaxime) in addition to topical agents. A systematic review included data from 36 ran-

domized controlled trials and concluded that SDD regimens consisting of combinations of topical and systemic antimicrobial agents reduce the risk for respiratory tract infection and overall mortality among adults receiving ICU care.<sup>29</sup> Despite supportive evidence, SDD has not been widely adopted as an infection prevention strategy in the United States mainly because of concerns regarding the potential risk for increasing antimicrobial resistance. Additional studies are needed to assess the impact of SDD on the epidemiology of antimicrobial resistance among gram-negative bacteria, particularly in a setting where the prevalence of MDR gram-negative bacilli is relatively high.

Misuse and overuse of antimicrobials facilitate the development of MDROs, making antimicrobial stewardship (AS) an important horizontal HAI prevention strategy that can complement other approaches. AS efforts ideally involve interdisciplinary collaboration aimed at providing prudent and appropriate antimicrobial use for patients across the continuum of care. AS has been shown to be critical in reducing rates of HAIs and the risks of other adverse events resulting from exposure to antimicrobial agents. Improving antimicrobial prescribing practices in conjunction with other infection prevention strategies has been effective in reducing *Clostridium difficile* infection (CDI) risk in outbreak and non-outbreak settings.<sup>30,31</sup> Additional research is needed to better quantify the impact of AS on MDRO risks.

Adequate cleaning of the healthcare environment is an important horizontal HAI prevention strategy. Evidence is increasing that contaminated surfaces play an important role in the transmission of several key pathogens including *Clostridium difficile*, VRE, MRSA, *Acinetobacter baumannii*, and norovirus. All of these organisms can persist from hours to days in the environment. Healthcare personnel can contaminate their hands not only through direct contact with a colonized or infected patient but also by touching contaminated hospital surfaces. Furthermore, recent studies have linked the risk of transmission to the colonization status of prior room occupants for MRSA and VRE,<sup>32,33</sup> CDI,<sup>34</sup> and multidrug-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.<sup>35</sup> Most important, improved environmental cleaning has led to reduced risk of VRE and *C. difficile* transmission.<sup>36</sup>

## CONCLUSION

Reliable implementation is critical for either vertical or horizontal strategies. As new data emerge, prevention measures known to be effective should be integrated into care, applied reliably, and sustained.<sup>37</sup> Quality improvement programs can play an important role in facilitating change and ensuring that implementation and intra-institutional spread respect local contexts. Unintended consequences should be anticipated and monitored.

It is important to recognize that there is no “one-size-fits-all” approach to improving practices. Local contextual factors matter, and specific components of the implementation plan

should be tested (Plan-Do-Study-Act [PDSA] cycles) and amended using standard quality improvement methods, such as those specified in the Model for Improvement.<sup>38</sup>

Our current ability to adequately compare the cost effectiveness of horizontal and vertical HAI prevention strategies or combinations of these strategies across healthcare settings is severely limited by the absence of robust data. Given the evolving epidemiology of MDROs and the complexity of managing the multiplicity of epidemiologically important pathogens across heterogeneous healthcare settings, however, we recommend (1) using robust quality improvement methods to ensure reliable performance of basic infection prevention practices known to mitigate transmission of MDROs and the infections they cause; (2) ensuring adherence to evidence-based universally applied HAI prevention strategies including hand hygiene, antimicrobial stewardship, and adequate environmental cleaning; (3) applying other evidence-based, horizontal strategies such as universal decolonization in settings where benefits are likely to outweigh risks and costs; and (4) using AST and other vertical approaches selectively when epidemiologically important pathogens are newly emerging and rare to a given institution or region or to control outbreaks of specific pathogens.

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