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Active Surveillance and Isolation of Asymptomatic Carriers of *Clostridium difficile* at Hospital Admission:

Containing What Lies Under the Waterline

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During the 2000s, the incidence of *Clostridium difficile* infection (CDI) increased dramatically, in large part due to the emergence of a hypervirulent strain, BI/NAP1/027, responsible for many hospital outbreaks in the United States. In 2011, *C difficile* accounted for 12% of all US health care–associated infections, surpassing *Staphylococcus aureus* as the most common cause of such infections.[1] Hospitalized patients with CDI are a recognized source of health care–associated (HA) transmission, and a primary control measure is to limit the spread of the organism from symptomatic patients. However, increasing molecular evidence, based on genomic sequence–based methods, indicates that asymptomatic patients colonized with *C difficile* also contribute to transmission.[2,3] A 2013 study[3] found that incident CDI cases in a hospital were as frequently linked to transmission from asymptomatic carriers as to symptomatic patients. Despite the potential for patients with asymptomatic colonization to serve as a reservoir for CDI, no data currently exist to determine whether interventions targeting asymptomatically colonized patients could be effective in reducing HA-CDI.

In this issue of *JAMA Internal Medicine*, Longtin et al[4] report findings from a quasi-experimental controlled study using time series analysis to determine the effect of active surveil-lance and isolation of asymptomatic carriers on the incidence of HA-CDI. The authors conducted rectal sampling of all patients admitted through the emergency department of a tertiary acute care hospital over an approximate 17-month period. *Clostridium difficile* testing was performed using a polymerase chain reaction (PCR) assay that targeted the *tcdB* gene and has been demonstrated to detect the subset of carriers with heavier organism loads who were more likely to contaminate the skin or environment.[5] All identified asymptomatic carriers were placed under isolation precautions until discharge. Among 7599 of 8218 patients screened, 4.8% were identified as asymptomatic carriers, which is similar to a previous study[6] that included additional Québec hospitals. However, other researchers have reported a higher prevalence of carriage on admission, ranging from 7% to 18%.[7] Longtin et al[4] did not provide the proportion of all patients admitted who were

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either transferred from other hospitals or directly admitted from long-term care facilities. Although these individuals are likely to be higher-risk patients, they were excluded from screening due to logistical restraints, and their exclusion could have contributed to the low prevalence of asymptomatic carriage. The limited sensitivity of direct screening using a commercial PCR (ie, insufficient for detecting carriers with lower organism burden) might be another reason for the lower prevalence.

Nonetheless, Longtin et al[4] found that the incidence of HA-CDI decreased by 7% per 4-week period during the intervention period, resulting in an overall decrease of 7.2 cases per 10 000 patient-days. The intervention was estimated to have prevented 63 of 101 expected cases. This meant that, for every single HA-CDI case prevented, 121 patients had to be screened, and 6 asymptomatic carriers had to be isolated. No concomitant decrease in the incidence of HA-CDI was detected among other hospitals in Québec City and throughout Québec province. It is conceivable that more cases would have been prevented if periodic screening was performed among patients after admission, identifying additional carriers who were missed during admission screening. In addition, a greater reduction of HA-CDI incidence might have been detected if it had not been for the previously mentioned limitations (ie, exclusion of direct admissions and transfers and use of a less sensitive screening method).

Several strengths of this study should be noted. Although the study design was not as rigorous as a cluster randomized approach, multiple statistical methods were used to measure the effect of the intervention, including segmented regression analysis and autoregressive integrated moving average modeling, and these analyses produced similar results, while accounting for seasonality and changes in diagnostic as-says. Multiple control hospitals were also included for inter-hospital comparison. Other important confounders that were assessed included hand hygiene compliance and antibiotic and proton pump inhibitor use. Hand hygiene compliance increased during the intervention phase, but almost all hand hygiene was performed with an alcohol-based hand sanitizer, which is not effective against *C difficile* spores.

The results of this study are promising for reducing HA-CDI. Additional information on patient-specific factors that could have affected the incidence of HA-CDI, such as whether asymptomatic carriers were less likely than noncarriers to receive antibiotics and therefore to develop CDI, would be helpful. Adherence to isolation precautions was also not assessed to ensure that the intervention was adequately implemented. In addition, isolation precautions were modified to allow asymptomatic carriers to share a room with noncarriers as long as the curtain separating the 2 beds was drawn. The effectiveness of this approach in preventing *C difficile* transmission is unknown, and no data were available regarding the proportion of noncarrier roommates who subsequently developed CDI. Furthermore, environmental cleaning was not as sessed to determine if there were improvements during the in tervention phase that could have affected HA-CDI rates.

The feasibility of implementing active surveillance for *C difficile* needs to be carefully considered. At present, there is no standardized method for detecting asymptomatic carriage of toxigenic *C difficile*. Limited data suggest that rectal culture might be as sensitive as stool

culture for detecting asymptomatic carriage among hospitalized patients. Perirectal sampling has been shown to be an accurate and efficient method for detecting toxigenic *C difficile* in symptomatic patients, but its effectiveness in asymptomatic carriers has not been widely studied. Moreover, none of the commercially available nucleic acid amplifications tests (eg, PCR) for diagnosing CDI have been approved by the US Food and Drug Administration for detection of asymptomatic carriers.

Practical challenges and disadvantages to implementing active surveillance and isolation precautions also exist. Screening all patients who are admitted can be labor and resource intensive, particularly given the cost of PCR assays, although Longtin et al[4] estimated that the intervention might have been cost-effective. Private rooms might not be readily available, and isolation of all detected carriers would contribute to the shortage of rooms. In addition, isolation has been shown to negatively affect patients' quality of life and can cause anxiety and depression, particularly in patients on long-term isolation.[8] Using a modified approach to isolation precau tions, as was done in the study by Longtin et al,[4] might mitigate some of the negative psychological effect, although the effectiveness of this strategy requires further evaluation. Other options to explore that could be potentially cost-effective and allow for a judicious use of resources include targeting active surveillance to patients at high risk for asymptomatic carriage, particularly those at high risk of spore shedding (eg, history of prior CDI with recent antibiotic use) or those admitted to high-risk wards (eg, intensive care units).

The severity of disease and complications associated with CDI can result in tremendous distress among patients and substantial increases in cost. Preventing transmission of *C difficile* is critical to limiting its serious effects, which might be more effectively achieved by targeting asymptomatic carriers in addition to symptomatic patients with CDI. Longtin et al[4] have shown the possible benefit of using active surveillance testing and isolation of asymptomatic carriers for preventing HA-CDI. Larger, well-designed studies, such as cluster randomized trials, are ultimately needed to confirm the effectiveness of this strategy. Similar investigations need to be conducted in long-term care settings, where there can be a larger reservoir of asymptomatic *C difficile* colonization. Further efforts are also needed to explore other strategies for reducing transmission of *C difficile* from asymptomatic carriers, including decolonization, enhanced disinfection of the skin and environment to reduce the burden of spores, and decreased use of antibiotics.

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