

Original Article

Clostridioides difficile dynamic electronic order panel, an effective automated intervention to reduce inappropriate inpatient ordering

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Abstract

Background: Ordering *Clostridioides difficile* diagnostics without appropriate clinical indications can result in inappropriate antibiotic prescribing and misdiagnosis of hospital onset *C. difficile* infection. Manual processes such as provider review of order appropriateness may detract from other infection control or antibiotic stewardship activities.

Methods: We developed an evidence-based clinical algorithm that defined appropriateness criteria for testing for *C. difficile* infection. We then implemented an electronic medical record–based order-entry tool that utilized discrete branches within the clinical algorithm including history of prior *C. difficile* test results, laxative or stool-softener administration, and documentation of unformed bowel movements. Testing guidance was then dynamically displayed with supporting patient data. We compared the rate of completed *C. difficile* tests after implementation of this intervention at 5 hospitals to a historic baseline in which a best-practice advisory was used.

Results: Using mixed-effects Poisson regression, we found that the intervention was associated with a reduction in the incidence rate of both *C. difficile* ordering (incidence rate ratio [IRR], 0.74; 95% confidence interval [CI], 0.63–0.88; $P = .001$) and *C. difficile*–positive tests (IRR, 0.83; 95% CI, 0.76–0.91; $P < .001$). On segmented regression analysis, we identified a sustained reduction in orders over time among academic hospitals and a new reduction in orders over time among community hospitals.

Conclusions: An evidence-based dynamic order panel, integrated within the electronic medical record, was associated with a reduction in both *C. difficile* ordering and positive tests in comparison to a best practice advisory, although the impact varied between academic and community facilities.

(Received 26 June 2022; accepted 29 September 2022; electronically published 16 March 2023)

Colonization with *Clostridioides difficile* commonly occurs in hospitalized patients. Available laboratory diagnostics alone cannot reliably differentiate between colonization and infection.^{1–3} Furthermore, inpatients commonly experience diarrhea that may be misdiagnosed as *C. difficile* infection, particularly with highly sensitive *C. difficile* laboratory assays. Such misdiagnosis may result in unnecessary and potentially harmful exposure to antibiotics in addition to increased reporting of hospital-onset *C. difficile* events using National Healthcare Safety Network (NHSN) criteria.^{4,5}

To aid clinicians in the appropriate ordering of *C. difficile* tests and to reduce unnecessary testing and potential misdiagnosis of

hospital-onset *C. difficile* events, several diagnostic stewardship interventions have been studied, including education, provider feedback, physician review, and electronic order-entry clinical decision support (CDS).^{6–15} Utilization of the electronic medical record (EMR) to guide *C. difficile* testing stewardship most commonly includes best-practice advisories (BPAs) or provider question prompts. Providers may ignore or provide inaccurate responses to these prompts.¹³ Although such interventions initially may be successful, sustainability may be limited.¹⁶ Furthermore, interventions that require continued provider support (eg, real-time order review or approval) may detract from other antimicrobial stewardship and infection control interventions. Thus, we studied the impact of an electronic order-entry aid that uses automated EMR data to provide contextualized, dynamic, clinical decision support to ordering physicians. This tool was paired with an evidence-based clinical algorithm that defined appropriateness criteria for testing for *C. difficile* infection. This “dynamic order

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Cite this article: Ziegler MJ, Flores EJ, Epps M, et al. *Clostridioides difficile* dynamic electronic order panel, an effective automated intervention to reduce inappropriate inpatient ordering. *Infect Control Hosp Epidemiol* 2023. 44: 1294–1299, doi: [10.1017/ice.2022.254](https://doi.org/10.1017/ice.2022.254)

Table 1. Characteristics of Study Hospitals

Hospital	Location	Bed Size	Teaching Hospital	Baseline Practice	DOP Implementation
Hospital of the University of Pennsylvania	Philadelphia, PA	807	Yes	Laxative BPA, ordering guideline ^a , nursing-led stewardship ^b	Pilot (3 units) 12/2019 All units 2/2020
Penn Presbyterian Medical Center	Philadelphia, PA	375	Yes	Laxative BPA, ordering guideline ^a	2/2020
Pennsylvania Hospital	Philadelphia, PA	475	Yes	Laxative BPA, ordering guideline ^a	2/2020
Chester County Hospital	West Chester, PA	252	No	Laxative BPA, ordering guideline ^a	Pilot (1 unit) 2/2020 All units 8/2020
Medical Center of Princeton	Princeton, NJ	429	No	Laxative BPA, ordering guideline ^a	Pilot (1 unit) 2/2020 All units 8/2020

Note. DOP, dynamic order panel; BPA, best-practice advisory.

^aGuideline for appropriate ordering of *C. difficile* tests posted on electronic repository.

^bBedside nurses and nurse managers reviewed *C. difficile* orders on their units and engaged providers if orders did not meet appropriateness criteria.

panel” (DOP) was developed to utilize clinical decision support to automatically adjust the display based on clinical criteria to drive appropriate order placement. To our knowledge, this approach to aligning ordering with evidence-based criteria is the first of its kind. In this study, we evaluated the impact this *C. difficile* DOP on *C. difficile* orders within the University of Pennsylvania Healthcare System (UPHS).

Methods

Study design

Using a quasi-experimental cohort design, we compared the impact of the DOP to a preintervention historical control period (January 2018 through DOP implementation). During the preintervention period, inpatient entities across the health system utilized a BPA within the EMR software (Epic Systems, Verona, WI) to prevent inappropriate *C. difficile* testing. The preintervention BPA interrupted providers ordering *C. difficile* testing when the patient had received a laxative or stool softener in the prior 24 hours. This “laxative BPA” also suggested discontinuing existing laxative orders and recommended that *C. difficile* testing orders not be placed. The intervention period included all months after the DOP was implemented through October 2021. Other interventions targeted at reducing inappropriate *C. difficile* testing are described in Table 1.

Study sites

The intervention was implemented across our 5-hospital health system. Hospitals in ranged in size from community-based to large academic hospitals. The characteristics of each hospital are displayed in Table 1.

Evidence-based clinical pathway development

To promote the uptake of evidence into clinical practice in our large health system, we rely on clinical pathways to operationalize evidence-based practices across multiple specialties and as a blueprint for subsequent EMR-based interventions. In this project, we used our existing 10-step framework for developing evidence-based clinical pathways.^{17,18} The clinical pathway was informed by the Infectious Disease Society of America 2017 clinical practice guidelines for *C. difficile* infection and the 2016 Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) report on *C. difficile* infection (Supplementary Fig. 1 online).^{3,19} A multidisciplinary stakeholder panel participated in the development

of the clinical pathway, including experts from infectious diseases, infection control, antimicrobial stewardship, pharmacy, hospital medicine, nursing, and clinical informatics.

Dynamic EMR CDS intervention

In December 2019, the DOP was implemented in a staged fashion among UPHS hospitals (Table 1). The dynamic EMR CDS consisted of 4 subpanels to guide appropriate testing, of which only 1 panel was presented to providers at a time (Supplementary Figs. 2–5 online). Three panels focused on appropriateness of clinical testing given the following clinical scenarios: (panel 1) retesting in the case of a positive *C. difficile* test in the prior 30 days or a negative result in the prior 7 days; (panel 2) testing when a laxative or stool softener was administered within the prior 48 hours; and (panel 3) testing when <3 unformed bowel movements documented in the prior 24 hours. EMR rules were developed for each panel, based on the clinical pathway. Panel rules were evaluated in a sequential fashion using patient data from the EMR. For instance, when a provider opened the DOP to place an order for a *C. difficile* test, panel 1 EMR rules were evaluated first. If appropriateness rules were met, then panel 2 rules were next evaluated, and so on. Panel 4, the last panel, displayed to the provider if all rules for panels 1–3 were met. If EMR-based appropriateness rules were not met for a particular panel, then the panel presented a message to the provider indicating that *C. difficile* testing was not indicated. However, providers could override guidance presented in the panel and place an order. The CDS intervention was implemented across all inpatient settings (ie, outpatient and emergency room orders were excluded). *C. difficile* stool-testing specimens not collected within 24 hours of order placement were automatically cancelled during both study periods.

Study outcomes

The primary study outcome was the number of completed *C. difficile* orders (ie, specimens that were collected and processed). The number of orders placed in each period was summarized as a rate of orders per 1,000 patient days to account for variation in patient census. Our secondary outcomes included the rate of positive tests, including both molecular and immunoassay-based *C. difficile* results. *C. difficile* testing was performed by the clinical microbiology laboratory. Stool specimens were first assessed with a PCR assay (Xpert *C. difficile*, Cepheid, Sunnyvale, CA). Stool specimens that were PCR-positive were then assessed using an

immunoassay test (C.dif Quick Chek Complete, Alere, Waltham, MA). Additionally, we investigated the impact of the CDS intervention on the number of days between admission and specimen collection date. This assessment was performed as a safety endpoint because delaying testing can result in delayed treatment and inappropriate attribution of community-onset *C. difficile* infection as hospital-onset *C. difficile* infection. This assessment was limited to the first 30 days of hospitalization to decrease the impact of outliers associated with prolonged lengths of stay.

Statistical analysis

To model the impact of the study intervention, accounting for the variation in baseline ordering rates by hospital and unit, mixed-effects Poisson regression was performed to determine the incidence rate ratio (IRR) associated with the study intervention. This model was created with an offset for the number of patient days attributed to each study unit and month, with a random effect of hospital and unit. We performed a secondary analysis limited to our 3 academic hospitals, where inpatient units are organized by service lines. Service lines included units that cared for primarily medicine, surgery, oncology, cardiovascular, or women's health patient populations. This analysis did not include hospitals where patient units were not clearly organized by service line (PMPH and CCH). Additionally, we assessed the impact of the intervention on orders placed by various provider types, categorized as resident or fellow, attending physician, and advanced practice provider (including nurse practitioners and physician assistants).

We performed a segmented regression analysis to assess the trends in *C. difficile* testing before and after the study intervention. To display an aggregate trend in testing across institutions, accounting for the variable timing of implementation of the dynamic order panel, study time was adjusted relative to starting the intervention (ie, months after intervention rather than calendar month).

Results

Impact of the dynamic order panel on *C. difficile* testing

During the preintervention period, an average of 7.73 *C. difficile* test orders were completed per 1,000 patient days compared to 6.49 per 1,000 patient days during the intervention period (Table 2). Ordering rates varied by institution (Fig. 1). Using mixed-effects Poisson regression with a random intercept for hospital and unit, the CDS intervention was associated with a reduction in the incidence of *C. difficile* testing (IRR, 0.82; 95% confidence interval [CI], 0.77–0.86; $P < .001$). After adjusting for time (month within each study period and month from beginning of study), the association remained (IRR, 0.74; 95% CI, 0.63–0.88; $P = .001$) (Table 3). The impact of the intervention varied by hospital type, with a greater reduction in *C. difficile* testing for both community hospitals (CCH and MCP) compared to the 3 academic hospitals (Supplementary Table 1 online). In the subanalysis of hospitals where patients are geographically grouped by service line, there was no significant difference for any service line (Supplementary Table 2 online). When stratifying *C. difficile* testing by specific provider types, we identified a significant reduction among both physicians (IRR, 0.55; 95% CI, 0.46–0.65; $P < .001$) and physicians in training (ie, resident and fellows) (IRR, 0.89; 95% CI, 0.81–0.97; $P = .007$) but not among advanced practice providers (IRR, 0.95; 95% CI, 0.88–1.02; $P = .13$). The intervention was also associated with a reduction in the incidence rate of

Table 2. *Clostridioides difficile* Tests Compared Between Baseline and Intervention Period

Order	Baseline Period	Intervention Period	P Value
Completed orders ^a	8.72 (8.10–9.32)	7.35 (7.01–7.79)	<.001
Attending physician	2.43 (2.14–2.76)	1.44 (0.90–1.59)	<.001
Housestaff	3.28 (2.80–3.59)	2.70 (2.65–3.06)	<.001
APP	3.15 (2.82–3.36)	3.17 (3.01–3.26)	.76
Positive orders ^a	1.15 (1.09–1.35)	0.99 (0.90–1.14)	.001
Immunoassay	0.30 (0.21–0.35)	0.28 (0.20–0.33)	.43
Molecular	0.82 (0.71–0.95)	0.76 (0.61–0.90)	.15

Note. APP, advanced practice provider.

^aPer 1,000 patient days.

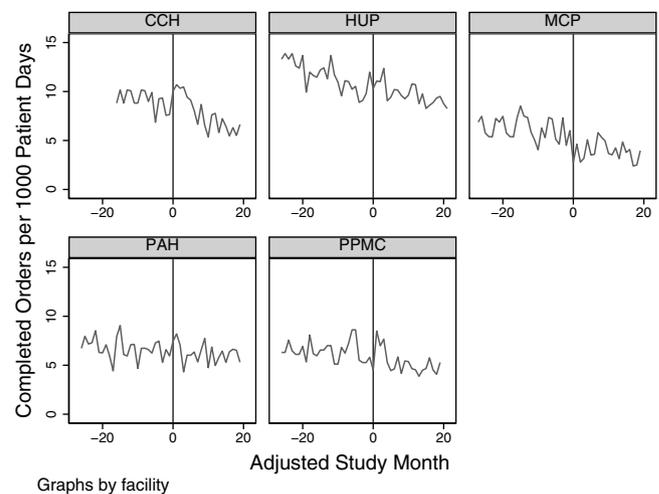


Fig. 1. *Clostridioides difficile* completed orders per 1,000 patient days. Note. Month 0 indicates the beginning of the study intervention.

C. difficile-positive tests from an average of 1.33 per 1,000 patient days in the preintervention period to 1.12 per 1,000 patient days in the intervention group (IRR, 0.83; 95% CI, 0.76–0.91; $P < .001$). When limited to specific test modality, the reduction was observed only among PCR positive tests (IRR, 0.85; 95% CI, 0.75–0.97; $P = .012$) and not immunoassay-positive tests (IRR, 0.92; 95% CI, 0.78–1.11; $P = .41$).

Using interrupted time-series analysis, assessing all hospitals in aggregate, we detected a decreasing trend in *C. difficile* order completion in the preintervention period (–0.087 orders per 1,000 patient days per month; 95% CI, –0.103 to –0.071; $P < .001$). Although we detected a continued trend of decreased testing in the postintervention period, this slope was increased compared to the preintervention period (–0.036 orders per 1,000 patient days per month; 95% CI, 0.073 reduction to 0.001 increase; $P = .058$) (Fig. 2). Among academic hospitals, we observed negative baseline slope (–0.090 orders per 1,000 patient days per month; 95% CI, –0.120 to –0.060; $P < .001$) and postintervention slope (–0.074 orders per 1,000 patient days per month; 95% CI, –0.121 to –0.026; $P = .003$), but the difference between slopes was not statistically significant ($P = .54$). Among community hospitals, we observed positive baseline slope that was not statistically significant (0.020 orders per 1,000 patient days per month; 95% CI, –0.017 to 0.057; $P = .29$), a negative postintervention slope (–0.085 orders

Table 3. Mixed-Effects Poisson Regression of Completed *Clostridioides difficile* Orders

Variable	Bivariable IRR (95% CI)	P Value	Multivariable IRR (95% CI)	P Value
Intervention	0.82 (0.77–0.86)	<.001	0.74 (0.63–0.88)	.001
Time from beginning of study, mo	0.99 (0.99–0.99)	<.001	1.00 (0.99–1.01)	.36
Time within study period, mo ^a	0.99 (0.99–0.99)	<.001	0.99 (0.98–0.99)	<.001

NOTE. IRR, incidence rate ratio; CI, confidence interval. Hospital and unit included as a random effect. All other covariates included as fixed effects.
^aNumber of months from beginning of either the baseline period or the intervention period.

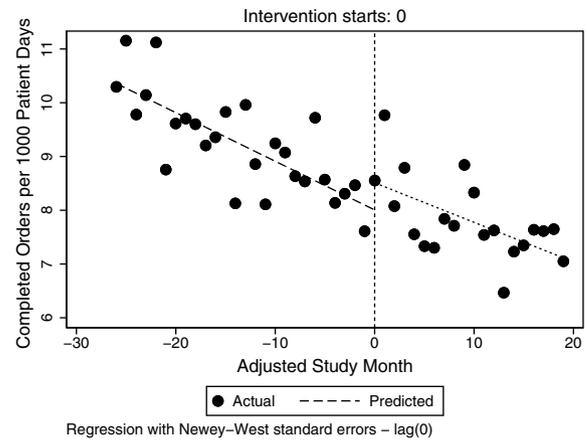


Fig. 3. Interrupted time-series analysis, academic hospitals.

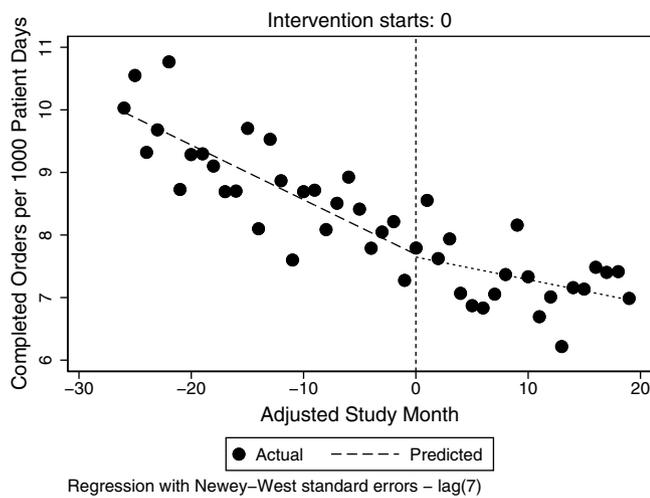


Fig. 2. Interrupted time-series analysis, all hospitals.

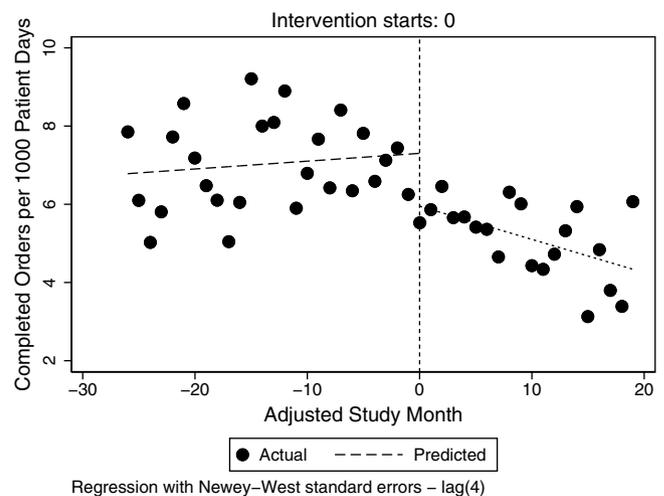


Fig. 4. Interrupted time-series analysis, community hospitals.

per 1,000 patient days per month; 95% CI, -0.125 to -0.045 ; $P < .001$), and a statistically significant difference in slopes ($P < .001$) with an immediate postintervention drop (ie, difference in intercepts) of 1.35 orders per 1,000 patient days (95% CI, -1.93 to -0.77 ; $P < .001$) (Figs. 3–4).

Impact of the intervention on time to order collection

The median times from admission to *C. difficile* test collection in the first 30 days of admission were similar in the baseline and intervention period: median, 4 days (interquartile range [IQR], 1–9) versus 4 days (IQR, 1–10; $P = .002$). Although the intervention was associated with decreased odds of testing on or before hospital day 3 (odds ratio [OR], 0.90; 95% CI, 0.84–0.97; $P = .003$), the rate of testing during the first 7 days of hospitalization was decreased overall (5.02 vs 3.82 per 1,000 patient days; $P < .001$) as did testing during the first 30 days (7.17 vs 5.68; $P < .001$).

Discussion

Implementation of a contextualized, dynamic EMR CDS intervention developed from an evidence-based clinical pathway significantly reduced *C. difficile* testing among hospitalized patients in our healthcare system. The reduction in *C. difficile* testing was greatest in community hospitals compared to academic hospitals.

This observation may have been due to *C. difficile*-targeted coin-terventions across the hospitals in 2017–2018 before the CDS tool was introduced. These historic interventions included an evidence-based *C. difficile* testing pathway embedded in the order panel and in-person “handshake” stool testing stewardship between nursing and ordering providers targeted at reducing inappropriate *C. difficile* testing. These testing interventions were likely accountable for the negative slope in *C. difficile* testing in the preintervention period; the largest proportion (42%) of testing occurred at our largest academic center (ie, HUP) where testing stewardship efforts were concentrated. These cointerventions likely reduced the observed impact of the CDS intervention at academic sites but were effort intensive and difficult to sustain, in contrast to our fully integrated EMR CDS tool. Additionally, we observed a larger reduction in completed orders among attending physicians compared to house staff and advanced practice providers. It is possible that the impact of the intervention is diminished when decision making occurs prior to interaction with the order set as may occur on academic rounds (eg, the attending physician or team decides to send *C. difficile* testing on rounds, but the house staff or APP team member places the order later in the day). Further research is needed to understand this difference. A limitation of this analysis is the potential that the distribution of provider types changed over time.

In addition to reduced testing, we observed a reduction in *C. difficile*-positive tests. This reduction may represent a lower rate of detection of asymptomatic colonization (ie, patients who did not meet testing criteria were unlikely to have *C. difficile* infection). This finding highlights the potential benefit of this intervention not only to decrease laboratory burden but also to reduce misdiagnosis of asymptomatic colonization as hospital-onset *C. difficile* infection. Due to concern that the intervention may delay appropriate testing of *C. difficile*, we investigated the time from admission to testing, finding a similar difference, when limited to tests performed within the first 30 days of admission. Thus, we did not observe a clinically significant shift or delay of orders within the month of hospitalization to suggest that the order panel delayed appropriate diagnostic testing.

In comparison to prior literature, Christensen *et al*⁷ reported that an intervention requiring provider attestation of clinical criteria, antibiotic stewardship preauthorization (ie, approval prior to ordering *C. difficile* tests), and verbal clinician feedback was associated with ~20% reduction in monthly positive *C. difficile* results. We found a similar and sustained reduction in the incidence of positive *C. difficile* results utilizing a fully automated approach. Mizusawa *et al*⁹ studied the impact of a multilevel BPA, which required approval from the microbiology laboratory to override *C. difficile* ordering. They achieved a large reduction in *C. difficile* testing of ~25% in their academic center and reductions of 31% and 38% at community partner hospitals.⁹ This observation mirrors the greater reduction we observed among community hospitals. However, our intervention differed in several ways. First, our baseline comparison period utilized a “soft stop” rather than a “hard stop” BPA (ie, the BPA could be bypassed) and was fully integrated in the EMR without requiring additional oversight or approval process. Mizusawa *et al*¹³ identified that providers commonly bypassed a soft-stop BPA, with only 15.4% of providers heeding advice to not order *C. difficile* testing. Among SHEA member hospitals, this mode of BPA was the most commonly reported EHR tool to reduce unnecessary *C. difficile* ordering.¹³ Finally, our intervention utilized electronic documentation of unformed bowel movements to further reduce inappropriate testing. Accurate documentation of stool output was emphasized because prior studies have shown that providers commonly order tests in the absence of clinically significant diarrhea.¹⁴

To compare the effectiveness of soft-stop to hard-stop BPAs, Rock *et al*²⁰ conducted a multicentered study comparing the impact of clinical decision support interventions. In this study, hard-stop interventions were the most effective at reducing *C. difficile* orders among centers with no alert at baseline, with a 33% reduction in the relative incidence rate compared to 23%. When they investigated the impact of hard-stop BPAs at centers where soft-stop BPAs had been utilized previously, they found a 22% reduction in the relative incidence rate of *C. difficile* ordering.²⁰ In our study, we detected a similar reduction of 26% by improving upon an existing “soft stop” BPA without requiring a “hard stop” approval process.

Our study had several limitations. First, we focused on a system-level analysis and did not account for patient or provider-level modifiers that may have influenced *C. difficile* test ordering over time. Second, we compared the impact of our intervention against existing tools, notably a soft-stop BPA, which may have reduced the relative impact of our intervention. Finally, our intervention period began shortly before the coronavirus disease 2019 (COVID-19) pandemic, which had multiple consequences for both HAI surveillance and interventions focused on prevention.²¹ However, because

the intervention was fully automated, the quality of the intervention was not affected.

In conclusion, utilization of a fully integrated, dynamic, contextualized EMR CDS tool was associated with significant and sustained reductions in both *C. difficile* testing and positive *C. difficile* results, although the impact varied between academic and community facilities.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2022.254>

Acknowledgments.

Financial support. M.J.Z. is supported by the National Institute for Allergy and Infectious Diseases (grant no. K23 AI143925) and CDC Epicenters for the Prevention of Healthcare Associated Infections (cooperative agreement FOA no. CK16-004). The funding agency had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

Conflicts of interest. All authors report no conflicts of interest relevant to this study.

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