MAYO CLINIC

Reduction in Health Care Facility—Onset *Clostridioides difficile* Infection: A Quality Improvement Initiative

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Abstract

Objective: To reduce health care facility—onset (HCFO) *Clostridioides difficile* infection (CDI) incidence by improving diagnostic stewardship and reducing the inappropriate testing of *C difficile* assays.

Patients and Methods: A multidisciplinary team conducted a quality improvement initiative from January 1, 2020, through March 31, 2021. *Clostridioides difficile* infection and inappropriate testing were identified via electronic health records using predefined criteria related to stool quantity/caliber, confounding medications, and laboratory data. An intervention bundle was designed including (1) provider education, (2) implementation of an appropriate testing algorithm, (3) expert review of *C difficile* orders, and (4) batch testing of assays to facilitate review and cancellation if inappropriate.

Results: Compared with a baseline period from January to September 2020, implementation of our intervention bundle from December 2020 to March 2021 resulted in an 83.6% reduction in inappropriate orders tested and a 41.7% reduction in HCFO CDI incidence.

Conclusion: A novel prevention bundle improved *C difficile* diagnostic stewardship and HCFO CDI incidence by reducing testing of inappropriate orders. Such initiatives targeting HCFO CDI may positively affect patient safety and hospital reimbursement.

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*C*lostridioides difficile infection (CDI) is estimated to annually cause approximately 500,000 cases per year, with 15,000 to 20,000 attributable deaths in the Unites States alone.[1] The Centers for Disease Control and Prevention (CDC) defines CDI as a positive *C difficile* toxin assay or a positive *C difficile* molecular assay (eg, polymerase chain reaction [PCR]) of a stool specimen from a patient of the surveillance catchment area who is 1 year of age or older.[2,3] Cases are further stratified into 2 major epidemiological categories: community-onset CDI, indicating a positive stool specimen collected in an outpatient setting or within 3 calendar days from a patient with no documented overnight stay in a health care facility during the 12 weeks previously; and health care facility—onset (HCFO) CDI, indicating a positive stool specimen collected more than 3 calendar days after admission to a health care facility.

Health care facility—onset CDI is one of several quality metrics chartered by the Centers for Medicare & Medicaid Services (CMS) and the Department of Health and Human Services to improve patient safety by reducing health care—associated infections (HAIs). Hospital performance is graded on rates of infection, readmission, and other metrics that

directly affect hospital reimbursement. The total annual CDI-attributable cost is estimated to exceed $6 billion dollars annually in the United States.[4]

The asymptomatic colonization rate in patients living in long-term care facilities is estimated to be 50%, and the previous literature has cited inappropriate *C difficile* testing to be as high as 40% on the basis of the Infectious Diseases Society of America (IDSA) and Society for Healthcare and Epidemiology guidelines for appropriate *C difficile* testing.[5-7] The availability of highly sensitive and specific molecular testing of *C difficile* has led to an increase of asymptomatic colonized patients incidentally meeting criteria for HCFO CDI. Given the patient morbidity and cost of unnecessary antimicrobial therapy, as well as the stringency of CMS-enforced quality metrics and their downstream effects on reimbursement, promotion and maintenance of diagnostic stewardship of CDI testing are essential.

The aim of our quality improvement (QI) initiative was to reduce the inappropriate testing for CDI in asymptomatic patients who may be colonized with *C difficile*. We hypothesized that a combination of diagnostic stewardship education, implementation of a *C difficile* assay appropriate testing algorithm (ATA), incorporation of infection prevention and control (IPAC) case review for diagnostic testing appropriateness, and laboratory batch testing to facilitate IPAC review of *C difficile* testing orders could reduce HCFO CDI incidence in asymptomatic patients who may be colonized with *C difficile*.

PATIENTS AND METHODS

Study Design

A multidisciplinary team conducted a QI initiative at Mayo Clinic in Florida from January 1, 2020, through March 31, 2021. Our project charter was to reduce the inappropriate testing of *C difficile* assays ordered 3 calendar days or more after hospital admission by 25% without increasing the hospital length of stay. Our target population was all patients admitted to Mayo Clinic in Florida. The Six-Sigma Define, Measure, Analyze, Improve, and Control framework guided by the Mayo Clinic Quality Academy curriculum was used.

This study was determined to be within the scope of routine HAI surveillance and therefore exempt from Mayo Clinic Institutional Review Board approval. The Mayo Clinic IPAC team identified cases of CDI diagnosed during a patient's index admission using Mayo Clinic's electronic health record (Epic). At our hospital, we used a 2-step algorithm for the detection of CDI as recommended by the IDSA guidelines.[7] The initial step uses the C. DIFF QUIK CHEK COMPLETE assay (TECHLAB), which tests for glutamate dehydrogenase and *C difficile* toxins A/B. This assay is highly accurate, with a reported sensitivity of 100% and a specificity of 99.6%.[8] If the glutamate dehydrogenase antigen is positive but the toxin test is negative, this is considered an "indeterminate" result and a laboratory-developed PCR based on the detection of the *tcdC* (for expansion of the gene symbol, use search tool at www.genenames.org) regulatory gene of toxin A/B is reflexively performed. The high specificity of the primers and detection probes used in the PCR assay allow the qualitative determination of toxigenic *C difficile* on the basis of crossing threshold and melting point analysis.[9]

Defining Variables

Our project charter defined inappropriate *C difficile* testing as stool consistency of less than 6 per Bristol Stool Scale,[10] less than 3 bowel movements per 24-hour time period, new-onset diarrhea in a patient receiving enteral tube feeds, laxatives, or stool softeners within the past 24 hours, repeat testing within 7 days before a negative assay, and/or testing in afebrile patients without leukocytosis (white blood cell count $\geq$ 10,500 cells/mm^3), leukopenia (white blood cell count < 4000 cells/mm^3), or systemic signs of infection (Table 1). Appropriateness of testing was based on the IDSA and Society for Healthcare Epidemiology of America guidelines for appropriate *C difficile* testing.[7] *Health care facility−onset CDI* was defined as a positive stool specimen collected more than 3 calendar days after hospital admission per CDC surveillance definition.[2,3]

Measure

Our QI initiative measured the incidence of *C difficile* orders that met testing criteria and

TABLE 1. Inappropriate Testing Criteria for *Clostridioides difficile*

Stool consistency of <6 per Bristol Stool Scale
Less than 3 bowel movements in a 24-h time period
New-onset diarrhea in a patient receiving enteral tube feeds, laxatives, or stool softeners
Repeat testing within 7 d before a negative *C difficile* assay
Testing in patients without objective signs of infection. Objective findings include fever (>38.1°C), leukocytosis (white blood cell count ≥ 10,500 cells/mm^3), and leukopenia (white blood cell count < 4000 cells/mm^3)

were processed (criteria met and tested), *C difficile* orders discontinued because of not meeting testing criteria (criteria not met and stopped), *C difficile* orders that did not meet testing criteria and were still processed (criteria not met and tested), and HCFO CDI identified by appropriate and inappropriate testing. An assessment of provider knowledge regarding CDI and diagnostic stewardship pre- and postintervention was also done.

Measurements were separated into 2 phases: a preintervention "measure phase" to obtain numerical baseline of quality gap and an "intervention phase" after the implementation of the intervention bundle. Our balancing measure was hospital length of stay. Our goal was to reduce inappropriate *C difficile* assay ordering and processing without increasing the hospital length of stay.

Intervention Bundle

Four interventions were bundled to address the quality gap and reduce HCFO CDI incidence:

1. *C difficile*—related provider education and diagnostic stewardship: A pre- and postintervention survey evaluating provider role (resident physician, advanced practice provider, and other), department, and self-reported number of *C difficile* tests ordered per month was distributed electronically. Questions assessed knowledge of *C difficile* testing, diagnostic standards, appropriateness of testing criteria, and applicable steps

in triaging suspected infections. Differing pre- and posttest questions to assess provider knowledge regarding CDI and diagnostic stewardship were standardized in all participants. This measure evaluated the effectiveness of provider educational interventions and their overall effect on the reduction of inappropriate *C difficile* assay ordering.

2. A *C difficile* ATA was modified from the previous testing algorithm created by Khanna et al[11] available on "Ask Mayo Expert," a clinical knowledge resource available to Mayo Clinic providers. Our modified algorithm was simplified, incorporated a color-coded workflow, and included a visual representation of the Bristol Stool Scale (Figure 1). This algorithm was distributed to providers in the form of laminated badge-sized cards, and posters were placed in workrooms and on hospital unit floors.

3. A multidisciplinary *C difficile* workgroup under the IPAC subcommittee composed of physicians and allied health professionals identified infection risk and intervened as necessary to mitigate infection transmission among visitors, patients, and hospital staff. When a *C difficile* order is placed, the nursing staff protocol is to confirm the presence of 3 or more stools within 24 hours that meet a consistency of 6 or 7 per Bristol Stool Scale. Floor providers then review current patient medication administrations for concurrent laxative or tube feedings, which contraindicate testing because of the confounding effect on clinical presentation (diarrhea). Once an order has been placed, IPAC reviews the case patient, and if deemed appropriate, the CDI assay is approved to be processed as outlined above in the Patients and Methods section. If inappropriate, discussion with the primary team ensued and test would be canceled if still deemed inappropriate. Infection prevention and control review of *C difficile* orders spanned both the measure phase and the intervention phase.

4. Weekday batch testing was implemented to reduce the number of inappropriate tests that were processed. Batch testing refers to processing of specimens in groups.

This intervention allowed IPAC to review *C difficile* orders before processing and ensure that evidence-based best practice testing criteria were met. Failure to meet appropriate testing criteria prompted discussion with the primary health care team to understand clinical context and advisement to reconsider ordering when inappropriate.

Statistical analyses

Descriptive statistics for continuous variables were reported as means and percentages. The Fisher exact test was used for categorical variables. Microsoft Office Excel was used to graph data points and statistical analysis (Microsoft Corporation) and REDCap (Research Electronic Data Capture) for provider educational assessment.[12,13] The standardized infection ratio (SIR) is a summary measure calculated by CDC's National Healthcare Safety Network to benchmark HAIs nationwide. The SIR compares the actual number of HAIs reported with a population risk-adjusted predicted number.[14]

RESULTS

Measure Phase

Our preintervention measure phase occurred from January 1, 2020, through September 30, 2020. A total of 224 *C difficile* assays were ordered more than 3 calendar days after hospital admission. One hundred three *C difficile* assays met testing criteria and were processed (criteria met and tested). Fifty *C difficile* assay orders were discontinued because of not meeting testing criteria (criteria not met and stopped). Sixty-one *C difficile* assays did not meet testing criteria and were still processed for an average of 6.78 inappropriate *C difficile* assays tested per month (criteria not met and tested) (Figure 2). Seven inappropriate *C difficile* assays tested per month served as our numeric baseline with respect to our project charter. Six HCFO CDI were identified by inappropriate testing during the measure phase.

Hospital length of stay served as our balancing measure. There were 11,161 hospital admissions from January 2020 through September 2020, with an average hospital length of stay of 5.75 days.
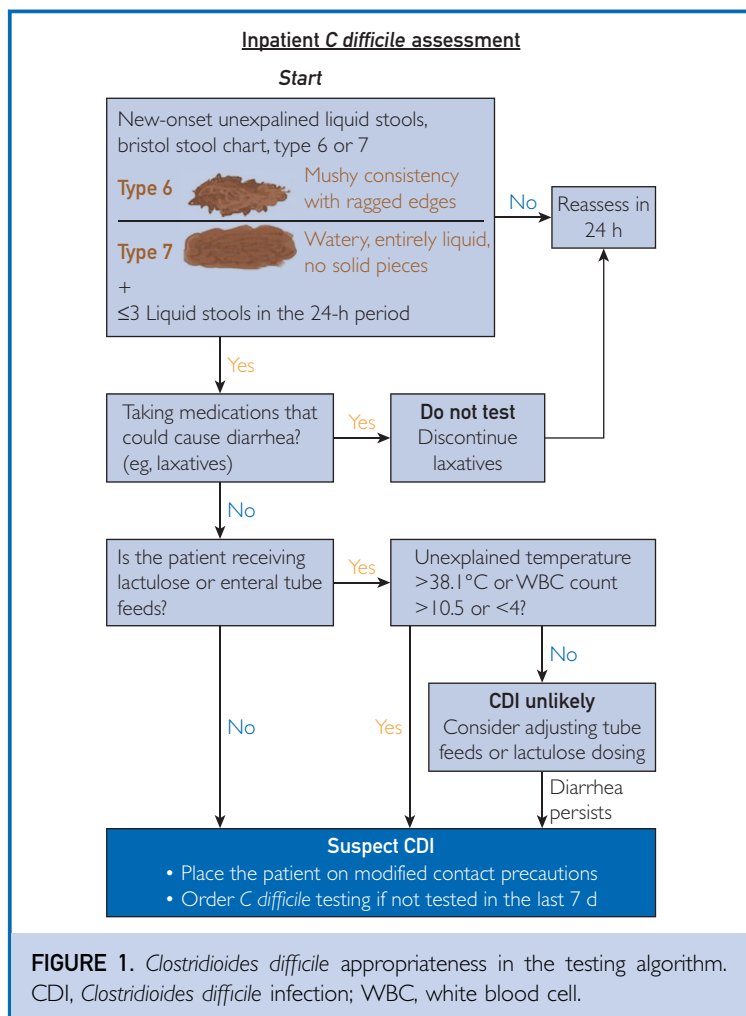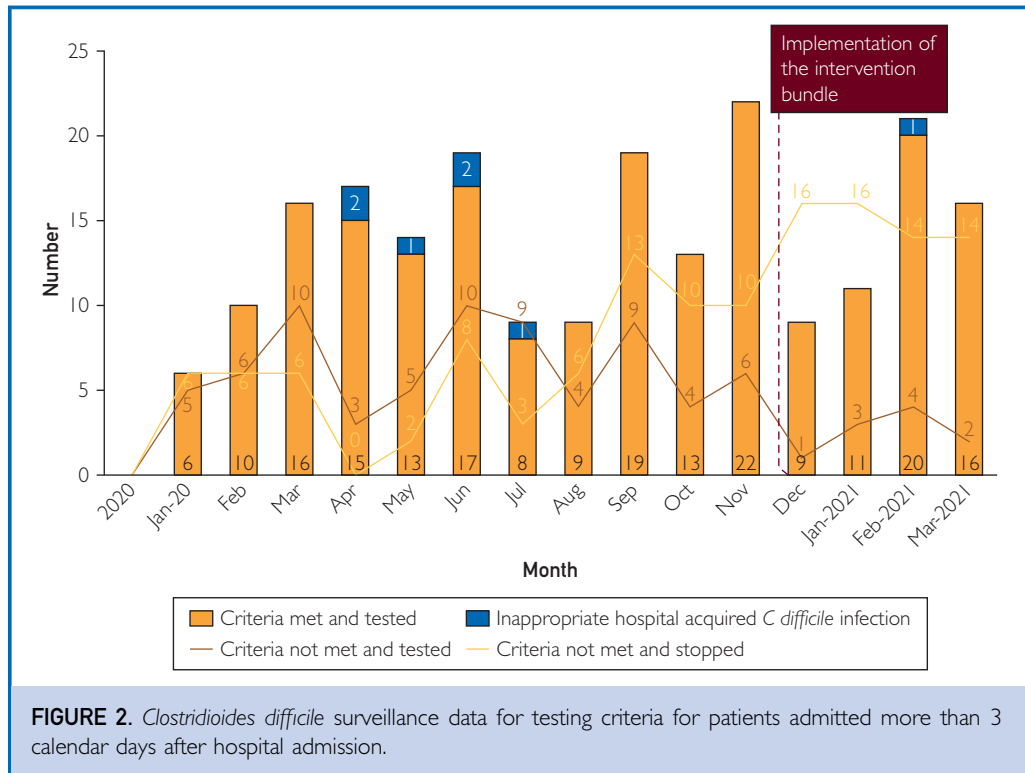

FIGURE 1. *Clostridioides difficile* appropriateness in the testing algorithm. CDI, *Clostridioides difficile* infection; WBC, white blood cell.

A provider educational assessment of *C difficile* clinical knowledge (pretest) was electronically sent out to 91 individuals preintervention, of whom 60 participated (66%). Advanced practice providers (physician assistant or nurse practitioner) accounted for 71.7% of responses (43 of 60) and 26.7% (16 of 60) were resident physicians with 1 *other* participant. The average test score was 82.4% in the preintervention group.

Intervention Phase

The intervention phase of our QI initiative spanned from December 1, 2020, through March 31, 2021. Interventions included distribution of the pretest survey (*C difficile* provider education on diagnostic stewardship),

FIGURE 2. *Clostridioides difficile* surveillance data for testing criteria for patients admitted more than 3 calendar days after hospital admission.

C difficile ATA (Figure 2), and implementation of batch testing.

A total of 135 *C difficile* tests were ordered more than 3 days after hospital admission. Of these, 56 met appropriateness criteria and were processed (criteria met and tested), 60 were reviewed and discontinued because of not meeting criteria (criteria not met and stopped), and 10 tests did not meet criteria, but were still tested for an average of 2.50 inappropriate *C difficile* assays tested per month (criteria not met and tested).

After the implementation of our intervention bundle, including batch testing, IPAC was able to comprehensively review orders for appropriateness of testing. During our measure phase, IPAC reviewed and stopped an average of 5.55 inappropriate orders per month compared with an average of 15 per month during the intervention phase. Compared with the numerical baseline (7) determined during the measure phase, the number of inappropriate *C difficile* assays tested per month during our intervention phase decreased to an average of 2.50

processed tests per month after the implementation of the intervention bundle.

Of the 10 inappropriate orders that were tested, 1 test was positive for a HCFO CDI (Figure 2). The average number of HCFO CDI cases per month identified through inappropriate testing criteria improved from 0.667 cases per month during the measure phase to 0.25 per month during the intervention phase.

We additionally sought to determine the incidence of active CDI in patients whose *C difficile* tests were canceled because of inappropriate testing criteria at the time of order. In reviewing the number of tests that were canceled and subsequently reordered from April 2020 through March 2021, a total of 112 *C difficile* orders were canceled (criteria not met and stopped) (Table 2). Of those tests, 28 were reordered and tested after cancellation. Reordered tests met both "criteria met and tested" and "criteria not met and tested" criteria. Only 1 test was positive (1 of 28 [3.57%]) after previous cancellation due to inappropriate testing criteria. This patient was identified during the intervention phase.

Per IPAC, the patient did not meet testing criteria at the time of the initial order (laxative use) but did meet testing criteria (off laxative >24 hours) when the test was reordered and conducted. The patient was identified as HCFO CDI from appropriate testing and treated for active CDI. When comparing our intervention measures to our balancing measure of hospital length of stay, the average hospital length of stay for December 2020 to March 2021 was 5.85 days, similar to the measure phase length of stay of 5.75 days.

The provider postintervention survey was sent to 91 individuals, of whom 31 providers participated (34%). The postintervention group exhibited improvement with an average test score of 87.0% compared with the preintervention test score of 82.4%. The postintervention assessment revealed an increase in the proportion of appropriate *C difficile* assays ordered, a decrease in the number of inappropriate *C difficile* assays processed, and an overall reduction in the number of HCFO CDI cases.

Compared to our measure phase (January-September 2020), there was a 41.7% reduction in overall HCFO CDI incidence. The number of inappropriate orders reviewed increased by 170.3%, with an 83.6% reduction in the number of inappropriate orders tested (Table 2). A comparison of the number of inappropriate *C difficile* assays tested per month with the number of inappropriate *C difficile* assay orders that were reviewed and stopped preintervention to postintervention trended toward statistical significance (Table 2).

Standardized Infection Ratio

The SIR is a summary measure calculated by CDC's National Healthcare Safety Network to benchmark HAIs nationwide. The SIR compares the number of HAIs reported by the hospital (numerator) with a population risk-adjusted predicted number (denominator). A SIR greater than 1.0 indicates that more HAIs were observed than predicted. Conversely, a SIR less than 1.0 indicates that fewer HAIs were observed than predicted. For reference, the SIR for CDIs across general acute care hospitals in 2019 was 0.58.[14]

Before the implementation of our intervention bundle in December 2020, the average *C difficile* SIR for Q1 through Q3 of 2020 was 0.497. When we compare this with the average *C difficile* SIR for Q4 of 2020 through Q1 of 2021, 0.1765, there was an improvement in SIR by 64.49% (Table 3). It is also worthy to note that the *C difficile* SIR for Q1 of 2021 (0.231) improved by 65% compared with Q1 of 2020 (0.661).

DISCUSSION

Our study aimed to reduce the inappropriate testing for CDI in asymptomatic patients who may be colonized with *C difficile*, specifically orders affecting the HCFO CDI SIR. A bundled approach consisting of (1) provider education, (2) implementation of a revised and improved *C difficile* ATA, (3) IPAC review of order appropriateness, and (4) batch testing reduced inappropriate testing by 83.6% and our hospital's HCFO CDI incidence by 41.7% (Table 2). Before the implementation of our intervention bundle, the average *C*

TABLE 2. Improvement Outcomes Pre- and Postintervention Bundle				
Variable	Measure phase	Intervention phase	Improvement	*P* value
Average number of inappropriate *Clostridioides difficile* assays tested per month (criteria not met and tested)	6.58	2.50	83.6% reduction	.0515
Average number of inappropriate *C difficile* assays reviewed and stopped per month (criteria not met and stopped)	5.55	15	170.3% increase	
Average number of HCFO CDI cases per month due to inappropriate testing criteria	0.667	0.25	41.7% reduction	
Diagnostic stewardship and *C difficile* education assessment (test average)	82.4%	87.0%	5.57% improvement	
CDI, *Clostridioides difficile* infection; HCFO, health care facility—onset.				

TABLE 3. Health Care Facility—Onset CDI Standardized Infection Ratio Quarterly Data

Quarter	HCFO CDI identified by inappropriate testing	HCFO CDI identified by appropriate testing	Total HCFO CDI	Standardized infection ratio
2020-Q1 (Jan-Mar)	1	9	10	0.661
2020-Q2 (Apr-Jun)	4	6	10	0.644
2020-Q3 (Jul-Sep)	1	2	3	0.188
2020-Q4 (Oct-Dec)	0	2	2	0.122
Cumulative 2020				0.397
2021-Q1 (Jan-Mar)	1	3	4	0.231

CDI, *Clostridioides difficile* infection; HCFO, health care facility—onset.

difficile SIR for 2020-Q1 through 2020-Q3 was 0.497. When we compare this with quarters after the implementation of our intervention bundle, 2020-Q4 (0.122) and 2021-Q1 (0.231), the average *C difficile* SIR was 0.177, reflecting an improvement in SIR by 64.49% (Table 3). Reduction in our overall hospital SIR was likely a contribution of both appropriate and inappropriate testing reductions during the time of our intervention phase. The use of appropriate testing criteria targeted HCFO CDI incidence through the improved assessment of timing of symptoms. Symptom identification on or early in hospital admission prompted providers to order *C difficile* assays earlier with positive tests within 3 days of hospital admission, appropriately identifying more community-onset CDI than HCFO CDI. Improved provider knowledge regarding the quantity/caliber of stool and other causes of diarrhea (laxative use, tube feeds, etc) reduced inappropriate testing and detection in colonized asymptomatic carriers. A reduction in HCFO CDI from appropriate testing was likely due to improved cleaning and disinfection interventions during the coronavirus disease 2019 (COVID-19) pandemic. Additional hypotheses include improved antimicrobial stewardship, improved adherence to personal protective equipment in patients undergoing *C difficile* assay testing, and improved patient isolation during the COVID-19 pandemic.

Despite improvement in provider test scores, the average number of inappropriate tests ordered during the intervention phase (17.55 tests per month) was higher than that during the measure phase (12.33 tests per month). In spite of this increase, the actual number of tests processed was reduced after the implementation of the intervention bundle (7 tests per month during the measure phase and 2.50 tests per month during the intervention phase). We believe that this improvement was due to the increased time allocated for IPAC review and approval of orders after the implementation of batch testing. With respect to our balancing measure, hospital length of stay was not markedly affected pre- and post-intervention, increasing minimally from 5.75 to 5.85 days (2.4 hours). We believe that the late identification of true HCFO CDI or sequelae of untreated infection would have increased the hospital length of stay by a more considerable margin and that the observed small increase in our balancing measure would be clinically insignificant. Based on the data available that spanned both our measure phase and intervention phase, there was a less than 5% chance that reordering and testing for CDI that was initially canceled because of inappropriate testing criteria will yield a positive result.

Major strengths of our study included our multidisciplinary approach, incorporating heavy resident physician engagement with IPAC personal and institutional buy-in of our intervention bundle. However, our results should also be interpreted in regard to our study's limitations. This was a single-center QI initiative with a limited sample size after a 4-month intervention phase. Future studies over longer durations are warranted. Infection prevention and control review was restricted by the availability of on-call personnel to normal weekday business hours. Batch testing and IPAC review were not conducted on weekends, accounting for some of the inappropriate

assays performed. This study was conducted during the COVID 2019 pandemic, which may have skewed both the admitted patient population and the overall antimicrobial stewardship focus, as the IPAC team rightly prioritized support for COVID 2019 patient care and infection control. We recognize the difference in sample size with respect to response rate when comparing the pretest cohort (35%) with the posttest cohort (60%), a discrepancy that may have led to participation bias. Finally, IPAC staff did not have institutional review board approval to chart review-specific patient cases, lending hospital length of stay to be our chosen balancing measure rather than alternative measures such as disease severity, index admission comorbidities, and mortality, which require laboratory or flow sheet data.

Future directions of this study may include assessment of balancing measures other than hospital length of stay. Examples may include hospital mortality due to HCFO CDI or incidence of severe or fulminant HCFO CDI in patients initially determined to not meet criteria for CDI testing.

Our study adds important depth to the existing literature regarding QI initiatives aimed at reducing HCFO CDI through combinations of diagnostic stewardship, prevention bundles, electronic health record clinical decision support, and real-time monitoring.[15-17]

With rates of CDI colonization estimated to be as high as 8.1% in asymptomatic patients with previous hospitalization and up to 50% in patients admitted from long-term care facilities, promoting increased diagnostic stewardship is an essential endeavor to avoid morbidity associated with unnecessary antibiotics.[5,6,18] Additionally, treating asymptomatic *C difficile* colonization through overdiagnosis imposes significant economic burden on patients and hospitals alike. With CMS and Department of Health and Human Services patient safety guidelines and payment models based on quality measures such as HCFO SIR, powerful financial incentives exist for hospitals to reduce the HCFO CDI rate.[19]

CONCLUSION

Inappropriate testing for CDI affects patient mortality and morbidity, draws on hospital and provider resources, and affects quality metrics set by government agencies. Our multipronged QI strategy included provider education, implementation of a *C difficile* ATA, IPAC review of testing appropriateness, and batch testing that together reduced inappropriate testing of CDI and lowered the HCFO CDI rate at our tertiary care center. Diagnostic stewardship initiatives specifically targeting HCFO CDI rates may positively affect patient safety and hospital reimbursement.

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