

Impact of a division-wide bundle on hospital-acquired *Clostridioides difficile* cases, antibiotic days of therapy, testing appropriateness, and associated financial costs

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ABSTRACT

Introduction: Updated international guidelines recommend the use of a two-step algorithm (glutamate dehydrogenase [GDH] or nucleic-acid amplification test [NAAT] plus toxin) rather than NAAT alone for the diagnosis of *Clostridioides difficile* (formerly *Clostridium difficile*) infections. The goal of our project was to evaluate the impact of a new bundle on the rate of hospital-acquired *C. difficile* infections (CDIs), hospital-acquired CDI standardized infection ratio (SIR), antibiotic days of therapy (DOT), and financial cost. **Materials and Methods:** The new bundle was implemented in April 2018. This bundle was implemented across five hospitals in Catholic Health Initiatives (CHI) Texas Division. The bundle included a switch from NAAT to a two-step process (GDH and toxin). We placed the new test in an order panel which included enteric isolation and required indications for *C. difficile* testing. We used quarterly data pre- and post-intervention to calculate SIR and DOT. **Results:** In the pre-intervention period, 15.5% of the total 3513 *C. difficile* NAAT was positive. In the post-intervention period, 5.7% of a total of 2845 GDH and toxin assays was positive for both GDH and toxin ($P < 0.0001$). SIR, which adjusts for denominator and change in testing methodology, also dropped from 1.02 to 0.43. The estimated cost associated with positive *C. difficile* cases dropped from 1,932,150 USD to 1,113,800 USD with an estimated yearly cost saving of 794,150 USD. Compliance with enteric isolation improved from 73.1% to 92.5% ($P = 0.008$). **Conclusion:** The new testing bundle led to a marked reduction in hospital-acquired CDI and unnecessary treatment, reduction in *C. difficile* testing, an increase in compliance with enteric isolation, and significant cost savings.

Key words: *C. difficile*, cost, diagnostic stewardship, DOT, testing

INTRODUCTION

Diagnosis of *Clostridioides difficile* infection (CDI) is a dynamic field: we have vacillated from the nucleic acid amplification test (NAAT) to glutamate dehydrogenase (GDH) and toxin enzyme immunoassays (EIA). Within the *C. difficile* community, no consensus can be reached on

the optimal testing method. The NAAT detects genes for toxigenic strains of *C. difficile*. Though highly sensitive, it does not test for active toxin production as it detects both

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asymptomatic carriers and toxin producers. Hence, using this test is associated with overdiagnosis and overtreatment.^[1] On the contrary, GDH is an essential enzyme produced by all isolates of *C. difficile* and the enzyme immunoassay for this enzyme has high sensitivity.^[2] However, it also does not distinguish between toxigenic vs. nontoxigenic strains; therefore, needs to be combined with a specific test, such as the EIA for *C. difficile* Toxin A and B.^[3] The gold standard testing for CDI with high sensitivity and specificity is the cell culture cytotoxicity neutralization assay.^[4] However, this test is highly labor and time intensive, making it impractical when we need rapid diagnosis and turnover.

The guidelines are ever changing as well. Five years ago, at our five hospitals, we were using the toxin EIA, followed by a switch to NAAT sometime in 2015, and then came the new Infectious Diseases Society of America (IDSA) *C. difficile* guidelines^[5] in 2018 which recommended a two-step approach using either NAAT and toxin or GDH and toxin. The European guidelines also recommended a similar two-step approach.^[6]

In response to the new guidelines and in order to improve diagnostic stewardship at our division, we decided to implement a new bundle in the electronic medical record (EMR). Components of the bundle include change of testing methodology from NAAT to GDH and toxin, screening questions to increase appropriateness of testing, and automatic implementation of enteric contact isolation. Our primary aim was to understand the impact of the intervention on hospital-acquired CDIs.

MATERIALS AND METHODS

This is a multicenter quasi-experimental interventional quality improvement study performed at five Catholic Health Initiatives (CHI) hospitals in Texas: CHI Baylor St. Luke's Medical Center, St. Luke's Sugar Land, The Woodlands Hospital, The Vintage Hospital, and St. Luke's Lakeside Hospital. In April 2018, we implemented the new bundle in the EMR across all five hospitals. Clinicians ordering *C. difficile* testing would have to open a bundle, in which they were required to list an indication for testing, as well as answer questions regarding laxative use in the last 24h and previous *C. difficile* testing in the last 7 days. The bundle also sets off automatic initiation of enteric contact isolation including alcohol gel and gown upon entering the room and handwashing upon exiting the room. Most importantly, the testing method was switched from NAAT to GDH and toxin. Providers were educated on the intervention through various methods (communication memo and in-person meetings) and test interpretations were provided in the

electronic health record. Figures 1 and 2 provide a more direct overview on the changes made based on the bundle [Figure 3] is a direct illustration of the bundle.

Previously, clinicians ordered NAAT with one click in the EMR if there was suspicion for CDI. A positive NAAT indicated the patient likely had CDI and antimicrobials were given. With the new bundle and the GDH and toxin assay, patients were only treated for CDI if GDH and toxin were both positive. A test of positive GDH and negative toxin was interpreted as unlikely CDI and clinicians were advised to use clinical judgment to guide treatment. Ordering NAAT to arbitrate in these cases was optional and restricted to infectious disease physicians only. A test of negative GDH and positive toxin was difficult to interpret and we recommended performing the NAAT to arbitrate as an option. When the GDH and toxin are both negative, patients were deemed unlikely to have CDI.

The pre-intervention period was 12 months in duration from April 2017 to March 2018, whereas the post-intervention period was also 12 months in duration from July 2018 to

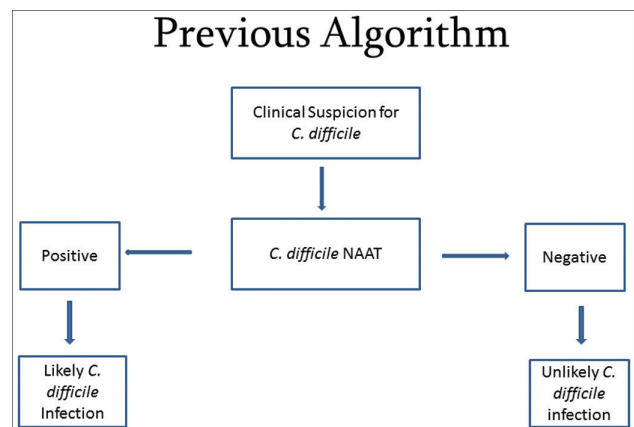


Figure 1: Previous algorithm of CDI testing

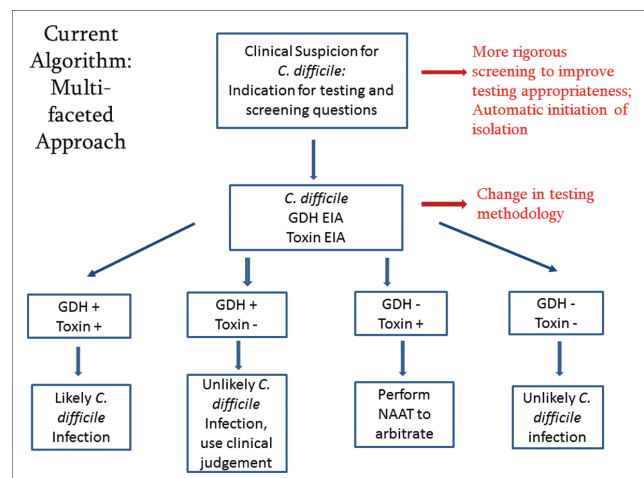


Figure 2: Current algorithm of CDI testing

June 2019. The post-intervention period did not include April to June 2018 as an attempt to avoid confounding of the SIR in that quarter of the year as the bundle was introduced in mid-April.

The primary outcome was hospital-acquired *C. difficile* SIR. Secondary outcomes included number of *C. difficile* tests ordered per 10,000 patient days, proportion of positive tests, rate of hospital-acquired *C. difficile* cases, oral vancomycin and fidaxomicin DOT/1000 days present, testing appropriateness, enteric isolation compliance and finally cost savings.

Clostridioides difficile tests ordered per 10,000 patient days, proportion of positive tests, and rate of hospital-acquired *C. difficile* cases were collected and calculated by our infection prevention department. Oral vancomycin and fidaxomicin days were determined by using the TheraDoc program (Premier Healthcare Solutions, Inc. Salt Lake City, UT). To evaluate testing appropriateness and compliance to enteric contact isolation, based on a power calculation (estimated appropriateness [based on previous clinical experience] preintervention 20%, postintervention 50%, alpha 0.05, power 0.9), we selected a random sample of 105 patients stratified by location (floor, intensive care unit, and emergency room) and test result (positive vs. negative). Fifty-two patients were selected from the pre-intervention period, and 53 patients from the post-intervention period. Testing was reviewed by an infectious disease fellow (E.W.) and was considered appropriate if the patient has not had laxatives in the last 24 h, has not had a positive test in the last 7 days, has an indication for testing including 3 or more watery loose stools in the last 24 h; leukocytosis, diarrhea and/or abdominal cramps and imaging findings consistent with colitis; endoscopic or pathologic evidence of pseudomembranous colitis; ileus suspected due to CDI. If any of these criteria were not met, testing was considered inappropriate. We chart reviewed the medication administration record for laxative use, laboratory results for previous positive testing, and nursing flow sheets and clinician documentation for the number of episodes of diarrhea and other clinical criteria that would support *C. difficile* testing. If a clinician listed 3 or more loose, watery stools as the indication for testing which was not supported by nursing flow sheet or clinician documentation, this was considered inappropriate testing. To determine compliance with enteric contact isolation, we reviewed EMR orders to see if this was ordered around the same time as *C. difficile* testing. In our new model, noncompliance would mean physician-initiated intentional discontinuation of isolation orders after the initiation of the bundle. Financial cost was calculated based on the article by Schroeder *et al.*^[7]

Chi-square was used to assess any difference in the rate of testing appropriateness and the rate of positive testing between pre- and post-intervention groups. The incidence-rate difference was used to examine the effect of our intervention on tests/10,000 patient days, infection rate/10,000 patient days, SIR, and vancomycin and fidaxomicin DOT/1000 days present. Significance was defined as $P < 0.05$. Statistical analysis was done through Stata version 13 (StataCorp, College Station, Texas). The study was approved by Baylor College of Medicine IRB (H-47898).

RESULTS

CDI tests

After the implementation of the new bundle, the rate of hospital-acquired CDI dropped significantly from 5.02 cases per 10,000 patient days in the pre-intervention period to 1.64 cases per 10,000 patient days in the post-intervention period ($P < 0.0001$). The number of tests ordered per 10,000 patient days went down from 90.38 to 76.64 ($P < 0.0001$). The percentage of positive tests decreased from 15.46% to 5.66% ($P < 0.0001$). Hospital-acquired *C. difficile* SIR, our primary outcome, decreased from 1.02 to 0.43 ($P < 0.0001$).

Testing appropriateness

Testing appropriateness pre-intervention was 48%, compared to 58% post-intervention. However, this increase was not statistically significant with $P = 0.29$. Compliance to enteric contact isolation did improve from 73% to 93% ($P = 0.008$).

Antibiotic treatment

Oral vancomycin days declined from 439.73 to 394.38 DOT/1000 days present ($P < 0.0001$). There was no significant change in fidaxomicin DOT/1000 days present pre- and post-intervention (14.23 and 21.39, respectively, $P = 0.1374$).

Financial cost

Total estimated cost in the pre-intervention period was 1,932,150 USD, compared to 1,113,800 USD in the post-intervention period. Estimated annual savings totaled to 794,150 USD. There was significant change in financial cost/10,000 patient days pre and post intervention (49.71 and 30.66, respectively, $P < 0.0001$) [Table 1].

DISCUSSION

Our study showed that diagnostic stewardship—modification of the process of ordering, performing, and reporting diagnostic tests—can be very powerful when supported by engaged clinicians and hospital leadership. Our intervention led to a substantial reduction in hospital-

Table 1: Pre- and post-intervention results of the *Clostridioides difficile* bundle

	Pre-intervention period (April 2017–March 2018)	Post-intervention period (July 2018–June 2019)	P
Total number of tests ordered	3513	2845	
Number of tests/10,000 patient days	90.38	76.64	<0.0001
Number of positive tests	543	161	
Rate of positive tests	15.46%	5.66%	<0.0001
Hospital-acquired cases of <i>C. difficile</i>	195	61	
Rate/10,000 patient days	5.02	1.64	<0.0001
SIR	1.015	0.427	<0.0001
Oral vancomycin days	4618	2841	
Vancomycin/1000 days present	429.73	394.38	<0.0001
Fidaxomicin days	226	196	
Fidaxomicin/1000 days present	14.23	21.39	0.1374
Financial costs	1,932,150 USD	1,138,000 USD	
Financial costs/10,000 patient days	49.71 USD	30.66 USD	<0.0001

acquired CDI. In addition, oral vancomycin and fidaxomicin use was reduced as the two-step method distinguished between active infection (GDH +/toxin +) and colonization (GDH+/toxin). The intervention was also associated with an increase in compliance with enteric isolation, and significant cost savings for the hospitals (personal protective equipment, testing, unnecessary treatment, and government penalties for CDI). In addition, switching to a two-step testing could allow clinicians to consider other diagnoses for patients with GDH-positive but are toxin-negative. These diagnoses could have been missed if using an NAAT-based algorithm alone.^[6]

Other investigators have shown that diagnostic stewardship methods reduce CDI rates. Truong *et al.*^[8] showed that using the laboratory to reject samples that did not meet testing criteria, *C. difficile* testing utilization, CDI rates, and oral vancomycin days decreased. Yen *et al.*^[9] used a multifaceted approach with hospital-wide education of providers, as well as diagnostic stewardship with canceling of orders if sample not received in the laboratory in 24h and if sample not consistent with diarrhea. They showed a decrease in SIR, laboratory testing costs and drug costs. Bischoff *et al.*^[10] showed that switching testing methodology from NAAT to GDH and toxin resulted in decrease in CDI, avoidance of unnecessary antibiotics, reduction in isolation, and significant cost savings. Furthermore, multiple studies have shown that computerized clinical decision support (CCDS)-based interventions can significantly reduce inappropriate *C. difficile* testing and CDI events.^[11,12] Our study is unique in that we employed a multifaceted approach and combined the change in testing methodology with CCDS in hopes to maximize our impact.

Due to the scope and focus of the study, we were not able to examine the outcomes of those patients who had GDH positive, toxin negative testing result, and were not treated for CDI. Madden *et al.*^[13] examined the outcomes of solid organ transplant patients in whom *C. difficile* testing was

prevented by CCDS tool and determined that none of the 38 tests prevented resulted in a poor outcome associated with delayed *C. difficile* diagnosis.

One observation we made was that determination of testing appropriateness is difficult when documentation is sparse. Clinicians often list 3 watery, loose stools in 24 h as an indication for testing; however, actual documentation of these bowel movements was nowhere to be found in the nursing flow sheets or clinician notes. Clinicians also continued to order *C. difficile* testing when patient has obviously received laxatives and/or in the absence of diarrhea.

Future plans include improving the appropriateness of testing by implementing a hard stop for laxative use in the previous 24h, hard stop for ordering testing if patient had positive testing in the previous 7 days, and pop-up display if there is an order that has not been collected over 48 h.

This study has several limitations. Our estimates for testing appropriateness pre- and post-intervention were different from actual results, which might have led to decreased power of the study. There was no control group. It is possible that the study findings were explained by other preventative CDI measures (e.g., hand hygiene, environmental cleaning, antimicrobial stewardship). We considered the lack of documentation in nursing flow sheet of stool quantity and consistency as the patient did not have diarrhea. This may have led to selection bias which may have increased the inappropriate testing rates.

Another limitation of this study is that as the bundle has three components, it is difficult to attribute whether the effects are driven largely by the change in methodology from NAAT to GDH and toxin versus the other components of the bundle including enteric isolation and indication for testing. The NHSN, in its calculation of the expected

number of cases for the SIR, takes into consideration the methodology used and adjust accordingly. However, it may not be a perfect adjustment. Nevertheless, regardless of the testing methodology, the number of tests ordered per 10,000 patient days did decrease significantly from our intervention.

CONCLUSION

Our project showed that a testing bundle led to a marked reduction in hospital-acquired CDI and *C. difficile* testing. In addition, it was associated with a reduction in unnecessary treatment, an increase in compliance with enteric isolation, and significant cost savings. Future plans will focus on improving the appropriateness of testing using CCDS.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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