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Reducing Overutilization of Testing for *Clostridium difficile* Infection in a Pediatric Hospital System: A Quality Improvement Initiative

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ABSTRACT

OBJECTIVES: Study objectives included addressing overuse of *Clostridium difficile* laboratory testing by decreasing submission rates of nondiarrheal stool specimens and specimens from children ≤ 12 months of age and determining resultant patient and laboratory cost savings associated with decreased testing.

METHODS: A multifaceted initiative was developed, and components included multiple provider education methods, computerized order entry modifications, and automatic declination from laboratory on testing stool specimens of nondiarrheal consistency and from children ≤ 12 months old. A run chart, demonstrating numbers of nondiarrheal plus infant stool specimens submitted over time, was developed to analyze the initiative's impact on clinicians' test-ordering practices. A p-chart was generated to evaluate the percentage of these submitted specimens tested biweekly over a 12-month period. Cost savings for patients and the laboratory were assessed at the study period's conclusion.

RESULTS: Run chart analysis revealed an initial shift after the interventions, suggesting a temporary decrease in testing submission; however, no sustained differences in numbers of specimens submitted biweekly were observed over time. On the p-chart, the mean percentage of specimens tested before the intervention was 100%. After the intervention, the average percentage of specimens tested dropped to 53.8%. Resultant laboratory cost savings totaled nearly \$3600, and patient savings on testing charges were ~\$32 000.

CONCLUSIONS: Automatic laboratory declination of nondiarrheal stools submitted for CDI testing resulted in a sustained decrease in the number of specimens tested, resulting in significant laboratory and patient cost savings. Despite multiple educational efforts, no sustained changes in physician ordering practices were observed.

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The diagnosis of pediatric *Clostridium difficile* infection (CDI) has increased over the past 10 to 20 years and has been associated with increased health care costs.^{1–3} Despite a recent American Academy of Pediatrics policy statement outlining appropriate indications for pediatric CDI testing, a significant number of institutions have few restrictions on testing.^{4,5} The American Academy of Pediatrics and Infectious Diseases Society of America guidelines recommend against CDI testing of nondiarrheal stool (formed or soft stool consistency, per visual inspection) specimens.^{4,6}

This recommendation is based in part on the statistical principle of a positive test result (in this situation, a positive test result for CDI) demonstrating poor predictive utility in the presence of a low pretest probability.⁷ For diagnosis of pediatric CDI, low prevalence rates of disease in children, when combined with the known sensitivities and specificities of testing methods such as stool enzyme immunoassay, lead to a poor positive predictive value for this testing method.⁴ Newer testing techniques, such as nucleic acid–based polymerase chain reaction (PCR) analysis for *C. difficile* strains that harbor toxin-producing genes, are highly sensitive and specific yet are plagued by the inability to differentiate asymptomatic colonization from symptomatic CDI.^{8,9} For the pediatric population, in whom rates of asymptomatic *C. difficile* colonization (particularly in infants ≤ 12 months of age) can be elevated⁴ and in whom gastroenteritis caused by etiologies other than *C. difficile* (eg, adenoviruses, noroviruses, and rotaviruses¹⁰) is exceedingly more common, close adherence to published recommendations for appropriate testing is therefore extremely important.

Before development of this quality improvement (QI) initiative, the Children's Mercy Hospital (CMH) microbiology laboratory began recording the consistency of stool specimens submitted for CDI testing in November 2010. This study was initiated after microbiology laboratory personnel data review revealed that

nondiarrheal stools (soft or formed) were frequently being submitted for CDI testing. In this study, we sought to work closely with the microbiology laboratory to develop, implement, and evaluate the impact of a multifaceted QI initiative, designed to reduce overuse of pediatric CDI testing at CMH. Reduction of testing overuse was facilitated by accomplishment of our primary aim: reducing rates of nondiarrheal specimens and those from infants ≤ 12 months old both submitted and tested for CDI (from both inpatients and outpatients, although baseline data review revealed that a majority of specimens were submitted from inpatients). Our secondary aim included calculation of cost savings resulting from the intervention. Before the implementation of the initiative, there was no routine process to notify the ordering physician that a nondiarrheal stool had been submitted for testing, and the study aimed to address this problem as well.

METHODS

Study Design

The CMH system, located in Kansas City, Missouri, includes a 302-bed tertiary hospital, a 53-bed satellite facility, and outpatient primary and subspecialty clinics. The system's main hospital campus serves as the primary training site for 72 categorical pediatrics resident physicians and 24 combined internal medicine and pediatrics residents. The multidisciplinary team included members of the Infectious Diseases Division, the microbiology laboratory director, the director of the Gastroenterology Division, members of the Quality and Safety Department, and the CMH Medical Informatics Committee. Laboratory testing for CDI at CMH throughout the study period entailed testing stool specimens for the presence of both glutamate dehydrogenase (GDH) antigen (Ag), an enzyme produced by both toxigenic and nontoxigenic strains of *C. difficile*, and *C. difficile* toxin antigen (toxin Ag). Reflex PCR testing for *C. difficile* toxin-producing gene was performed on specimens testing positive for GDH Ag but negative for toxin Ag, to optimize testing sensitivity.⁸

Planning the Intervention

Multiple formative discussions were held between the microbiology laboratory director and members of the Infectious Diseases Division. Active input was subsequently sought from the director of the Gastroenterology Division, after analysis of preexisting laboratory data, which revealed that a majority of specimens submitted for CDI testing were directly ordered either by gastroenterology or by hospital medicine physicians at the behest of consulting gastroenterology physicians. Review of the existing literature on indications for pediatric CDI testing and additional collaboration between the aforementioned parties resulted in development of the intervention's educational components and the proposed plan for modification of computerized order entry for CDI and automatic laboratory declination of nondiarrheal stool specimens submitted for testing.

Multidisciplinary team attendance at monthly meetings of the CMH Quality and Safety Department, as well as the CMH Medical Informatics Committee, allowed widespread dissemination of educational materials and formulation of computerized order entry changes according to team specifications.

Tested nondiarrheal stool specimens obtained from patients >12 months old, in whom concern existed for toxic megacolon or severe ileus, were not included in the study analysis (as per review of medical record documentation before the intervention, $n = 2$, and as indicated by computerized order entry documentation after the intervention, $n = 2$). All other specimens tested during the study that were either nondiarrheal in consistency or from patients ≤ 12 months old were also stratified by testing result (positive or negative). After the intervention, ordering clinicians could choose to override the automatic declination by contacting the clinical microbiology laboratory within 24 hours of test declination. In certain circumstances as deemed necessary by laboratory personnel, subsequent clinical microbiology discussion with the Infectious Diseases Division (regarding the

appropriateness of testing) occurred before an order of automatic declination could be overridden.

Intervention

The initiative involved development and simultaneous implementation of several intervention components. Educational facets included teaching pediatric residents through a didactic lecture, because review of baseline data revealed that ~30% of all nondiarrheal specimens testing positive for CDI were ordered by resident physicians. Education of CMH-affiliated providers was facilitated by publication of an article in a monthly hospital-based newsletter that outlined clinical features, risk factors, and appropriate diagnosis and treatment of CDI. Most importantly, an evidence-based algorithm was developed to optimize CDI test ordering. The algorithm was made available on the hospital's clinical practice guidelines Web site (https://www.childrensmercy.org/Health_Care_Professionals/Medical_Resources/Clinical_Practice_Guidelines/Clostridium_Difficile/Clostridium_Difficile/).

The second component involved development of computerized order entry modifications for CDI testing, including mandatory completion of 2 additional fields before submission that included whether the patient age was ≤ 12 months and whether the clinician suspected toxic megacolon or the patient had evidence of severe ileus. The requirement of having the ordering clinician enter the patient's age as part of the order entry process was instituted to facilitate automatic laboratory declination of specimens submitted from patients ≤ 12 months old, given the increased prevalence of asymptomatic *C. difficile* colonization in this age group.⁴ Because the clinician was prompted to indicate whether toxic megacolon or severe ileus was suspected, the laboratory was notified that a submitted specimen needed to be tested, even if it was of a nonliquid consistency (because toxic megacolon and severe ileus, which occur in $< 2\%$ of children with CDI, are the only clinical scenarios for which testing of nonliquid specimens should be performed).^{1,6}

Finally, automatic laboratory declination was implemented for nondiarrheal stools submitted for testing, unless severe ileus was present or toxic megacolon was suspected. Automatic declination was communicated to submitting providers by laboratory posting of a comment in the patient's electronic medical record, which stated, "Test not performed. Non-liquid stool is not acceptable for testing. Notify lab within 24 hours if testing is clinically warranted."

The evidence-based algorithm, computerized order entry modifications, and automatic laboratory declination of nondiarrheal stool submissions were all implemented on April 15, 2013. The educational lecture and the newsletter article occurred on April 10, 2013 and upon publication of the March/April newsletter issue, respectively.

Submitted specimens were stratified according to patient age at the time of specimen submission (ie, ≤ 12 months vs > 12 months). Specimens submitted from infants ≤ 12 months of age were automatically declined throughout the study period, unless the ordering clinician contacted the clinical microbiology laboratory.

Project Measures

This study's primary process measure was the percentage of stool specimens submitted for CDI testing over time that were either nondiarrheal or from children ≤ 12 months old, while the primary outcome measure was the number of these stool specimens tested for *C. difficile*.

Data Collection

Data were collected and recorded in 2-week time periods over a 12-month duration (October 15, 2012 to October 15, 2013) and included specimen numbers submitted for testing and numbers of specimens actually tested.

By using QI Macros for Excel software (Microsoft Corporation, Redmond, WA), we created a run chart to track the number of specimens submitted on a biweekly basis over the study period. A p-chart was also generated, to demonstrate the percentage of tests performed on a biweekly basis

(relative to those submitted for testing) during the study period.

Laboratory cost savings were calculated from costs incurred for both materials and labor needed to perform testing in 2013. GDH Ag plus toxin Ag cost per test was \$12.46, whereas the cost of performing 1 *C. difficile* toxin gene PCR test at the reference laboratory was \$45.00 per test. Cost of PCR testing was not included in the analysis, because this reflex step was avoided by automatic nondiarrheal stool testing declination after the intervention. Laboratory technician time cost was determined to be \$4.00 per test, based on time needed to perform 1 test (estimated to be 10 minutes).

Patient savings on testing charges were calculated from unadjusted (ie, before insurance authorization) 2013 CMH charge data and included a GDH Ag plus toxin Ag charge of \$147.00 per test. Toxin gene PCR charges (not included in the analysis) were \$137.00 per test.

RESULTS

During the baseline period of the study (October 15, 2012–April 14, 2013), 534 specimens were submitted, including 21 (4%) from children ≤ 12 months old. Of the 513 specimens obtained from children > 12 months old, 318 (62%) were nondiarrheal. A total of 47 out of 318 (15%) tested positive (ie, either GDH Ag positivity plus toxin Ag positivity or GDH Ag positivity with toxin Ag negativity, plus a positive toxin gene PCR test result). Of 21 specimens submitted from children ≤ 12 months old, 16 (76%) were tested, with 1 specimen yielding a positive result. With respect to antibiotic therapy receipt, 94% (45 out of 48; 47 nondiarrheal positives plus 1 positive test from a child ≤ 12 months old) of patients received antibiotic therapy directed against CDI after return of positive testing results.

During the postintervention period (April 15, 2013–October 15, 2013), 485 specimens were submitted, including 11 (2%) from those ≤ 12 months old and 474 from children > 12 months old (Fig 1). A total of 257 out of 474 (54%) tests were performed on specimens obtained from children

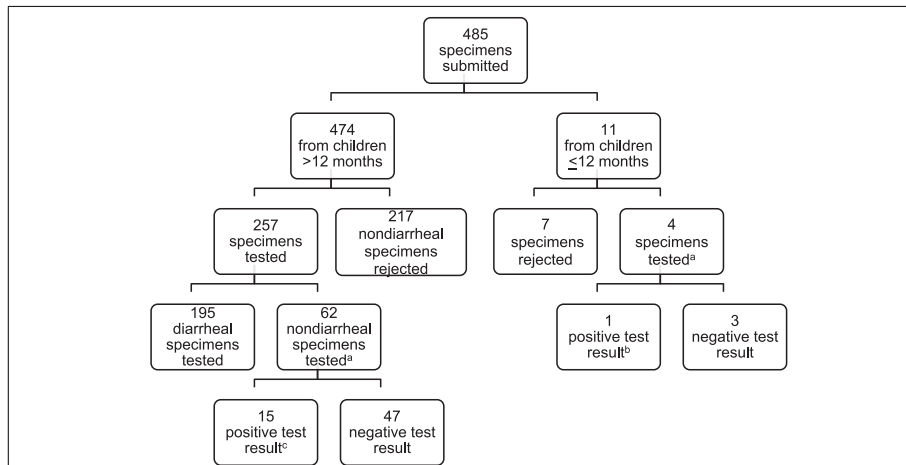


FIGURE 1 Specimens submitted, tested, and rejected during the postintervention period. ^aAfter ordering clinician discussion with the laboratory. ^bPatient treated with antibiotic therapy for CDI after return of positive test result. ^c12 of 15 patients treated with antibiotic therapy for CDI after return of positive test result.

>12 months old, after automatic laboratory declination of nondiarrheal stool specimens ($n = 217$; 46%). Of the 257 specimens tested, 62 (24%) were determined to be inappropriate but were tested after ordering clinician discussion with the laboratory. Fifteen (24%) of 62 specimens tested positive. Of the 11 specimens submitted from individuals ≤ 12 months old, 4 (36%) were tested after clinician discussion with the laboratory, and 1 (9%) specimen tested positive. With respect to antibiotic therapy, 81% (13 out of 16; 15 nondiarrheal positives plus 1 positive test from a child ≤ 12 months old) of patients received antibiotic therapy directed against CDI after return of positive testing results.

From the date of implementation of the intervention's major components on April 15, 2013 through completion of week 42 of the study period on August 4, 2013, an initial shift, reflecting a decrease in the numbers of specimens submitted on a biweekly basis over time, was detected via run chart analysis. However, subsequent data collected pertaining to nondiarrheal and infant stool specimen submission failed to show a continued shift (Fig 2).

The percentage of tests performed on a biweekly basis (relative to the total numbers of specimens submitted for testing) declined sharply after the intervention (Fig 3).

Between October 15, 2012 and April 14, 2013, a total of 334 tests (318 nondiarrheal specimens and 16 specimens from children ≤ 12 months old) accounted for \$5497.64 in laboratory costs. Corresponding unadjusted patient charges for these tests totaled \$49 098.00. From April 15, 2013 to October 15, 2013, a total of 66 tests (performed on 62 nondiarrheal specimens and 4 specimens from children ≤ 12 months old) accounted for \$1086.36 in laboratory costs, with corresponding unadjusted patient charges of \$9702.00.

The 217 nondiarrheal specimens automatically declined by the laboratory after the intervention represent laboratory cost savings of \$3571.82 and unadjusted patient charge savings totaling \$31 899.

DISCUSSION

Diagnostic guidelines to optimize identification of those with CDI specifically recommend against testing nondiarrheal stools in the absence of toxic megacolon and from infants < 12 months of age.^{4,6} Yet this is a common practice that results in excessive expense and potential exposure to unnecessary antibiotics. For instance, 1 previous study evaluating optimization of CDI testing in adults found that 39% of all CDI testing at the study institution could have been avoided if clinicians had only submitted specimens from patients with both diarrhea and a history of antibiotic

use.¹¹ After our intervention, we observed a 45% decrease in the number of specimens tested (217 out of 485 submitted nondiarrheal stool specimens automatically declined by the laboratory and subsequently not tested). Development of an initiative that eliminated testing of nondiarrheal stool specimens resulted in a substantial decline in inappropriate CDI testing, accounting for $> \$35 000$ in overall savings, thus demonstrating a clear financial benefit to optimizing CDI testing. Additionally, laboratory testing costs and patient charge savings are probably underestimated, because automatic declination negated the need for any potential reflex PCR testing in the postintervention period.

This study is limited by the fact that we did not correlate the number of inpatient tests ordered to the inpatient census at the time of testing, which impeded our ability to determine whether the rate of inpatient test ordering changed over time. However, our average patient census was fairly stable throughout the study period and thus is unlikely to have introduced much bias.

Although it appears that there may have been an initial decrease in the frequency of nondiarrheal stool specimens submitted for testing in the postintervention period, a sustained decline in submission of such specimens was not confirmed over time. This observation suggests the need for

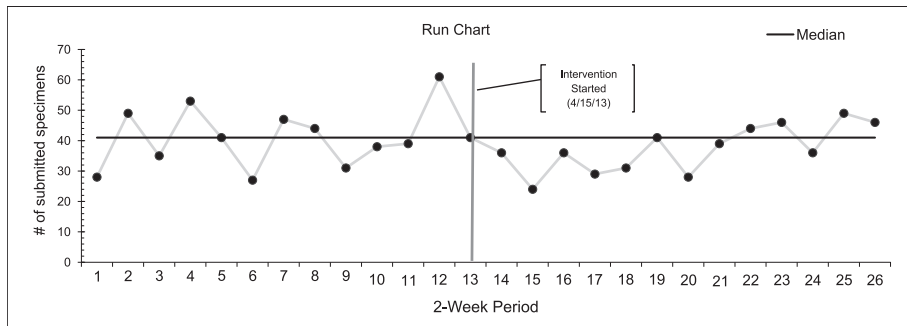


FIGURE 2 Run chart showing the number of specimens submitted during the study period. The x-axis is in 2-week increments. Number 1 represents October 15 to 28, 2012, and number 26 represents September 30 through October 15, 2013. The y-axis is the number of specimens submitted. The vertical line represents intervention implementation.

provision of additional and ongoing feedback and education, rooted in evidence-based practice, and targeted toward the specialties and individual clinicians continuing to consistently demonstrate inappropriate ordering tendencies.

Among the most common reasons given by clinicians for overriding an automatic laboratory declination was that the patient being tested had a concurrent diagnosis of inflammatory bowel disease and therefore was more likely to have symptomatic CDI, regardless of the submitted stool specimen consistency. Although the diagnosis of inflammatory bowel disease in and of itself has been shown to be a risk factor for development of CDI, rates of colonization with toxigenic strains of *C. difficile* in this pediatric patient subpopulation may be up to 14% greater than in otherwise healthy children; therefore, application of

judicious testing according to published guidelines also applies to this patient population.^{12,13}

Another common indication given by clinicians for overriding an automatic laboratory testing declination was that “it [the stool specimen] was liquid, but it had to be scraped out of a diaper . . . so that’s why it appears to be non-liquid.” Additional measures to reduce these types of inappropriate specimen submissions might also include timely nursing-to-ordering provider notification, in the event that a diarrheal stool specimen cannot be obtained for CDI testing.

Still other measures that could be undertaken to reduce submission of nondiarrheal specimens could include instructing ordering clinicians to advise parents of pediatric outpatients that if stools subsequently develop a formed

consistency, then specimen submission for CDI testing is longer indicated.

CONCLUSIONS

Our study highlights the need for judicious pediatric CDI testing and thus treatment according to published guidelines and standards.^{4,6} Reducing overuse of CDI testing has the potential to improve patient care by reducing unnecessary antibiotic exposure in patients with a positive test who do not have symptoms consistent with CDI. Furthermore, this is a good example of financial stewardship in this era in which reduction of unnecessary costs and patient charges are becoming increasingly important. Finally, this study also underscores the importance of active, ongoing collaboration between physicians and microbiology laboratory professionals and the necessity of this partnership for timely institution of hospital policies pertaining to infectious diseases.

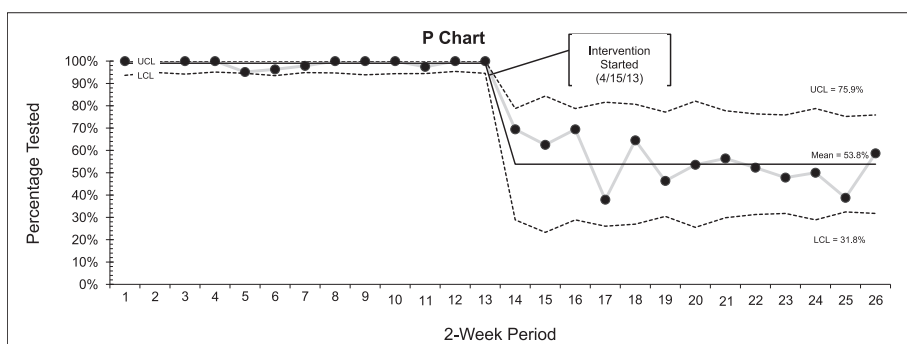


FIGURE 3 P-chart showing the percentage of tests performed (relative to those submitted for testing) in 2-week increments during the study period. Number 1 represents October 15 to 28, 2012, and number 26 represents September 30 through October 15, 2013. The y-axis is the percentage of tests performed. LCL, lower control limit; UCL, upper control limit.

Development of a hospital-specific, best practice model for appropriate CDI diagnosis and testing is a primary step toward development of a CDI stewardship initiative.¹⁴

Several core components of this initiative, including automatic laboratory declination of nondiarrheal stool specimens submitted for testing, computerized order entry modifications, and access to the evidence-based algorithm, have remained in place after the conclusion of this study. A recent increase in clinicians' requesting of testing on automatically rejected specimens has been observed, and the multidisciplinary team is planning additional interventions to address this issue.

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