ORIGINAL ARTICLE

The Use of a Computerized Provider Order Entry Alert to Decrease Rates of *Clostridium difficile* Testing in Young Pediatric Patients

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BACKGROUND. Infants and young children are frequently colonized with *C. difficile* but rarely have symptomatic disease. However, *C. difficile* testing remains prevalent in this age group.

OBJECTIVE. To design a computerized provider order entry (CPOE) alert to decrease testing for *C. difficile* in young children and infants.

DESIGN. An interventional age-targeted before-after trial with comparison group.

SETTING. Monroe Carell Jr. Children's Hospital at Vanderbilt University, Nashville, Tennessee.

PATIENTS. All children seen in the inpatient or emergency room settings from July 2012 through July 2013 (pre-CPOE alert) and September 2013 through September 2014 (post-CPOE alert).

INTERVENTION. In August of 2013, we implemented a CPOE alert advising against testing in infants and young children based on the American Academy of Pediatrics recommendations with an optional override. We further offered healthcare providers educational seminars regarding recommended *C. difficile* testing.

RESULTS. The average monthly testing rate significantly decreased after the CPOE alert for children 0–11 months old (11.5 pre-alert vs 0 post-alert per 10,000 patient days; $P < .001$) and 12–35 months old (61.6 pre-alert vs 30.1 post-alert per 10,000 patients days; $P < .001$), but not for those children ≥36 months old (50.9 pre-alert vs 46.4 post-alert per 10,000 patient days; $P = .3$) who were not targeted with a CPOE alert. There were no complications in those children who testing positive for *C. difficile*.

CONCLUSIONS. The average monthly testing rate for *C. difficile* for children <35 months old decreased without complication after the use of a CPOE alert in those who tested positive for *C. difficile*.

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Clostridium difficile is the most common cause of nosocomial and antibiotic-associated diarrhea in adults and is increasingly prevalent among children.[1] However, healthy newborns can harbor large concentrations of toxigenic *C. difficile* yet remain entirely healthy.[2] Pooled data demonstrate that *C. difficile* colonizes 37% of newborns, decreasing to 3% by 3 years of age.[3–5] In addition, *C. difficile*–associated diarrheal illness before 12 months of age is rare. In a US survey of 20,642 *C. difficile*–associated deaths from 1999 to 2004, only 17 occurred in the first year of life.[6] Testing among these patient leads to unnecessary antibiotic use and increased medical costs.[5] The American Academy of Pediatrics (AAP) made formal recommendations in 2012 to avoid *C. difficile* testing in children <1 year of age and to only consider testing in children 1–2 years of age after alternative etiologies were sought.[7]

Despite these recommendations, healthcare providers continue to test young children for the presence of *C. difficile*.[8,9] Implementing sustainable provider behavior changes pose numerous challenges even with multifaceted interventions.[10] Computerized provider order entry (CPOE) alerts can effectively minimize testing and decrease medication errors.[11,12] No studies to our knowledge have investigated the impact of age-targeted CPOE alerts to decrease rates of testing for *C. difficile* in infants and young children. A single recent study used a CPOE alert to describe scenarios in which asymptomatic carriage is more likely than *C. difficile* infection (CDI) in pediatric patients. The results demonstrated decreases in testing rates per patient encounters, but this alert was not targeted toward specific age groups.[13] Thus, we investigated the impact of an age-specific CPOE alert and educational presentation on

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the rate of *C. difficile* testing in children <36 months of age in a tertiary-care hospital in Nashville, Tennessee.

METHODS

We determined monthly *C. difficile* testing rates by age at our tertiary-care pediatric hospital from July 2012 to July 2013 and from September 2013 to September 2014. In August of 2013, we implemented a CPOE alert (Online Supplementary Figure 1) and offered pediatric healthcare providers brief educational seminars regarding acceptable *C. difficile* testing per AAP guidelines. These recommendations were presented in a PowerPoint presentation at the time of a scheduled conference. One month was deemed an appropriate intervention period because CPOE alerts can effect provider behavior within a short period of implementation.[7] Study methods were reviewed and approved by the Vanderbilt University Institutional Review Board.

Study Site and Intervention

Monroe Carell Jr. Children's Hospital at Vanderbilt (MCJCHV) is a tertiary-care hospital with 271 beds, including a 36-bed pediatric intensive care unit (PICU), 100-bed neonatal intensive care unit (NICU), and a 38-bed emergency room. We initiated a CPOE alert in August of 2013 informing providers of the AAP *C. difficile* testing guidelines. The CPOE alert was activated for any child <36 months of age at the time of order entry for those in an inpatient or emergency room setting. The alerts were considered advisory only and allowed the clinician an opportunity to place the order by providing an overriding reason. There were no consequences to the clinicians who elected to order the test.

Inclusion Criteria

All patients who were seen in the emergency room or were admitted to any pediatric inpatient setting between July 2012 and July 2013 (pre-CPOE alert) and between September 2013 and September 2014 (post-CPOE alert) were included in the study. We gathered additional clinical and demographic information on all patients younger than 36 months of age on whom testing for *C. difficile* was ordered. If the patient tested positive for *C. difficile*, we collected additional outcome variables. Complications including toxic megacolon, pneumatosis intestinalis, gastrointestinal perforation, need for an ICU admission, need for a surgical intervention, or death were carefully collected on all patients who tested positive for *C. difficile*.

Statistical Analyses

The primary outcome of the study was the rate of *C. difficile* testing among 3 different age groups: 0–11 months old, 12–35 months old, and ≥36 months old. These groups were selected due to the variable recommendations per age with a stronger recommendation against *C. difficile* testing in those infants from 0 to 11 months of age than those 12–35 months of age per the AAP guidelines.[7] Children ≥36 months of age served as our comparison group because they received no alert at the time of order entry. We defined a single patient day as 1 inpatient day or 1 emergency room encounter. We presented monthly *C. difficile* tests per patient days in each of the 3 age groups before and after the intervention as our monthly *C. difficile* testing rates.

Patient characteristics were summarized and described as a frequency (percentage) or median and interquartile range (IQR) where appropriate. Categorical variables were compared using the Pearson χ^2 test, and continuous variables were compared using the Wilcoxon rank-sum test. The primary endpoint was the number of patients tested for *C. difficile* per patient days per month. We fit a Poisson model to assess the primary outcome change over time with the total number of patient days as the offset. Time was included in the model as a nonlinear relationship to the outcome implemented by restricted cubic splines with 4 knots. We included time by age-group interaction to allow for the different patterns among age groups. All analyses were performed using statistical software R version 3.1.2 (R Core Team, Vienna, Austria) and Stata (StataCorp, College Station, TX).

RESULTS

Providers ordered 922 *C. difficile* tests in the emergency department or inpatient settings during the 26-month study period, including 307,647 patient days. The average monthly testing rate was significantly decreased pre-CPOE alert versus post-CPOE alert for children 0–11 months old (11.5 vs 0 per 10,000 patient days; $P < .001$) and 12–35 months old (61.6 vs 30.1 per 10,000 patients days; $P < .001$), but not for those children ≥36 months old (50.9 vs 46.4 per 10,000 patient days; $P = .30$) where no CPOE alert was issued (Table 1).

Poisson regression model with time as a continuous variable demonstrated an overall decreasing trend in rates of testing. Age groups 0–11, 12–35, and ≥36 months old demonstrated a decrease in *C. difficile* testing by time ($P < .001$) and age ($P < .001$) (Figure 1).

During the study period, 196 patients (141 patients pre-CPOE alert, 55 patients post-CPOE alert) who were younger than 36 months old were tested for *C. difficile* (Table 2). There were no differences in gender or race between these young children pre- and post-CPOE alert. Of these 196 young children tested, 43 (22%) tested positive for *C. difficile* on initial testing. In addition, 11 children (26%) did not receive therapy directed at the treatment of *C. difficile* and 4 (9%) children had either a poor response to antibiotic therapy or an additional potential etiology of symptoms was identified. There were no complications associated with CDI in any patients in the cohort. Of the 55 patients <36 months of age that were tested post-CPOE alert, the most common overriding reasons were the following: antibiotic use within 30 days (N = 34 tested,

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TABLE 1. *Clostridium difficile* Tests Ordered per 10,000 Patient Days

Age Group	Before Intervention	After Intervention	*P* Value
0–11 months old, median (IQR)	11.5 (8.2–14.8)	0 (0–6.6)	<.001
12–35 months old, median (IQR)	61.6 (42.6–69.9)	30.1 (27.7–46.7)	<.001
0–35 months old, median (IQR)	30.0 (11.4–61.8)	10.9 (0–31.2)	.009
≥36 months old, median (IQR)	50.9 (45.6–59.6)	46.4 (40.0–56.6)	.300

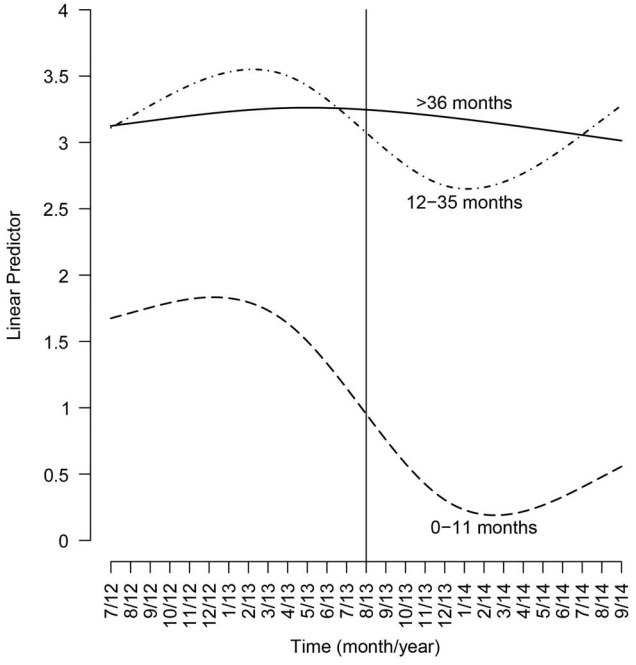


FIGURE 1. Poisson regression modeled over time stratified by age. A significant change was noted in monthly testing rates over time ($P < .001$) and by age ($P < .001$).

8 positive), bloody diarrhea and a close contact with *C. difficile* (N = 5 tested, 0 positive), and Hirschsprung's disease or gastrointestinal motility disorder (N = 4 tested, 0 positive).

DISCUSSION

Colonization with *C. difficile* is common in children and infants, and symptomatic disease is rare.[14] Testing for *C. difficile* in this population leads to increased medical costs and unnecessary antibiotic use. Using an age-targeted CPOE alert and provider educational interventions, we demonstrated a significant decrease in the rate of *C. difficile* testing for children <36 months old and had no *C. difficile*-associated complications, suggesting that any potential delays in testing associated with this alert did not result in unintended adverse outcomes.

Although high rates of *C. difficile* colonization in young infants and toddlers has previously been described,[15] there are more recent concerns about further increase in colonization detection related to changes in *C. difficile* testing modalities. Enzyme immunoassay (EIA) was previously the mainstay for clinical laboratory detection of *C. difficile* but has been mainly replaced by highly sensitive nucleic acid amplification testing (NAAT) of toxin A and B genes, which provides rapid turnaround time as well as increased sensitivity and specificity.[16] Notably, since implementation of NAAT, hospitals have reported a 50%–100% increase in the rate of CDI.[17,18] A single study in adults demonstrated that virtually all CDI-related complications occurred in patients with a positive EIA and that those patients with a negative EIA and positive molecular test were clinically comparable to those without CDI.[19] Concerns involving the increased rates of colonization detection with newer testing modalities make our attempts to decreasing testing rates in young children through the use of a CPOE alert particularly timely.

Decreasing the rates of *C. difficile* testing in young children and infants is important for multiple reasons, including decreased contact isolation needs, less inappropriate use of antibiotics, and decreased costs. At MCJCHV, children who are tested for *C. difficile* are placed on contact precautions until the test is resulted as negative. If the test results are positive, the children commonly remain on contact precautions throughout their admissions. But such protocols may engender less care for isolated patients. Studies on patients who were placed on contact isolation due to the presence of MRSA have demonstrated that these patients received fewer bedside visits and tended to have longer hospital stays and more preventable complications.[20]

As medical costs continue to increase, the use of judicial evidence-based testing is paramount. The use of a CPOE alert is a cost-effective strategy to encourage thoughtful testing approaches. The direct cost of a *C. difficile* test at Vanderbilt is $112. We observed 115 fewer tests postintervention among children <36 months old, for a total direct cost savings of $12,880 in the year post-CPOE alert in the cost of tests alone.

Our study has several limitations. We did not have a formal control group for this study; all children <36 months of age received the CPOE alert. However, the use of a comparator group (children >36 months of age who did not received the CPOE alert) allowed for additional comparisons. It remains possible that changes in *C. difficile* ordering were impacted by changes in the types of patients admitted during the study period, which may not have been entirely captured with the current study design. In addition, although there were no *C. difficile*–associated complications in the 11 children who tested positive for *C. difficile* post-CPOE alert, it is plausible that a delay in testing due to the CPOE alert may have led to increased

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TABLE 2. Demographic and Clinical Characteristics of Patients <36 Months Old Tested for *Clostridium difficile*

Patient Characteristics	Before Intervention, No. (%) ($n = 141$)	After Intervention, No. (%) ($n = 55$)	Combined, No. (%) ($n = 196$)	*P* Value
Age, mo median (IQR)	13 (7–21)	17 (9–26)	14 (7–23)	.06[a]
Male gender	79 (56)	34 (62)	113 (58)	.50[b]
Race/Ethnicity				.50[b]
White	106 (75)	40 (73)	146 (74)	
Black	27 (19)	9 (16)	36 (18)	
Other/Unknown	8 (6)	6 (11)	8 (4)	
Hirschsprung's disease	4 (3)	2 (4)	6 (3)	.80[b]
Antibiotic exposure 30 d prior to symptom onset	93 (66)	43 (78)	136 (70)	.10[b]
No. patients testing positive	32 (23) (n = 140)	11 (20)	43 (22) (n = 195)	.70[b]
	Before Intervention, No. (%) ($n = 32$)	After Intervention, No. (%) ($n = 11$)	Combined, No. (%) ($n = 43$)	
Type of infection				.30[b]
Community associated	13 (41)	4 (36)	17 (40)	
Hospital onset	11 (34)	5 (46)	16 (37)	
Community onset, healthcare associated	6 (19)	0 (0)	6 (14)	
Community onset, indeterminate	2 (6)	2 (18)	4 (9)	
No. patients receiving treatment	21 (64)	7 (64)	28 (64)	1[b]

[a]Wilcoxon Test.
[b]Pearson Test.

medical encounters related to a persistence of symptoms and delay in therapy. Of the 11 pediatric patients who tested positive for *C. difficile* post-CPOE alert, 1 patient had had an emergency department visit 30 days prior to *C. difficile* diagnosis. During this encounter, an alternative enteropathogen was identified, but *C. difficile* testing was not ordered. This finding may suggest that the use of a CPOE alert could lead to a delay in the identification of *C. difficile,* but the clinical relevance of this occurrence needs to be evaluated. Also, outpatients were not targeted by this intervention. Therefore, the evaluation of a CPOE alert to address testing in an outpatient setting cannot be determined by the current study.

In summary, our findings suggest that a CPOE alert and educational presentations to decrease inappropriate testing for *C. difficile* in young children and infants may be an effective, safe, and cost-efficient intervention. As concern for increase rates of *C. difficile* detection in colonized patients escalate, the use of a CPOE alert in clinical settings will become essential.

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SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2017.16

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