Title

The Effect of Clostridioides difficile Diagnostic Stewardship Interventions on the Diagnosis of Hospital-Onset Clostridioides difficile Infections

Journal

The Joint Commission Journal on Quality and Patient Safety, 46(8)

ISSN

1553-7250

Authors

Kang, Minji
Abeles, Shira R
El-Kareh, Robert
et al.

Publication Date

2020-08-01

DOI

10.1016/j.jcjq.2020.05.004

The Joint Commission Journal on Quality and Patient Safety 2020; 46:457–463

The Effect of *Clostridioides difficile* Diagnostic Stewardship Interventions on the Diagnosis of Hospital-Onset *Clostridioides difficile* Infections

Minji Kang, MD; Shira R. Abeles, MD; Robert El-Kareh, MD; Randy A. Taplitz, MD; Elizabeth Nyheim; Sharon L. Reed, MD; Ian H. Jenkins, MD; Gregory B. Seymann, MD; Frank E. Myers, MA; Francesca J. Torriani, MD, for the UCSDH CDI task force

Background: Public reporting of *Clostridioides difficile* infection (CDI) using laboratory-identified events has led some institutions to revert from molecular-based tests to less sensitive testing modalities. At one academic medical center, researchers chose to use nucleic acid amplification test alone in CDI diagnosis with institutional protocols aimed at diagnostic stewardship.

Methods: A single-center, quasi-experimental study was conducted to introduce and analyze the effects of various diagnostic stewardship interventions. In April 2017 an order report was created to inform providers of patients' recent bowel movements, laxative use, and prior *Clostridioides difficile* (CD) testing (Intervention 1). In November 2017 nursing staff were empowered to not send nondiarrheal stools for testing (Intervention 2). In February 2019, an interruptive alert was implemented to prevent testing that was not indicated (Intervention 3). CD testing rates and healthcare facility-onset CDI (HO-CDI) rates were compared before and after the interventions using one-way analysis of variance (ANOVA).

Results: At baseline, testing for CD after 3 days of admission was performed at mean ± standard deviation of 15.9 ± 1.7 tests/1,000 patient-days. After Intervention 1, it decreased to 12.1 ± 1.1 tests. This further decreased to 10.6 ± 0.8 after Intervention 2 and to 8.1 ± 0.1 after Intervention 3 ($p < 0.001$). HO-CDI cases per 10,000 patient-days declined from 12.7 ± 1.4 cases at baseline to 10.7 ± 1.2 after Intervention 1, to 8.7 ± 2.4 after Intervention 2, and to 5.8 ± 0.2 after Intervention 3 ($p = 0.03$).

Conclusion: A multidisciplinary approach optimizing electronic health record support tools and leveraging nursing education can reduce both testing and HO-CDI rates while using the most sensitive testing modality.

Clostridioides difficile infection (CDI) is one of the most common health care–associated infections and is associated with high morbidity and mortality.[1] The incidence of CDI diagnosis has risen dramatically since the early 2000s,[1,2] with the initial increase attributed to the emergence of a new hypervirulent strain, NAP1/BI/027.[3] The more recent increase, however, has been attributed to the greater detection and diagnosis of CDI with the highly sensitive molecular-based tests.[4,5] The choice of laboratory test significantly influences CDI rates, with a > 50% increase in CDI diagnosis seen when performing molecular-based tests instead of stool toxin tests as part of a multistep algorithm.[4]

In 2009 the National Healthcare Safety Network (NHSN) introduced an MDRO (multidrug-resistant organism)/CDI module with two core reporting options, including Laboratory-Identified (LabID) Event reporting. The NHSN categorized positive laboratory tests for *Clostridioides difficile* (CD) as "community-onset" (CO), "community-onset healthcare facility-associated" (CO-HCFA), or "healthcare facility-onset" (HO) CDI events.[6] To allow interfacility comparison, the NHSN implemented the standardized infection ratio (SIR) in 2013, which compared the number of observed HO-CDI LabID events for each facility to the number of predicted HO-CDI events for a comparable hospital. In 2016 the Centers for Medicare & Medicaid Services added the HO-CDI SIR to the list of quality metrics used to rank hospitals and set inpatient reimbursements.[7] Although the SIR is risk adjusted for the testing method used, the adjustment formula is insufficient and underestimates the impact of testing modalities.[8]

Given that nucleic acid amplification test (NAAT) detects genes specific to toxigenic strains but not active toxin protein production, using molecular-based tests without institutional protocols can result in the overdiagnosis of CDI. Overdiagnosis and subsequent treatment of patients with colonization rather than true infection harm patients by exposing them to unnecessary antibiotics, increasing hospital length of stay, and reducing patient satisfaction.[9] In addition, it puts hospitals at significant financial risk by falsely elevating CDI rates, which are tied to value-based performance payment penalties.[10] In response, many hospitals have reverted to the less sensitive multistep algorithm

1553-7250/$-see front matter

https://doi.org/10.1016/j.jcjq.2020.05.004

involving CD toxin enzyme immunoassay (EIA) for CDI diagnosis.[10]

At our large academic medical center, CD NAAT alone is used in the diagnosis of CDI, as opposed to a multistep algorithm including the CD toxin EIA to improve sensitivity of CD diagnosis. To combat the potential for overdiagnosis, we implemented various systemwide interventions focused on CD diagnostic stewardship in the inpatient setting.

METHODS

Study Setting

We performed a single-center, quasi-experimental study to evaluate the impact of CD diagnostic stewardship interventions from January 1, 2016, to June 30, 2019. University of California, San Diego Health (UCSDH) consists of two campuses within the same health care system with a combined capacity of 799 beds.

At our institution, CD testing is performed with CD toxin B polymerase chain reaction (PCR) (Focus Diagnostics, Cypress, California) or BioFire FilmArray gastrointestinal (GI) panel (Biofire Diagnostics, Salt Lake City), which tests for bacterial (including CD), viral, and parasitic DNA, and viral RNA for various community-acquired diarrheal diseases. This study was reviewed by the Institutional Review Board at University of California, San Diego and was deemed to be exempt from approval as a category 4 study under subsection 3 for the purposes of health care operations.

Intervention

In September 2016 the CDI Task Force, which consisted of infectious diseases physicians, hospitalists, infection preventionist, nursing educator, and director of microbiology, was created. Prior to and throughout the interventions, we reviewed and quantified the frequency of attempted CD test orders that were not indicated. Consistent with the 2017 Infectious Diseases Society of America and Society for Healthcare Epidemiology of America guideline, CD testing was deemed not indicated if patients had (1) < 3 diarrheal stools in the past 24 hours, (2) laxative use within the past 24 hours, or (3) recent CD testing completed within the past 7 days.[11] Biofire GI panel was considered not indicated if ordered after 48 hours of hospital admission. GI panels completed after 2 days were of interest, as GI panels are to be used for diagnosis of community-acquired diarrheal diseases and should ideally be obtained at admission or within 2 days of admission.

In April 2017 we implemented an order report within the electronic health record (Epic; Epic Systems Corporation, Verona, Wisconsin) to provide the ordering clinicians with a clinical context regarding the CD test being ordered. Providers were informed of the following at the time of CD PCR order entry: laxative administration within the past 24 hours, CD test results within the past 7 days, and the frequency and quality of documented bowel movements within the past 24 hours (Intervention 1). In November 2017 nursing educators taught nursing staff on stool appearance using the Bristol Stool Scale[12] to reinforce the proper documentation of stool form and frequency in the electronic health record. Nursing educators then reviewed compliance with this measure, and additional training was performed in units with low compliance. Nurses were then empowered within the testing order protocol to not send stool with Bristol Stool Scale < 6 (Intervention 2). In the absence of at least 3 diarrheal stool, nurses were empowered to document "not sent based on order criteria" to inactivate the order. In February 2019 three interruptive alerts were implemented to prevent providers from ordering (1) GI panels more than 2 days after admission, (2) CD PCRs after laxative administration within 24 hours, and (3) repeat CD testing within 7 days of a resulted CD test (Intervention 3). The following subclasses of laxatives were included: bulk, emollients/fecal softeners, osmotic, saline, and stimulants. All CD test orders with laxative use within 24 hours regardless of patient risk factors required the adjudication of the on-call infectious diseases physician. To override this alert, providers were required to contact the on-call infectious diseases physician for adjudication. If deemed appropriate by the on-call infectious diseases reviewing provider, an approval code was provided for placement in the order entry to bypass the alert and continue with test ordering.

Data Collection

Epic Bugsy (Epic Systems Corporation, Verona, Wisconsin), a data reporting module used in infection surveillance, was used to obtain the aggregate number of GI panels completed after 2 days of admission, repeat CD tests within 7 days of a prior result, and all completed CD tests resulting after 3 days of admission per quarter from January 1, 2016, to June 30, 2019. The number of tests completed was normalized to 1,000 patient-days. NHSN–reported HO-CDI cases, CO-CDI cases, and our institutional HO-CDI SIR per quarter from January 1, 2016, to June 30, 2019, were obtained from UCSDH's Infection Prevention/Epidemiology Unit. NHSN–reported HO-CDI cases were normalized to 10,000 patient-days.

Statistical Analysis

Data were analyzed using SPSS Statistics 25 (IBM Corp., Armonk, New York). Continuous variables were reported as means with standard deviations (SDs). Changes in CD testing rates, CD diagnoses, and SIR at baseline and after the interventions were assessed using one-way analysis of variance (ANOVA). All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Table 1. CD Tests Completed and Percent Positive Before and After the Interventions

	Baseline	Intervention 1	Intervention 2	Intervention 3	*P* Value
All tests completed (mean ± SD/1,000 patient-days)	15.9 ± 1.7	12.1 ± 1.1	10.6 ± 0.8	8.1 ± 0.1	< 0.001
Percent positive (mean ± SD %)	8.4 ± 0.9	10.2 ± 0.3	11.9 ± 1.2	9.1 ± 0.3	< 0.001
Cost ($ mean ± SD)	21,771 ± 2,961	19,107 ± 1,017	15,988 ± 1,300	13,337 ± 576	0.002
Repeat tests within 7 days (mean ± SD/1,000 patient-days)	2.8 ± 0.8	1.4 ± 0.3	0.8 ± 0.2	0.3 ± 0.03	< 0.001
Percent positive (mean ± SD %)	6.8 ± 2.4	5.6 ± 3.6	4.2 ± 5.2	0.0 ± 0.0	0.21
GI PCR after 2 days of admission (mean ± SD/1,000 patient-days)	1.9 ± 0.3	2.2 ± 0.3	2.0 ± 0.2	1.6 ± 0.1	0.09
Percent positive (mean ± SD %)	11.5 ± 2.4	15.7 ± 2.5	18.6 ± 3.5	18.1 ± 1.5	0.01

CD, *Clostridioides difficile*; SD, standard deviation; GI PCR, gastrointestinal polymerase chain reaction.

RESULTS

Hospital-Based CD Testing Rates

During the baseline period (January 1, 2016, to March 31, 2017), a mean ± SD of 15.9 ± 1.7 CD tests/1,000 patient-days per quarter were completed among hospitalized patients after 3 days of admission. This decreased to 12.1 ± 1.1 after Intervention 1 (April 1, 2017, to September 30, 2017), to 10.6 ± 0.8 after Intervention 2 (October 1, 2017, to December 31, 2018), and to 8.1 ± 0.1 after Intervention 3 (January 1, 2019, to June 30, 2019) ($p < 0.001$) (Table 1, Figure 1a). Repeat testing for CD within 7 days of a prior result decreased from 2.8 ± 0.8 tests/1,000 patient-days per quarter at baseline to 1.4 ± 0.3 after Intervention 1, to 0.8 ± 0.2 after Intervention 2, and to 0.3 ± 0.03 after Intervention 3 ($p < 0.001$) (Table 1, Figure 1b). GI panel testing after 2 days of admission remained unchanged during the study period, from 1.9 ± 0.3 tests/1,000 patient-days per quarter at baseline to 2.2 ± 0.3 after Intervention 1, to 2.0 ± 0.2 after Intervention 2, and to 1.6 ± 0.1 after Intervention 3 ($p = 0.09$) (Table 1, Figure 1b).

The percent positivity of total tests for CD increased from 8.4% ± 0.9% to 10.2% ± 0.3% after Intervention 1 and to 11.9% ± 1.2% after Intervention 2 but dropped again to 9.1% ± 0.3% after Intervention 3 ($p < 0.001$) (Table 1). Although the percentage of repeat tests that were positive within 7 days decreased from 2.8% ± 0.8% to 1.4% ± 0.3% after Intervention 1, to 0.8% ± 0.2% after Intervention 2, and to no positive tests after Intervention 3, this was not statistically significant (Table 1). The percentage of CD positive GI panels after 2 days of admission increased from 11.5% ± 2.4% to 15.7% ± 2.5% after Intervention 1, to 18.6% ± 3.5% after Intervention 2, and to 18.1% ± 1.5% after Intervention 3 ($p = 0.01$) (Table 1).

Laboratory Cost

During the study period, estimated cost of CD PCR was $25, and GI panel was $140 for laboratory material alone. The cost of all CD tests completed after 3 days of admission was $21,771 ± $2,961 per quarter at baseline and decreased to $19,107 ± $1,017 after Intervention 1. The cost decreased to $15,988 ± $1,300 after Intervention 2 and to $13,337 ± $576 after Intervention 3 ($p = 0.002$) (Table 1). Cost savings from CD treatment, personnel time, length of stay, or patient isolation efforts were not included in this calculation.

CD Test Orders Not Meeting Indication

The absence of diarrhea was the most common reason for a not indicated CD testing order. On average, 53.9 ± 11.4 orders did not meet the criteria for diarrhea. Laxative use within 24 hours was seen in 28.7 ± 7.2 orders per week. GI panels after 48 hours of admission were ordered 8.6 ± 3.7 times per week, and repeat CD tests within 7 days were ordered 7.7 ± 4.2 times per week (Figure 2).

CDI Diagnoses and SIR

NHSN–reported HO-CDI cases per 10,000 patient-days declined from 12.7 ± 1.4 per quarter at baseline to 10.7 ± 1.2 after Intervention 1, to 8.7 ± 2.4 after Intervention 2, and to 5.8 ± 0.2 after Intervention 3 ($p = 0.003$) (Table 2, Figure 1c). NHSN–reported CO-CDI cases per quarter remained unchanged with each intervention ($p = 0.80$) (Table 2, Figure 1c). SIR was 1.05 ± 0.24 at baseline and 1.09 ± 0.16 after Intervention 1. There was a downward trend in SIR to 0.99 ± 0.20 after Intervention 2 and to 0.71 ± 0.06 after Intervention 3, though this change was overall not statistically significant ($p = 0.24$) (Table 2, Figure 1d).

DISCUSSION

Our results emphasize that CDI rates based on positive NAAT alone led to an overestimation of the true burden of disease but that HO-CDI rate can be dramatically improved with diagnostic stewardship. In addition, we reduced the testing frequency for CD tests after 3 days of admission while increasing the percent positivity, suggesting that testing was performed when high index of suspicion for CD was present.

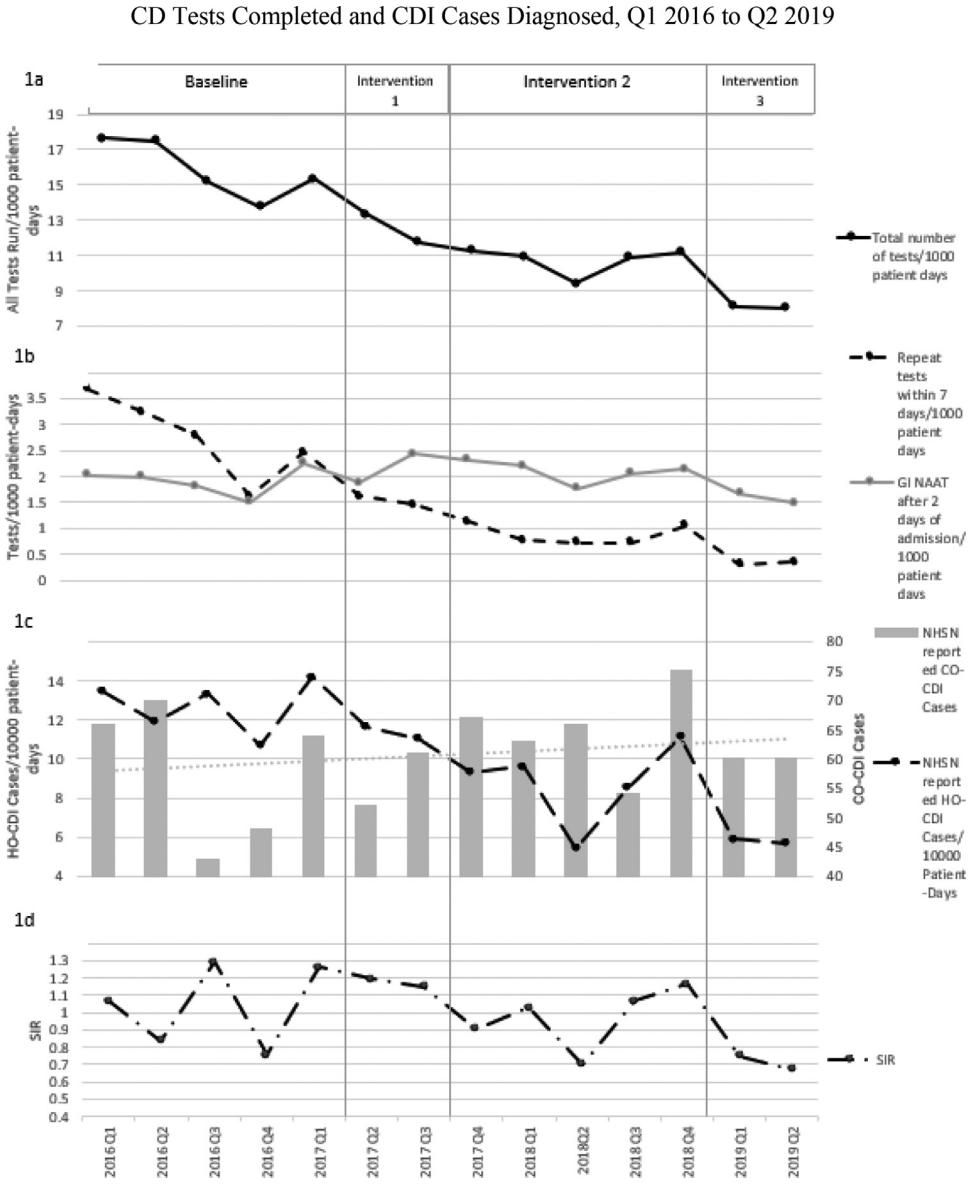

Figure 1: Shown in 1a are the total CD tests completed per quarter at baseline and throughout Interventions 1–3. 1b shows repeat CD tests within 7 days and GI PCR after 2 days of admission completed per quarter at baseline and throughout Interventions 1–3. Gray line represents GI PCR after 2 days of admission and dotted line represents repeat CD tests within 7 days. Shown in 1c are NHSN–reported HO- and CO-CDI cases diagnosed per quarter at baseline and throughout Interventions 1–3. Bar graph represents CO-CDI cases diagnosed, and dashed line represents HO-CDI cases diagnosed. 1d shows SIR per quarter at baseline and throughout Interventions 1–3. CD, *Clostridioides difficile*; CDI, *Clostridioides difficile* infection; Q, quarter; GI NAAT, gastrointestinal nucleic acid amplification test; HO-CDI, healthcare facility-onset *Clostridioides difficile* infection; NHSN, National Healthcare Safety Network; CO-CDI, community-onset *Clostridioides difficile* infection; SIR, standardized infection ratio; GI PCR, gastrointestinal polymerase chain reaction; Q, quarter.

Table 2. *Clostridioides difficile* Cases Diagnosed Before and After the Intervention

	Baseline	Intervention 1	Intervention 2	Intervention 3	*P* Value
NHSN–reported HO-CDI cases (mean± SD/10,000 patient-days)	12.7 ± 1.4	10.7 ± 1.2	8.7 ± 2.4	5.8 ± 0.2	0.003
NHSN–reported CO-CDI cases (mean ± SD)	58.2 ± 11.9	60.0 ± 7.6	64.5 ± 8.7	60.0 ± 0.0	0.80
SIR (mean ± SD %)	1.05 ± 0.24	1.09 ± 0.16	0.99 ± 0.20	0.71 ± 0.06	0.24

NHSN, National Healthcare Safety Network; HO-CDI, healthcare facility-onset *Clostridioides difficile* infection; SD, standard deviation; CO-CDI, community-onset *Clostridioides difficile* infection; SIR, standardized infection ratio.

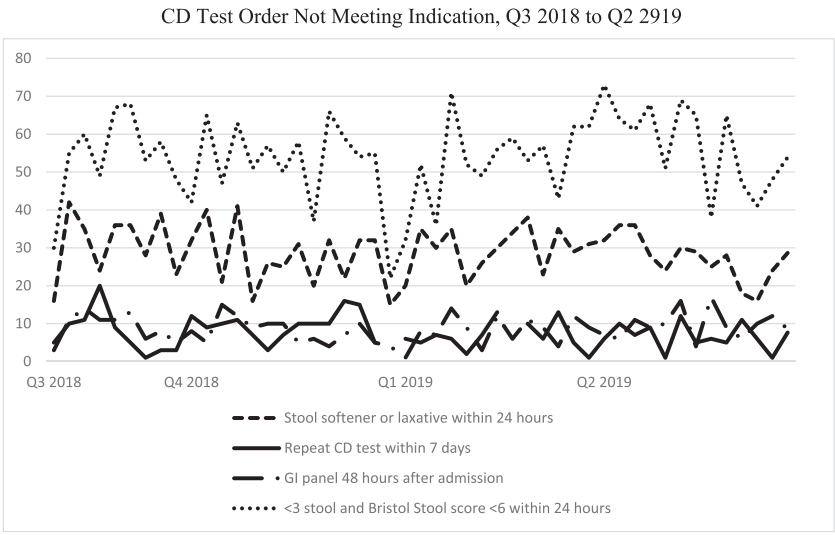

Figure 2: Shown are the number of times an alert was triggered for following reason: laxative use within 24 hours, repeat CD test within 7 days, GI panel 48 hours after admission, < 3 stools and Bristol Stool score < 6 within 24 hours. CD, *Clostridioides difficile*; Q, quarter; GI, gastrointestinal.

Prior studies have reported various approaches to implementing CD diagnostic stewardship. Use of computerized clinical decision support including "hard stops" has decreased CD testing rates but showed variable impact on HO-CDI rates.[13–19] Educational interventions informing health care providers on the limitations of PCR reduced overall CD testing but did not decrease HO-CDI rates.[20] Hospitalwide educational campaigns combined with measures taken by the microbiology laboratory to reject nonliquid stool samples or delayed receipt of stool samples led to marked reductions in CD testing and CDI rates.[21] At our institution, prior protocols that made the microbiology laboratory responsible for rejecting nonliquid stool samples were met with limited success and pushback from providers.

Our approach to CD diagnostic stewardship engaged nursing staff and leveraged computerized clinical decision support while limiting the need for direct oversight by infectious diseases physicians to scenarios when CD testing outside of guidelines was felt to be clinically indicated. Although some initiatives required increasing workforce, which make interventions more costly, time-consuming, and more difficult to sustain,[22] our multidisciplinary approach leveraging electronic health record support tools and nursing education reduced testing frequency and HO-CDI rates with minimal increase in workforce, resulting in significant cost savings. Per providers, the interruptive alert minimally interfered with the workflow and did not add significant burden to the workload.

Recently, some groups have expressed concerns that diagnostic stewardship efforts such as requiring the discontinuation of laxatives may delay the diagnosis of CDI and result in serious adverse outcomes.[23] However, at our institution, at most 3.4% of cases were delayed due to the interruptive alert in patients with laxative use within 24 hours. In addition, there were no severe CDI cases that led to ICU admission, colectomy, or death.[24]

Some have advocated for a two-step algorithm with glutamate dehydrogenase (GDH) and CD toxin A/B EIA to avoid the risk of overdiagnosis with NAATs, but this does not address the problem of excessive test ordering by providers. It does, however, decrease the sensitivity of testing and increase time to results.[25] The GDH assays have a lower sensitivity for specimens positive for ribotypes other than 027, which can affect the detection of CDI.[26] In addition, studies have reported that 12% to 13% of samples required additional testing with molecular tests or cell culture for definitive results due to discrepant results in GDH and toxin A/B EIA.[27,28] Although such three-step testing can reduce the number of specimens that would require the more expensive molecular tests, this increases time to result.[25] Instead, enforcing limits on overall testing of liquid stool in hospitalized patients via low-cost interventions can minimize false positive results.

Limitations to this study include the single academic medical center and the quasi-experimental study design. No other major interventions occurred concurrently, so it is unlikely that other factors had major contributions to the changes seen in CD test ordering and diagnoses rates during the time of this study. CO-CDI rates remained similar over time as well. Given that all three interventions were implemented sequentially together, we cannot directly estimate the impact of a single intervention on test ordering and CDI rates. In addition, the number of times in which the alert was triggered for CD test order not meeting indication remained relatively unchanged from quarter 3 2018 to quarter 2 2019. Unfortunately, there were shortcomings in retrieving the number of times in which the alert was triggered prior to quarter 3 2018. Given this is reflective of only the last four quarters of the study period, its impact on not

indicated CD test order was unable to be fully captured. Finally, although the absence of at least 3 diarrheal stools within the past 24 hours was by far the most common reason for CD test order not indicated throughout the interventions, we opted not to pursue it beyond informational purposes until documentation on frequency and quality of stools in the electronic medical records became highly consistent and accurate. With stepwise improvement on the accuracy of this process measure, future focus will concentrate on implementing an interruptive alert on patients without diarrhea. We expect that this will lead to a further decline in unnecessary tests and optimize the accuracy of CDI diagnosis.

CONCLUSION

Although decreases in true HO-CDI can be obtained through infection prevention practices and antimicrobial stewardship initiatives,[29,30] diagnostic stewardship is key to guiding appropriate clinical behavior to limit testing to patients in whom a high index of suspicion is present. Optimizing test utilization to reduce unnecessary tests and diagnostic errors remains crucial in CDI diagnosis, allowing for institutions to better focus on prevention of true CDI through improved infection prevention and antibiotic stewardship efforts.

Conflicts of Interest. All authors report no conflicts of interest.

Minji Kang, MD, is Clinical Fellow, Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California, San Diego (UCSD). **Shira R. Abeles, MD**, is Assistant Clinical Professor, Division of Infectious Diseases and Global Public Health, UCSD. **Robert El-Kareh, MD**, is Assistant Professor, Divisions of Hospital Medicine and Biomedical Informatics, Department of Medicine, UCSD. **Randy A. Taplitz, MD**, is Professor, Division of Infectious Diseases and Global Public Health, and Clinical Director, Infection Prevention and Clinical Epidemiology, UCSD. **Elizabeth Nyheim** is Director of Nursing Quality, Education, Development & Research, Department of Nursing, UCSD. **Sharon L. Reed, MD**, is Director of the Clinical Microbiology Laboratory. **Ian H. Jenkins, MD**, is Associate Professor, Division of Hospital Medicine, UCSD. **Gregory B. Seymann, MD**, is Professor, Division of Hospital Medicine, UCSD. **Frank E. Myers, MA**, is Interim Director, Infection Prevention and Clinical Epidemiology, UCSD. **Francesca J. Torriani, MD**, is Professor, Division of Infectious Diseases and Global Public Health, and Medical Director, Infection Prevention and Clinical Epidemiology, UCSD. Please send correspondence to Francesca J. Torriani, ftorriani@ucsd.edu.

REFERENCES

1. Lessa FC, et al. Burden of *Clostridium difficile* infection in the United States. N Engl J Med. 2015 Feb 26;372:825–834.
2. Zilberberg MD, Shorr AF, Kollef MH. Increase in adult *Clostridium difficile*–related hospitalizations and case-fatality rate, United States, 2000–2005. Emerg Infect Dis. 2008;14:929–931.
3. McDonald LC, et al. An epidemic, toxin gene-variant strain of *Clostridium difficile*. N Engl J Med. 2005 Dec 8;353:2433–2441.
4. Longtin Y, et al. Impact of the type of diagnostic assay on *Clostridium difficile* infection and complication rates in a mandatory reporting program. Clin Infect Dis. 2013;56:67–73.
5. Gould CV, et al. Effect of nucleic acid amplification testing on population-based incidence rates of *Clostridium difficile* infection. Clin Infect Dis. 2013;57:1304–1307.
6. Dudeck MA, et al.. Centers for Disease Control and Prevention. Risk Adjustment for Healthcare Facility-Onset *C. difficile* and MRSA Bacteremia Laboratory-Identified Event Reporting in NHSN, Mar 12. Accessed May 25, 2020. https://www.cdc.gov/nhsn/PDFs/mrsa-cdi/RiskAdjustment-MRSA-CDI.pdf.
7. Centers for Medicare & Medicaid Services Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and policy changes and fiscal year 2017 rates; quality reporting requirements for specific providers; graduate medical education; hospital notification procedures applicable to beneficiaries receiving observation services; technical changes relating to costs to organizations and Medicare cost reports; finalization of interim final rules with comment period on LTCH PPS payments for severe wounds, modifications of limitations on redesignation by the Medicare Geographic Classification Review Board, and extensions of payments to MDHs and low-volume hospitals. Final rule. Fed Regist.. 2016 Aug 22;81:56762–567345. Accessed May 25, 2020. https://www.govinfo.gov/content/pkg/FR-2016-08-22/pdf/2016-18476.pdf .
8. Marra AR, et al. Failure of risk-adjustment by test method for *C. difficile* laboratory-identified event reporting. Infect Control Hosp Epidemiol. 2017;38:109–111.
9. Lagu T, et al. The impact of hospital-onset *Clostridium difficile* infection on outcomes of hospitalized patients with sepsis. J Hosp Med. 2014;9:411–417.
10. Diekema DJ. Rising stakes for health care-associated infection prevention: implications for the clinical microbiology laboratory. J Clin Microbiol. 2017;55:996–1001.
11. McDonald LC, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis.. 2018 Mar 19;66:987–994.
12. O'Donnell LJ, Virjee J, Heaton KW. Detection of pseudodiarrhoea by simple clinical assessment of intestinal transit rate. BMJ. 1990 Feb 17;300:439–440.
13. Madden GR, et al. Reduced *Clostridium difficile* tests and laboratory-identified events with a computerized clinical decision support tool and financial incentive. Infect Control Hosp Epidemiol. 2018;39:737–740.
14. White DR, et al. The impact of a computerized clinical decision support tool on inappropriate *Clostridium difficile* testing. Infect Control Hosp Epidemiol. 2017;38:1204–1208.
15. Nicholson MR, et al. The use of a computerized provider order entry alert to decrease rates of *Clostridium difficile* testing in young pediatric patients. Infect Control Hosp Epidemiol. 2017;38:542–546.
16. Friedland AE, et al. Use of computerized clinical decision support for diagnostic stewardship in *Clostridioides difficile* testing: an academic hospital quasi-experimental study. J Gen Intern Med. 2019;34:31–32.
17. Khoury JA, et al. Sustained reduction in rates of hospital-onset *Clostridium difficile* infection using an automated

electronic health record protocol. Am J Infect Control. 2018;46:542–548.
18. Mizusawa M, et al. Prescriber behavior in *Clostridioides difficile* testing: a 3-hospital diagnostic stewardship intervention. Clin Infect Dis. 2019 Nov 13;69:2019–2021.
19. Drees M, et al. Testing stewardship: a 'hard stop' to reduce inappropriate *C. diff* testing. Open Forum Infect Dis. 2017;4(Suppl 1):S1–S2.
20. Kociolek LK, et al. Impact of a healthcare provider educational intervention on frequency of *Clostridium difficile* polymerase chain reaction testing in children: a segmented regression analysis. J Pediatric Infect Dis Soc. 2011 Jun 1;6:142–148.
21. Yen C, et al. Reducing *Clostridium difficile* colitis rates via cost-saving diagnostic stewardship. Infect Control Hosp Epidemiol. 2018;39:734–736.
22. Christensen AB. et al. Diagnostic stewardship of *C. difficile* testing: a quasi-experimental antimicrobial stewardship study. Infect Control Hosp Epidemiol. 2019;40:269–275.
23. White NC, et al. Laxative use does not preclude diagnosis or reduce disease severity in *Clostridiodes difficile* infection. Clin Infect Dis. Epub. 2019 Oct 4.
24. Torriani F, et al. *C. difficile* infection (CDI) testing stewardship inclusive of hard stop in the presence of laxative use is an effective and safe strategy with expert clinical evaluation. In: presentation scheduled for Society for Healthcare Epidemiology of America Conference, Atlanta [conference canceled].
25. Eastwood K, et al. Comparison of nine commercially available *Clostridium difficile* toxin detection assays, a real-time PCR assay for *C. difficile* tcdB, and a glutamate dehydrogenase detection assay to cytotoxin testing and cytotoxigenic culture methods. J Clin Microbiol. 2009;47:3211–3217.
26. Tenover FC, et al. Impact of strain type on detection of toxigenic *Clostridium difficile*: comparison of molecular diagnostic and enzyme immunoassay approaches. J Clin Microbiol. 2010;48:3719–3724.
27. Quinn CD, et al. C. Diff Quik Chek Complete enzyme immunoassay provides a reliable first-line method for detection of *Clostridium difficile* in stool specimens. J Clin Microbiol. 2010;48:603–605.
28. Sharp SE, et al. Evaluation of the C.Diff Quik Chek Complete assay, a new glutamate dehydrogenase and A/B toxin combination lateral flow assay for use in rapid, simple diagnosis of *Clostridium difficile* disease. J Clin Microbiol. 2010;48:2082–2086.
29. Price J, et al. Impact of an intervention to control *Clostridium difficile* infection on hospital- and community-onset disease; an interrupted time series analysis. Clin Microbiol Infect. 2010;16:1297–1302.
30. Barker AK, Alagoz O, Safdar N. Interventions to reduce the incidence of hospital-onset *Clostridium difficile* infection: an agent-based modeling approach to evaluate clinical effectiveness in adult acute care hospitals. Clin Infect Dis. 2018 Apr 3;66:1192–1203.