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Reduction of *C. difficile* standardized infection ratio by limiting testing in patients with low probability of infection

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ABSTRACT

Background: *Clostridium difficile* is a spore-forming, anaerobic gram-positive bacillus that is a major cause of healthcare-associated infections. *C. difficile* can be transmitted from symptomatic individuals as well as from asymptomatic carriers, however, compliance with recommended precautions can minimize the risk of transmission. Testing of patients with a low probability of *C. difficile* Infection (CDI), based on the presence or absence of risk factors and symptoms, can result in the identification of asymptomatic carriers. This can lead to 1) the unnecessary institution of contact isolation; 2) unnecessary administration of antibiotics for the treatment of *C. difficile*; and 3) an increased length of stay, all of which contribute towards increased healthcare-related expenditures on an individual and system wide level. In order to reduce the amount of unnecessary testing and subsequent treatment of patients colonized, but not infected with *C. difficile*, a "C. diff SWAT team" was created.

Methods: Starting January 2015, all orders for *C. difficile* toxin B gene (PCR) at Clements University Hospital (CUH) placed or collected while in an inpatient location were considered. CUH is a 460-bed acute care hospital associated with the University of Texas Southwestern Medical School. The following measures were monitored using individual-moving range control charts (XmR):

Outcomes measures: (1) National Healthcare Safety Network (NHSN) *C. difficile* hospital-onset standardized infection ratio (SIR) and (2) inpatient facility *C. difficile* healthcare facility-onset incidence rate per 10,000 patient days.

Process measures: (1) percentage of *C. difficile* testing ordered when laxatives were given within the prior 48 hours, (2) percentage of *C. difficile* samples ordered on day 1-3 but collected on hospital day 4 or greater, and (3) percentage of samples collected greater than 24 hours after the order was placed.

Balances measures: Total community-onset *C. difficile*.

Results: Both the process measures and the NHSN *C. difficile* hospital onset rate per 10,000 days demonstrate statistically significant shifts on the control charts. Overall, the SIR in 2015 quarter Q1-Q3 was 1.20 (107/89.38), and from initiation of the project through 2017 Q2, the SIR is 0.87 (151/174.28) ($p = 0.011$).

Conclusion: With the aid of clinical decision support (CDS) and clinical education, the project team was able to successfully hardwire *C. difficile* testing and diagnosis best practice guidelines into the diagnostic pathway and significantly reduce the *C. difficile* SIR and subsequent burden of treatment.

INTRODUCTION

Clostridium difficile is a spore-forming, anaerobic gram-positive bacillus that is a major cause of healthcare-associated infections [1]. Evidence shows that only 1-2% of hospitalized patients may have active *C. difficile* infection (CDI), while up to 20% may actually be colonized with *C. difficile* [3]. The rates of CDI have risen nationally, partly thought to be due to inappropriate testing in patients with a low probability of infection, as well as the use of the PCR (polymerase chain reaction) assay for the toxin B gene. It is a sensitive diagnostic modality able to detect a small amount of genetic material, but cannot distinguish between active infection or colonization. A positive test in an asymptomatic individual would essentially identify patients who are colonized and not infected, which can lead to
1) the unnecessary institution of Contact isolation;
2) unnecessary administration of antibiotics for the treatment of *C. difficile*; and 3) an increased length of stay, all of which contribute to increased healthcare-related expenditures on an individual and system-wide level [3].

Problem description

Inappropriate ordering of *C. difficile* testing with subsequent identification of colonized (rather than infected) patients can harm the patient and the institution in several ways.

1) The administration of antibiotics for the treatment of *C. difficile* is known to disrupt the normal flora of the intestine and, in the case of oral vancomycin, may allow the proliferation of vancomycin-resistant enterococci (VRE) [4].
2) A diagnosis of *C. difficile* based primarily on a positive PCR test can distract clinicians along the diagnostic pathway, delaying the identification of the actual cause of illness and having a negative impact on patient treatment [5].

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3) The judicious use of testing for *C. difficile* can protect the patient from experiencing any feelings of social or physical isolation that can result from being placed in isolation. In our institution, contact precautions for CDI constitutes the use of gloves, gown and subsequent hand washing with soap and water. For example, staff are required to wear personal protective equipment (which would include at the least, an impervious isolation gown and gloves) when entering the rooms of known or suspected *C. difficile* patients to prevent the risk of acquiring and transmitting *C. difficile* spores throughout the hospital environment. The financial cost of contact precautions is due to usage of disposable gowns, gloves and medical equipment, as well as the enhanced cleaning of these rooms with Oxycide and a UV light disinfection system (Xenex). The psychological impact of contact isolation on patients is related to fewer room entries by staff and limited physical interaction with others; this can also consequently impact patient and family satisfaction [6].

Rationale

Diagnostic stewardship refers to choosing the right diagnostic assay for the right reason at the right time for the right patient. Modifying the ways in which tests are ordered, performed and resulted can result in improving the quality of patient care and subsequent clinical outcomes. The diagnostic pathway encompasses the three phases of lab testing: pre-analytic, analytic, and post-analytic. Leveraging efforts to address the pre-analytic phase of care can help prevent the subsequent consequences of inappropriate testing.

The Society for Healthcare Epidemiology of America (SHEA) and Infectious Diseases Society of America (IDSA) joint expert panel established best practice guidelines on the testing and diagnosis of *C. difficile* [7]. Recommendations adopted from SHEA-IDSA are as follows: (1) testing should only be performed on diarrheal stool, and (2) the testing of stool from asymptomatic patients is not advisable [7].

Specific aims

Stewardship of diagnostic testing and "choosing wisely" are important concepts to control cost in care delivery and to avoid unnecessary treatment. Our approach to improve diagnostic stewardship included clinical decision support to guide testing and analytic interventions to improve Best Practice Advisory (BPA) utility. Working as a multidisciplinary team allowed for a diversified perspective and interdepartmental project buy-in. The project team aim was to reduce *C. difficile* SIR from 1.20 to 0.92[1] for Clements University Hospital (CUH).

METHODS

Context

The project was implemented via rapid cycle changes using performance improvement methodologies such as Plan-Do-Study-Act. Each new improvement change was selected by the project team for implementation. Compliance with the change was monitored and infection rates were analyzed for evaluation of efficacy.

All positive *C. difficile* tests in which a stool was collected after hospital day 3 were reviewed thoroughly by the Department of Infection Prevention & Control (IPC). These positive tests were divided into one of two categories (HO vs. HAI). HO cases were defined as a positive PCR test for *C. difficile* toxin, but the positive test was attributed to colonization or infection upon admission. Common HO scenarios included: diarrhea that was attributed to laxative usage without evidence of colitis, history of *C. difficile* colonization, delay in stool being sent to the lab, and inappropriate ordering of testing in patients with less than three watery stools in a 24-hour time period. HAI cases were defined as positive PCR test for *C. difficile* toxin and the patients were truly infected showing signs and symptoms of CDI such as fever, leukocytosis, and abdominal pain.

A multidisciplinary "*C. difficile* SWAT team" was created to address these concerns. The core project team members included representatives from Infection Prevention, Laboratory Services, Nursing, Medical Staff, Quality Analytics, and Performance Improvement. Reporting of progress was presented at periodic intervals to the hospital Performance Improvement Committee, the Medical Executive Committee, and the Hospital Board. Expectations and requirements established by Executive sponsorship were identified at project kickoff and used as a project tollgate to validate quality parameters and customer requirements.

To reduce the incidence of inappropriate ordering, the project team opted to emphasize *C. difficile* diagnosis and rejection guidelines through the use of 1) clinical decision support (CDS) and 2) revised lab policy:

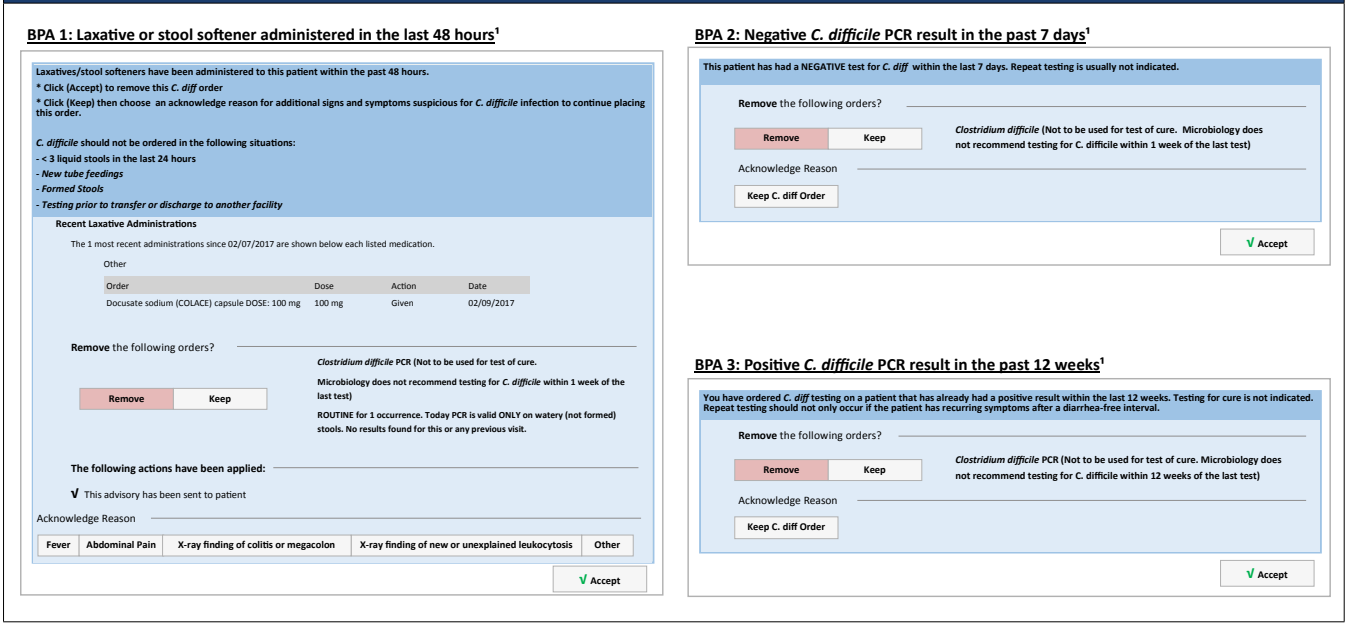
1) CDS design was based on discouraging (a) the testing of patients for whom laxatives, stool softeners or enemas have been administered in the past 48 hours, (b) "test of cure" or ordering test for patients treated for *C. difficile* infection after symptom resolution, or (c) repeat testing within one week of last test due to ongoing concern for CDI. These testing algorithms are founded on best practice and supported by CDS to guide ordering habits. This is preferable to relying on clinical education, which is subject to the deterioration of recall.
2) The Cepheid Xpert *C. difficile/Epi* Assay is a rapid, automated in vitro diagnostic test for detection of toxin producing *C. difficile* directly from unformed stool specimens. If the sample fails to meet specimen requirements (i.e., the specimen does not conform to the container), it would be subject to rejection per lab policy. The lab resolved to emphasize policy as of November 2015.

Interventions

1. *C. difficile* notifications for providers: All Hospital Onset (HO) C. diff Laboratory Identified (LabID) events are reviewed by Infection Prevention and a clinical summary is provided in an email notification.

[1] At project kickoff, 0.92 represented the 50th percentile of facilities reporting.

FIGURE 1: C. difficile Best Practice Advisories*



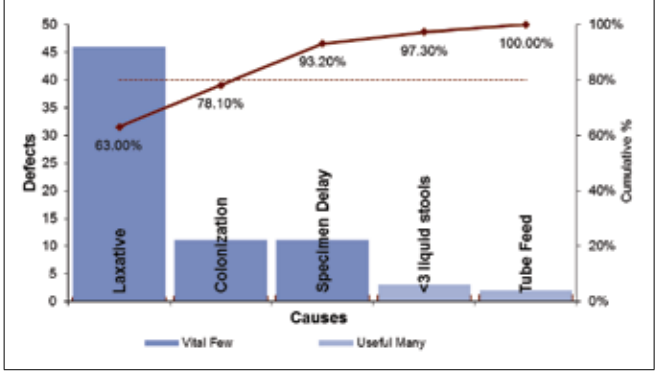
* Figure 1 depicts generic renderings of Best Practice Advisories.

2. Lab rejection of formed stool specimens: The *C. difficile* PCR assay is only intended for use on diarrheic stool samples that conform to the shape of the collection container. Three or more diarrheic stools within a 24-hour time period are required before testing should be considered. The lab is empowered to reject specimens that do not meet the requirements of the test or the clinical criteria for CDI (no diarrhea).
3. *C. difficile* order laxative question: a clinical justification is required if the ordering provider responds affirmatively to the question, "Have laxatives, stool softeners or enemas been administered in the last 48 hours?"
4. Nursing cancellation of *C. difficile* orders after 24 hours: Nurses may discontinue *C. difficile* testing orders if no specimen was collected in the 24 hours after the order was placed and the provider agreed with the cancellation in the text of the original order.
5. Clinical Decision Support using BPAs (Best Practice Advisories):
    1. Laxative or stool softener administered in the last 48 hours (modified from 24 to 48 hours in February 2017) – the BPA will prompt providers entering an order for *C. difficile* PCR when the patient has had a stool softener, laxative, and/or enema administered in the past 48 hours. The provider may either remove or keep the order and provide an explanation in the comments box.
    2. Negative *C. difficile* PCR result in the past seven days – the BPA will prompt providers entering an order for *C. difficile* PCR when the patient has had a negative *C. difficile* PCR result in the past 7 days. The provider may either remove the order or keep the order and provide an explanation in the comments box.
    3. Positive *C. difficile* PCR result in the past 12 weeks – the BPA will prompt providers entering an order for *C. difficile* PCR when the patient has had a positive *C. difficile* PCR result in the past 12 weeks. The provider may either remove the order or keep the order and provide an explanation in the comments box.

Measures

Beginning in January 2015, all *C. difficile* PCR orders placed while in an inpatient location or collected at an inpatient location were considered. Process and outcome measures were tracked using individual-moving range control charts (XmR). In addition, a Pareto chart of frequent causes revealed that laxative use was the most common factor involved (Figure 2).

FIGURE 2: 2016 UTSW HO C. difficile Attribution Types



Process and balance measures were determined based on the National Healthcare Safety Network (NHSN) reporting definition of laboratory-identified CDI event (LabID). At least 12 months of data were collected for each process and outcome measure to establish pre-intervention baselines. The Center for Disease Control (CDC) will factor Community-Onset (CO) *C. difficile* into the risk adjustment calculation of CDI SIR, hence this balance

measure was included to assess the impact of lab's rejection of formed stool samples on the CO count [9]. The project team also used the Pareto chart to analyze aggregate hospital-onset data by attribution type (Figure 2). The Pareto chart guided our efforts to focus on the few causes that produce more than 80% of defects. Optimizing resources proved to be critical in the eventual realization of our project goal.

- Outcomes measure: NHSN *C. difficile* hospital onset standardized infection ratio.[2]
- Outcomes measure: Inpatient facility *C. difficile* healthcare facility-onset incidence rate per 10,000 patient days.
- Process measure #1: the percentage of *C. difficile* testing ordered when laxatives had been given within the prior 48 hours.
- Process measure #2: the percentage of samples collected on hospital day 4 or greater that were ordered on day 1-3.
- Process measure #3: the percentage of samples collected greater than 24 hours after the order.
- Balance measure #1: total community-onset *C. difficile*.

RESULTS

Outcomes measures

The SIR in calendar 2015 Q1 - Q3[3] was 1.20 (107/89.38). From initiation of the project through 2017 Q2, the SIR is 0.87 (151/174.28) ($p = 0.011$) (Table 1; Figure 3). The XmR control charts demonstrated two statistically significant declines in the healthcare facility-onset incidence rate per 10,000 patient days at CUH (Figure 4). The process has demonstrated stability since December 2016.

TABLE 1: Healthcare Facility-Onset Change in Incidence

	Pre-Intervention	Post-Intervention
Observed	107	151
Expected	89.38	174.28
SIR	1.197	0.866

Relative ratio of SIRs (data column 2/data column 1: 0.866/1.97=0.723 (72.3%)
Two-tailed p-value: 0.0114
95% Confidence Interval: 0.565, 0.929

Process measures

Process measure #1 (percent of *C. difficile* orders with laxatives given <48 hours prior to order improved from) improved from its initial baseline average of 26.39% (January – October 2015) to a re-baselined average of 11.24% (February 19 – April 9, 2017). This was confirmed by a signal of process change indicated by 8 consecutive data points below the baseline (February 19 – April 9, 2017). The change was observed 2-8 months following the launch of the *C. difficile* laxatives BPA (September 2016) and the implemented changes to the *C diff BPA* timeframe (February 2017; 24 to 48 hours).

Process measure #2 (the percentage of samples collected on hospital day 4 or greater that were ordered on day 1-3) improved from its initial baseline average of 6.4% (January – December 2015) to 3.4% (January – November 2016). The process change was observed 4 months post the implementation of the nursing cancellation of C. diff orders after 24 hours. The post-intervention group is within expected boundaries, indicating the process is in control.

Process measure #3 (the percentage of samples collected greater than 24 hours after the order) improved from its initial baseline average of 10.9% (January 2015 – March 2016) to 5.8% (April – November 2016). The process change was observed 3 months subsequent to the initiation of nursing cancellation of *C. diff* orders after 24 hours. The post-intervention group performance is being maintained within the control limits.

Balance measures

Balance measure # 1 (total community onset *C. difficile)* declined from its initial baseline average of 30.5 per month (January 2015 – October 2016) to 18.4 per month (November 2016 – October 2017). The decrease correlated with Lab's rejection of formed stool specimens, beginning in November 2016.

Summary

The process measures and the NHSN *C. difficile* hospital-onset rate per 10,000 days demonstrated statistically significant control chart shifts (Figure 2). The CO count decreased substantially and resulted in an SIR average difference of 0.1 – 0.2 but ultimately did not offset the benefits of the lab's rejection of formed stool samples. The project successfully achieved its SIR target as well as the process targets for each of the indicated measures.

DISCUSSION

CDI is a publicly reported hospital acquired infection per the Affordable Care Act's Hospital Acquired Condition (HAC) Reduction Program. Pursuant to HAC, relative institutional performance above or below the 75th percentile nationally can affect payments from the Centers for Medicaid and Medicare Services (CMS). In quarter Q3 of calendar year 2015, CUH performed at the 72nd percentile for *C. difficile* SIR. The SIR is calculated by the NHSN and is a comparison between the observed number of infections that occur in a facility to the number expected (or predicted) to have occurred, based on the national baseline. A positive *C. difficile* test that results on day 4 or later of the patient's admission factors into the standardized infection ratio (SIR) calculation. Being a LabID event, consideration for clinical symptoms is not taken into account and, thus, CMS does not differentiate between colonized and infected patients [8]. Inappropriate testing leading

[2] Not monitored in an XmR due to limited data points.

[3] The project team could not continue comparing beyond 2015 into 2016 using 2014 data due to the change in NHSN risk modeling, switching to their new 2015 re-baseline version.

FIGURE 3: CUH Facwideln *C. diff* SIR

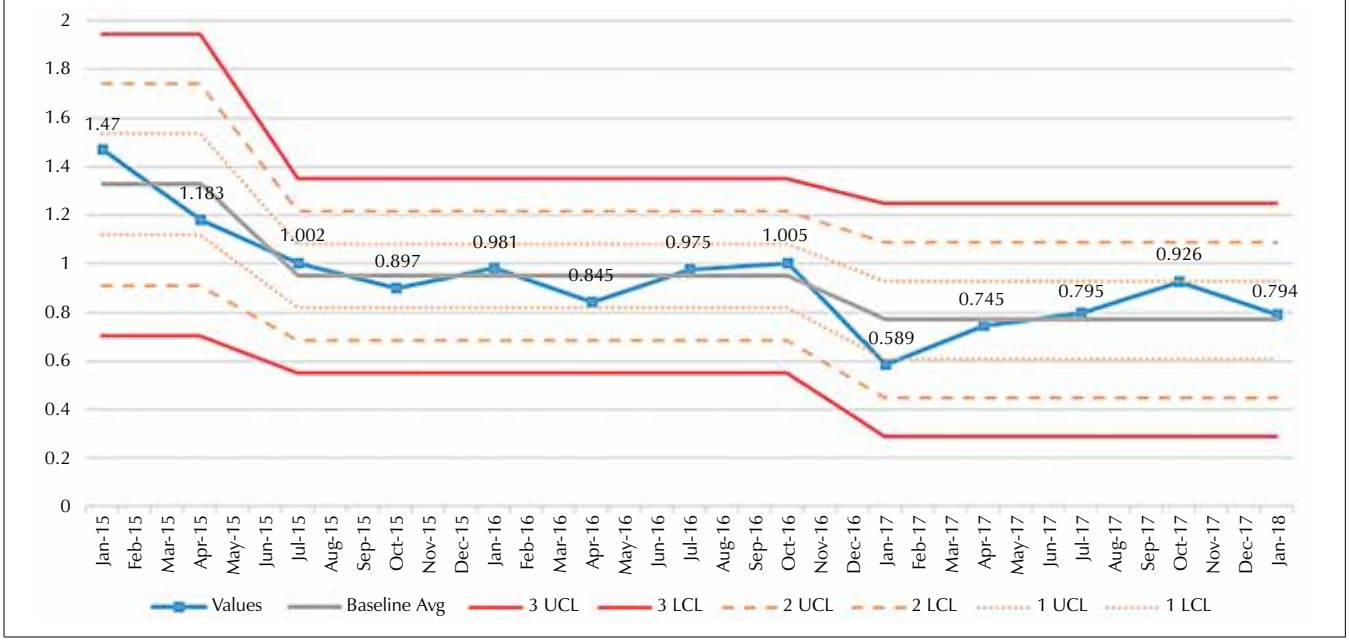
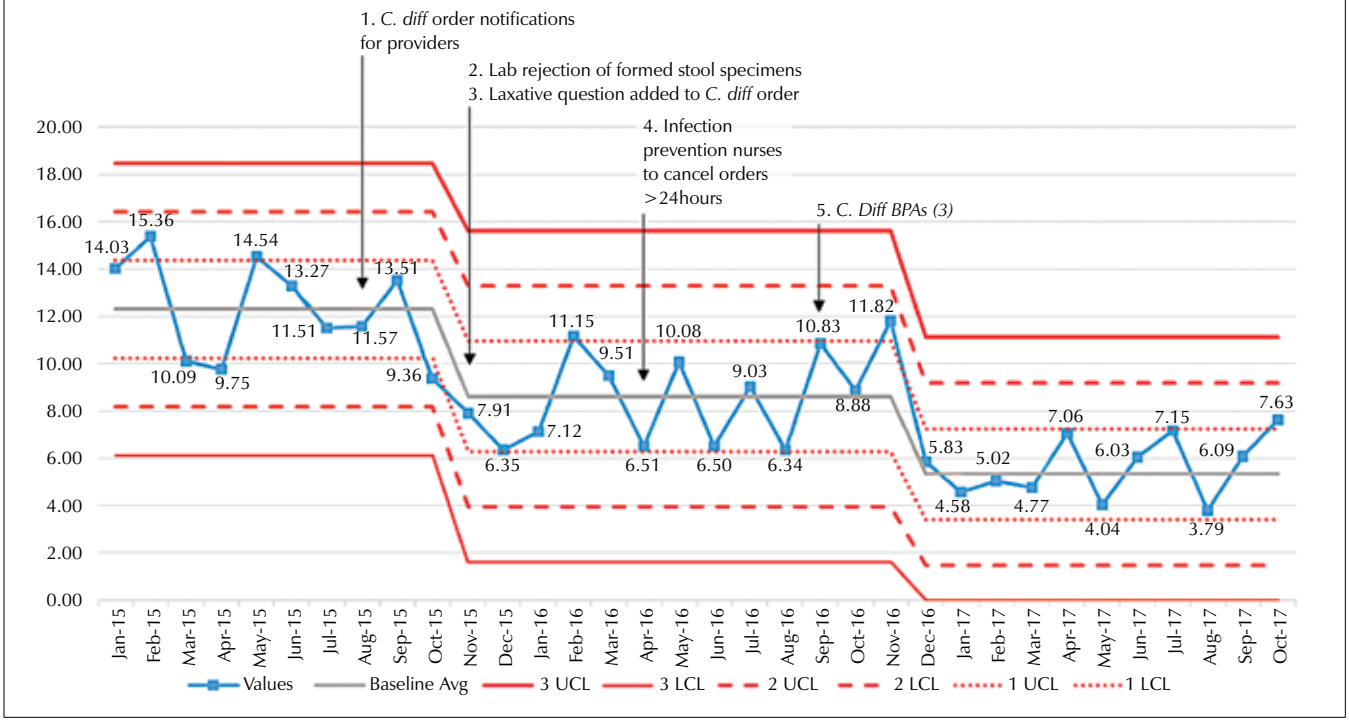


FIGURE 4: CUH Inpatient Facility *C. diff* Healthcare Facility-Onset Incidence Rate per 10,000 Patient Days



to the identification of colonized patients increases the number of LabID events which negatively affects the SIR, can result in a monetary penalty and reflects poorly on the institution.

Limitations

With the in-depth analysis and categorization of positive tests as HO or HAI, it became more evident that improvements could be made to more appropriately use the *C. difficile* PCR assay. These areas included: 1) re-education of laboratory personnel to reject formed stools; 2) reminding staff to send stool within the first 3 days of admission if CDI suspected; 3) providing nursing staff with the authority to cancel an outstanding order for *C. difficile* PCR when a stool sample was not collected within 24 hours of the order; and 4) not testing within 48 hours of administering stool softeners, laxatives and enemas. Positive tests for *C. difficile* in the setting of

diarrhea associated with laxative usage was a significant problem and accounted for the majority of patients thought to be colonized and not truly infected. The creation of Best Practice Advisories and having specific questions in the order set resulted in a reduction in the overall amount of testing. This, in conjunction with other measures to reduce the burden of *C.difficile* in the hospital, resulted in a decrease in true infections from 40%
pre-intervention to 31% post intervention.

Due to the financial incentive for hospitals with lower rates of CDI, under-reporting has become a potential issue in that testing is not performed, even when appropriate. In these situations, patients are often treated empirically for CDI without any documentation of a positive test. To address this issue, some states, including Texas, perform random audits of hospital infection rates. The issue of diagnostic testing is further thrust into the spotlight with discussions revolving around the utility of two-step testing to differentiate between colonization and true infection.

The process and outcome measure control charts indicate that our intervention-driven approach to improving *C. difficile* SIR has resulted in new baselines and control limits. Continued performance within these boundaries is expected. However, even within our stable processes,[4] variation remains, and, while some degree of variation is inevitable, our current control limits are such that expected variation could cause our SIR rate to fail to meet performance targets during given reporting periods. To prevent common cause variation from exceeding specification limits, additional interventions or process changes may be necessary to reduce the spread of the distribution.

CONCLUSIONS

With the aid of CDS and clinical education, the project team was able to successfully hardwire *C. difficile* testing and diagnosis best practice guidelines into the diagnostic pathway. Infection Prevention's *C. difficile* notifications for providers and the launch of the *C. difficile* BPAs preceded two of the largest shifts in *C. difficile* healthcare facility-onset incidence rate, per the process behaviour chart. The BPA provider bypass rate varied by service and BPA type, but the overall effectiveness of the BPAs in influencing behaviour change was modest. However, even a modest (25-50%) improvement in adherence to *C. difficile* best practice guidelines correlated with the attainment of project targets.

As a teaching institution, we benefitted from trainee engagement to disseminate knowledge identified as part of this project. Specifically, a Urology resident reviewed all of the HAI CDI cases in his department and presented data on over-testing at a teaching conference. Also, a resident in Internal Medicine used one of our cases to write a clinical vignette in *JAMA Internal Medicine* [10].

There were unintentional byproducts of the project's success that resulted in benefits to areas not directly involved. In 2016, following enforcement of the lab's rejection of formed stool policy, 1,250 orders were cancelled, which resulted in an approximate yearly savings of $60,000. Other important but less quantifiable benefits of the project include the empowerment of nursing through the addition of the *C. difficile* order question, "Order may be discontinued if sample not collected within 24 hours," as well a renewed interest in antimicrobial stewardship as part of the multifaceted approach to reducing infections due to *C. difficile*.

Ultimately, the multidisciplinary approach to integrate quality analytics with performance improvement and informatics proved to be effective as we were able to incorporate *C. difficile* testing and diagnosis best practices into clinical workflows.

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[4] Processes remain stable as of October 2017.