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Major Article

Impact of a *C. difficile* infection (CDI) reduction bundle and its components on CDI diagnosis and prevention

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Hospital infection control
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Background: Published bundles to reduce *Clostridioides difficile* Infection (CDI) frequently lack information on compliance with individual elements. We piloted a computerized clinical decision support-based intervention bundle and conducted detailed evaluation of several intervention-related measures.

Methods: A quasi-experimental study of a bundled intervention was performed at 2 acute care community hospitals in Maryland. The bundle had five components: (1) timely placement in enteric precautions, (2) appropriate CDI testing, (3) reducing proton-pump inhibitor (PPI) use, (4) reducing high-CDI risk antibiotic use, and (5) optimizing use of a sporicidal agent for environmental cleaning. Chi-square and Kruskal-Wallis tests were used to compare measure differences. An interrupted time series analysis was used to evaluate impact on hospital-onset (HO)-CDI.

Results: Placement of CDI suspects in enteric precautions before test results did not change. Only hospital B decreased the frequency of CDI testing and reduced inappropriate testing related to laxative use. Both hospitals reduced the use of PPI and high-risk antibiotics. A 75% decrease in HO-CDI immediately postimplementation was observed for hospital B only.

Conclusion: A CDI reduction bundle showed variable impact on relevant measures. Hospital-specific differential uptake of bundle elements may explain differences in effectiveness, and emphasizes the importance of measuring processes and intermediate outcomes.

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BACKGROUND

Despite continuing efforts, *Clostridioides difficile* has proven to be difficult to control in health care settings with only modest declines in hospital-onset *C. difficile* infection (HO-CDI) in recent years.^{1–3} The epidemiology surrounding *C. difficile* infection (CDI), although complex, is key to creating appropriate interventions. The multifaceted epidemiologic triad of host, agent, and environment provide the essential factors that must be addressed simultaneously to

successfully reduce CDI rates (Fig 1) and formed the basis of a pilot intervention as a precursor for a statewide CDI reduction initiative in Maryland.

The intervention bundle included: (1) institution of enteric precautions at initial suspicion of CDI before test results are returned, (2) optimization of *C. difficile* testing via decision support at the time of electronic order entry, (3) decreasing unnecessary prescribing of proton-pump inhibitors (PPI), (4) reducing the use of selected high-CDI-risk antibiotics (fluoroquinolones, third generation cephalosporins, and clindamycin), and (5) optimization of CDI-related disinfection. In addition, to improve efficiency of multiple interventions, our bundle leveraged the use of computerized clinical decision support (CCDS) for implementation. CCDS tools provide patient-specific data to clinicians through the electronic medical record (EMR) at the point of care and decision-making.⁴ While a bundle approach has been

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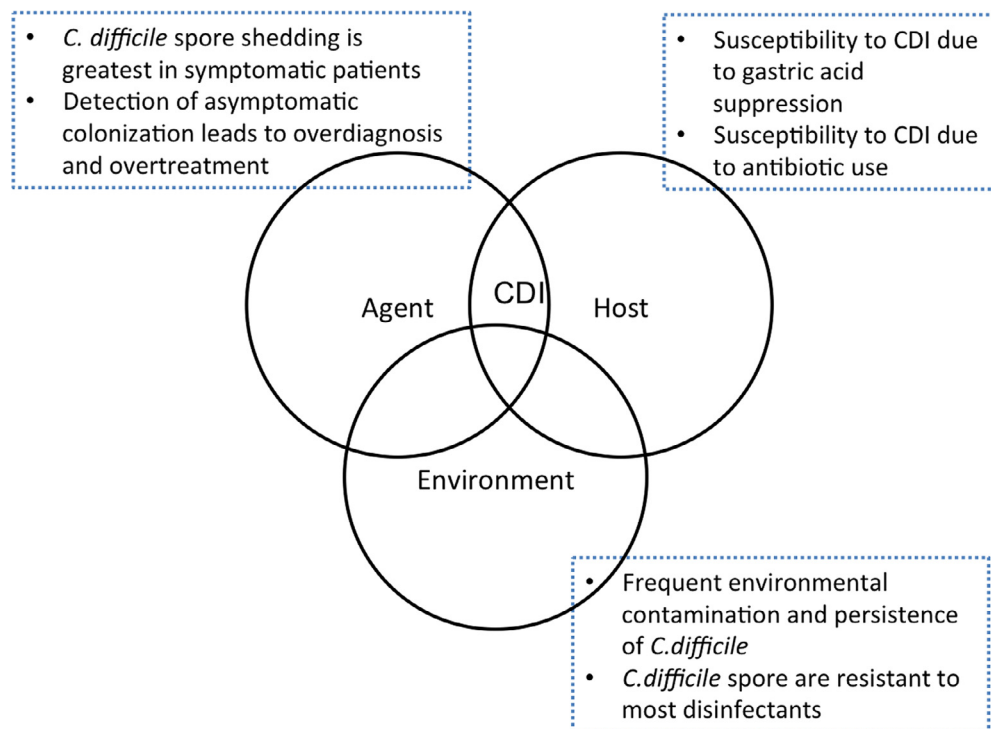


Fig 1. *C. difficile* infection epidemiological triad.

effective for reducing healthcare-associated infections,^{5–7} it is frequently difficult to tease out the relative contribution of each bundle component because compliance with bundle elements is not reported.^{5–7}

This pilot study aimed to measure the effect of the overall “bundle” in reducing CDI, as well as the impact of the deconstructed bundle components on intermediate outcomes and process measures to inform a future statewide CDI reduction initiative.

METHODS

Study design and study population

We performed a quasi-experimental study to evaluate the impact of a *C. difficile* intervention bundle at 2 acute care community hospitals in Maryland. Hospital A had 256 beds and an average baseline HO-CDI rate of 11.5 cases per 10,000 patient-days during the last 6 months of 2016, while Hospital B had 223 beds and 4.9 HO-CDI cases per 10,000 patient-days during the same period.

Intervention

The *C. difficile* bundle described above was introduced at in-person meetings with existing multidisciplinary teams at each hospital in October 2016. Teams included representatives from infection prevention, quality, infectious diseases (ID), pharmacy, microbiology, nursing, environmental services, and informatics. Prior to implementation, in November 2016, we gauged healthcare worker perceptions of proposed interventions through semistructured interviews, and incorporated those into the intervention design and implementation process.⁸ From January to June 2017, the study team and hospital teams collaborated on the development and implementation of the bundle. Within the overall framework (Fig 1), each hospital team decided which specific tools would be implemented based on perceived priorities, and requested necessary changes to hospital guidelines and policies. From January to December 2017, the study team

visited each site 3 times to discuss progress on implementation and educate clinicians, with intervening phone check-ins. Component implementation was staggered through this time period. June 2017 was assigned as the end of the preimplementation period based on the following criteria: at least 1 component of the EMR interventions was fully implemented at each hospital, and guideline changes to antibiotics and PPI had been approved and shared with clinicians (but not yet implemented in electronic order-sets).

Data collection

Each participating hospital provided monthly HO CDI rates as reported to the Centers for Disease Control and Prevention National Healthcare Safety Network. Specific study periods were established for evaluating process measures for each bundle component (Fig 2). For the overall effect of the bundle on CDI incidence, for hospital A, a preimplementation period was established from January 1, 2016 to June 30, 2017, before the bundle was fully implemented. For hospital B, the preimplementation period was April 1, 2016 to June 30, 2017, due to changes in the laboratory algorithm in early 2016 (change from toxin-based testing to PCR-only testing in March 2016). For both hospitals, the postimplementation period was from July 1, 2017 to June 31, 2018.

Timely institution of enteric precautions and appropriateness of CDI testing

Each hospital provided a dataset of all *C. difficile* tests ordered with patient demographics and enteric precaution orders during the hospital stay. Electronically retrieved data were validated through chart review for institution of enteric precautions and appropriateness of testing on a random sample of 50 per hospital for each period. Tests ordered in patients who did not meet diarrhea criteria (≥ 3 loose stools in 24 hours), received laxatives within 48 hours before the test, had a previous *C. difficile* positive result in the last 21 days or a negative result in the last 5 days were considered inappropriate. If the



Fig 2. Defined study periods for the overall bundle and its components per hospital.

patient had a suspicion of ileus due to *C. difficile* documented the test was considered appropriate even in the presence of laxatives.

Reducing PPI and high-CDI risk antibiotic use

Each hospital provided hospital-wide aggregated data on the use of PPI and high-CDI risk antibiotics (Fig 2). The frequency of electronic order-set use for ordering antibiotics was determined on a random sample of 50 orders each for ceftriaxone and levofloxacin per hospital, pre- and postimplementation. Only electronically validated data were reported.

Optimization of environmental cleaning

A baseline assessment through a structured survey of at least 30 *C. difficile* patient rooms and the CDI patient's nurse were completed at each hospital between January 1 and February 30, 2017. The survey inquired about the disinfectant present in the patient's room and the isolation cart. Nurses were asked to indicate the appropriate disinfectant to use in the CDI positive patient room. If appropriate responses were lower than expected, the assessment was repeated during the postperiod.

Data analyses

Component-specific measures

The time between the *C. difficile* diagnostic test order and placement in enteric precautions was estimated based on the isolation order. Kruskal-Wallis test was used to compare differences in time to enteric precautions, changes in the frequency of *C. difficile* testing, and the median use of PPI and antibiotics (days of therapy per 1,000 patient-days) between periods. Chi-square was used to evaluate changes in *C. difficile* testing appropriateness, order-set use for antibiotics, and the environmental survey responses.

Hospital-onset CDI rates

We performed interrupted time series analysis to examine changes in level (intercept change) and trend (linear slope change (on a log scale) of monthly rates of HO-CDI post- vs preimplementation, separately for each hospital. Negative-binomial regression was used due to

over-dispersion relative to the Poisson distribution. Terms in the model included: an indicator variable for implementation period, consecutive month starting with the first month of the preperiod, and an interaction term between these 2 variables.

RESULTS

Timely institution of enteric precautions

Hospital A did not create an automatic order entry link between CDI test order and enteric precaution order. The median time between order entry for a *C. difficile* test and enteric precautions for a CDI suspected patient was 1 hour (IQR = –10 hour, 4 hour) preimplementation and 2 hours (IQR = 1 hour, 5 hour) in the postimplementation period ($P = .23$, Table 1). No significant difference was observed in overall proportions of CDI suspected patients placed under enteric precautions before CDI test results were back (72% pre- vs 66% postimplementation, $P = .52$). However, while compliance with enteric precautions order was high among CDI positive patients (100% and 97% pre- and postimplementation, respectively), it was low among those where test was negative or not performed (5/20 pre- and 1/20 postimplementation).

Hospital B implemented an electronic link between the order of enteric precautions and the order of *C. difficile* test. In the same order set, the user could order the appropriate precautions. However, the selection of any or the appropriate enteric precautions depended on the user as the default option was “no contact precautions.” The median time between ordering a *C. difficile* test and ordering enteric precautions was 8 hours (IQR = 1 hour, 20 hour) during the preimplementation and 6 hours (IQR = 1 hour, 21 hour; $P = .79$) postimplementation (Table 1). No significant difference was observed in the proportions of CDI suspected patients placed under enteric precautions before CDI test results were back (62% vs 68%, $P = .53$). Similar to Hospital B, 100% of the reviewed positive CDI patients ($n = 30$) had an enteric precautions order both pre- and postimplementation ($P = .79$) but among patients with a negative/not performed CDI test result ($n = 20$), only 6 and 4 patients were ever placed on enteric precautions in the pre- and post-preimplementation periods, respectively.

Table 1
Pre and postimplementation process measures by hospital

Interventions	Measure	Hospital A			Hospital B		
		Pre	Post	P value*	Pre	Post	P value*
Link contact precautions order with CDI test order	Time (hr) to CP <i>Median (IQR)</i> (n = 200; 50 per hospital pre and post)	1 (–10, 4)	2 (1, 5)	.23	8 (1, 20)	6 (1, 21)	.79
Provide a hard stop/alert	Frequency of CDI testing <i>median of monthly frequency (no. of tests/1,000 pt days [IQR])</i>	15 (10, 18)	13 (12, 14)	.34	10 (9, 12)	7 (6, 9)	.02
	Frequency of inappropriate testing (N = 50) <i>N (%)</i>	32 (64)	31 (62)	.84	29 (53)	22 (44)	.37
	Among inappropriate tests						
	Testing in the presence of laxative No significant diarrhea	15 (47) 14 (44)	9 (29) 21 (67)	.14 .06	7 (24) 16 (55)	1 (5) 16 (73)	.06 .20
Mandatory PPI indication; PPI removal from order-sets	PPI doses/per 1,000 pt days <i>Median (IQR)</i>	256 (249, 259)	203 (188, 213)	<.01	238 (220, 248)	210 (204, 213)	.05
Antibiotic guideline and order-set changes favoring lower-CDI risk antibiotics, short duration therapy	Overall use high-risk antibiotics (days of therapy/1,000 pt days) <i>Median (IQR)</i>	138 (137, 148)	121 (110, 121)	<.01	112 (103, 118)	92 (83, 97)	.01
<i>C. difficile</i> status alert in nursing electronic board	Levofloxacin	30 (26, 31)	21 (21, 23)	.02	56 (52, 65)	38 (36, 44)	<.01
	Ceftriaxone	100 (94, 103)	86 (80, 92)	.02	49 (43, 52)	49 (41, 51)	.75
	Clindamycin	11 (9, 11)	8 (6, 8)	.04	4 (4, 5)	3 (3, 4)	.15
	Bleach disinfectant present in CDI room n (%)	40 (80)	23 (85)	.83	30 (100)	-	
Use of electronic order sets for prescription of targeted antibiotics	Nurses knowledgeable about the need to clean with bleach n (%)	44 (88)	24 (89)	.33	30 (100)	-	
	Levofloxacin n (%) (n = 200; 50 per hospital pre and post)						
	Order set used	-	-		10 (20)	8 (16)	.80
	Order set not used	-	-		40 (80)	42 (84)	
Use of electronic order sets for prescription of targeted antibiotics	Ceftriaxone n (%) (n = 200; 50 per hospital pre and post)						
	Order set used	-	-		5 (10)	2 (4)	.44
	Order set not used	-	-		45 (90)	48 (96)	

NOTE. P values below 0.05 are bolded.

*P value for categorical variables obtained through Pearsons Chi-square test or Fisher's exact test. Kruskal-Wallis test was used to compare medians between groups.

Nevertheless, among 50 reviewed CDI suspected patients during the postperiod, only for 12 cases (24%) were the enteric precautions ordered using the *C. difficile* test order panel. Among these 12 patients, the median placement time was 0 (IQR = 10.5). Similarly, among these patients, the contact precaution order was placed a median of 4 hours before the CDI test result was back. A significant difference in placement timing was observed between those patients whose enteric precautions were ordered at the same time as their *C. difficile* test than those for whom no enteric precautions were ordered at the time of *C. difficile* testing ($P = .01$).

Appropriateness of CDI testing

Both hospitals implemented an order panel that incorporated a hard stop for *C. difficile* test orders, inquiring about occurrence of diarrhea/loose stools, use of laxatives in the last 24 hours, and previous CDI tests performed. The main difference between the hard stops was that hospital B prepopulated the laxative history requested in the test order pulling from the patient's current medical record, while the clinician in hospital A was responsible for accurately answering this question. If the requirements for testing were not met, the ordering clinicians at both facilities were not allowed to continue ordering in the EMR and instead directed to the laboratory or the ID/GI attending if they wanted to proceed with the test.

During the preimplementation period, in Hospital A, 32 (64%) reviewed CDI suspected cases had a *C. difficile* test inappropriately ordered. Forty-four percent (14 out of 32) of these patients did not meet the diarrhea definition for ordering a *C. difficile* test. Additionally, 47% received laxatives within 48 hours before testing (Table 1). If the definitional requirements of diarrhea were relaxed to having any amount of loose stools, 25% of the CDI tests were still inappropriate. During the post period, 62% of *C. difficile* tests were considered inappropriate using the more restrictive definition. No significant difference in the proportion of inappropriate testing by period was observed ($P = .84$). There were no significant changes in the reasons for inappropriateness across periods either. Furthermore, there was no significant difference in *C. difficile* testing frequency between the 2 study periods in Hospital A ($P = .34$; Table 1).

In contrast in Hospital B, during the pre-period, 29 (53%) reviewed CDI suspected cases had a *C. difficile* test inappropriately ordered. Fifty-five percent (16 out of 29) of these patients did not meet the diarrhea definition for ordering a *C. difficile* test. Additionally, at least 24% received laxatives within 48 hours before testing (Table 1). If the definitional requirements of diarrhea were relaxed to having any amount of loose stools, 24% of the CDI tests were inappropriate. During the post period, 44% of *C. difficile* tests were considered inappropriate using the more restrictive definition. No significant difference in the proportion of inappropriate testing by period was observed ($P = .37$). However, only 1 case (5%) was considered inappropriate due to laxative use during the postperiod, which showed a borderline significant difference from the pre-implementation period ($P = .06$). Additionally, a significant reduction in the frequency of *C. difficile* testing from 10 orders per 1,000 patient-days to 8 orders per 1,000 patient-days from pre- to postimplementation was observed in Hospital B ($P = .02$; Table 1).

Reducing PPI use

Hospital A and B implemented a mandatory PPI indication when prescribing PPIs through EMR orders. In addition, both hospitals removed all PPIs from other hospital order-sets. Both hospitals observed a reduction of PPI use between study periods (Fig 3D). Hospital A went from prescribing a median of 256 days of therapy/1,000 patient-days to 203 days of therapy/1,000 patient-days ($P < .01$). Similarly, Hospital B went from prescribing a median of 238 days of

therapy/1,000 patient-days to 210 days of therapy/1,000 patient-days ($P = .05$; Table 1).

Reducing high-CDI risk antibiotic use

While both hospital A and B implemented antibiotic guidelines and order-sets favoring lower-CDI risk antibiotics and shorter durations of therapy, the use of electronic order-sets for ordering antibiotics was low (overall 13% preintervention and 7% postintervention, Table 1). Both hospitals observed a reduction in the overall use of high-CDI risk antibiotics between the study periods (Fig 3A–C). Reported total days of therapy for levofloxacin, ceftriaxone, and clindamycin decreased pre to postimplementation from 138 per 1,000 patient-days to 121 per 1,000 patient-days ($P < .01$) for Hospital A, and from 112 to 92 per 1,000 patient-days ($P = .01$) for Hospital B. Hospital A was able to achieve significant reductions in the use of levofloxacin, ceftriaxone, and clindamycin. However, hospital B achieved a significant reduction only in fluoroquinolone use (Table 1).

Optimization of use of sporicidal agent for environmental cleaning

In hospital A, 80% of the evaluated CDI rooms at baseline had bleach as the disinfectant inside the patient's room while in hospital B, all evaluated rooms had bleach. Similarly, 88% and 100% of surveyed nurses knew bleach was needed to clean surfaces in CDI positive rooms in hospitals A and B respectively. Hospital A decided to build an improved status board in their EMR that allowed easy identification of the CDI status of the patient. No significant change in the proportion of CDI positive rooms with bleach (80% vs 85%, $P = .83$) or nurses' knowledge about the need of using bleach in CDI positive rooms (88% vs 89%, $P = .33$) was observed after this intervention.

Hospital-onset CDI rates

The mean reported CDI incidence rate for hospital A over the preimplementation months was 8.7 (standard deviation [SD] = 4.9) HO CDI cases per 10,000 patient-days and 9.9 (SD = 4.3) cases per 10,000 patient-days over the postimplementation months. The mean reported CDI rate for hospital B was 5.7 (SD = 3.3) per 10,000 patient-days preimplementation and 3.2 (SD = 2.9) per 10,000 patient days over the post-implementation months. In interrupted time-series analysis in hospital A, there was an estimated increase in CDI incidence of 2.8% per month (95% confidence interval [CI]: –1.8%, 7.3%) during the preperiod. This month-to-month increase was estimated to be 1.3% (95% CI: –6.4%, 9.6%) during the postperiod; however, the change was not significant ($P = .75$) and nor was the level change immediately postimplementation ($P = .44$; Fig 4). In hospital B, the trend over the preperiod was estimated to be virtually flat (month-to-month increase 0.39%, 95% CI: –6.3%, 7.5%). There was a substantial (74.8%) level decrease in incidence rate post- vs preimplementation (95% CI: –92.9, –10.6, $P = .044$). Over the postimplementation months, there was an estimated monthly increase of 12.5% per month (95% CI: –1.5%, +28.4%), however, this change in trend was not significant ($P = .14$).

DISCUSSION

A pilot study of a multifaceted CCDS CDI reduction bundle showed a variable impact on CDI-relevant process and outcome measures in 2 community hospitals. Overall reduction in CDI rates was seen in 1 hospital and detailed review of the process measures and intermediate outcomes helped understand bundle element uptake, and opportunities for improvement.

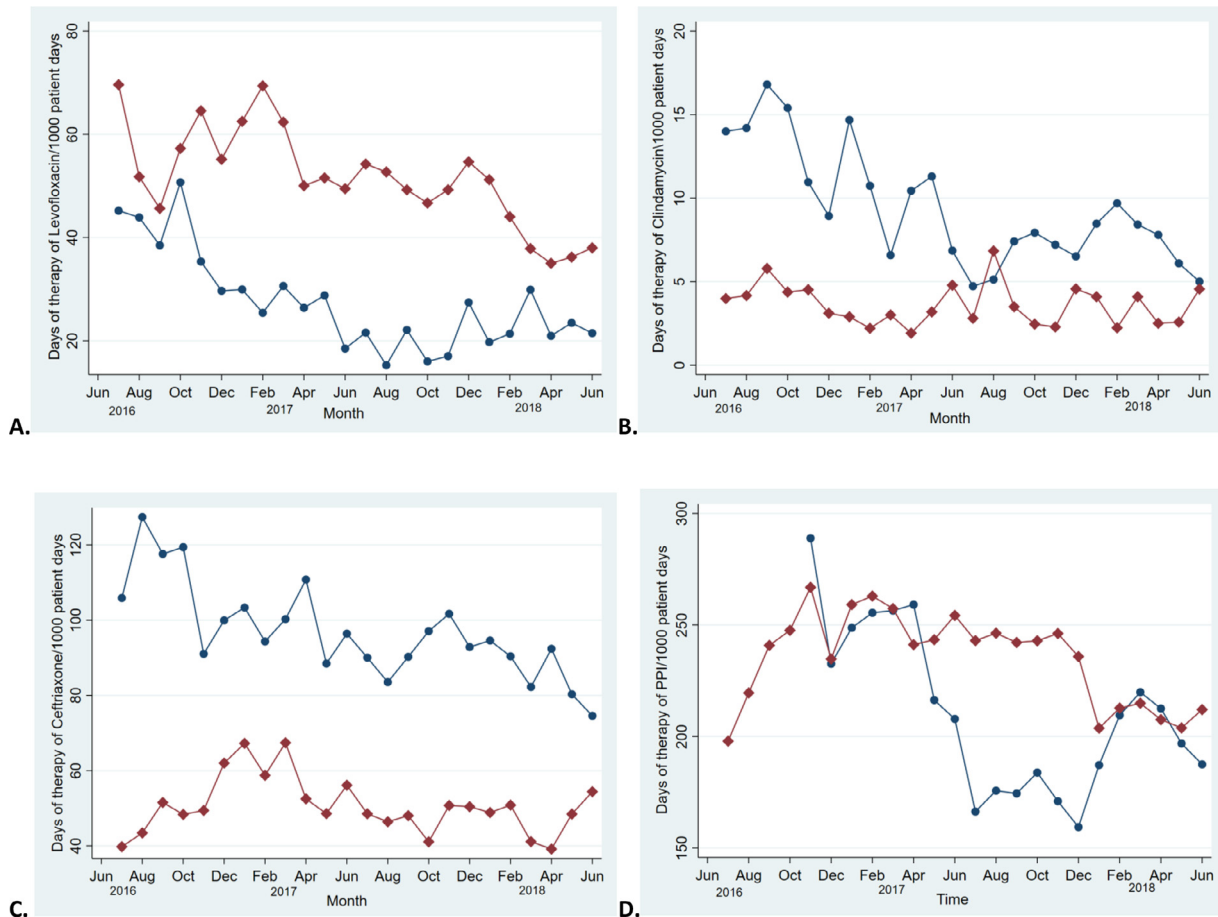


Fig 3. Antibiotic and PPI use across the study period by hospital (Circle marker = Hospital A and Diamond marker = Hospital B). Panels: A (levofloxacin), B (Clindamycin), C (Ceftriaxone), and D (Proton pump inhibitors [PPI]).

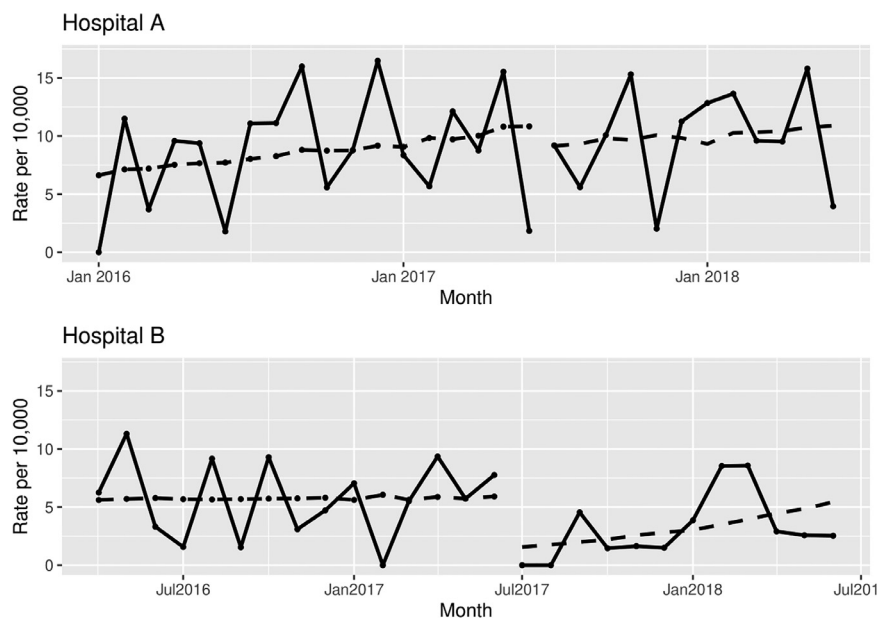


Fig 4. Interrupted time-series analysis of hospital-associated CDI rates across the study periods in hospital A (Panel A) and in hospital B (Panel B).

We did not observe an overall improvement in compliance or timeliness of enteric precautions for CDI suspects prior to test results except when providers used the order panel where the *C. difficile* test

order and the enteric precautions order were electronically linked. This is similar to a prior study.⁹ However, our results demonstrated that such a link is most effective when it is automatic; in other words,

ordering enteric precautions should always be the default option when ordering a *C. difficile* test. Nevertheless, the user should have the option to modify precautions to a higher level in case of a comorbid risk such as tuberculosis.

A hard stop for optimizing *C. difficile* testing when not indicated proved to be challenging as well. Neither hospital significantly decreased overall test inappropriateness after applying a hard stop for testing; however, hospital B reduced the proportion of patients considered inappropriately tested by recent previous use of a laxative. This suggests that prepopulating the hard stop questions or criteria using EMR data may be essential because this can provide timely and accurate information to the clinician and facilitate decision making without requiring the user to manually verify the patient's testing requirements.

Electronic alerts and hard stops to reduce unnecessary *C. difficile* testing are well described. Quan et al. found a 64% reduction in inappropriate *C. difficile* testing and HO-CDI after a real-time order entry alert informing the prescriber that the patient did not meet testing criteria, and directing them to obtain ID or gastroenterology approval.¹⁰ A hard stop alert described by Rock et al. found similar reduction in inappropriate testing and HO-CDI and no negative outcomes associated with the hard stop.¹¹ While the test orders in the EMR had similar designs at both hospitals, our discussions with Hospital A's team revealed that despite the "hard stop," clinicians would frequently call the microbiology laboratory directly to "bypass" the EMR barrier, highlighting the importance of reviewing user uptake of decision support.

Both hospitals observed a decrease in PPI use following implementation of a mandatory indication for PPI orders and removal of PPI from several order-sets. Herzig et al. similarly reported a reduction in the use of acid suppressive medications through CCDS that guided appropriate PPI use at the time of ordering.¹² Likewise, Clay et al. also reported the reduction of intravenous (IV) PPI use after implementing an electronic order set designed to guide PPI use based on indication.¹³

Finally, both hospitals observed a significant reduction in high-CDI risk antibiotics after the implementation of revised antibiotic guidelines. Facility-specific treatment guidelines are considered a priority antimicrobial stewardship intervention because they can enhance the effectiveness of both prospective audit and feedback and preauthorization by establishing clear recommendations for appropriate antibiotic use.¹⁴ The use of CCDS to guide appropriate antibiotic use has also been described^{15,16} and use of electronic order-sets is recommended for antimicrobial stewardship.¹⁷ Despite clinicians stating a preference for guideline and order-set changes over EMR alerts in our preimplementation evaluation,⁸ we found that use of electronic order-sets for ordering high-risk antibiotics was low at baseline and even lower postintervention. The latter may be due to clinicians being forced to order outside the order-sets because these antibiotics were removed from preferred order-set choices. However, the overall poor uptake of electronic order-sets for hospital antibiotic prescribing requires future study.

In this bundle, we did not focus on environmental cleaning because both hospitals had implemented environmental cleaning initiatives prior to the start of this study, and both were using UV light for terminal disinfection of *C. difficile* rooms with near 100% compliance. We assessed staff knowledge of need for, and placement of, bleach-based disinfectants in *C. difficile* patient rooms for daily cleaning. Baseline awareness was high at both hospitals, with no intervention implemented at Hospital B, and no change postimplementation of a CDI-specific indicator in the patient status board in Hospital A.

Comparing post- to preimplementation, overall HO CDI rates were reduced in one hospital (Hospital B) that had a significant level change; however, no significant change in slope was observed in either hospital. The variability in implementation of bundle elements

described above could explain these results. Specifically, we suspect that the level-change observed for hospital B was most closely temporally associated with the electronic hard stop for inappropriate testing particularly related to laxative use. While both hospitals reduced the use of fluoroquinolones, this was not reflected in significant CDI reduction as seen in prior studies.^{18,19} This could be related to a low baseline proportion of fluoroquinolone-resistant *C. difficile* strain (~20% in Maryland hospitals reported through the Emerging Infection Program), need for additional reduction in high-risk and overall antibiotic use, or the need to measure the impact on CDI over a longer time period. This latter point underscores a key limitation of this study in that this was designed as an implementation pilot in 2 medium-sized hospitals under endemic conditions and therefore not adequately powered to study the impact on CDI rates. We also did not have data on overall antibiotic use trends which may have impacted CDI risk.

Variable results have been reported on the impact of CDI bundles^{7,20–22} on CDI rates. Davis et al. described an insignificant difference in HO-CDI following a multicomponent bundle (antimicrobial and drug management, detection, cleaning, contact precautions and equipment practices, and people practices).²⁰ Bishop et al. described a reduction of HO-CDI in surgical patients after the introduction of a bundle (hand-washing initiative, maintaining gastric acidity, antibiotic stewardship, and a modification to the rounding protocol to limit patient exposure).²² Neither study described the level of compliance with bundle elements. Similarly, in a systematic review of published results of CDI bundles, most studies reported measuring compliance with the bundle, but rarely reported the compliance measure results.⁷

Our study was unique in its multifaceted approach to reducing CDI under endemic conditions, using CCDS where possible, and in measuring the extent to which each component was implemented. Additionally, our study follows several recommended best practices for reporting CCDS-based interventions.²³ We used evidence-based strategies to inform intervention development, directly incorporated EMR data when possible, incorporated hospital guidelines, workflows and user feedback, selected and measured both process and outcome measures, and have presented our results in context.

Collectively these findings demonstrate the need to critically evaluate processes and intermediate outcomes and deconstruct bundled interventions, to better measure both effectiveness and gaps.

References

1. Lessa FC, Mu Y, Bamberg WM, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med*. 2015;372:825–834.
2. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med*. 2014;370:1198–1208.
3. Guh AY, Mu Y, Winston LG, et al. Trends in U.S. burden of *clostridioides difficile* infection and outcomes. *N Engl J Med*. 2020;382:1320–1330.
4. Bright T, Wong A, Dhurjati R, et al. Effect of clinical decision-support systems. *Ann Intern Med*. 2012;157:29–43.
5. Saint S, Greene MT, Krein SL, et al. A program to prevent catheter-associated urinary tract infection in acute care. *N Engl J Med*. 2016;374:2111–2119.
6. Pronovost P, Needham D, Berenholtz S, et al. An Intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;355:2725–2732.
7. Barker AK, Ngam C, Musuza JS, Vaughn VM, Safdar N. Reducing *Clostridium difficile* in the inpatient setting: a systematic review of the adherence to and effectiveness of *C. difficile* prevention bundles. *Infect Control Hosp Epidemiol*. 2017;38:639–650.
8. Blanco N, O'Hara LM, Robinson GL, et al. Health care worker perceptions toward computerized clinical decision support tools for *Clostridium difficile* infection reduction: a qualitative study at 2 hospitals. *Am J Infect Control*. 2018;46:1160–1166.
9. Dewart CM, Blanco N, Foxman B, Malani AN. Electronic *clostridium difficile* infection bundle reduces time to initiation of contact precautions. *Infection Control and Hospital Epidemiology*. Cambridge University Press; 2017:242–244.
10. Quan KA, Yim J, Merrill D, et al. Reductions in *clostridium difficile* infection (CDI) rates using real-time automated clinical criteria verification to enforce appropriate testing. *Infect Control Hosp Epidemiol*. 2018;39:625–627.
11. Rock C, Mizusawa M, Small B, et al. Implementation of electronic medical record hard stop alerts for inappropriate *clostridium difficile* tests in academic and community hospital setting; impact on testing rates and clinical outcomes. *Open Forum Infectious*

- Disease. 2017:S608. Available at: https://academic.oup.com/ofid/article-abstract/4/suppl_1/S608/4295111. Accessed November 14, 2020.
12. Herzig SJ, Guess JR, Feinbloom DB, et al. Improving appropriateness of acid-suppressive medication use via computerized clinical decision support. *J Hosp Med.* 2015;10:41–45.
 13. Clay B. Reduction in utilization of intravenous proton pump inhibitors following implementation of a computerized physician order entry order set (abstract). *Hosp Med.* 2007;2(suppl 2). Available at: <https://www.shmabstracts.com/abstract/reduction-in-utilization-of-intravenous-proton-pump-inhibitors-following-implementation-of-a-computerized-physician-order-entry-order-set/>. Accessed November 14, 2020.
 14. Centers for Disease Control and Prevention. *Core Elements of Hospital Antibiotic Stewardship Programs [Internet]*. 2020. Atlanta, Georgia. Available at: <https://www.cdc.gov/antibiotic-use/core-elements/hospital.html>. Accessed November 14, 2020.
 15. Monteiro L, Maricoto T, Solha I, Ribeiro-Vaz I, Martins C, Monteiro-Soares M. Reducing potentially inappropriate prescriptions for older patients using computerized decision support tools: systematic review. *J Med Internet Res.* 2019;21:e15385.
 16. Curtis CE, Al Bahar F, Marriott JF. The effectiveness of computerised decision support on antibiotic use in hospitals: a systematic review. *PLoS One.* 2017;12:1–15.
 17. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis.* 2016;62:e51–e77.
 18. Shea KM, Hobbs ALV, Jaso TC, et al. Effect of a health care system respiratory fluoroquinolone restriction program to alter utilization and impact rates of clostridium difficile infection. *Antimicrob Agents Chemother.* 2017;61:1–8.
 19. Dingle KE, Didelot X, Quan TP, et al. Effects of control interventions on Clostridium difficile infection in England: an observational study. *Lancet Infect Dis.* 2017;17:411–421.
 20. Davis BM, Yin J, Blomberg D, Fung ICH. Impact of a prevention bundle on Clostridium difficile infection rates in a hospital in the Southeastern United States. *Am J Infect Control.* 2016;44:1729–1731.
 21. Olson B, Floyd R, Howard J, Hassanein T, Warm K, Oen R. A multipronged approach to decrease the risk of clostridium difficile infection at a community hospital and long-term care facility. *J Clin Outcomes Manag.* 2015;22:398.
 22. Bishop J, Parry M, Hall T. Decreasing clostridium difficile infections in surgery: impact of a practice bundle incorporating a resident rounding protocol. *Connecticut Med.* 2013;77:69–75.
 23. Kawamoto K, McDonald CJ. Designing, conducting, and reporting clinical decision support studies: recommendations and call to action. *Ann Intern Med.* 2020;172:S101–S109.