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Compliance with *Clostridium difficile* treatment guidelines: effect on patient outcomes

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SUMMARY

Guidelines for the severity classification and treatment of *Clostridium difficile* infection (CDI) were published by Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) in 2010; however, compliance and efficacy of these guidelines has not been widely investigated. This present study assessed compliance with guidelines and its effect on CDI patient outcomes as compared with before these recommendations. A retrospective study included all adult inpatients with an initial episode of CDI treated in a single academic center from January 2009 to August 2014. Patients after guideline publication were compared with patients treated in 2009–2010. Demographic, clinical, and laboratory data were collected to stratify for disease severity. Outcome measures included compliance with guidelines, mortality, length of stay (LOS), and surgical intervention for CDI. A total of 1021 patients with CDI were included. Based upon the 2010 guidelines, 42 (28·8%) of 146 patients treated in 2009 would have been considered undertreated, and treatment progressively improved over time, as inadequate treatment decreased to 10·0% (15/148 patients) in 2014 ($P = 0{\cdot}0005$). Overall, patient outcomes with guideline-adherent treatment decreased CDI attributable mortality twofold ($P = 0{\cdot}006$) and CDI-related LOS by 1·9 days ($P = 0{\cdot}0009$) when compared with undertreated patients. Compliance with IDSA/SHEA guidelines was associated with a decreased risk of mortality and LOS in hospitalized patients with CDI.

Key words: Adherence to guidelines, *Clostridium difficile*, overtreatment, undertreatment.

INTRODUCTION

Clostridium difficile remains an important hospital-acquired infection associated with significant cost, morbidity, and increased mortality. In the USA, *C. difficile* infection (CDI) is now the most common healthcare-associated infection (HAI) [1]. The incidence of CDI was increasing from 2001 to 2010 [2], but with the more recent focus on improving patient safety and reducing HAI, the rate has begun to decline. From 2012 to 2013 a 10% reduction in incidence was achieved in hospitalized patients nationwide [3]. Despite the declining rate, CDI still places

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a significant burden on the healthcare industry as a CDI is associated with a 2·5-fold increase in 30-day mortality [4], and the average additional cost of an initial hospital-acquired CDI is approximately US$12 000 [5]. In 2009, it was estimated that CDI contributed US$1.5 billion in cost to the care of adult patients at US acute care hospitals [6].

As CDI is beginning to be evaluated as a national quality indicator for hospitals, defining the current state of treatment could identify areas for improvement. CDI rates are collected through the Centers for Disease Control and Prevention (CDC)'s National Healthcare Safety Network (NHSN), and individual hospital rates are now publicly available on the Hospital Compare website. With the recent movement to link reimbursement with quality measures, CDI rates and/or compliance with treatment guidelines may become important for determining hospital policies and reimbursement.

In 2010, the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) jointly published guideline recommendations for CDI treatment based upon the severity of an episode [7]. Other recommendations have been published with additional variables used to classify disease severity without altering treatment regimens [8, 9]; nonetheless, the IDSA/SHEA guidelines remain commonly used. Since the guidelines were published, two studies at tertiary care hospitals have determined compliance with the guidelines, which ranged from 43% to 52% [10, 11]. There are limited data comparing guideline-compliant treatment with CDI outcomes. The aims of the present study were to assess whether treatment patterns for CDI were affected by the guideline publication, define the degree of compliance to those guidelines, and test the hypothesis that guideline-concordant treatment improved patient outcomes.

METHODS

Study design

We conducted an IRB (Institutional Review Board) approved retrospective analysis of patients over the age of 18 diagnosed with CDI from 1 January 2009 to 25 August 2014 at Penn State Hershey Medical Center, a 551 bed tertiary hospital. All inpatients or patients in the emergency department with a positive *C. difficile* assay were identified.

Laboratory investigation

A positive *C. difficile* assay was based on a cell culture cytotoxicity assay prior to March of 2011. Subsequently, a nucleic acid amplification test specific for a *C. difficile* toxin gene was used; this assay has greater sensitivity and negative predictive value, and results are available more rapidly [12–14]. The laboratory only runs the assay on diarrheal specimens, not formed stools, and our laboratory does not routinely test for the specific strain of *C. difficile*. To control for the difference in processing time for the two assays, we included only the medications continued after resulting of the assay. Patients studied prior to March 2011 were started on treatment when the specimen was sent to the laboratory, but only medications that started and continued after the result was positive, were included in this study.

Data collection

Data from the medical records were collected for patients over the age of 18. As this study targeted initial episodes, patients with recurrent or persistent episodes were excluded except for the index occurrence. Patient demographics were obtained including age, gender, ethnicity, ASA (American Society of Anesthesiologists) score, diagnosis of inflammatory bowel disease (IBD), and use of chemotherapy and radiation therapy. Laboratory values, including white blood cell count (WBC) and creatinine at diagnosis and up to 5 days surrounding the diagnosis were collected to assess for pre-CDI values and trends following diagnosis. All surgical procedures performed during the hospitalization, including surgical treatment for CDI, were recorded. Medications prescribed during the hospitalization, such as antibiotics, vasopressors, inotropes, and steroids were recorded. The date of admission, date of discharge (or death if the patient expired), discharge disposition, need for surgical treatment for CDI, and intensive care unit (ICU) or intermediate care unit (IMC) level of care were collected. A chart review was performed for each patient with in-hospital mortality to determine cause of death. The cause of death is stated on the death note, but patients given a more generic cause of death such as overwhelming sepsis were further reviewed to identify a more definitive cause of death. To decrease researcher bias, patient charts were reviewed in a random order.

Severity and treatment

Disease severity was classified based on the IDSA/SHEA guidelines [7]. An initial mild–moderate

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episode was defined as WBC <15 000 cells/μl and a creatinine level <1·5 times the premorbid value on the day the stool specimen was collected for analysis of *C. difficile*. An initial severe episode was defined as WBC ≥15 000 cells/μl or a creatinine level ≥1·5 times the premorbid value. An initial severe-complicated episode was defined as hypotension or shock requiring vasopressors or inotropes at the time of diagnosis.

Adherence to treatment guidelines was assessed based on disease severity. Treatment was considered concordant if medications were prescribed as per the guidelines. The recommended medications are: metronidazole 500 mg PO or IV for mild–moderate disease, vancomycin 125 mg (we also accepted 250 mg) PO for severe disease, and vancomycin 500 mg PO or per rectum plus metronidazole 500 mg IV for severe-complicated disease. Undertreatment included a lack of drug treatment for any disease category, sole metronidazole therapy for severe disease, or omission of either vancomycin or metronidazole or doses of either drug that were less than 500 mg for severe-complicated disease. Overtreatment was defined as vancomycin alone or metronidazole plus vancomycin for a mild–moderate episode, or metronidazole in addition to vancomycin for a severe episode. Surgical intervention for CDI included total abdominal colectomy with end or end-loop ileostomy, subtotal colectomy with ileostomy, or simple creation of a loop ileostomy with subsequent colonic irrigation. Patients were treated for a total of 10–14 days as inpatients. If patients were discharged during the treatment regimen, we were only able to retrieve the discharge medication but not the length of treatment; however, since all patients were treated with the appropriate length as inpatients, we assumed the correct duration was continued at discharge.

Patients were divided into two groups based upon time points relative to the guideline publication. Patients diagnosed from January 2009 to December 2010 were classified as the before guidelines group, and patients diagnosed from January 2011 to August 2014 formed the after guidelines group. Although the guidelines were published in mid-2010, we placed patients diagnosed through December 2010 into the before guideline group to allow a brief period for dissemination of the guidelines and potential changes in practice. The guidelines were retrospectively applied to patients treated in 2009 and 2010 to establish the baseline treatment patterns in our institution, and this control group was compared with patients treated after the guidelines had been published. Although there is an antimicrobial stewardship program at our institution overseeing appropriate use of antibiotics, there were no strict hospital-wide policies enforcing appropriate treatment of CDI during any period of this study.

Outcome measures included in-hospital mortality, CDI-related mortality, hospital length of stay (LOS), CDI-related LOS (LOS after the CDI test was positive), and surgical intervention for CDI. All patients who expired during the hospitalization were further reviewed to determine whether the cause of death was directly attributable to CDI or to another cause, although CDI may have played an indirect role in the patient's demise.

Statistical analysis

All categorical variables were compared by using the χ^2 test. Mean values of quantitative variables were compared by using Student's t test and one-way analysis of variance (ANOVA) (IBM SPSS Statistics, Version 22·0. Armonk, NY). P values ≤0·05 were considered as statistically significant.

RESULTS

Patient characteristics

A total of 1384 positive *C. difficile* assays between January 2009 and August 2014 were identified. We excluded 368 tests: 132 from patients with recurrent disease, 75 that were duplicate tests or related to persistent episodes, and 161 for which there was incomplete documentation regarding severity or treatment. Patients excluded for lack of documentation were distributed throughout all years included in this study. The remaining 1021 patients were included in this study, including 293 (28·7%) in the before guidelines group and 728 (71·3%) in the after guidelines group. Overall, the mean age was 62·5 ± 0·5 years, with 481 (47%) over the age of 65. A majority of the patients, 938 (92%), in this study were Caucasian. The distribution of disease severity included 761 (75%) cases classified as mild–moderate, 116 (11%) cases that were severe, and 144 (14%) cases that were severe-complicated. There were no differences between the before and after guidelines groups in terms of patient sex, presence of IBD, chemotherapy, radiation, steroid use, or disease severity (Table 1). Moreover, the proportion of

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Table 1. *Characteristics of patients treated before or after CDI guideline publication*

Variable	Before guidelines ($N = 293$)	After guidelines ($N = 728$)	P value
Age (mean ± S.D.)	64·3 ± 16·8	61·9 ± 18·5	0·052
Gender			0·347
Male, *n* (%)	152 (52%)	354 (49%)	
Service			0·409
Medicine, *n* (%)	237 (81%)	572 (79%)	
Surgery, *n* (%)	56 (19%)	156 (21%)	
IBD			
Crohn's, *n* (%)	8 (3%)	27 (4%)	0·437
UC, *n* (%)	6 (2%)	24 (3%)	0·285
Chemotherapy, *n* (%)	63 (22%)	155 (21%)	0·941
Radiation, *n* (%)	22 (8%)	51 (7%)	0·778
LOS (mean ± S.D.)	11·9 ± 13	12·7 ± 14	0·458
ICU			0·02
IMC, *n* (%)	99 (34%)	232 (32%)	
ICU, *n* (%)	41 (14%)	172 (24%)	
Discharge			<0·0001
To home, *n* (%)	226 (77%)	436 (60%)	
To rehab/facility, *n* (%)	39 (13%)	292 (40%)	
Disease severity			0·248
Mild–moderate, *n* (%)	208 (71%)	558 (76%)	
Severe, *n* (%)	37 (13%)	79 (11%)	
Severe-complicated, *n* (%)	48 (16%)	144 (14%)	
Steroids, *n* (%)	73 (25%)	214 (29%)	0·15
Medication usage			
Metronidazole, *n* (%)	258 (88%)	668 (92%)	0·065
Vancomycin oral, *n* (%)	133 (45%)	370 (51%)	0·116
Vancomycin enema, *n* (%)	0 (0%)	32 (4·4%)	0·001

patients in each severity classification did not change over the time period in this study (Fig. 1).

Treatment adherence to guidelines

Of the total 1021 patients, 471 (46%) received appropriate, or guideline-adherent, treatment, 383 (38%) were overtreated, and 167 (16%) were undertreated. Retrospectively applying the guidelines to the patients diagnosed with CDI in 2009, 42 (28·8%) of 146 patients would have been considered undertreated, while guideline-adherent treatment improved such that only 15 (10·0%) of 148 patients in 2014 received inadequate treatment ($P = 0·0005$). Using the 2 years prior to the guidelines, 2009–2010, as the baseline, we found that the rate of undertreatment decreased from 25% of patients treated prior to the guidelines to 13% of patients treated after guideline publication. Furthermore, the overtreatment of patients increased from 32% to 40%, and guideline-concordant treatment increased slightly from 43% to 47% after guideline implementation ($P < 0·0001$; Fig. 2).

Age differed between treatment classification ($P = 0·04$) as patients in the undertreated group (65·2 ± 17·0 years) were older than either the overtreated (62·8 ± 18·7 years) or appropriately treated (61·5 ± 17·8 years) groups. Guideline adherence did not differ with admitting service, sex, race, diagnosis of ulcerative colitis (UC), history of chemotherapy, radiation administration, or steroid use (Table 2).

The subgroup of patients with Crohn's disease had the lowest likelihood of undertreatment (3 of 35 patients; 9%) and a high likelihood of overtreatment (21 of 35 patients; 60%; $P = 0·02$). When all IBD patients, including both Crohn's and UC, were analyzed, the preferential improvement in guideline-concordant treatment did not reach statistical significance. Although we expected the IBD patients to present with worse disease severity, a majority of Crohn's patients (89%) had mild–moderate disease severity. The gastroenterology service was involved in the management of CDI in 68% of Crohn's disease patients.

As treatment is based upon severity of CDI episode, we compared treatment adherence to guidelines

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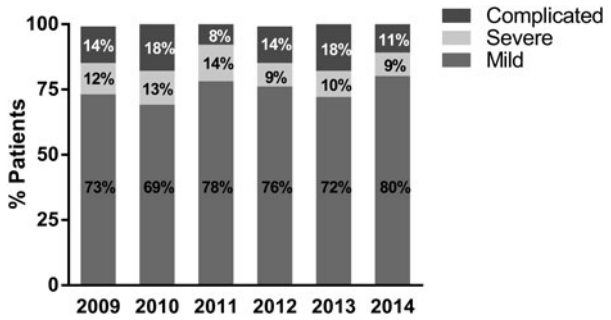

Fig. 1. Disease severity by year. Each bar represents the proportion of patients assigned to the severity of CDI episode, mild–moderate (mild), severe, or severe-complicated (severe), in each year of the study ($P = 0{\cdot}16$ by one-way ANOVA).

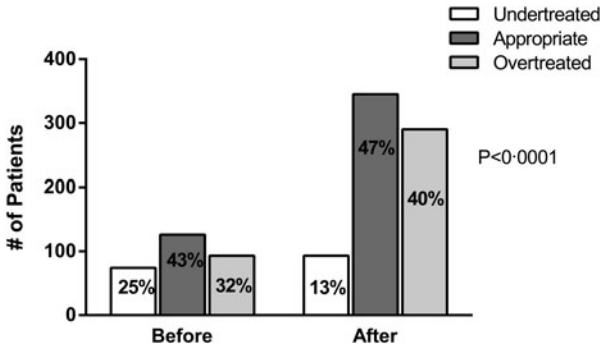

Fig. 2. Treatment adherence improved after guideline publication. Bars represent the number of patients classified by guideline adherence retrospectively applied before (2009–2010) or after (2011–2014) guideline publication ($P < 0{\cdot}0001$ by χ^2 test). The percentage of patients in each time frame is noted within the bar. Undertreatment improved from 25% before to 13% after publication of guidelines.

within each severity group. Overall, undertreatment increased proportionally with disease severity ($P < 0{\cdot}001$). Overtreatment was similar in the mild–moderate and severe episodes; there was no overtreatment in the severe-complicated group as all medications investigated were recommended for this group. Appropriate treatment was lowest in patients with a severe episode (Table 3).

Following publication of the guidelines, treatment patterns shifted toward the recommended treatment or overtreatment in the patients with mild–moderate severity CDI episodes ($P = 0{\cdot}0005$). In the severe group, although the same trend over time was found, it did not reach statistical significance ($P = 0{\cdot}1$). Moreover, treatment patterns became more adherent to the guideline recommendations in the severe-complicated group ($P = 0{\cdot}02$; Table 3).

Patient outcomes

Overall, mortality occurred in 80 (7·8%) patients, and 23 (2·0%) patients required surgical intervention for CDI. A twofold increase in overall mortality (15·0%) was found in undertreated patients compared with appropriate and overtreated patients (7·2% and 5·5%, respectively; $P < 0{\cdot}05$ for each comparison; Table 4). Over the time period included in this study, mortality decreased from 9·6% in 2009 and 9·5% in 2010, to 4% in 2011, 4·5% in 2012, and 7·4% in 2014. Only in 2013 did mortality clearly increase, to 12·1%, without any obviously distinguishing factor that year and despite the fact that undertreatment only occurred in 12% of patients that year.

CDI was the direct cause of death for nearly half of the patients who had in-hospital mortality, with 39 (49%) of the 80 deaths attributed to CDI, and 3·8% of all patients (39 of 1021) had mortality attributable to CDI. Patients with an initial diagnosis of a mild–moderate episode had the lowest risk of overall mortality, 2·9% (22 of 761 patients), as well as the lowest risk of CDI-related mortality, with 3 of the 761 (0·4%) patients dying directly from CDI. Severe and severe-complicated episodes were more likely to be associated with in-hospital CDI-related mortality as 10 of 116 (8·6%) severe episodes and 26 of 114 (22·8%) severe-complicated episodes had deaths attributed to CDI ($P < 0{\cdot}001$ via one-way ANOVA and $P < 0{\cdot}05$ for each comparisons). Furthermore, mortality directly related to CDI decreased from 7·8% in undertreated patients (13 of 167 patients) to 3·8% in appropriately treated patients (18 of 471 patients) and 2·0% in overtreated patients (8 of 383 patients; $P = 0{\cdot}006$; Table 4).

Hospital LOS also varied with disease severity. Undertreatment was associated with a 2·5 day longer LOS (14·6 ± 14·5 days) compared with both guideline adherence and overtreatment (12·1 ± 10·1 and 12·2 ± 11·2 days, respectively; $P = 0{\cdot}005$). However, the LOS did not change over the time course of this study ($P = 0{\cdot}2$; data not shown). The mean LOS after diagnosis of CDI was 9·4 ± 9·7 days for undertreated, 7·5 ± 8·9 days for appropriately treated, and 9·8 ± 9·3 days for overtreated patients ($P = 0{\cdot}0009$). There was a significant decrease in CDI-attributed LOS in appropriately treated compared with undertreated patients by an average of 1·9 days ($P < 0{\cdot}05$; Table 4).

Surgical intervention for CDI was included as an outcome measure as surgery can suggest failure of

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Table 2. *Patient characteristics within treatment classification*

Variable	Undertreatment ($N = 167$)	Appropriate ($N = 471$)	Overtreatment ($N = 383$)	P value
Age (mean ± S.D.)	65·2 ± 17·0	61·5 ± 17·8	62·8 ± 18·7	0·04
Sex				0·67
Male, *n* (%)	86 (51·5%)	183 (47·8%)	237 (50·3%)	
Service				0·69
Medicine, *n* (%)	128 (76·6%)	373 (79·2%)	308 (80·4%)	
Surgery, *n* (%)	39 (23·4)	98 (20·8)	75 (19·6)	
IBD				
Crohn's, *n* (%)	3 (9%)	11 (31%)	21 (60%)	0·02
UC, *n* (%)	3 (10%)	15 (50%)	12 (40%)	0·71
Chemotherapy, *n* (%)	103 (22%)	78 (20%)	37 (22%)	0·85
Radiation, *n* (%)	13 (8%)	39 (8%)	21 (6%)	0·29
ICU				0·05
IMC, *n* (%)	86 (52%)	133 (28%)	99 (26%)	
ICU, *n* (%)	20 (12%)	88 (19%)	101 (26%)	
Steroids, *n* (%)	48 (29%)	125 (27%)	113 (30%)	0·19

Table 3. *Treatment adherence based upon disease severity and guideline publication*

Variable	Undertreatment ($N = 167$)	Appropriate ($N = 471$)	Overtreatment ($N = 383$)	P value
Disease severity				<0·001
Mild, *n* (%)	26 (3%)	400 (53%)	335 (44%)	
Severe, *n* (%)	51 (44%)	18 (15%)	47 (41%)	
Complicated, *n* (%)	90 (63%)	54 (37%)		
Mild disease				0·0005
Before guidelines, *n* (%)	16 (8%)	109 (52%)	83 (40%)	
After guidelines, *n* (%)	10 (2%)	291 (53%)	252 (45%)	
Severe disease				0·1
Before guidelines, *n* (%)	21 (57%)	6 (16%)	10 (27%)	
After guidelines, *n* (%)	30 (38%)	12 (15%)	37 (47%)	
Complicated disease				0·02
Before guidelines, *n* (%)	37 (77%)	11 (23%)		
After guidelines, *n* (%)	53 (56%)	42 (44%)		

medical treatment; however, the rate of patients requiring surgery did not change over time in this study. Surgery for CDI ranged from 1% to 5% per year with an overall rate of 2·2% per year. The need for surgical intervention also did not differ as a function of the appropriateness of treatment (Table 4).

DISCUSSION

CDI is the most burdensome nosocomial infection for the healthcare system, and the national rate has started to decline only recently [1, 6]. Guidelines published by the IDSA/SHEA in 2010 recommend treatment based on the severity of the CDI episode. The burden of CDI on the healthcare system is substantial due to increased cost and mortality; thus, targeting compliance with treatment recommendations may improve patient outcomes and reduce healthcare expenditures. This study provides an assessment of the treatment patterns and associated outcomes based on guideline adherence. The results of this study indicate that after the 2010 guidelines were published, treatment became more aligned with those guidelines and the rate of undertreatment decreased. Moreover, treatment adherence to guidelines is beneficial as undertreated patients in our study were at an increased risk of mortality.

Previous reports have shown poor adherence with the 2010 IDSA/SHEA CDI guidelines [10, 11], and consistent with our new results, that guideline-concordant therapy or overtreatment decrease both mortality and the rate of recurrence [11]. However,

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Table 4. *Patient outcomes*

Variable	Undertreatment ($N = 167$)	Appropriate ($N = 471$)	Overtreatment ($N = 383$)	P value
Mortality, *n* (%)	25 (15·0%)	34 (7·2%)	21 (5·5%)	0·0005
CDI-related mortality, *n* (%)	13 (7·7%)	18 (3·8%)	8 (2·0%)	0·006
LOS, mean ± S.D.	14·6 ± 13·3	7·6 ± 15·8	7·8 ± 11·5	0·005
CDI-related LOS, mean ± S.D.	9·4 ± 9·7	7·5 ± 9·0	9·7 ± 9·3	0·0009
Surgery for CDI, *n* (%)	4 (2·4%)	13 (2·8%)	6 (1·6%)	0·51

those prior studies assessed compliance only in 2011, the year after guideline publication, and their sample sizes were relatively small. We were able to show an improvement in compliance from a baseline period (2009–2010) before publication of the guidelines compared with a 3-year period (2011–2014) after the guidelines became available. Additionally, Jardin *et al.* [15] found improved outcomes after implementation of an antimicrobial stewardship program that promoted the use of vancomycin in severe CDI episodes, as per the IDSA/SHEA recommendations. Our study expands upon these findings by having a larger sample size, documenting the impact of the guideline publication on treatment regimens, and analyzing several years of data.

In this study, the rates of undertreatment throughout all years (ranging 12–29%) were lower than the previously published studies (50–60%) [10, 11]. This finding could be explained by the local expertise in IBD and the prevalence of gastroenterology, infectious diseases, and colorectal surgery teams who are often consulted in our institution for assistance in CDI management. Nonetheless, the rate of undertreatment decreased over time following guideline publication compared with our retrospective application of these guidelines to assess treatment before their publication, with 28·8% of patients undertreated in 2009 compared with only 11·6% of patients in 2014. In episodes of CDI categorized as mild–moderate severity, the rate of undertreatment decreased the most after guideline publication, while the rate of overtreatment increased proportionately in this group. The increase in overtreatment can be attributed to vancomycin use in patients for whom metronidazole as sole therapy is recommended. Although vancomycin is appropriate for patients categorized as having severe disease, we also identified patients with mild–moderate disease who received vancomycin alone and together with metronidazole. The reasons underlying the cases of overtreatment could not be ascertained, but we suspect it may be due to confusion over the nomenclature for categorizing disease severity [9].

Patients receiving guideline-adherent treatment had improved survival and an associated decreased LOS. More specifically, mortality attributed to CDI decreased twofold with appropriate treatment or overtreatment (3·8% and 2·0%; respectively) compared with undertreatment (7·7%), and mortality trended down over the years correlating with the decrease in undertreatment. As patients with severe and severe-complicated episodes were more likely to have deaths that were attributed to CDI, targeting appropriate treatment in these patients potentially could decrease mortality. The LOS after CDI diagnosis also decreased by 1·9 hospital days when treatment was appropriate compared with undertreatment. Although we did not investigate cost or charges, the decreased LOS implies a decreased cost of hospitalization.

Prior studies combined the appropriate and overtreated groups when reporting patient outcomes [10, 11], but these groups were kept separate in this present study. We were able to identify that overtreatment did not further improve in mortality compared with appropriate treatment, and overtreatment increased the CDI-related LOS similar to undertreated patients. Thus, treatment according to guidelines is preferential to overtreatment. The use of vancomycin should be reserved for severe or severe-complicated episodes of CDI, especially as vancomycin has an increased cost compared with metronidazole and can lead to an increased prevalence of vancomycin-resistant *Enterococcus*.

We also included surgical intervention as an outcome measure, but we did not see an improvement in the need for surgical intervention as we did with mortality and LOS. The rate of surgical intervention at this institution (2·2%) is below the average of 3–5% estimated nationwide; thus, our rate could have been too low to detect a change.

There are several limitations to this study. This was a single-institution study in a university-affiliated medical center which included mostly inpatients; therefore, the results may not be generalizable to other settings. The study is retrospective and thus limited by missing data and patient confounders, such as other conditions

leading to elevated WBC or creatinine level or shock that could skew the severity classification and thus introduce misinterpretation of the appropriateness of treatment. The severity category and appropriateness of treatment were assessed by the authors based on data at the time of diagnosis, and thus did not adjust for patients who developed worsening disease or had a change in management. Univariate analyses were performed on the groupings of patients (severity of illness and before/after guidelines) as these important differences between groups were lost when attempting to combine the data for a single multivariate analysis. Finally, we did not control for concurrent use of other antibiotics or additional sources of infection.

In conclusion, treatment that would be considered adherent to the 2010 IDSA/SHEA guidelines for CDI improved after guideline publication. Importantly, however, mortality and LOS attributable to CDI were higher in patients who received undertreatment according to these guidelines, and there was no evidence that overtreatment protected against mortality, CDI-related LOS or the need for surgical intervention. Efforts should continue to focus on adherence with these guidelines to improve outcomes in patients with CDI.

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DECLARATION OF INTEREST

None.

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