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MAJOR ARTICLE

Short- and Long-Term Attributable Costs of *Clostridium difficile*–Associated Disease in Nonsurgical Inpatients

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(See the editorial commentary by Paladino and Schentag on pages 505–6)

Background. The incidence of *Clostridium difficile*–associated disease (CDAD) is increasing. There are few data on the short-term and long-term attributable costs of CDAD. The objective of this study was to determine the acute and 180-day attributable inpatient costs of CDAD.

Methods. We performed a retrospective cohort study of all patients without operating room costs who were admitted for ⩾48 h to Barnes-Jewish Hospital, a tertiary care hospital in St. Louis, Missouri, 1 January 2003–31 December 2003 ($n = 24{,}691$). Attributable costs of CDAD were determined by multivariable linear regression and propensity-score matched-pairs analyses ($n = 684$) for the hospitalization in which CDAD occurred and per patient over a 180-day period, including the initial hospitalization.

Results. CDAD was associated with $2454 (95% confidence interval, $2380–$2950; increase in cost, 41%) attributable costs per CDAD episode by linear regression and with $3240 attributable costs ($P < .001$; increase in cost, 33%) by propensity-score matched-pairs analysis. CDAD was associated with $5042 (95% confidence interval, $3797–$6481; increase in cost, 53%) attributable inpatient costs over 180 days by linear regression and with $7179 attributable costs for inpatient care ($P < .001$; 48% increase in costs) by propensity-score matched-pairs analysis.

Conclusions. CDAD was associated with a significant increase in costs for inpatient care and increased costs at 180 days after the initial hospitalization when the CDAD episode occurred.

Clostridium difficile–associated disease (CDAD) is the most common infectious cause of hospital-associated diarrhea [1]. A recent study using *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9), codes to measure CDAD prevalence found that the proportion of hospital discharges that were assigned the CDAD ICD-9 code (008.45) increased from 0.37% in 2000 to 0.51% in 2003, for an estimated 178,000 CDAD cases in patients discharged from short-stay hospitals in 2003 [2]. The occurrence of recent outbreaks with unexpectedly high numbers of severe CDAD cases, many caused by the North American pulsed field gel electrophoresis type 1 strain of *C. difficile*, suggests that the epidemiology of CDAD is changing [3–7]. Despite its importance as a hospital pathogen, there are few studies of the financial burden of CDAD. No studies have evaluated costs associated with CDAD beyond the hospitalization when CDAD occurred [8–12]. The objective of the present study was to determine the attributable total costs of treatment of CDAD infections in nonsurgical inpatients, both for the index hospitalization and over a 180-day period starting with the index hospitalization.

METHODS

Study design. This study was conducted at Barnes-Jewish Hospital (BJH), a 1250-bed tertiary care hospital in St. Louis, Missouri. Data were collected electronically from the hospital's Medical Informatics and Trendstar financial databases. The Informatics database was queried to identify all patients admitted to BJH from 1 January 2003, through 31 December 2003. Data were

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collected on demographic characteristics, hospital ward(s), inpatient mortality, ICD-9 discharge and procedure codes, inpatient medications ordered, vital signs, and laboratory results. Total hospital costs (direct, indirect, and fixed) were collected from the Trendstar financial database for each patient. Case patients with CDAD were defined as any inpatient with a positive stool toxin assay for *C. difficile* (TechLab). Because the hospital laboratory performs a test for *C. difficile* only on unformed stool samples from patients with a clinical suspicion of CDAD, all patients with positive toxin results were considered to be case patients with CDAD. The analyses included health care–onset and community-onset CDAD cases.

Attributable costs of CDAD were assessed both for individual hospitalizations and per patient over a 180-day period. For the former analysis, all nonsurgical admissions with a stay ⩾48 h during the study period were included. Admissions with a stay <48 h were excluded, to limit the number of patients not at risk or at very low risk for CDAD. Nonsurgical admissions were defined by the absence of operating room costs. Surgical patients were excluded, because preliminary data analysis indicated that the distribution and predictors of costs were very different in patients with operating room costs compared with those of other hospitalized patients. For the 180-day analysis, the index hospitalization for case patients with CDAD was the patient's first toxin-positive admission during the study period. For noncases with >1 admission during the study period, 1 admission per patient during the study period was randomly selected as the index admission. For both patients with and without CDAD, the Informatics database was then queried to identify all subsequent admissions to BJH within 180 days after the index admission. Total hospital costs for each admission, including the index hospitalization, were summed to obtain a total for all admissions over the 180-day period. Diagnoses, procedures, and medications from the index hospitalization were used to predict costs over the 180-day period.

Data analysis. The first method for determining attributable cost used in this study was multivariable linear regression. Natural log–transformed total costs were used as the outcome variable, to normalize the distribution of costs. The primary independent variable was CDAD case status. Frequency analyses were performed on ICD-9 code data, to identify other variables that might be important predictors of costs. Comorbidities were classified by the Deyo adaptation of the Charlson Comorbidity Index [13, 14]. A modified Acute Physiology Score was calculated on the basis of laboratory results and vital signs collected within 24 h after admission [15]. The Acute Physiology Score was modified, because data for respiratory rate and Glasgow Coma Score were not available electronically. In addition, albumin levels measured within 24 h after admission were collected and categorized into normal (>3.5 g/dL), low (2.5–3.5 g/dL), and very low (<2.5 g/dL). Missing laboratory results and vital signs were classified in the normal range. Case patients with CDAD were considered to be exposed to a medication only if the order start date was before the collection date of the patient's first positive stool toxin assay.

Linear regression models were built using backwards stepwise regression, with use of $P \leqslant .05$ for entry and $P > .15$ for exclusion criteria. All biologically plausible variables met entry criteria. Variables that applied to <10 patients were excluded. Of the continuous variables, only the modified Acute Physiology

Table 1. Characteristics of study cohort (n = 24,691).

Characteristic	Case patients with CDAD (n = 439)	Patients without CDAD (n = 24,252)
Age, median years (range)	67 (18–101)	54 (13–106)
Male sex, no. (%)	214 (49)	9470 (39)
White race, no. (%)	288 (66)	13,595 (56)
Length of stay, median days (range)	10 (2–87)	4 (2–290)
Total costs[a], median US$	15,906	6821
Direct costs, median US$	8581	3563
Charges, median US$		
Total	32,597	14,068
Room and board	7179	3220
Pharmacy	5971	1781
Laboratory	7297	2786
Radiology	3449	2083
Respiratory therapy	2843	1238
Physical therapy	647	456

NOTE. $P < .001$ for all comparisons (by Mann-Whitney U test for continuous variables and by χ^2 test for categorical variables).

[a] Total costs include direct, indirect, and fixed costs.

Table 2. Linear regression analysis of total hospital costs per hospitalization (selected variables).

Variable	Coefficient	*P*
CDAD case	0.35	<.001
Age, years		
⩽20	Reference	
21–25	−0.04	<.001
26–30	−0.04	.01
36–40	−0.04	.02
61–65	0.03	.04
65–70	0.05	<.001
71–75	0.04	.01
76–80	0.05	<.001
81–85	0.06	<.001
86–90	0.05	.01
Male sex	−0.01	.04
White race	−0.03	<.001
Modified Acute Physiology Score	0.01	<.001
Albumin level		
Normal (>3.5 g/dL)	Reference	
Low (2.5–3.5 g/dL)	0.06	<.001
Very low (<2.5 g/dL)	0.11	<.001
Received gastric acid suppressor	0.09	<.001
Received chemotherapy	0.30	<.001
Leukemia/lymphoma	0.29	<.001
Transplantation	0.49	<.001
Bacteremia, septicemia, or fungemia	0.07	<.001
Received treatment with a fluoroquinolone		
0 days	Reference	
>4–7 days	0.24	<.001
>7–14 days	0.41	<.001
>14 days	0.50	<.001
Received treatment with a third- or fourth-generation cephalosporin		
0 days	Reference	
>2–4 days	0.06	<.001
>4–7 days	0.24	<.001
>7–14 days	0.34	<.001
>14 days	0.35	<.001

NOTE. Other variables included in the model were age, 31–35, 41–60, and ⩾91 years; receiving treatment with >0–2 days or >2–4 days of fluoroquinolone; receiving treatment with >0–2 days of third- or fourth–generation cephalosporin; staying on the chronic ventilation floor; receiving an antidiarrheal, laxatives, or narcotics; congestive heart failure; cerebral vascular disease; chronic obstructive pulmonary disease; peripheral vascular disease; moderate or severe liver disease; paraplegia/hemiplegia; cancer (excluding leukemia/lymphoma); metastatic solid tumor; obesity; endoscopy; G tube placement; insertion, repair, or removal of a pacemaker or defibrillator; angioplasty and stent placement (coronary and non-coronary), cardiac stress tests, pacemaker, and defibrillator checks; cardiac arrest; cardiac catheterization; atrial fibrillation; aneurysm repair; acute renal failure; pleurisy, pneumothorax, or pulmonary collapse; central venous catheter placement; minor surgery or procedures on colon or small intestine; anemia; neutropenia; cystic fibrosis; deep venous thrombosis or pulmonary embolism; gunshot wound or motor vehicle accident; cesarean section; preeclampsia or eclampsia; vaginal delivery; other obstetrical procedures; early or threatened labor; polyhydramnios, oligohydramnios, or other amniotic cavity or membrane problems; staying on psychiatry ward; dementia; episodic mood disorders; psychiatric somatotherapy; convulsions; urinary tract infection or pyelonephritis; nausea and/or vomiting; adverse drug event or overdose; cardiomyopathy; schizophrenia; obsessive-compulsive disorder; depression; receiving amoxicillin or ampicillin, receiving clindamycin, receiving metronidazole, receiving intravenous vancomycin, receiving macrolide, receiving first- or second-generation cephalosporin, receiving antifungal treatment, receiving antiviral treatment; number of procedures performed; number of days in an intensive care unit; and time to death after admission.

Table 3. Attributable costs of *Clostridium difficile*–associated disease (CDAD) per hospitalization.

Variable	Matched-pairs estimate, median US$	Linear regression estimate, mean US$ (95% CI)
Non-CDAD admissions[a]	9753	5940 (5761–6125)
CDAD admissions[b]	14,570	8394 (8141–9074)
Attributable costs	3240[c]	2454 (2380–2950)
Increase in costs, %	33	41

[a] Admissions for linear regression, 24,252; admissions for matched-pairs analysis, 342.
[b] Admissions for linear regression, 439; admissions for matched-pairs analysis, 342.
[c] Median difference in costs between case-control pairs.

Score met the assumptions for inclusion as a continuous variable; all other variables were analyzed categorically. All levels of categorical variables were retained in the regression models. All independent variables were checked for colinearity. The models were checked for functional form misspecification with Ramsey's regression specification error test and for heteroskedasticity with the Breusch-Pagan test [16]. Both linear regression models (hospitalization costs and 180-day costs) were found to have significant heteroskedasticity ($P < .05$). A general linear model (GLM) with calculation of feasible generalized least-squares parameter estimates was used to adjust for heteroskedasticity. Because the GLM model used the natural logarithm of costs—ln(costs)—as the dependent variable, an intermediate regression was performed to predict costs [16]. Attributable costs of CDAD were calculated as follows. The regression coefficient of each variable (other than CDAD) was multiplied by the mean value for each variable or the fraction of patients in the entire cohort who were positive for the variable of interest and was added to the constant. The regression equation was solved individually for the case patients (CDAD = 1) and for the comparison group (CDAD = 0) and was back-transformed by taking the exponent of the result. The attributable costs of CDAD were calculated by subtracting the difference in calculated costs between the 2 models.

The second method for determining attributable costs used in this study was propensity-score matched-pairs analysis [17]. A logistic regression model to predict risk of CDAD was created that contained all variables that might impact either risk of CDAD or hospital costs, with CDAD as the outcome. Predicted probabilities to develop CDAD from this model were used to match case patients to control subjects by the nearest-neighbor method [18]. One control subject was selected per case patient. Case patients for whom a suitable control subject could not be found were excluded. Attributable costs were calculated using the median difference in costs between case-control patient pairs.

Analyses were performed with SPSS, version 14.0 (SPSS), and Stata, version 9.2 (StataCorp). The Washington University Human Research Protection Office approved this study.

RESULTS

Characteristics of the cohort are given in table 1. The cohort included 439 CDAD admissions and 24,252 non-CDAD admissions. Case patients with CDAD were significantly older, had a longer length of stay, and were more likely to be male or white than were subjects without CDAD (for all, $P < .001$). Median unadjusted total costs were higher for case patients with CDAD than for patients without CDAD ($15,906 vs. $6821; $P < .001$). When total hospitalization costs were categorized by selected departments, case patients with CDAD had significantly higher costs than did noncase patients for each cost center analyzed ($P < .001$).

Selected variables from the final linear regression model for CDAD costs per hospitalization in the nonsurgical cohort are given in table 2. More than 100 variables were included in the final model. CDAD remained an independent predictor of total costs after adjustment for a variety of variables ($P < .001$). Other variables that strongly impacted costs include chemotherapy, insertion or repair of a pacemaker or defibrillator, coronary angioplasty or stent placement, aneurysm repair, cystic fibrosis, transplantation, psychiatric somatotherapy, treatment with antimicrobials for >1 week, having a large number of procedures performed, staying in an intensive care unit for ⩾1 week, and death ⩾2 weeks after hospital admission.

In the propensity-score matched-pairs analyses, 342 case patients were matched with 342 control patients ($n = 684$). Appropriate control patients could not be found for 48 patients with CDAD. Unmatched case patients had significantly higher modified Acute Physiology Scores than did matched case patients (median, 7.5 vs. 5.0; $P < .001$), and unmatched case patients were more likely to have leukemia or lymphoma than were matched case patients (33% vs. 11%; $P < .001$). Unmatched case patients had significantly higher costs than did matched case patients, both during the index hospitalization (median, $35,751 vs. $14,570; $P < .001$) and over 180 days (median, $47,827 vs. $27,385; $P < .001$).

In the cohort, after back-transformation, the adjusted costs of a non-CDAD admission were $5940, and the adjusted costs

Table 4. Linear regression analysis of total hospital costs over 180 days (selected variables).

Variable	Coefficient	*P*
CDAD case	0.43	<.001
Age, years		
⩽20	Reference	
21–25	−0.04	.01
26–30	−0.05	<.001
31–35	−0.06	<.001
36–40	−0.06	.01
51–55	0.05	.04
56–60	0.05	.03
61–65	0.05	.05
65–70	0.06	.02
>95	−0.12	.05
Male sex	−0.03	.01
White race	−0.03	<.001
Modified Acute Physiology Score	0.01	<.001
Albumin level		
Normal (>3.5 g/dL)	Reference	
Low (2.5–3.5 g/dL)	0.10	<.001
Very low (<2.5 g/dL)	0.13	<.001
Received gastric acid suppressor	0.12	<.001
Received chemotherapy	0.40	<.001
Leukemia/lymphoma	0.50	<.001
Received treatment with a fluoroquinolone		
0 days	Reference	
>4–7 days	0.24	<.001
>7–14 days	0.37	<.001
>14 days	0.50	<.001
Received treatment with a third- or fourth-generation cephalosporin		
0 days	Reference	
>0–2 days	0.08	<.001
>4–7 days	0.18	<.001
>7–14 days	0.22	<.001
>14 days	0.34	<.001

NOTE. Other variables included in the model were age, 41–50 or 71–95 years; receiving >0–2 or >2–4 days of treatment with fluoroquinolone; receiving >2–4 days of treatment with third- or fourth–generation cephalosporin; staying on the chronic ventilation floor; receiving antidiarrheals; receiving laxatives; receiving narcotics; congestive heart failure; cerebrovascular disease; moderate or severe liver disease; diabetes with chronic complications; cancer (excluding leukemia/lymphoma); metastatic solid tumor; G tube placement; insertion, repair, or removal of a pacemaker or defibrillator; angioplasty and stent placement (coronary and noncoronary); cardiac stress tests, pacemaker, and defibrillator checks; cardiac arrest; atrial fibrillation; aneurysm repair; acute renal failure; pleurisy, pneumothorax, pulmonary collapse; central venous catheter placement; minor surgery or procedures on colon or small intestine; anemia; neutropenia; cystic fibrosis; deep venous thrombosis or pulmonary embolism; cesarean section; preeclampsia or eclampsia; vaginal delivery; early or threatened labor; polyhydramnios, oligohydramnios, or other amniotic cavity or membrane problems; staying on psychiatry ward; dementia; episodic mood disorders; psychiatric somatotherapy; convulsions; obesity; incision of pleura/thoracentesis; urinary tract infection or pyelonephritis; receiving antifungal; receiving antiviral; number of procedures performed; number of days in an intensive care unit; time to death after index admission; dialysis; hypertension; diabetes; adverse drug event or drug overdose; schizophrenia; depression; sickle cell anemia; number of admissions in previous 60 days; received treatment with amoxicillin or ampicillin; received treatment with metronidazole; received treatment with intravenous vancomycin; received treatment with macrolide; received first- or second-generation cephalosporin.

Table 5. Attributable costs of *Clostridium difficile*–associated disease (CDAD) over 180 days.

Variable	Matched-pairs estimate, median US$	Linear regression estimate, mean US$ (95% CI)
Non-CDAD admission[a]	14,970	9518 (9107–9947)
CDAD admission[b]	27,385	14,560 (12,905–16,428)
Difference (attributable costs)	7179[c]	5042 (3797–6481)
Increase in costs, %	48	53

[a] Admissions for linear regression, 17,663; admissions for matched-pairs analysis, 342.
[b] Admissions for linear regression, 390; admissions for matched-pairs analysis, 342.
[c] Median difference in costs between case-control pairs.

of a CDAD admission were $8394, for attributable costs of $2454 (95% CI, $2380–$2950) (table 3). In the propensity-score matched-pairs analysis, the median costs of a control admission were $9753, and the median costs of a case admission were $14,570 ($P < .001$, by Wilcoxon signed rank test); the median attributable costs of CDAD calculated from the matched pairs were $3240. When multiplied by the 439 CDAD admissions, the resulting median attributable costs of CDAD in nonsurgical inpatients per admission over a 1-year period at BJH were estimated to be between $1,077,306 (regression model estimate) and $1,422,360 (matched-pairs estimate).

The analysis of attributable inpatient costs over 180 days included 390 patients with CDAD and 17,663 patients without CDAD. Selected variables from the final linear regression model for CDAD costs over the 180-day follow-up period are given in table 4. CDAD remained an independent predictor of total inpatient costs over 180 days, after adjustment for many variables ($P < .001$). Other important predictors of increased costs over the follow-up period included chemotherapy, leukemia/lymphoma, insertion or repair of a pacemaker or defibrillator, coronary or noncoronary angioplasty or stent placement, aneurysm repair, minor abdominal surgery or procedures, cystic fibrosis, psychiatric somatotherapy, treatment with antimicrobials for >1 week, having a large number of procedures performed, staying in an intensive care unit for ⩾6 days, and death within 1 week after hospital admission.

After back-transformation, the adjusted sum cost for admissions for patients without CDAD over the 180-day period was $9518, and the adjusted sum for patients with CDAD was $14,560, for attributable costs of $5042 (95% CI, $3797–$6481) (table 5). In the propensity-score analysis, the median sum cost of inpatient admissions over the 180-day period for CDAD cases was $27,385. The median sum cost of control admissions was $14,970 ($P = .001$, by Wilcoxon signed rank test). The median attributable costs of CDAD calculated from the matched-pairs analysis were $7179. When multiplied by the 390 CDAD admissions, the resulting median attributable costs of CDAD over 180 days at BJH were estimated to be between $1,966,380 (regression model estimate) and $2,799,810 (matched-pairs estimate).

DISCUSSION

In this study, to our knowledge the largest to date evaluating the attributable costs of CDAD, CDAD was associated with increased costs during the CDAD hospitalization and increased inpatient costs extending 180 days from the initial CDAD admission. These estimates were established using 2 different methods for determining attributable costs: multivariable GLM regression and propensity-score matched pairs. The attributable costs of CDAD ranged from $2454 (41% increase in costs over non-CDAD admissions) by regression analyses to $3240 (33% increase in costs) by propensity-score matched-pairs analyses. The increase in 180-day attributable costs of CDAD ranged from $5042 (53% increase in costs) by regression analyses to $7179 (48% increase in costs) by propensity-score matched-pairs analyses.

A key strength of this analysis is the use of 2 different methods to estimate costs. The "true" attributable costs of CDAD are unknown, but the different models used here provide a realistic range in which the true attributable costs may fall. Both analysis methods have advantages and disadvantages. A weakness of the propensity-scores method is the loss of some cases that could not be matched to controls; the GLM-regression method allows analysis of the entire cohort. The GLM-regression model may have unmeasured confounders, but in the propensity-scores method, case and control patients are matched using data from a large number of variables, to minimize potential confounding.

The attributable costs estimates generated by both methods are remarkably consistent. A closer look at the findings of this study reveals how the results are complementary. Patients who develop CDAD tend to be older and more severely ill than patients who do not develop CDAD. The GLM-regression method uses all of the cohort data, thereby including a large number of patients at low risk for CDAD. Propensity-score matching identifies control patients who are as similar to the

case patients as possible and minimizes the number of control patients who are not severely ill. The estimated per hospitalization cost for a non-CDAD admission by GLM is $5940, with attributable CDAD costs of $2454, compared with $9753 for the matched pairs, with attributable CDAD costs of $3240 (table 3). Although the absolute attributable CDAD cost by GLM is lower, the relative increase in costs due to CDAD is higher (41% vs. 33%). CDAD may cost more for patients who are sicker, but the relative increase in costs may not be as great compared with that for less sick patients who develop CDAD. The similarities in relative increase in costs further highlight the consistency of these estimates. The relative increases in costs in the 180-day analyses (by regression, 53%; by propensity-score matched pairs, 48%) differ by only 5%.

Both analysis methods are conservative and may underestimate the true attributable cost of CDAD. The large number of variables included in the GLM regression may have biased costs toward a lower value by attributing some of the costs associated with CDAD to other variables that occurred after CDAD diagnosis (for example, admission to an intensive care unit after CDAD diagnosis). In the propensity-score matched-pairs analysis, 48 CDAD cases were excluded. These case patients were more severely ill than were the matched case patients and had higher median costs for both the index hospitalization and over the 180 days after the index hospitalization.

Data on the cost of CDAD are surprisingly rare, and data on attributable costs are even rarer. Wilcox et al. [11] estimated the costs of a CDAD infection to be £4107. Miller et al. [10] estimated the costs of hospital readmission due to CDAD in Canada to be $128,200 (in Canadian dollars) per hospital per year. In 1 of only 3 published CDAD cost analyses performed in the United States, Kofsky et al. [8] estimated overall charges of $334,000 for treatment of 155 patients with CDAD, for an individual cost of ~$2000 per patient. The greatest limitation of these previous studies is that none of them calculated the attributable costs of CDAD; instead, costs were estimated by either summing various patient charges or by extrapolating general costs (e.g., cost to be hospitalized 1 day) over averages for a known number of patients with CDAD. Similarly, in the recent study by O'Brien et al. [12], the mean excess costs of CDAD were estimated to be $13,675 per case. This estimate is much higher than those of previously published estimates, but the estimate was derived from differences in length of stay between CDAD and non-CDAD patients (stratified by severity of illness) and does not constitute a true attributable costs. Notably, the median excess costs of $5442 reported by O'Brien et al. [12] for secondary case patients with CDAD was much closer to those of other published estimates.

Kyne et al. [9] performed the only analysis of CDAD-attributable costs published to date. The researchers used a cohort study design and linear regression to estimate attributable costs and found the attributable costs of CDAD to be $3669 (95% CI, $1126–$7024) per episode. The analysis presented here has several advantages over the analysis performed by Kyne et al. [9]. The first is sample size; the study population at BJH included 439 CDAD cases, compared with 47 in the study of Kyne et al. [9]. Second, the analysis presented here may be more generalizable than is the analysis performed by Kyne et al. [9], which was limited to 3 medical wards. Finally, Kyne et al. [9] estimated total hospital costs by adjusting hospital charges with the overall Medicare cost-to-charge ratio for their institution. In the present analysis, the cost-to-charge ratio was individualized by department, thereby providing a more accurate estimate of the actual costs of each inpatient admission.

The analysis of CDAD costs over 180 days performed in this study indicated that CDAD continues to be a significant predictor of inpatient costs extending beyond the costs of a patient's initial CDAD hospitalization. This finding has not been reported previously. The attributable costs of the index admission plus readmissions within 180 days are likely to be in the range between our linear regression estimate ($5042) and our propensity-score estimate ($7179). However, these figures underestimate the overall long-term attributable costs of CDAD, because we did not have data on outpatient costs (e.g., outpatient clinic visits, outpatient medication use, or rehabilitation), long-term care facility costs, cost of admissions to another acute care facility, or costs from loss of work due to CDAD. The lack of these data is a limitation of this study. Furthermore, because this study included only inpatients without operating room costs, patients with CDAD who received colectomies were excluded. A future study that incorporates all health care costs and includes information about surgical patients would provide a more accurate estimate of the true total attributable costs of CDAD.

CDAD significantly increases hospital costs, even when the conservative estimates presented here are applied. On the basis of these results, in 2003, CDAD infections cost >$1 million at BJH alone. McDonald et al. [2] found the CDAD ICD-9 code cited in 178,000 discharges from short-stay hospitals in the United States in 2003. With use of this estimate, the national attributable costs of CDAD per CDAD hospitalization in 2003 were $436–$580 million. The long-term costs of CDAD may be even greater. In 2003, patients who developed CDAD incurred 180-day costs of $1.9–$2.8 million at BJH. When multiplied by the estimate of McDonald et al. [2] of 178,000 US CDAD cases, the estimated attributable 180-day costs of CDAD cases in the United States in 2003 were ~$897 million—$1.3 billion.

Anecdotal reports of outbreaks with the North American pulse-field type 1 strain of *C. difficile* since 2003 indicate that CDAD rates are increasing. More-recent estimates suggest that as many as 250,000 hospitalizations in the United States during

2005 were complicated by CDAD (Centers for Disease Control and Prevention, unpublished data). In addition, CDAD severity may also be increasing. Thus, the financial burden of CDAD is likely increasing as well. The high attributable costs of CDAD may help justify allocation of resources to CDAD prevention in hospitals and emphasize the need for additional scientific research on CDAD [19, 20]. Future studies of CDAD interventions can assess cost-effectiveness of those interventions with use of the estimates provided here.

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