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Mortality, Hospital Costs, Payments, and Readmissions Associated With *Clostridium difficile* Infection Among Medicare Beneficiaries

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Background: The management of *Clostridium difficile* infection (CDI) among hospitalized patients is costly, and ongoing payment reform is compelling hospitals to reduce its burden. To assess the impact of CDI on mortality, hospital costs, healthcare use, and Medicare payments for beneficiaries who were discharged with CDI listed as a secondary *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* claim diagnosis.

Methods: Data were analyzed from the 2009 to 2010 5% random sample Medicare Standard Analytic Files of beneficiary claims. Patients with index hospitalizations with CDI as a secondary diagnosis and no previous hospitalization within 30 days were identified. Outcomes included inpatient and 30-day mortality, inpatient costs, index hospital payments, all-provider payments, net hospital losses, payment to cost ratio, length of stay (LOS), and 30-day readmission; outcomes were each risk adjusted using propensity score matching and regression modeling techniques.

Results: A total of 3262 patients with CDI were identified after matching to patients without a CDI diagnosis. After risk adjustment, secondary CDI was associated with statistically significantly (all $P < 0.05$) greater inpatient mortality (3.1% vs. 1.7%), 30-day mortality (4.1% vs. 2.2%), longer LOS (7.0 days vs. 3.8 days), higher rates of 30-day hospital readmissions (14.8% vs. 10.4%), and greater hospital costs ($16,184 vs. $13,954) compared with the non-CDI cohort. The risk-adjusted payment-to-cost ratio was shown to be lower for patients with CDI than those without (0.76 vs. 0.85).

Conclusions: Secondary CDI is associated with greater adjusted mortality, costs, LOS, and hospital readmissions, while receiving similar hospital reimbursement compared with patients without CDI in a Medicare population.

Key Words: clostridium difficile, cost, hospital readmission, mortality

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Clostridium difficile infection (CDI) is one of the most common healthcare-associated infections (HAIs) and is a significant cause of morbidity and mortality that disproportionately affects elderly hospitalized patients.[1,2] Between 2000 and 2009, the number of hospitalized patients in the United States with any CDI discharge diagnosis increased from approximately 139,000 to 336,600, whereas the number with a primary CDI diagnosis increased from 33,000 to 111,000.[3] *Clostridium difficile* infection most commonly manifests as colitis, leading to diarrhea, commonly referred to as *C. difficile*–associated diarrhea. Risk factors for CDI include age older than 65 years, female sex, previous or concomitant antibiotic exposure, prolonged stay in a healthcare facility, immune compromise, renal impairment, previous antibiotic exposure, and chemotherapy.[4–8]

Clostridium difficile infection imposes a significant burden to the US health system, resulting in an estimated $1.01 to $1.62 billion in direct medical costs.[9] Cases of CDI can result in incremental hospital costs in excess of $6000 per case for patients diagnosed with CDI compared with those without CDI.[10] In addition, costs for hospital stays among patients with CDI are greater for patients with secondary diagnoses of CDI compared with primary diagnoses ($31,500 vs. $10,100), potentially due to a greater severity of illness.[3] Approximately two thirds of CDI-related hospital stays involve CDI as a secondary diagnosis.[3] Optimal management of CDI is complicated by the risk of recurrence; approximately 20% to 30% of patients with CDI experience a recurrence of the infection within 60 days of initial treatment.[11–14] If CDI recurs, it typically does so within 1 to 3 weeks after completion of therapy for the initial infection.[15–18] Furthermore, approximately 29% of patients hospitalized with CDI are readmitted within 30 days, and approximately 13% are readmitted with CDI.[19] Rehospitalizations for CDI are estimated to cost in excess of $13,000 per patient.[20]

In recognition of the burden of CDI and HAIs, the US Department of Health and Human Services initiated a National Action Plan to Prevent HAIs with goals of a 30% reduction in CDI rates and hospitalizations by 2013.[21] Furthermore, the Centers for Medicare and Medicaid Services (CMS) require public reporting of CDI infection rates as part of the Inpatient Quality Reporting Program, with financial penalties for underperforming hospitals in 2017.[22,23] Through the Hospital Readmission

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This document contains the risk-adjusted outcomes for inpatient mortality, 30-day mortality, mean length of stay, mean index hospital costs, mean index hospital payments, and mean index all-provider inpatient payments for the entire sample (Table S1), patients with renal insufficiency (Table S2), and patients eligible for the Medicare Hospital Readmissions Reduction Program.

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Reduction Program (HRRP), CMS has also established penalties to hospitals with excess all-cause readmissions in selected patient populations (ie, congestive heart failure, pneumonia, and acute myocardial infarction), with plans to implement additional measures for chronic obstructive pulmonary disorder as well as total hip and knee arthoplasty.[24,25] Given the risk of recurrence among patients with CDI, this may constitute a significant cause of readmissions among patients with these target conditions and procedures.

Although previous estimates on the costs among patients with a secondary CDI have been performed,[3] an evaluation of both costs and payments among patients with secondary CDI has not been conducted to our knowledge. Given ongoing Medicare payment reform and the ensuing cost pressures imposed on hospitals, an understanding of the impact of secondary CDI on patient outcomes (eg, readmissions), costs, and resource use among Medicare beneficiaries may be of interest to hospital administrators and policy makers. In this study, we evaluate the differences in costs and payments between patients with and without secondary CDI among hospitalized Medicare beneficiaries.

MATERIALS AND METHODS

Data Sources And Study Population

The analysis was conducted using the 2009 and 2010 Medicare 5% Standard Analytic Files. These files contain medical claims and eligibility files from a 5% random sample of Medicare "fee-for-service" beneficiaries and allow for longitudinal analyses of health outcomes, healthcare use, and Medicare payments across years.

Inclusion criteria included (1) continuous enrollment in fee-for-service Medicare parts A and B for all of 2009 and 2010, with the exception of death during the study period and (2) secondary *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* (*ICD-9-CM*) diagnosis of CDI on an inpatient claim for short-term acute care hospitals (008.45, intestinal infection due to *C. difficile*). Exclusion criteria included the following: (1) primary (ie, first listed) *ICD-9-CM* diagnosis for CDI, for whom CDI was the main reason for hospitalization and (2) previous hospital stay within the 30 days preceding the index hospital stay to reduce the likelihood that the observed outcomes from the index hospital stay would be influenced by recently provided hospital care. Eligible controls were identified from those admitted to an acute care hospital in 2009 or 2010 for which a diagnosis code for CDI was absent.

We also evaluated the outcomes of interest in separate subgroups of patients (ie, renal insufficiency and Medicare HRRP eligible patients). The renal insufficiency subgroup was selected because these patients may represent a more homogenous group patients at high risk of CDI compared with other subgroups (eg, immune compromised) and had a sufficiently large number of sample patients. Those with an *ICD-9-CM* diagnosis for renal insufficiency and/or an *ICD-9-CM* procedure code for dialysis were grouped into the renal insufficiency subgroup. Those with a principal diagnosis of acute myocardial infarction, heart failure, or pneumonia were grouped as Medicare HRRP patients. These conditions were chosen because these were the ones that were finalized as the HRRP conditions at the time of the analysis. The *ICD-9-CM* diagnosis or procedure codes for each of these conditions are provided in Table 1.

TABLE 1. The *ICD-9-CM* Diagnosis and Procedure Codes for Selected Conditions

Condition	The *ICD-9-CM* Diagnosis and/or Procedure Codes
C. difficile	008.45
Renal insufficiency	250.4x, 403.xx, 404.xx, 405.01, 405.11, 409.11, 581.xx-589.x, 753.0, 753.1x, 791.0, V42.0
Dialysis	V45.1x, V56.x, E871.2, E872.2, E874.2, E879.1
Acute myocardial infarction	410.x0, 410.x1
Heart failure	402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0, 428.1, 428.20–428.23, 428.30–428.33, 428.40–428.43, 428.9
Pneumonia	480.x-483.x, 485, 486, 487.0, 488.11

Outcomes

To evaluate the impact of CDI on hospital costs and use, we evaluated the following outcomes: inpatient mortality, 30-day mortality, length of stay (LOS), 30-day all cause readmissions, index hospital costs, and index hospital payments. Each of these outcomes was evaluated in the renal insufficiency and HRRP subgroups, with the exception of mortality for the HRRP subgroup. Costs were calculated by conversion of the applicable hospital's cost-to-charge ratio to hospital charges. The 2011 and 2012 Medicare Inpatient Prospective Payment System Impact Files were used to obtain the appropriate cost-to-charge ratios. Index hospital Medicare payments were determined using Medicare part A claims, whereas all-provider payments included payments to the hospital (ie, part A) and professional fees (ie, part B) during the index hospital stay matched to the hospital by admission and discharge dates and place of service. We also estimated the net loss (costs minus payments) and the payment-to-cost ratio for the CDI and non-CDI groups.

Matching Procedure

A 1:1 propensity score match was performed between patients with and without a CDI diagnosis using a "greedy matching" algorithm (specifically, nearest neighbor). The propensity score was constructed using a probit regression, including covariates for age, sex, dual (Medicare and Medicaid) eligibility, mechanical ventilation, parenteral or enteral feeding, indwelling catheter, Agency for Healthcare Research and Quality Clinical Classification Software categories,[26] Medicare Severity Diagnosis Related Groups (MS-DRGs), Charlson Comorbidity Index (CCI) associated with the inpatient stay, and 30-day history of skilled nursing facility (SNF) stays and infused drugs administered in the 90 days before admission (antibiotics, glucocorticoids, immunomodulators, chemotherapeutic agents). Postmatching baseline characteristics were compared with check for balance between the CDI and non-CDI groups.

Statistical Analysis

Descriptive comparisons (CDI vs. non-CDI) were performed on the matched sample. For continuous variables, a paired *t* test or Wilcoxon signed rank test was performed, where appropriate. Differences in categorical variables were assessed using McNemar χ^2 test. Because of residual differences in baseline characteristics after matching, additional regression models were used to test differences in outcomes between the CDI and non-CDI matched groups while adjusting for covariates, including age, dual eligibility status, admission source, Agency for Healthcare Research and Quality Clinical Classification Software diagnosis groups,[26] CCI,

TABLE 2. Baseline Characteristics Between Patients With CDI and Patients Without CDI

Variable	No CDI (n = 3262)	CDI (n = 3262)	*P*
Age, %			
0–44	113 (3.5)	104 (3.2)	<0.001*
45–54	193 (5.9)	171 (5.2)	
55–64	396 (12.1)	277 (8.5)	
65–74	1362 (41.8)	831 (25.5)	
75–84	931 (28.6)	1071 (32.8)	
≥85	267 (8.2)	808 (24.8)	
Female, %	1788 (54.8)	1891 (58.0)	0.01
Dual eligible, %	675 (20.7)	995 (30.5)	<0.001
Mean (SD) CCI	1.03 (1.19)	1.40 (1.64)	<0.001
SNF stays in past 30 days, %	70 (2.1)	653 (20.0)	<0.001
Antibiotic use in past 30 days, %	52 (1.6)	328 (10.1)	<0.001
Use of mechanical ventilation, %	17 (0.5)	318 (9.8)	<0.001
Enteral/parenteral feeding, %	13 (0.4)	181 (5.6)	<0.001
Indwelling catheters during index stay, %	18 (0.6)	54 (1.7)	<0.001
Subgroups			
Renal insufficiency, %	404 (12.4)	1357 (41.6)	<0.001
Medicare HRRP	328 (10.1)	365 (11.2)	0.133

**P* value corresponds to the categorical differences in the distribution of age groups.

mechanical ventilation, parenteral feeding, presence of indwelling catheter, previous intravenous 30-day antibiotic use, previous 30-day immunosuppressant use, previous 30-day intravenous chemotherapy use, and previous 30-day SNF use. For costs and payments, a generalized linear model with a gamma distribution and a log-link function was used. A negative binomial regression was fit for LOS to account for overdispersion. Thirty-day readmission, inpatient death, and 30-day mortality were modeled with logit regression. Estimates of effect for costs and payments comparing patients with CDI with patients without CDI were reported as the exponentiated coefficient, interpreted as a multiplicative factor applied to the costs and payments for patients with CDI compared with those without. Incidence rate ratios were reported for LOS, and odds ratios were reported for inpatient mortality, 30-day mortality, and 30-day readmissions. *P* values of <0.05 were considered to be statistically significant. The analysis was conducted using Stata Statistical Software (Release 12, College Station, Tex).

RESULTS

A total of 3264 admissions with CDI as a secondary diagnosis were identified after applying the inclusion and exclusion criteria. After the propensity score match, 3262 patients with CDI were matched with patients without CDI. Characteristics for the 2 groups after matching are shown in Table 2. Significant differences were observed for each of the baseline variables, indicating poor matches and necessitating additional risk adjustment using multivariate regression models.

Inpatient And 30-Day Mortality

Risk-adjusted inpatient and 30-day mortality were significantly different between patients with CDI and patients without CDI (Tables 3, 4). Tables S1 to S3 (available in supplemental digital content, http://links.lww.com/IDCP/A17) provide additional data on 95% confidence intervals (CIs) around estimates for the entire sample, for patients with renal insufficiency and among those meeting Medicare HRRP criteria. Patients with CDI had 1.87 (95% CI, 1.32–4.54; $P = 0.004$) times greater odds of inpatient mortality compared with those without CDI. Similarly, patients with CDI had 1.88 (95% CI, 1.33–3.68; $P = 0.002$) times greater odds of 30-day mortality compared with those without CDI. Among patients with renal insufficiency, patients with CDI experienced 2.19 (95% CI, 1.02–4.72; $P = 0.045$) and 2.89 (95% CI, 1.33–6.32; $P = 0.0008$) times greater odds of inpatient and 30-day mortality, respectively.

Hospital LOS And 30-Day Readmission Rate

Risk-adjusted differences in the 30-day readmission rates and LOS between the CDI and non-CDI groups were significant (Tables 3, 4). In the CDI group, patients had 1.55 (95% CI,

TABLE 3. Estimated Risk-Adjusted Effects* Between Patients With CDI and Patients Without CDI by All Patients, Patients With Renal Insufficiency, and Medicare HRRP Patients

	All Patients (N = 6524)			Renal Insufficiency (n = 1761)			Medicare HRRP* (n = 693)		
Outcomes	Effect Estimate†	95% CI	*P*	Effect Estimate†	95% CI	*P*	Effect Estimate†	95% CI	*P*
Inpatient mortality	1.87	1.32–4.54	0.004	2.19	1.02–4.72	0.045	—	—	—
30-Day mortality	1.88	1.33–3.68	0.002	2.89	1.33–6.32	0.008	—	—	—
LOS	1.82	1.68–1.98	<0.001	1.57	1.38–1.78	<0.001	1.87	1.60–2.20	<0.001
30-Day readmission rate	1.55	1.14–2.11	0.005	1.73	1.10–2.73	0.017	3.13	1.22–8.00	0.017
Index hospital cost	1.16	1.07–1.26	<0.001	1.13	1.02–1.26	0.025	1.26	1.04–1.53	0.019
Index hospital payments	1.05	0.97–1.13	NS	1.02	0.93–1.13	NS	0.98	0.85–1.13	*NS*
Index all-provider inpatient payments	1.08	1.01–1.17	0.037	1.06	0.95–1.17	NS	1.04	0.90–1.21	*NS*

*Models were risk adjusted using the following characteristics: age, dual eligible status, admission source, primary and secondary diagnoses, CCI, mechanical ventilation, parenteral feeding, presence of indwelling catheter, previous intravenous 30-day antibiotic use, previous 30-day immunosuppressant use, previous 30-day intravenous chemotherapy use, and previous 30-day SNF use.

†Effect estimates compare the CDI group with the non-CDI group (referent group). Multiplicative factors are reported for costs and payments. Odds ratios are reported for mortality and 30-day readmission. Incidence rate ratios are reported for LOS. Mortality odds ratios for HRRP patients are not shown because there were insufficient numbers of mortality cases among HRRP patients Without CDI.

HRRP indicates Hospital Readmissions Reduction Program (acute myocardial infarction, heart failure, pneumonia); NS, non-significant findings.

TABLE 4. Risk-Adjusted Outcomes Between Patients With CDI and Patients Without CDI by All Patients, Patients With Renal Insufficiency, and Medicare HRRP Patients

	All Patients (N = 6524)			Patients With Renal Insufficiency (n = 1761)			Medicare HRRP Patients (n = 693)		
Outcomes	**No CDI**	**CDI**	**Difference**	**No CDI**	**CDI**	**Difference**	**No CDI**	**CDI**	**Difference**
Inpatient mortality, %	1.7	3.1	1.4*	9.1	14.3	5.2*	—	—	—
30-Day mortality, %	4.1	2.2	1.9*	7.3	15.0	7.7*	—	—	—
LOS, mean, d	3.8	7.0	3.2*	5.2	8.2	3.0*	3.6	6.7	3.1*
30-Day readmission rate, %	10.4	14.8	4.4*	16.8	24.0	7.2*	11.7	22.4	10.7*
Index hospital cost, mean	$13,954	$16,184	$2230*	$15,264	$17,296	$2032*	$16,534	$20,847	$4313*
Index hospital payments, mean	$11,808	$12,359	$551	$13,609	$13,941	$332	$12,264	$12,020	-$244
Index all-provider inpatient payments, mean	$14,728	$15,955	$1227*	$17,441	$18,412	$971	$14,907	$15,551	$644

Outcomes were risk adjusted using the following characteristics: age, dual eligible status, admission source, primary and secondary diagnoses, CCI, mechanical ventilation, parenteral feeding, presence of indwelling catheter, previous intravenous 30-day antibiotic use, previous 30-day immunosuppressant use, previous 30-day intravenous chemotherapy use, and previous 30-day SNF use. See supplemental appendix (Tables S1-S3, http://links.lww.com/IDCP/A17) for 95% CIs on risk-adjusted rates and means.

*Denotes statistically significant differences ($P < 0.05$).

HRRP indicates Hospital Readmissions Reduction Program (acute myocardial infarction, heart failure, pneumonia).

1.14–2.11; $P = 0.005$) times greater odds of readmission compared with those in the non-CDI group. The LOS for patients with CDI was 1.82 (95% CI, 1.68–1.98; $P < 0.001$) times greater than patients without CDI.

Healthcare use differed according to the subgroups under evaluation (Tables 3, 4). Compared with patients without CDI, patients with CDI with renal insufficiency had 1.73 (95%, 1.10–2.73; $P = 0.017$) times greater odds of readmission within 30 days of discharge and a 1.57 (95% CI, 1.38–1.78; $P < 0.001$) times longer LOS. Patients with CDI eligible for HRRP had 3.13 (95% CI, 1.22–8.00; $P = 0.017$) times greater odds of readmission compared with patients without CDI. Finally, patients with CDI eligible for HRRP had a 1.87 (95% CI, 1.60–2.20; $P < 0.001$) times longer LOS.

Hospital Cost And Medicare Payments

After risk adjustment, there were significant differences between patients with CDI's and patients without CDI's hospital cost and all-provider inpatient payments. Patients with CDI had 1.16 (95% CI, 1.07–1.26; $P < 0.001$) times greater hospital costs than patients without CDI (Fig. 1). Patients with CDI also had 1.08 (95% CI, 1.01–1.17) times greater all-provider inpatient payments. Significant differences in hospital payments were not observed.

In evaluating adjusted costs and payments for each of the subgroups, only differences in hospital costs were observed between patients with CDI and patients without CDI. Among patients with renal insufficiency, patients with CDI had 1.13 (95% CI, 1.02%-1.26%; $P = 0.025$) times greater hospital costs than patients without CDI. For patients meeting the Medicare HRRP eligibility criteria, hospital costs were 1.26 (95% CI, 1.04-1.53; $P = 0.019$) times greater for patients with CDI (Tables 3, 4).

Net Loss And Payment-To-Cost Ratios

Comparing Medicare payments with hospital costs, net losses were estimated to be $1679 worse for patients with CDI compared with patients without CDI. Differences in net losses were similar for patients with renal insufficiency ($1700) but were higher for patients with CDI meeting Medicare HRRP criteria

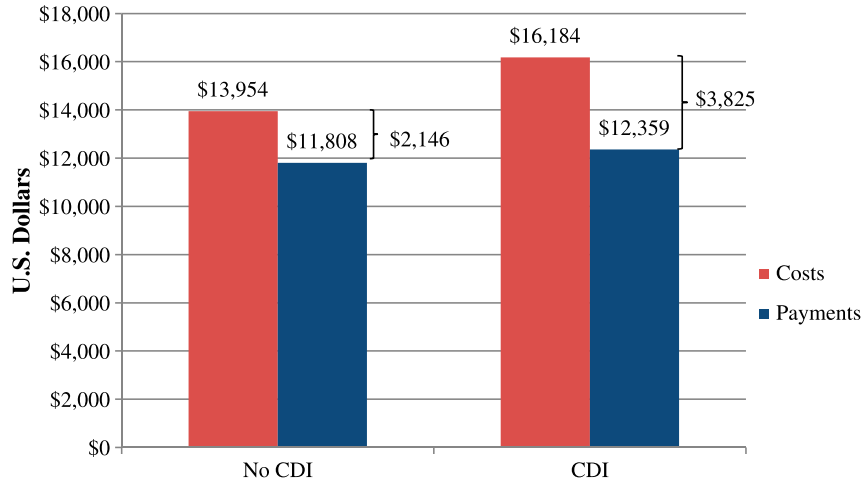

FIGURE 1. Adjusted mean costs and payments according to CDI status as a secondary diagnosis.*

TABLE 5. Average Risk-Adjusted Medicare Payment-to-Cost Ratios and Net Losses for All Patients, Patients With Renal Insufficiency, and Medicare HRRP Patients

	Payment-to-Cost Ratio			Net Loss (US Dollars*)		
	No CDI	CDI	Difference	No CDI	CDI	Difference
All patients	0.85	0.76	−0.08	$2146	$3825	$1679
Renal insufficiency	0.89	0.81	−0.09	$1655	$3355	$1700
Medicare HRRP	0.74	0.58	−0.17	$4270	$8827	$4557

*2010 US dollars.

HRRP indicates Hospital Readmissions Reduction Program (acute myocardial infarction, heart failure, pneumonia).

($4557). Among all patients, the payment-to-cost ratio was lower for patients with CDI (0.76 vs. 0.85, respectively), implying a lower return for patients with CDI. This ratio was also lower in each of the subgroups, with the largest differences observed for Medicare HRRP patients (Table 5).

DISCUSSION

This is the first study to our knowledge that evaluated the impact of CDI as a secondary diagnosis on both costs and payments. Although not all Medicare patients in the current study were elderly, approximately 80% were 65 years or older, and thus, the data are generalizable to elderly patients and provide direct information on the burden of the disease in this high-risk population. Patients with CDI were not only shown to have greater net losses (ie, costs minus payments) compared with those without CDI but also greater mortality, LOS, and hospital readmissions. This information can be used to inform policy decisions regarding reimbursement for CDI and can be used in planning prevention and treatment strategies aimed at reducing the occurrence and recurrence of CDI in this population.

In this analysis, patients with a secondary diagnosis of CDI were shown to have greater risk-adjusted inpatient mortality and 30-day mortality. The negative impact of CDI as a secondary diagnosis was also illustrated in a previous study that showed patients with a secondary diagnosis of CDI were sicker and had higher mortality than those with a primary diagnosis of CDI.[3] Patients with a secondary CDI diagnosis had a higher risk of major or extreme loss of function (93.0% vs. 61.2%), increased death (11.7% vs. 3.7%), and higher risk of mortality scores (68.3% vs. 40.5%).[3] Of note, the effect of CDI on mortality was more pronounced for patients with renal insufficiency in our study; these patients may represent a vulnerable subgroup for which timely, optimal treatment can especially be impactful.

In our study, CDI was also associated with increased healthcare use and costs among hospitalized patients. Specifically, patients with a secondary diagnosis of CDI had greater LOS and 30-day readmission rates compared with those without CDI. Our results were consistent with results from previous analyses evaluating LOS or readmissions among patients with CDI.[27,28] When evaluating the renal insufficiency and HRRP (ie, acute myocardial infarction, heart failure, and pneumonia) subgroups in our study, readmission rates were even higher and underscore the need for closer monitoring and optimal treatment in these populations to prevent recurrences and subsequent readmissions.

We calculated the difference in adjusted costs between patients with CDI and patients without CDI to be approximately $2230, which was somewhat lower than previous estimates.[27] However, our results were consistent with previous findings when evaluating total costs for secondary CDI.[20] In our study, CDI was found to impact costs similarly across subgroups, although the effect was higher for Medicare HRRP patients, indicating that these patients may constitute those for which CDI has a considerable impact on costs.

Although greater costs were observed for patients with CDI, hospital payments were not found to significantly differ for patients with CDI versus patients without CDI, suggesting potentially greater underpayment for patients with CDI. Most strikingly, we estimated that hospitals recovered less costs for patients with CDI compared with patients without CDI, with the largest differences observed for Medicare HRRP patients, suggesting greater underpayment for patients with CDI and even greater underpayment for patients with CDI meeting the Medicare HRRP criteria.

The results of this analysis have important implications for hospitals, especially given increased anticipated cost pressures. Hospitals incur higher costs for Medicare patients with a secondary diagnosis of CDI, compared with those without; however, they receive lower payments relative to those costs. In our study, results indicated a lower payment-to-cost ratio among hospitalized patients with a secondary CDI diagnosis compared with those without, with pronounced differences among patients who meet HRRP measure criteria (ie, admission with acute myocardial infarction, heart failure, or pneumonia). This is especially important because increased readmissions among these patients can lead to further potential financial impact. Because CMS continues to establish financial incentives to reduce all-cause readmissions for an expanding list of principal diagnoses, hospitals may be incented to reduce common causes of readmissions such as CDI to improve quality reporting benchmarks and to avoid financial penalties. Hospitals should employ strategies to deliver optimal management and treatment of CDI to improve outcomes and reduce downstream attributable costs.

This study contains several limitations. As with any study that uses retrospective claims data, identification of patients according to specific diagnoses is limited to the use of *ICD-9-CM* codes. It should be noted that the positive predictive value for secondary *ICD-9-CM* codes has been reported to be low, resulting in potential misclassification bias due to false positives.[29] However, this would likely bias the results toward the null hypothesis (ie, no difference between patients with CDI and patients without CDI), rather than serving to overstate the findings.

Although we used propensity score matching to attempt to account for potential confounders between the CDI and non-CDI cohorts, the groups were unbalanced across various characteristics after the matching procedure was performed. This may be due to the inclusion of MS-DRGs as covariates in the propensity score regression model, thus giving more weight to the MS-DRGs coded during the inpatient stay and less weight toward the demographics and other characteristics. Although significant differences in baseline characteristics were observed after the propensity score match was performed, these differences were controlled for by performing additional risk adjustment via regression models on the matched sample.

Separate propensity score models were not conducted for each of the subgroups and were performed only for the entire sample. Thus, these subgroups may not be matched on the same propensity score. Although this raises the risk of bias especially for these subgroup analyses, we attempted to control for differences in observed characteristics by using separate regression models for these subgroups of patients, conditioning on the same covariates used in the regression models for overall sample.

In conclusion, patients hospitalized with a secondary diagnosis of CDI experience greater mortality, hospital costs, LOS, and readmissions compared with the patients hospitalized for other reasons, whereas hospitals receive similar reimbursement for these patients. Costs were significantly higher among patients with renal insufficiency and patients eligible for inclusion in Medicare HRRP (ie, acute myocardial infarction, heart failure, pneumonia). Our findings suggest that comprehensive prevention and treatment strategies are needed to decrease resource use and burden among patients who develop secondary CDI.

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