Attributable Healthcare Resource Utilization and Costs for Patients With Primary and Recurrent *Clostridium difficile* Infection in the United States

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Background. The economic burden of *Clostridium difficile* infection (CDI), the leading cause of nosocomial infectious diarrhea, is not well understood. The objective of this study was to estimate the healthcare resource utilization (HCRU) and costs attributable to primary CDI and recurrent CDI (rCDI).

Methods. This is a database (MarketScan) study. Patients without CDI were matched 1:1 by propensity score to those with primary CDI but no recurrences to obtain HCRU and costs attributable to primary CDI. Patients with primary CDI but no recurrences were matched 1:1 by propensity score to those with primary CDI plus 1 recurrence in order to obtain HCRU and costs attributable to rCDI. Adjusted estimates for incremental cumulative hospitalized days and healthcare costs over a 6-month follow-up period were obtained by generalized linear models with a Poisson or gamma distribution and a log link. Bootstrapping was used to obtain 95% confidence intervals (CIs).

Results. A total of 55 504 eligible CDI patients were identified. Approximately 25% of these CDI patients had rCDI. The cumulative hospitalized days attributable to primary CDI and rCDI over the 6-month follow-up period were 5.20 days (95% CI, 5.01–5.39) and 1.95 days (95% CI, 1.48–2.43), respectively. The healthcare costs attributable to primary CDI and rCDI over the 6-month follow-up period were $24 205 (95% CI, $23 436–$25 013) and $10 580 (95% CI, $8 849–$12 446), respectively.

Conclusions. The HCRU and costs attributable to primary CDI and rCDI are quite substantial. It is necessary to reduce the burden of CDI, especially rCDI.

Keywords. *Clostridium difficile*; healthcare resource utilization; recurrence; hospitalization; risk factors.

Clostridium difficile is an anaerobic, gram-positive, spore-forming, toxin-producing bacillus. *Clostridium difficile* infection (CDI) is the leading cause of nosocomial infectious diarrhea in adults [1]. CDI caused 453 000 new and 83 000 recurrent infections and was associated with approximately 29 000 deaths in the United States in 2011 [2]. The most important risk factor for CDI is disruption of the normal intestinal flora by exposure to prolonged use of antibiotics [3, 4]. Advanced age, immunosuppression, surgical procedures, increased severity of underlying illness, use of antiulcer medications, chemotherapeutic agents, and hospitalization (including stays at long-term care facilities) are risk factors for healthcare-associated CDI [3, 4].

The rate of healthcare-associated CDI has been increasing, and the diagnosis of CDI is estimated to raise the cost of

a hospitalization stay by 54% in the United States [1, 5–7]. In addition, CDI has been associated with increasing morbidity and mortality, likely due to a combination of the changing virulence of *C. difficile* strains and the greater number of risk factors among vulnerable hospitalized patients [8–12].

A key issue with the management of CDI is recurrent infection. Recurrent CDI (rCDI) occurs due to relapse or reinfection [13]. Reports have shown that 18%–25% of patients will experience their first primary episode of CDI recurrence following the completion of treatment with vancomycin or metronidazole [14–16]. In patients with at least 1 recurrence, the risk for subsequent recurrences increases to 45%–65% [17]. A recent meta-analysis showed several risk factors for rCDI, including continuation of non–*C. difficile* antibiotics, advanced age, and use of antacid medications [18].

CDI places a substantial economic burden on the healthcare system. The cost of CDI was estimated at $5.4 billion in the United States, with $4.7 billion (86.7%) incurred in healthcare settings and $725 million (13.3%) incurred in the community [19]. The main driver of the economic burden is hospitalization and recurrence. rCDI is associated with excessive costs, mostly because of longer hospital stays and admittance in to intensive care units [20–22]. Despite this burden associated with rCDI, the cost attributable to rCDI in the United States

is not well understood, and studies estimating these costs are limited. Dubberke et al [23] compared the average cost of all patients in an academic, urban, tertiary care hospital that had at least 1 recurrence to a matched cohort with no recurrence over a 6-month period. The estimated attributable cost of rCDI was $11 631 (2010 dollars). Patients with rCDI were significantly more likely to have hospital costs compared with those without a recurrence. Other studies have assessed the cost of primary CDI and not the recurrence [24, 25].

Given the substantial burden of CDI and its association with increased hospital stay, there is a need to assess the cost and healthcare resource utilization (HCRU) that can be attributed to primary CDI (compared to having no CDI) and to rCDI (compared to having a primary CDI only). Therefore, the objectives of this study were (1) to describe patient characteristics with primary CDI and rCDI; (2) to assess the rate of rCDI after an episode of primary CDI; (3) to estimate cumulative hospitalized days and healthcare costs attributable to primary CDI, and; (4) to estimate cumulative hospitalized days and healthcare costs attributable to rCDI.

METHODS

Study Design and Data Source

This was a retrospective observational study. Two Truven Health MarketScan databases were used: (1) the Commercial Claims and Encounters database and (2) the Medicare Supplemental and Coordination of Benefits database. The commercial database represents approximately 100 employer-sponsored private health plans with coverage of an estimated 45 million members. The Medicare Supplemental database covers approximately 4.2 million retirees covered by their previous employers. Both databases record patient demographic data, health plan information, medical diagnosis/procedure codes, prescriptions, and cost data. Each member in the datasets has a unique identifier used to track patients over time across the sites of service and providers.

The Medicare Supplemental database contains the amount paid by Medicare in the field of Coordinate of Benefit. If Medicare is the primary payer and a service is 100% covered by Medicare, the Medicare Supplemental database will not capture the claim as there is no need for the service provider to send the claim to the employer-sponsored supplemental plan for further payment. Institutional review board approval was not obtained because this study was an analysis of de-identified secondary data. The study was conducted in accordance with Guidelines for Good Pharmacoepidemiology Practices [26].

Study Sample and Cohorts

Subjects were included in this study if they (1) had a CDI diagnosis (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] code = 008.45) from 1 July 2010 to 30 June 2014 (the earliest CDI diagnosis date was defined as the index date); (2) were continuously enrolled in a health plan for 12 months prior to and 6 months after the index date (subjects who died within 6 months after the index date were included in the analysis). Subjects were excluded from the study if they had a CDI diagnosis during the 84 days prior to the index date, had multiple primary CDI episodes during the follow-up period (ie, 6 months from the index date), or had potentially invalid payment data (eg, negative values or extremely large values).

CDI diagnoses overlapping within 14 days were collapsed and combined to build CDI episodes. This accounts for multiple diagnoses that may be due to refractoriness and longer treatment periods needed with intervening retesting. The CDI episode starting from the index date was defined as the primary episode. Those CDI episodes that occurred within 84 days of the previous episode were classified as recurrences. Details are provided in Supplementary Appendix 1.

To estimate the incremental hospitalized days and healthcare costs, 4 cohorts were further constructed for 2 comparisons. For the first comparison, patients without CDI were matched 1:1 by propensity score (non-CDI) to patients with primary CDI only ($CDI_{PRIMARY1}$) to obtain hospitalized days and costs attributable to primary CDI. For the second comparison, patients with primary CDI only were matched 1:1 by propensity score ($CDI_{PRIMARY2}$) to patients with 1 recurrence ($CDI_{RECURRENT}$) to obtain hospitalized days and costs attributable to an rCDI. While all the patients with primary CDI were included in $CDI_{PRIMARY1}$ for the first comparison, only the patients with primary CDI who matched with those having a recurrence were included in $CDI_{PRIMARY2}$ for the second comparison. The index date of patients without CDI was randomly selected from the service dates of all the medical claims during 1 July 2010 to 30 June 2014. Propensity score was calculated based on covariates related to primary or rCDI.

STUDY VARIABLE MEASUREMENTS

Outcomes

The outcomes of this study are rCDI rate, cumulative hospitalized days, total healthcare costs, and healthcare costs within different settings (inpatient, outpatient, and emergency department) during the 6 months after the index date. The rCDI rate was measured as the proportion of patients with a primary CDI episode that had a recurrence. Cumulative hospitalized days were measured as total number of days admitted in the hospital during the 6-month follow-up period. The total healthcare costs were calculated as the amount paid by primary and secondary insurers and by patients (ie, copayment and deductibles) across all claims (medical and pharmacy) during the 6 months after the index date. Healthcare costs were inflation-normalized to 2014 US dollars using the Consumer Price Index All Urban Consumers for Medical Care Services in accordance with the International Society for Pharmacoeconomics and Outcomes Research recommendations [27].

Covariates

Covariates were used to describe the characteristics of CDI patients and to create propensity scores for matching the 4 comparison cohorts. Covariates included age, sex, geographic region of residence, health plan type, Charlson comorbidity index, specific comorbidities, immunocompromised status, use of certain medications, and previous 3-month HCRU. Charlson comorbidity index and specific comorbidities were identified by *ICD-9-CM* diagnosis codes during the 12 months prior to the index date (see Supplementary Appendix 2). Conditions used to imply immunocompromised status were identified by ICD-9-CM diagnosis/procedure codes during the 6 months prior to the index date (see Supplementary Appendix 3). Medications were identified by National Drug Codes during the 3 months prior to the index date.

Subgroup Analyses

In addition to overall CDI patients, subgroup analysis was conducted by age (<65 years vs ≥65 years), sex, immunocompromised status, and antibiotic use prior to the primary CDI episode.

Statistical Analysis

Descriptive statistics such as frequencies and percentages for categorical variables and mean (standard deviation [SD]) for continuous variables were used to describe the characteristics of the patients. Differences of characteristics between the 4 comparison cohorts ($CDI_{PRIMARY1}$ vs non-CDI and $CDI_{RECURRENT}$ vs $CDI_{PRIMARY2}$) were assessed for significance using standardized difference scores [28]. Adjusted estimates of cumulative hospitalized days and healthcare costs for the 4 comparison cohorts were obtained by generalized linear models with a Poisson (hospitalized days) or gamma (costs) distribution and a log link. This approach resolves the issue of skewed distribution that is common in claims data [29]. Furthermore, it has been demonstrated that a generalized linear model can provide more robust coefficient estimates than logged ordinary least squares regression, where the log transformation is often used to address skewed data [30]. Bootstrapping was used to obtain the 95% confidence interval (CI) of the estimates. A *P* value of .05 was the threshold for statistical significance. All statistical analyses were performed using SAS version 9.3 software (SAS Institute, Cary, North Carolina).

RESULTS

After applying the inclusion and exclusion criteria, a total of 55504 CDI patients were identified for the study (Table 1). Full CDI patient demographics are reported in Table 2. The mean age of these patients was 61.3 years (SD, 21.1 years), and 62.0% were female. The most commonly reported health plan type was Preferred/Exclusive Provider Organization (45.9%). Approximately 31.8% and 29.9% of the patients resided in the

Table 1. ***Clostridium difficile* Infection Cohort Construction**

Inclusion/Exclusion Criteria	No. of Subjects
Diagnosis of CDI from 1 July 2010 to 30 June 2014 (the earliest diagnosis was the index date)	146942
Continuous health plan enrollment for 12 mo before and 6 mo after the index date (subjects who died during the follow-up were included in the study)	59837
No diagnosis of CDI during 84 d before the index date	59262
No multiple primary CDI episodes during the follow-up period	56646
No invalid cost data (eg, negative values or extremely large values)	55504

Abbreviation: CDI, *Clostridium difficile* infection.

Table 2. **Baseline Characteristics of Patients With *Clostridium difficile* Infection (N = 55504)**

Characteristic	No. of Subjects (%)
Age, y	
Mean (SD)	61.3 (21.1)
<65	29667 (53.5)
≥65	25837 (46.6)
Sex	
Female	34389 (62.0)
Male	21115 (38.0)
Health plan type [1]	
HMO	7697 (13.9)
PPO/EPO	25447 (45.9)
POS	3386 (6.1)
HDHP/CDHP	2862 (5.2)
Comprehensive	14956 (27.0)
Unknown	1156 (2.1)
Geographic region of residence	
Northeast	10399 (18.7)
North Central	17673 (31.8)
South	16605 (29.9)
West	10321 (18.6)
Unknown	506 (0.9)
Medical conditions 12 mo prior to primary CDI	
Charlson comorbidity score, mean (SD)	3.1 (3.4)
Diabetes	14530 (26.2)
Cardiovascular disease	11693 (21.1)
Renal dysfunction	13066 (23.5)
Pulmonary disease	37201 (67.0)
Inflammatory bowel disease	3618 (6.5)
Immunocompromised	12884 (23.2)
Medications 3 mo prior to primary CDI	
Antibiotics	35432 (63.8)
Gastric acid suppression	8332 (15.0)
Laxatives	1953 (3.5)
NSAIDs	22938 (41.3)
Healthcare resource utilization 3 mo prior to primary CDI	
Hospitalizations, mean (SD)	0.6 (0.8)
Emergency department visits, mean (SD)	0.2 (0.5)
Doctor office visits, mean (SD)	4.7 (4.9)

Abbreviations: CDHP, consumer-driven health plan; CDI, *Clostridium difficile* infection; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; NSAID, nonsteroidal anti-inflammatory drug; POS, point of service; PPO, preferred provider organization; SD, standard deviation.
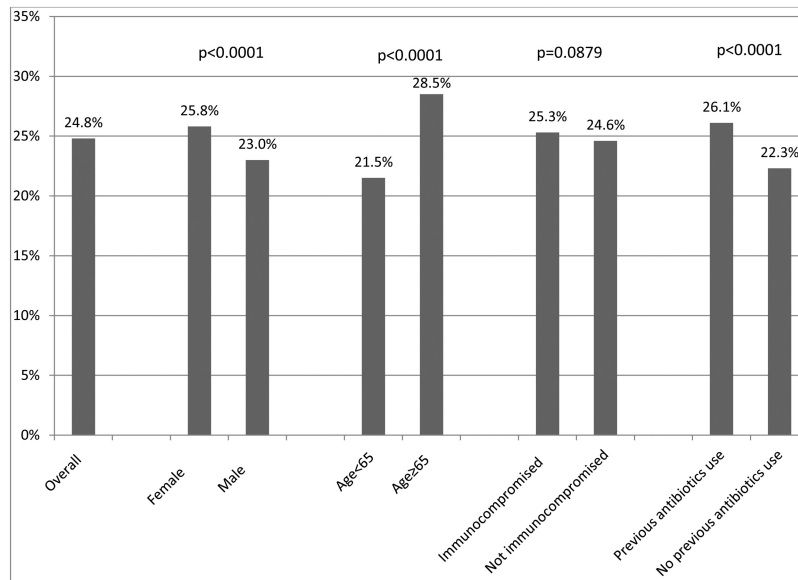
Figure 1. *Clostridium difficile* recurrence rates, overall and by subgroup.

North Central and South regions, respectively, of the United States. Approximately 64% of the CDI patients had used antibiotics prior to the primary episode. On average, the CDI patients had 0.6 (SD, 0.8) hospitalizations, 0.2 (SD, 0.5) emergency department visits, and 4.7 (SD, 4.9) doctor office visits during the 3 months prior to the primary episode.

Figure 1 shows CDI recurrence rates overall and by subgroup. Among the 55 504 CDI patients, 24.8% had a recurrence. The recurrence rate was significantly higher in patients who were female (25.8%), were ≥65 years old (28.5%), and used antibiotics (26.1%) prior to the primary episode than those patients who were male (23.0%), were <65 years old (21.5%), and did not use antibiotics (22.3%), respectively (all *P* < .0001).

Supplementary Table 1 presents the comparison of the baseline characteristics of the patients with CDI primary episode only vs the matched non-CDI patients and the CDI patients with recurrences vs the matched patients who only had CDI primary episode. The standardized differences of all the baseline characteristics across the 2 comparisons are <0.2 (small effect), suggesting that the propensity score matching algorithm was effective in minimizing these baseline differences.

Table 3 describes the cumulative hospitalized days attributable to the primary CDI, overall and by subgroups. The average hospitalized days across all primary CDI patients without recurrences is 8.01 days (95% CI, 7.83–8.17 days) vs 2.81 days (95% CI, 2.71–2.90 days) across the matched non-CDI patients. Therefore, the hospitalized days of 5.20 days (95% CI, 5.01–5.39 days) is attributable to a primary CDI episode.

Table 4 describes the cumulative hospitalized days attributable to an rCDI, overall and by subgroups. The average cumulative hospitalized days across all rCDI patients is 9.27 days (95%

Table 3. Cumulative Hospitalized Days Attributable to Primary *Clostridium difficile* Infection, Overall and by Age, Sex, and Immunocompromising Status

Characteristic	Cumulative Hospitalized Days in CDI_PRIMARY1 Cohort (n = 41 767)	Cumulative Hospitalized Days in Non-CDI Cohort (n = 41 767)	Cumulative Hospitalized Days Attributable to Primary CDI
Overall	8.01 (7.83–8.17)	2.81 (2.71–2.90)	5.20 (5.01–5.39)
Age <65 y	7.99 (7.74–8.22)	2.46 (2.34–2.59)	5.53 (5.26–5.80)
Age ≥65 y	8.05 (7.82–8.27)	3.24 (3.10–3.38)	4.81 (4.54–5.08)
Male	9.59 (9.28–9.90)	3.37 (3.21–3.54)	6.22 (5.86–6.54)
Female	7 (6.80–7.20)	2.45 (2.34–2.56)	4.55 (4.34–4.76)
Not immunocompromised	7.07 (6.89–7.24)	2.21 (2.12–2.31)	4.86 (4.64–5.05)
Immunocompromised	11.07 (10.69–11.49)	4.74 (4.49–4.98)	6.33 (5.87–6.84)

Data are presented as mean (95% confidence interval).

Abbreviations: CDI, *Clostridium difficile* infection; CDI_PRIMARY1, cohort with primary CDI only matched to those without CDI.

Table 4. Cumulative Hospitalized Days Attributable to Recurrent *Clostridium difficile* Infection, Overall and by Age, Sex, and Immunocompromising Status

Characteristic	Cumulative Hospitalized Days in CDI_{RECURRENT} Cohort (n = 8502)	Cumulative Hospitalized Days in CDI_{PRIMARY2} Cohort (n = 8502)	Cumulative Hospitalized Days Attributable to Recurrent CDI
Overall	9.27 (8.87–9.66)	7.33 (7.01–7.67)	1.95 (1.48–2.43)
Age <65 y	8.82 (8.32–9.33)	7.32 (6.90–7.85)	1.49 (.80–2.16)
Age ≥65 y	9.72 (9.18–10.26)	7.33 (6.88–7.79)	2.39 (1.76–3.07)
Male	11.57 (10.81–12.33)	8.88 (8.24–9.57)	2.68 (1.71–3.59)
Female	7.98 (7.54–8.41)	6.44 (6.10–6.84)	1.53 (1.04–2.04)
Not immunocompromised	8.18 (7.75–8.60)	6.54 (6.16–6.92)	1.64 (1.11–2.17)
Immunocompromised	12.84 (11.93–13.70)	9.89 (9.17–10.64)	2.95 (1.84–3.98)

Data are presented as mean (95% confidence interval).

Abbreviations: CDI, *Clostridium difficile* infection; CDI_{PRIMARY2}, cohort with primary CDI only matched to those with recurrent CDI; CID_{RECURRENT}, cohort with recurrent CDI.

CI, 8.87–9.66 days) vs 7.33 days (95% CI, 7.01–7.67 days) across the matched primary CDI patients in CDI_{PRIMARY2}; therefore, the hospitalized days of 1.95 (95% CI, 1.48–2.43 days) is attributable to an rCDI episode.

Table 5 describes the healthcare costs attributable to the primary CDI, overall and by subgroup. The average healthcare cost across all patients with primary CDI only is $43718 (95% CI, $43001–$44572) vs $19513 (95% CI, $19053–$20046) for those matched patients without CDI. Therefore, the healthcare cost of $24205 (95% CI, $23436–$25013) is attributable to primary CDI, compared to those without CDI.

When looking at healthcare cost by settings (Supplementary Table 2), the average inpatient cost of the patients with primary CDI only is $28014 (95% CI, $26767–$29737) vs $6918 (95% CI, ($6521–$7287) for those matched non-CDI patients, suggesting that inpatient cost is the main driver of the total healthcare cost.

Table 6 describes the healthcare costs attributable to a rCDI, overall, and by subgroup. The average healthcare cost for patients with recurrence in the CDI_{RECURRENCE} cohort is $49456 (95% CI, $47847–$50997) vs $38876 (95% CI, $37550–$40291) for those matched primary CDI patients in the CDI_{PRIMARY2} cohort. Therefore, the total healthcare cost attributable to a rCDI, compared to those with primary CDI only, is $10580 (95% CI, $8849–$12446).

When looking at healthcare costs by settings (Supplementary Table 3), similar to the comparison between primary CDI patients and non-CDI patients, the inpatient cost of patients with primary CDI plus 1 recurrence is $32190 (95% CI, $29983–$36110) compared with $22456 (95% CI, $21008–$25072) for those matched patients with primary CDI only.

DISCUSSION

This study is consistent with previous literature that has demonstrated a significant and substantial increase in HCRU for CDI over and above similar patients without CDI. It has also shown that having rCDI is associated with substantial healthcare resource use as compared to similar CDI patients who do not have a recurrence. The subgroup analyses comparing the incremental HCRU for those patients with rCDI compared to those with primary CDI only are consistent with the concept that more vulnerable patients, such as immunocompromised and older patients, incur even greater need for healthcare resources.

Estimating the cost of rCDI is complex because of potential confounding factors that are independently associated with both recurrence of CDI and more healthcare utilization regardless of recurrence. To estimate the true burden, it is necessary to account for this confounding. Multivariable analysis is one method, but this is generally not as robust as a carefully done propensity score matching that also allows for more statistical robustness by the

Table 5. Healthcare Costs Attributable to Primary *Clostridium difficile* Infection, Overall and by Age, Sex, and Immunocompromising Status

Characteristic	Healthcare Costs in CDI_{PRIMARY1} Cohort, $ (n = 41767)	Healthcare Costs in Non-CDI Cohort, $ (n = 41767)	Healthcare Costs Attributable to Primary CDI, $
Overall	43718 (43001–44572)	19513 (19053–20046)	24205 (23436–25013)
Age <65 y	44704 (43585–45861)	18041 (17423–18652)	26663 (25551–27846)
Age ≥65 y	42497 (41513–43549)	21337 (20646–22042)	21160 (20016–22335)
Male	53450 (51931–55105)	22378 (21569–23351)	31073 (29542–32700)
Female	37463 (36668–38369)	17672 (17161–18196)	19791 (18944–20736)
Not immunocompromised	33213 (32571–33900)	12998 (12650–13334)	20215 (19556–20913)
Immunocompromised	77801 (75468–80618)	40653 (39028–42320)	37148 (34561–40070)

Data are presented as mean (95% confidence interval).

Abbreviations: CDI, *Clostridium difficile* infection; CDI_{PRIMARY1}, cohort with primary CDI only matched to those without CDI.

Table 6. Healthcare Costs Attributable to Recurrent *Clostridium difficile* Infection, Overall and by Age, Sex, and Immunocompromising Status

Characteristic	Healthcare Costs in CDI$_{RECURRENT}$ Cohort, $ (n = 8502)	Healthcare Costs in CDI$_{PRIMARY2}$ Cohort, $ (n = 8502)	Healthcare Costs Attributable to Recurrent CDI, $
Overall	49 456 (47 847–50 997)	38 876 (37 550–40 291)	10 580 (8849–12 446)
Age <65 y	48 342 (46 013–50 858)	39 597 (37 595–41 831)	8 745 (6039–11 354)
Age ≥65 y	50 532 (48 562–52 724)	38 180 (36 420–40 046)	12 352 (9911–14 736)
Male	58 552 (55 540–61 732)	45 528 (43 160–48 078)	13 024 (9624–16 479)
Female	44 300 (42 528–46 019)	35 105 (33 603–36 772)	9 194 (7 110–11 166)
Not immunocompromised	39 316 (37 915–40 681)	30 484 (29 334–31 722)	8 832 (7 218–10 414)
Immunocompromised	82 410 (77 362–87 666)	66 151 (62 112–70 403)	16 259 (10 726–22 207)

Data are presented as mean (95% confidence interval).

Abbreviations: CDI, *Clostridium difficile* infection; CDI$_{PRIMARY2}$, cohort with primary CDI only matched to those with recurrent CDI; CID$_{RECURRENT}$, cohort with recurrent CDI.

matching approach [31]. Most of the literature on CDI-associated costs assesses only the cost of primary CDI. To our knowledge, there is only one other study using an appropriate approach in the United States. Dubberke and colleagues [23] used a matched cohort approach to determine the cost of rCDI. Their overall estimate of the inpatient 6-month cost of rCDI was $11 631 (2010 US dollars). Most of the incremental cost over and above primary CDI only in our study is almost solely due to inpatient expenses. Moreover, our study also enables us to estimate the cost associated with primary episode compared with those without any CDI. One difference in the Dubberke et al study is that our recurrent population contains those having a single recurrence in the 84-day period. As a result, our study estimated the cost attributable to a single recurrence, while Dubberke et al's paper includes costs of all subsequent recurrences.

The other uniqueness of this study was the ability to describe HCRU by high-risk subgroup and shows the particular importance to prevent this disease, primary or recurrent, in these groups. The subgroups of immunocompromised patients and those ≥65 years old reveal even greater incremental costs of an rCDI with payments of $16 259 and $12 352, compared with $8 832 and $8 745 for immunocompetent patients and those <65 years old, respectively. This is consistent with there being more of an adverse effect of CDI or rCDI in these more vulnerable patients. The anomaly of those <65 years old incurring more costs than those ≥65 years old for primary CDI could be because of partial reporting of costs in this database for claims that were fully adjusted by Medicare. Comparing rCDI patients to those with primary only CDI by these age groups, the situation is reversed, consistent with the other high-risk group of immunocompromised patients.

A significant strength of this study is that our data were drawn from a much broader sample of the US population, which increases its external validity. Recurrence rates by risk group were consistent with that in the published literature. The baseline comparisons of the patients with CDI primary episode only vs the matched non-CDI patients and the CDI patients with recurrences vs the matched patients with CDI primary episode only are quite similar in their characteristics, which demonstrates the effectiveness of the matching algorithm. The ability to examine the different sources of costs (eg, inpatient, outpatient, and emergency department), as well as the high-risk groups that extend the view and the consistency of these relationships, all amplify the robustness of these findings.

Several limitations inherent to administrative claims data apply to this study. First, due to unknown and/or unmeasured factors, residual confounding might still exist despite the use of the propensity score method. The propensity score method, when successfully implemented, can adjust for observed imbalances between treatment arms. However, it cannot correct imbalances that may exist between treatment arms with regard to potentially important unobserved characteristics. Second, CDI and comorbidity status were based only on claims database information (without any medical record review). The database captures only an outpatient prescription fill and does not record what was actually taken by the patients. These could likely result in some misclassification. Third, as the Medicare Supplemental database is sourced from the employer-sponsored supplemental plans, if a service is 100% covered by Medicare and there is no need for the service provider to send the claim to the employer-sponsored supplemental plan for further payment, the Medicare Supplemental database will not capture the claim. Therefore, this study may underestimate the total number of days staying in hospital and total healthcare costs for patients aged ≥65 years. Finally, as MarketScan includes only commercially insured patients, results may not be generalizable to the overall population in the United States.

In conclusion, the HCRU and economic burden associated with primary and rCDI are quite substantial. Better prevention and treatment of CDI, especially rCDI, are needed.

Supplementary Data

Notes

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