Healthcare Resource Utilization and Costs of Recurrent CDI

ID Week
New Orleans, LA
October 26-30, 2016

Omneya Mohamed, PhD[1]; Damion Nero, PhD[2]; Ellen Riehle, MPH[2]; Paul Juneau, MS[2]; Stephen Marcella, MD[1]

[1]Merck & Co., Inc., Kenilworth, NJ, USA; [2]Truven Health Analytics, Ann Arbor, MI, USA

Abstract

Background

Clostridium difficile infection (CDI) management poses a burden on the US healthcare system due to the high rates of recurrence. It costs more than $1 billion annually. Current studies are mostly from single institutions.

Study aim

This study sought to quantify the difference in healthcare resource utilization and costs among adult CDI patients with and without recurrent CDI (rCDI) using a generalizable dataset.

Study design

This is a retrospective study of CDI patients with and without rCDI from June 2011 through September 2014 using Truven Health MarketScan® Commercial Claims and Encounters and Medicare Supplemental Databases. A cohort of CDI patients treated with metronidazole, vancomycin, or fidaxomicin were followed for 6 months following an index episode, tracking all healthcare utilization, costs, and subsequent recurrences. Two subcohorts were defined: a subcohort without rCDI and a subcohort with rCDI. rCDI was defined as a CDI episode 15-84 days following the index episode. We estimated the incremental cost of recurrence over and above that associated with having only a single episode. Propensity score matching was used to match CDI patients with and without rCDI on a 1:1 basis. The rCDI patients had the time marked from the date of diagnosis of their first episode to the diagnosis date of the recurrent episode. This time was added to the discharge date of the single CDI patients. Follow-up of the matched pair started from this point onwards for 6 months.

Results

A total of 12,025 CDI patients were identified (N=8,906 without rCDI; N=2,994 with rCDI). Patients were mainly female (63%), and the average age was 59 years old. Healthcare utilization and costs were significantly higher among CDI patients with rCDI compared with those without rCDI after controlling for baseline differences through matching. The total mean all-cause healthcare expenditures was $35,025 (SD: $76,637) and $19,959 (SD: $55,332), respectively, for patients with and without rCDI. The difference of the means was $21,912.15 (*P*-value <0.001). *C diff*-related costs were also higher among patients with rCDI, with expenditures of $10,287 (SD: $30,730) and $5,169 (SD: $13,277), respectively, for those with and without recurrence.

Conclusion

CDI patients with recurrences had higher healthcare utilization and expenditures compared to those without recurrences. Prevention of rCDI may reduce the economic burden that CDI management poses on the US healthcare system.

Background

- *Clostridium difficile* (*C diff*) is one of the main causes of infectious diarrhea (*Clostridium difficile* infection, CDI) in hospitalized patients
- Within US acute-care facilities, the current estimated cost associated with CDI is more than $1 billion annually[1]
- CDI is difficult to treat because *C diff* spores are easily communicable; they can survive up to 5 months on various surfaces.[2] In addition, almost 20% of patients treated for *C diff* will have a recurrence of the disease[3]
- CDI's high communicability and recurrence among patients admitted to hospitals, nursing homes, and long-term-care facilities pose a significant burden on the healthcare system, particularly due to the additional cost of care for already-sick patients

Study Aims

- This study quantified the difference in healthcare utilization and costs between patients having only one episode of CDI and those having at least one recurrence of CDI
- The quantification of this difference in healthcare utilization and expenditures offers supporting evidence for the value of preventing a recurrence of *C diff* infection

Study Objectives

- To identify the baseline demographic and clinical characteristics of patients having only one episode of CDI and those having at least one recurrence of CDI
- To assess the difference in all-cause and *C diff*-related healthcare resource utilization and costs for patients with recurrent infections in the 6 months following a first recurrence in comparison with those having only one episode of CDI during an identical time period

Methods

- A retrospective observational study of CDI patients with and without rCDI from June 2011 through September 2014 using Truven Health MarketScan® Commercial Claims and Encounters and Medicare Supplemental Databases
- A cohort of CDI patients were followed for 6 months following an index episode, which was defined as the first claim for metronidazole, vancomycin, or fidaxomicin with a CDI diagnosis (ICD-9-CM 008.45) occurring 6 months prior to or up to 7 days after the first claim, covering all healthcare utilization, costs, and subsequent recurrences. Two subcohorts were defined: a subcohort without rCDI and a subcohort with rCDI
- rCDI was defined as a CDI episode 15-84 days following the index episode
- We estimated the incremental cost of recurrence over and above that associated with having only a single episode
  - CDI-related costs included only administrative claims containing a ICD-9-CM diagnosis code for *C diff* (008.45) or *C diff* medications: metronidazole, vancomycin, and fidaxomicin
- Propensity score matching was used to match CDI patients with and without rCDI on a 1:1 basis to control for baseline demographic and clinical characteristic differences
- The rCDI patients had the time marked from the date of diagnosis of their first episode to the diagnosis date of the recurrent episode. This time was added to the discharge date of the single CDI patient to serve as an offset to match the relative time after the first CDI from which the rCDI patient was followed
- Follow-up of the matched single CDI patient in the pair started from this point onwards for 6 months

Results

- A total of 12,025 CDI patients were identified (N=8,906 without rCDI; N=2,994 with rCDI). Patients were mainly female (63%), and the average age was 59 years old. **Table 1** summarizes patients' characteristics
- Healthcare utilization and costs were significantly higher among patients with rCDI compared with those without rCDI after controlling for baseline differences through matching
  - The total mean all-cause healthcare expenditures were $35,025 (SD: $76,637) and $19,959 (SD: $55,332), respectively, for patients with and without rCDI
  - The difference of the means was $21,912.15 (*P*-value <0.001)
- **Figure 1** shows the difference in all cause healthcare expenditure for CDI patients with and without rCDI

Results (continued)

Table 1a. Demographic characteristics of the study sample

Demographic Characteristics	Total		CDI Patients Without rCDI		CDI Patients With rCDI	
	N = 12,025		N = 8,906		N = 2,994	
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD
Age (mean, SD)	58.8	18.0	58.2	18.0	60.7	17.9
Age group (N, %)						
18-29	920	7.7%	716	8.0%	190	6.4%
30-39	957	8.0%	735	8.3%	206	6.9%
40-49	1,521	12.7%	1,165	13.1%	344	11.5%
50-64	4,218	35.1%	3,145	35.3%	1,031	34.4%
65+	4,409	36.7%	3,145	35.3%	1,223	40.9%
Sex (N, %)						
Male	4,457	37.1%	3,413	38.3%	997	33.3%
Female	7,568	62.9%	5,493	61.7%	1,997	66.7%
Payer (N, %)						
Commercial	7,494	62.3%	5,673	63.7%	1,738	58.1%
Medicare	4,531	37.7%	3,233	36.3%	1,256	42.0%
Index year (N, %)						
2012	6,894	57.3%	5,169	58.0%	1,640	54.8%
2013	5,131	42.7%	3,737	42.0%	1,354	45.2%
Geographic region (N, %)						
Northeast	2,721	22.6%	1,981	22.2%	701	23.4%
North Central	3,299	27.4%	2,423	27.2%	845	28.2%
South	3,734	31.1%	2,845	31.9%	860	28.7%
West	2,102	17.5%	1,525	17.1%	552	18.4%
Unknown	169	1.4%	132	1.5%	36	1.2%

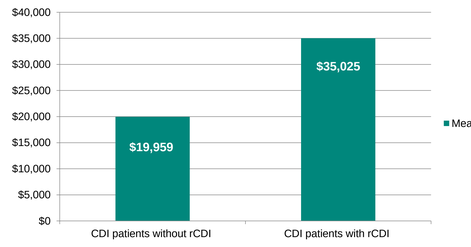
[1]Demographic characteristics are measured on the index date for patients in the total cohort and the subcohort of CDI patients without rCDI and on the latest of up to three recurrence index dates for the subcohort of CDI patients with rCDI

Table 1b. Clinical characteristics of the study sample

Clinical Characteristics	Total		CDI Patients Without rCDI		CDI Patients With rCDI	
	N = 12,025		N = 8,906		N = 2,994	
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD
Deyo-Charlson comorbidity index (DCI) – pre-period (mean, SD)	1.8	2.5	1.9	2.5	1.7	2.4
Baseline antibiotic use – pre-period (N, %)						
Any antibiotic use	8,705	72.4%	6,360	71.4%	2,240	74.8%
Top 5 most commonly prescribed antibiotics:						
Amoxicillin	1,882	15.7%	1,357	15.2%	501	16.7%
Azithromycin	1,536	12.8%	1,134	12.7%	380	12.7%
Ciprofloxacin	2,246	18.7%	1,643	18.5%	581	19.4%
Clindamycin	1,668	13.9%	1,156	13.0%	484	16.2%
Sulfamethoxazole	1,413	11.8%	1,057	11.9%	340	11.4%
Comorbid conditions – pre-period (N, %)						
Anemia	3,191	26.5%	2,342	26.3%	806	26.9%
Cancer	1,936	16.1%	1,462	16.4%	443	14.8%
Colorectal cancer	297	2.5%	231	2.6%	59	2.0%
Cardiovascular events	4,652	38.7%	3,463	38.9%	1,141	38.1%
Crohn's disease	387	3.2%	292	3.3%	93	3.1%
Gastrointestinal disease	4,520	37.6%	3,340	37.5%	1,130	37.7%
Renal impairment/ disease/failure	2,601	21.6%	1,919	21.6%	651	21.7%
Ulcerative colitis	573	4.8%	419	4.7%	148	4.9%
Total Healthcare Cost – 6 Month Pre-Period						
Mean, SD	$49,410	$91,753	$51,104	$95,330	$43,192	$76,849
Min	$0		$0		$0	
Median	$20,620		$21,102		$18,863	
Max	$1,709,055		$1,709,055		$971,980	

[1]Clinical characteristics are measured in the six months prior to the index date.

Figure 1: Total all cause healthcare costs



- *C diff*-related costs were also higher among patients with rCDI, with expenditures of $10,287 (SD: $30,730) and $5,169 (SD: $13,277), respectively, for those with and without recurrence
- **Table 2** presents CDI-related healthcare utilization and expenditures for CDI patients with and without rCDI

Table 2. CDI-related healthcare utilization and cost

Utilization and Expenditure Outcomes[1]	Matched CDI Patients Without rCDI		Matched CDI Patients with rCDI		Difference Between Matched Cohorts			
	N=2,994		N=2,994					
	N/Mean	%/SD	N/Mean Diff	%/SD	Mean Diff	Median Diff	SD Diff	*P*-value Diff
C. diff-related[2]								
Inpatient: Patients with an inpatient admission (N, %)	78	2.6%	589	19.7%	0.2	0.0	0.4	0.718
Number of inpatient admissions					0.2	0.0	0.7	**<0.001**
Mean, SD	0.0	0.2	0.3	0.6				
Min	0.0		0.0					
Median	0.0		0.0					
Max	4.0		8.0					
Total inpatient admission costs					$6,376	$0	$28,891	**<0.001**
Mean, SD	$3,874	$12,695	$6,968	$29,608				
Min	$0		$0					
Median	$0		$0					
Max	$119,978		$832,335					
Outpatient: Patients with an ER visit (N, %)	29	1.0%	213	7.1%	0.1	0.0	0.3	0.829
Number of ER visits					0.07	0.00	0.34	**<0.001**
Mean, SD	0.0	0.1	0.1	0.3				
Min	0.0		0.0					
Median	0.0		0.0					
Max	2.0		4.0					
Total ER visit costs					$51	$0	$353	0.153
Mean, SD	$48	$236	$59	$339				
Min	$0		$0					
Median	$0		$0					
Max	$3,010		$6,699					

Table 2. CDI-related healthcare utilization and cost (continued)

Utilization and Expenditure Outcomes[1]	Matched CDI Patients Without rCDI		Matched CDI Patients with rCDI		Difference Between Matched Cohorts			
	N=2,994		N=2,994					
	N/Mean	%/SD	N/Mean Diff	%/SD	Mean Diff	Median Diff	SD Diff	*P*-value Diff
C. diff-related[2]								
Number of outpatient office visits					1.3	1.0	1.6	**<0.001**
Mean, SD	0.1	0.3	1.4	1.6				
Min	0.0		0.0					
Median	0.0		1.0					
Max	3.0		16.0					
Total outpatient visit costs					$165	$104	$272	**<0.001**
Mean, SD	$47	$78	$173	$270				
Min	$0		$0					
Median	$0		$106					
Max	$623		$5,322					
Total other outpatient costs					$1,323	$23	$5,322	**<0.001**
Mean, SD	$281	$1,286	$1,367	$5,298				
Min	$0		$0					
Median	$0		$29					
Max	$16,408		$99,073					
Total medical: Total medical costs					$7,916	$324	$29,632	**<0.001**
Mean, SD	$4,249	$12,815	$8,566	$30,319				
Min	$0		$0					
Median	$102		$360					
Max	$122,420		$832,335					
Outpatient pharmacy: Number of *C. diff* medication pharmacy prescriptions					1.2	1.0	2.1	**<0.001**
Mean, SD	0.2	0.7	1.4	2.0				
Min	0.0		0.0					
Median	0.0		1.0					
Max	9.0		20.0					
Total outpatient pharmacy costs for *C. diff* medications					$1,580	$9	$3,788	**<0.001**
Mean, SD	$920	$2,531	$1,720	$3,629				
Min	$0		$0					
Median	$14		$13					
Max	$24,194		$36,660					
Total costs: Total *C. diff*-related healthcare costs[3]					$9,496	$1,075	$30,111	**<0.001**
Mean, SD	$5,169	$13,277	$10,287	$30,730				
Min	$2		$15					
Median	$204		$1,276					
Max	$122,420		$832,335					

All values cover the full 6 month follow up period for these patients; *p*-value: comparing the subcohorts of CDI patients with and without rCDI by matched pair, bold=statistically significant at α=0.05; Mean Diff: Mean difference between matched pairs, Median Diff: Median difference between matched pairs, SD Diff: Standard Deviation between matched pairs.

[1]Utilization and expenditure variables are measured among propensity score matched by CDI patients with and without rCDI during the 6 months following the first recurrence index date for CDI patients with rCDI and during equivalent periods of time beginning at recurrent patients' recurrence index dates for CDI patients without rCDI. Expenditures averaged among patients with non-zero all-cause total healthcare costs.

[2]*C. diff*-related: administrative claims containing the diagnosis code for *C. diff* (008.45); *C. diff* medications included in outpatient pharmacy measures: metronidazole, vancomycin and fidaxomicin.

[3]The total cost included the total outpatient pharmacy costs, excluding *C. diff* medications that is not shown here.

Limitations

- This study was limited to only those individuals with commercial health coverage or private Medicare supplemental coverage. Consequently, results of this analysis may not be generalizable to *C diff* patients with other insurance or without health insurance coverage
- The potential for misclassification of *C diff*, covariates, or study outcomes was present, as patients were identified through administrative claims data as opposed to medical records. As with any administrative claims, data are subject to data coding limitations and data entry error
- We identified initial episodes using both pharmacy claims for CDI medications as well as ICD-9 codes for CDI; thus, patients' selection was biased to those fully or partially treated in the outpatient environment. CDI patients who finished their course of treatment while still in the hospital were not captured in our sample
- Patients were followed for 6 months following a single CDI or rCDI; therefore, we may have missed some or all of the costs incurred after 2 or more recurrences
- The second CDI episode (first recurrent CDI) was identified by using only the ICD-9 code, which is less specific but more sensitive for picking up recurrences; thus, there might be some false-positive rCDI patients in the rCDI subcohort

Conclusion

- CDI patients with recurrences had higher healthcare utilization and expenditures compared to those without recurrences. Prevention of rCDI may reduce the economic burden that CDI management poses on the US healthcare system

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