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Contemporary Total Cost of Care Among Medicare Patients with Primary and Recurrent Clostridioides Difficile Infection

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FERRING PHARMACEUTICALS

Introduction

- *Clostridioides difficile* infection (CDI) is the most common healthcare-associated infection in the U.S., especially in older patients, affecting an estimated 462,100 persons in 2017. Recurrent CDI remains one of the most difficult treatment challenges for clinicians.[1-3]
- Up to 35% of patients who develop CDI will experience a recurrence (rCDI), and up to 65% of patients who develop one recurrence will develop a subsequent recurrence.[4-9] rCDI is associated with higher likelihood of death and higher healthcare utilization compared with CDI without recurrence (primary CDI or pCDI).[10-11]

Objective

- To evaluate mortality, total healthcare costs, and the main drivers of cost among contemporary Medicare patients with pCDI and rCDI.

Methods

- This retrospective study utilized 100% Medicare Fee-for-Service (FFS) claims data from 2009-2017 to identify patient's aged ≥65 with ≥1 CDI episode. The study population included patients with CDI diagnosis between January 1, 2010 through December 31, 2016 and continuously enrolled in Parts A, B, and D for 12 months prior to first CDI diagnosis date with no evidence of CDI, and up to 12 months after index CDI episode.
- The pCDI index episode began on the date of the first CDI medical claim and included all subsequent claims with CDI diagnosis with no more than a 14-day gap. (Figure 1)
- The pCDI episode was identified as ≥1 inpatient stay with CDI diagnosis (primary or secondary diagnosis field) (ICD codes 008.45; A04.7, A04.71, A04.72), or ≥1 outpatient medical claim with CDI diagnosis plus evidence of CDI treatment (use of antibiotics including vancomycin, fidaxomicin, metronidazole, rifaximin, and bezlotoxumab, or fecal microbiota transplant).
- rCDI episodes started within 8-weeks from the end of a previous CDI episode. CDI episodes starting beyond the 8-week window were considered new episodes and were excluded from the analysis.[12]
- Total costs of care were calculated per-patient-per-month (PPPM) overall and separately for patients with CDI-linked death which was defined as patients whose most proximal healthcare visit on or near date of death had CDI in primary/secondary diagnosis field.

RESULTS

Baseline Patient Characteristics (Table 1)

- 497,489 CDI patients are included; 42.8% of all CDI patients died.
- Mean (median) follow-up time from index CDI to death was 63 (17) days for patients with pCDI and 118 (86) days for patients with rCDI.
- CDI-related deaths were almost 10 times higher for patients with recurrences (rCDI 25.4% vs pCDI 2.7%) within 12 months. Compared to survivors, patients who died were older, had higher Charlson Comorbidity Index scores, and were more likely Black.

Post-Index Healthcare Resource Utilization and Costs (Table 2 and Figure 1)

- During the 12-month follow-up period, patients who died had higher likelihood of ≥1 acute hospital stay, ICU use, and 30-day readmission compared to those who survived.
- 99.9% of patients with recurrence and CDI-linked death were hospitalized, with 52.7% requiring intensive care, and 77.9% readmitted at least once.
- For both pCDI and rCDI cohorts, total costs per patient per month (PPPM) were about 4.5 times higher among patients who died compared to those who survived.
  - Mean costs for pCDI patients who died were $29,150 PPPM versus $6,348 PPPM for those who survived.
  - Mean costs for rCDI patients who died were $35,767 PPPM versus $7,959 PPPM for those who survived.
  - Mean costs for CDI-linked deaths were $24,883 PPPM for pCDI who died versus $28,443 PPPM for rCDI who died.
- Costs were driven largely by inpatient stays including 30-day readmissions, comprising 41%-75% of total cost across all CDI cohorts. Skilled nursing facility care was the next largest contributor to PPPM costs across all cohorts.

Table 1. Baseline Patient Characteristics

CDI-related deaths 10x higher for recurring CDI

Patient Characteristics (12-Month Pre-Index)	Primary CDI Only (N = 345,893)								Any Recurrence (N = 151,596)							
	Total Survived N = 186,996		Total Deaths N=158,897		CDI-Related N = 4,317 (2.7%)		Not CDI-Related N = 154,580 (97.3%)		Total Survived N = 97,738		Total Deaths N = 53,858		CDI-Related N = 13,689 (25.4%)		Not CDI-Related N = 40,169 (74.6%)	
Post-Index Follow-Up Days																
Mean (SD)	351.9 (55.5)		63.2 (91.4)		131.8 (109.0)		61.3 (90.1)		354.8 (47.0)		118.4 (92.0)		133.9 (93.8)		113.1 (90.7)	
Median	365.0		17.0		116.0		16.0		365.0		86.0		106.0		80.0	
Age (N, %) at Index Date																
Mean (SD)	78.41 (8.02)		81.50 (8.49)		81.68 (8.17)		81.49 (8.50)		78.00 (7.94)		80.41 (8.38)		81.38 (8.21)		80.08 (8.41)	
Gender (N, %)																
Female	128,911	68.9%	98,009	61.7%	2,763	64.0%	95,246	61.6%	66,759	68.3%	32,734	60.8%	8,806	64.3%	23,928	59.6%
Male	58,085	31.1%	60,888	38.3%	1,554	36.0%	59,334	38.4%	30,979	31.7%	21,124	39.2%	4,883	35.7%	16,241	40.4%
Race (N, %)																
White	160,046	86.7%	129,987	82.9%	3,734	87.2%	126,253	82.8%	85,236	88.3%	43,955	82.7%	11,768	86.9%	32,187	81.3%
Black	16,350	8.9%	18,415	11.7%	355	8.3%	18,060	11.8%	7,535	7.8%	6,504	12.2%	1,202	8.9%	5,302	13.4%
Hispanic or Latino	4,108	2.2%	4,107	2.6%	84	2.0%	4,023	2.6%	1,949	2.0%	1,388	2.6%	348	2.6%	1,040	2.6%
Asian	2,965	1.6%	3,378	2.2%	81	1.9%	3,297	2.2%	1,244	1.3%	995	1.9%	151	1.1%	844	2.1%
Other Race	3,527	1.9%	3,010	1.9%	63	1.5%	2,947	1.9%	1,774	1.9&	1,016	1.9%	220	1.6%	796	1.9%
Dual Eligible (Medicaid) Status (N, %)																
Non-Dual	120,312	64.6%	94,323	59.4%	2,730	63.2%	91,593	59.3%	65,501	67.1%	29,917	55.5%	8,466	61.8%	21,451	53.4%
Dual	66,042	35.4%	64,574	40.6%	1,587	36.8%	62,987	40.7%	32,138	32.9%	23,941	44.5%	5,223	38.2%	18,718	46.6%
Original Reason for Entitlement to Medicare (N, %)																
Age	151,088	80.8%	130,713	82.3%	3,619	83.8%	127,094	82.2%	78,400	80.2%	43,151	80.1%	11,449	83.6%	31,702	78.9%
Disability/ESRD	35,908	19.2%	28,184	17.7%	698	16.2%	27,486	17.8%	19,338	19.8%	10,707	19.9%	2,240	16.4%	8,467	21.1%
Charlson Comorbidity Index (CCI) (N, %)																
Mean (SD)	5.03 (3.39)		7.16 (3.61)		6.66 (3.56)		7.17 (3.61)		5.20 (3.45)		7.19 (3.58)		6.72 (3.54)		7.34 (3.57)	

CCI = Charlson Comorbidity Index; CDI = Clostridioides difficile infection; ESRD = end-stage renal disease; SD = standard deviation

Table 2. Post-Index Healthcare Resource Utilization

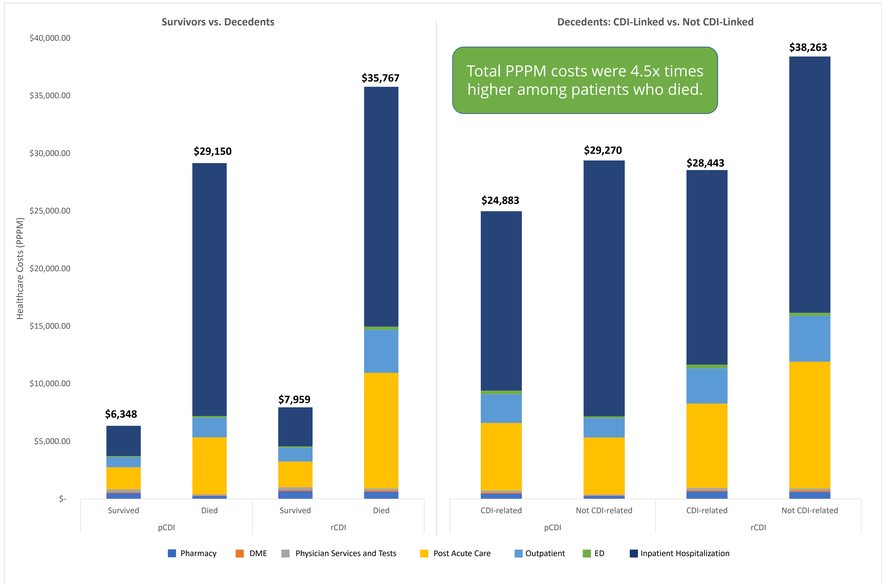
HRU Per Patient Per Month		Primary CDI Only (N = 345,893)				Patients with Any Recurrence (N = 151,596)			
		Total Survived	Total Deaths	CDI-Related	Not CDI-Related	Total Survived	Total Deaths	CDI-Related	Not CDI-Related
Hospitalizations									
Utilization	N	161,015	148,663	4,308	144,355	86,617	52,006	13,681	38,325
	%	86.1	93.6	99.8	93.4	88.6	96.6	99.9	95.4
Inpatient Days	Mean (SD)	7.6 (7.5)	11.3 (12.2)	8.4 (6.1)	11.3 (12.3)	7.6 (6.7)	10.6 (10.3)	8.8 (8.9)	11.3 (10.7)
Intensive Care Unit (ICU) Stay									
	%	21.3	22.5	48.1	21.8	29.8	53.2	52.7	53.4
30-Day All-Cause Readmissions									
	%	20.2	22.2	63.7	21.0	37.8	58.0	77.9	51.2

CDI = Clostridioides difficile infection; HRU = health resource utilization; ICU = Intensive Care Unit; SD = Standard Deviation

CONCLUSIONS

- CDI-related mortality rates among older Medicare beneficiaries were almost 10 times higher for patients who experienced recurrent CDI relative to patients who experienced primary CDI only.
- Along with high mortality, CDI is associated with high cost and healthcare utilization near the end of life. During the 12-month follow-up period, 99.9% of patients with recurrence and CDI-linked death were hospitalized, with 52.7% requiring intensive care, and 77.9% readmitted at least once.
- For both pCDI and rCDI cohorts, total costs per patient per month (PPPM) were about 4.5 times higher among patients who died compared to those who survived. Mean costs for rCDI patients who died were 23-25% higher than costs for pCDI patients who died: $35,767 PPPM versus $7,959 PPPM for those who survived. Costs were driven largely by inpatient stays including 30-day readmissions (41%-75% of total cost).
- Advances in therapeutic options to reduce recurrent CDI can potentially ease the economic, physical, and mortality burden among the frail elderly Medicare population.

Figure 1. Post-Index Cost of Care Per Member Per Month: Primary vs. Recurrent CDI Patients and CDI-Linked vs. Not Linked Deaths



Limitations

- The Medicare claims data do not include claims for Medicare beneficiaries enrolled in private Medicare Advantage plans. Patients insured by other payers such as commercial, Medicaid and Veterans Administration coverage are not captured in the data.
- This study was descriptive in nature and cannot be used to determine cause and effect as temporality cannot be truly established with the use of claims data. In addition, the identification of the subpopulation conditions relies on accurate reporting of the ICD9/10 diagnosis codes on clams; therefore, misclassification of the cohorts is possible.

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Disclosures

- Dr. Amy Guo is an employee of Ferring Pharmaceuticals
- Dr. Amin Alpesh serves as PI or co-I of clinical trials sponsored by NIH/NIAID, NeuroRx Pharma, Pulmotect, Blade Therapeutics, Novartis, Takeda, Humanigen, Eli Lilly, PTC Therapeutics, OctaPharma, Fulcrum Therapeutics, Alexion, unrelated to the present study; speaker and/or consultant for BMS, Pfizer, BI, Portola, Sunovion, Mylan, Salix, Alexion, AstraZeneca, Novartis, Nabriva, Paratek, Bayer, Tetraphase, Achogen LaJolla, Ferring, Seres, Eli Lilly, Spero, Millenium, PeraHealth, HeartRite, Aseptiscope, Sprightly, unrelated to the present study.
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