

A SYSTEMATIC REVIEW OF HEALTHCARE RESOURCE USE AND COST OF THE TREATMENT OF CLOSTRIDIODES DIFFICILE INFECTIONS

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Background

- Clostridioides difficile* infection (CDI) is the most common healthcare-associated infection in the US.
- Patients with CDI have a higher risk of hospitalization, complications, and mortality compared to patients without CDI
- CDI and particularly recurrent CDI (rCDI) have been shown to have a significant impact on patient's physical, psychological, and social well-being
- As one of the greatest risk factors for rCDI is a history of rCDI, these patients may be particularly vulnerable to repeated, increased costs and healthcare resource use
- Given the complex nature of CDI and rCDI, and the heterogeneity of the patient population and the various sites of care, it is necessary to establish a comprehensive overview of associated costs and resource use with CDI

Methods

Objective

The objective of this analysis was to conduct a systematic review and assess the real-world evidence of healthcare resource use and burden of illness associated with CDI

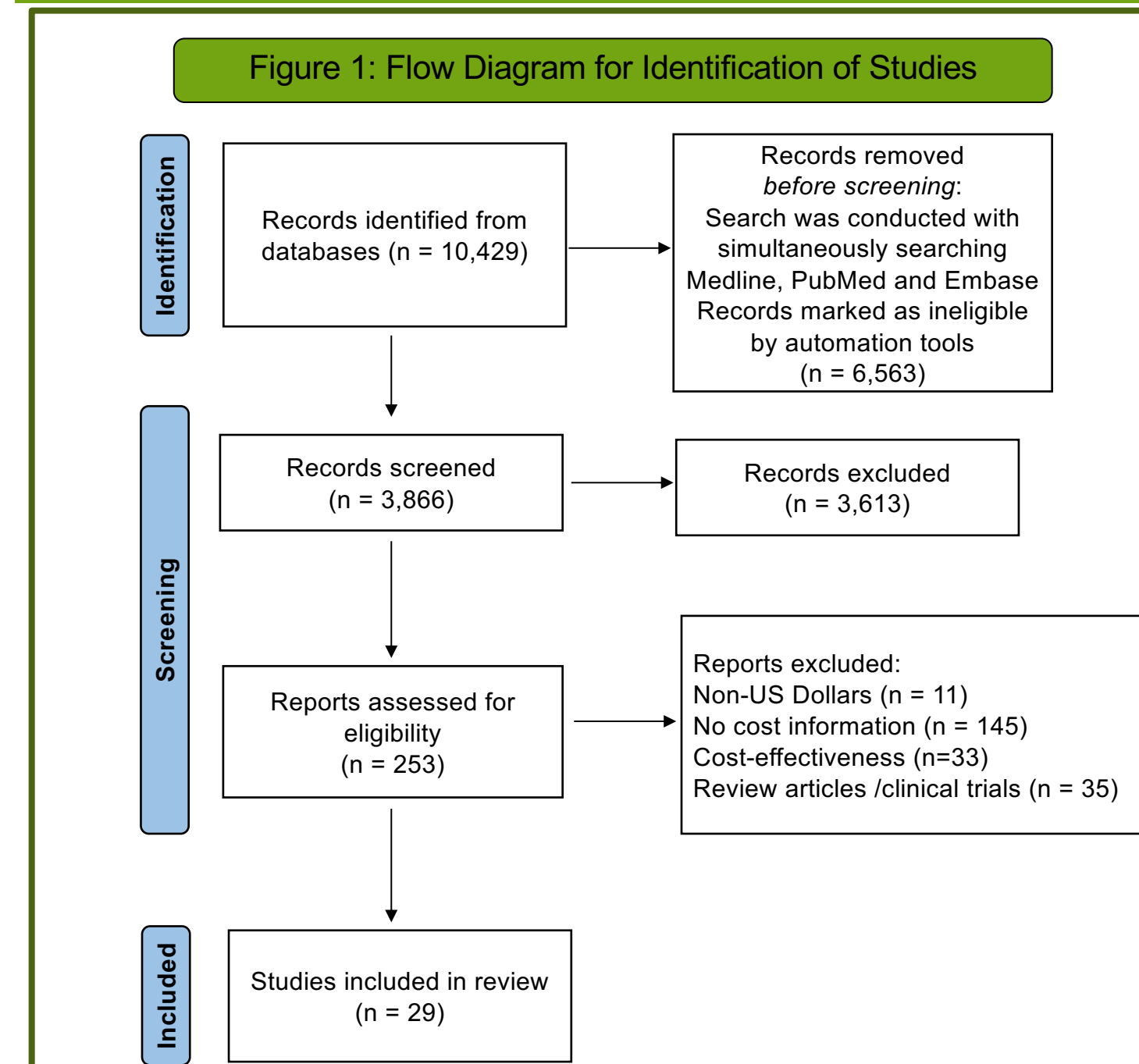
Approach

- Abstracting services of PubMed, Embase, and the Cochrane Collaboration were searched to identify supporting evidence for economic studies of CDI
- Search restricted to English-language publications from 2010 to 2021
- Terms of interest included: *Clostridioides difficile*, cost, healthcare cost, economic, cost of illness, budget impact, resource use
- Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed in this analysis
- Eligible studies:
 - Articles reporting economic outcomes and healthcare resource use associated with CDI
 - Published in English
 - Studies conducted within the United States
 - Cost-effectiveness analysis and studies with non-economic endpoints were excluded (e.g., clinical trials)
- Article titles and abstracts reviewed by two individuals (EA and DCM). Full manuscripts retrieved and evaluated for eligibility

Conclusions

- The studies identified in this systematic review consistently found CDI to be a costly disease, with inpatient hospitalizations being the main cost driver
- Compared to primary CDI, rCDI can lead to additional, substantial increases in healthcare costs and it should be of particular focus to prevent any recurrent episodes after an initial CDI episode

Results



- 29 articles met the inclusion criteria
- Data came from a variety of sources: Medicare/Medicaid (N=6), MarketScan (N=3), HealthCore (N=2), Premier (N=2) and various other sources (N=16)
- Just over half of the articles included a comparison group only a third of articles utilized propensity-score matching
- Across multiple studies, the presence of CDI was regularly associated with a significant cost and resource burden compared to those without CDI
- Additionally, further episodes associated with rCDI require significant resource allocation compared to the primary CDI episode with escalating costs for each subsequent episode
- Hospital length of stay was reported by 16 studies, with most studies reporting CDI (primary or rCDI) adding between 4 to 26 additional hospitalized days

Table 1: Real-World Evidence for CDI and rCDI Burden of Illness and Resource Utilization

Author	Database	Sample Size	Comparator Match	Propensity Score Match	Relevant Endpoints	Results
Nelson WW, et al. ¹ 2021	Medicare	268,762	No	No	Resource use, costs	Mean total all-cause direct costs were \$76,024 for no CDI recurrence and \$96,517 for at least 3 CDI recurrence episodes
Duhaide L, et al. ² 2020	Truven Health MarketScan	622	Yes	No	Hospital LOS, inpatient costs	The average cost for cancer and CDI was \$196,524 versus \$136,365 for cancer without CDI. The average time in the hospital was 23.1 days longer with CDI
Feuerstadt P, et al. ³ 2020	PharMetrics Plus	46,571	No	No	Costs	The mean annual total all-cause direct medical costs per CDI patient were \$71,980 with no recurrence and \$207,733 for those with 3 or more recurrences
Garg SK, et al. ⁴ 2020	HCUP / ED	909,236	No	No	Charges, admission, hospital LOS	There were 909,236 emergency department visits for CDI and 90% were admitted to the hospital. Charges per visit escalated to \$2,900. LOS declined to 5.8 days
Hall BR, et al. ⁵ 2019	Vizient	1,059	No	No	Mortality, hospital LOS, costs	More days from admission to surgery were associated with higher mortality, hospital LOS, infectious complications, and hospital charges
Mollard S, et al. ⁶ 2019	Truven Health MarketScan	46,097	Yes, for subset	No	Hospital LOS, inpatient costs	Inpatients with CDI primary diagnosis had mean cost of \$10,528 and LOS of 5.9 days. CDI as comorbidity had mean additional cost of \$11,938 and added hospital LOS of 4.4 days
Shrestha MP, et al. ⁷ 2016	HCUP	587,799	No	No	Mortality, hospital LOS, costs	Hospital charges for patients with a principal diagnosis of CDI increased from \$24,535 in 2004 to \$35,898 in 2014. Mortality decreased from 3.6% in 2004 to 1.6% in 2014
Zhang D, et al. ⁸ 2018	Truven Health MarketScan	55,504	Yes	Yes	Hospital days, healthcare costs	24.8% patients had recurrence. Average hospital days for CDI was 8.01 versus 2.81 for matched non-CDI. Average healthcare cost across all patients with primary CDI was \$43,718 versus \$19,513 for matched group without CDI
Kulayat AN, et al. ⁹ 2017	HCUP / Project Kids	1,438	Yes	Yes	Hospital LOS, inpatient costs	The mean excess hospital LOS and costs attributable to CDI were 5.8 days and \$12,801
Kuntz JL, et al. ¹⁰ 2017	Kaiser Perm. Northern CA	4,174	Yes	No (optimal matching algorithm)	Health resources	Recurrent CDI patients had substantially higher levels of healthcare utilization than both patients with nonrecurrent CDI and patients that never had CDI
Mehrotra P, et al. ¹¹ 2017	HCUP / Project Kids	8,527	Yes	Yes	Hospital LOS, inpatient costs	The attributable cost of CDI ranged from \$1,917 to \$8,317 and the increase in hospital LOS was 4 days
Rodriguez R, et al. ¹² 2017	Partners Healthcare	98	No	No	Healthcare utilization, estimated costs	84% of patients had a CDI hospitalization and total CDI-associated cost was \$34,104 per patient
Zilberberg MD, et al. ¹³ 2017	Medicare and Medicaid	14,472	No	No	Hospital days, healthcare costs	Adjusted excess hospital days per patient was 20.3 and Medicare reimbursements were \$12,043 in the group with recurrence
Shah DN, et al. ¹⁴ 2016	Single hospital	540	No	No	Recurrence, hospital LOS, costs	18% of primary CDI had a recurrence. Total hospital median hospital LOS and costs increased with recurrence
Shorr AF, et al. ¹⁵ 2016	Medicare and Medicaid	6,838	Yes	Yes	Mortality and costs	CDI was associated with near doubling of both mortality and total healthcare costs
Yu H, et al. ¹⁶ 2016	Medicare, Medicaid, MDS	32,807	Yes	Yes	Incidence, mortality, healthcare costs	Total healthcare costs within 2 months following first CDI episode were significantly higher for CDI residents (\$28,621 vs \$13,644) for combined Medicare and Medicaid costs. Mortality rates higher in CDI group
Drozdz EM, et al. ¹⁷ 2015	Medicare	3,262	Yes	Yes	Mortality and costs	Patients with CDI have 1.87 times greater odds of inpatient mortality compared to those without CDI. Hospital LOS with CDI was 1.82 times greater than those without CDI. Patients with CDI had 1.16 times greater hospital cost than patients without CDI
Gallagher JC, et al. ¹⁸ 2015	Premier	95	No	No	90-day readmission	Recurrence occurred in 20.4% of patients on fidaxomicin and 41.3% on vancomycin. Costs estimated to be \$454,800 for vancomycin and \$196,200 for fidaxomicin
Magee G, et al. ¹⁹ 2015	Premier	84,225	Yes	Yes	Hospital LOS, inpatient costs	Hospital LOS and total costs were higher with CDI than non-CDI
Palli SR, et al. ²⁰ 2015	HealthCore	500	No	No	Resource use, costs	Mean cost was \$35,621 (SD \$100,502). Two-thirds of patients had GI or ID consult
Dubberke ER, et al. ²¹ 2014	Single hospital	421	No	No	Costs	The attributable cost of recurrent CDI was \$11,631
Campbell R, et al. ²² 2013	Cerner	4,521	Yes	Yes	Hospital LOS, inpatient costs	Adjusted total hospital LOS was significantly greater with CDI in 4 of 5 subgroups. Total hospital costs were greater with CDI in patients who were at least 65 years of age and those on antibiotics
Quimbo RA, et al. ²³ 2013	HealthCore	21,177	Yes	No	Hospital LOS, inpatient costs	Incremental hospital LOS and hospitalization cost was increased for CDI across all subgroups compared to matched comparator groups
Sammons JS, et al. ²⁴ 2013	Pediatric Health Information System	5,107	Yes	Yes	Mortality, hospital LOS, costs	In-hospital mortality was higher with CDI than matched controls. Also, mean differences in hospital LOS and total cost were higher with both community-acquired and hospital-acquired CDI than matched controls
Tabak YP, et al. ²⁵ 2013	CareFusion	282	Yes	Yes	Mortality, hospital LOS, costs	CDI patients had higher mortality, longer hospital LOS, and higher costs
Lipp MJ, et al. ²⁶ 2012	New York State Dept of Health	1,913	No	No	Charges and hospital LOS	Hospital-acquired CDI impacted both charges (\$29,000 increase) and hospital LOS (12 additional hospital days)
McGlone SM, et al. ²⁷ 2012	Computer simulation	N/A	N/A	N/A	Costs	Median CDI cost ranged from \$9,179 to \$11,456 from a hospital perspective, \$8,932 to \$11,679 from third party payer perspective, and \$13,310 to \$16,464 from a societal perspective
Pakyz A, et al. ²⁸ 2011	University HealthSystem Consortium	10,857	Yes	No	Hospital LOS, inpatient costs	Adjusted mean cost for patients with CDI was \$55,769 compared to \$28,609 for controls. There was also a longer hospital LOS with cases than controls
Stewart DB, et al. ²⁹ 2011	Medicare	41,207	Yes	Yes	Mortality, hospital LOS, costs	Mean cost of hospitalization, hospital LOS, and mortality were higher with CDI than matched controls

Information on references available from study authors

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