

Burden of *Clostridium difficile* on the Healthcare System

Erik R. Dubberke and Margaret A. Olsen

Department of Medicine, Washington University School of Medicine, St Louis, Missouri

There are few high-quality studies of the costs of *Clostridium difficile* infection (CDI), and the majority of studies focus on the costs of CDI in acute-care facilities. Analysis of the best available data, from 2008, indicates that CDI may have resulted in \$4.8 billion in excess costs in US acute-care facilities. Other areas of CDI-attributable excess costs that need to be investigated are costs of increased discharges to long-term care facilities, of CDI with onset in long-term care facilities, of recurrent CDI, and of additional adverse events caused by CDI.

Clostridium difficile places a significant burden on the healthcare system. However, there are few data defining the cost of *C. difficile* infection (CDI) on the healthcare system, and much of the burden has yet to be fully quantified. These costs will only continue to increase as the incidence of CDI continues to increase. Fully understanding the burden CDI places on healthcare is important to ensure that adequate resources are dedicated to CDI treatment and prevention efforts and to identify which treatment and prevention efforts are cost-effective.

There have been 2 recent reviews of the costs of CDI [1, 2]. Most notably, these reviews highlight the relative lack of studies that determine the costs attributable to CDI. Most published studies are limited by small sample size and either do not or inadequately control for confounders when estimating the cost of CDI. Because patients at highest risk for CDI often are older, have more comorbid conditions, and have higher acuity of illness than patients who do not develop CDI,

studies that do not completely adjust for confounders likely will overestimate the costs of CDI [3, 4].

It is likely that the total burden of CDI on the healthcare system is significantly underestimated. Nearly all studies in the literature are based on CDI diagnosed and treated in acute-care hospitals. CDI was associated with an increased likelihood of being discharged to a long-term care facility (LTCF) in our previous study [5]. Statewide CDI surveillance in Ohio found that more cases of CDI were diagnosed in LTCFs than in acute-care hospitals [6]. For some patients, especially those with multiple recurrent episodes of CDI, CDI is diagnosed and treated in the outpatient setting [7]. Therefore, the focus of published studies solely on inpatient hospital diagnosis and treatment of CDI ignores the contribution of other healthcare costs to the economic burden of CDI.

Because most data for the cost of CDI come from the United States and the costs of a disease are dependent on the healthcare system in which the disease is managed, this review focuses on the burden of CDI on the US healthcare system [1, 2]. In this review, we provide updated estimates of healthcare costs due to CDI in acute-care facilities. Because data for CDI prevalence from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP) are based on 2008 data, costs in this review are adjusted to 2008 dollars with the medical care component of the Consumer Price Index. We have

Correspondence: Erik R. Dubberke, MD, MSPH, 660 S Euclid, Box 8051, St. Louis, MO 63110 (edubberk@dom.wustl.edu).

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attempted to estimate the burden of CDI outside of acute-care facilities as well.

CDI BURDEN AND ACUTE-CARE FACILITIES

Four studies have examined the costs attributable to CDI in acute-care facilities. At face value, the estimated costs due to CDI in these studies appear to be different, although many of these differences likely are related to variations in study design. O'Brien et al [8] conducted a retrospective analysis of all patients in the Massachusetts hospital discharge database from 1999 to 2003. All costs for discharges with the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* code for CDI (008.45) listed as the principal diagnosis or a possible CDI-related symptom (eg, diarrhea) or condition (eg, intestinal disorder) listed as the principal diagnosis and CDI as a secondary diagnosis were attributed to CDI. Discharges with a secondary diagnosis of CDI without a primary diagnosis of a CDI-related symptom or diagnosis were considered hospital-onset CDI cases. Costs due to CDI for hospital-onset CDI were determined by calculating the difference in lengths of stay between discharges that were and those that were not assigned the *ICD-9-CM* code for CDI, stratified by all-patient refined diagnosis-related group (APR-DRG) severity level, and then applying this proportional difference in length of stay to the total costs incurred by the discharges assigned the *ICD-9-CM* code for CDI. They determined the mean cost of CDI to be \$11 498 (inflation adjusted to 2008 dollars) for a principal diagnosis and \$15 397 when CDI was hospital onset (Table 1) [8].

Both Kyne et al [9] and Dubberke et al [3] used linear regression to estimate the costs attributable to CDI. Dubberke et al [3] also used propensity score-matched pairs to estimate costs attributable to CDI. Kyne et al [9, 10] performed a secondary analysis of patients enrolled in a study to assess

whether antibody responses to *C. difficile* toxins affected the risks for colonization, diarrhea, and asymptomatic carriage. With 40 of 271 patients (15%) developing hospital-onset CDI, Kyne et al [9, 10] controlled for 11 variables in their cost model and found the mean CDI-attributable costs to be \$7000 (in 2008 dollars). Dubberke et al [3], while controlling for 130 variables, found the mean costs of CDI for 439 cases of CDI (community and hospital onset) to be \$3006 (in 2008 dollars). These 2 calculations by Kyne et al and Dubberke et al estimated the mean costs for an individual hospital admission attributable to CDI. Dubberke et al also examined additional attributable inpatient costs, including hospital readmissions up to 6 months after the original discharge in which CDI was diagnosed, and found that CDI contributed to \$6176 in excess costs during the 6-month follow-up period. Although the study by O'Brien et al [8] included all patients, the studies by Kyne et al and Dubberke et al were limited to adults. As expected, the costs attributable to CDI decreased as the number of confounders included in the model increased. Interestingly, all 3 studies had similar results for attributable length of stay and proportionate increase in costs (Table 1) [3, 5, 8, 9]. It is possible that some of the differences in absolute costs of CDI in the studies also may be related to regional differences in healthcare expenditures.

Song et al [11] used a matched-cohort design to determine the length of stay and direct costs attributable to CDI in adults between 2000 and 2005 (Table 1). A total of 540 of 741 CDI cases were matched to a control by using a number of matching characteristics, including APR-DRG. Overall, they found CDI to be associated with an increase of 4 days in length of hospital stay and \$375 (in 2008 dollars) in costs. However, CDI was associated with a 5.5-day increase in length of stay and a \$7123 increase in costs in 2004 to 2005. The reason for this difference in CDI-attributable outcomes between times is not clear. However, the epidemic *C. difficile* strain (North American pulsed-field gel electrophoresis type 1) was

Table 1. Acute-Care Facility Costs Attributable to *Clostridium difficile* Infection in 2008, According to Estimates From the Literature

Study	Attributable Length of Stay (d)	Proportionate Increase in Costs (%)	Attributable Costs per Case, 2008 (US\$)	No. of CDI Cases, HCUP 2008	Total Costs, 2008 (US\$)
O'Brien et al [8]					
Principal diagnosis	6.4	Not applicable	11 498	113 956	1.3 billion
Hospital onset	2.9	46	15 397	234 994	3.6 billion
Kyne et al [9]	3.6	54	7000	340 401	2.4 billion
Dubberke et al [3, 5]					
Index	2.8	41	3006	...	1.0 billion
Hospitalization 180-d follow-up	Not applicable	53	6176	340 401	2.1 billion
Song et al [11] (after 2004)	5.5	29	7123	340 401	4.8 billion

Abbreviations: CDI, *Clostridium difficile* Infection; HCUP, Healthcare Cost and Utilization Project.

identified at their institution in 2005 (no *C. difficile* typing data before 2005 were provided). The variations in attributable lengths of stay and costs also may be related to their methods and/or changes in *C. difficile* testing practices during the study period [4, 11, 12].

According to the 2008 HCUP Nationwide Inpatient Sample, 348 950 discharges in the United States were assigned the ICD-9-CM code for CDI in either the primary or a secondary position [13]. Of these discharges, 340 401 involved patients ≥ 18 years of age, and CDI was the principal diagnosis for 113 956 discharges. In 2008, CDI costs in acute-care hospitals during the hospitalization in which CDI was diagnosed totaled \$4.9 billion on the basis of estimates by O'Brien et al [8], \$2.4 billion on the basis of estimates by Kyne et al [9], and \$1.0 billion on the basis of estimates by Dubberke et al [3] (Table 1). On the basis of estimates by Dubberke et al [3], costs attributable to CDI in the 180 days after diagnosis were \$2.1 billion. The cost for 2008, calculated using the estimates by Song et al [11] for the period after 2004, was \$4.8 billion.

It is important to note that these studies have examined only costs directly related to CDI. It is reasonable to assume that there are numerous indirect effects of CDI that also increase costs. It is recommended to place patients with a diagnosis of CDI into contact precautions, including isolation [14]. In hospitals with a limited number of private rooms, patients with hospital-onset CDI may need to be transferred from nonprivate to private rooms when placed on contact precautions. This may necessitate moving several patients to accomplish this. Not only does moving several patients to place a single patient with CDI on contact precautions take additional administrative time to identify suitable transfer locations, it also requires additional housekeeping time for nondischarge terminal cleanings and additional nursing time for intake assessments if the patients are transferred to different units. There also may be lost opportunity costs if the patient with CDI remains alone in a semiprivate room because of a lack of private rooms to accommodate the need for an isolation room. To maintain isolation, the patient with CDI may prevent another patient from being admitted to an otherwise available bed. More insidiously, CDI contributes to healthcare costs because each patient with CDI contributes to the transmission of *C. difficile* within the hospital, thereby increasing other patients' risks for developing CDI [15].

CDI BURDEN AND LTCFS

There have not been studies that assess the costs of CDI in LTCFs, but presumably the costs of CDI extend to LTCFs. We found that 32% of patients with CDI were discharged to an LTCF, compared with 23% of propensity-score-matched patients without CDI, resulting in an increase in odds of

discharge to an LTCF of 62% (compared with home discharge; $P = .01$) [5]. This also likely increases the burden of CDI on the healthcare system. On the basis of the number of discharges with CDI in the 2008 HCUP data, if 9% of adult hospital discharges coded for CDI were sent to an LTCF because of CDI, there would have been >30 600 excess discharges to nursing homes attributable to CDI. The 2008 estimate of the average daily charge for LTCF residents was \$192 [16]. The average postacute length of stay for individuals admitted to an LTCF in the 1999 National Nursing Home Survey was 24 days (most postacute stays at an LTCF are temporary as the patient convalesces) [17]. Therefore, if CDI resulted in a short-term need for additional care that could not be provided in the patient's home, CDI could have contributed an additional \$141 million in healthcare costs due to LTCF transfers in 2008.

There also are costs of managing CDI with onset within an LTCF. CDI was a publicly reported condition in Ohio during 2006 for both nursing homes and hospitals [6]. Although the incidence of CDI was lower in nursing homes than in hospitals (1.7–2.9 vs 6.4–7.9 cases/10 000 patient-days in hospitals), there were more total cases of CDI at nursing homes. Of 14 329 CDI cases reported, 6376 were diagnosed in hospitals (5217 initial cases and 1159 recurrent cases), compared with 7953 diagnosed in nursing homes (4880 initial cases and 3073 recurrent cases). After adjustment for missing months of data, it was estimated that there were 7000 hospital-based and 11 200 LTCF-based cases. If 61.5% of healthcare facility-associated CDI cases occur in nursing homes, on the basis of the number of CDI cases diagnosed in hospitals in the 2008 HCUP data, there may have been as many as 558 320 CDI cases acquired in nursing homes in 2008.

In addition to costs related to the diagnosis and treatment of CDI in nursing homes, there likely are other costs to the patient and healthcare system. According to the 2004 National Nursing Home Survey, 47.7% of LTCF residents were not continent of bowel [18]. In addition, only 15.9% of residents were completely independent in toileting, and 2.1% were completely independent in bathing. CDI can cause incontinence as a result of severe diarrhea, but elderly patients who do not have severe diarrhea also can become incontinent because of the increase in urgency and frequency of bowel movements caused by CDI. Not only does this decrease the patient's quality of life, it also increases demands on nursing home staff. Another potential complication due to CDI is an increase in pressure ulcers. The 2004 National Nursing Home Survey found that 10.7% of residents had a pressure ulcer at the time of the survey and that 77.6% of all patients required at least some, if not complete, assistance to transfer. Increases in incontinence and frequency of watery bowel movements, combined with an inability to bathe or transfer independently, also likely

increase the risk for development of pressure ulcers. This is true for acute-care settings, as well.

Another adverse event that CDI likely contributes to in LTCFs and hospitals is falls. Among elderly individuals, falls are the most common reason for emergency department visits (accounting for 10%–30% of visits), and 30% of these patients are admitted to the hospital, with an average length of stay of 5.5 days [19, 20]. The 2004 National Nursing Home Survey found that one-third of patients reported a fall in the 180 days before the survey, and falls with injuries accounted for 36% of potentially preventable emergency department admissions [18, 21]. Almost 50% of falls in hospitalized patients are associated with toileting [22]. The odds of falling associated with incontinence were reported to be 2.3 in a hospital setting and 2.1 in a rehabilitation setting [23, 24]. In addition to more frequent toileting and increasing incontinence, diarrhea due to CDI also can lead to orthostatic hypotension and the need to toilet at night, both of which also increase the risk for falls [22].

CDI BURDEN AND RECURRENT CDI

One study from the United States assessed the costs of recurrent CDI [7]. Cost data were collected retrospectively for past CDI episodes from patients enrolled in a randomized trial for recurrent CDI. Data collected included medical billing records or laboratory charges for clinic visits, standard antibiotics, and findings from laboratory tests conducted to evaluate the cause of diarrhea. For patients who were hospitalized, data collected included charges for daily room use (for a double room), 1 physician visit, and (if performed) sigmoidoscopy, colonoscopy, or abdominal radiography. The costs of CDI recurrences during the 2-month prospective study (repeated antibiotic treatment and laboratory tests for enteric pathogens and *C. difficile*) also were included. At enrollment, patients reported a mean (\pm SD) of 2.6 ± 1.9 prior episodes (range, 1–14 episodes) of CDI. The total costs of treating CDI through the end of the study were \$17 493, with a per-episode cost for treating recurrent CDI of \$4948. Patients admitted for recurrent CDI had a mean (\pm SD) length of hospital stay of 8.8 ± 8.6 days.

Presumably, the cost of recurrent CDI varies on the basis of whether it is managed as an outpatient or inpatient. Although most recent treatment trials indicate that CDI recurs in 20%–30% of patients 30–60 days after CDI treatment is stopped [25, 26], some of these patients are not readmitted for management of CDI. Hospital-level data indicate that approximately 15% of patients with a diagnosis of CDI are readmitted with recurrent CDI 30–60 days after the initial episode [27, 28]. This indicates that 50%–75% of first recurrences result in a new hospital admission. Similar to CDI with onset in the hospital, there likely are additional indirect costs associated with

recurrent CDI when the patient is readmitted. These include lost opportunity costs if the patient occupies a semiprivate room while on contact precautions and an increased risk for CDI among other hospitalized patients due to the patient's contribution to *C. difficile* transmission.

CONCLUSION

Despite limited data, studies to date indicate that CDI has a significant burden on the healthcare system. In 2008, CDI may have resulted in as much as \$4.8 billion in excess health-care costs in acute-care facilities alone. There may be more cases of CDI treated in LTCFs than in acute-care facilities; however, the cost of treating CDI in nursing homes is not known at this time. There also are additional costs of CDI that have yet to be quantified, such as increases in discharges to LTCFs, lost opportunity costs if the patient with CDI is isolated in a semiprivate room, and contributions to the transmission of *C. difficile* and additional new cases of CDI. Additional areas of study needed to fully understand the impact CDI has on the healthcare system and society include the costs of recurrent CDI; costs of CDI managed in the outpatient setting; adverse events associated with CDI, particularly in elderly individuals; and the impact of CDI on quality of life. A full appreciation of the burden that CDI has on the healthcare system is necessary to ensure that adequate resources are allocated to CDI prevention and treatment efforts.

Notes

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