

ORIGINAL ARTICLE

Clostridium difficile Infection in Ohio Hospitals and Nursing Homes During 2006

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CONTEXT. Healthcare data suggest that the incidence and severity of *Clostridium difficile* infection (CDI) in hospitals are increasing. However, the overall burden of disease and the mortality rate associated with CDI, including the contribution from cases of infection that occur in nursing homes, are poorly understood.

OBJECTIVE. To describe the epidemiology, disease burden, and mortality rate of healthcare-onset CDI.

METHODS. In 2006, active public reporting of healthcare-onset CDI, using standardized case definitions, was mandated for all Ohio hospitals and nursing homes. Incidence rates were determined and stratified according to healthcare facility characteristics. Death certificates that listed CDI were analyzed for trends.

RESULTS. There were 14,329 CDI cases reported, including 6,376 cases at 210 hospitals (5,217 initial cases [ie, cases identified more than 48 hours after admission to a healthcare facility in patients who had not had CDI during the previous 6 months] and 1,159 recurrent cases [ie, cases involving patients who had had CDI during the previous 6 months]) and 7,953 cases at 955 nursing homes (4,880 initial and 3,073 recurrent cases). After adjusting for missing data, the estimated total was 18,200 cases of CDI, which included 7,000 hospital cases (5,700 initial and 1,300 recurrent cases) and 11,200 nursing homes cases (6,900 initial and 4,300 recurrent cases). The rate for initial cases was 6.4–7.9 cases/10,000 patient-days for hospitals and 1.7–2.9 cases/10,000 patient-days for nursing homes. The rate for initial cases in nursing homes decreased during the study ($P < .001$). Nonpediatric hospital status ($P = .011$), a smaller number of beds ($P = .003$), and location in the eastern or northeastern region of the state ($P = .011$) were each independently associated with a higher rate of initial cases in hospitals. Death certificates for 2006 listed CDI among the causes of death for 893 Ohio residents; between 2000 and 2006, this number increased more than 4-fold.

CONCLUSION. Healthcare-onset CDI represents a major public health threat that, when considered in the context of an increasing mortality rate, should justify a major focus on prevention efforts.

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Clostridium difficile is an anaerobic, spore-forming, toxigenic bacteria that is the most commonly recognized cause of infectious nosocomial diarrhea and one of the most common healthcare-associated pathogens.^{1,2} *C. difficile* infection (CDI) presents with a spectrum of severity ranging from uncomplicated diarrhea to pseudomembranous colitis that can lead to toxic megacolon and death; CDI is especially problematic among elderly individuals, the group in which infection is most common. Admission to inpatient healthcare facilities and antibiotic use are associated with an increased risk of CDI.³

Because CDI is not a reportable condition nationwide, there are few national or regional data on its incidence in the United States (US). Nonetheless, data based on discharges from acute care hospitals suggest that both the incidence and severity of CDI are increasing, both in the Midwest and

nationally.^{4,5} There are no similar data to indicate the incidence or disease burden of CDI in nursing homes. In recent years, there has been an increasing trend for US states to make healthcare-acquired infections publicly reportable. Currently, approximately half of all states have mandated public reporting for some healthcare-acquired infections and at least another dozen are either currently considering legislation or have study bills in place.⁶ Ohio initiated public reporting for all initial and recurrent cases of healthcare-onset CDI that occurred in acute care hospital and nursing home patients, effective January 1 through December 31, 2006. The purpose of this public reporting system was to better determine the burden of healthcare-onset CDI infection among Ohio residents and to establish facility-level baseline CDI rates to assist in identifying unusual disease activity. In the present article, we summarize the major findings drawn from Ohio's 2006

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statewide reporting to provide better understanding of the regional epidemiology and disease burden of CDI. In addition, we assessed the changes that occurred between 2000 and 2006 in the mortality rate associated with CDI.

METHODS

All 210 Ohio acute care hospitals and 955 Ohio nursing homes were required to report the number of CDI cases that occurred in their facilities between January 1 and December 31, 2006. The long-term care facilities under surveillance were limited to nursing homes (ie, facilities that housed low acuity patients who required long-term skilled care) by legislative mandate. Hospitals and nursing homes reported cases by fax or telephone to the local health jurisdiction for their area. Local health departments initially made a paper report to the Ohio Department of Health (ODH), followed by an electronic report to the ODH that was made through a secure public health system. Hospitals or nursing homes that opened or closed during the study period were not required to report and are not included in these analyses.

Patient-days became reportable for hospitals on April 1, 2006, retroactive to January 1, 2006. Effective July 1, 2006, nursing homes were also required to report patient-day information for this same time period. The reporting period for cases identified more 48 hours after admission to a health-care facility that occurred in patients who had not had CDI during the previous 6 months (hereafter, "initial cases") and cases involving patients who had had CDI during the previous 6 months (hereafter, "recurrent cases") changed from weekly to monthly beginning July 1, 2006. Only those hospitals and nursing homes that reported the number of initial and/or recurrent CDI infections and the number of patient-days for a given month were included in the analyses. Case and patient-day reports that were received at ODH by January 30, 2007, were included.

All rates were calculated as the number of cases per 10,000 patient-days. Missing months of data (numerators and/or denominators) were estimated by imputing the value from the preceding or subsequent reporting period, if available; otherwise imputed values were randomly selected from the distribution of values for similar facilities. Values were only imputed if facilities reported at least 1 month of data (ie, no facilities had all 12 months of data imputed). All statistical analyses used only data that were not imputed. Sensitivity analyses were performed using only data from facilities with complete data reported for the entire year. Facilities were classified as urban, suburban, or rural using 1990 census data, in accordance with the following classifications: urban counties contained at least 1 metropolitan area with population 50,000 or greater, suburban counties had urban areas and were contiguous with urban counties, and rural counties were all other nonurban, nonsuburban counties. The hospital's number of beds, as well as its pediatric and teaching status, were obtained from the Ohio Hospital Association. The list

of Ohio nursing homes was obtained from the ODH Division of Quality Assurance. Hospitals and nursing homes were contacted to obtain the facility's number of beds if this information was missing.

Statistical analyses were performed with SAS, version 9.13 (SAS Institute), and Microsoft Excel (Microsoft). Repeated-measures Poisson regression models were used to evaluate variables associated with CDI rates and to conduct trend analyses (for rates of initial cases only). All variables with a *P* value less than .20 on univariate analysis were included in the initial multivariate model. Variables with a *P* value greater than .05 were then removed sequentially, starting with the highest *P* value. Statistical significance was defined as *P* less than .1.

Death data for the years from 2000 through 2006 were obtained from Vital Statistics at the ODH, and deaths were classified as caused by CDI if the primary or any other reported cause of death on the death certificate was *International Classification of Diseases and Related Health Problems, 10th Revision*, code A04.7 ("enterocolitis due to *Clostridium difficile*").

A case patient was defined as a patient who had a laboratory diagnostic test result positive for *C. difficile* (enzyme immunoassay, cytotoxin, antigen, and/or culture), pseudomembranes seen on endoscopy, or a positive histologic test result from a tissue specimen obtained during surgery or autopsy; if the case patient was identified by laboratory test results, the result had to be a first positive result—that is, it had to have been more than 2 weeks since the patient's last result positive for *C. difficile*. The presence or absence of diarrhea was not included in the definition for logistical reasons; we relied instead on recommended laboratory practices that indicate *C. difficile* testing should be performed only on unformed stool. Only healthcare-onset cases of CDI were captured in this reporting scheme.

A healthcare-onset initial case was defined as occurring in a patient who had a laboratory diagnostic test, endoscopy, or biopsy result positive for *C. difficile* more than 48 hours after admission to a health-care facility. A subsequent episode of CDI that occurred more than 6 months after an initial infection was also classified as an initial infection. A healthcare-onset recurrent case was defined as occurring in a patient who had had an initial case of CDI and then, within 6 months after the initial case, had a subsequent laboratory diagnostic test, endoscopy, or biopsy result positive for *C. difficile*.

Monthly patient-days were defined as the sum of the daily facility census for that month. All patient-specific data used to determine case assignment (ie, initial or recurrent) were captured and saved at the facility level, and only monthly summary data of the number of initial and recurrent cases (ie, numerators) and the number of patient-days (ie, denominators) were sent to the health department. There was no formal data sharing agreement between facilities to ensure that patients were correctly identified as having recurrent or

initial cases of CDI, other than the medical records that accompanied patient transfers.

RESULTS

During the 12-month reporting period, a total of 14,329 cases of CDI were reported. Hospitals ($n = 210$) reported 6,376 cases, of which 5,217 were initial and 1,159 were recurrent. Nursing homes ($n = 955$) reported 7,953 cases, of which 4,880 were initial and 3,073 were recurrent. After adjusting for missing data, the estimated total number of cases was 18,200; hospitals accounted for 7,000 cases (5,700 initial and 1,300 recurrent cases), and nursing homes accounted for 11,200 cases (6,900 initial and 4,300 recurrent cases). The mean percentage of acute care hospitals that reported both the number of initial cases and the number of patient-days each month was 90% (range, 77%–95%), and the mean percentage of nursing homes that reported both the number of initial cases and the number of patient-days each month was 75% (range, 57%–87%).

The mean number of initial cases for all Ohio hospitals was 435 cases/month (475 cases/month after adjusting for missing data). The rate of initial cases (hereafter, “initial case rate”) ranged from 6.4 to 7.9 cases/10,000 patient-days during the reporting period (Figure 1). The mean number of recurrent cases for Ohio hospitals was 97 cases/month (108 cases/month after adjusting for missing data). The rate of recurrent cases ranged from 1.1 to 2.0 cases/10,000 patient-days for the reporting period (Figure 1). There was a downward trend in the rates of both initial and recurrent cases during the year. There was concern that, in the early months of the reporting system, facilities may not have reported 0 as a number of cases, thereby potentially biasing the case estimates upward, so analyses were conducted using only the 130 hospitals (62%) that reported complete data during the 12-

month period. The decrease in the initial case rate for these hospitals was not significant ($P = .104$).

The mean number of initial cases for all Ohio nursing homes was 407 cases/month (575 cases/month after adjusting for missing data). The reported initial case rate ranged from 1.7 to 2.9 cases/10,000 patient-days for the reporting period (Figure 1). The mean number of recurrent cases reported for Ohio nursing homes was 256 cases/month (358 cases/month after adjusting for missing data) per month. The reported rate of recurrent cases ranged from 0.8 to 2.4 cases/10,000 patient-days for the reporting period (Figure 1). There was also a downward trend for the rate of both initial and recurrent cases in nursing homes during the year; this decrease was statistically significant for initial cases ($P < .001$). An analysis restricted to the 401 nursing homes (42%) that reported complete data yielded similar results.

The mean initial case rate per 10,000 patient-days in hospitals had a strong inverse relationship with the number of beds ($P = .014$). Rates were highest in hospitals with 24 or fewer beds (20.6 cases/10,000 patient-days) and lowest in hospitals with 400–499 beds (5.9 cases/10,000 patient-days) (Table and Figure 2). The mean initial case rate was slightly higher in hospitals in rural counties (8.0 cases/10,000 patient-days) than in hospitals in suburban counties (7.4 cases/10,000 patient-days) or urban counties (7.1 cases/10,000 patient-days), but this difference was not statistically significant (Table). The initial case rate in teaching hospitals was 6.3 cases/10,000 patient-days, compared with 7.6 cases/10,000 patient-days in nonteaching hospitals ($P = .063$); the rate was 2.6 cases/10,000 patient-days in pediatric hospitals, compared with 7.4 cases/10,000 patient-days for nonpediatric hospitals ($P = .027$). The rate for initial cases in hospitals was generally higher for hospitals located in the northeast and east central regions of Ohio than for hospitals located in other parts of

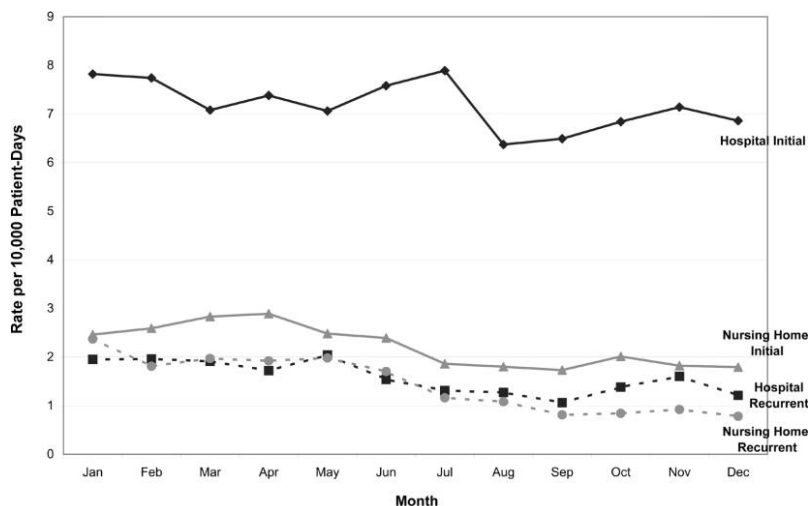


FIGURE 1. Rates of *Clostridium difficile* infection in Ohio acute care hospitals ($n = 210$) and nursing homes ($n = 955$) from January 1 to December 31, 2006, according to month. See Methods for definitions of initial and recurrent cases.

TABLE. Rate of Initial Cases of *Clostridium difficile* Infection in Ohio Acute Care Hospitals and Nursing Homes During 2006, According to Facility Characteristics

Characteristic	Hospitals (n = 210)			Nursing homes (n = 955)		
	Unadjusted mean rate, cases/10,000 patient-days	P		Unadjusted mean rate, cases/10,000 patient-days	P	
		Univariate	Multivariate		Univariate	Multivariate
County type		NS	NS		.064	NS
Urban	7.1			2.5		
Suburban	7.4			1.8		
Rural	8.0			2.0		
No. of beds		.014	.003		NS	NS
6–24	20.6			3.1		
25–49	12.4			2.5		
50–99	9.8			2.2		
100–199	7.7			2.2		
200–299	6.8			2.3		
300–399	7.3			2.5		
400–499	5.9			0		
≥500	6.2			NA		
Region		.175	.011		<.001	<.001
Northwest	5.7			1.3		
West central	5.7			0.9		
Southwest	7.2			2.5		
Central	6.0			1.8		
Southeast	8.0			2.3		
East Central	7.9			2.8		
Northeast	8.4			2.9		
Teaching status		.063	NS		NA	NA
Teaching	6.3			NA		
Nonteaching	7.6			NA		
Pediatric status		.027	.011		NA	NA
Pediatric	2.6			NA		
Nonpediatric	7.4			NA		

NOTE. An initial case was defined as occurring in a patient who had a laboratory diagnostic test, endoscopy, or biopsy result positive for *C. difficile* more than 48 hours after admission to a healthcare facility. A subsequent *C. difficile* infection that occurred more than 6 months after an initial infection was also classified as an initial infection. NA, not applicable; NS, nonsignificant ($P > .1$).

the state. Multivariate analysis showed that nonpediatric hospital status ($P = .011$), a smaller number of beds ($P = .003$), and location in the east central or northeastern region ($P = .011$) were each independently associated with a higher initial case rate (Table).

The mean initial case rate in nursing homes was higher in urban counties (2.5 cases/10,000 patient-days) than in rural counties (2.0 cases/10,000 patient-days) or suburban counties (1.8 cases/10,000 patient-days) ($P = .064$) (Table). In contrast to hospitals, in nursing homes there was no correlation between the initial case rate and the number of beds (Table and Figure 2). There were, however, higher rates of initial cases in nursing homes in the east central and northeastern regions of Ohio ($P < .001$). County-level mean rates for hospitals and nursing homes were positively correlated with one another for both initial cases (Pearson $r = 0.22$; $P = .054$) and recurrent cases (Pearson $r = 0.29$; $P = .011$) (data not shown).

The number of Ohio resident deaths for which CDI was

the primary or any other reported cause of death increased during the period from 2000 to 2006 (Figure 3). In 2006, there were 893 deaths for which the death certificate reported CDI as any cause of death, 528 (59%) of which reported CDI as the primary underlying cause of death. Age-adjusted mortality rates were consistently higher and increased fastest in the oldest age groups (data not shown), and they were similar for male and female subjects. However, rates for white subjects were higher than those for black subjects. Mortality rates were highest in northeast Ohio.

DISCUSSION

Our results indicate a substantial CDI burden for the state of Ohio, with an estimated total of 12,600 initial and 5,600 recurrent cases. If the data for Ohio (which has a population of approximately 11.5 million) are extrapolated to the entire US population (300 million), then there may have been 333,000 initial and 145,000 recurrent cases of CDI nationwide

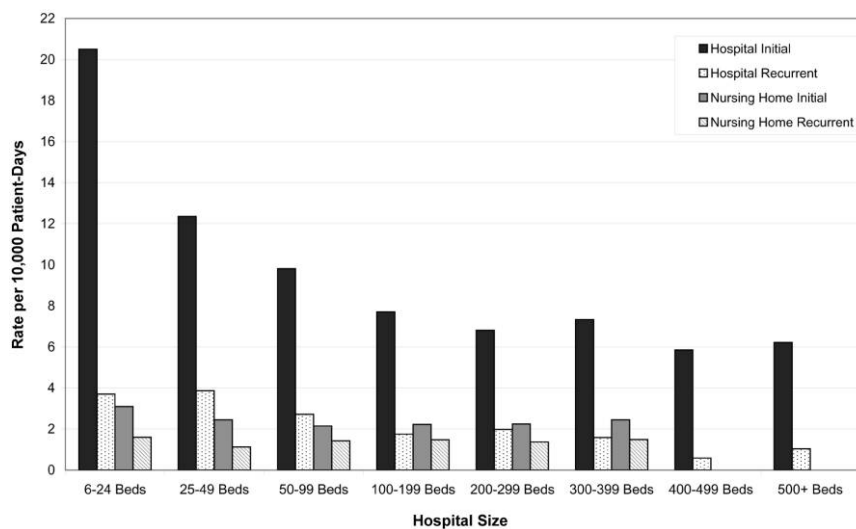


FIGURE 2. Mean rates of *Clostridium difficile* infection per month in Ohio hospitals ($n = 210$) and nursing homes ($n = 955$) from January 1 to December 31, 2006, according to the number of beds in a facility. See Methods for definitions of initial and recurrent cases.

in 2006. Nonetheless, the true overall burden of CDI in Ohio and elsewhere may be much greater, because community-onset disease, which was not included in this report, may represent up to half of all cases of CDI.⁷

This report highlights the significant disease burden of CDI in nursing homes, where over half of all healthcare-onset cases of CDI occurred in this study. Furthermore, long-term care facilities other than nursing homes, such as rehabilitation or mental health facilities or group homes, were not included in this study, so the total number of healthcare facility-onset cases of CDI is likely higher than this estimate. Similar to the results of other recent reports, we found evidence of a rapidly increasing mortality rate for CDI during the period from 2000 to 2006; in 2006, there were 893 death certificates that indicated CDI as a cause of death. No other infectious disease listed as a cause of death showed any increase during the same time period, and the number of mortality codes in 2006 for CDI was substantially higher than that for any other infectious disease except unspecified septicemia (data not shown). It is possible that many patients who have CDI recorded on their death certificate die while they have the disease rather than *from* the disease, whereas other deaths that truly are attributable to CDI go unrecognized. Nonetheless, recent reports indicate that the attributable mortality rate for CDI ranges from 5.7% to 15% for initial, hospital-onset cases.⁸⁻¹⁰ This suggests 297–782 deaths in 2006 in Ohio that were attributable to initial cases of hospital-onset CDI, which extrapolates to 7,752–20,000 such deaths nationally.

The overall initial case rate in acute care hospitals observed in this study, which ranged from 6.4 to 7.9 cases/10,000 patient-days, is similar to previously reported rates of endemic CDI in North American hospitals.¹¹⁻¹³ There are no similar

background data against which to compare the overall rate for initial cases of CDI among nursing home patients, which ranged from 1.7 to 2.9 cases/10,000 patient-days in this Ohio study. We observed a lower initial case rate in nursing home patients than in acute care patients, despite a similar rate of recurrent cases in both groups, which may reflect the longer mean length of stay and increased risk of colonization among nursing home patients rather than a truly reduced risk of *C. difficile* transmission. One recent study suggested that more than 50% of asymptomatic nursing home patients may be colonized with *C. difficile* and that such carriage is frequently associated with a previous case of CDI or antimicrobial exposure.¹⁴ The correlation of county rates for acute care hospitals and nursing homes in our data and the increasing proportion of patients with CDI who are transferred between acute care and nursing home facilities (as reflected in hospital discharge data²) both suggest significant movement of recently infected or colonized patients between acute and long-term facilities. In turn, this suggests that the control of a highly transmissible pathogen such as *C. difficile* may best be addressed through communitywide prevention strategies that align both healthcare quality and public health initiatives.

CDI rates in both acute care and nursing home facilities appeared to decrease during the study period; however, this trend was statistically significant only in nursing homes. Although the effectiveness of public reporting of health process and outcome data is still largely unproven, one goal of public reporting initiatives is to motivate healthcare facilities and providers to improve infection control measures¹⁵—in this case, to implement CDI prevention measures. However, it is unknown whether this significant decrease the rate of CDI in nursing homes represents merely a trend toward baseline

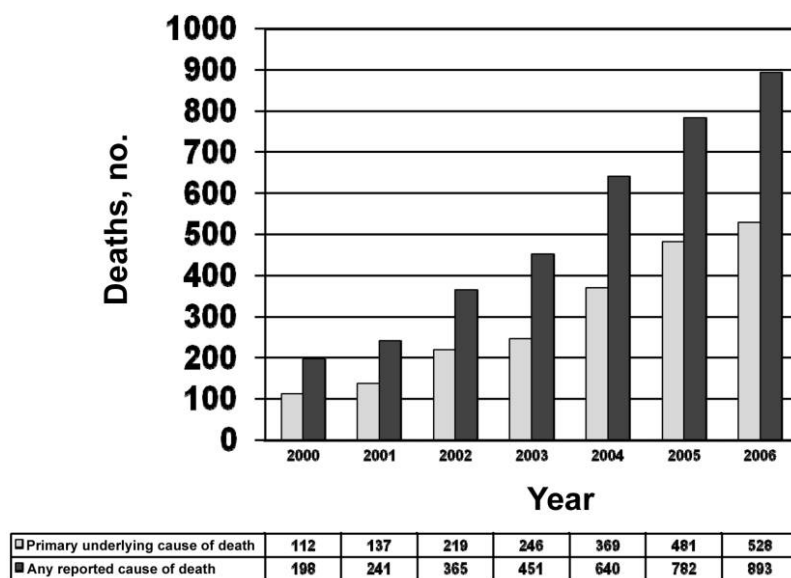


FIGURE 3. Deaths of Ohio residents during the period from 2000 through 2006 for which enterocolitis due to *Clostridium difficile* (*International Classification of Diseases and Related Health Problems, 10th Revision, code A04.7*) was reported as the primary or any cause of death. Data are from the Ohio Department of Health, Vital Statistics, death certificates for 2000–2006.

after an earlier statewide outbreak, seasonal variation, or actual improvement in infection control and antimicrobial use practices in Ohio nursing homes.

In acute care hospitals, we found an inverse association between the number of beds and the CDI rate. Typically, larger hospitals are more likely to provide specialty care to patients with greater severity of illness, who may in turn have an increased risk of acquiring multidrug-resistant organisms, including *C. difficile*. However larger hospitals may also be more likely to have better-developed infection control and antimicrobial stewardship programs and/or the expertise needed for such programs.¹⁶ Alternatively, smaller hospitals may be more likely to provide care to patients with demographic factors other than increased severity of illness that lead to an increased risk of CDI. For example, advanced age is one of the most important host factors that increases patient risk of CDI, and smaller hospitals may be more likely to provide care to elderly patients. An analysis of national discharge estimates from 2006 indicates that smaller hospitals—variably defined in terms of urban versus rural, teaching status, and regional location—had a larger percentage of patients aged 65 years or older (39.9% [2,140,559 of 5,358,106; 95% confidence interval {CI}, 36.3%–43.6%]) than did medium-sized hospitals (33.4% [3,351,891 of 10,024,172; 95% CI, 31.1%–35.8%]) or large hospitals (33.2% [7,961,687 of 23,988,670; 95% CI, 30.9%–35.5%]; $P < .001$) (unpublished analysis of data from Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, Rockville, Maryland).

One major limitation of this study was the fact that re-

porting was limited only to healthcare facility-onset cases. There is increasing evidence that not only is the burden of community-onset CDI large, but many cases appear in association with inpatient healthcare exposures.^{7,17,18} Unfortunately, the Ohio public reporting efforts occurred before the current interim CDI surveillance definitions became available.¹⁹ The 6-month interval during which a subsequent episode of CDI was considered to be a recurrent case rather than a new initial case was longer than the 8-week interval used in the current definitions. Therefore, under these newer definitions, the Ohio healthcare facility reporting for 2006 underestimates the number of initial cases. Another limitation is the relatively large proportion of data that were missing and therefore imputed for nursing homes (3,247 [40.8%] of 7,953 reported cases), relative to the amount of imputed data for hospitals (624 [9.8%] of 6,376 reported cases), which suggests that our calculation of the total burden and rates of CDI in Ohio nursing homes may be less accurate than our calculation for hospitals. There was no attempt to stratify patient populations for risk with regard to age or underlying illness. We did not include symptom criteria in our case definition but relied instead on recommended laboratory practices, which indicate that *C. difficile* testing should be performed only on unformed stool. In particular, the number of recurrent cases may have been inflated if laboratories routinely accepted formed stool for testing, because patients commonly shed toxin after resolution of symptoms. Conversely, the number of reported cases may be an underestimate, owing to the insensitivity of commonly used toxin enzyme immunoassays; in rare instances, severe cases of CDI

that occurred in patients with ileus may not have satisfied the case definition.

The public reporting described in this study resulted in a significant resource burden borne by both healthcare facilities and public health institutions. A cost survey conducted by use of a questionnaire issued by the ODH estimated the state-wide personnel costs associated with the reporting of CDI from January through December of 2006. The estimated total cost of reporting was \$2,486,000 (95% CI, \$2,159,000–\$2,813,000). This included \$164,000 paid by the ODH, \$295,000 paid by local health departments, \$560,000 paid by acute care hospitals, and \$1,467,000 paid by nursing homes. The decision to make CDI publicly reportable was not accompanied by an increase in financial resources to cover these costs for either healthcare facilities or public health institutions. When considered in the context of the significant financial impact of CDI on excess healthcare costs, supporting surveillance with the ultimate goal of reducing the rate of CDI may be a wise investment. Given recent estimates,^{20,21} it is likely that the excess healthcare costs for just initial, hospital-onset cases of CDI were between \$21 and \$41 million in Ohio and between \$548 million and \$1 billion when the Ohio data were extrapolated to the nation.

Given the significant burden in terms of human suffering and excess healthcare costs associated with CDI, resources should be directed toward prevention. Evidence-based recommendations for infection control and antimicrobial stewardship appear to reduce CDI rates in outbreak situations, including outbreaks caused by the current epidemic strain.^{22–24} However, additional data are needed to demonstrate the preventability of CDI in environments where it is endemic or in a larger group of hospitals, much as has been demonstrated with the reduction of other healthcare-acquired infections.^{25,26} Although such data may not define the incremental impact of each intervention, they could provide evidence of what proportion of infections are preventable in a range of inpatient healthcare settings and set the stage for national efforts to reduce CDI rates and mortality.

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The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of either the Ohio Department of Health or the Centers for Disease Control and Prevention.

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