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Erik R. Dubberke

Washington University School of Medicine in St. Louis

Anne M. Butler

Washington University School of Medicine in St. Louis

Deborah S. Yokoe

Harvard University

Jeanmarie Mayer

University of Utah

Bala Hota

Rush University

See next page for additional authors

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Authors

Erik R. Dubberke, Anne M. Butler, Deborah S. Yokoe, Jeanmarie Mayer, Bala Hota, Julie E. Mangino, Yosef M. Khan, Kyle J. Popovich, Kurt B. Stevenson, Clifford McDonald, Margaret A. Olsen, Victoria J. Fraser, and Prevention Epicenters Program of the Centers for Disease Control and Prevention

ORIGINAL ARTICLE

Multicenter Study of Surveillance for Hospital-Onset *Clostridium difficile* Infection by the Use of ICD-9-CM Diagnosis Codes

Erik R. Dubberke, MD; Anne M. Butler, MS; Deborah S. Yokoe, MD, MPH; Jeanmarie Mayer, MD; Bala Hota, MD, MPH; Julie E. Mangino, MD; Yosef M. Khan, MD; Kyle J. Popovich, MD; Kurt B. Stevenson, MD, MPH; L. Clifford McDonald, MD; Margaret A. Olsen, PhD, MPH; Victoria J. Fraser, MD; for the Prevention Epicenters Program of the Centers for Disease Control and Prevention

OBJECTIVE. To compare incidence of hospital-onset *Clostridium difficile* infection (CDI) measured by the use of *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* discharge diagnosis codes with rates measured by the use of electronically available *C. difficile* toxin assay results.

METHODS. Cases of hospital-onset CDI were identified at 5 US hospitals during the period from July 2000 through June 2006 with the use of 2 surveillance definitions: positive toxin assay results (gold standard) and secondary ICD-9-CM discharge diagnosis codes for CDI. The χ^2 test was used to compare incidence, linear regression models were used to analyze trends, and the test of equality was used to compare slopes.

RESULTS. Of 8,670 cases of hospital-onset CDI, 38% were identified by the use of both toxin assay results and the ICD-9-CM code, 16% by the use of toxin assay results alone, and 45% by the use of the ICD-9-CM code alone. Nearly half (47%) of cases of CDI identified by the use of a secondary diagnosis code alone were community-onset CDI according to the results of the toxin assay. The rate of hospital-onset CDI found by use of ICD-9-CM codes was significantly higher than the rate found by use of toxin assay results overall ($P < .001$), as well as individually at 3 of the 5 hospitals ($P < .001$ for all). The agreement between toxin assay results and the presence of a secondary ICD-9-CM diagnosis code for CDI was moderate, with an overall κ value of 0.509 and hospital-specific κ values of 0.489–0.570. Overall, the annual increase in CDI incidence was significantly greater for rates determined by the use of ICD-9-CM codes than for rates determined by the use of toxin assay results ($P = .006$).

CONCLUSIONS. Although the ICD-9-CM code for CDI seems to be adequate for measuring the overall CDI burden, use of the ICD-9-CM discharge diagnosis code for CDI, without present-on-admission code assignment, is not an acceptable surrogate for surveillance for hospital-onset CDI.

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Clostridium difficile is the most commonly recognized cause of infectious diarrhea in hospitalized patients. Several reports suggest that the incidence and severity of *C. difficile* infection (CDI) have been increasing in recent years, due in part to transmission of a single, fluoroquinolone-resistant epidemic strain with enhanced virulence characteristics.^{1–7} Given the increase in the incidence and severity of CDI, a surveillance system to track rates of CDI is necessary. In the absence of a national surveillance system, *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes assigned at hospital discharge have been used as a surrogate. Current national CDI rate estimates are based on a national probability sample of patient discharge records from

nonfederal, short-stay hospitals.⁸ In early 2009, the US Department of Health and Human Services identified the reduction of endemic CDI rates as a high-priority goal in their Action Plan to Prevent Healthcare-Associated Infections and proposed ICD-9-CM codes as a metric to measure CDI case rates.⁹ Surveillance with administrative discharge data is advantageous, because the data are inexpensive to obtain and readily available at all hospitals in the United States, thus providing a nationally representative method for tracking CDI rates.^{10,11} Conversely, case ascertainment by means of current surveillance definitions (ie, symptoms of diarrhea or toxic megacolon, combined with a positive result of a laboratory assay and/or endoscopic or histopathologic evidence of pseu-

From the Washington University School of Medicine, St Louis, Missouri (E.R.D., A.M.B., M.A.O., V.J.F.); the Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts (D.S.Y.); the University of Utah Hospital, Salt Lake City, Utah (J.M.); the Stroger Hospital of Cook County/Rush University Medical Center, Chicago, Illinois (B.H., K.J.P.); the Ohio State University Medical Center, Columbus, Ohio (J.E.M., Y.M.K., K.B.S.); and the Centers for Disease Control and Prevention, Atlanta, Georgia (L.C.M.).

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domembranous colitis), the gold standard for CDI surveillance, is labor intensive and expensive, because it requires both microbiologic test results and medical record review.¹²

Data from 2 single-institution studies suggest that the *ICD-9-CM* code for CDI may be an acceptable surrogate for tracking the overall CDI burden in the absence of toxin testing results.^{13,14} However, no multicenter studies have been conducted to evaluate CDI surveillance by means of *ICD-9-CM* codes, nor have there been any studies reporting more than 1 year of data. There have not been any investigations of the ability of *ICD-9-CM* codes to track rates of hospital-onset CDI.

The objective of this study was to compare hospital-onset CDI incidence rates measured by the use of *ICD-9-CM* discharge diagnosis codes with CDI rates measured by the use of electronically available *C. difficile* toxin assay results—the gold standard—at multiple healthcare facilities during a 6-year study period. We sought to determine the utility of *ICD-9-CM* codes for overall hospital-onset CDI surveillance, as well as for intrahospital and interhospital comparisons of hospital-onset CDI incidence. In addition, we evaluated the effect of surveillance with *ICD-9-CM* codes on the proportion of cases of hospital-onset CDI relative to cases of community-onset CDI and recurrent CDI.

METHODS

The study population included all adult patients admitted and discharged during the period from July 1, 2000, through June 30, 2006, at 5 hospitals participating in the Prevention Epicenters Program of the Centers for Disease Control and Prevention. These hospitals included Barnes-Jewish Hospital (St Louis, Missouri), Brigham and Women's Hospital (Boston, Massachusetts), the Ohio State University Medical Center (Columbus, Ohio), Stroger Hospital of Cook County (Chicago, Illinois), and University of Utah Hospital (Salt Lake City, Utah). Eligibility was limited to patients aged at least 18 years. Approval for this study was obtained from the institutional review boards of the Centers for Disease Control and Prevention and all participating centers.

Retrospective data were collected from hospital medical informatics databases; the data included dates of hospital admission, discharge, and stool collection, as well as *C. difficile* toxin assay results and the *ICD-9-CM* discharge diagnosis code for CDI (008.45). Medical coders are trained to assign this code to hospitalizations for which there is medical record documentation by the treating clinician of gastroenteritis or colitis due to *C. difficile*; positive laboratory test results alone are not sufficient to warrant application of the code. This is the only *ICD-9-CM* code specific for CDI.¹⁵

Case Definitions

Cases of hospital-onset CDI, defined as cases that occurred for patients with nonrecurrent CDI that had onset more than 48 hours after admission, were identified by using 2 sur-

veillance definitions: positive toxin assay results and the secondary *ICD-9-CM* diagnosis code for CDI. Cases of CDI identified from a positive toxin assay result were not considered to be hospital-onset CDI if the first positive toxin assay result was for a sample obtained no more than 48 hours after admission or if the patient had a positive toxin assay result during the previous 8 weeks (which defined a case as recurrent CDI). Because the presence of a primary *ICD-9-CM* code for CDI suggests that CDI was the primary reason for hospitalization, cases identified by an *ICD-9-CM* code for CDI were not considered to be hospital-onset CDI if the *ICD-9-CM* diagnosis code was the primary discharge code. In addition, since cases of CDI that occur in the same patient within 8 weeks after a previous case are considered recurrent, hospitalizations identified by an *ICD-9-CM* code for CDI were considered recurrent if an *ICD-9-CM* code for CDI had been assigned to a hospitalization for the same patient during the previous 8 weeks.

Cases of community-onset CDI were defined as cases that occurred for patients with nonrecurrent CDI and a positive toxin assay result for a sample obtained no more than 48 hours after admission (by the toxin assay definition) or for patients with a primary *ICD-9-CM* diagnosis code for CDI (by the *ICD-9-CM* code definition). Cases of CDI were attributed to the month of stool sample collection for the positive toxin assay result definition and to the month of discharge from the hospital for the *ICD-9-CM* code definition. For patients who had multiple positive toxin assay results during a single hospitalization, only the first positive toxin assay result was included in the analysis.

Statistical Analysis

Monthly CDI rates were calculated as the number of cases per 1,000 patient discharges for each surveillance definition (ie, positive *C. difficile* toxin assay result and *ICD-9-CM* code). Patient discharges, rather than patient-days, were used for the denominator because the date of CDI onset was not known for cases of CDI indicated by *ICD-9-CM* code, and the codes are assigned at discharge. Rates were compared with the χ^2 test, with Bonferroni adjustment for multiple comparisons. Linear regression analysis was used to estimate the annual change in CDI incidence, and the test of equality was used to compare the slopes. The κ statistic was calculated to measure the agreement between *C. difficile* toxin assay results and *ICD-9-CM* codes. Data from hospital D were incomplete for the first 14 months and the last 14 months of the study period; therefore, these months were excluded from the analysis for hospital D. All tests were 2-tailed, and a *P* value of less than .05 was considered to indicate a significant difference. Statistical analyses were performed with Epi Info, version 6 (Centers for Disease Control and Prevention), SPSS for Windows, version 14.0 (SPSS), and Stata, version 9.2 (StataCorp).

TABLE 1. Method of Identifying Cases of *Clostridium difficile* Infection among 930,692 Patient Discharges from 5 Hospitals

ICD-9-CM code	Toxin assay result		Total
	Positive	Negative	
Positive	6,545	3,033	9,578
Negative	1,831	919,283	921,114
Total	8,376	922,316	930,692

NOTE.—Data are no. of patient discharges.

RESULTS

The number of patient discharges from each hospital varied (range, 84,984–318,847); a total of 930,692 patient discharges occurred during the 6-year study period (Table 1). *C. difficile* toxin assays had positive results for 8,376 (0.9%) of the discharges, of which 3,435 (41%) cases were identified from samples obtained within 48 hours after admission of the patient (ie, consistent with community-onset CDI) and 4,941 (59%) cases were identified from samples obtained more than 48 hours after admission (ie, consistent with hospital-onset CDI). The ICD-9-CM code for CDI was assigned to 9,578 (1%) of the discharges, for which the primary diagnosis code for CDI was present in the medical record for 1,339 (14%) and the secondary diagnosis code for CDI was present for 8,239 (86%). Six hundred twenty-four (7%) cases of CDI identified by means of toxin assays occurred for patients who had a prior positive toxin assay result during the previous 8 weeks, and 1,237 (13%) cases of CDI identified by means of the ICD-9-CM code for CDI occurred for patients who had a CDI code assigned to a hospitalization during the previous 8 weeks. Compared with toxin assay results, the sensitivity and specificity of ICD-9-CM codes for tracking the overall CDI burden were 78.1% and 99.7%, respectively.

Of 8,670 cases of hospital-onset CDI identified during the study period by use of a secondary ICD-9-CM diagnosis code and/or toxin assay result, 3,335 cases (38%) were identified by both toxin assay result and code, 1,419 cases (16%) were identified by toxin assay result alone, and 3,916 cases (45%) were identified by code alone (Figure 1). The use of secondary diagnosis codes identified 53% more cases of hospital-onset CDI than did the use of toxin assay results. The agreement between toxin assay results and diagnosis codes was moderate; the overall κ value was 0.509, and hospital-specific κ values were 0.489–0.570. Compared with the toxin assay definition, the diagnosis code definition classified a significantly higher proportion of cases of CDI as hospital-onset CDI (76% vs 57%; $P < .001$) rather than community-onset CDI or recurrent CDI. Of the 3,916 discordant cases classified as hospital-onset CDI by the secondary ICD-9-CM diagnosis code definition but not by the toxin assay definition, the toxin assay definition classified 1,828 (47%) as community-onset CDI, 84 (2%) as recurrent CDI, and 2,004 (51%) as not CDI (Figure 2).

Table 2 presents hospital-onset CDI rates according to surveillance definition. Overall, the rates of hospital-onset CDI were significantly higher with the use of ICD-9-CM codes than with the use of toxin assays (7.8 vs 5.1 cases per 1,000 discharges; $P < .001$). The rates of hospital-onset CDI for the entire study period found with the use of ICD-9-CM codes were higher than the rates found with the use of toxin assay results at all 5 hospitals, with significant differences at 3 of 5 hospitals ($P < .001$ for hospitals A, C, and E) and a marginally significant difference at a fourth hospital ($P = .092$ for hospital D). Figures 3 and 4 present annual rates of hospital-onset CDI according to surveillance definition, overall and stratified by hospital. Across hospitals, there was significant variation in the number of additional cases of hospital-onset CDI identified with the use of ICD-9-CM codes, compared with the use of toxin assay results (test of equality, $P < .001$). The use of the codes identified 6% more cases of hospital-onset CDI than did the use of toxin assays at hospital B, 14% more at hospital D, 36% more at hospital A, 129% more at hospital C, and 142% more at hospital E.

The annual rates of hospital-onset CDI were also significantly higher with the use of ICD-9-CM codes than with the use of toxin assay results for the entire study population ($P < .001$ for each year) (Figure 3). Within hospitals, the number of years during which there was a significant difference in the incidence of hospital-onset CDI detected with different

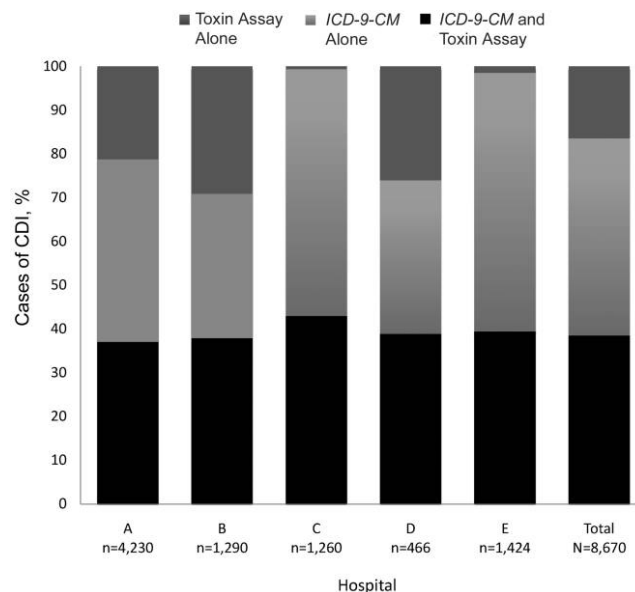


FIGURE 1. Identification of cases of hospital-onset *Clostridium difficile* infection (CDI) identified with use of toxin assay results and/or International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, by hospital. The hospital-specific κ values were as follows: hospital A, 0.489; hospital B, 0.494; hospital C, 0.570; hospital D, 0.499; and hospital E, 0.527. The overall κ value was 0.509.

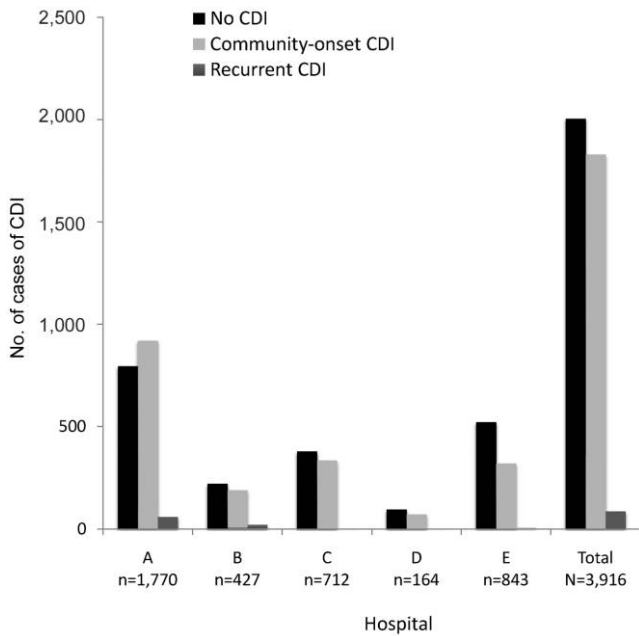


FIGURE 2. Classification of cases of *Clostridium difficile* infection (CDI) by use of the toxin assay result definition for the 3,916 discordant cases classified as hospital-onset *C. difficile* infection by the *International Classification of Diseases, Ninth Revision, Clinical Modification* code definition alone.

surveillance definitions varied (range, 0–6 cases per 1,000 discharges) (Figure 4). Of the 28 annual time points in the analysis (ie, 6 years for hospitals A, B, C, and E and 4 years for Hospital D), half (14 time points) had rates of hospital-onset CDI that differed significantly by surveillance definition, after correction for multiple comparisons ($P < .001$ for all). Hospitals C and E had significantly higher rates with the use of *ICD-9-CM* codes than with the use of toxin assay results for every year of the 6-year study period. Hospital A had significantly higher rates with the use of the codes than with the use of toxin assay results for the last 4 years of the

study period. At hospitals B and D, the rates of hospital-onset CDI did not differ by surveillance definition for any year.

While the overall annual incidences of hospital-onset CDI increased almost every year of the study period regardless of the surveillance definition used, the annual increase in incidence was significantly higher for the rates found with the use of *ICD-9-CM* codes than for the rates found with the use of toxin assay results (β , 0.908 vs 0.327; $P = .006$; Figure 3). At 3 hospitals, the annual increase in CDI incidence was higher for rates found with the use of *ICD-9-CM* codes than for rates found with the use of toxin assay results (Figure 4), with significant differences at hospital A (β , 0.990 vs -0.035 ; $P = .014$) and hospital C (β , 0.583 vs 0.151; $P = .025$) and a nonsignificant difference at hospital E (β , 0.900 vs 0.447; $P = .129$).

DISCUSSION

The results of this multicenter study of patients admitted to 5 geographically diverse academic medical centers suggest that *ICD-9-CM* codes may be an adequate surrogate for tracking the overall CDI burden, but comparison with toxin assay results reveals that *ICD-9-CM* codes are of little to no use for tracking hospital-onset CDI incidence. Consistent with previous reports, the sensitivity and specificity of *ICD-9-CM* codes for tracking the overall CDI burden were 78.1% and 99.7%, respectively, compared with the use of toxin assay results, which suggests that these codes are an adequate surrogate for tracking CDI prevalence. However, *ICD-9-CM* codes demonstrated only moderate agreement with toxin assay results for identification of cases of hospital-onset CDI. Use of the codes significantly overreported the incidence of hospital-onset CDI compared with use of toxin assay results, and the degree to which hospital-onset CDI incidence was overreported with use of the codes varied by year and by hospital. In addition, the annual increase found in the incidence of hospital-onset CDI was greater with the use of *ICD-9-CM* codes than that found with the use of toxin assay results overall and at 3 of the individual hospitals. These results indicate that *ICD-9-CM* codes would not have been

TABLE 2. Incidences of Hospital-Onset *Clostridium difficile* Infection (CDI) Identified by Surveillance with *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* Codes and Toxin Assay Results

Hospital	No. of patient discharges	<i>ICD-9-CM</i> code		Toxin assay result		<i>P</i>
		No. of cases of CDI	No. of cases of CDI per 1,000 discharges	No. of cases of CDI	No. of cases of CDI per 1,000 discharges	
A	318,847	3,334	10.5	2,460	7.7	<.001
B	110,437	915	8.3	863	7.8	.219
C	254,073	1,253	4.9	548	2.2	<.001
D	84,984	345	4.1	302	3.6	.092
E	162,351	1,404	8.6	581	3.6	<.001
Total	930,692	7,251	7.8	4,754	5.1	<.001

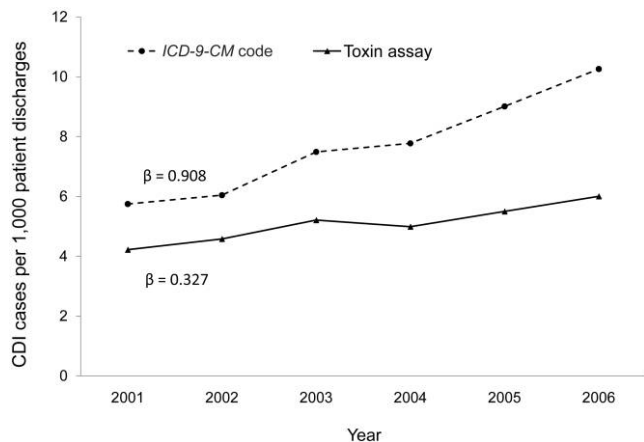


FIGURE 3. Overall annual incidence of hospital-onset *Clostridium difficile* infection (CDI) at the study hospitals, according to surveillance definition. The annual increase in incidence was significantly higher for the rates found with the use of *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes than the rates found with the use of toxin assay results (β , 0.908 vs 0.327; $P = .006$).

useful for overall hospital-onset CDI surveillance, nor would they be useful for intrahospital or interhospital comparisons of CDI incidence during the study period.

Previous studies of CDI surveillance with the use of *ICD-9-CM* codes have focused on the overall CDI burden rather than hospital-onset CDI. Data from 2 single-institution studies suggest that *ICD-9-CM* codes are an acceptable surrogate for tracking the overall CDI burden in the absence of toxin testing results.^{13,14} In a cohort of patients hospitalized in 2003 at Barnes-Jewish Hospital, there was good agreement between *ICD-9-CM* codes and toxin assay results for CDI case ascertainment ($\kappa = 0.72$).¹³ In this study, *ICD-9-CM* codes had a sensitivity of 78.0% and a specificity of 99.7%. These results were remarkably similar to those of a study by Scheurer and colleagues¹⁴ of patients hospitalized in 2004 at Brigham and Women's Hospital. These investigators reported a sensitivity of 71% and a specificity of 99% for CDI surveillance with the use of *ICD-9-CM* codes, compared with the use of positive toxin assay results. In the present study, the sensitivity (78.1%) and specificity (99.7%) of *ICD-9-CM* codes for tracking the overall CDI burden were consistent with those of previous reports. This suggests that *ICD-9-CM* codes may be an adequate surrogate for tracking overall CDI prevalence, compared with the use of toxin assay results. It is possible that the disparity in the ability of *ICD-9-CM* codes to track overall CDI compared with their ability to track hospital-onset CDI can be explained by an inherent limitation of surveillance based on *ICD-9-CM* codes: the codes are assigned to the date of discharge rather than the date of diagnosis and thus do not give any information regarding the date of CDI onset. In our study, 47% of the cases of CDI discordantly classified as hospital-onset CDI according to the *ICD-9-CM*

code definition but not according to the toxin assay result definition occurred for patients who had their first positive toxin assay result for a sample obtained within 48 hours after admission and therefore were cases of community-onset CDI, according to the gold standard definition. In the future, present-on-admission codes, which became mandatory for the records of Medicare patients discharged on or after October 1, 2007 (ie, after the study period), may add precision to CDI surveillance based on *ICD-9-CM* codes by providing a mechanism to distinguish preexisting conditions, ultimately reducing misclassification of cases of community-onset CDI.¹⁶

Medical record review was not performed for this study; however, prior studies have used medical record review to investigate discrepancies in CDI case ascertainment between toxin assay and *ICD-9-CM* code surveillance definitions. In our study, 3,916 (45%) cases of CDI were identified as hospital-onset CDI by use of the *ICD-9-CM* code surveillance definition but not by use of the toxin assay surveillance definition. We found that 1,912 (49%) of these cases were misclassified as hospital-onset CDI according to the *ICD-9-CM* codes, because according to the toxin assay results, they were community-onset CDI (1,828 cases) or recurrent CDI (84 cases). There were no corresponding positive toxin assay results for the remaining 2,004 (51%) of these cases. Scheurer et al¹⁴ performed medical record review for the 35 patients with an *ICD-9-CM* code for CDI but without a positive toxin assay result in their study and reported that all of these patients had a prior history of CDI documented in their medical history but did not have active disease during the hospital stay. In our previous study at Barnes-Jewish Hospital, 142 patients (59%) with an *ICD-9-CM* code for CDI but without a positive toxin assay result had a past history of CDI.¹³ In addition, 137 patients (57%) with an *ICD-9-CM* code but without a positive toxin assay result had at least 1 order for toxin testing, and 130 (95%) of these had at least 1 negative toxin test result. It is possible that many of the patients in this study identified as having hospital-onset CDI without a corresponding toxin assay result had only a past history of CDI. Alternatively, some of these cases could have occurred among patients with diarrhea whose physicians noted a high clinical suspicion of CDI but who never had a positive toxin assay result.

In our current study, 16% of the cases of hospital-onset CDI were identified using the toxin assay surveillance definition alone. This discrepancy may have occurred, in part, because toxin assay results were pending at discharge. We previously reported that hospitalizations of patients who had only a positive toxin assay result and no *ICD-9-CM* code for CDI were more likely than hospitalizations of patients with concordant CDI classification to have their first positive toxin assay result for a sample obtained within the 48 hours before discharge (44% vs 14%; $P < .01$).¹³ In our current study, the median duration between obtaining the first sample with a positive toxin assay result and hospital discharge was significantly shorter for hospitalizations of patients with only a

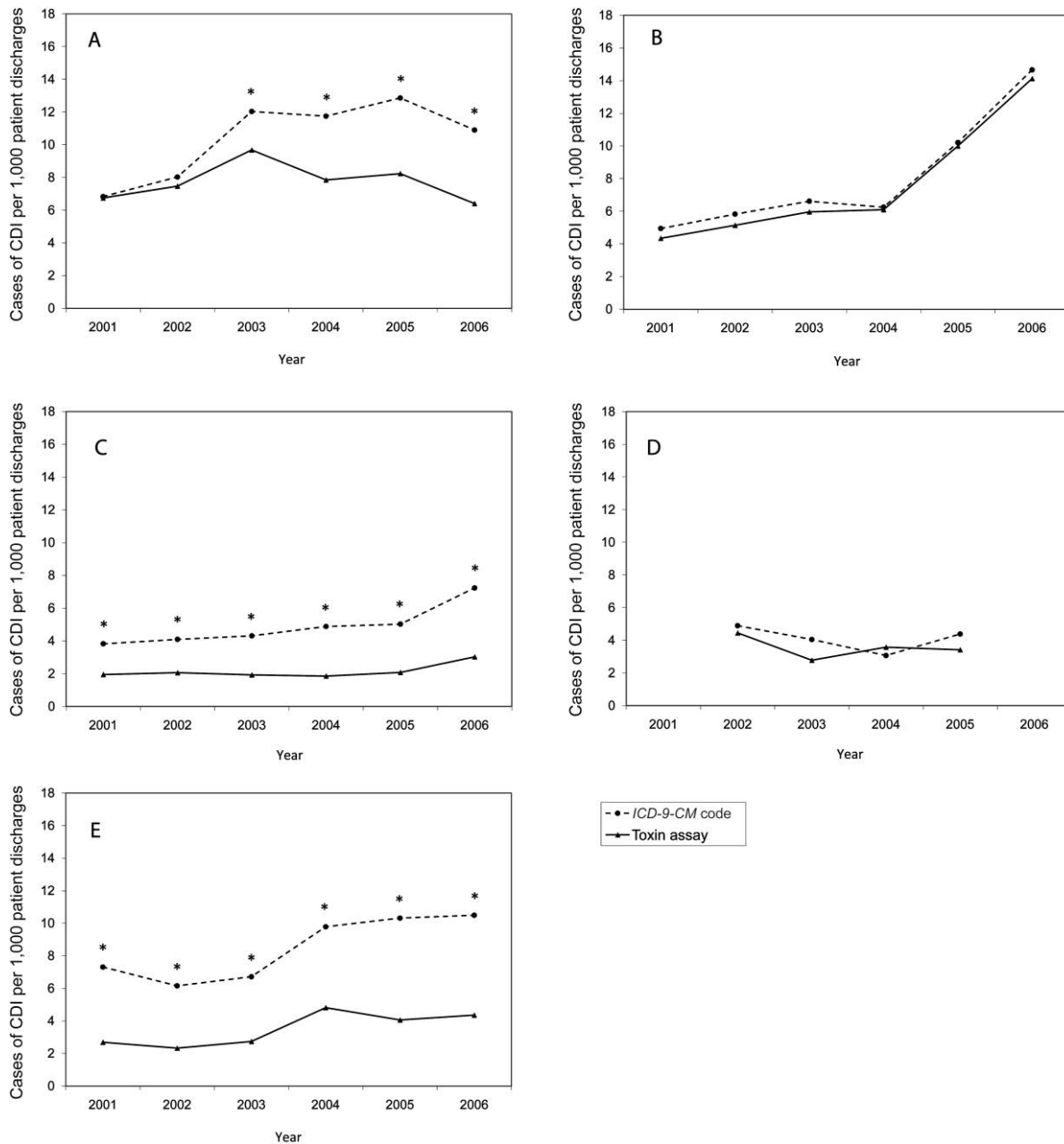


FIGURE 4. Annual incidence of hospital-onset *Clostridium difficile* infection (CDI) at individual study hospitals, according to surveillance definition. Asterisks indicate significantly higher annual incidences found with the use of *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes compared with rates found with the use of toxin assay results ($P < .001$).

positive toxin assay result than for hospitalizations of patients with concordant CDI classification (4 vs 9 days; Mann-Whitney U test, $P < .001$). The first stool sample positive for CDI was collected within 2 days before discharge for 541 (38%) of 1,419 hospitalizations of patients with a positive toxin assay result only, compared with 357 (11%) of 3,335 hospitalizations of patients with concordant CDI classification ($P < .001$). For these hospitalizations, toxin assay results may not yet have been known at the time of patient discharge and

therefore were not noted in the physician's discharge summary for medical coders to capture.

There are several additional limitations to surveillance for hospital-onset CDI based on *ICD-9-CM* codes. First, the retrospective nature of administrative data causes a time lag in code assignment, since *ICD-9-CM* codes are assigned after patients are discharged from the hospital. Second, discharge diagnosis codes reflect conditions diagnosed or treated during the entire hospitalization but do not give information re-

garding the hospital location or date of CDI onset. Therefore, surveillance based on *ICD-9-CM* codes cannot be used for ward-level surveillance. Last, CDI is currently slated for Phase III of Centers for Medicare and Medicaid Services nonreimbursable diagnoses. This may affect the utility of *ICD-9-CM* codes for conducting CDI surveillance, if the frequency of hospital-onset CDI coding is altered.

This study was limited to academic medical centers located in urban areas. Although medical coding practices are theoretically standardized across institutions, there may be differences in coding practices according to hospital size, geographic location, or teaching status. In addition, there may be differences in patient populations or physician practices at urban, academic medical centers, compared with other acute care settings, that influence the likelihood that a patient has CDI diagnosed or is assigned the *ICD-9-CM* code for CDI.

Despite these limitations, the utilization of *ICD-9-CM* codes is potentially valuable for CDI surveillance because the data are readily available from hospital billing databases and provide a universal method of surveillance. The codes appear to be adequate for measuring the overall CDI burden; however, our data from 2000 through 2006 indicate that *ICD-9-CM* codes are not an adequate substitution for toxin assay results for surveillance of hospital-onset CDI. The recent implementation of present-on-admission code assignment offers a potential mechanism to differentiate community-onset CDI from hospital-onset CDI and ultimately to improve the accuracy of surveillance based on *ICD-9-CM* codes. Additional work is needed to evaluate the effect that present-on-admission codes have on hospital-onset CDI surveillance in multiple acute care settings before *ICD-9-CM* codes can be considered for hospital-onset CDI surveillance.

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Address reprint requests to Erik R. Dubberke, MD, Box 8051, 660 South Euclid, St Louis, MO 63110 (edubberk@im.wustl.edu).

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