The Impact of ICD-9-CM Code Rank Order on the Estimated Prevalence of Clostridium difficile Infections

Erik R. Dubberke,1 Anne M. Butler,1 Humaa A. Nyazee,1 Kimberly A. Reske,1 Deborah S. Yokoe,2 Jeanmarie Mayer,3 Julie E. Mangino,4 Yosef M. Khan,4 Victoria J. Fraser,1 and Centers for Disease Control and Prevention Epicenters Program

1Department of Medicine, Washington University School of Medicine, St Louis, Missouri; 2Department of Medicine, Brigham and Women’s Hospital and Harvard Medical School, Boston, Massachusetts; 3Department of Medicine, University of Utah Hospital, Salt Lake City, Utah; and 4Department of Medicine, The Ohio State University Medical Center, Columbus, Ohio

Background. US estimates of the Clostridium difficile infection (CDI) burden have utilized International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes. Whether ICD-9-CM code rank order affects CDI prevalence estimates is important because the National Hospital Discharge Survey (NHDS) and the Nationwide Inpatient Sample (NIS) have varying limits on the number of ICD-9-CM codes collected.

Methods. ICD-9-CM codes for CDI (008.45), C. difficile toxin assay results, and dates of admission and discharge were collected from electronic hospital databases for adult patients admitted to 4 hospitals in the United States from July 2000 through June 2006. CDI prevalence per 1000 discharges was calculated and compared for NHDS and NIS limits and toxin assay results from the same hospitals. CDI prevalence estimates were compared using the χ² test, and the test of equality was used to compare slopes.

Results. CDI prevalence measured by NIS criteria was significantly higher than that measured using NHDS criteria (10.7 cases per 1000 discharges versus 9.4 cases per 1000 discharges; P < .001) in the 4 hospitals. CDI prevalence measured by toxin assay results was 9.4 cases per 1000 discharges (P = .57 versus NHDS). However, the CDI prevalence increased more rapidly over time when measured according to the NHDS criteria than when measured according to toxin assay results (β = 1.09 versus 0.84; P = .008).

Conclusions. Compared with the NHDS definition, the NIS definition captured 12% more CDI cases and reported significantly higher CDI rates. Rates calculated using toxin assay results were not different from rates calculated using NHDS criteria, but CDI prevalence appeared to increase more rapidly when measured by NHDS criteria than when measured by toxin assay results.

The incidence and severity of Clostridium difficile infection (CDI) have been increasing in recent years [1–7], but national surveillance efforts and interhospital comparisons have been limited by the lack of a standard CDI surveillance system. As a result, the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes assigned at hospital discharge have been used as a proxy to estimate CDI prevalence in the United States [8–12].

Using administrative data (ICD-9-CM codes) to compare CDI rates between hospitals has several potential advantages. Administrative discharge data are inexpensive to obtain, are systematically collected, and utilize a single ICD-9-CM code to designate CDI (008.45), thus potentially providing a nationally representative method for tracking CDI rates [8, 13, 14]. Two administrative databases have been used to estimate CDI prevalence in the United States: the National Hospital...
Discharge Survey (NHDS) and the Nationwide Inpatient Sample (NIS). ICD-9-CM code data are collected differently in each database; neither data set collects all potential ICD-9-CM codes assigned at hospital discharge. The NHDS is collected annually by the National Center for Health Statistics at the Centers for Disease Control and Prevention (CDC), and about 90% of a panel of 500 hospitals participate [8]. The NIS, on the other hand, is collected from all states that participate in the Healthcare Cost and Utilization Project and includes information from about 1000 US hospitals [15]. The NHDS collects up to the first 7 ICD-9-CM codes assigned per patient, and the NIS collects up to the first 9–15 codes assigned per patient (the number of codes captured varies by state).

Despite their advantages, a recent study suggests that ICD-9-CM codes may not be acceptable for hospital-onset CDI surveillance. A multicenter study performed at the CDC Prevention Epicenters hospitals compared the incidences of hospital-onset CDI as measured by ICD-9-CM codes with toxin assay results. ICD-9-CM codes overestimated the incidence of hospital-onset CDI, compared with toxin assay results, indicating that ICD-9-CM codes are not an acceptable surrogate for hospital-onset CDI surveillance [16]. The degree to which ICD-9-CM codes overreported the incidence of hospital-onset CDI varied by year and by hospital, indicating that ICD-9-CM codes would not have been useful for intrahospital or interhospital CDI surveillance.

No previously published CDI prevalence study using ICD-9-CM codes has differentiated between the NHDS and NIS criteria. The data collection discrepancies between these 2 data sets may account for the conflicting results of previous studies of CDI prevalence. It is not known how the differences in the number of ICD-9-CM codes available for prevalence estimation affect the estimated CDI prevalence and how CDI burden estimates based on ICD-9-CM codes compare with toxin assay results. Therefore, we investigated how the NHDS and NIS criteria affect CDI prevalence and how these definitions compare with toxin assay results at multiple healthcare facilities during a 6-year study period.

**METHODS**

The study population included all adult patients admitted to 4 US hospitals participating in the CDC Epicenters Program from 1 July 2000 through 30 June 2006. These hospitals included Barnes-Jewish Hospital (St Louis, Missouri), Brigham and Women’s Hospital (Boston, Massachusetts), Ohio State University Medical Center (Columbus, Ohio), and University Hospital (Salt Lake City, Utah). Patients aged ≥18 years were included in our analyses. During the study period, 3 of the 4 laboratories at the study hospitals rejected formed stool specimens for *C. difficile* testing.

Dates of hospital admission and discharge, rank order of CDI ICD-9-CM code, and positive *C. difficile* toxin assay results were obtained from hospital databases. The toxin test assays used at the 4 hospitals during the study period are as follows: Hospital A used the cytotoxicity assay until June 2002 and then switched to an enzyme immunoassay; hospital B used an enzyme immunoassay; and hospitals C and D used the cytotoxicity assay. For each discharged patient, the NHDS collects ICD-9-CM code data up to the first 7 diagnoses and the NIS collects data up to the first 15 diagnoses. The number of ICD-9-CM diagnoses collected for the NIS varies by state and year (eg, 15 in Massachusetts, Missouri, and Ohio; 9 in Utah from 2000 to 2002 and 10 in Utah from 2003 to 2006). The institutional review boards at the CDC and all participating hospitals gave approval for this study.

**Statistical Analysis**

Rates of CDI cases per 1000 discharges were calculated and compared for the overall administrative data set, NHDS and NIS criteria, and toxin assay results. Discharges, rather than patient-days, were used for the denominator because the date of CDI onset was not known and ICD-9-CM codes are assigned at discharge. CDI prevalence estimates were compared using the χ² test, and slopes were compared using the test of equality. Calculation of κ statistics was performed to measure the agreement between *C. difficile* toxin assay results and ICD-9-CM codes. Statistical analyses were performed with Epi Info, version 6 (CDC); SPSS for Windows, version 17.0 (SPSS), and Stata, version 9.2.

**RESULTS**

We identified a total of 10,832 cases of CDI, of which 2925 (27%) had an ICD-9-CM code alone, 1643 (15.2%) had a positive toxin assay result alone, and 6264 (57.8%) had both the ICD-9-CM code and positive toxin assay result. The overall CDI prevalence of all ICD-9-CM codes (ie, ICD-9-CM code in any position) was 10.9 per 1000 discharges, and the median rank-order of the ICD-9-CM code was 4. Compared with the total CDI cases captured by ICD-9-CM codes in any position, the NIS and NHDS criteria captured 99% (n = 9056) and 87% (n = 7978), respectively (Figure 1).

The overall CDI prevalence calculated with the NIS criteria (10.7 per 1000 discharges) was significantly higher than the CDI prevalence calculated with the NHDS criteria (9.4 per 1000 discharges; P < .001) but was no different from the CDI prevalence of all ICD-9-CM codes (10.9 per 1000 discharges; P = .33). The CDI prevalence measured by means of toxin assay results (9.4 per 1000 discharges) was no different from the CDI prevalence measured by NHDS (P = .57). The agreement between the NHDS criteria and toxin assay was good, with an overall κ value of 0.638, and hospital-specific κ values ranging from 0.560 to 0.702.
Figures 2 and 3 present annual CDI prevalence by surveillance definition, overall and stratified by hospital, respectively. Overall, the CDI prevalence by means of the NIS criteria was the highest across the study period (Figure 2). The median rank order of the ICD-9-CM code for CDI was 3 at hospitals A and B and 4 at hospitals C and D. Hospital B is the only hospital where the annual CDI prevalence was highest by means of toxin assay results during every year of the study (Figure 3). The toxin assay rate was the highest rate only at Hospital B (Figure 3). Compared with the NHDS criteria, the toxin assay rate was higher at hospital A (toxin assay rate, 13.7 cases per 1000 discharges versus NHDS rate, 13.1 cases per 1000 discharges; \(P = .03\)) and hospital B (toxin assay rate, 12.0 cases per 1000 discharges versus NHDS rate, 9.4 cases per 1000 discharges; \(P < .001\)), whereas the toxin assay rate was lower at hospital C (toxin assay rate, 4.3 cases per 1000 discharges versus NHDS rate, 5.3 cases per 1000 discharges; \(P < .001\)) and hospital D (toxin assay rate, 6.9 cases per 1000 discharges versus NHDS rate, 8.7 cases per 1000 discharges; \(P < .001\)).

Overall, ICD-9-CM codes overestimated the number of cases of CDI relative to use of the toxin assay (Figure 2). While the overall annual rates increased almost every year of the study period regardless of the surveillance definition, the annual increase in the prevalence of CDI varied by definition. The annual increase in prevalence according to the NIS criteria was greater than that according to the NHDS criteria (\(\beta = 1.34\) versus \(\beta = 1.09\); \(P = .003\)). The annual increase in prevalence according to the NHDS criteria was greater than that according to the toxin assay (\(\beta = 1.09\) versus \(\beta = 0.84\); \(P = .008\)).

DISCUSSION

To our knowledge, this is the first study to examine how current methods used to estimate the prevalence of CDI in the United States compare with the use of toxin assay results to estimate the prevalence of CDI. The results of this multicenter study suggest that the CDI prevalence measured using all ICD-9-CM codes was higher than the CDI prevalence measured using the NIS, which, in turn, was higher than the CDI prevalence measured using the NHDS. These results were not surprising, given that the NIS captures more ICD-9-CM codes than the NHDS but does not capture all ICD-9-CM codes. In this study, the overall CDI prevalence measured by the NHDS criteria was the same as the CDI prevalence measured by the positive toxin assay results. Previous research indicates that ICD-9-CM codes overestimate CDI prevalence [16–18]. NHDS, by limiting the data set to the first 7 ICD-9-CM codes in each discharge record, may eliminate patients who do not truly have CDI. However, in this study, the annual increase in CDI prevalence as measured by the NHDS criteria was greater than that revealed by positive toxin assay results, indicating at some point that the CDI prevalence identified by the NHDS criteria may become greater than the CDI prevalence identified by toxin assay results.

When comparing the CDI prevalence measured using the NHDS criteria with the toxin assay results at the hospital level, the CDI prevalence was higher by toxin assay results at hospitals A and B, whereas the prevalence was higher by the NHDS criteria at hospitals C and D. Hospital A’s results may be due in part to the fact that this institution became more vigilant to ensure that all medical records were adequately reviewed by medical coders in a timely fashion midway through the study period. Hospital B’s results may reflect laboratory practices at this institution. During the study period, this hospital’s
microbiology laboratory tested formed stools for *C. difficile* toxin. This practice is discouraged because testing asymptomatic patients may falsely elevate the CDI prevalence by 2 mechanisms: asymptomatically colonized patients without CDI can have positive toxin assay results, and testing for *C. difficile* in low-prevalence populations will increase the number of false-positive test results [19, 20]. This may explain the higher CDI prevalence by toxin assay results than that by the NHDS criteria at this institution. Last, the NIS and NHDS databases do not exclude on the basis of stool consistency either. Therefore, it was unknown what effect this might have on our results.

There are limitations to the use of administrative data for disease surveillance purposes. The ICD-9-CM codes are assigned by medical coders. Not all medical coders have the same level of training and certification, which may result in variable coding practices from coder to coder and facility to facility. For a patient to receive an ICD-9-CM code, the diagnosis must be clearly stated in the medical records by a treating physician. Additional variability may occur if physician documentation is inconsistent. Patients who receive the ICD-9-CM code for CDI but who do not have laboratory confirmation frequently have a history of CDI but lack ongoing symptoms of CDI [17, 18]. Furthermore, ICD-9-CM codes are assigned after discharge, creating a time lag in the availability of data, and ICD-9-CM codes do not provide any information about date or place of onset of CDI. Therefore, ICD-9-CM codes alone are not ideal for CDI incidence surveillance.

Despite the limitations of ICD-9-CM codes, there are limitations to the use of laboratory results on *C. difficile* toxin tests for CDI surveillance as well. The “gold standard” to detect pathogenic *C. difficile* from stool, toxigenic culture, is labor and resource intensive and takes several days until results are final. As a result, there are an increasing number of methods and algorithms to detect *C. difficile* or its toxins in stool, all of which differ in sensitivity and specificity. Stool handling and processing can also affect the sensitivity and

---

**Figure 3.** Yearly hospital *Clostridium difficile* infection rates by surveillance definition at hospitals A, B, C, and D. ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; NHDS, National Hospital Discharge Survey; NIS, Nationwide Inpatient Sample.
specificity of an assay. Testing practices vary in interpretation of positive results. Although this practice is uncommon, the diagnoses for some patients are made by means of endoscopy alone [18]. Indiscriminate repeated testing for C. difficile can falsely elevate CDI incidence by as much as 27% [20]. Most importantly, CDI is a clinical diagnosis. Testing stool samples obtained from patients who do not have clinical symptoms compatible with CDI will result in positive test results for patients without CDI. In addition, the NIS and NHDS databases do not exclude patients with recurrent disease or patients with repeated toxin assay tests. To keep comparisons consistent, we did not exclude these patients either. As a result, this may have overestimated the true CDI prevalence by toxin assay.

An alternative CDI surveillance system already in use is that of the National Healthcare Safety Network (NHSN), which has been augmented by mandatory C. difficile public reporting requirements of many states in the United States. Currently, the NHSN is collecting data on C. difficile using 2 different reporting methods: (1) infection surveillance and (2) laboratory-identified events [21]. To date, 166 facilities are participating in the NHSN C. difficile infection surveillance reporting, 576 facilities are participating in the C. difficile laboratory-identified event reporting, and 36 facilities are participating in both reporting methods (D. Sievert, PhD, personal communication, 4 June 2010). Review of data from the 36 facilities performing both methods of surveillance will be important to further our understanding as to whether use of laboratory data alone in the absence of clinical information from facilities that do not test formed stool for C. difficile is a valid method for CDI surveillance.

This study indicates that current estimates of CDI prevalence in the United States based on ICD-9-CM codes may be falsely elevated. Fortunately, the NHSN is currently collecting data for CDI surveillance. The NHSN system provides a standardized method of CDI surveillance and will be able to assess the utility of laboratory-based CDI surveillance. Thus, the NHSN system may represent a substantial improvement in the quality of data available for hospital-based CDI surveillance, national CDI prevalence estimates, and interhospital CDI prevalence comparisons.

Acknowledgments

Findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Financial support. This work was supported by grants from the Centers for Disease Control and Prevention (UR8/CCU715087-06/1 and 5U01CI000333 to Washington University, 5U01CI000344 to the Ohio State University, and 5U01CI000334 to the University of Utah) and from the National Institute of Allergy and Infectious Diseases (K23AI065806).

Potential conflicts of interest. V. J. F. holds stock options in Express Scripts. J. M. has received institutional financial support for a lecture on candidemia from Fallon Medical CME. E. R. D. has received payment from Optimer, Merck, Pfizer, Steris, BD, and Merck for consultancy; payment for lectures from Schering-Plough; and payment for development of educational presentations from the Robert Michaels Educational Institute. His institution has received grant support on his behalf from Optimer and Merck. All other authors: no conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed in the Acknowledgments section.

References

16. Dubberke ER, Butler AM, Yokoe DS, et al. Multicenter study of candidemia from Fallon Medical CME. E. R. D. has received payment from Optimer, Pfizer, Steris, BD, and Merck for consultancy; payment for lectures from Schering-Plough; and payment for development of educational presentations from the Robert Michaels Educational Institute. His institution has received grant support on his behalf from Optimer and Merck. All other authors: no conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed in the Acknowledgments section.

