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Multicenter study of the impact of communityonset Clostridium difficile infection on surveillance for C. difficile infection

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Multicenter Study of the Impact of Community-Onset Clostridium difficile Infection on Surveillance for C. difficile Infection •

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ORIGINAL ARTICLE

Multicenter Study of the Impact of Community-Onset *Clostridium difficile* Infection on Surveillance for *C. difficile* Infection

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

OBJECTIVE. To evaluate the impact of cases of community-onset, healthcare facility (HCF)-associated *Clostridium difficile* infection (CDI) on the incidence and outbreak detection of CDI.

DESIGN. A retrospective multicenter cohort study.

SETTING. Five university-affiliated, acute care HCFs in the United States.

METHODS. We collected data (including results of *C. difficile* toxin assays of stool samples) on all of the adult patients admitted to the 5 hospitals during the period from July 1, 2000, through June 30, 2006. CDI cases were classified as HCF-onset if they were diagnosed more than 48 hours after admission or as community-onset, HCF-associated if they were diagnosed within 48 hours after admission and if the patient had recently been discharged from the HCF. Four surveillance definitions were compared: cases of HCF-onset CDI only (hereafter referred to as HCF-onset CDI) and cases of HCF-onset and community-onset, HCF-associated CDI diagnosed within 30, 60, and 90 days after the last discharge from the study hospital (hereafter referred to as 30-day, 60-day, and 90-day CDI, respectively). Monthly CDI rates were compared. Control charts were used to identify potential CDI outbreaks.

RESULTS. The rate of 30-day CDI was significantly higher than the rate of HCF-onset CDI at 2 HCFs (P < .01). The rates of 30-day CDI were not statistically significantly different from the rates of 60-day or 90-day CDI at any HCF. The correlations between each HCF's monthly rates of HCF-onset CDI and 30-day CDI were almost perfect (ρ range, 0.94–0.99; P < .001). Overall, 12 time points had a CDI rate that was more than 3 standard deviations above the mean, including 11 time points identified using the definition for HCF-onset CDI and 9 time points identified using the definition for 30-day CDI, with discordant results at 4 time points ($\kappa = 0.794$; P < .001).

Conclusions. Tracking cases of both community-onset and HCF-onset, HCF-associated CDI captures significantly more CDI cases, but surveillance of HCF-onset, HCF-associated CDI alone is sufficient to detect an outbreak.

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Clostridium difficile is the most common cause of infectious diarrhea among hospitalized patients, causing significant morbidity, mortality, and increase in healthcare costs.^{1,2} Inpatient stay in a healthcare facility (HCF) is a well-established risk factor for both *C. difficile* colonization and *C. difficile* infection (CDI).^{3,4} Although earlier studies suggest a relatively short incubation period (ie, 3–7 days),^{4,5} patients often develop CDI after discharge from an HCF.⁶⁻⁹ More recent evidence indicates that CDI onset after discharge from an HCF may be increasing.¹⁰ The majority of patients with CDI onset after discharge from an HCF have symptom onset within 4

weeks of discharge,^{6,8} although CDI symptom onset may occur in patients as many as 2–3 months after discharge.^{7,9}

Current surveillance definitions of CDI—which were developed to assess disease trends, detect outbreaks, and facilitate comparison of CDI rates among similar institutions incorporate previous HCF exposure information.¹⁰ However, the decision of individual HCFs to report cases of community-onset, HCF-associated CDI in addition to cases of HCFonset CDI is dependent on their ability to accurately and efficiently collect HCF exposure information, categorize cases, and report rates. Because of the limited infection prevention

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TABLE 1. Definitions of Healthcare Facility (HCF)-Associated Clostridium difficile Infection (CDI) According to Recent HCF Exposure

| Type of CDI | Definition | | |
|---------------|--|--|--|
| HCF-onset CDI | Patient's stool sample tested positive >48 h after admission to study hospital | | |
| 30-day CDI | Patient's stool sample tested positive >48 h after admission to study hospital or tested positive \leq 48 h after admission to study hospital and \leq 30 d after last study hospital discharge, with no other HCF exposure prior to readmission | | |
| 60-day CDI | Patient's stool sample tested positive >48 h after admission to study hospital or tested positive ≤48 h after admission to study hospital and ≤60 d after last study hospital discharge, with no other HCF exposure prior to readmission | | |
| 90-day CDI | Patient's stool sample tested positive >48 h after admission to study hospital or tested positive ≤48 h after admission to study hospital and ≤90 d after last study hospital discharge, with no other HCF exposure prior to readmission | | |

NOTE. Cases of 30-day, 60-day, and 90-day CDI are cases of HCF-onset and community-onset, HCF-associated CDI diagnosed within 30, 60, and 90 days, respectively, after the last discharge from the study hospital.

and control resources, it is important to determine whether tracking cases of community-onset, HCF-associated CDI improves the ability of an HCF to detect an abnormal increase in CDI rates. A recent study that was limited to medical wards at a single institution reported that CDI rates that included cases of community-onset, HCF-associated CDI closely reflect CDI rates that include only cases of HCF-onset CDI.⁷ The purpose of this study was to evaluate the impact of HCF exposure on the incidence and outbreak detection of CDI at 5 geographically diverse hospitals in the United States.

METHODS

Our retrospective multicenter cohort study was conducted by collecting data on all of the adult patients admitted to 5 university-affiliated, acute care medical facilities during the period from July 1, 2000, through June 30, 2006. Eligibility was limited to patients who were 18 years of age or older. All 5 hospitals in our study participated in the Prevention Epicenters Program of the Centers for Disease Control and Prevention and are as follows: Barnes-Jewish Hospital (St. Louis, MO), Brigham and Women's Hospital (Boston, MA), The Ohio State University Medical Center (Columbus, OH), John H. Stroger Jr. Hospital (formerly known as Cook County Hospital; Chicago, IL), and University of Utah Hospital (Salt Lake City, UT). Data on the results of C. difficile toxin assays of stool samples, number of patient-days, and dates of hospital admission, hospital discharge, and assay testing were collected from electronic databases. Toxin assay results from 1 hospital were not available for the period from July 1, 2000, through June 30, 2001. Patients with CDI were defined as any inpatient whose stool sample tested positive for C. difficile by use of toxin assay. Chart review was performed for all patients who had tested positive for C. difficile within 48 hours after admission, to ascertain whether there was any HCF exposure during the 90 days prior to hospital admission. Recurrent cases of CDI-which were defined as a repeated episode of CDI within 8 weeks of a previous episode of CDIwere excluded from the analysis.¹⁰ Cases of community-onset, community-associated CDI-which were defined as the onset of symptoms within 48 hours after hospital admission and no HCF exposure during the previous 90 days—and cases of community-onset, HCF-associated CDI that were not attributed to a study hospital were also excluded.

Cases of CDI were classified as HCF-onset cases or community-onset, HCF-associated cases, according to a modified version of published surveillance definitions.¹⁰ A patient with HCF-onset CDI was defined as a patient whose stool sample tested positive for C. difficile more than 48 hours after hospital admission. A patient with community-onset, HCF-associated CDI was defined as a patient whose stool sample tested positive for C. difficile within 48 hours after hospital admission, provided that the diagnosis of CDI was received within 90 days after the last discharge from the study hospital and that there was no other HCF exposure prior to readmission. To evaluate the usefulness of incorporating recent HCF exposure information into CDI surveillance definitions, 4 definitions of HCF-associated CDI were compared: (1) HCF-onset CDI; (2) HCF-onset and community-onset, HCF-associated CDI diagnosed within 30 days after the last discharge from the study hospital (hereafter referred to as 30-day CDI); (3) HCFonset and community-onset, HCF-associated CDI diagnosed within 60 days after the last discharge from the study hospital (hereafter referred to as 60-day CDI); and (4) HCF-onset and community-onset, HCF-associated CDI diagnosed within 90 days after the last discharge from the study hospital (hereafter referred to as 90-day CDI) (Table 1).

Data Analysis

For all 5 hospitals, monthly CDI rates (ie, cases per 10,000 patient-days) were calculated for each CDI definition. Cases of HCF-onset CDI were attributed to the month of stool collection for the *C. difficile* toxin assay, and cases of community-onset, HCF-associated CDI were attributed to the month of discharge from the HCF before symptom onset. Rates were compared with summary χ^2 tests with Bonferroni correction (a *P* value of less than .01 was considered to be statistically significant). Cross-correlation coefficients (ρ) were calculated to assess the correlation in rate variability



FIGURE 1. Time to onset for cases of community-onset healthcare facility-associated *Clostridium difficile* infection (CDI) after most recent discharge from 5 hospitals, from July 1, 2000, through June 30, 2006.

over time (in months) between CDI definitions. The annual and overall hospital rankings by CDI rates were described. These analyses excluded the last 3 months of the study period, because we did not assess whether patients discharged in the last 3 months of the study period presented to the study hospital with CDI after the study period.

Statistical control charts were constructed for the surveillance definitions of HCF-onset CDI and 30-day CDI, stratified by hospital, to provide a standardized, objective method to compare CDI rates by surveillance definition and to monitor for the occurrence of abnormal increases in CDI rates. Of primary interest was the comparison of the definition of HCF-onset CDI with the definition of 30-day CDI, because insignificant differences in CDI rates were found when we compared the definition of 30-day CDI with the definition of 60-day CDI and when we compared the definition of 60day CDI with the definition of 90-day CDI. This analysis excluded the last month of the study period, because we did not assess whether patients discharged in the last month of the study period presented to the study hospital with *C. difficile* after the study period.

Shewhart u control charts were used, as described by Benneyan11 and Sellick.12 Because of the discrete count data following a Poisson distribution with unequal size of monthly patient-day subgroups, u control charts were the appropriate choice of chart type. The primary indication for an abnormal CDI rate was a value of more than 3 standard deviations (SDs) from the mean.¹¹ In addition, a supplementary set of within-limit criteria, as described by Benneyan,13 was used to identify nonrandom variation, such as trends, cycles, shifts above the mean, and other forms of nonrandom or lowprobability behavior. For each hospital, incidence rates of HCF-onset CDI and 30-day CDI were plotted. Time points with abnormally high rates of CDI were identified by determining whether the monthly rate was more than 3 SDs above the mean rate for the study period and by using the withinlimit criteria; abnormal time points that were defined by the within-limit criteria were labeled at the first time point, to meet the criteria. The κ statistic was calculated to measure the agreement between the number of times an abnormal CDI rate was detected by use of the definitions of HCF-onset CDI and 30-day CDI.

All tests were 2-tailed, and a *P* value of less than .05 was considered to be statistically significant. Statistical analyses were performed by use of SPSS for Windows, version 14.0 (SPSS). Approval for our study was obtained from the human research protection offices of all 5 participating medical centers.

RESULTS

During the 6-year study period, the participating hospitals identified 4,668 cases of HCF-onset CDI and 1,027 cases of community-onset, HCF-associated CDI with the most recent discharge from the study hospital within 90 days. Of the 1,027 cases of community-onset, HCF-associated CDI, 744 (72%) were diagnosed within 30 days after last hospital discharge, 211 (21%) were diagnosed within 31–60 days, and 72 (7%) were diagnosed within 61–90 days (Figure 1).

The incidence rates of CDI that are based on the 4 definitions of HCF-associated CDI are presented in Table 2 and are stratified by hospital. The overall HCF-onset CDI rate was significantly lower than the 30-day CDI rate (8.94 vs 10.36 cases per 10,000 patient-days; P < .001). There were no significant differences between the HCF-onset CDI rate and the 30-day CDI rate at 3 hospitals (ie, hospitals B, C, and D). Overall incidence rates of CDI were not statistically significantly different between 30-day CDI and 60-day CDI (10.36 vs 10.77 cases per 10,000 patient-days; P = .05) or between 60-day CDI and 90-day CDI (10.77 vs 10.90 cases per 10,000 patient-days; P = .50). Overall incidence rates

 TABLE 2. Incidence Rates of *Clostridium difficile* Infection (CDI)

 From July 1, 2000, Through June 30, 2006, Based on 4 Definitions

 of Healthcare Facility (HCF)–Associated CDI

| | Rate of CDI, cases per 10,000 patient-days | | | | |
|-------------------------|--|---------------|---------------|---------------|--|
| HCF | HCF-onset CDI | 30-day CDI | 60-day CDI | 90-day CDI | |
| Hospital A ^a | 15.60 | 18.26 | 18.93 | 19.17 | |
| Hospital B | 15.81 | 17.81 | 18.59 | 18.82 | |
| Hospital C | 3.94 | 4.49 | 4.69 | 4.75 | |
| Hospital D ^b | 6.23 | 7.05 | 7.27 | 7.33 | |
| Hospital E ^a | 4.49 | 5.39 | 5.62 | 5.72 | |
| Overall ^{a,c} | 8.94 | 10.36 | 10.77 | 10.90 | |

NOTE. Cases of 30-day, 60-day, and 90-day CDI are cases of HCF-onset and community-onset, HCF-associated CDI diagnosed within 30, 60, and 90 days, respectively, after the last discharge from the study hospital.

^a The rate of HCF-onset CDI was significantly lower than that of 30-day CDI (P < .01).

^b The study period was restricted to September 2001–March 2006.

^c The overall rate of 30-day CDI was significantly lower than that of 90-day CDI (P < 0.01).



FIGURE 2. Rates of *Clostridium difficile* infection (CDI) according to 2 surveillance definitions at hospitals A (*top*) and B (*bottom*). Solid black circles, abnormally high incidence of healthcare facility (HCF)–onset CDI (which was determined by a monthly rate that was more than 3 standard deviations [SDs] above the mean); open circles, abnormally high incidence of HCF-onset CDI (which was determined on the basis of within-limit criteria); solid black triangles, abnormally high incidence of HCF-onset and community-onset, HCF-associated CDI diagnosed within 30 days after the last discharge from the study hospital (30-day CDI; which was determined by a monthly rate was more than 3 SDs above the mean); open triangles, abnormally high incidence of 30-day CDI (which was determined on the basis of within-limit criteria).

were significantly lower for 30-day CDI than for 90-day CDI (10.36 vs 10.90 cases per 10,000 patient-days; P < .01) but not at any of the individual hospitals.

The rank order of hospitals by CDI rates remained constant across all definitions within each study year. In addition, the hospital rankings for the entire study period remained constant across the different definitions: hospital B maintained the highest rate, followed by hospitals A, D, E, and C (Table 2). The correlations between each hospital's monthly rates of HCF-onset CDI and 30-day CDI were almost perfect (ρ range, 0.94–0.99; P < .001). There were similar correlations between the rate of 30-day CDI and the rate of 60-day CDI (ρ range, 0.98–1.00; $P \leq .001$) and between the rate of 60-day CDI and the rate of 60-day CDI and the rate of 90-day CDI ($\rho = 1.00$ for all; P < .05).

Figures 2 and 3 present the incidence rates and the abnormal time points for the HCF-onset CDI and 30-day CDI



FIGURE 3. Rates of *Clostridium difficile* infection (CDI) according to 2 surveillance definitions at hospitals C (*top*), D (*middle*), and E (*bottom*). Solid black circles, abnormally high incidence of healthcare facility (HCF)–onset CDI (which was determined by a monthly rate that was more than 3 standard deviations [SDs] above the mean); open circles, abnormally high incidence of HCF-onset CDI (which was determined on the basis of within-limit criteria); solid black triangles, abnormally high incidence of HCF-onset and community-onset, HCF-associated CDI diagnosed within 30 days after the last discharge from the study hospital (30-day CDI; which was determined by a monthly rate was more than 3 SDs above the mean); open triangles, abnormally high incidence of 30-day CDI (which was determined on the basis of within-limit criteria)

definitions, stratified by hospital. During the study period, 4 (80%) of the 5 hospitals detected at least 1 time point at which the monthly CDI rate was more than 3 SDs above the center line (Table 3), with a range of 1-7 abnormal time points per hospital. Overall, 12 time points were identified as having a monthly CDI rate that was more than 3 SDs above the center line, including 11 time points identified using the definition for HCF-onset CDI and 9 time points identified using the definition for 30-day CDI, with discordant results at 4 time points ($\kappa = 0.794$; P < .001). There was perfect agreement between the HCF-onset CDI rate and the 30-day CDI rate at 2 hospitals (ie, hospitals A and D), with a total of 3 time points at which the monthly CDI rate was more than 3 SDs above the center line. There was almost perfect agreement at 3 hospitals (ie, hospitals B, C, and E). At hospital B, there were 7 months during which the monthly CDI rates were more than 3 SDs above the center line: for 5 months, the rates were identified by use of both the definition for HCF-onset CDI and the definition for 30-day CDI, and for 2 months, the rates were identified by use of the definition for HCF-onset CDI only. At hospital C, there was 1 month during which the HCF-onset CDI rate was more than 3 SDs above the center line, but no abnormally high monthly CDI rates were identified using the definition for 30-day CDI. At hospital E, there was 1 month during which the 30-day CDI rate was more than 3 SDs above the center line, but no abnormally high monthly CDI rates were identified using the definition for HCF-onset CDI. In addition to the 11 time points identified as having HCF-onset CDI rates that were more than 3 SDs above the center line, the more conservative supplementary within-limit criteria identified 5 more months with abnormally high HCF-onset CDI rates (1 month each at hospitals A, B, and C and 2 months at hospital E). Similarly, the more conservative supplementary withinlimit criteria identified 8 more months with abnormally high 30-day CDI rates (1 month at hospitals A and C, 2 months at hospital E, and 4 months at hospital B) in addition to the 9 time points identified as having 30-day CDI rates that were more than 3 SDs above the center line. When combining the results of abnormally high CDI rates that were detected either on the basis of whether the monthly rate was more than 3 SDs above the center line of the within-limit criteria, the overall κ statistic decreased to 0.669 (P < .001) (Table 3).

DISCUSSION

To our knowledge, this is the first multicenter study to compare standardized CDI surveillance definitions across institutions to determine the influence that these different definitions have on perceived CDI incidence and on the detection of abnormal increases in CDI rates. The results of our investigation suggest that tracking cases of both communityonset and HCF-onset, HCF-associated CDI captures significantly more cases of CDI but does not improve the ability of HCFs to detect abnormally high rates of CDI. Compared with the surveillance of only cases of HCF-onset CDI, the expanded surveillance definitions that also track cases of community-onset, HCF-associated CDI had excellent correlation over time and almost perfect agreement for detection of abnormally high CDI rates. The rank order of hospitals by CDI rates did not vary by surveillance definition; instead, the hospital rankings remained constant within each study year as well as during the 6-year study period. From a public health perspective, the primary purposes of CDI surveillance are to guide the implementation of interventions to control CDI in HCFs and to monitor the impact of such interventions. Therefore, it is critical that surveillance definitions have the

TABLE 3. Comparison of Abnormal Monthly Rates Identified by Use of 2 Surveillance Definitions of Healthcare Facility (HCF)–Associated *Clostridium difficile* Infection (CDI) at 5 HCFs, July 1, 2000–June 30, 2006

| 2000 | | | | | | | | | | | |
|------------|---|------------|-----------------------------|---|------------|------------------|--|--|--|--|--|
| | No. of months with monthly rate >3 SDs above the center line | | | No. of months with monthly rate >3 SDs above the center line and the within-limit criteria ^a | | | | | | | |
| HCF | HCF-onset CDI | 30-day CDI | ĸ | HCF-onset CDI | 30-day CDI | $\kappa^{\rm b}$ | | | | | |
| Hospital A | 3 | 3 | 1.00 | 4 | 4 | 0.735 | | | | | |
| Hospital B | 7 | 5 | 0.818 | 8 | 9 | 0.666 | | | | | |
| Hospital C | 1 | 0 | Not calculated ^c | 2 | 2 | 1.00 | | | | | |
| Hospital D | 0 | 0 | 1.00 | 0 | 0 | 1.00 | | | | | |
| Hospital E | 0 | 1 | Not calculated ^c | 3 | 3 | 0.304 | | | | | |
| Total | 11 | 9 | 0.794 | 17 | 18 | 0.669 | | | | | |
| | | | | | | | | | | | |

NOTE. Cases of 30-day CDI are cases of HCF-onset and community-onset, HCF-associated CDI diagnosed within 30 days after the last discharge from the study hospital.

^a Supplementary within-limit criteria were considered in the absence of time points with abnormal rates during which the monthly CDI rate was >3 standard deviations (SDs) above the center line.

^b $P \leq .01$ for all comparisons.

^c The κ statistic was not calculated because the values for either the HCF-onset CDI or 30-day CDI surveillance definition were constant.

ability to accurately identify outbreaks. Our findings provide evidence that surveillance of HCF-onset, HCF-associated CDI alone is sufficient to detect an outbreak.

We found excellent correlation of rates over time between the HCF-onset and the community-onset, HCF-associated surveillance definitions, which reflects the high proportion of CDI cases captured by the HCF-onset definition. In our study, of the 5,695 cases of HCF-associated CDI, 4,668 (82%) were cases of HCF-onset CDI. This proportion is consistent with that from a study by Kutty et al.,8 who reported that 77% of the cases of HCF-associated CDI that occurred within 90 days after hospital discharge were cases of HCF-onset CDI. Although uncertainty exists regarding the typical incubation period from exposure to infection,^{4,5} the high proportion of cases with HCF-onset CDI is not surprising, because inpatient stay at an HCF is a major risk factor for the development of C. difficile colonization or infection. Biological explanations for the increased risk of CDI at an HCF include exposure to concurrently admitted patients with CDI, antimicrobial use, and the advanced age and severity of illness in patients at HCFs.^{3,4,14}

Current surveillance definitions classify cases of community-onset, HCF-associated CDI on the basis of the timing of recent HCF exposures. Published studies report that the majority of patients who experience symptoms of CDI later do so within 4 weeks after discharge from an HCF,⁶⁻⁸ although there are some patients who experience symptoms as many as 2-3 months after discharge.^{7,9} For instance, Kutty et al.⁸ identified 70% of the cases of community-onset, HCF-associated CDI within the first 30 days after hospital discharge, and Chang et al.⁶ identified 85% of the cases of communityonset, HCF-associated CDI within the first 30 days after hospital discharge. Unlike our study, which focused exclusively on hospital-based surveillance, these studies employed surveillance strategies that captured cases managed in outpatient settings. Because the availability of toxin assay results for outpatients varies across HCFs, we focused exclusively on hospital-based surveillance to increase the generalizability of our findings. Despite different surveillance approaches, our study identified 744 (72%) of the 1,027 cases of communityonset, HCF-associated CDI within the first 30 days after hospital discharge, an estimate that falls between the Kutty et al.⁸ and Chang et al.⁶ estimates.

A unique strength of this study was the use of statistical control charts to evaluate the influence of surveillance of community-onset, HCF-associated CDI on outbreak detection. Use of the definitions for 60-day and 90-day CDI did not result in significantly higher CDI rates at any of the hospitals, compared with use of the definition for 30-day CDI. In fact, the CDI rates that were reported using the definitions for 60-day and 90-day CDI were approximately 100% concordant with the CDI rates that were reported using the definition for 30-day CDI; therefore, we focused the control chart analysis on the definitions for HCF-onset CDI and 30-day CDI. Despite the significantly higher 30-day CDI rates than

HCF-onset CDI rates at 2 of the 5 hospitals, use of the HCFonset CDI and 30-day CDI definitions resulted in the detection of similar totals of abnormally high time points using the more than 3 SDs criteria with the addition of the more conservative within-limit criteria. The κ values for HCF-onset CDI and 30-day CDI surveillance indicate substantial concordance between the 2 definitions to identify abnormally high CDI rates. Many of the discordant time points determined by 1 definition were different by only 1 month, compared with the time points determined by the other definition. The κ value improved to 0.899 when the months with abnormally high HCF-onset CDI rates (which were determined either on the basis of whether the monthly rate was more than 3 SDs above the center line or on the basis of the withinlimit criteria) that occurred within 1 month of abnormally high 30-day CDI rates, and vice versa, were considered to be concordant. From a clinical perspective, the almost-perfect κ value calculated in the latter analysis provides evidence that the simpler HCF-onset CDI surveillance definition accurately identifies increases from endemic to epidemic CDI rates.

Statistical control charts provide a standardized, objective method to monitor CDI rates but do not preclude the need for visual inspection of CDI rates by infection prevention and control practitioners. Despite the gradual increase in CDI incidence during the study period at hospital E, an abnormal time point based on a monthly rate that was more than 3 SDs above the center line was not identified until April 2006. Other limitations of our study include a lack of generalizability to smaller, community hospitals. Because the academic medical centers included in our study were large, there was less variability in the rates of CDI, compared with the rates in hospitals with lower patient-day totals and fewer cases of CDI. This may explain the consistency in the rank order of hospitals by annual CDI rates across our surveillance definitions as well as the excellent correlation between surveillance definitions. In addition, the definitions of patient-days varied slightly across study hospitals. However, the expected impact on the results is minimal, because all comparisons were intrahospital and used the same patient-day total for the CDI rate denominator.

Although surveillance of HCF-onset, HCF-associated CDI is currently considered to be the minimum surveillance required in healthcare settings,¹⁰ there is rationale for additional tracking of cases of community-onset, HCF-associated CDI. Currently, the transmission source for community-onset, HCF-associated CDI is poorly understood. Past studies indicate that patients with prior HCF exposures are more likely to be colonized with *C. difficile* than are patients without prior HCF exposures, which suggests acquisition from an HCF.^{4,5} However, patients with community-onset, HCF-associated CDI frequently present to the hospital with symptoms of CDI more than 7 days after hospital discharge, which is beyond the understood incubation period for CDI.^{4,5} Furthermore, the strains of *C. difficile* present at hospital readmission may differ from the strains present at hospital discharge.⁵ The potential for acquisition of CDI after hospital discharge has implications for HCFs, because this type of acquisition may introduce new strains into the healthcare setting and may be a source of CDI transmission, contributing to rates of HCF-onset CDI.⁵ In addition, studies indicate that the risk factors for community-onset, community-associated CDI may differ from the risk factors for HCF-onset CDI.^{15,16} It is also possible that the risk factors for community-onset, HCF-associated CDI may differ from the risk factors for the trisk factors for HCF-onset CDI.⁷ Therefore, HCFs may need to tailor CDI prevention efforts to target the more prevalent types of CDI in their institution. Future studies are needed to provide insight into recent increases in the incidence of both HCF-onset and community-onset CDI, as well as to identify the transmission source and risk factors for community-onset CDI.

To our knowledge, this is the first study to compare different standardized CDI surveillance definitions across institutions to determine whether the definitions impact the perceived burden of CDI or alter the ability to detect a CDI outbreak. Our findings suggest that 30 days after hospital discharge is a reasonable time frame for surveillance of CDI to detect cases associated with an HCF, but that HCFs have the ability to accurately detect abnormal increases in CDI rates with a more simplistic HCF-onset, HCF-associated case definition. Given limited infection control resources, these findings could have important implications for surveillance methods in HCFs.

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REFERENCES

- Johnson S, Gerding DN. Clostridium difficile–associated diarrhea. Clin Infect Dis 1998; 26:1027–1034.
- Dubberke ER, Reske KA, Olsen MA, McDonald LC, Fraser VJ. Shortand long-term attributable costs of *Clostridium difficile*–associated disease in nonsurgical inpatients. *Clin Infect Dis* 2008; 46:497–504.
- Dubberke ER, Reske KA, Olsen MA, et al. Evaluation of *Clostridium difficile*-associated disease pressure as a risk factor for *C difficile*-associated disease. *Arch Intern Med* 2007; 167:1092–1097.
- McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of *Clostridium difficile* infection. N Engl J Med 1989; 320:204–210.
- Clabots CR, Johnson S, Olson MM, Peterson LR, Gerding DN. Acquisition of *Clostridium difficile* by hospitalized patients: evidence for colonized new admissions as a source of infection. J Infect Dis 1992; 166:561–567.
- Chang HT, Krezolek D, Johnson S, Parada JP, Evans CT, Gerding DN. Onset of symptoms and time to diagnosis of *Clostridium difficile*-associated disease following discharge from an acute care hospital. *Infect Control Hosp Epidemiol* 2007; 28:926–931.
- Dubberke ER, McMullen KM, Mayfield JL, et al. Hospital-associated *Clostridium difficile* infection: is it necessary to track community-onset disease? *Infect Control Hosp Epidemiol* 2009; 30:332–337.
- Kutty PK, Benoit SR, Woods CW, et al. Assessment of *Clostridium difficile*–associated disease surveillance definitions, North Carolina, 2005. *Infect Control Hosp Epidemiol* 2008; 29:197–202.
- Palmore TN, Sohn S, Malak SF, Eagan J, Sepkowitz KA. Risk factors for acquisition of *Clostridium difficile*–associated diarrhea among outpatients at a cancer hospital. *Infect Control Hosp Epidemiol* 2005; 26:680–684.
- McDonald LC, Coignard B, Dubberke E, Song X, Horan T, Kutty PK. Recommendations for surveillance of *Clostridium difficile*–associated disease. *Infect Control Hosp Epidemiol* 2007; 28:140–145.
- Benneyan JC. Statistical quality control methods in infection control and hospital epidemiology, part I: introduction and basic theory. *Infect Control Hosp Epidemiol* 1998; 19:194–214.
- 12. Sellick JA Jr. The use of statistical process control charts in hospital epidemiology. *Infect Control Hosp Epidemiol* 1993; 14:649–656.
- Benneyan JC. Statistical quality control methods in infection control and hospital epidemiology, part II: chart use, statistical properties, and research issues. *Infect Control Hosp Epidemiol* 1998; 19:265–283.
- Dubberke ER, Reske KA, Yan Y, Olsen MA, McDonald LC, Fraser VJ. *Clostridium difficile*-associated disease in a setting of endemicity: iden-tification of novel risk factors. *Clin Infect Dis* 2007; 45:1543–1549.
- Centers for Disease Control and Prevention (CDC). Severe Clostridium difficile-associated disease in populations previously at low risk—four states, 2005. MMWR Morb Mortal Wkly Rep 2005; 54:1201–1205.
- Centers for Disease Control and Prevention (CDC). Surveillance for community-associated Clostridium difficile—Connecticut, 2006. MMWR Morb Mortal Wkly Rep 2008; 57:340–343.