The Importance of Considering Different Healthcare Settings When Estimating the Burden of *Clostridium difficile*

Jennifer L. Kuntz¹ and Philip M. Polgreen²

¹Kaiser Permanente Northwest Center for Health Research, Portland, Oregon; and ²University of Iowa, Iowa City

**Background.** Traditional surveillance methods may underestimate the true burden of *Clostridium difficile* infection (CDI) because they fail to capture cases brought to medical attention in outpatient settings or diagnosed during non–face-to-face patient–provider interactions.

**Methods.** We identified CDIs diagnosed among Kaiser Permanente Northwest patients between 1 June 2005 and 30 December 2012. We categorized infections by whether they were diagnosed during an inpatient or outpatient encounter and whether they were diagnosed during a face-to-face (eg, hospitalization, outpatient visit) or non–face-to-face encounter (eg, phone, e-mail). We constructed a baseline surveillance estimate that included CDIs identified during hospitalization, representing burden captured through traditional surveillance approaches. We then constructed 2 additional estimates: 1 that included CDIs identified during outpatient face-to-face encounters and 1 that also included CDIs identified during non–face-to-face encounters.

**Results.** We identified 8024 CDIs. Twenty-four percent occurred during a hospitalization, while the remaining CDIs were recognized in the outpatient setting. Surveillance focused on hospitalized patients would have captured less than one-quarter of total burden. The addition of cases identified during outpatient face-to-face encounters would account for 80% of CDIs. An additional 1702 CDIs would not be captured without inclusion of non–face-to-face encounters; thus, surveillance approaches that do not include telephone or e-mail encounters would miss 21% of CDIs.

**Conclusions.** Surveillance approaches that do not include outpatient or nontraditional encounters miss a substantial proportion of CDIs. Failure to capture these cases leads to underestimation of disease burden and difficulty in measuring interventions to control CDI.

**Keywords.** *Clostridium difficile*, surveillance, incidence.

*Clostridium difficile* infection (CDI) is a major cause of morbidity and mortality [1]. Over the past decade, the incidence and severity of CDI have increased dramatically [2]. Historically, CDI was considered primarily a hospital-associated infection; however, in recent years, the frequency of community-associated CDI has been increasing [3–7].

Available estimates of CDI burden typically rely on the *International Classification of Diseases, 9th revision* (ICD-9) code or microbiological test data generated during hospitalizations [8]. However, substantial proportions of patients acquire CDI during a hospitalization and develop clinical disease after hospital discharge [9]. Thus, current hospital-based surveillance approaches likely miss these healthcare-associated CDIs, unless patients are readmitted to have their infections treated. Underestimation may be especially common in healthcare settings where inpatient and outpatient health records are not fully integrated. Furthermore, surveillance systems are especially prone to underestimation in cases where patients receive care from multiple healthcare systems or in multiple geographic locations.
Most current surveillance efforts only account for cases identified via traditional face-to-face meetings between patients and healthcare providers. However, patients and healthcare providers increasingly communicate via telephone, e-mail, and other forms of electronic communication (e.g., Internet-based patient portals) [10–14]. Access to information about these nontraditional encounters is needed in order to identify and track cases diagnosed and/or empirically treated without face-to-face contact with a clinician.

Here, our goal was to determine the potential degree to which the burden of CDI is underestimated. We specifically examined cases brought to medical attention in outpatient settings or diagnosed and managed during non–face-to-face patient–provider interactions, which most traditional surveillance approaches fail to capture.

**METHODS**

We identified CDI cases among Kaiser Permanente Northwest (KPNW) patients between 1 June 2005 and 30 December 2012. All care at KPNW, including but not limited to healthcare encounters, pharmacy orders and dispensings, and laboratory services, is captured through an electronic medical record (EMR). Information about healthcare received outside of the KP system is obtained from submitted claims. Electronic databases capture all aspects of patient care provided or underwritten by KPNW from both inpatient and outpatient settings. In the outpatient setting, KPNW keeps complete information regarding whether a patient’s healthcare encounter occurred face-to-face with a provider, through a telephone conversation, or through electronic communications such as e-mail or secure messaging through a patient web portal.

We identified CDIs in the inpatient setting using ICD-9 code 008.45 (“Intestinal infection due to C. difficile”). In the outpatient setting, we identified CDIs through ICD-9 code 008.45 or a positive C. difficile test with metronidazole or vancomycin dispensed in the 7 days before or after a positive test. *Clostridium difficile* testing was conducted at a centralized laboratory for patients receiving care at a KPNW-owned facility using a 2-stage testing method. We used the C.Diff Quik Chek Complete assay to test for the presence of glutamate dehydrogenase and C. difficile toxins A and B. For discordant results, a rapid polymerase chain reaction assay was performed. Testing could occur outside the system for patients receiving care in non–KPNW facilities. Different identification criteria were used for the inpatient and outpatient settings due to incomplete medication use or *C. difficile* testing data among hospitalized patients. We based infection dates on the first indication of CDI.

We included both incident and recurrent CDIs and based our definitions on recommended surveillance definitions [15]. We defined an incident of CDI as a new infection with no indication of CDI (i.e., ICD-9 code, positive toxin test) in the previous 56 days. Recurrent CDI was a diagnosis of infection 15–56 days after a prior CDI diagnosis. If a CDI diagnosis was present 1–14 days after a previous incident or recurrent CDI, we counted it as an ongoing infection (i.e., the same infection).

We categorized infection by the type of encounter during which the first indication for CDI occurred. Encounter types included inpatient, ambulatory care, emergency department (ED), telephone, e-mail, and “other encounters.” Other encounters originated in home health, skilled nursing, and long-term care settings. We also included laboratory toxin testing alone with evidence of treatment in the other encounters group because we were unable to fully describe where these laboratory orders originated from and, thus, where the infections were occurring. We further categorized CDIs by inpatient or outpatient diagnosis. Inpatient encounters occurred during a hospitalization. ED visits were coded as outpatient encounters, unless the patient was admitted to the hospital on the same day. Ambulatory care, telephone, e-mail, and other encounters occurred in the outpatient setting.

We further classified CDIs by whether they were identified during a face-to-face or a non–face-to-face encounter. Hospitalizations, ED visits, ambulatory care visits, home health visits, and other encounters were categorized as face-to-face encounters. Non–face-to-face encounters included telephone and e-mail encounters. Note that we only included telephone and e-mail encounters that occurred between a provider and the patient, thus eliminating communications for non-patient care reasons such as scheduling or cancelling an appointment.

Based on our data, we constructed a baseline surveillance estimate that included only CDIs identified during hospitalization. This estimate represented the percentage of CDI cases that were captured through traditional, hospital-based surveillance approaches. Our second estimate expanded on the first by adding CDIs identified during outpatient face-to-face encounters, including ED, ambulatory care, and other encounters. This estimate represented the proportion of CDI cases that would be identified through surveillance approaches that are accounted for in both inpatient and outpatient settings. Our third estimate further included CDIs identified during non–face-to-face encounters. Thus, the final estimate represented CDIs that were identified throughout the KPNW population (Figure 1).

Next, we determined how cases would be defined according to the Centers for Disease Control and Prevention’s (CDC’s) recommended surveillance definitions. We categorized the CDIs as hospital acquired (also referred to as healthcare associated), community onset, healthcare associated, community associated, or indeterminate [15]. Hospital-acquired CDI was defined as an infection identified in the inpatient setting. Community-onset, healthcare-associated CDI was identified in the outpatient setting among patients with a history of hospital...
discharge in the prior 4 weeks. Community-associated CDI was identified in the outpatient setting among patients with no history of being discharged from a hospital in the previous 12 weeks. Finally, indeterminate CDI was identified in the outpatient setting among patients with a history of being discharged from a hospital 4–12 weeks prior to identification.

RESULTS

We identified 8024 CDIs. Among the cases identified, 74.7% (5990 of 8024) were incident infections. This represented an overall incidence of 15.9 CDIs per 10 000 patient-years of observation; 4491 patients experienced the 8024 CDIs that we identified. Twenty-four percent of all CDIs (1944 of 8024) occurred during a hospitalization, while 6080 (76%) were recognized in the outpatient setting. Seventy-two percent of incident CDIs and 89% of recurrent infections were identified in the outpatient setting (Table 1). The proportion of inpatient vs outpatient CDI was stable during the course of the study. Each year, between 69% and 74% of CDIs were identified in the outpatient setting.

Seventy-nine percent of CDIs (6322 of 8024) were identified during face-to-face healthcare encounters, including hospitalizations, ED visits, ambulatory care visits, or other healthcare encounters. An additional 1702 CDIs (21% of the total) were identified during non–face-to-face telephone or Internet-mediated encounters. One-fifth (21%) of incident CDIs and 22% of recurrent CDIs were diagnosed through a non–face-to-face healthcare encounter (Table 1).

Based on our data, surveillance methods that focus on hospitalized patients would capture 1727 incident and 217 recurrent CDIs, representing only 24% of the entire CDI burden within our population. The addition of CDIs identified during ED visits, ambulatory care visits, and other healthcare encounters (ie, from all face-to-face encounters) would account for 79% of CDIs (6322 of 8024). Finally, an additional 1702 CDIs would not be accounted for without the inclusion of non–face-to-face encounters. Thus, surveillance approaches that do not include telephone or electronic communication encounters would miss 21% of CDIs in the KPNW healthcare system (Figure 1).

When we applied CDC surveillance definitions, 1944 of 8024 (23.9%) CDIs were hospital acquired (ie, developed and identified during inpatient encounters); the second approach includes CDIs identified in face-to-face inpatient and outpatient encounters including hospitalization, emergency department visits, ambulatory care visits, and other care encounters. The third approach includes CDIs identified during inpatient and outpatient face-to-face encounters and non–face-to-face encounters (eg, phone, Internet).

Table 1. Incident and Recurrent *Clostridium difficile* Infection by Encounter Type, Whether the Encounter was Face-to-Face or Non–Face-to-Face, and Healthcare Setting

<table>
<thead>
<tr>
<th>Inpatient Setting N = 1944</th>
<th>Outpatient Setting N = 6080</th>
<th>Non-Face-to-Face Encounter N = 1702</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face-to-Face Encounter N = 6322</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization (N=1944)</td>
<td>Emergency Department (N=252)</td>
<td>Ambulatory Care Visit (N=1520)</td>
</tr>
<tr>
<td>Incident CDI N = 5990</td>
<td>1727 (88.8)</td>
<td>199 (78.9)</td>
</tr>
<tr>
<td>Recurrent CDI N = 2034</td>
<td>217 (11.2)</td>
<td>53 (21.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: CDI, *Clostridium difficile* infection.
in the previous 12 weeks). Indeterminate CDIs, that is, infections among patients with a hospitalization in the previous 4–12 weeks, accounted for 971 CDIs (11.6%).

We found that only 29% of all incident infections were hospital acquired (ie, developed and diagnosed during hospitalization); CDIs diagnosed in the outpatient setting without recent hospitalization accounted for the largest percentage of incident cases (42.5%; 2546 of 5990). Recurrent CDIs were commonly diagnosed in the outpatient setting. Thirty-four percent of all recurrent infections were community associated, and an additional 38% were identified in the community setting in the 4 weeks after a hospitalization (ie, were community onset, healthcare associated).

DISCUSSION

Our results show that traditional surveillance methods may dramatically underestimate the true burden of CDI in the United States. We found that surveillance of only hospitalized patients would capture <25% of the CDI burden among KPNW patients. The addition of cases from the ED and ambulatory care settings would only account for roughly 80% of all CDIs. By using an integrated EMR system that captures outpatient and non–face-to-face encounters, we were able to estimate the burden of CDI missed by more traditional investigations and surveillance systems.

The US incidence and recurrence of CDI has dramatically increased over the past 15 years [16–18]. In fact, as of 2010, the CDC estimates that 250 000 people require hospital care and 14 000 people die as a result of CDI each year, leading the CDC to categorize CDI as an urgent threat [19]. This particular estimate is based on the CDC Emerging Infections Program’s (EIP’s) CDI active surveillance system [20]. EIP captures all positive C. difficile toxin or molecular assay reports from laboratories within a defined catchment area (eg, counties). All CDIs are investigated using a case report form that includes demographic, clinical, and risk factor information. These data provide greater insight into population-level CDI incidence compared with hospital discharge data alone. However, it is difficult to assess the completeness of case ascertainment and longitudinal follow-up for patients who cross healthcare institutional and geographic boundaries.

Additional national CDI estimates on which public health policies are based are obtained from hospital discharge data such as the National Hospital Discharge Survey [17] or the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS) [2, 21–23]. These systems capture national probability samples of patient discharge records, to which ICD-9 diagnosis codes are applied in order to estimate CDI prevalence. In general, these approaches cannot be used to follow patients in the outpatient setting. Based on our results, it is clear that more CDI cases occur than can be captured from hospitalization data alone. In fact, we found that the majority (76%) of cases occurred in the outpatient setting or during non–face-to-face encounters.

Our data support observations of a shift in CDI burden to the community setting [7, 24–26]. We found that 40% of CDIs were not preceded by a healthcare stay and, thus, were community associated. This proportion of cases is slightly higher than previous estimates where 20%–28% of CDIs were found to be community associated [27, 28]. This variation may be explained by differences in the population studied, timing of the investigation, or case ascertainment methods. Our higher rate may also, in part, be explained by our ability to capture cases that other investigations could not account for.

This shift of CDI to ambulatory care populations has implications not only for surveillance efforts but also for infection control and patient care. From an infection control standpoint, the development of CDI in the home setting rather than in a busy inpatient ward may actually be “safer” for other patients who have not yet acquired CDI. However, infection control professionals and healthcare administrators may speculate that infection rates are improving when cases are merely being shifted to the outpatient setting. Thus, as hospitals work toward lowering CDI rates, perhaps surveillance systems should attempt to track post-discharge CDI cases. This is likely an important issue, in general, because shorter lengths of stay may make it more difficult to measure the true burden of other healthcare-associated infections, in addition to CDI that occur during inpatient hospital stays. The inability of infection control and surveillance efforts to identify CDI in the outpatient setting also reduces the potential to more fully understand the transmission of this pathogen across healthcare and home settings. Without accurate estimates of CDI cases, the effectiveness of infection control measures may be reduced.

In regard to patient care, the first opportunity to diagnose and treat a CDI case is increasingly occurring in the outpatient care setting. As such, the results of our study can be used to increase clinician awareness of C. difficile as a cause of diarrhea and inform efforts to improve timely recognition and treatment of infection among outpatients, thus, potentially preventing prolonged illness, adverse outcomes, and need for additional healthcare.

Interaction between patients and healthcare providers continues to change. For example, more patients are interacting with their healthcare providers electronically [10–14]. Unless these encounters are captured consistently in patient medical records and by surveillance systems, a substantial proportion of CDI cases may be missed. Changing communication patterns have certainly affected other surveillance efforts. For example, the shift away from fixed phone lines to cell phones has negatively impacted the ability to generate random samples for population-
Based investigations [29]. Surveillance efforts must identify methods to account for these new means of communication and interaction between patients and healthcare providers. The emergence of EMRs will facilitate complete documentation of patient and healthcare interactions, thus allowing for generalization of the results presented here. However, it may remain difficult to track CDIs among patients who seek care in multiple healthcare settings and in multiple geographic regions, as they may acquire CDI in one setting (eg, a tertiary care center) but have that infection recognized in another setting (eg, remote ambulatory clinic). Our results provide motivation for integration of EMRs across healthcare settings and systems. Without such integration it will be difficult to not only estimate disease burden but also to attribute some CDIs to their source.

While cost estimates for individual cases of CDI vary greatly, the underestimation inherent in CDI burden estimates has substantial implications for national cost estimation. In a recent metaanalysis, an annual incidence of 133,657 CDIs and costs of $11,285 (95% confidence interval [CI], $9118–$13,574) per case leading to a total annual cost of $1.5 billion (95% CI, $1.2–$1.8 billion) were estimated. This accounts for 15% of US annual costs for the 5 most common healthcare-associated infections [30]. Variations in cost estimation depend on the methods used and the population captured; however, our estimates suggest a sizable burden omitted from traditional surveillance methods and, as a result, a financial impact that may be greater than widely thought. While we acknowledge that the most expensive component of a CDI case is likely increased lengths of stay for inpatients with CDI, the large number of cases that occur in the outpatient setting also contributes to healthcare costs. In addition, outpatient CDI is undoubtedly expensive in terms of the opportunity cost of lost wages and productivity, as well as personal suffering and emotional distress [31,32].

Our study has several limitations. First, our findings may not be completely generalizable to other healthcare settings. KPNW patients likely have more access to their clinicians through nontraditional means such as telephone and e-mail, and when compared with patients with similar access to these resources, may use a nontraditional approach more frequently. Nevertheless, electronic communication, which is currently available at KPNW, will likely emerge in other settings in the near future. In addition, we considered that KPNW patients may be admitted for shorter periods of time than patients in other healthcare systems, thus increasing the proportion of infections recognized in the outpatient setting. However, the mean length of stay for KPNW hospitalizations in 2013 was 4.6 days; this is comparable to the average duration of hospitalizations in 2011 Healthcare Cost and Utilization Project NIS data [33].

In addition, we were not able to capture encounters that occurred outside of care provided or underwritten by the KPNW system, thus leading to potential underestimation of CDI burden. However, there is a strong financial incentive for patients to use the KPNW healthcare system, thus minimizing this limitation. Furthermore, we did not require a run-in period for this study, as we sought to imitate a surveillance effort and capture all CDIs over the time period. The classification of CDI as incident or recurrent may be inaccurate if a patient had a CDI in a non-KPNW setting prior to membership; however, 95% of cases had at least 6 months of membership prior to their infection during which we did not identify a CDI. In addition, we could not clearly delineate the origin of CDIs that were identified through toxin testing and treatment alone and of those that occurred during long-term or skilled nursing facility encounters. Thus, rather than include these as separate categories of encounters, we used the generic label of “other encounters.”

Finally, we may have missed encounters in which CDI was identified but for which an ICD-9 code was not documented, although the majority of these cases would be captured through positive toxin tests and prescribed treatment. In turn, our requirement that positive toxin tests be accompanied by dispensing of treatment may have led to the exclusion of true CDI cases. However, the majority of KPNW members (more than 90%) have a pharmacy benefit. Also, we found that only 4% of positive C. difficile tests were not accompanied by treatment or an ICD-9 diagnosis within 1 week.

**CONCLUSION**

Our research shows that traditional hospital-centric surveillance approaches likely lead to underestimation of the true burden of CDI. Future hospital- and ambulatory-based surveillance systems that seek to estimate CDI incidence and recurrence should attempt to capture CDI episodes that are not associated with face-to-face interactions and may need to incorporate more syndrome-based approaches [34]. Finally, failure to capture cases that occur outside the hospital setting will not only lead to underestimates of population disease burden but will also make it difficult to measure the impact of interventions to control CDI.

**Notes**

**Financial support.** This work was supported by the Kaiser Permanente Center for Effectiveness & Safety Research (CESR). CESR facilitates interregional research conducted by the research programs in each of the 7 regional entities (Colorado, Georgia, Hawaii, Mid-Atlantic States [Virginia, Maryland, District of Columbia], Northern California, Northwest [Oregon, Washington], and Southern California) that comprise the Kaiser Permanente integrated healthcare organization.

**Potential conflict of interest.** Both authors: No potential conflicts of interest.

Both 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.
References


32. Madeo M, Boyack M. Using the lived experiences of patients with *Clostridium difficile* infection to improve care. Nurs Times 2014; 106:10–3.
