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ORIGINAL ARTICLE

Frequent Hospital Readmissions for *Clostridium difficile* Infection and the Impact on Estimates of Hospital-Associated *C. difficile* Burden

Courtney R. Murphy, MS;¹ Taliser R. Avery, MSc;² Erik R. Dubberke, MD, MSPH;³ Susan S. Huang, MD, MPH¹

OBJECTIVE. *Clostridium difficile* infection (CDI) is associated with hospitalization and may cause readmission following admission for any reason. We aimed to measure the incidence of readmissions due to CDI.

DESIGN. Retrospective cohort study.

PATIENTS. Adult inpatients in Orange County, California, who presented with new-onset CDI within 12 weeks of discharge.

METHODS. We assessed mandatory 2000–2007 hospital discharge data for trends in hospital-associated CDI (HA-CDI) incidence, with and without inclusion of postdischarge CDI (PD-CDI) events resulting in rehospitalization within 12 weeks of discharge. We measured the effect of including PD-CDI events on hospital-specific CDI incidence, a mandatory reporting measure in California, and on relative hospital ranks by CDI incidence.

RESULTS. From 2000 to 2007, countywide hospital-onset CDI (HO-CDI) incidence increased from 15 per 10,000 to 22 per 10,000 admissions. When including PD-CDI events, HA-CDI incidence doubled (29 per 10,000 in 2000 and 52 per 10,000 in 2007). Overall, including PD-CDI events resulted in significantly higher hospital-specific CDI incidence, although hospitals had disproportionate amounts of HA-CDI occurring postdischarge. This resulted in substantial shifts in some hospitals' rankings by CDI incidence. In multivariate models, both HO and PD-CDI were associated with increasing age, higher length of stay, and select comorbidities. Race and Hispanic ethnicity were predictive of PD-CDI but not HO-CDI.

CONCLUSIONS. PD-CDI events associated with rehospitalization are increasingly common. The majority of HA-CDI cases may be occurring postdischarge, raising important questions about both accurate reporting and effective prevention strategies. Some risk factors for PD-CDI may be different than those for HO-CDI, allowing additional identification of high-risk groups before discharge.

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Hospital length of stay has steadily decreased over the past 30 years,¹ and increasingly, complex medical care is provided after discharge through home health and skilled nursing facilities. In turn, adverse events related to hospitalization, including hospital-associated infection, may increasingly be present after discharge and result in readmission.²⁻⁵ The costs and sequelae of hospital readmission have made it a target for hospital quality indicators and value-based purchasing.^{6,7} Currently, the Centers for Medicare and Medicaid Services reports hospitals' rates of readmission following treatment for myocardial infarction, congestive heart failure, and pneumonia, prompting a national focus on preventing readmission.8 However, readmission rates for other important conditions, such as hospital-associated infections (HAIs), are not well studied despite national and state requirements for reporting hospital-specific rates of HAIs.9-12

Clostridium difficile infection (CDI) is a common cause of diarrhea in healthcare settings and may be an important source of hospital readmissions.¹³⁻¹⁵ Hospital-associated C. difficile acquisition may not be evident until after hospital discharge, especially since the average hospital length of stay is 3–5 days and acquisition may initially be asymptomatic.^{1,16} In addition, risk factors related to medical care, such as predisposing antibiotics, may require time to deplete the normal intestinal flora and allow C. difficile to flourish and produce symptoms. The exact incubation period for CDI is unknown, but 3 studies found the incubation period to be less than 1 week.^{22,23} However, several studies have found patients may be at an increased risk for developing CDI up to 3 months after hospital discharge.¹⁸⁻²¹ One recent study found that among patients who developed CDI within 100 days postdischarge, 89% of patients developed CDI in the first 60 days

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	Characteristics of Hospital Admissions, N (%)						
Characteristic	All	HO-CDI	PD-CDI	CA-CDI	Total CDI		
No. of patients	N = 1,768,686	N = 1,952	N = 3,077	N = 5,667	N = 10,750		
Male gender	675,111 (38)	919 (47)	1,213 (39)	2,416 (43)	4,580 (43)		
Age, years							
18-<40	497,982 (28)	146 (7)	194 (6)	364 (6)	703 (7)		
40-49	220,320 (13)	164 (9)	218 (7)	443 (8)	819 (8)		
50-59	220,859 (13)	243 (13)	255 (8)	596 (11)	1,105 (10)		
60-<75	365,572 (21)	590 (31)	758 (25)	1,518 (28)	2,878 (28)		
75+	434,378 (25)	762 (40)	1,569 (52)	2,572 (47)	4,929 (47)		
Race							
White	1,419,979 (80)	1,582 (81)	2,698 (88)	4,775 (84)	9,103 (85)		
Black	42,500 (3)	40 (2)	34 (1)	117 (2)	193 (2)		
Asian	167,465 (9)	212 (11)	174 (6)	429 (8)	823 (7)		
Other	138,761 (8)	118 (6)	171 (5)	346 (6)	631 (6)		
Hispanic ethnicity	281,701 (16)	208 (11)	290 (9)	643 (11)	1,164 (11)		
Romano score							
0	880,857 (50)	349 (18)	704 (23)	1,203 (21)	2,120 (20)		
1–2	407,651 (23)	405 (21)	750 (24)	1,187 (21)	2,275 (21)		
3–4	221,440 (12)	397 (20)	621 (20)	1,068 (19)	2,110 (20)		
5+	258,757 (15)	801 (41)	1,002 (33)	2,209 (39)	4,245 (39)		
Recent surgery ^a	570,445 (32)	869 (44)	986 (32)	1,143 (20)	2,848 (26)		

TABLE 1. Characteristics of Hospital Inpatients, Orange County, California, 2000–2007

NOTE. HO-CDI, hospital-onset *Clostridium difficile* infection; PD-CDI, postdischarge CDI; and CA-CDI, community-associated CDI.

^a Recent surgery includes surgery during the current admission or within the previous 30 days.

and 85% occurred in the first month.¹⁷ To account for the range of incubation period, national guidance considers CDI occurring within 4 weeks of hospitalization as hospital associated, and CDI occurring within 4–12 weeks of a hospitalization as potentially hospital associated.^{22,23}

Concerns about CDI have been increasing in the United States. Hospitals' incidence of CDI has been rising in the past decade.²⁴ This has been associated with the emergence of a new epidemic strain, BI/NAP1/027, that produces 20-fold more toxin than other strains and is associated with high rates of colectomy and death.²⁵⁻²⁹ In fact, there is evidence in some hospitals that CDI prevalence may have surpassed that of methicillin-resistant *Staphylococcus aureus* (MRSA).³⁰ With continued pressure to reduce hospital length-of-stay, the frequency of postdischarge CDI (PD-CDI)—defined here as community-onset CDI within 12 weeks after any hospitalization—may be increasing, along with the opportunity for prevention.

In response to rising CDI incidence, the Centers for Disease Control and Prevention (CDC) and the Society for Healthcare Epidemiology of America (SHEA) have recommended surveillance of healthcare-associated CDI (HA-CDI) rates, which includes both hospital-onset as well as community-onset healthcare-associated CDI.^{9,10} In addition, reporting of CDI rates has been legislated or is under legislative consideration in several states.^{31,32} Despite national guidance that postdischarge CDI events occurring within 4 weeks should be considered hospital associated and events between 4–12 weeks of discharge could potentially be hospital associated, hospitals performing CDI surveillance often do not track PD-CDI events. However, tracking postdischarge events may facilitate efforts to prevent readmissions and may be helpful for reporting hospital-specific CDI incidence. Moreover, patients requiring readmission for PD-CDI may not return to the original facility, suggesting that the incidence of HA-CDI may be significantly underestimated if PD-CDI events are not uniformly identified among hospitals.¹⁴

We sought to identify CDI cases occurring at all hospitals in a large California county (population 3 million). We assessed the frequency of admission for new-onset CDI after a recent hospitalization and the impact of including PD-CDI events resulting in readmission on hospital-specific CDI incidence.

METHODS

Description of Data Set

We conducted a population-based retrospective cohort study to assess the frequency of postdischarge CDI events among adult inpatients in all 29 hospitals serving adults in Orange County, California, from January 1, 2000, to December 31, 2007. We used mandatory California hospital discharge data which provides line-item demographic and insurer information, ICD-9 codes (up to 25), and a unique identifier (record linking number) that allows patients to be tracked across hospital admissions.³³ This data also includes a code



FIGURE 1. *Clostridium difficile* infection (CDI) burden among hospitalized adult patients in Orange County, California, from 2000 to 2007. Incidence of hospital-onset CDI (HO-CDI), postdischarge CDI (PD-CDI), and hospital-associated CDI (HA-CDI) is expressed per 10,000 adult admissions; incidence of community-associated CDI (CA-CDI) is expressed per 100,000 Orange County adult population. HA-CDI consists of HO-CDI and PD-CDI.

to indicate whether a given condition was present when the patient was admitted, known as the "present on admission" (POA) code, which has been used in California since 1996.³⁴

We identified CDI cases using the ICD-9 diagnostic code 008.45 for pseudomembranous colitis. We defined 4 types of CDI cases: (1) hospital-onset CDI (HO-CDI) cases defined by POA = N (no); (2) PD-CDI cases defined by POA = Y (yes) with a history of hospitalization for any reason in the prior 12 weeks; (3) HA-CDI cases defined as the sum of HO-CDI and PD-CDI; and (4) community-associated CDI (CA-CDI) cases defined by POA = Y with no prior history of hospitalization in the previous 12 weeks. While we used 12 weeks for our primary analysis, we repeated all analyses using a 4-week cutoff for comparison. To reduce the chance that a code represented a past history of CDI without active infection during hospitalization, we limited cases with POA = Y to the first 3 coding positions. For POA = N cases, all coding positions were accepted. We excluded 932 cases of recurrent CDI, defined as cases occurring within 8 weeks of a previous CDI episode.9,22 Finally, we assessed the fraction



FIGURE 2. Time to readmission for postdischarge *Clostridium difficile* infection cases (PD-CDI), 2000–2007, for cases occurring within 1 year after discharge (N = 1,766).

of postdischarge events that occurred within 4 weeks of discharge. This study was approved by the Institutional Review Boards of the University of California Regents and the California Committee for the Protection of Human Subjects.

DATA ANALYSIS

Patient Characteristics

We collected demographic information for all patients in our cohort, including gender, age, race and ethnicity, and insurance type. We also assessed the proportion of hospitalized patients with select comorbidities using the Romano score³⁴ and the proportion that had undergone surgery in the previous month. These characteristics were collected for all admissions and for those with CDI (HO-CDI, PD-CDI, and CA-CDI).

Annual Incidence of CDI

Annual CDI incidence across Orange County was determined for 2000–2007 and analyzed by χ^2 tests for trend. We identified all cases and subsets of CDI as defined above. Incidences of HO-CDI, PD-CDI, and HA-CDI were expressed per 10,000 admissions. CA-CDI incidence was expressed per 100,000 residents.

Hospital Readmission for CDI

We defined a PD-CDI readmission as a case with symptoms present on admission (POA = Y) that occurred within 12 weeks after a prior hospitalization for any reason, as described above. We calculated the percentage of all-cause readmissions that are due to PD-CDI. We excluded readmissions for recurrent CDI, which we defined as community-onset (POA = Y) cases readmitted within 8 weeks of a previous admission for CDI.²² We also determined how often patients readmitted for PD-CDI went to a different facility for their readmission.



FIGURE 3. Hospital-specific rankings by hospital-associated *Clostridium difficile* infection (HA-CDI) versus hospital-onset CDI (HO-CDI) incidence for 2007. Shaded areas indicate the quartile of hospitals with the highest CDI incidence based on HA-CDI versus HO-CDI.

Impact of Including Postdischarge CDI Readmissions in Hospital-Specific CDI Incidence

For each hospital, we determined the annual incidence of HO-CDI and HA-CDI for the years 2000–2007. Differences between annual HO-CDI and HA-CDI incidence were compared using paired t tests. We determined whether relative rankings by quartile of hospitals by CDI incidence were affected by inclusion of PD-CDI.

Identifying Individual and Hospital Predictors of CDI

We identified the primary admission diagnoses of admissions that were associated with HO-CDI and PD-CDI. For primary admission diagnoses associated with greater than 25 HO-CDI or PD-CDI events, we calculated the frequency of CDI compared to those without that primary admission diagnosis.

We performed bivariate analyses using χ^2 tests to identify individual and hospital level variables associated with the individual outcomes of HO-CDI and PD-CDI. For the PD-CDI outcome, we used characteristics from the PD-CDI (vs the index) admission and removed all hospitalizations that resulted in death, since these hospitalizations could not result in readmission. Individual variables included demographics, comorbidities, primary admission diagnosis, recent surgery, insurance type, year of hospital admission, and length of stay. Hospital variables included annual admissions, average length of stay, and hospital type (acute vs long-term acute care facility). Variables with P < .1 from bivariate testing were entered into a generalized linear mixed model which accounted for clustering by hospital (ProcGLIMMIX, SAS 9.2; SAS). Variables were retained at $\alpha = 0.05$.

RESULTS

Patient Characteristics

Patients admitted with CDI were older, had more comorbidities, and were less likely to have undergone surgery in the past month compared to all hospitalized patients (Table 1). Among those with CDI, patients with HO-CDI and PD-CDI had similar distributions of age, race and ethnicity, and comorbidities, but those with HO-CDI were more likely to be male and to have undergone surgery in the past month.

Annual Incidence of HO-CDI and HA-CDI

Annual incidence of HO-CDI in Orange County increased from 2000 to 2007, as shown in Figure 1 (P < .001 for test of trend). After including PD-CDI events, the annual incidence of HA-CDI increased 1.9-fold during the same period, from 28.7 to 52.2 per 10,000 admissions (χ^2 , P < .001). By 2007, PD-CDI comprised the majority of HA-CDI cases (increasing from 46% in 2000 to 57% in 2007; P < .001 for test of trend). Restricting PD-CDI cases to the 4 weeks following discharge captured 73% of PD-CDI cases and resulted in similar annual incidences of HA-CDI, increasing 1.8-fold from 28.0 per 10,000 admissions in 2000 to 51.6 per 10,000 admissions in 2007 (χ^2 , P < .001).

Frequency of New-Onset CDI as Reason for Hospital Readmission

Over 2000–2007, PD-CDI events resulting in readmission represented 1.8% (2,998 of 170,995) of all-cause readmissions within 12 weeks after discharge. When evaluating all admissions related to CDI occurring within 365 days of discharge, we found that the risk of readmission for CDI was higher in the first 12 weeks postdischarge, and highest in the first 4 weeks postdischarge (Figure 2). Of PD-CDI events occurring within 12 weeks of discharge, 58% (624 of 1071) occurred within the 4 weeks after discharge. After 12 weeks, the risk of readmission for CDI dropped to a stable, low level. Among PD-CDI cases readmitted within 12 weeks, 25% (746 of 2,998) were readmitted to a different hospital than the initial hospitalization.

Impact of Including CDI Readmissions on Hospital-Specific Rates

Figure 3 shows hospital-specific rankings according to CDI incidence for 2007, with and without including PD-CDI events (HO-CDI vs HA-CDI, respectively). The proportion of hospitals' HA-CDI comprised by PD-CDI varied greatly (median 60% PD-CDI, range 0%–100%, for 2007). Hospital ranking by CDI incidence changed by a mean of 3 places after including PD-CDI events; only 5 of 29 hospitals did not change rank. Three hospitals became ranked in the worst quartile after including PD-CDI, including 1 hospital that had been ranked in the best quartile when PD-CDI events were excluded. Another 3 hospitals were no longer ranked in the worst quartile when PD-CDI events were included.

When restricting PD-CDI events to 4 weeks postdischarge, the proportion of HA-CDI comprised by PD-CDI similarly varied from 0%–100% (median 46%). Hospital rankings changed by a mean of 2.5 places, and 10 of 30 hospitals

Primary admission diagnosis	N (%) with HO-CDI	OR	P value	N (%) with PD-CDI	OR	P value
Staphylococcus aureus septicemia	31 (0.6)	10.09	<.001			
S. aureus pneumonia	33 (0.7)	9.76	<.001			
Acute respiratory failure	117 (2.4)	8.56	<.001	31 (0.4)	1.22	.007
Aspiration pneumonitis	99 (2.1)	6.55	<.001	69 (0.8)	2.47	<.001
Infection of vascular device	33 (0.7)	6.16	<.001	26 (0.3)	2.65	
Chemotherapy	30 (0.6)	5.43	<.001			
E. coli septicemia	26 (0.5)	5.39	<.001	26 (0.3)	2.94	<.001
Septicemia	68 (1.4)	3.72	<.001	184 (1.2)	3.20	<.001
Postoperative infection	28 (0.6)	3.28	<.001	26 (0.3)	1.67	<.001
Acute renal failure	39 (0.8)	2.80	<.001	47 (0.5)	1.85	<.001
Pneumonia	98 (2.0)	1.69	<.001	184 (2.1)	1.74	<.001
Acute pancreatitis	31 (0.6)	1.51	.002	26 (0.3)	0.69	.8
Urinary tract infection	37 (0.8)	1.43	.19	96 (1.1)	2.04	<.001
Hip fracture				31 (0.4)	1.76	<.001
Cellulitis				45 (0.5)	1.69	<.001
Colon diverticulitis				45 (0.5)	1.68	<.001

 TABLE 2.
 Frequent Primary Admission Diagnoses for Hospital Patients at High Risk for Clostridium difficile Infection (CDI)

NOTE. HO-CDI, hospital-onset CDI; PD-CDI, postdischarge CDI; OR, odds ratio.

changed quartile. Nine hospitals did not change rank; these hospitals all had zero CDI events.

Identifying Individual and Hospital Predictors of CDI

Primary admission diagnoses that occurred most often during HO-CDI and PD-CDI admissions are listed in Table 2. Several primary admission diagnoses were significantly associated with both HO-CDI and PD-CDI admissions on bivariate analysis, including septicemia, pneumonia, postoperative infection, and urinary tract infection.

Results from bivariate analysis (Table 3) were similar to those from multivariate analysis (Table 4). In multivariate analysis, HO-CDI and PD-CDI were both associated with increasing age, longer length of stay, Medicare insurance, recent surgery, comorbidities, select primary admission diagnoses (septicemia, postoperative infection, and pneumonia), and hospitals with a high percent of patients with a high comorbidity index. Nonwhite race, Hispanic ethnicity, and male gender were protective against PD-CDI but not HO-CDI.

Annual Incidence of Community-Associated CDI

Orange County's incidence of CA-CDI also rose during 2000 to 2007. In this period, CA-CDI incidence increased 2.1-fold from 9.1 to 19.4 cases per 100,000 residents (χ^2 , P < .001), exclusive of PD-CDI cases. These rates were similar when PD-CDI was restricted to events within 4 weeks of discharge (9.5 to 19.8 cases per 100,000 residents; χ^2 , P < .001).

DISCUSSION

Clostridium difficile disease is a major cause of healthcareassociated infection and morbidity. Due to the known delay in presentation following antibiotic exposure, national guidelines consider cases up to 12 weeks following hospital discharge as potentially healthcare-associated and possibly preventable. Nevertheless, the majority of hospitals do not track postdischarge cases, and the impact of postdischarge cases has remained largely unknown. Remarkably, we found that PD-CDI cases within 12 weeks after hospital discharge accounted for the majority of HA-CDI and led to a 2-fold increase in HA-CDI incidence across hospitals in a large metropolitan county. These effects were largely driven by PD-CDI events within 4 weeks after hospital discharge. This finding illustrates the need to expand prevention and education strategies to include the postdischarge period and thereby reduce the frequency of PD-CDI events.

Inclusion of postdischarge CDI events substantially altered hospital-specific CDI incidence, but the impact varied widely by hospital. For example, PD-CDI cases accounted for all HA-CDI cases in one hospital and none of the cases in another. This suggests that tracking PD-CDI events may impact the validity of interfacility comparisons, since hospitals are affected differentially by including or excluding PD-CDI. These discrepancies could be magnified if only some, but not all, hospitals track PD-CDI. When we ranked hospitals by HO-CDI incidence, half the hospitals captured in the quartile with the highest HO-CDI incidence changed when PD-CDI was included. In fact, one hospital changed from the best quartile to the worst quartile when PD-CDI cases were captured. Further, changes in rank were similar when PD-CDI was restricted to events within 4 weeks postdischarge, with one-third of hospitals changing quartile after inclusion of PD-CDI. In addition, since 75% of patients with PD-CDI returned to the same hospital for readmission, hospitals may be able to track most PD-CDI cases by performing postdischarge surveillance for PD-CDI cases that readmit to their own facility. Additional notification of PD-CDI cases back to

Individual variables (%)	HO-CDI	Non-HO-CDI	P value	PD-CDI	Non-PD-CDI	P value
N	2,403	1,766,753		3,077	1,725,165	
Age, years			<.001			<.001
18-<40	6.7	28.7		6.5	29.3	
40-49	7.8	12.7		7.3	12.8	
50–59	11.9	12.7		8.5	12.8	
60-<75	31.7	21.0		25.3	20.9	
75+	41.9	24.9		52.4	24.2	
Male gender	48.2	38.2	<.001	39.4	37.9	.08
Race			.01			<.001
White	80.9	80.3		87.7	80.2	
Black	2.2	2.4		1.1	2.4	
Asian	10.6	9.5		5.6	9.5	
Other	6.3	7.8		5.6	7.9	
Hispanic ethnicity	11.1	16.2	<.001	9.5	16.4	<.001
Medicare insurance	36.8	59.8	<.001	29.9	60.6	<.001
Medicaid insurance	92.0	89.5	<.001	95.2	89.4	<.001
Admit to acute hospital (vs LTAC) ^a	87.2	96.8	<.001	96.3	96.8	.08
Admission year			<.001			<.001
2000	10.2	11.7		7.9	11.6	
2001	10.6	12.2		9.1	12.2	
2002	11.7	12.4		9.6	12.4	
2003	10.8	12.9		10.9	12.9	
2004	11.8	12.7		12.2	12.7	
2005	13.5	12.7		16.3	12.7	
2006	16.3	12.5		17.6	12.6	
2007	15.1	12.9		16.4	12.9	
Length of stay >5 days	96.7	27.4	<.001	56.2	26.8	<.001
Surgery ^b	42.3	32.2	<.001	25.7	30.5	<.001
Comorbidities						
Diabetes	29.6	16.9	<.001	24.7	16.6	<.001
Cancer	15.1	7.8	<.001	13.5	7.5	<.001
Dementia	5.9	2.9	<.001	5.8	2.8	<.001
Ulcer	4.6	1.8	<.001	2.7	1.7	<.001
AIDS	0.6	0.2	<.001	0.4	0.2	.02
High comorbidity index ^c	64.5	27.1	<.001	52.8	26.0	<.001
Admitted to high-volume hospital ^d	61.9	61.1	<.001	72.2	67.2	<.001
Admitted to hospital with high length of stay ^e	85.4	77.2	<.001	71.5	77.1	<.001

TABLE 3. Bivariate Analysis of Predictors of Hospital-Onset *Clostridium difficile* Infection (HO-CDI) and Postdischarge CDI (PD-CDI) Among All Adult Inpatients

NOTE. Data other than N and P shown as percentage. AIDS, acquired immune deficiency syndrome.

^a LTAC, long-term acute care facility.

^b Surgery indicates surgery during the current admission or within the previous 30 days.

^c Comorbidity index measured by Romano score.

^d High volume, >10,000 annual admissions.

^e High length of stay, >5 days.

transferring or recently discharging hospitals may also improve accuracy of CDI rates.

For prevention, patient characteristics may be utilized to identify populations at elevated risk for postdischarge CDI. We found that risk factors for HO-CDI and PD-CDI were often the same, including increasing age, higher length of stay, and overall poor health, including diabetes, cancer, and AIDS, in agreement with prior studies.²⁴ In addition, prevention may be targeted at patients with specific primary admission diagnoses such as septicemia, postoperative infection, and pneumonia. These primary admission diagnoses all represent conditions likely to be treated with antibiotics, the main risk factor for CDI. The immediate postdischarge period should be considered an extension of the risk of CDI that begins during a hospital stay. This heightens the importance of educating high-risk patients before hospital discharge about the potential for postdischarge diarrhea and of identifying prophylactic solutions to prevent disease in the highrisk patient population.

In addition, we found that white and non-Hispanic patients

	HO-CDI vs non-HO-CI	PD-CDI vs all non-HO-CDI		
Individual variables	OR (95% CI)	P value	OR (95% CI)	P value
Age, years		<.001		<.001
18-<40	Reference		Reference	
40-49	1.93 (1.29-2.89)		2.20 (1.53-3.17)	
50–59	1.82 (1.23-2.71)		2.21 (1.54-3.17)	
60-<75	1.83 (1.28-2.61)		2.76 (1.99-3.82)	
75+	2.16 (1.51-3.09)		3.93 (2.85-5.44)	
Male gender	1.04 (0.93-1.16)	.49	0.87 (0.80-0.95)	.001
Race		.01		<.001
White	Reference		Reference	
Black	0.94 (0.61-1.45)		0.49 (0.31-0.78)	
Asian	1.27 (1.06-1.52)		0.64 (0.53-0.77)	
Other	0.79 (0.59-1.05)		1.04 (0.85-1.28)	
Hispanic ethnicity	0.94 (0.77-1.15)	.56	0.73 (0.6286)	<.001
Medicare insurance	0.61 (0.4877)	<.001	0.70 (0.5687)	.001
Admission year	1.07 (1.05-1.09)	<.001	1.11 (1.09–1.13)	<.001
2000 (reference)				
2001	1.03 (0.81-1.33)		0.92 (0.75-0.86)	
2002	1.12 (0.88-1.43)		1.04 (0.86-1.27)	
2003	0.94 (0.73-1.21)		1.14 (0.94–1.38)	
2004	1.22 (0.96-1.55)		1.35 (1.12–1.62)	
2005	1.25 (0.99–1.58)		1.67 (1.40-1.99)	
2006	1.55 (1.24–1.94)		1.83 (1.53-2.18)	
2007	1.39 (1.10-1.74)		1.71 (1.43-2.04)	
Length of stay	1.02(1.02-1.02)	<.001	1.01 (1.01-1.01)	<.001
Surgery ^a	2.16 (1.91-2.43)	<.001	1.23 (1.12-1.35)	<.001
Comorbidities				
Diabetes	1.36 (1.20-1.53)	<.001	1.14 (1.03-1.25)	.009
Cancer	1.32 (1.13-1.55)	<.001	1.24 (1.09–1.42)	.001
Dementia	1.57 (1.28–1.93)	<.001	1.03 (0.87-1.21)	.74
Ulcer	1.92 (1.49-2.47)	<.001	1.31 (1.04–1.67)	.02
AIDS	4.15 (2.02-8.50)	<.001	3.27 (1.60-6.65)	.001
High comorbidity index ^b	1.06 (1.02–1.11)	<.001	1.02 (1.01-1.03)	.001
Primary admission diagnosis				
Chemotherapy	7.08 (4.04-12.42)	<.001		
Staphylococcus aureus pneumonia	5.13 (3.23-8.16)	<.001		
Infection due to vascular device	3.05 (1.87-4.97)	<.001		
Septicemia	2.70 (3.71-1.96)	<.001	3.55 (2.87-4.40)	<.001
Postoperative infection	2.36 (3.89–1.43)	<.001	2.39 (1.51-3.76)	<.001
Acute respiratory failure	2.25 (1.63-3.10)	<.001		
Pneumonia	1.47 (1.93-1.11)	.006	1.82 (1.54-2.16)	<.001
Cellulitis			2.41 (1.72-3.38)	<.001
Colon diverticulitis			2.37 (1.64-3.43)	<.001
Urinary tract infection			1.86 (1.48-2.33)	<.001
Acute renal failure			1.73 (1.25-2.39)	<.001

TABLE 4. Multivariate Analysis of Predictors of Hospital-Onset *Clostridium difficile* Infection (HO-CDI) and Postdischarge CDI (PD-CDI) Aamong All Adult Inpatients

NOTE. CI, confidence interval; OR, odds ratio.

^a Surgery indicates surgery during the current admission or within the previous 30 days.

^b Comorbidity index measured by Romano score.

had a higher risk of PD-CDI. While we did not evaluate reasons for this difference, racial and ethnic disparities, including access to health care, have been well documented and may be magnified in the outpatient arena.^{36,37} Differences in

access to outpatient care are likely to impact antibiotic use in these groups and their subsequent risk of PD-CDI. In addition, male gender was associated with lower risk of PD-CDI but not with HO-CDI. This difference may not be due to an increased postdischarge risk for women but may instead reflect men's reduced tendency to seek care and therefore be hospitalized for PD-CDI.^{38,39} More research is needed to understand the reasons for differential risk in these groups in order to develop effective prevention strategies for the post-discharge setting.

Our study has several limitations. We did not capture PD-CDI cases treated in the outpatient setting, which may have led to an underestimate of PD-CDI incidence. Nevertheless, the focus on PD-CDI associated with rehospitalization ensured capture of the most serious cases. While errors present in administrative data may lead to an under- or overestimation of CDI incidence, previous studies indicate reasonable agreement between medical records and ICD-9 codes for identification of total CDI burden.40,41 Nevertheless, without POA codes, ICD-9 codes alone have been variably successful at distinguishing between community versus healthcareassociated C. difficile disease.42 We anticipate that the POA code, which has been in standard use in California for over a decade, improves this determination. In fact, POA codes have proven useful in other diseases (pneumonia, myocardial infarction) for distinguishing between hospital versus community-onset disease.43 We also minimized the chances that a code represented a history of CDI only versus active disease by limiting diagnoses to the first 3 coded positions. Another limitation is that we did not account for certain known risk factors (such as antibiotic use) that were unavailable in administrative data. However, we included primary admission diagnoses that are frequently treated with antibiotics. Finally, we attributed a PD-CDI event to the most recent hospitalization within 12 weeks. This definition does not account for multiple hospital exposures during that period or for intervening nursing home admissions, which may also contribute to CDI acquisition. Further, since the incubation period for CDI is unknown, some cases occurring within our 12-week window may be due to exposures in the community, including outpatient antibiotic use, household pets, and contamination of food. Nonetheless, over half of PD-CDI cases detected in this study occurred within the first 4 weeks after discharge, a time window that is accepted by national guidance to most likely reflect healthcare-associated CDI events.

In summary, tracking PD-CDI cases doubled the incidence of HA-CDI in a large county. Since the majority of hospitals do not track PD-CDI cases, the frequency and impact of PD-CDI may be widely underestimated, resulting in missed opportunities to prevent readmissions. Importantly for public reporting purposes, including PD-CDI affected individual hospitals differently, leading to substantial changes in hospital rankings by CDI incidence. Uniform tracking of PD-CDI events would allow more accurate estimates of overall CDI incidence and more equitable hospital-to-hospital comparisons. We found that the vast majority of cases can be captured if hospitals track PD-CDI cases that return to the same facility. We also identified several patient characteristics that were associated with PD-CDI, suggesting that preventative strategies may effectively focus upon specific patient groups. Targeted education and prevention for CDI may become increasingly important to help hospitals lower their readmission rates.

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REFERENCES

- Meltzer DO, Chung JW. U.S. trends in hospitalization and generalist physician workforce and the emergence of hospitalists. J Gen Intern Med 2010;25:453–459.
- Yokoe DS, Avery TR, Huang SS. Surgical Site Infection Surveillance following Total Hip and Knee Arthroplasty Using California Administrative Data. Oral presentation, Society for Healthcare Epidemiology of America; April 1–4, 2011; Dallas, TX.
- Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillinresistant *Staphylococcus aureus* infections in the United States. *JAMA* 2007;298:1763–1771.
- Datta R, Huang SS. Risk of infection and death due to methicillin-resistant *Staphylococcus aureus* in long-term carriers. *Clin Infect Dis* 2008;47:176–181.
- 5. Huang SS, Platt R. Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. *Clin Infect Dis* 2003;36:281–285.
- Weinberger M, Oddone EZ, Henderson WG. Does increased access to primary care reduce hospital readmissions? N Engl J Med 1996;334:1441–1447.
- Jweinat JJ. Hospital readmission under the spotlight. J Healthc Manag 2010;55:252–264.
- Centers for Medicare and Medicaid Services/Joint Commission. http://www.jointcommission.org/home_care_-_reducing __hospital_readmissions_bibliography/. Accessed November 11, 2011.
- Cohen AL, Calfee D, Fridkin SK, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC Position Paper. *Infect Control Hosp Epidemiol* 2008;29:901–913.
- National Health Safety Network, Centers for Disease Control and Prevention. *Multidrug-resistant organism and* Clostridium difficile *infection (MDRO/CDI) module*. http://www.cdc.gov/ nhsn/mdro_cdad.html. Accessed July 5, 2011.
- Healthcare-Associated Infection Working Group of the Joint Public Policy Committee (SHEA/APIC/CSTE/CDC). Essentials

of Public Reporting of Healthcare-Associated Infections: A Tool Kit. http://www.shea-online.org/Assets/files/Essentials_of _Public_Reporting_Tool_Kit.pdf. Accessed July 5, 2011.

- Association for Professionals in Infection Control and Epidemiology. *Healthcare-Associated Infection Legislation in Progress* 2010. http://www.apic.org/downloads/legislation/HAI_map.gif. Accessed July 5, 2011.
- 13. Dubberke ER, Gerding DN, Classen D, et al. Strategies to prevent *Clostridium difficile* infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29(suppl 1):S81–S92.
- 14. Huang SS, Avery TR, Song Y, et al. Quantifying inter-hospital patient sharing as a mechanism for infectious disease spread. *Infect Control Hosp Epidemiol* 2010;31:1160–1169.
- 15. Dubberke ER, Butler AM, Reske KA, et al. Attributable outcomes of endemic *Clostridium difficile*–associated disease in non-surgical patients. *Emerg Infect Dis* 2008;14:1031–1038.
- Issa M, Ananthakrishnan AN, Binion DG. *Clostridium difficile* and inflammatory bowel disease. *Inflamm Bowel Dis* 2008;14: 1432–1442.
- 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. Hospitalassociated *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 *Clostrid-ium 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.
- Kelly CP, Pothoulakis C, Lamont JT. Clostridium difficile colitis. N Engl J Med 1994;330:257–262.
- 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.
- Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol* 2010;31:431–455.
- Elixhauser A, Jhung M. *Clostridium difficile*–Associated Disease in U.S. Hospitals, 1993–2005. Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, 2008. Statistical Brief 50.
- Campbell RJ, Giljahn L, Machesky K, et al. *Clostridium difficile* infection in Ohio hospitals and nursing homes during 2006. *Infection Control Hosp Epidemiol* 2009;30:526–533.
- Hookman P, Barkin JS. *Clostridium difficile* associated infection, diarrhea and colitis. *World J Gastroenterol* 2009;15:1554–1580.
- Warny M, Pepin J, Fang A, et al. Toxin production by an emerging strain of *Clostridium difficile* associated with outbreaks of severe disease in North America and Europe. *Lancet* 2005;366: 1079–1084.
- 28. Miller M, Gravel D, Mulvey M, et al. Healthcare-associated Clos-

tridium difficile infection in Canada: patient age and infecting strain type are highly predictive of severe outcome and mortality. *Clin Infect Dis* 2010;50:194–201.

- 29. McDonald LC, Killgore GE, Thompson A, et al. An epidemic, toxin gene-variant strain of *Clostridium difficile*. N Engl J Med 2005;353:2433–2441.
- 30. Miller BA, Chen LF, Sexton DJ, Anderson DJ. The Impact of Hospital-Onset Healthcare Facility Associated (HO-HCFA) *Clostridium difficile* Infection (CDI) In Community Hospitals: Surpassing Methicillin-Resistant *Staphylococcus aureus* (MRSA) As the New Superbug. Oral presentation, top four abstracts at the Fifth Decennial International Conference on Healthcare-Associated Infections. March 2010, Atlanta, GA.
- Association for Professionals in Infection Control and Epidemiology. Clostridium difficile *Legislation in Progress 2010*. http:// www.cqstatetrack.com/texis/viewrpt/+yeOlOjemuAB?report = 4cab75bbeb1. Accessed July 5, 2011.
- Committee to Reduce Infection Deaths. State Legislation and Initiatives on Healthcare-Associated Infections. Updated March 2010. http://www.hospitalinfection.org/legislation.shtml. Accessed July 5, 2011.
- Office of Statewide Health Planning and Development. http:// www.oshpd.ca.gov/. Accessed July 5, 2011.
- 34. Leibson CL, Needleman J, Buerhaus P, et al. Identifying inhospital venous thromboembolism (VTE): a comparison of claims-based approaches with the Rochester Epidemiology Project VTE cohort. *Med Care* 2008;46:127–132.
- Musher DM, Aslam S, Logan N. Relatively poor outcome after treatment of *Clostridium difficile* colitis with metronidazole. *Clin Infect Dis* 2005;40:1586–1590.
- 36. Nelson A. Unequal treatment: confronting racial and ethnic disparities in health care. J Natl Med Assoc 2002;94:666–668.
- 37. Williams DR. Racial variations in adult health status: patterns, paradoxes and prospects. In: Smelser N, Wilson WJ, Mitchell F, eds. *America Becoming: Racial Trends and Their Consequences*. Vol 2. Washington, DC: National Academy of Sciences, 2001: 371–410.
- Courtenay W. Constructions of masculinity and their influence on men's well-being: a theory of gender and health. *Soc Sci Med* 2000;50:1385–1401.
- 39. Lee C, Owens RG. Issues for a psychology of men's health. J Health Psychol 2002;7:209–217.
- Schmiedeskamp M, Harpe S, Polk R, Oinonen M, Pakyz A. Use of international classification of diseases, ninth revision: clinical modification codes and medication use data to identify nosocomial *Clostridium difficile* infection. *Infect Control Hosp Epidemiol* 2009;30:1070–1076.
- Dubberke ER, Reske KA, McDonald LC, Fraser VJ. ICD-9-CM codes and surveillance for *Clostridium difficile*-associated disease. *Emerg Infect Dis* 2006;12:1576–1579.
- 42. Dubberke ER, Butler AM, Yokoe DS, et al. Multicenter study of surveillance for hospital-onset *Clostridium difficile* infection by the use of ICD-9-CM diagnosis codes. *Infect Control Hosp Epidemiol* 2010;31:262–268.
- 43. Goldman LE, Chu PW, Prothro C, Osmond D, Bindman AB. Accuracy of condition present on admission, do not resuscitate, and E-codes in California patient discharge data. Prepared for the Office of Statewide Health Planning and Development, spring 2011.