ORIGINAL ARTICLE

Trends in U.S. Burden of *Clostridioides difficile* Infection and Outcomes

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ABSTRACT

BACKGROUND

Efforts to prevent *Clostridioides difficile* infection continue to expand across the health care spectrum in the United States. Whether these efforts are reducing the national burden of *C. difficile* infection is unclear.

METHODS

The Emerging Infections Program identified cases of *C. difficile* infection (stool specimens positive for *C. difficile* in a person ≥1 year of age with no positive test in the previous 8 weeks) in 10 U.S. sites. We used case and census sampling weights to estimate the national burden of *C. difficile* infection, first recurrences, hospitalizations, and in-hospital deaths from 2011 through 2017. Health care–associated infections were defined as those with onset in a health care facility or associated with recent admission to a health care facility; all others were classified as community-associated infections. For trend analyses, we used weighted random-intercept models with negative binomial distribution and logistic-regression models to adjust for the higher sensitivity of nucleic acid amplification tests (NAATs) as compared with other test types.

RESULTS

The number of cases of *C. difficile* infection in the 10 U.S. sites was 15,461 in 2011 (10,177 health care–associated and 5284 community-associated cases) and 15,512 in 2017 (7973 health care–associated and 7539 community-associated cases). The estimated national burden of *C. difficile* infection was 476,400 cases (95% confidence interval [CI], 419,900 to 532,900) in 2011 and 462,100 cases (95% CI, 428,600 to 495,600) in 2017. With accounting for NAAT use, the adjusted estimate of the total burden of *C. difficile* infection decreased by 24% (95% CI, 6 to 36) from 2011 through 2017; the adjusted estimate of the national burden of health care–associated *C. difficile* infection decreased by 36% (95% CI, 24 to 54), whereas the adjusted estimate of the national burden of community-associated *C. difficile* infection was unchanged. The adjusted estimate of the burden of hospitalizations for *C. difficile* infection decreased by 24% (95% CI, 0 to 48), whereas the adjusted estimates of the burden of first recurrences and in-hospital deaths did not change significantly.

CONCLUSIONS

The estimated national burden of *C. difficile* infection and associated hospitalizations decreased from 2011 through 2017, owing to a decline in health care–associated infections. (Funded by the Centers for Disease Control and Prevention.)

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N Engl J Med 2020;382:1320-30.
DOI: 10.1056/NEJMoa1910215
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THE INCIDENCE OF *CLOSTRIDIOIDES DIFFICILE* (formerly *Clostridium difficile*) infection and associated hospitalizations increased in the 2000s,[1,2] largely because of the emergence of the epidemic strain ribotype 027.[3,4] The introduction of more sensitive *C. difficile* assays in the late 2000s, such as nucleic acid amplification tests (NAATs), probably contributed to the rising incidence of *C. difficile* infection.[5,6] Concerns have been increasing about the potential overdiagnosis of *C. difficile* infection by NAAT, since this test detects the gene encoding the toxin rather than the actual toxin; these concerns have called into question the appropriate approach for diagnosis of *C. difficile* infection. Although in the United States there is currently no consensus on the best laboratory test for *C. difficile* infection, whether an institution or laboratory has prespecified criteria for *C. difficile* testing can help guide the choice of testing method.[7] The higher sensitivity of NAATs as compared with other assays should be taken into account when estimating the burden of and trends in *C. difficile* infection.

Although traditionally considered an infection affecting patients in health care facilities, *C. difficile* infection is increasingly identified in the community among persons with no recent hospitalizations or stays in a long-term care facility.[8,9] To monitor the changing epidemiology of *C. difficile* infection and generate national estimates of disease burden, the Centers for Disease Control and Prevention (CDC) Emerging Infections Program (EIP) has been conducting population-based surveillance of *C. difficile* infection in 10 U.S. sites since 2011.[10] Using EIP data, we previously estimated that 453,000 episodes of *C. difficile* infection (95% confidence interval [CI], 397,100 to 508,500) occurred in the United States in 2011.[11] Those data were based on a 2011 rate of NAAT use of 52%, which we have since updated to 55%.

Prevention of *C. difficile* infection has long been a national priority,[12] as efforts to improve infection prevention and antibiotic stewardship continue to expand across the health care spectrum. To assess national progress in reducing *C. difficile* infection, we used EIP data to determine trends in the national estimates of the burden and incidence of *C. difficile* infection and associated outcomes from 2011 through 2017.

METHODS

SURVEILLANCE POPULATION

EIP surveillance of *C. difficile* infection involves 35 counties in 10 states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee), with a surveillance population of more than 12 million persons in 2017. A total of 34 of these counties have participated in surveillance of *C. difficile* infection since 2011. The surveillance protocol underwent ethical review by the CDC and all EIP sites and either was deemed to be a nonresearch activity or received institutional review board approval with a waiver of informed consent.

We defined an incident case as a positive result on a *C. difficile* toxin or molecular assay of a stool specimen obtained from a person at least 1 year of age with no positive test in the previous 8 weeks. This definition did not require the presence of diarrhea. Laboratories that serve the surveillance areas reported positive *C. difficile* tests to EIP staff and were audited at least annually for case ascertainment.

DATA COLLECTION

Data-collection methods have been described previously.[10,13] EIP staff performed chart reviews on all cases at eight EIP sites and on a random sample of cases at two EIP sites (Colorado and Georgia) to collect selected data, including hospitalization on the day of or in the 6 calendar days after diagnosis of *C. difficile* infection. Cases were initially classified as having had onset in the community or onset associated with a health care facility (positive stool collected >3 days after hospital admission or from a resident of a long-term care facility) (see the Supplementary Appendix, available with the full text of this article at NEJM.org). All community-onset cases and a 10% random sample of cases that had an onset associated with a health care facility underwent subsequent chart review for additional data, including first recurrent episode (a positive stool specimen within 2 to 8 weeks after the last positive test) and in-hospital death. Community-onset cases were further classified as community-associated if there was no documented admission to a health care facility in the preceding 12 weeks;

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all other community-onset cases, along with cases that had an onset associated with a health care facility, were classified as health care–associated. We surveyed laboratories annually regarding their *C. difficile* testing method to determine the percentage of cases diagnosed by NAAT (used alone or in a multistep algorithm in which NAAT was almost always the last test performed).

ISOLATE CHARACTERIZATION

A convenience sample of stool specimens (see the Supplementary Appendix) was cultured for *C. difficile* at either the Edward Hines, Jr. Veterans Affairs Hospital or the Minnesota Department of Health Public Health Laboratory. Recovered isolates underwent strain typing at the CDC, with the use of capillary-based polymerase-chain-reaction ribotyping starting in 2012[14]; results were analyzed against a library of standard profiles with the use of BioNumerics software (Applied Maths). *C. difficile* isolates that were obtained in 2011 underwent a different typing method (pulsed-field gel electrophoresis) and have been described previously[11]; therefore, we focused primarily on the isolates from 2012 through 2017.

STATISTICAL ANALYSIS

In cases of *C. difficile* infection in which the patient's race was unknown (18.7%) or the epidemiologic class was unknown (0.9%), we performed multiple imputation separately for each site and year on the basis of the distribution of known values stratified according to age and sex. At the two EIP sites where sampling was conducted, we estimated nonsampled cases that were aggregated according to age, sex, race, and epidemiologic class through domain analysis. We used the estimated cases to build two random-intercept models with negative binomial distribution to account for site clustering and overdispersion, one for community-associated cases and another for health care–associated cases, adjusting for age, sex, race, and the percentage of cases diagnosed by means of NAAT. Because NAAT is more sensitive than other test types and its use increased from 2011 through 2017, to appropriately compare burden estimates over time, we used the NAAT coefficients from the models to arbitrarily fix NAAT use at the 2011 rate of 55% (as if NAAT use had remained constant since 2011) in order to perform trend analyses.

For cases that did not undergo additional chart review, we performed another domain analysis to estimate the following outcomes, stratified according to the patient's age, sex, and race: first recurrence of *C. difficile* infection, hospitalization, and in-hospital death. We used cases with complete data to build a separate community-associated and health care–associated logistic-regression model for each of these outcomes, adjusting for age, sex, race, and diagnostic method (NAAT vs. other test types), and used the NAAT coefficients from these models to adjust NAAT use to 55% for each year to perform trend analyses.

The calculation of sampling weights for generating national estimates of the burden of *C. difficile* infection and associated outcomes and for performing trend analyses is described in the Supplementary Appendix. We also performed a sensitivity analysis to estimate the 2017 national burden of *C. difficile* infection according to different levels of NAAT use.

RESULTS

BURDEN AND INCIDENCE OF *C. DIFFICILE* INFECTION

The percentage of EIP cases that were diagnosed by means of NAAT increased from 55% in 2011 to 84% in 2016, then decreased to 83% in 2017 (Fig. 1). The number of reported EIP cases was 15,461 in 2011 (10,177 health care–associated and 5284 community-associated cases) and 15,512 in 2017 (7973 health care–associated and 7539 community-associated cases) (Table 1).

Without adjustment for NAAT use, the estimated total national burden of *C. difficile* infection was 476,400 cases (95% CI, 419,900 to 532,900) in 2011, with an estimated incidence of 154.9 (95% CI, 136.5 to 173.3) per 100,000 population, and 462,100 cases (95% CI, 428,600 to 495,600) in 2017, with an estimated incidence of 143.6 (95% CI, 133.2 to 154.0) per 100,000 population (Fig. 2). The estimated national burden of health care–associated *C. difficile* infection was 306,500 cases (95% CI, 269,000 to 343,900) in 2011, with an estimated incidence of 99.6 (95% CI, 87.5 to 111.8) per 100,000 population, and 235,700 cases (95% CI, 221,700 to 249,700) in 2017, with an estimated incidence of 73.3 (95% CI, 68.9 to

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77.6) per 100,000 population. The estimated national burden of community-associated *C. difficile* infection was 170,000 cases (95% CI, 150,900 to 189,000) in 2011, with an estimated incidence of 55.3 (95% CI, 49.1 to 61.4) per 100,000 population, and 226,400 cases (95% CI, 206,900 to 245,900) in 2017, with an estimated incidence of 70.4 (95% CI, 64.3 to 76.4) per 100,000 population.

After adjustment of NAAT use to the 2011 rate of 55%, the estimated burden of *C. difficile* infection decreased from 2012 through 2017 (Fig. 2). Trend analyses showed the adjusted estimate of the total national burden of *C. difficile* infection changed annually by −4% (95% CI, −1 to −6), which resulted in a decrease of 24% (95% CI, 6 to 36) from 2011 through 2017. The adjusted estimate of the national burden of health care–associated *C. difficile* infection changed annually by −6% (95% CI, −4 to −9), which resulted in a decrease of 36% (95% CI, 24 to 54) from 2011 through 2017, whereas there was no change in the adjusted estimate of the national burden of community-associated *C. difficile* infection (0%; 95% CI, −2 to 3). In the sensitivity analysis, the estimated national burden of *C. difficile* infection in 2017 ranged from 244,600 cases (95% CI, 227,300 to 261,800) if no laboratories used NAAT to 508,900 cases (95% CI, 472,600 to 545,200) if all laboratories used NAAT (Fig. S1 in the Supplementary Appendix).

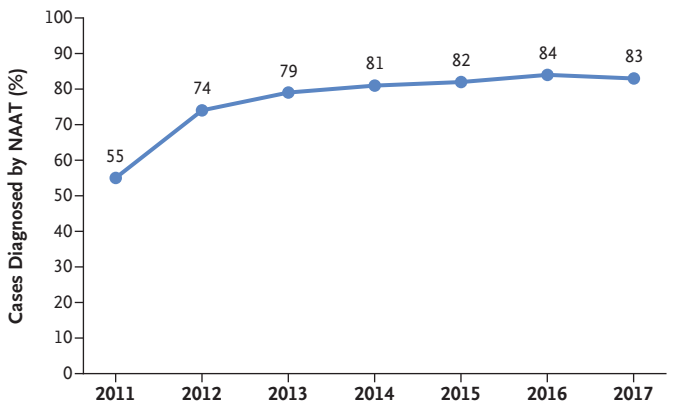

Figure 1. Percentage of Cases of *Clostridioides difficile* Infection (CDI) Diagnosed by Means of NAAT at 10 U.S. Emerging Infections Program Sites, 2011–2017.

Diagnosis of CDI by nucleic acid amplification test (NAAT) was defined as a positive *C. difficile* stool test conducted with the use of NAAT alone or with a multistep testing algorithm in which NAAT was almost always the last test performed. The non-NAAT methods that were used by participating laboratories consisted primarily of an enzyme immunoassay for toxins, used either alone or in combination with an enzyme immunoassay for glutamate dehydrogenase. Less than 1% of participating laboratories used other methods, such as the cell-culture cytotoxicity neutralization assay.

C. DIFFICILE RECURRENCES, HOSPITALIZATIONS, AND IN-HOSPITAL DEATHS

The frequency of first recurrence of *C. difficile* infection, hospitalizations for *C. difficile* infection (with onset of infection in either the community

Table 1. Reported Cases of *Clostridioides difficile* Infection (CDI) and Crude Incidence, According to Epidemiologic Class, at 10 U.S. Emerging Infections Program Sites, 2011–2017.*

Surveillance Year	Population ≥1 Yr of Age	Community-Associated CDI		Health Care–Associated CDI		All CDI	
		No. of Cases	Incidence per 100,000 Persons	No. of Cases	Incidence per 100,000 Persons	No. of Cases	Incidence per 100,000 Persons
	no.						
2011	10,971,319	5284	48.16	10,177	92.76	15,461	140.92
2012†	11,283,326	5967	52.88	10,482	92.90	16,449	145.78
2013	11,552,955	6441	55.75	9,938	86.02	16,379	141.77
2014	11,533,856	6669	57.82	9,662	83.77	16,331	141.59
2015	11,682,427	7697	65.89	9,655	82.65	17,352	148.53
2016	11,777,482	7915	67.20	8,881	75.41	16,796	142.61
2017	11,906,512	7539	63.32	7,973	66.96	15,512	130.28

* The population for each surveillance year is based on estimates from the U.S. Census Bureau. The weighted frequency of cases in Colorado and Georgia was based on 33% random sampling for cases in persons 18 years of age or older.

† Data presented in the table exclude cases from Olmsted County, Minnesota, where CDI surveillance began midyear. The total number of reported CDI cases in 2012 would be 16,564 if CDI cases from Olmsted County, Minnesota, were included.

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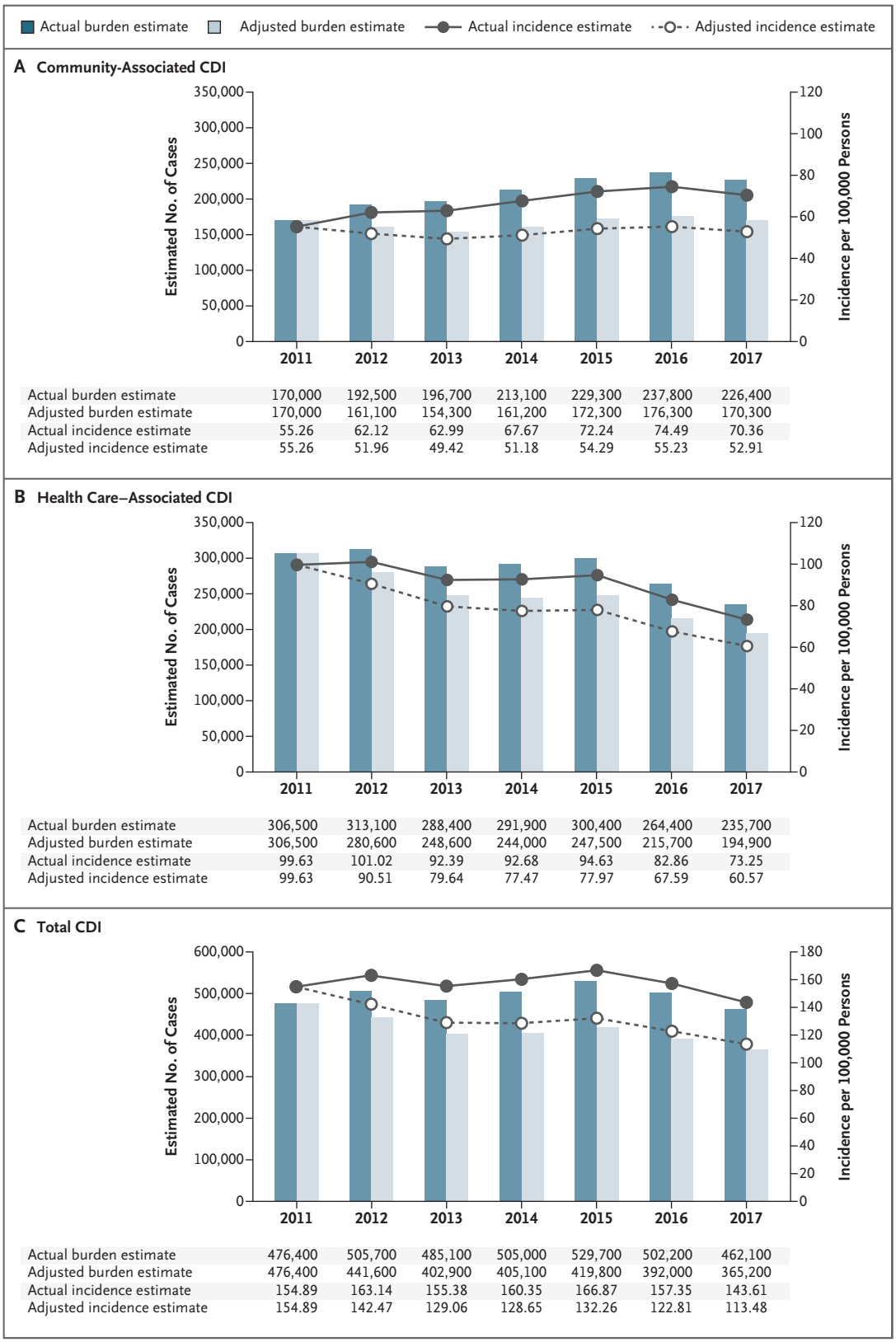

	2011	2012	2013	2014	2015	2016	2017
Actual burden estimate	170,000	192,500	196,700	213,100	229,300	237,800	226,400
Adjusted burden estimate	170,000	161,100	154,300	161,200	172,300	176,300	170,300
Actual incidence estimate	55.26	62.12	62.99	67.67	72.24	74.49	70.36
Adjusted incidence estimate	55.26	51.96	49.42	51.18	54.29	55.23	52.91

	2011	2012	2013	2014	2015	2016	2017
Actual burden estimate	306,500	313,100	288,400	291,900	300,400	264,400	235,700
Adjusted burden estimate	306,500	280,600	248,600	244,000	247,500	215,700	194,900
Actual incidence estimate	99.63	101.02	92.39	92.68	94.63	82.86	73.25
Adjusted incidence estimate	99.63	90.51	79.64	77.47	77.97	67.59	60.57

	2011	2012	2013	2014	2015	2016	2017
Actual burden estimate	476,400	505,700	485,100	505,000	529,700	502,200	462,100
Adjusted burden estimate	476,400	441,600	402,900	405,100	419,800	392,000	365,200
Actual incidence estimate	154.89	163.14	155.38	160.35	166.87	157.35	143.61
Adjusted incidence estimate	154.89	142.47	129.06	128.65	132.26	122.81	113.48

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Figure 2 (facing page). U.S. National Estimates of the Burden and Incidence of Community-Associated CDI, Health Care–Associated CDI, and Total CDI, 2011–2017.
The estimates of the actual national burden and incidence for each year are based on the actual rate of use of the nucleic acid amplification test (NAAT) in that year, with adjustment for the age, sex, and race of the U.S. population. The estimates of the adjusted national burden and incidence for each year are based on an adjustment of NAAT use to the 2011 rate of 55%, with additional adjustment for the age, sex, and race of the U.S. population. The estimates of the national burden of community-associated CDI and health care–associated CDI do not always add up to the estimated total burden of CDI because of rounding.

or the hospital), and in-hospital deaths at the 10 EIP sites fluctuated from 2011 through 2017 and was higher among health care–associated infections than among community-associated infections (Table 2). A similar pattern was observed with the estimates of the national incidence and burden of first recurrence of *C. difficile* infection, hospitalizations, and in-hospital deaths (Table 3). When the rate of NAAT use was held at 55%, there were no significant changes in the adjusted estimates of the national burden of first recurrences and in-hospital deaths. In contrast, the adjusted estimate of the total national burden of hospitalizations for *C. difficile* infection changed annually by –4% (95% CI, –8 to 0), which resulted in a decrease of 24% (95% CI, 0 to 48) from 2011 through 2017. The adjusted estimate of the national burden of hospitalizations among health care–associated infections changed annually by –5% (95% CI, –1 to –9), but there was no significant change among community-associated infections.

ISOLATE CHARACTERIZATION

From 2012 through 2017, a total of 969 to 1443 *C. difficile* isolates were submitted annually to the CDC (Table S1), consisting of 275 distinct community-associated and 227 distinct health care–associated strain types. Ribotypes 027, 106, 014, 002, and 020 were the most common community-associated and health care–associated ribotypes identified each year, except in 2017, when ribotype 020 was replaced by 076 as one of the top health care–associated ribotypes. From 2012 through 2017, ribotype 027 decreased significantly among health care–associated isolates (21% vs. 15%; P=0.02) and community-associated isolates (17% vs. 6%; P<0.001). Including the 2011 isolates,[10] there was an even greater decline in the prevalence of the North American Pulsed Field 1 (NAP1) strain (which represents mostly ribotype 27) or of ribotype 027 among health care–associated isolates (31% in 2011 vs. 15% in 2017; P<0.001) and among community-associated isolates (19% in 2011 vs. 6% in 2017; P<0.001).

Because ribotype 027 is more likely than other strains to be detected by enzyme immunoassays for toxins in stool because of its increased toxin production[15] and because the decreased use of enzyme immunoassays for toxins might affect its prevalence, we analyzed data from laboratories that used NAAT and found a similar decreasing trend of ribotype 027 during this period. Despite its decline, ribotype 027 remained the predominant health care–associated ribotype during this period, whereas ribotype 106 has been the most prevalent community-associated ribotype since 2014.

DISCUSSION

The estimated burden of *C. difficile* infection in the United States declined from 2011 through 2017, despite the increasing use of the more sensitive diagnostic test of NAAT. When NAAT use was held constant over this period, we observed a significant decrease in the adjusted estimate of the national burden of *C. difficile* infection, which supports a true decline in *C. difficile* infection. This decrease was driven by the decline in health care–associated infections, which decreased annually by an adjusted 6%, whereas there was no change in the adjusted estimate of the burden of community-associated infections. In contrast, a 2015 U.S. acute care point-prevalence survey indicated that the prevalence of health care–associated *C. difficile* infection had not changed as compared with 2011; however, the survey did not account for increased NAAT use, which could have masked a true reduction in *C. difficile* infection.[16]

The decrease in health care–associated *C. difficile* infection probably reflects a decline in both cases with an onset associated with a long-term care facility and hospital-onset cases. We previously observed a 55% decrease in the adjusted incidence of *C. difficile* infection with an onset

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Table 2. Estimates of First Recurrences, Hospitalizations, and In-Hospital Deaths Associated with CDI, According to Epidemiologic Class, at 10 U.S. Emerging Infections Program Sites, 2011–2017.*

Surveillance Year	Estimated First Recurrences		Estimated Hospitalizations		Estimated In-Hospital Deaths	
	Community-Associated CDI	Health Care–Associated CDI	Community-Associated CDI	Health Care–Associated CDI	Community-Associated CDI	Health Care–Associated CDI
2011	678	1959	1691	6145	159	889
2012	703	1848	2130	6527	161	571
2013	879	1665	2259	6398	202	581
2014	843	1690	2320	6537	142	670
2015	1066	1740	2633	6643	198	812
2016	1092	1380	2740	6024	190	750
2017	967	1221	2505	5483	164	573

* The frequency of cases was weighted to account for sampling in two of the Emerging Infections Program sites (Colorado and Georgia) and sampling of health care–associated CDI cases. Recurrence refers to the first recurrent episode, defined as a positive stool specimen within 2 to 8 weeks after the initial positive test. Hospitalization includes admission on the day of or in the 6 calendar days after diagnosis of CDI. In-hospital deaths refer to deaths that occurred during hospitalization.

associated with a long-term care facility across EIP sites from 2011 through 2015.[17] According to the CDC National Healthcare Safety Network, the *C. difficile* standardized infection ratio, which is a risk-adjusted measure of hospital-onset *C. difficile* infection, declined by 20% from 2015 through 2017.[18] Several factors probably contributed to the decrease in health care–associated *C. difficile* infection, including a decline in ribotype 027, which might be partly driven by reduced fluoroquinolone use in U.S. hospitals.[17,19] The association between fluoroquinolones and *C. difficile* infection is well described,[3,4,20] and in one study, hospitals that achieved a 30% reduction in fluoroquinolone use observed a 19% reduction in hospital-onset *C. difficile* infection.[21] In England, the restriction of fluoroquinolone prescribing probably contributed to the drastic reduction of *C. difficile* infection through a deselection of fluoroquinolone-resistant strains, including ribotype 027.[22] Adherence to recommended infection-prevention practices may have also decreased health care–associated infections, as shown by several successful local and regional initiatives for the prevention of *C. difficile* infection.[23,24] Public reporting of *C. difficile* infection and pay-for-performance programs probably increased prevention efforts. With the rise in NAAT use and the potential for overdiagnosis of *C. difficile* infection, there has been a greater emphasis on diagnostic stewardship to counter the effects of the increased sensitivity of NAAT by reducing inappropriate testing,[25] which may have also reduced health care–associated infections.

In contrast, estimates of community-associated *C. difficile* infection did not change after accounting for NAAT use. Several factors might have contributed to the high burden of community-associated *C. difficile* infection, such as changes in testing practices. This may include increased frequency of *C. difficile* testing owing to increased awareness among outpatient providers. Diagnostic stewardship efforts have primarily targeted inpatient settings, and little is known regarding the extent to which overtesting might be occurring in outpatient settings. High use of outpatient antibiotics is another contributing factor. In studies of community-associated *C. difficile* infection, approximately 60% of patients had recent antibiotic use.[8,26] Although U.S. outpatient antibiotic prescription rates decreased from 2011 to 2016,[27] at least 30% of outpatient antibiotic prescriptions are estimated to be unnecessary,[28] which highlights the need to improve outpatient prescribing.

Other contributing factors might be related to community exposures, given that 18% of patients with community-associated *C. difficile* infection had no recent outpatient health care exposures.[8,26] *C. difficile* transmission among households and between humans and domestic and farm animals has been reported,[29,30] and although a

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Table 3. U.S. National Estimates of First Recurrences, Hospitalizations, and In-Hospital Deaths Associated with CDI, According to Epidemiologic Class, 2011–2017.*

Variable	2011	2012	2013	2014	2015	2016	2017
Estimated first recurrences							
Community-associated CDI							
No. (95% CI)	24,100 (19,000–29,300)	23,400 (19,500–27,400)	28,800 (24,900–32,800)	29,300 (24,100–34,500)	35,300 (29,700–40,900)	33,600 (29,000–38,300)	31,300 (26,600–36,000)
Incidence per 100,000 persons (95% CI)	7.9 (6.2–9.5)	7.6 (6.3–8.8)	9.2 (8.0–10.5)	9.3 (7.7–11.0)	11.1 (9.4–12.9)	10.5 (9.1–12.0)	9.7 (8.3–11.2)
Health care–associated CDI							
No. (95% CI)	60,500 (50,100–70,800)	53,900 (44,100–63,700)	48,500 (41,800–55,100)	55,600 (46,800–64,400)	58,100 (51,300–64,900)	43,500 (37,500–49,400)	38,500 (32,100–44,800)
Incidence per 100,000 persons (95% CI)	19.7 (16.3–23.0)	17.4 (14.2–20.6)	15.5 (13.4–17.7)	17.7 (14.9–20.5)	18.3 (16.2–20.5)	13.6 (11.8–15.5)	12.0 (10.0–13.9)
Estimated hospitalizations							
Community-associated CDI							
No. (95% CI)	52,500 (43,800–61,100)	61,800 (54,200–69,500)	66,000 (58,900–73,200)	71,600 (61,200–81,900)	76,300 (68,200–84,300)	79,100 (68,000–90,300)	69,900 (61,100–78,600)
Incidence per 100,000 persons (95% CI)	17.1 (14.3–19.9)	20.0 (17.5–22.4)	21.2 (18.9–23.5)	22.7 (19.4–26.0)	24.0 (21.5–26.6)	24.8 (21.3–28.3)	21.7 (19.0–24.4)
Health care–associated CDI							
No. (95% CI)	186,600 (155,500–217,600)	189,600 (165,700–213,500)	178,400 (158,300–198,500)	190,200 (171,400–209,000)	196,000 (179,700–212,300)	173,100 (158,900–187,200)	154,100 (140,700–167,400)
Incidence per 100,000 persons (95% CI)	60.7 (50.6–70.8)	61.2 (53.5–68.9)	57.2 (50.7–63.6)	60.4 (54.4–66.4)	61.8 (56.6–66.9)	54.2 (49.8–58.7)	47.9 (43.7–52.0)
Estimated in-hospital deaths							
Community-associated CDI							
No. (95% CI)	5000 (3200–6700)	5100 (3000–7100)	5700 (3600–7700)	5800 (3800–7900)	5800 (3900–7700)	7200 (3400–11,000)	4300 (2300–6300)
Incidence per 100,000 persons (95% CI)	1.6 (1.0–2.2)	1.6 (1.0–2.3)	1.8 (1.2–2.5)	1.9 (1.2–2.5)	1.8 (1.2–2.4)	2.3 (1.1–3.4)	1.3 (0.7–2.0)
Health care–associated CDI							
No. (95% CI)	25,600 (18,200–33,000)	15,300 (11,000–19,700)	16,700 (12,400–21,100)	19,000 (14,500–23,400)	23,200 (19,800–26,600)	19,500 (15,800–23,200)	16,200 (13,300–19,200)
Incidence per 100,000 persons (95% CI)	8.3 (5.9–10.7)	5.0 (3.6–6.4)	5.4 (4.0–6.8)	6.0 (4.6–7.5)	7.3 (6.2–8.4)	6.1 (5.0–7.3)	5.0 (4.1–6.0)

* Recurrence refers to the first recurrent episode, defined as a positive stool specimen within 2 to 8 weeks after the initial positive test. Hospitalization includes admission on the day of or in the 6 calendar days after diagnosis of CDI. In-hospital deaths refer to deaths that occurred during hospitalization.

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direct foodborne link has not been established, toxigenic *C. difficile* has been cultured from retail meat and vegetables.[31,32] A distinct pattern of genetic relatedness between some *C. difficile* isolates has been observed in Europe that does not show the country, regional, or within-hospital clustering that would suggest local person-to-person transmission but instead seems to suggest dissemination through other routes, such as the food chain.[33]

We observed a decrease in the adjusted estimate of the burden of hospitalizations among health care–associated *C. difficile* infections, which resulted in a 24% decrease in the total adjusted burden of all hospitalizations for *C. difficile* infection, as included in the CDC's *Antibiotic Resistance Threats in the United States, 2019*.[34] This is not surprising, given that health care–associated *C. difficile* infection has declined, thereby reducing the burden of hospitalizations. The adjusted estimate of the burden of in-hospital deaths did not change; however, we did not assess for attributable mortality. The adjusted estimate of the burden of first recurrences also did not change, which underscores the need to improve the identification of patients at high risk for recurrence to help target prevention strategies.

Although community-associated strains were more diverse than health care–associated strains, the most common ribotypes were the same in both groups and have been frequently observed in Europe.[33] In a finding consistent with data from the U.S. Veterans Health Administration and from other countries,[35,36] ribotype 027 decreased significantly from 2011 through 2017, even among isolates from laboratories that used NAAT, which indicates that the decrease is not likely to be due to decreased use of enzyme immunoassays for toxins. Although ribotype 027 could have declined naturally, the widespread decrease in fluoroquinolone use was probably a factor.[17,19] Other strains that are associated with severe disease, such as ribotypes 078 and 244,[37,38] have rarely been identified among U.S. clinical isolates.

This analysis has several limitations. The case definition was based on a laboratory diagnosis, and it is possible that some identified cases were only colonized with *C. difficile*. We attempted to identify every case occurring in catchment-area residents, but it is possible that some cases were missed (e.g., in residents hospitalized outside the catchment area). Additional limitations are discussed in the Supplementary Appendix.

The estimated burden of *C. difficile* infection in the United States decreased by an adjusted 24% from 2011 through 2017, owing to a decline in health care–associated infections. Community-associated infections did not decrease and contributed to nearly 50% of the burden of *C. difficile* infection in 2017. Continued efforts are needed to improve infection prevention and diagnostic and antibiotic stewardship in both inpatient and outpatient settings. The CDC Targeted Assessment for Prevention Strategy helps facilities target wards with the highest rates of *C. difficile* infection to improve infection-prevention practices.[39] The CDC Core Elements of Antibiotic Stewardship provide a framework to improve antibiotic use across the health care spectrum.[40] Additional efforts include incentivizing facilities to work collaboratively across a region and improving our understanding of the role of non–health care reservoirs in *C. difficile* transmission. The development of a *C. difficile* vaccine and exploration of innovative strategies, such as gut microbiome restoration for primary prevention of *C. difficile* infection, might also further reduce the burden of *C. difficile* infection.

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Supported by the Centers for Disease Control and Prevention.

Dr. Dumyati reports receiving fees for serving on a drug safety monitoring board from Seres Therapeutics; Dr. Kainer, receiving fees for serving on a board and travel support from Infectious Disease Consulting, fees for the production of CME materials and travel support from WebMD, and consulting fees and travel support from Pfizer; and Dr. Gerding, receiving advisory board fees from Ferring Pharmaceuticals, Rebiotix, Merck, Da Volterra, Summit Therapeutics, and Actelion, receiving consulting fees from Pfizer, Sanofi Pasteur, MGB Biopharma, and Medpace, and holding patents (US No. 6,635,260, CAN No. 2,232,001, and EU No. 0952773) on methods and compositions for the prevention and treatment of *Clostridium difficile*–associated diseases. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank the following persons for their contribution to the Emerging Infections Program *C. difficile* infection surveillance activity: Fernanda Lessa, Jessica Cohen, and Jamie Barnes from the Centers for Disease Control and Prevention; Erin Parker, Joelle Nadle, and Karen Click from the California Emerging Infections Program; James Hadler from the Connecticut Emerging Infections Program; Wendy Baughman, Leigh Ann Clark, Olivia Almendares, Zirka Smith, and Andrew Revis from the Georgia Emerging Infections Program and the Atlanta Research and

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Education Foundation; Ruth Lynfield from the Minnesota Department of Health; Nicole Kenslow and Kristina Flores from the University of New Mexico and the New Mexico Emerging Infections Program; Corinne Davis and Rose Devasia from the Tennessee Department of Health; and Susan Sambol and Laurica Petrella-Zitco from the Edward Hines, Jr. Veterans Affairs Hospital.

APPENDIX

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