

Emerging Infections Program
Healthcare-Associated Infections–Community Interface Report
***Clostridioides difficile* Infection Surveillance, 2021**

Surveillance Catchment Areas

California (1 county San Francisco area), Colorado (5 county Denver area); Connecticut (1 county New Haven area); Georgia (8 county Atlanta area); Maryland (9 Eastern Shore and 2 western counties); Minnesota (5 counties); New Mexico (1 county Albuquerque area); New York (1 county Rochester area); Oregon (1 rural county); and Tennessee (1 county Nashville area).

Population

The surveillance area represents 12,109,721 persons.

Source: U.S. Census Bureau, Population Division, Vintage 2021 Special Tabulation.

Case Definition

An incident case of *Clostridioides difficile* infection (CDI) was defined as a *C. difficile*-positive stool test (toxin or molecular assay) from a person ≥ 1 year old with no positive test in the prior 8 weeks.

Methods

Case finding was active, laboratory-based, and population-based. Laboratories serving the surveillance catchment areas reported positive *C. difficile* tests to EIP staff and were routinely audited with a goal of complete case ascertainment.

An initial chart review was performed on all CDI cases in eight EIP sites and on all pediatric cases and a 1/3 random sample of cases age 18 years and older in the two remaining EIP sites with the largest surveillance catchment areas (CO and GA). A subsequent comprehensive chart review was performed on all community-onset cases and a subset of healthcare-facility onset cases.

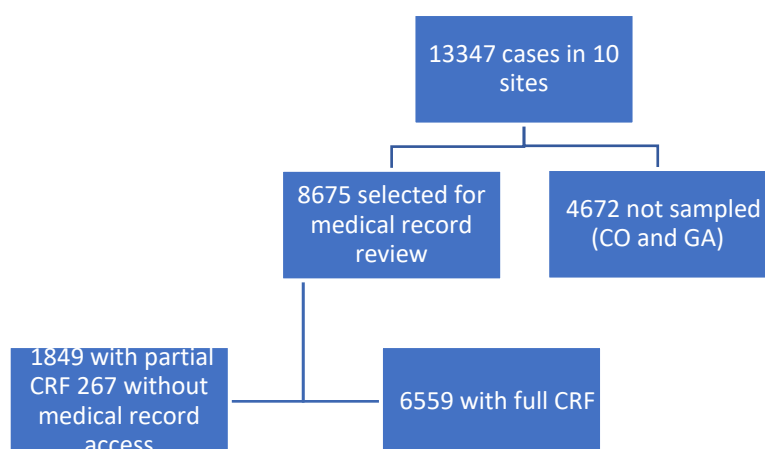
A standardized case report form (CRF) was completed for each incident case through review of medical records. Inpatient and outpatient medical records were reviewed for information on patient demographics, clinical syndrome, outcome of illness, and relevant healthcare exposures.

A convenience sample of stool specimens and swabs was sent to reference laboratories for *C. difficile* isolation. Recovered isolates were sent to CDC for molecular typing and characterization. From 2012-2018, PCR-ribotyping was used for EIP strain typing. Beginning in 2018, whole genome sequencing (WGS) and analysis were used for the molecular characterization of *C. difficile* isolates. *C. difficile* isolates were sequenced

(Illumina MiSeq or NovaSeq) by the CDC or the Minnesota Department of Health Public Health Laboratory. Assembly and multi-locus sequence typing (MLST) were performed using CDC's in-house Portable Healthcare Nextgen Informatics (PHoeNix) pipeline (<https://github.com/CDCgov/phoenix>).

A CDI case was classified as community-associated (CA) if the *C. difficile*-positive stool specimen was collected on an outpatient basis or within 3 days after hospital admission in a person with no documented overnight stay in a healthcare facility in the preceding 12 weeks. All CDI cases that did not meet the aforementioned criteria were classified as healthcare-associated (HA). HA cases with disease onset outside of a healthcare facility but with documented overnight stay in a healthcare facility in the preceding 12 weeks were classified as community-onset, healthcare-facility associated (CO-HCFA). HA cases with disease onset in a healthcare facility were classified as healthcare-facility onset (HCFO). HCFO cases were further classified into hospital onset or long-term care facility onset. Incidence rates were calculated using US Census population estimates.

CDI surveillance data undergo regular data cleaning to ensure accuracy and completeness. Patients with case data as of 01/31/2024 were included in this analysis. Because data can be updated as needed, analyses of datasets generated on a different date may yield slightly different results.



Results

Table 1 – Reported Number of CDI Cases and Crude Incidence by Sex, Age Group, Race, and Epidemiologic Classification Among the 10 EIP Sites

Sex	Population ≥1 Year of Age	Community-Associated CDI ^a , No. ^c	Community-Associated CDI ^a , Incidence ^b	Healthcare-Associated CDI ^a , No. ^c	Healthcare-Associated CDI ^a , Incidence ^b	All CDI, No. ^c	All CDI, Incidence ^b
Male	5,952,832	2497	42.0	3081	51.7	5578	93.7
Female	6,156,889	4310	70.0	3459	56.2	7769	126.2

Age group	Population ≥1 Year of Age	Community-Associated CDI ^a , No. ^c	Community-Associated CDI ^a , Incidence ^b	Healthcare-Associated CDI ^a , No. ^c	Healthcare-Associated CDI ^a , Incidence ^b	All CDI, No. ^c	All CDI, Incidence ^b
1-17 years	2,506,710	417	16.6	179	7.2	596	23.8
18-44 years	4,728,721	1668	35.3	838	17.7	2506	53.0
45-49 years	764,997	339	44.3	298	39.0	637	83.3
50-54 years	794,283	502	63.3	365	45.9	867	109.2
55-59 years	780,720	539	68.8	550	70.4	1087	139.2
60-64 years	732,551	653	89.2	697	95.1	1350	184.3
65-70 years	613,116	608	99.1	735	119.9	1343	219.0
70-74 years	499,997	723	144.7	868	173.5	1591	318.2
75-79 years	310,774	558	179.6	770	247.7	1328	427.3
80+ years	377,852	802	212.2	1240	328.2	2042	540.4

Race ^a	Population ≥1 Year of Age	Community-Associated CDI ^a , No. ^c	Community-Associated CDI ^a , Incidence ^b	Healthcare-Associated CDI ^a , No. ^c	Healthcare-Associated CDI ^a , Incidence ^b	All CDI, No. ^c	All CDI, Incidence ^b
White	8,022,836	5341	66.0	4623	57.6	9965	124.3
Other	4,086,885	1466	35.9	1916	46.9	3382	82.8

Total	Population ≥1 Year of Age	Community-Associated CDI ^a , No. ^c	Community-Associated CDI ^a , Incidence ^b	Healthcare-Associated CDI ^a , No. ^c	Healthcare-Associated CDI ^a , Incidence ^b	All CDI, No. ^c	All CDI, Incidence ^b
Total	12,109,721	6808	56.2	6539	54.0	13347	110.2

^a The epidemiologic classification was statistically imputed for 3% of the CDI cases selected for medical record review, and race was statistically imputed for 15% of the CDI cases selected for medical record review. The weighted frequency of cases in Colorado and Georgia was based on 33% random sampling for cases aged ≥18 years.

^b Cases per 100,000 persons.

^c Subcategories may not add to total due to rounding.

Table 2 – Diagnostic Assay Results of CDI Cases (N=13347)

Diagnostic assay	N	%
Toxin positive	4140	31
Nucleic acid amplification test (NAAT) positive/toxin negative	4465	33
NAAT positive/toxin result unknown ^a	4741	36
Unspecified assay	1	<1

^a Includes cases diagnosed mainly by NAAT or multiplex PCR panel (i.e., toxin enzyme immunoassay or cell cytotoxicity assay was not performed) or by NAAT as part of a multistep algorithm where the toxin result was not readily known

Table 3 – CDI Cases by Epidemiologic Classification (N=13347)

Epidemiologic classification	N	%
Hospital onset	1710	13
LTCF onset	632	5
COHCFA	1774	13
CA	4292	32
Unknown ^a	4939	37

^a Includes 4672 non-sampled cases

Table 4 – CDI Cases by Race and Ethnicity (N=13347)

Race/Ethnicity	N	%
Hispanic, any race	892	7
Not known to be Hispanic ^a - White ^b	6463	48
Not known to be Hispanic ^a - Black or African American ^c	2110	16
Not known to be Hispanic ^a - Asian ^d	322	2
Not known to be Hispanic ^a - Other or multiple races ^e	118	<1
Non-Hispanic- Unknown race	225	2
Unknown ethnicity and race	3217	24

^a Records either indicated ethnicity was non-Hispanic, or ethnicity was not known.

^b 528 cases with unknown ethnicity

^c 99 cases with unknown ethnicity

^d 47 cases with unknown ethnicity

^e American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported; 11 cases with unknown ethnicity

Table 5 – Location of CDI Cases on the Third Calendar Day Before Incident Specimen Collection (N=8675)

Location of patient before incident specimen collection	N	%
Private residence	5971	69
Long-term care facility	649	7
Acute-care hospital (inpatient)	1633	19
Long-term care acute care hospital	45	<1
Homeless	96	1
Incarcerated	7	<1
Other	7	<1
Unknown	267	3

Table 6 – Location of CDI Cases at Time of Incident Specimen Collection (N=8675)

Location of incident specimen collection	N	%
Outpatient setting or emergency department	4371	50
Acute care hospital	3566	41
Long-term care facility	427	5
Long-term acute care hospital	39	<1
Other	3	<1
Unknown	269	3

Table 7 – Selected Clinical Characteristics of CDI Cases (N=6559, except where indicated)

Clinical characteristic	N	%
Charlson comorbidity index - 0	2642	40
Charlson comorbidity index - 1	1254	19
Charlson comorbidity index - ≥ 2	2663	41
Underlying conditions - Cardiovascular disease ^{a,b}	1382	21
Underlying conditions - Diabetes mellitus ^a	1407	21
Underlying conditions - Chronic pulmonary disease ^{a,c}	1419	22
Underlying conditions - Gastrointestinal disease ^{a,d}	1665	25
Underlying conditions - Gastrointestinal disease – Diverticular disease ^a	747	11
Underlying conditions - Gastrointestinal disease – Inflammatory bowel disease ^a	453	7
Underlying conditions - Gastrointestinal disease – Peptic ulcer disease ^a	174	3
Underlying conditions - Gastrointestinal disease – Short gut syndrome ^a	20	<1
Underlying conditions - Gastrointestinal disease – Liver disease ^a	439	7
Underlying conditions - Chronic renal disease ^a	1241	19
Underlying conditions - Neurologic condition, any ^a	1309	20
Underlying conditions - Malignancy (hematologic or solid organ) ^a	1122	17
Underlying conditions - Transplant (hematopoietic stem cell or solid organ) ^a	205	3
Positive test for SARS-CoV-2 during hospitalization and on or before date of incident specimen collection ^e	94	3

^a Underlying conditions are not mutually exclusive.

^b Defined as myocardial infarction, congestive heart failure, congenital heart disease, stroke, transient ischemic attack, or peripheral vascular disease.

^c Defined as cystic fibrosis or any chronic respiratory condition resulting in symptomatic dyspnea.

^d Defined as diverticular disease, inflammatory bowel disease, peptic ulcer disease, short gut syndrome, or liver disease.

^e Among patients in the hospital on the date of incident specimen collection (N=2757). Excludes patients who were admitted to the hospital after the date of incident specimen collection. A positive SARS-CoV-2 test was defined as any positive viral test for SARS-CoV-2, including antigen and nucleic acid amplification tests.

Table 8 – Selected Healthcare Exposures and Risk Factors of Incident CDI Cases in the 12 Weeks Before the Date of Incident Specimen Collection by Epidemiologic Classification (N=6559)

	CA (N=4292)		COHCFA (N=1774)		HCFO (N=493)	
Healthcare Exposure ^a	N	%	N	%	N	%
Acute care hospitalization	0	0	1735	98	244	49
Long-term care facility residence	0	0	187	11	178	36
Long-term acute care hospitalization	0	0	7	<1	9	2
Surgery	196	5	491	28	125	25
Emergency room	881	21	741	42	142	29
Observation unit	69	2	103	6	17	3
Chronic dialysis	106	2	163	9	51	10

^a Healthcare exposure categories are not mutually exclusive.

Table 9 – Antibiotic Use in the 12 Weeks Before the Date of Incident Specimen Collection (N=6559)

Antibiotic ^a	N	%
Any antibiotic	4006	61
Aminoglycosides	83	1
Beta-lactam / beta-lactamase inhibitor combinations	1284	20
Carbapenems	164	3
Cephalosporins	2062	31
Clindamycin	464	7
Fluoroquinolones	805	12
Glycopeptides	1178	18
Macrolides	261	4
Monobactam	16	<1
Penicillins	385	6
Trimethoprim or Trimethoprim/Sulfamethoxazole	366	6
Tetracyclines	274	4
Other antibiotic	1153	18

^a Antibiotic use categories are not mutually exclusive.

Table 10 – Treatment of Incident CDI Cases (N=6559)

Treatment ^a	N	%
Any treatment ^b	5605	85
Oral or rectal vancomycin (excluding vancomycin tapers) ^c	4725	72
Vancomycin tapers	390	6
Metronidazole	1079	16
Fidaxomicin	409	6
Bezlotoxumab	25	<1
Stool transplant	33	<1

^a Treatment categories are not mutually exclusive.

^b Includes any course of CDI antibiotic therapy, bezlotoxumab, or stool transplant.

^c Includes 3 patients receiving vancomycin prophylaxis after treatment of incident CDI.

Table 11 – Outcomes of Incident CDI Cases (N=6559, except where indicated)

Outcome	N	%
Toxic megacolon ^a	18	<1
Ileus ^a	156	2
Pseudomembranous colitis ^a	32	<1
White blood cell count $\geq 15,000/\mu\text{l}$ ^a	1107	17
Recurrent infection ^a	763	12
Hospitalization on the day of or within 6 days after the date of incident specimen collection ^{a, b}	2868	44
ICU admission one day before, the day of, or within 6 days after the date of incident specimen collection ^a	384	6
In-hospital death ^a	176	3
Discharge location after acute-care hospitalization among patients who survived ^c - Private Residence	2184	81
Discharge location after acute-care hospitalization among patients who survived ^c - Long-term care facility	402	15
Discharge location after acute-care hospitalization among patients who survived ^c - Long-term acute care hospital	12	<1
Discharge location after acute-care hospitalization among patients who survived ^c - Other	75	3
Discharge location after acute-care hospitalization among patients who survived ^c - Unknown	19	<1

^a Outcomes, except for location of discharge from acute care hospitalization, are not mutually exclusive.

^b Data include 345 cases considered to be hospital-onset.

^c N=2692

Laboratory Characterization

In 2021, 1099 *C. difficile* isolates were characterized by CDC. The total number of isolates received from each site ranged from 38 to 300, with a median of 76. Most isolates (95%) were collected from patients residing in metropolitan areas.

Among all isolates submitted, 113 distinct sequence types were detected. Among the 597 community-associated isolates, 87 STs were observed. ST42 was most common (13.1%), followed by ST2 (10.7%), ST8 (7.7%), and ST3 (4.7%); all other STs accounted for <4% of isolates (Table 12). Among the 502 healthcare-associated isolates, 67 STs were observed. ST2 was most common (12.7%), followed by ST8 and ST42 (11.4% each), ST1 (8.4%), ST34 (4.4%), and ST110 (4.2%); all other STs accounted for <4% of isolates (Table 13). A crosswalk to assist with evaluation of ST data with previous ribotype data is provided in the appendix.

Table 12 – Frequency of Sequence Types Among Community-Associated *C. difficile* Isolates, 2021 (N=597)

Sequence Type (ST)	Number of Isolates	Percentage of Isolates
ST42	78	13.1%
ST2	64	10.7%
ST8	46	7.7%
ST3	28	4.7%
ST14	23	3.9%
ST110	20	3.4%
ST11	20	3.4%
ST1	20	3.4%
ST34	19	3.2%
ST43	18	3.0%
All Other STs	261	43.7%

Table 13 – Frequency of Sequence Types Among Healthcare-Associated *C. difficile* Isolates, 2021 (N=502)

Sequence Type (ST)	Number of Isolates	Percentage of Isolates
ST2	64	12.7%
ST8	57	11.4%
ST42	57	11.4%
ST1	42	8.4%
ST34	22	4.4%
ST110	21	4.2%
ST58	17	3.4%
ST14	17	3.4%
ST53	13	2.6%
ST3	13	2.6%
ST11	13	2.6%
All Other STs	166	33.1%

Summary

Surveillance data from 2021 represent the eleventh year of population-based surveillance for CDI conducted among all 10 Emerging Infections Program sites. The crude overall incidence rate of CDI in 2021 was 110.2 cases per 100,000 persons, with a slightly higher incidence of community associated cases (56.2 cases per 100,000 persons) compared with healthcare-associated cases (54.0 cases per 100,000 persons). The incidence rate of CDI increased with age and was higher in women than in men and higher in White persons than in persons of other races.

Underlying conditions were commonly reported among CDI cases, with 41 percent having a Charlson comorbidity index of ≥ 2 . Antibiotic use in the prior 12 weeks was reported for 61 percent of CDI cases. Eighty-

five percent of CDI cases were treated, with vancomycin being the most common treatment given. CDI-related complications, such as toxic megacolon and ileus, were rare.

Citation

Centers for Disease Control and Prevention. 2024. Emerging Infections Program, Healthcare-Associated Infections – Community Interface Surveillance Report, *Clostridioides difficile* infection (CDI), 2021. Available at: [Insert link to the report].

For more information, visit our web sites:

- *Clostridioides difficile* Infection (CDI) Tracking [[Clostridioides difficile Infection \(CDI\) Surveillance | HAIs | CDC](https://www.cdc.gov/healthcare-associated-infections/php/haic-eip/cdiff.html?CDC_AAref_Val=https://www.cdc.gov/hai/eip/cdiff-tracking.html)] (https://www.cdc.gov/healthcare-associated-infections/php/haic-eip/cdiff.html?CDC_AAref_Val=https://www.cdc.gov/hai/eip/cdiff-tracking.html)
- Healthcare-Associated Infections - Community Interface Data Visualization (HAICViz) [[HAICViz | HAIs | CDC](https://www.cdc.gov/healthcare-associated-infections/php/haic-eip/haicviz.html)] (<https://www.cdc.gov/healthcare-associated-infections/php/haic-eip/haicviz.html>)
- *Clostridioides difficile* Infection [[About C. diff | C. diff | CDC](https://www.cdc.gov/c-diff/about/?CDC_AAref_Val=https://www.cdc.gov/hai/organisms/cdiff/cdiff_infect.html)] (https://www.cdc.gov/c-diff/about/?CDC_AAref_Val=https://www.cdc.gov/hai/organisms/cdiff/cdiff_infect.html)

Appendix

A collection of isolates representing common ribotypes observed from previous EIP surveillance years underwent whole genome sequencing and MLST. Some STs corresponded to a single ribotype and some to multiple or overlapping ribotypes. Table A1 represents a crosswalk to assist with evaluation of previous ribotype data for the top community-associated and healthcare-associated STs observed from 2018–2021.

Table A1. *C. difficile* Multi-locus Sequence Types and Associated PCR Ribotype(s)

Sequence Type (ST)	Associated PCR Ribotype(s)
ST1	027, 036, A75
ST2	014, 020, 076, 077, 207, A27, A30
ST3	001_072, 009, 305
ST8	002
ST10	015
ST11	078, 126
ST14	014, 077, 207, A27
ST34	056
ST41	106, 153, 171, A32, B14
ST42	106, 002, 077
ST43	054
ST53	024, 103, 351
ST55	070, A12
ST58	056, A05
ST110	014, 020, 076, 154, 207, A27