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Characterization of Healthcare-Associated and Community-Associated *Clostridioides difficile* Infections among Adults, Canada, 2015–2019

Appendix

Surveillance Case Definitions and Eligibility Criteria

Clostrioides difficile Infection (CDI)

A "primary" episode of CDI is defined as either the first episode of CDI ever experienced by the patient or a new episode of CDI, which occurs greater than eight weeks after the diagnosis of a previous episode in the same patient.

A patient is identified as having CDI if:

- The patient has diarrhea or fever, abdominal pain and/or ileus AND a laboratory confirmation of a positive toxin assay or positive polymerase chain reaction (PCR) for *C. difficile* (without reasonable evidence of another cause of diarrhea)

OR

- The patient has a diagnosis of pseudomembranes on sigmoidoscopy or colonoscopy (or after colectomy) or histological/pathological diagnosis of CDI

OR

- The patient is diagnosed with toxic megacolon (in adult patients only)

Diarrhea is defined as one of the following:

- More watery/unformed stools in a 36-h period
- or more watery/ unformed stools in a 24-h period and this is new or unusual for the patient (in adult patients only)

Exclusion:

- Any patients younger than one year
- Any pediatric patients (aged one year to younger than 18 y) with alternate cause of diarrhea found (i.e., rotavirus, norovirus, enema or medication, etc.) are excluded even if *C. difficile* diagnostic test result is positive

CDI Case Classification

Once a patient has been identified with CDI, the infection will be classified further based on the following criteria and the best clinical judgment of the healthcare and/or infection prevention and control practitioner.

Healthcare-associated (acquired in your facility) CDI case definition

- Related to the current hospitalization
    - The patient's CDI symptoms occur in your healthcare facility three or more days (or ≥72 h) after admission
- Related to a previous hospitalization
    - The patient's CDI symptoms occur less than three days after the current admission (or less than 72 h) AND the patient had been previously hospitalized at your healthcare facility and discharged within the previous four weeks
- Related to a previous healthcare exposure at your facility
    - The patient's CDI symptoms occur less than three days after the current admission (or less than 72 h) AND the patient had a previous healthcare exposure at your facility within the previous four weeks

Healthcare-associated (acquired in any other healthcare facility) CDI case definition

- Related to a previous hospitalization at any other healthcare facility
    - The patient's CDI symptoms occur less than three days after the current admission (or less than 72 h) AND the patient is known to have been previously hospitalized at any other healthcare facility and discharged/transferred within the previous four weeks
- Related to a previous healthcare exposure at any other healthcare facility
    - The patient's CDI symptoms occur less than three days after the current admission (or <72 h) AND the patient is known to have a previous healthcare exposure at any other healthcare facility within the previous four weeks

Community-Associated CDI Case Definition

The patient's CDI symptoms occur less than three days (or less than 72 h) after admission, with no history of hospitalization or any other healthcare exposure within the previous 12 weeks.

Appendix Table 1. Number of Canadian Nosocomial Infection Surveillance Program adult and mixed (adult and pediatric) hospitals in each region included in a study of *Clostridioides difficile* infection among adults, Canada, 2015–2019*

Region	2015	2016	2017	2018	2019
Healthcare-associated					
Western	22	22	22	22	22
Central	22	22	23	23	26
Eastern	14	15	15	15	15
Northern	0	0	0	0	1
All	58	59	60	60	64
Community-associated					
Western	12	12	12	12	12
Central	20	21	23	23	26
Eastern	14	15	15	15	15
Northern	0	0	0	0	1
All	46	48	50	50	54

*Western region includes British Columbia, Alberta, Saskatchewan, and Manitoba; Central includes Ontario and Quebec; Eastern includes Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador; and Northern includes Nunavut. The Northern region was included in national rates but not displayed in regional stratification due to zero reported cases of *Clostridioides difficile*.

Appendix Table 2. Clinical characteristics and outcome trends of patients with *Clostridioides difficile* infection over time, Canada, 2015–2019*

Characteristics	2015	2016	2017	2018	2019	p value
Healthcare-associated *C. difficile* infection						
Sex, no. (%)†						
M	1,487 (50.1)	1,452 (50.4)	1,454 (51.7)	1,326 (49.9)	1,268 (52.5)	NS
F	1,479 (49.9)	1,430 (49.6)	1,360 (48.3)	1,329 (50.1)	1,149 (47.5)	NS
Median age, y (IQR)†	71 (59–82)	70 (58–81)	71 (59–81)	70 (59–81)	71 (59–81)	NS
ICU admission, no./total (%)‡						
All cause	46/507 (9.1)	33/466 (7.1)	29/492 (5.9)	22/433 (5.1)	26/442 (5.9)	**0.0188**
Complication from CDI	13/507 (2.6)	8/466 (1.7)	11/492 (2.2)	5/433 (1.2)	9/442 (2.0)	NS
30-day outcome death, no./total (%)‡						
All cause death	68/504 (13.5)	51/442 (11.5)	49/486 (10.1)	49/429 (11.4)	46/441 (10.4)	NS
Attributable to CDI	21/504 (4.2)	14/442 (3.2)	16/485 (3.3)	6/424 (1.4)	12/438 (2.7)	NS
Community-associated *C. difficile* infection						
Sex, no. (%)†						
M	426 (44.0)	384 (42.7)	453 (45.9)	445 (44.6)	367 (42.3)	NS
F	543 (56.0)	516 (57.3)	533 (54.1)	553 (55.4)	500 (57.7)	NS
Median age, y (IQR)†	67 (54–79)	66 (54–79)	66 (54–78)	67 (54–78)	67 (55–79)	NS
ICU admission, no./total (%)‡						
All cause	16/164 (9.8)	11/146 (7.5)	4/141 (2.8)	11/145 (7.6)	9/137 (6.6)	NS
Complication from CDI	3/164 (1.8)	2/146 (1.4)	3/141 (2.1)	1/145 (0.7)	2/137 (1.5)	NS
30-day outcome death, no./total (%)‡						
All cause death	11/164 (6.7)	12/146 (8.2)	7/141 (5.0)	7/144 (4.9)	16/136 (11.8)	NS
Attributable to CDI	4/164 (2.4)	4/146 (2.7)	1/140 (0.7)	3/143 (2.1)	5/133 (3.8)	NS

*Missing or unknown values were excluded from the analysis. The Cochran–Armitage test was used for categorical variables and the Mann–Kendall test for continuous variables to assess significant trends over time. Bolde text indicates statistical significance. CDI, *Clostridioides difficile* infection; ICU, intensive care unit; NS, not significant.
†Patient demographic characteristics data (age and sex) collected year-round.
‡ICU admission and mortality data are collected during a 2-month targeted surveillance period (March–April) each year.

Appendix Table 3. Top 15 most prevalent healthcare-associated and community-associated *Clostridioides difficile* ribotypes among adults, Canada, 2015–2019

Ribotypes	2015	2016	2017	2018	2019
Healthcare-associated, %					
027	24.59	15.30	18.72	9.92	9.36
106	7.33	13.31	8.87	11.29	18.13
014	8.04	8.22	7.39	8.82	11.11
020	6.38	6.80	5.91	7.16	5.85
002	7.33	5.10	4.43	6.06	5.56
056	3.07	4.53	3.94	4.68	3.80
015	1.89	2.83	1.97	4.13	3.80
076	3.31	1.70	3.94	2.48	0.88
057	2.13	2.27	2.96	3.03	0.88
012	1.18	1.70	0.99	3.58	2.63
103	0.95	2.55	0.74	2.48	2.34
072	3.31	1.98	1.97	0.28	0.29
078	2.13	1.13	2.22	0.83	1.46
629	1.18	1.42	0.99	1.65	2.05
153	1.18	2.27	1.72	1.10	0.58
Other	26.00	28.90	33.25	32.51	31.29
Community-associated, %					
106	6.45	9.48	15.32	14.73	17.59
020	8.39	9.48	8.11	8.53	7.41
014	5.16	7.76	9.91	10.08	8.33
027	14.84	10.34	6.31	3.10	2.78
056	4.52	5.17	2.70	8.53	3.70
002	5.81	5.17	5.41	3.88	4.63
015	2.58	1.72	5.41	3.88	9.26
012	3.23	2.59	4.50	4.65	3.70
629	3.23	0.00	0.90	1.55	2.78
153	0.65	2.59	3.60	1.55	0.93
019	1.29	2.59	1.80	2.33	0.00
328	3.23	0.86	0.90	2.33	0.00
078	2.58	2.59	0.00	0.78	0.93
076	0.65	1.72	1.80	1.55	1.85
054	0.00	1.72	0.90	1.55	3.70
Other	37.42	36.21	32.43	31.01	32.41

Appendix Table 4. Prevalence of livestock-associated *Clostridioides difficile* ribotypes 078/126, Canada, 2015–2019

Ribotype 078/126	2015	2016	2017	2018	2019	2015–2019
Healthcare-associated, no. (%)	10 (2.4)	7 (2.0)	13 (3.2)	9 (2.2)	7 (2.1)	2.4
Community-associated, no. (%)	5 (3.2)	3 (2.6)	1 (0.9)	1 (0.8)	2 (1.9)	1.9

Appendix Table 5. Outcomes of ribotype 027 and ribotype 106 by healthcare-associated and community-associated *Clostridioides difficile* infection, 2015–2019, Canada*

Ribotypes	All-cause death			*C. difficile*–attributable death			Severe outcomes†		
	HA	CA	p value	HA	CA	p value	HA	CA	p value
RT027	43/277 (15.5)	1/48 (2.1)	0.0102	22/275 (8.0)	1/48 (2.1)	0.2217	33/282 (11.7)	2/48 (4.2)	0.1348
RT106	26/204 (12.8)	4/73 (5.5)	0.1227	7/204 (3.4)	1/73 (1.4)	0.6853	10/210 (4.8)	3/74 (4.1)	1.0000

*Values represent no. deaths/no. cases (%) unless otherwise noted. CA, community-associated; HA, healthcare-associated; RT, ribotype.
†Severe outcomes include CDI attributable ICU admission, colectomy and death combined.

Appendix Table 6. MIC_{50} and MIC_{90} of healthcare-associated and community-associated *Clostridioides difficile* infection, Canada, 2015–2019*

		2015			2016			2017			2018			2019			Study period average		
Ant	Set	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range
Mox	HA	1.5	>32	0.25 to >32	1.5	>32	0.38 to >32	1.5	>32	0.38 to >32	1.5	>32	0.50 to >32	1.5	>32	0.50 to >32	1.5	>32	0.25 to >32
	CA	1.5	>32	0.50 to >32	1.5	>32	0.38 to >32	1	3	0.38 to >32	1.5	2	0.50 to >32	1.5	32	0.75 to >32	1.5	>32	0.38 to >32
Cli	HA	3	>256	0.125 to >256	3	256	0.047 to 256	3	96	0.094 to >256	4	>256	0.25 to >256	4	>256	0.25 to >256	3	>256	0.047 to >256
	CA	3	>256	0.094 to >256	2	256	0.094–256	3	96	0.25 to >256	6	12	0.75 to >256	3	12	0.25 to >256	3	128	0.094 to >256
Rif	HA	0.002	0.003	<0.002 to >32	0.002	0.003	<0.002 to >32	0.002	0.003	<0.002 to >32	0.002	0.004	<0.002 to >32	0.002	0.003	<0.002 to >32	0.002	0.003	<0.002 to >32
	CA	0.002	0.003	<0.002 to >32	0.002	0.003	<0.002 to >32	<0.002	0.002	<0.002 to >32	0.002	0.004	<0.002 to >32	0.002	0.004	<0.002 to >32	0.002	0.003	<0.002 to >32
Van	HA	0.5	0.75	0.19–3	0.5	0.75	0.25–4	0.5	0.75	0.19–3	0.75	1	0.25–3	0.75	1	0.38–6	0.5	1	0.19–6
	CA	0.5	0.75	0.25–1.5	0.5	0.75	0.19–1.5	0.5	0.75	0.25–1.0	0.75	1	0.38–1.5	0.75	1	0.25–2	0.5	1	0.19–2
Met	HA	0.25	1	0.032 to 2	0.25	0.75	0.032 to 3	0.25	1	0.023 to 3	0.38	0.5	0.023 to 3	0.38	0.75	0.064 to 4	0.38	0.75	0.023–4
	CA	0.19	0.5	0.047–1.5	0.25	0.75	0.047–2.0	0.25	0.5	0.047–2.0	0.38	0.5	0.094–2.0	0.38	0.75	0.047–3.0	0.25	0.5	0.047–3
Tig	HA	0.064	0.125	<0.016–0.25	0.032	0.047	<0.016–0.094	0.032	0.047	<0.016–0.38	0.032	0.047	0.016–0.25	0.047	0.125	0.023–0.38	0.047	0.094	<0.016–0.38
	CA	0.064	0.125	<0.016–0.19	0.032	0.047	<0.016–0.38	0.032	0.047	0.016–0.094	0.047	0.047	0.016–0.094	0.047	0.125	0.016–0.5	0.047	0.094	<0.016–0.5

*Values expressed as µg/mL. MIC_{50}, MIC required to inhibit the growth of 50% of the isolates; MIC_{90}, MIC required to inhibit the growth of 90% of the isolates. Ant, antimicrobial drug tested; CA, community-associated; Cli, clindamycin; HA, healthcare-associated; Met, metronidazole; Mox, moxifloxacin; Rif, rifampin; Set, setting; Tig, tigecycline; Van, vancomycin.

Appendix Table 7. Antimicrobial resistance interpretation healthcare-associated and community-associated *Clostridioides difficile* infection, Canada, 2015–2019*

	2015						2016						2017						2018						2019					
	HA, n = 423; CA, n = 155						HA, n = 353; CA, n = 116						HA, n = 406; CA, n = 111						HA, n = 363; CA, n = 129						HA, n = 342; CA, n = 108					
	Sus		Inter		Res		Sus		Inter		Res		Sus		Inter		Res		Sus		Inter		Res		Sus		Inter		Res	
Ant	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Mox																														
HA	273	64.5	5	1.2	145	34.3	271	76.8	7	2.0	75	21.3	312	76.9	0	0	94	23.2	309	85.1	4	1.1	50	13.8	294	86.0	2	0.6	46	13.5
CA	126	81.3	0	0.0	29	18.7	97	83.6	4	3.5	15	12.9	99	89.2	1	0.9	11	9.9	117	90.7	2	1.6	10	7.8	93	86.1	3	2.8	12	11.1
Cli																														
HA	183	43.3	131	31.0	109	25.8	160	45.3	105	29.8	88	24.9	196	48.3	120	29.6	90	22.2	80	22.0	115	31.7	168	46.3	117	34.2	94	27.5	131	38.3
CA	75	48.4	25	22.6	45	29.0	59	50.9	27	23.3	30	25.9	50	45.1	40	36.0	21	18.9	24	18.6	35	27.1	70	54.3	42	38.9	24	22.2	42	38.9
Rif																														
HA	412	97.4	2	0.5	9	2.1	346	98.0	0	0	7	2.0	393	96.8	2	0.5	11	2.7	358	98.6	0	0	5	1.4	339	99.1	0	0	3	0.9
CA	152	98.1	0	0	3	1.9	115	99.1	0	0	1	0.9	110	99.1	0	0	1	0.9	127	98.5	0	0	2	1.6	106	98.2	0	0	2	1.9
Tig																														
HA	423	100	0	0	0	0	353	100	0	0	0	0	406	100	0	0	0	0	363	100	0	0	0	0	342	100	0	0	0	0
CA	155	100	0	0	0	0	116	100	0	0	0	0	111	100	0	0	0	0	129	100	0	0	0	0	108	100	0	0	0	0
Van																														
HA	423	100	0	0	0	0	353	100	0	0	0	0	406	100	0	0	0	0	363	100	0	0	0	0	341	99.7	1	0.3	0	0
CA	155	100	0	0	0	0	116	100	0	0	0	0	111	100	0	0	0	0	129	100	0	0	0	0	108	100	0	0	0	0
Met																														
HA	423	100	0	0	0	0	353	100	0	0	0	0	406	100	0	0	0	0	363	100	0	0	0	0	342	100	0	0	0	0
CA	155	100	0	0	0	0	116	100	0	0	0	0	111	100	0	0	0	0	129	100	0	0	0	0	108	100	0	0	0	0

*Per Clinical and Laboratory Standards Institute guidelines; Methods for antimicrobial susceptibility testing of anaerobic bacteria, 9th edition. CLSI standard M11. Wayne, PA: The Institute; 2018. Ant, antimicrobial drug; CA, community-associated; HA, healthcare-associated; Inter, intermediate; Res, resistant; Sus, susceptible.

†Values expressed as µg/mL. Antimicrobial susceptibility interpretation: Moxifloxacin (Mox), susceptible ≤2, intermediate = 4, resistant ≥8; clindamycin (Cli), susceptible ≤2, intermediate = 4, resistant ≥8; rifampin (Rif), susceptible ≤1, intermediate = 2, resistant ≥4; vancomycin (Van), susceptible ≤4, intermediate = 8–16, resistant ≥32; metronidazole (Met), susceptible ≤8, intermediate = 16, resistant ≥32; tigecycline (Tig), susceptible ≤4, intermediate = 8, resistant ≥16.