ASM Microbe 2018 FRIDAY - 454



Antimicrobial Susceptibility Testing of Clostridium difficile Ribotypes Infecting Canadian Patients: The Canadian Clostridium difficile Surveillance Study (CAN-DIFF) 2013-2016

Introduction

Clostridiodes difficile (formerly Clostridium difficile) is the most frequently identified infectious cause of nosocomial diarrhea. C. difficile infection (CDI) occurs primarily in patients previously receiving antimicrobial agents. Antimicrobial susceptibility testing of C. difficile is rarely performed in clinical laboratories because of its complexity, cost, and dubious clinical significance.

Management of patients with CDI includes withdrawal of the predisposing antimicrobial agent, if possible, and empiric therapy with either oral vancomycin or fidaxomicin recommended over metronidazole (1). Fidaxomicin was approved by the FDA to treat CDI in 2011. Fidaxomicin is an oral, narrowspectrum macrocycle that inhibits the RNA polymerase of Gram-positive bacteria, especially C. difficile.

Treatment failure and CDI recurrence in patients treated with metronidazole occurs with considerable frequency (2-5). Vancomycin treatment of CDI may increase the risk for selection of vancomycin resistance in enterococci and staphylococci (6).

As the epidemiology and pathogenesis of C. difficile evolves, routine surveillance of clinical isolates to determine their ribotypes and in vitro susceptibility to both established and newer agents is warranted.

Materials and Methods

Bacterial Isolates Studied

1,747 isolates of C. difficile were cultured on C. difficile Moxalactam Norfloxacin (CDMN) Selective Supplement agar (Oxoid Canada, Nepean, ON, Canada) from toxin-positive stool specimens (following an ethanol shock step) by the clinical microbiology laboratory at the Winnipeg Health Sciences Centre. Each isolate's identity was confirmed by Gram stain, typical odor, latex agglutination (Microgen Bioproducts Ltd., Surrey, UK) or a positive L-proline aminopeptidase test, and chartreuse fluorescence under UV light (7). Chi-square testing was used to establish statistical significance (significance level, $P \leq 0.05$).

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed using the CLSI agar dilution reference method (8). Fidaxomicin and OP-1118 were supplied by Merck & Co., Inc.; the solvent for both of these compounds was DMSO and water was used as the diluent. C. difficile ATCC 700057 was used as the quality control strain for testing fidaxomicin; its reference MIC range for fidaxomicin is 0.06-0.25 µg/mL. In vitro antimicrobial susceptibility testing MIC interpretive criteria have not been established for fidaxomicin. CLSI breakpoints were used to interpret MICs for the other antimicrobial agents tested (9) except vancomycin. Vancomycin MICs were interpreted using the epidemiological cut-off value (ECOFF) established by EUCAST for vancomycin tested against C. difficile (vancomycin-wild-type [susceptible], $\leq 2 \mu g/mL$; reduced susceptibility to vancomycin, >2 μ g/mL) (10).

PCR Ribotyping

Isolates were ribotyped at the National Microbiology Laboratory, Public Health Agency of Canada, using an internationally-standardized, high-resolution capillary gel-based electrophoresis PCR-ribotyping protocol for *C. difficile* (11).

PCR for Toxin Genes

DNA extraction was performed using a commercial kit (InstaGene Matrix; Bio-Rad, Richmond, CA). The presence of the genes coding for toxin A (tcdA), toxin B (*tcdB*), negative regulator of toxin production (*tcdC*), binary toxin (*cdtB*), and triose phosphate isomerase (tpi) were determined for each cultured isolate using previously described PCR methods (12-14). PCR products were separated by electrophoresis on a 1.5% agarose gel and visualized with ethidium bromide staining, and images captured using Alpha Imager software (Alpha Innotech Corp., San Leandro, CA). The presence of a deletion or mutations in the *tcdC* gene was investigated by PCR amplification of the *tcdC* gene by following the methods outlined by Spigaglia and Mastrantonio (15). PCR products were purified and sequenced. All PCR testing was performed at the National Microbiology Laboratory, Public Health Agency of Canada.

Table 1. PCR ribotype composition of the 1,747 isolates of toxin-positive *C. difficile* collected by the CAN-DIFF surveillance study from 2013 to 2016

PCR ribotype	Number of isolates
	(% of all isolates)
027	379 (21.7%)
106	131 (7.5%)
014	126 (7.2%)
020	116 (6.6%)
002	86 (4.9%)
056	63 (3.6%)
072	44 (2.5%)
078	43 (2.5%)
015	43 (2.5%)
057	40 (2.3%)
012	34 (1.9%)
076	32 (1.8%)
087	29 (1.7%)
054	25 (1.4%)
005	24 (1.4%)
176	23 (1.3%)
103	22 (1.3%)
153	21 (1.2%)
019	20 (1.1%)
Ribotypes with <20	446 (25.5%)
isolates	
Total number of different r	ibotypes: 172

	- (/			-														
012	34 ((1.9%)		35									MIC (µg	ı/mL)			MIC inte	rpretatio	on
076	32 ((1.8%)		o D						Antimicrobial agent	Ribotype ^a	Range	Mode	MIC ₅₀	MIC ₉₀	% 5	%	6 I	% R
087	29 (1.7%)		ar 30 —															
054	25 ((1.4%)		ohic C						Amoxicillin-clavulanate	027	≤0.25-2	2	2	2	100	(0	0
005	24 ((1.4%)		Grap Grap							014	0.5-2	1	1	2	100	(0	0
176	23 (1.3%)		0 0 0 0 0							020	0.5-2	1	1	2	100	(0	0
103	22 ((1.3%)		E							106	0.5-2	1	1	2	100	(0	0
153	21 ((1.2%)		ي چ 15 —							002	1-4	1	1	2	100	(0	0
100	21 ((1.2/0)		olate							All non-027 ribotypes	≤0.25-8	1	1	2	100	(0	0
	20 (1.1%)		<u> </u>						Ceftriaxone	027	8->128	64	64	64	1.3	23	3.5	75.2
Ribotypes with <20	446 (25.5%)		tota		_					014	8-128	32	32	64	7.9	69	9.9	22.2
isolates				5 –							020	16-128	32	32	64	7.8	79	9.3	12.9
Total number of different	ent ribotypes: 1	172		~							106	16->128	32	32	64	5.3	62	2.6	32.1
				0							002	16->128	32	32	32	5.8	86	5.1	8.1
^a West (British Columbia, Al	berta, Manitoba; 3 la	boratory		()27	014	020	106	002		All non-027 ribotypes	8->128	32	32	64	8.9	71	1.8	19.3
Sites/year), Central (Ontario Fast (Quebec, Nova Scotia)	; 2-3 laboratory sites	s/year), and ear)			oct (627)		(525)	Eact (59	25)	Clindamycin	027	1->64	8	8	>64	4	27	7.9	68.1
		our).			51 (037)		u (525)		55)		014	2->64	8	8	8	5.6	37	7.3	57.1
Table 5 Prevalence of	common PCR rih	notvnes ar	mona tovi	n-nositive C	difficile	collected	l hy the C				020	≤0.12->64	8	8	8	8.6	21	1.6	69.8
surveillance study		otypes a			. unnene	Jonecleu					106	1->64	8	8	8	3.1	23	3.6	73.3
											002	1-8	8	8	8	2.3	33	3.7	64
Year (number of isolates)	Ribotyp	e, number	of isolates (%		olates fro	om study	year)	002		All non-027 ribotypes	≤0.12->64	8	8	>64	5.6	3	32	62.4
2013 (411)	113 (27 59	26)	33 (8 0%)	17 (4 1%)	24 ((5.8%)	16	002 (3.9%)	Fidaxomicin	027	0.12-1	0.5	0.5	0.5	NA	N	IA	NA
2014 (410)	98 (23.9%	~o) (a)	37 (9.0%)	32 (7.8%)	20 ((4.9%)	10	(4.6%)		014	0.06-1	0.25	0.25	0.5	NA	N	IA	NA
2015 (485)	109 (22.59	%)	31 (6.4%)	38 (7.8%)	36 ((7.4%)	25	(5.2%)		020	0.06-0.5	0.25	0.25	0.25	NA	N	IA	NA
2016 (441)	59 (13.4%	6)	25 (5.7%)	29 (6.6%)	51 (*	11.6%)	26	(5.9%)		106	0.03-2	0.5	0.5	0.5	NA	N	IA	NA
											002	0.06-0.5	0.12	0.25	0.5	NA	Ν	IA	NA
Table 6. CAN-DIFF 2013	3-2016 surveillan	ce study a	antimicro	bial suscepti	bility test	ing resul	Its for 1,7	747 toxin-			All non-027 ribotypes	≤0.015->8	0.25	0.25	0.5	NA	N	IA	NA
positive isolates of C. d	lifficile	-		-	-	•				Metronidazole	027	0.25-4	2	2	4	100	(0	0
		MIC (µg	/mL)			М	IIC interp	retation			014	0.25-4	0.5	0.5	1	100	(0	0
Antimicrobial agent	Range	Mode	MIC ₅₀	MIC ₉₀	(% S	% I		% R		020	0.25-4	0.5	0.5	1	100	(0	0
Amoxicillin-clavulanate	≤0.25-8	1	1	2	Q	9.8	0.2		0		106	0.25-2	0.5	0.5	1	100	(0	0
Ceftriaxone	8->128	32	32	64		7.3	61.3	3	31.4		002	0.25-2	0.5	0.5	1	100	(0	0
Clindamycin	≤0.12->64 <0.015.9	8	8	>64		5.3 Maa	31.1	1	63.6		All non-027 ribotypes	0.12-4	0.5	0.5	1	100	(0	0
Metronidazole	≤0.015-8 0.12-4	0.25	0.25	0.5		NA≏ 100				Moxifloxacin	027	1->32	>32	32	>32	10.3	(0	89.7
Moxifloxacin	0.5->32	1	2	32	-	1.8	0.9		27.3		014	1->32	2	2	16	84.1	1	.6	14.3
OP-1118	0.12-64	4	4	16		NA	NA		NA		020	1-16	2	2	2	92.2	1	.8	6
Vancomycin	≤0.25-4	1	1	2	g	8.7 ^b	NA		NA		106	1-32	2	2	2	92.4	1	.5	6.1
^a NA, CLSI MIC interpreta	tive breakpoints no	t available;	^b MICs w	ere interpreted	using the	EUCAST	epidemiol	ogical cut-	off value		002	0.5-32	1	1	2	90.7	1	.2	8.1
(ECOFF) for vancomycin											All non-027 ribotypes	0.5->32	1	2	4	88.9	1	.1	10
										OP-1118	027	1-32	16	16	16	NA	Ν	IA	NA
Table 7. CAN-DIFF 201	3-2016 surveillar	nce study	distributi	on of MICs f	or antimic	robial ag	gents tes	ted agair	st 1,747		014	0.5-16	4	4	8	NA	N	IA	NA
toxin-positive isolates	of C. difficile										020	1-16	4	4	8	NA	Ν	IA	NA
	Nur	mber of iso	plates for v	which the anti	microbial a	agent MIC	C (µg/mL)	was:			106	0.5-16	8	8	16	NA	N	IA	NA
Antimicrobial agent	0.015 0.03 0.0	0.125	0.25	0.5 1	2	4	8	16 32	2 ≥64		002	1-16	4	4	8	NA	Ν	IA	NA
Amoxicillin-clavulanate			5 ^a	73 979	674	13	3				All non-027 ribotypes	0.12-64	4	4	8	NA	N	A	NA
Ceftriaxone							3 1	124 10 [.]	71 549 ^b	Vancomycin	027	≤0.25-4	1	1	2	97.6	• N	IA	NA
Clindamycin	•	. 2 ^a		17	72	544	878	15 2	216 ^c		014	0.5-2	1	1	2	100	Ν	IA	NA
Fidaxomicin	3 ^a 28 74	426	634	534 46	1	67	1ª				020	0.5-2	1	1	2	100	Ν	IA	NA
		6	203	190 349 3 670	326 582	07 15	20	185 07	D e		106	0.5-4	1	1	2	99.2	Ν	A	NA
0P-1118		1	5	33 97	283	554	464 ?	100 Z/ 308 1	∠ [∞] 1 ^f		002	0.5-4	1	1	2	98.8	Ν	A	NA
Vancomvcin			1 ^a	192 1184	347	23					All non-027 ribotypes	0.5-4	1	1	2	99	Ν	IA	NA

		MIC (µg	g/mL)		M	IC interpretation	on
Antimicrobial agent	Range	Mode	MIC ₅₀	MIC ₉₀	% S	% I	% R
Amoxicillin-clavulanate	≤0.25-8	1	1	2	99.8	0.2	0
Ceftriaxone	8->128	32	32	64	7.3	61.3	31.4
Clindamycin	≤0.12->64	8	8	>64	5.3	31.1	63.6
Fidaxomicin	≤0.015-8	0.25	0.25	0.5	NA ^a	NA	NA
Metronidazole	0.12-4	0.5	0.5	2	100	0	0
Moxifloxacin	0.5->32	1	2	32	71.8	0.9	27.3
OP-1118	0.12-64	4	4	16	NA	NA	NA
Vancomycin	≤0.25-4	1	1	2	98.7 ^b	NA	NA

	34	(1.9%)		35								MIC (µg	g/mL)		М	IC interpret	ition
076	32	(1.8%)		30					Antimicrobial agent	Ribotype ^a	Pango	Mode	MIC	MIC.		94.1	% P
087	29	(1.7%)		06 ^a g							Kange	woue	WIIC 50	WIC ₉₀	/6 3	/0 1	70 K
054	25	(1.4%)		hica	_				Amoxicillin-clavulanate	027	≤0.25-2	2	2	2	100	0	0
005	24	(1.4%)		Ida 25						014	0.5-2	1	1	2	100	0	0
176	23	(1.1%)		eog						020	0.5-2	1	1	2	100	0	0
400	20	(1.370)		ຫ 20 ຮຸ						106	0.5-2	1	1	2	100	0	0
103	22	(1.3%)		i tro						002	1-4	1	1	2	100	0	0
153	21	(1.2%)		cr ates						All non-027 ribotypes	≤0.25-8	1	1	2	100	0	0
019	20	(1.1%)		^{io} : 10					Ceftriaxone	027	8->128	64	64	64	1.3	23.5	75.2
Ribotypes with <20	446	(25.5%)		otal						014	8-128	32	32	64	7.9	69.9	22.2
isolates				, [∓] 5			_			020	16-128	32	32	64	7.8	79.3	12.9
Total number of differer	t ribotvpes:	172		%						106	16->128	32	32	64	5.3	62.6	32.1
				0						002	16->128	32	32	32	5.8	86.1	8.1
^a West (British Columbia, Albe	erta, Manitoba; 3 I	aboratory			027	014	020	106 002		All non-027 ribotypes	8->128	32	32	64	8.9	71.8	19.3
sites/year), Central (Ontario; 2	2-3 laboratory site	s/year), and	1						Clindamycin	027	1->64	8	8	>64	4	27.9	68.1
East (Quebec, Nova Scotta; 3	laboratory sites/y	ear).		,	West (63	37) ■ Cen [•]	tral (525)	■East (585)		014	2->64	8	8	8	5.6	37.3	57.1
		- .	<i>.</i> .	,.	•					020	≤0.12->64	8	8	8	8.6	21.6	69.8
Table 5. Prevalence of co	ommon PCR ri	potypes a	mong toxi	n-positiv	ve C. ditti	cile collect	ed by the C	SAN-DIFF		106	1->64	8	8	8	3.1	23.6	73.3
surveillance study										002	1-8	8	8	8	2.3	33.7	64
Vear (number of isolates)		Ribotyp	e, number	of isolate	es (% of to	tal isolates	from study	year)		All non-027 ribotypes	≤0.12->64	8	8	>64	5.6	32	62.4
	027	- ()	014		020		106	002	Fidaxomicin	027	0.12-1	0.5	0.5	0.5	NA	NA	NA
2013 (411)	113 (27.5	%)	33 (8.0%)		17 (4.1%)) 2	4 (5.8%)	16 (3.9%)		014	0.06-1	0.25	0.25	0.5	NA	NA	NA
2014(410) 2015(485)	90 (23.9 100 (22 F	%) :0/_\	31 (9.0%)		32 (1.8%) 29 (7.8%)	/ ∠' \ 3	U (4.9%) G (7 1%)	19 (4.6%) 25 (5.2%)		020	0.06-0.5	0.25	0.25	0.25	NA	NA	NA
2015 (405) 2016 (441)	59 (13.4	<i>701</i> %)	25 (5 7%)	i	29 (6.6%)) 5' N 5'	0 (7.47%) 1 (11 6%)	25 (5.2%)		106	0.03-2	0.5	0.5	0.5	NA	NA	NA
	00(1011	/0/	20 (0.1 70)			<u> </u>	(11.070)	20 (0.070)		002	0.06-0.5	0.12	0.25	0.5	NA	NA	NA
	0040eillei	() , ,				1 1	tta fan 4 7	- 4		All non-027 ribotypes	<0.000 0.00	0.25	0.25	0.5	NA	NA	NA
1able 6. CAN-DIFF 2013-2	2016 Surveillar Ficilo	Ce study a	antimicro	Jai susc	eptionity	testing res	Suits for 1,7	4/ toxin-	Metronidazole	027	0.25-4	2	2	4	100	0	0
										014	0 25-4	- 0.5	-05	1	100	0	0
Antimicrobial agent	Pango	Mile (µg	/mL)	MIC		0/ S	MIC interpr			020	0.25-4	0.5	0.5	1	100	0	õ l
	<0 25-8	1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2)	99.8	0.2	<u> </u>		106	0.25-2	0.0	0.0		100	0	
Ceftriaxone	8->128	32	32	<u>_</u> 64		55.0	0.2	314		100	0.20 2	11 7	05	1	100		
Clindamycin	≤0.12->64	8	8			7.3	61.3		•	002	0 25-2	0.5	0.5	1	100 100	0	0
Fidaxomicin	≤0.015-8	0.25		>64		7.3 5.3	61.3 31.1	63.6		002	0.25-2	0.5 0.5	0.5 0.5	1 1 1	100 100 100	0	0
Metronidazole	0.12-4	0 5	0.25	>64 0.5		7.3 5.3 NAª	61.3 31.1 NA	63.6 NA	Maviflavaaia	002 All non-027 ribotypes	0.25-2	0.5 0.5 0.5	0.5 0.5 0.5	1 1 1	100 100 <u>100</u>	0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
		0.5	0.25 0.5	>64 0.5 2		7.3 5.3 NAª 100	61.3 31.1 NA 0	63.6 NA 0	Moxifloxacin	002 All non-027 ribotypes 027	0.25-2 0.12-4 1->32	0.5 0.5 0.5 >32	0.5 0.5 0.5 32	1 1 1 >32	100 100 100 10.3 84.1	0	0 0 0 89.7
Moxifloxacin	0.5->32	0.5	0.25 0.5 2	>64 0.5 2 32		7.3 5.3 NA ^a 100 71.8	61.3 31.1 NA 0 0.9	63.6 NA 0 27.3	Moxifloxacin	002 All non-027 ribotypes 027 014	0.25-2 0.12-4 1->32 1->32	0.5 0.5 	0.5 0.5 0.5 32 2	1 1 >32 16 2	100 100 100 10.3 84.1	0 0 1.6	0 0 0 89.7 14.3
Moxifloxacin OP-1118	0.5->32 0.12-64	0.5 1 4	0.25 0.5 2 4	>64 0.5 2 32 16		7.3 5.3 NA ^a 100 71.8 NA	61.3 31.1 NA 0 0.9 NA	63.6 NA 0 27.3 NA	Moxifloxacin	002 All non-027 ribotypes 027 014 020	0.25-2 0.12-4 1->32 1->32 1-16	0.5 0.5 >32 2 2	0.5 0.5 0.5 32 2 2	1 1 >32 16 2	100 100 100 10.3 84.1 92.2	0 0 1.6 1.8	0 0 0 89.7 14.3 6
Moxifloxacin OP-1118 Vancomycin	0.5->32 0.12-64 ≤0.25-4	0.5 1 4 1	0.25 0.5 2 4 <u>1</u>	>64 0.5 2 32 16 2		7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b	61.3 31.1 NA 0 0.9 NA NA	63.6 NA 0 27.3 NA NA	Moxifloxacin	002 All non-027 ribotypes 027 014 020 106	0.25-2 0.12-4 1->32 1->32 1-16 1-32	0.5 0.5 >32 2 2 2 2	0.5 0.5 0.5 32 2 2 2 2	1 1 >32 16 2 2 2	100 100 100 10.3 84.1 92.2 92.4	0 0 1.6 1.8 1.5	0 0 0 89.7 14.3 6 6.1
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ	0.5->32 0.12-64 ≤0.25-4 ′e breakpoints n	0.5 1 4 <u>1</u> ot available;	0.25 0.5 2 4 <u>1</u> ; ^b MICs we	>64 0.5 2 32 16 2 ere interpr	reted using	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo	63.6 NA 0 27.3 NA NA ogical cut-off value	Moxifloxacin	002 All non-027 ribotypes 027 014 020 106 002	0.25-2 0.12-4 1->32 1->32 1-16 1-32 0.5-32	0.5 0.5 >32 2 2 2 2 1	0.5 0.5 0.5 32 2 2 2 2 1	1 1 >32 16 2 2 2 2	100 100 100 10.3 84.1 92.2 92.4 90.7	0 0 1.6 1.8 1.5 1.2	0 0 0 89.7 14.3 6 6.1 8.1
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n	0.5 1 4 <u>1</u> ot available;	0.25 0.5 2 4 1 ; ^b MICs we	>64 0.5 2 32 16 2 >re interp	reted using	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo	1 63.6 NA 0 27.3 NA NA ogical cut-off value	Moxifloxacin	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes	0.25-2 0.12-4 1->32 1->32 1-16 1-32 0.5-32 0.5-32	0.5 0.5 >32 2 2 2 1 1	0.5 0.5 0.5 32 2 2 2 2 1 2 1 2	1 1 >32 16 2 2 2 2 4	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9	0 0 1.6 1.8 1.5 1.2 1.1	0 0 0 89.7 14.3 6 6.1 8.1 10
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n	0.5 1 4 1 ot available;	0.25 0.5 2 4 1 ; ^b MICs wo	>64 0.5 2 32 16 2 >re interp	reted using	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA <u>NA</u> 3T epidemiolo	63.6 NA 0 27.3 NA NA ogical cut-off value	Moxifloxacin OP-1118	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027	0.25-2 0.12-4 1->32 1->32 1-16 1-32 0.5-32 0.5->32 1-32	0.5 0.5 >32 2 2 2 2 1 1 1 16	0.5 0.5 0.5 32 2 2 2 2 1 2 1 2 16	1 1 >32 16 2 2 2 2 4 16	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA	0 0 1.6 1.8 1.5 1.2 1.1 NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013 - toxin-positive isolates of	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n •2016 surveilla	0.5 1 4 <u>1</u> ot available	0.25 0.5 2 4 ; ^b MICs we	>64 0.5 2 32 16 2 ∍re interp	reted using	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA ST epidemiolo	ted against 1,747	Moxifloxacin OP-1118	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014	0.25-2 0.12-4 1->32 1->32 1-16 1-32 0.5-32 0.5-32 1-32 0.5-16	0.5 0.5 >32 2 2 2 1 1 1 16 4	0.5 0.5 0.5 32 2 2 2 1 2 1 2 16 4	1 1 >32 16 2 2 2 2 4 16 8	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n •2016 surveilla ⁵ C. difficile	0.5 1 4 ot available	0.25 0.5 2 4 ; ^b MICs we	>64 0.5 2 32 16 2 эre interp	reted using Cs for ant	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo agents test	63.6 NA 0 27.3 NA NA ogical cut-off value ted against 1,747	Moxifloxacin OP-1118	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020	0.25-2 0.12-4 1->32 1->32 1-16 1-32 0.5-32 0.5->32 1-32 0.5-16 1-16	0.5 0.5 >32 2 2 2 1 1 16 4 4	0.5 0.5 32 2 2 2 1 2 1 2 16 4 4	1 1 >32 16 2 2 2 2 4 16 8 8	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n •2016 surveilla [±] C. difficile	0.5 1 4 1 ot available n ce study	0.25 0.5 2 4 ; ^b MICs w distribution	>64 0.5 2 32 16 2 ere interp	reted using Cs for ant antimicrot	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo agents test	63.6 NA 0 27.3 NA NA ogical cut-off value ted against 1,747 was:	Moxifloxacin OP-1118	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106	0.25-2 0.12-4 1->32 1->32 1-16 1-32 0.5-32 0.5->32 1-32 0.5-16 1-16 0.5-16	0.5 0.5 >32 2 2 2 1 1 16 4 4 8	0.5 0.5 0.5 32 2 2 2 1 2 1 2 16 4 4 8	1 1 -32 16 2 2 2 2 4 16 8 8 8 16	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.0	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n -2016 surveilla ⁱ <i>C. difficile</i> <u>Nu</u> 015 0.03 0.0	0.5 1 4 ot available nce study mber of iso 06 0.125	0.25 0.5 2 4 1 ; ^b MICs w distribution	>64 0.5 2 32 16 2 эre interp on of MI <u>hich the</u> 0.5	reted using Cs for ant antimicrot	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo agents test IIC (μg/mL) 8	63.6 NA 0 27.3 NA 0 27.3 NA NA NA second control value ted against 1,747 was: 16 32 ≥64	Moxifloxacin OP-1118	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 002	$\begin{array}{c} 0.25-2\\ 0.12-4\\ \hline 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ \hline 0.5-32\\ \hline 1-32\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ \hline 1-16\\ \hline 1-16\\ \end{array}$	0.5 0.5 >32 2 2 2 1 1 1 16 4 4 8 4	0.5 0.5 0.5 32 2 2 2 2 1 2 1 2 16 4 4 8 4	1 1 >32 16 2 2 2 4 16 8 8 16 8	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.0 Amoxicillin-clavulanate	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n -2016 surveilla f <i>C. difficile</i> <u>Nι</u> 015 0.03 0.0	0.5 1 4 ot available nce study mber of iso 06 0.125	0.25 0.5 2 4 1 ; ^b MICs we distribution <u>olates for we</u> 0.25 5 ^a	>64 0.5 2 32 16 2 ere interp on of MI <u>hich the</u> 0.5 73	reted using Cs for ant antimicrot 1 2 979 67	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS imicrobial	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo agents test IIC (μg/mL) 8 3	63.6 NA 0 27.3 NA NA ogical cut-off value ted against 1,747 was: 16 32 ≥64	Moxifloxacin OP-1118	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 020 106 002 All non-027 ribotypes	$\begin{array}{r} 0.25-2\\ 0.12-4\\ 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ 0.5-32\\ 0.5->32\\ 1-32\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.12-64\\ \end{array}$	0.5 0.5 0.5 >32 2 2 2 1 1 16 4 4 8 4 4 4 4	0.5 0.5 0.5 32 2 2 2 1 2 1 6 4 4 8 4 4 4	1 1 -32 16 2 2 2 2 4 16 8 8 16 8 16 8 8 8	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.0 Amoxicillin-clavulanate Ceftriaxone	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n -2016 surveilla i <i>C. difficile</i> Nt 015 0.03 0.0	0.5 1 4 nce study mber of iso 06 0.125	0.25 0.5 2 4 1 ; ^b MICs w distribution olates for w 0.25 5 ^a	>64 0.5 2 32 16 2 ere interp on of MI <u>hich the</u> 0.5 73	reted using Cs for ant antimicrot 1 2 979 67	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS imicrobial pial agent M 2 4 74 13	61.3 31.1 NA 0 0.9 NA NA ST epidemiolo agents test <u>IIC (μg/mL)</u> 8 1 3 3 1	63.6 NA 0 27.3 NA ogical cut-off value ted against 1,747 was: 16 32 ≥64 24 1071 549 ^b	Moxifloxacin OP-1118 Vancomycin	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 002 106 002 All non-027 ribotypes 027	$\begin{array}{c} 0.25-2\\ 0.12-4\\ 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ 0.5-32\\ 0.5->32\\ 1-32\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.12-64\\ \leq 0.25-4\\ \end{array}$	0.3 0.5 0.5 >32 2 2 2 1 1 16 4 4 4 8 4 4 4 1	0.5 0.5 0.5 32 2 2 2 1 2 1 6 4 4 8 4 4 8 4 4 1	1 1 32 16 2 2 2 4 16 8 8 16 8 16 8 8 16 8 8 2	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA NA NA NA NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.0 Amoxicillin-clavulanate Ceftriaxone Clindamycin	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n -2016 surveilla f <i>C. difficile</i> Nt 015 0.03 0.	0.5 1 4 1 ot available nce study mber of iso 06 0.125 2 ^a	0.25 0.5 2 4 1 ; ^b MICs w distribution olates for w 0.25 5 ^a	>64 0.5 2 32 16 2 ere interp on of MI <u>hich the</u> 0.5 73	reted using Cs for ant antimicrot 1 2 979 67 17 72	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS imicrobial <u>pial agent N</u> 2 4 4 4 2 544	61.3 31.1 NA 0 0.9 NA NA ST epidemiolo agents test 1IC (μg/mL) 8 3 3 1 878 10	63.6 NA 0 27.3 NA ogical cut-off value ted against 1,747 was: 16 32 ≥64 124 1071 549 ^b 15 2 216 ^c	Moxifloxacin OP-1118 Vancomycin	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014	$\begin{array}{r} 0.25-2\\ 0.12-4\\ \hline 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ \hline 0.5-32\\ \hline 0.5-32\\ \hline 1-32\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.12-64\\ \hline \le 0.25-4\\ 0.5-2\\ \end{array}$	0.3 0.5 0.5 >32 2 2 2 1 1 16 4 4 8 4 4 4 1 1 1	0.5 0.5 0.5 32 2 2 2 1 2 1 2 16 4 4 8 4 4 4 1 1	1 1 32 16 2 2 2 4 16 8 8 16 8 8 16 8 8 2 2 2	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA NA NA NA NA NA NA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.0 Amoxicillin-clavulanate Ceftriaxone Clindamycin Fidaxomicin 3 Matropidazala	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n -2016 surveilla f <i>C. difficile</i> Nt 015 0.03 0. 3ª 28 7	0.5 1 4 1 ot available nce study mber of iso 06 0.125 2 ^a 4 426 6	0.25 0.5 2 4 1 ; ^b MICs w distribution olates for w 0.25 5 ^a 634 202	>64 0.5 2 32 16 2 ere interp on of MI /hich the 0.5 73 534	reted using Cs for ant antimicrot 1 2 979 67 17 72 46 1 240 32	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS imicrobial <u>pial agent N</u> 2 4 74 13 2 544	61.3 31.1 NA 0 0.9 NA NA ST epidemiolo agents test 1IC (μg/mL) 8 3 3 1 878 1 ^d	i 63.6 NA 0 27.3 NA NA NA ogical cut-off value ted against 1,747 was: 16 32 ≥64 124 1071 549 ^b 15 2 216 ^c	Moxifloxacin OP-1118 Vancomycin	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 027 014 020	$\begin{array}{c} 0.25-2\\ 0.12-4\\ \hline 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ \hline 0.5-32\\ \hline 0.5-32\\ \hline 0.5-32\\ \hline 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.12-64\\ \hline \leq 0.25-4\\ 0.5-2\\ \hline 0.5-2\\ \hline 0.5-2\\ \hline 0.5-2\end{array}$	0.3 0.5 0.5 >32 2 2 2 1 1 16 4 4 4 8 4 4 4 1 1 1 1	0.5 0.5 0.5 32 2 2 1 2 16 4 4 8 4 4 8 4 1 1 1	1 1 332 16 2 2 2 2 4 16 8 8 16 8 8 16 8 8 16 8 8 2 2 2 2 2	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA NA NA NA NA NA 100 100	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA NA NA NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.(Amoxicillin-clavulanate Ceftriaxone Clindamycin Fidaxomicin 3 Metronidazole Moviflovacin	0.5->32 0.12-64 ≤0.25-4 /e breakpoints n -2016 surveilla f <i>C. difficile</i> Nt 015 0.03 0. 3ª 28 7	0.5 1 4 1 ot available nce study mber of iso 06 0.125 2 ^a 4 426 6	0.25 0.5 2 4 1 ; ^b MICs w distribution olates for v 0.25 5 ^a 634 203	>64 0.5 2 32 16 2 ere interp on of MI /hich the 0.5 73 534 796 3	reted using Cs for ant <u>antimicrol</u> 1 2 979 67 17 7 46 1 349 32 670 58	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS imicrobial oial agent N 2 4 74 13 2 544 2 544 2 544	61.3 31.1 NA 0 0.9 NA NA 3T epidemiolo agents test 1IC (μg/mL) 8 3 3 1 878 1 ^d 20 1	63.6 NA 0 27.3 NA 0 27.3 NA NA ogical cut-off value ted against 1,747 was: 16 32 24 1071 5 2 216 ^c	Moxifloxacin OP-1118 Vancomycin	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 027 014 020 104 020 106	$\begin{array}{c} 0.25-2\\ 0.12-4\\ \hline 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ \hline 0.5-32\\ \hline 0.5-32\\ \hline 1-32\\ 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.12-64\\ \hline \le 0.25-4\\ 0.5-2\\ 0.5-2\\ 0.5-2\\ 0.5-4\\ \end{array}$	0.5 0.5 0.5 >32 2 2 2 1 1 16 4 4 8 4 4 4 4 1 1 1 1 1 1 1	0.5 0.5 0.5 32 2 2 2 1 2 16 4 4 8 4 4 4 1 1 1 1	1 1 32 16 2 2 2 4 16 8 8 16 8 8 16 8 8 16 8 8 2 2 2 2 2 2 2 2 2	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA NA NA NA NA 07.6 ^b 100 100 99.2	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA NA NA NA NA NA NA
Moxifloxacin OP-1118 Vancomycin ^a NA, CLSI MIC interpretativ (ECOFF) for vancomycin Table 7. CAN-DIFF 2013- toxin-positive isolates of Antimicrobial agent 0.(Amoxicillin-clavulanate Ceftriaxone Clindamycin Fidaxomicin 3 Metronidazole Moxifloxacin OP-1118	0.5->32 0.12-64 ≤0.25-4 ve breakpoints n -2016 surveilla f <i>C. difficile</i> Nt 015 0.03 0. 3ª 28 7	0.5 1 4 1 ot available nce study mber of iso 06 0.125 2 ^a 4 426 6 1	0.25 0.5 2 4 1 ; ^b MICs w distribution olates for v 0.25 5 ^a 634 203 5	>64 0.5 2 32 16 2 ere interp on of MI /hich the 0.5 73 534 796 3 33	reted using Cs for ant antimicrol 1 2 979 67 17 72 46 1 349 32 670 58 97 28	7.3 5.3 NA ^a 100 71.8 NA 98.7 ^b the EUCAS imicrobial $\frac{1}{2}$ $\frac{1}{4}$ $\frac{1}{3}$ $\frac{1}{2}$ $\frac{1}{5}$ $\frac{1}{3}$ $\frac{5.3}{554}$	61.3 31.1 NA 0 0.9 NA NA ST epidemiolo agents test 1IC (μg/mL) 8 3 3 1 878 1 ^d 20 1 464 3	I 63.6 NA 0 27.3 NA NA NA ogical cut-off value ted against 1,747 was: 16 32 ≥64 124 1071 549 ^b 15 2 216 ^c 85 272 ^e 208 308 1 1 ^f	Moxifloxacin OP-1118 Vancomycin	002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 106 002 All non-027 ribotypes 027 014 020 104 020 106 020 106 020	$\begin{array}{c} 0.25-2\\ 0.12-4\\ \hline 1->32\\ 1->32\\ 1-16\\ 1-32\\ 0.5-32\\ \hline 0.5-32\\ \hline 0.5-32\\ \hline 0.5-32\\ \hline 0.5-16\\ 1-16\\ 0.5-16\\ 1-16\\ 0.12-64\\ \hline \le 0.25-4\\ 0.5-2\\ \hline 0.5-2\\ \hline 0.5-2\\ \hline 0.5-4\\ \hline 0.5-4\\ \hline 0.5-4\\ \hline \end{array}$	0.5 0.5 0.5 >32 2 2 2 1 1 16 4 4 4 8 4 4 4 1 1 1 1 1 1 1 1 1 1 1 1 1	0.5 0.5 0.5 32 2 2 1 2 16 4 4 8 4 4 8 4 1 1 1 1 1 1	1 1 -32 16 2 2 2 2 4 16 8 8 16 8 8 16 8 8 2 2 2 2 2 2 2 2 2 2 2 2 2	100 100 100 10.3 84.1 92.2 92.4 90.7 88.9 NA NA NA NA NA NA NA NA NA NA NA SA SA SA SA SA SA SA SA SA SA SA SA SA	0 0 1.6 1.8 1.5 1.2 1.1 NA NA NA NA NA NA NA NA NA NA NA	0 0 0 89.7 14.3 6 6.1 8.1 10 NA NA NA NA NA NA NA NA NA NA NA NA NA

^a Isolate count shown for lowest the dilution tested; some MICs may be lower than the lowest dilution tested; ^b 79/549 isolate MICs for ceftriaxone were >64 µg/mL; ^c 206/216 isolate MICs for clindamycin were >64 µg/mL; ^d One isolate MIC for fidaxomicin was >8 µg/mL; ^e 175/272 isolate MICs for moxifloxacin were >32 µg/mL; ^f One isolate MIC for OP-1118 was 64 µg/mL.

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Results

Table 2. Annual prevalence of PCR ribotype 027 among toxin-positive C. difficile stratified by Canadian geographic region^a

	Canadian g (% of tot	eographic region, numb al isolates from geogra	per of isolates phic region)
isolates)	West	Central	East
2013 (411)	27 (17.4%)	25 (25.3%)	61 (38.9%)
2014 (410)	21 (13.5%)	30 (30.0%)	47 (30.5%)
2015 (485)	20 (12.8%)	21 (12.7%)	68 (41.7%)
2016 (441)	29 (17.1%)	12 (7.5%)	18 (16.2%)

Table 3. Prevalence of common PCR ribotypes among toxin-positive *C. difficile* stratified by patient age^a

Age group (number of	Ribotype, number of isolates (% of total isolates from patient age group)							
isolates)	027	014	020	106	002			
≤64 years (815)	110 (13.5%)	63 (7.7%)	57 (7.0%)	74 (9.1%)	39 (4.8%)			
65-79 years (494)	100 (20.2%)	32 (6.5%)	36 (7.3%)	33 (6.7%)	26 (5.3%)			
≥80 years (435)	167 (38.4%)	31 (7.1%)	23 (5.3%)	24 (5.5%)	21 (4.8%)			

^a Patient age was unknown for 3 of 1,747 (0.2%) isolates





Table 4. CAN-DIFF 2013-2016 antimicrobial susceptibility testing results for 1,747 toxin-positive isolates of C. difficile stratified according to PCR ribotype

^a There were 379 isolates with ribotype 027 and 1368 non-ribotype 027 isolates. Non-ribotype 027 isolates with >85 isolates are shown individually and are also included in the "All non-027 ribotypes" group. ^b MICs were interpreted using the EUCAST epidemiological cut-off value (ECOFF) (vancomycin-wild-type [susceptible], ≤2 µg/mL; reduced susceptibility to vancomycin, $>2 \mu g/mL$)



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Conclusions

- Ribotype 027 was the most common ribotype identified among isolates of toxin-positive C. difficile infecting Canadian patients from 2013 to 2016. Ribotype 027 isolates were frequently resistant to moxifloxacin (fluoroquinolones) and MDR. However, the prevalence of ribotype 027 is decreasing in both central and eastern Canada.
- Ribotype 027 accounted for 13.5, 20.2, and 38.4% of isolates from patients aged ≤ 64 , 65-79, and ≥ 80 years, respectively (*P*<0.00001).
- 89.7% of ribotype 027 isolates were resistant to moxifloxacin compared with only 10.0% of non-ribotype 027 isolates.
- Ribotype 027 was found more commonly among isolates of toxin-positive C. difficile in eastern Canada (33.2%) than among isolates from central (16.8%) and western (15.2%) Canada (*P*<0.00001).
- The prevalence of ribotype 106 increased significantly in western Canada (P=0.002) and the prevalence of both ribotype 106 (P=0.039) and ribotype 002 (P=0.045) significantly increased in central Canada from 2013 to 2016.
- 49.9% of ribotype 027 isolates were multidrug-resistant (MDR defined as resistant to ceftriaxone, clindamycin, and moxifloxacin) compared to 3.9% for non-027 ribotypes.
- All isolates of toxin-positive C. difficile tested were susceptible to metronidazole and had vancomycin MICs of ≤0.25-4 µg/mL (98.7% of vancomycin MICs were $\leq 2 \mu g/mL$).
- Fidaxomicin demonstrated greater in vitro potency than metronidazole, vancomycin and all other antimicrobial agents tested based upon their MIC₉₀ values and MIC distributions.
- Fidaxomicin demonstrated potent in vitro activity (MIC₉₀, 0.5 µg/mL) against all genotypes of toxin-positive C. difficile including ribotype 027 (NAP1/BI).
- Metronidazole had an MIC_{50} and MIC_{90} two doubling-dilutions higher for ribotype 027 isolates than for non-ribotype 027 isolates; vancomycin and fidaxomicin MIC₅₀s and MIC₉₀s were identical for both ribotype 027 and non-ribotype 027 isolates.

Acknowledgements

The authors would like to thank the laboratory staffs at the CAN-DIFF sites for their assistance with specimen collection. The study was supported in part by the Health Sciences Centre, University of Manitoba, National Microbiology Laboratory, and Merck & Co., Inc.

References

- 1. McDonald LC et al. 2018. Clin Infect Dis 66:e1-48.
- 2. Musher DM et al. 2005. Clin Infect Dis 40:1586-90.
- 3. Pepin J et al. 2005. Clin Infect Dis 40:1591-7.
- 4. McDonald LC et al. 2006. Emerg Infect Dis 12:409-15.
- 5. Johnson S et al. Clin Infect Dis. 2014 59:345-54.
- 6. HICPAC. 1995. Infect Control Hosp Epidemiol 16:105-13.
- 7. CLSI. 2008. M35-A2
- 8. CLSI. 2012. M11-A8.
- 9. CLSI. 2018. M100, 28th Edition.
- 10. EUCAST. 2018. http://www.eucast.org/mic_distributions_and_ecoffs/.
- 11. Fawley WN et al. 2015. PLOS One DOI:10.1371/journal.pone.0118150 Feb 13, 2015:1-14.
- 12. Kato H et al. 1998. J Clin Microbiol 36:2178-82.
- 13. Lemee L et al. 2004. J Clin Microbiol 42:5710-4.
- 14. Stubb S et al. 2000. FEMS Microbiol Lett 186:307-12.
- 15. Spigaglia P et al. 2002. J Clin Microbiol 40:3470-5.