

CIPARS Human Surveillance Component

Salmonella and *Campylobacter* AMR – 2023 Results

Presented by Melissa MacKinnon, PhD, MSc, DACVS-LA, DVM

World Antimicrobial Resistance Awareness Week

November 19, 2024



Agenda

- Background
- *Salmonella*
- *Campylobacter*
- Take away messages
- Questions

AMR descriptions and colour gradient used throughout presentation

Description	Resistance (%)	Gradient
Rare	< 0.1%	Dark Green
Very low	0.1% to 1%	Medium Green
Low	>1% to 10%	Light Green
Moderate	>10% to 20%	Very Light Green
High	>20% to 50%	Yellow
Very High	>50% to 70%	Orange
Extremely High	>70%	Red

<https://www.efsa.europa.eu/en/efsajournal/pub/7867>

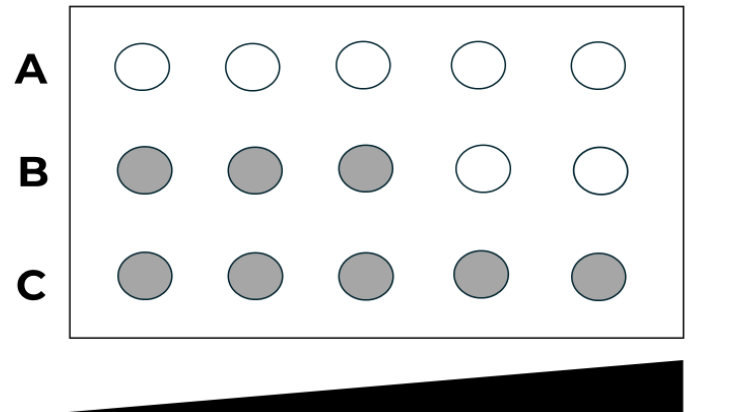
Methods for AMR evaluation

Campylobacter

Salmonella

Broth Microdilution

Whole Genome Sequencing (WGS)



Increasing concentrations of antimicrobial

S I R



Predicted phenotypes based on the resistance genes and/or mutations detected

Methods for AMR Interpretation

Campylobacter



For **CIPROFLOXACIN**,
use CLSI breakpoint to
classify MICs as either
susceptible, intermediate
or resistant



Report as resistant

R

Salmonella



For **CIPROFLOXACIN**,
cannot discriminate
between resistant and
intermediate using the
resistance genes



Report as non-susceptible

I/R

Human *Salmonella*

Most non-typhoidal *Salmonella* infections do NOT require treatment with antimicrobials

- Non-typhoidal *Salmonella* have an animal reservoir and typhoidal *Salmonella* do not
- Non-typhoidal *Salmonella* infections most commonly cause self-limiting diarrhea
 - Treatment with antimicrobials is not required or recommended
- Treatment with antimicrobials is considered:
 - When clinical signs are severe or prolonged
 - >6 diarrheal episodes/day, bloody diarrhea, diarrhea lasting >1 week, persistent fever
 - When patient is immunocompromised
- Treatment options include ciprofloxacin, azithromycin (alternative) or trimethoprim-sulfamethoxazole (alternative)

Invasive *Salmonella* infections require treatment with antimicrobials

- Typhoidal *Salmonella* infections most commonly cause bloodstream infections
- Invasive infections including bloodstream infections can occur with non-typhoidal *Salmonella* infections, but are less common than gastrointestinal infections
 - Treatment with antimicrobials is required
 - Treatment options include ceftriaxone, ciprofloxacin, or trimethoprim-sulfamethoxazole

***Salmonella* has the highest incidence rate of the enteric pathogens tracked by NESP**

- Incidence rates of Canadians with *Salmonella* in 2023

	2023 Incidence Rates* (Cases/100,000 population)
Total <i>Salmonella</i>	15.67
Non-typhoidal <i>Salmonella</i>	14.47
Typhoidal <i>Salmonella</i>	1.20

*2023 incidence rates are preliminary and subject to change with final validation of the data

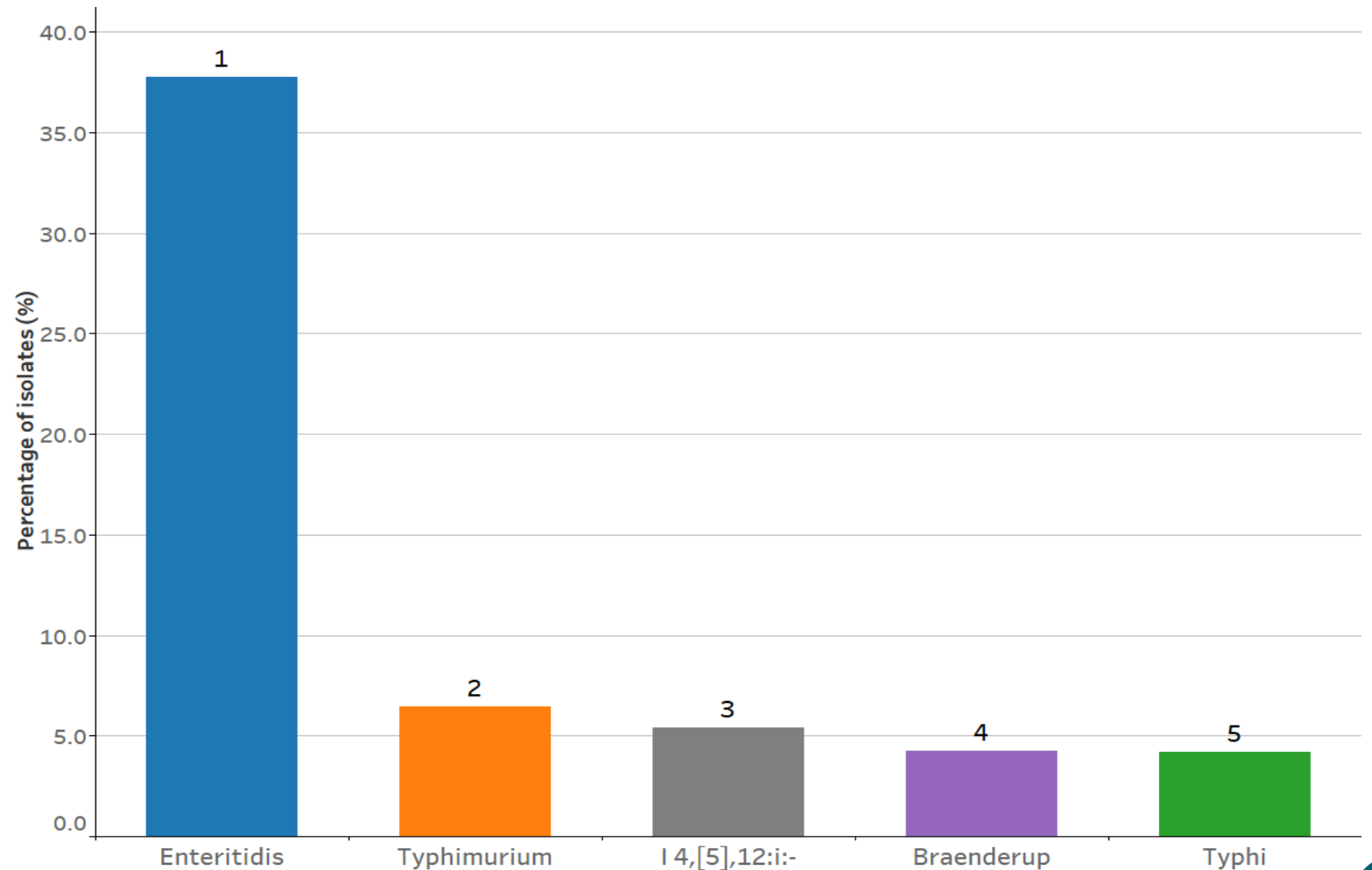
Source of data – [National Enteric Surveillance Program \(NESP\) - Canada.ca](https://www.canada.ca/en/health-canada/services/enteric-surveillance-program/nesp.html)

CIPARS human *Salmonella* surveillance reports temporal and regional variation in the prevalence of AMR

- Reporting of *Salmonella* infections is mandatory through laboratory notification of reportable diseases to the National Notifiable Disease Reporting System
 - However, forwarding of *Salmonella* isolates to provincial reference laboratories is voluntary and passive
- Isolates undergo whole genome sequencing
 - Predictive serotyping with SISTR
 - AMR prediction using Staramr
- Data from 2019-2023 are presented

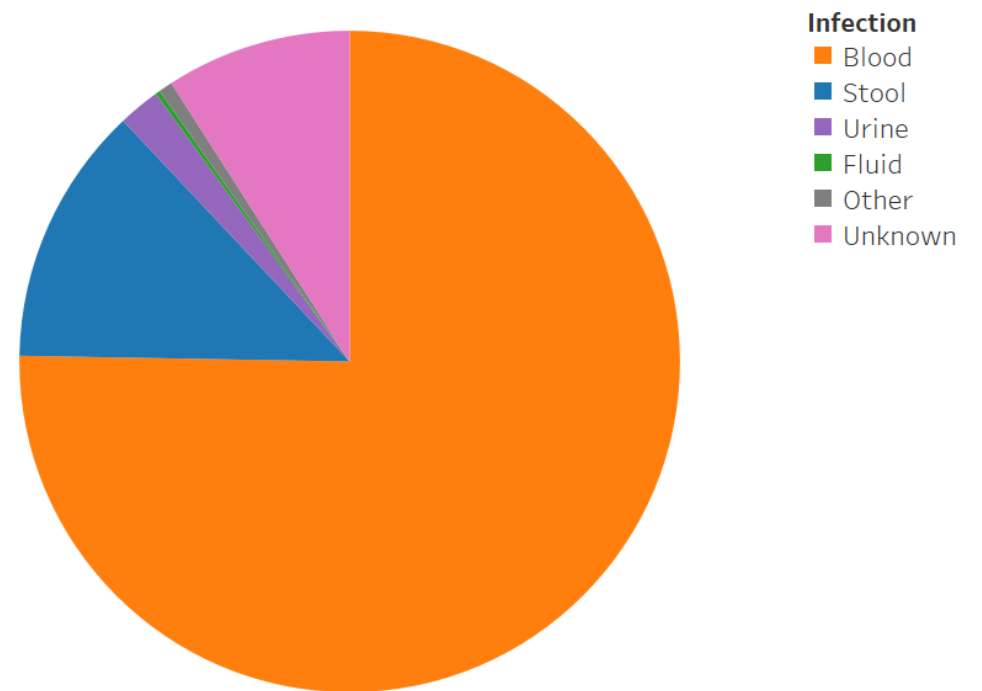
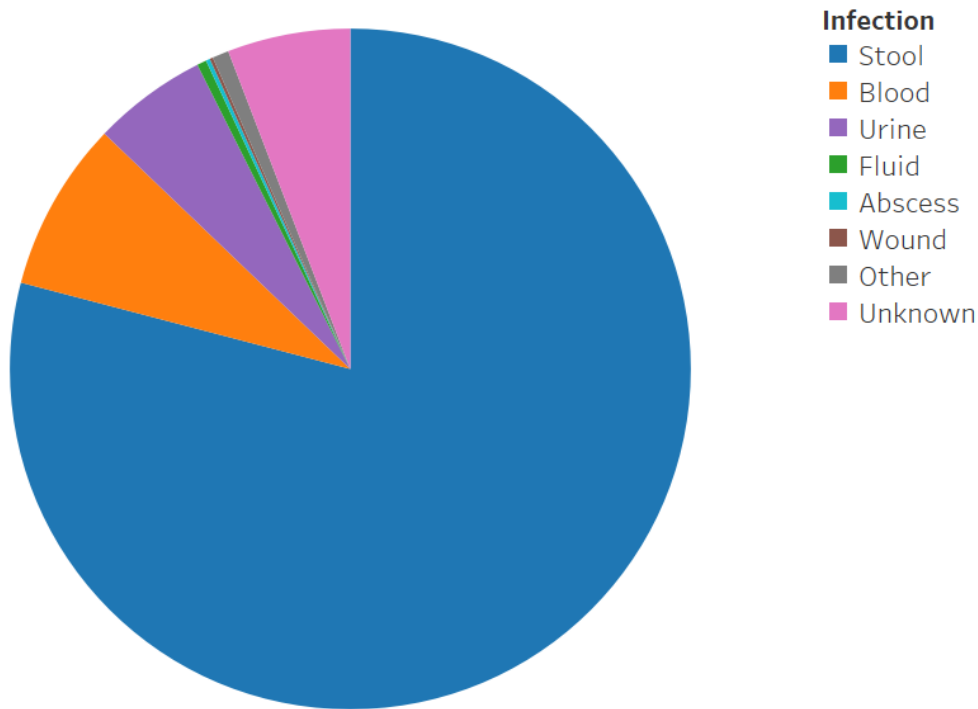
S. Enteritidis has been the top serovar nationally since 2005; ranking of other serovars varies from year to year

- In 2023, 38% of the isolates were *S. Enteritidis*
- *S. Heidelberg* was not in the top 10 serovars nationally for the first time in 2023
- There are regional differences in the frequency of serovars



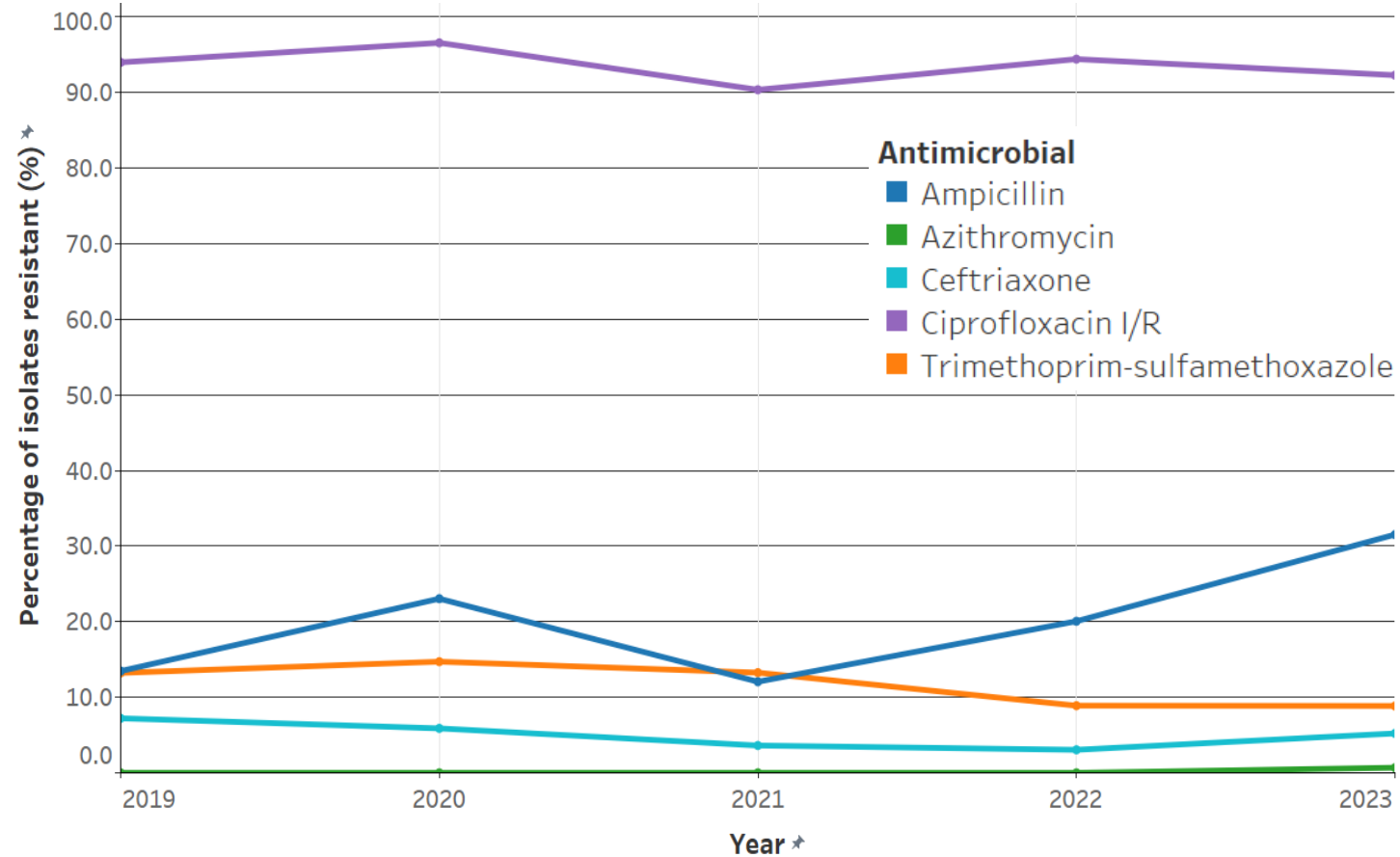
Non-typhoidal *Salmonella* generally from non-invasive infections, whereas typhoidal *Salmonella* generally from invasive infections

- Non-typhoidal *Salmonella* predominantly from gastrointestinal infections (79% stool in 2023)
- Typhoidal *Salmonella* predominantly from bloodstream infections (75% blood in 2023)










Extremely high non-susceptibility to ciprofloxacin has implications for treatment selection

- **Extremely high** non-susceptibility to ciprofloxacin (ranging from 90% to 97%)
- **Low** resistance to ceftriaxone; decreased from 2019 (7%) to 2022 (3%) and increased in 2023 (5%)
- **Moderate** resistance to ampicillin **increased to high** resistance (2019; 14% and 2023; 32%)
- **Moderate** resistance to trimethoprim-sulfamethoxazole **decreased to low** resistance (2019; 13% and 2023; 9%)
- **No** resistance to azithromycin from 2019-2022 and **very low** resistance in 2023 (0.7%)



Wide regional variation, sparse data and small numbers of isolates make interpretation of regional difference challenging

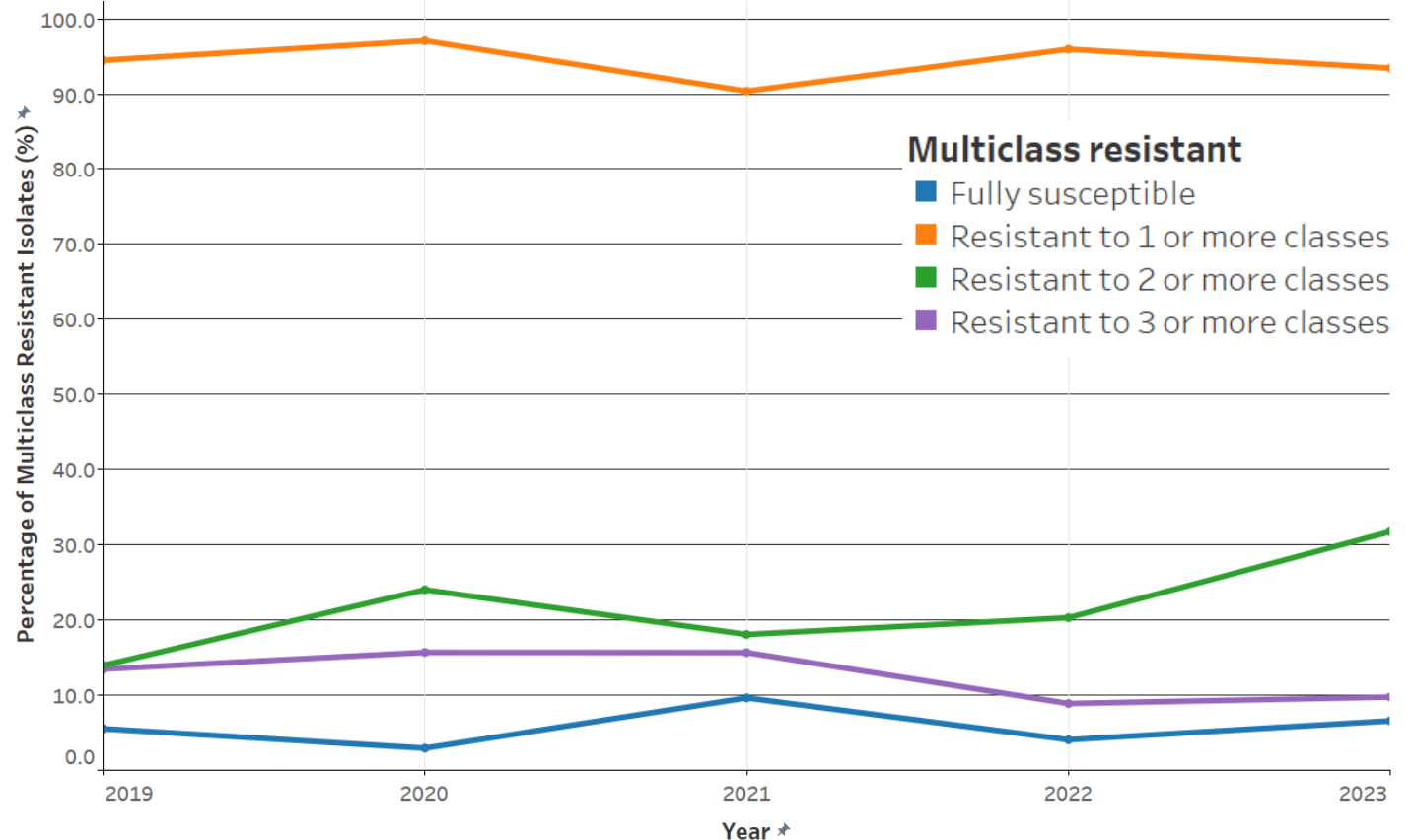
Region	2019		2020		2021		2022		2023	
	% R AMP	Total Isolates	% R AMP	Total Isolates	% R AMP	Total Isolates	% R AMP	Total Isolates	% R AMP	Total Isolates
National	14	416	23	204	12	83	20	394	32	441
Atlantic	0	2	--	--	0	2	25	8	0	7
British Columbia	0	84	6	32	16	19	3	76	0	99
Ontario	21	236	25	124	9	46	31	204	53	231
Prairies	5	72	41	34	9	11	8	85	15	79
Québec	9	22	0	14	40	5	19	21	20	25

% R and Gradient	
< 0.1%	
0.1 - 1%	
>1 - 10%	
>10 - 20%	
>20 - 50%	
>50 - 70%	
>70%	

Bolded numbers highlight < 20 total isolates tested

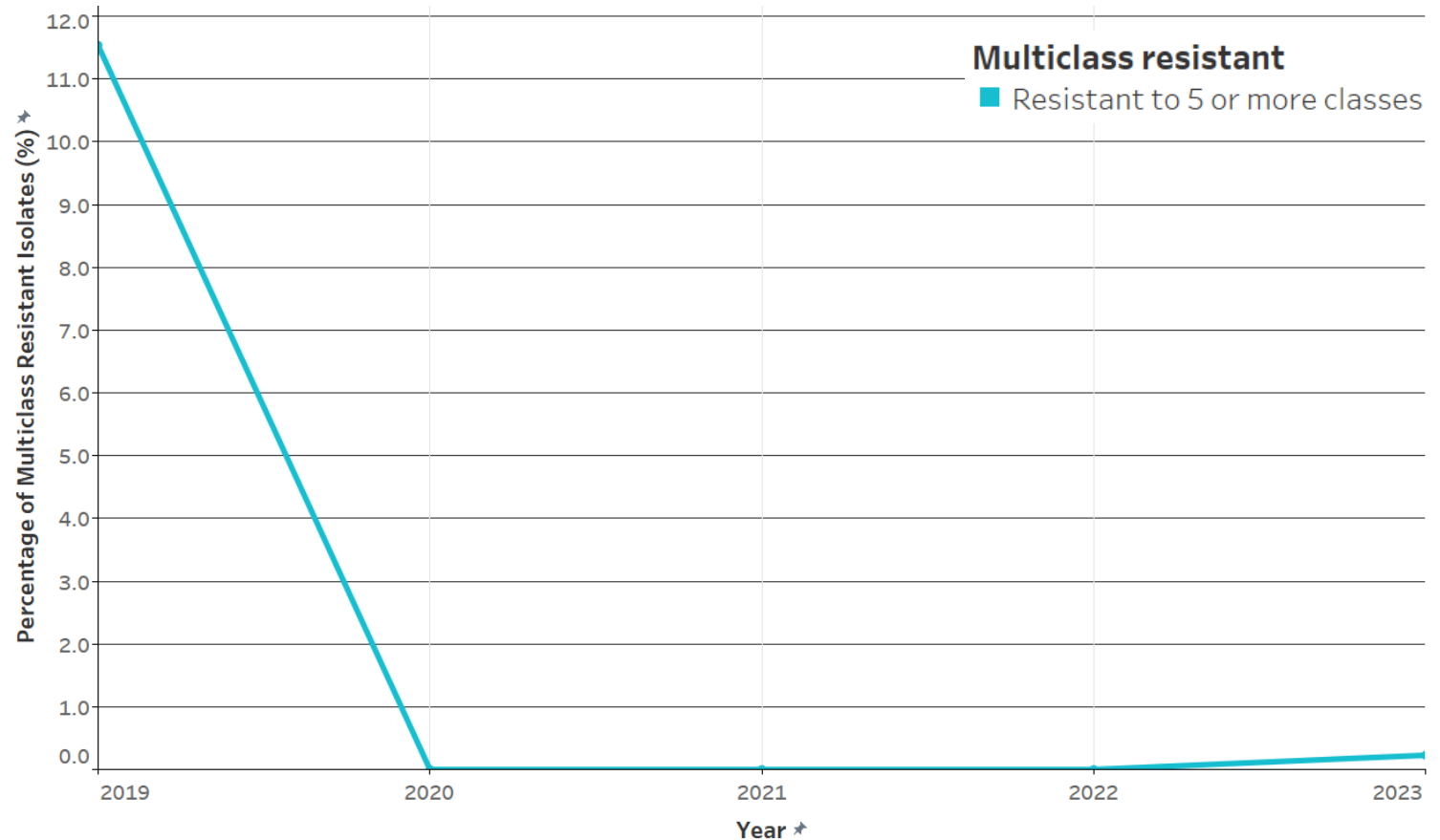
Increasing resistance to 2 or more classes and extremely low full susceptibility

- **Variable** full susceptibility (2019; 6% and 2023; 7%)
- **Variable and increased from moderate to high** resistance to 2 or more classes (2019; 14% and 2023; 32%)
- **Decreased from moderate to low** resistance to 3 or more classes (2019; 14% and 2023; 10%)



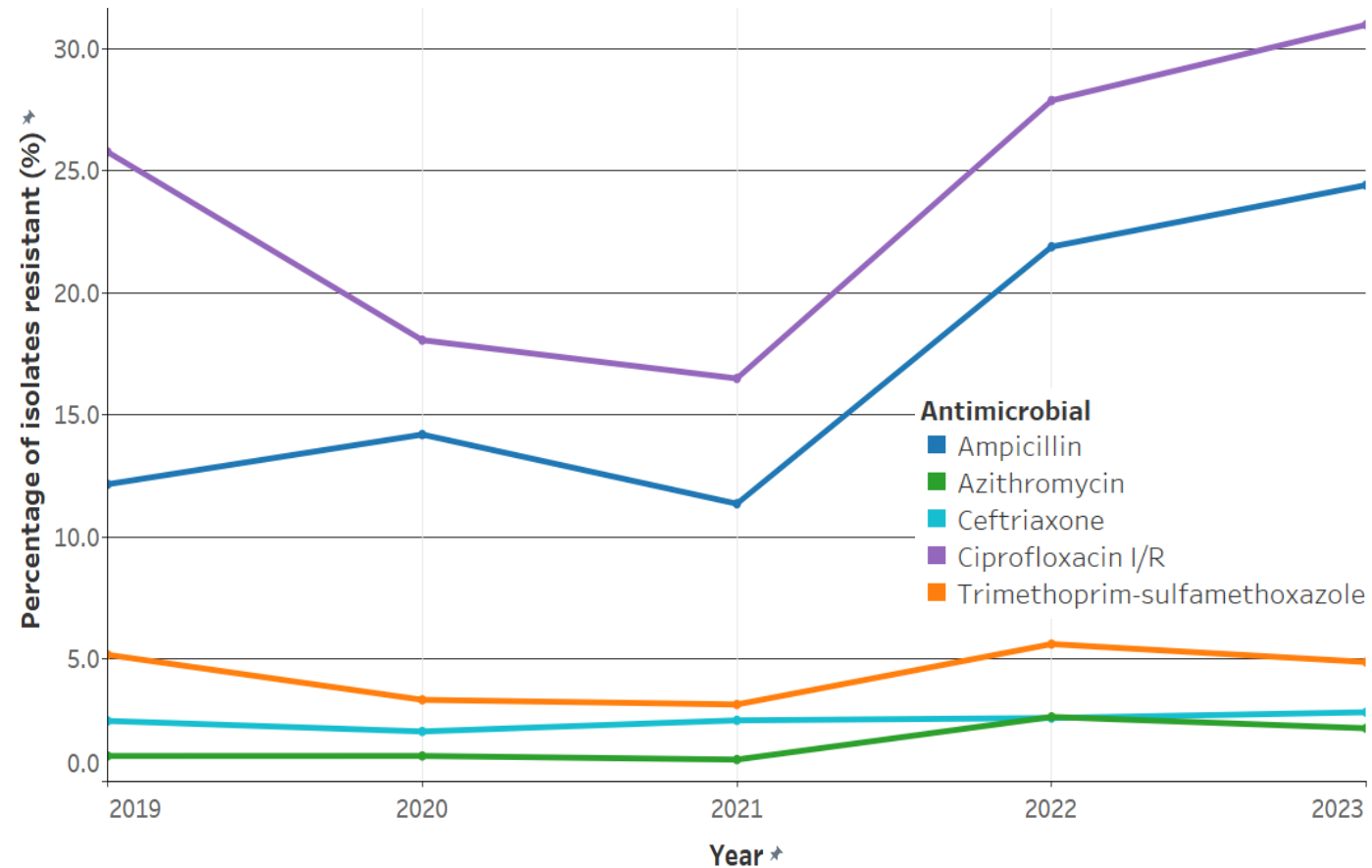
Decreasing resistance to 5 or more classes (returned to expected prevalence)

- **Decreased from moderate to very low** resistance to 5 or more classes
 - 2019; 12% - 48 isolates (importation of outbreak strain)
 - 2023; 0.2% - 1 isolate
- Since 2019, **no** resistance to 6 or more classes



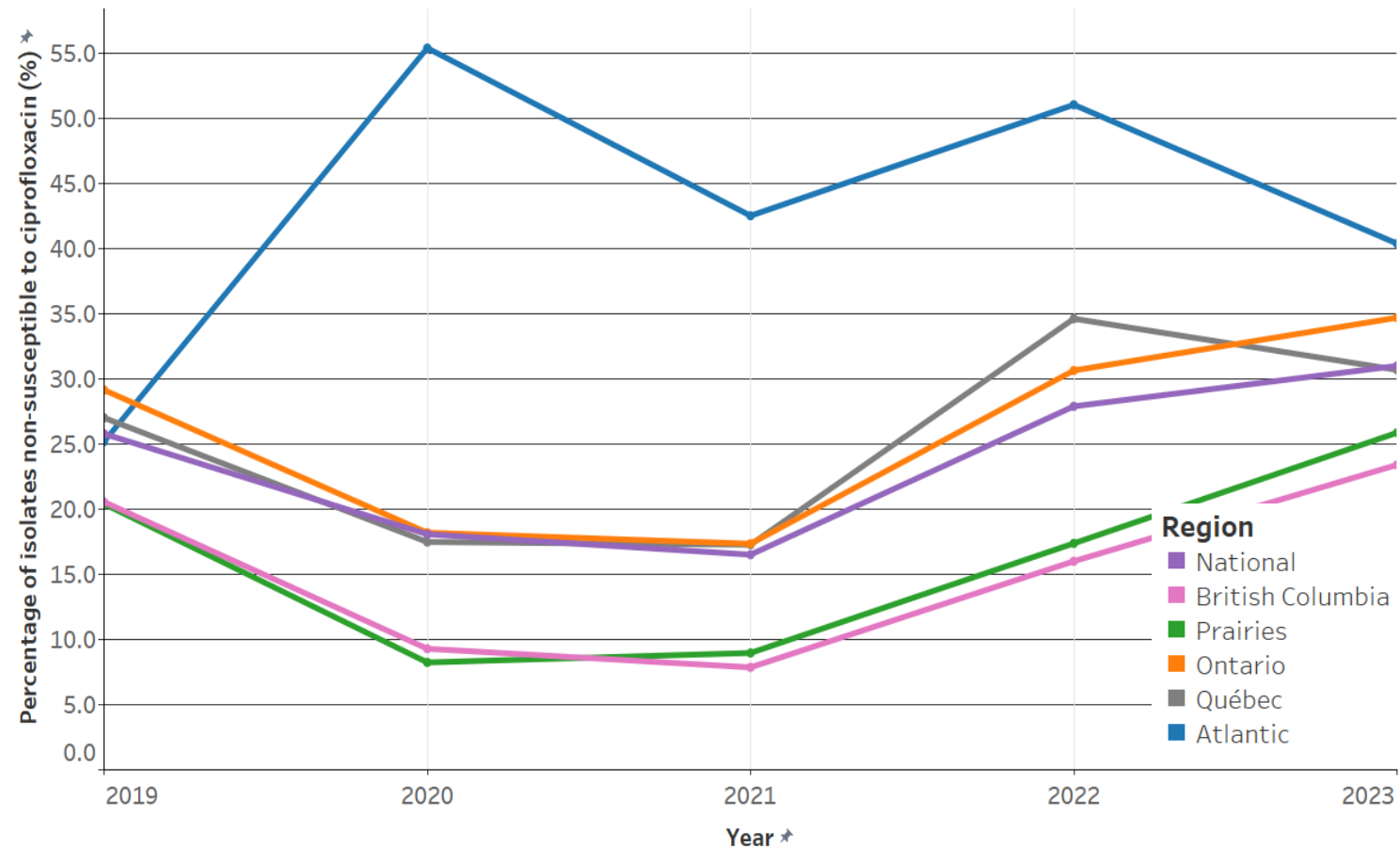
Increasing non-susceptibility to ciprofloxacin and resistance to ampicillin

- **High** non-susceptibility to ciprofloxacin **decreased to moderate** between 2019 (26%) and 2021 (17%), but **increased to high** in 2022 (28%) and 2023 (31%)
- **Low** and relatively stable resistance to ceftriaxone (ranging from 2% to 3%)
- **Moderate** resistance to ampicillin **increased to high** resistance (2019; 12% and 2023; 24%)
- **Low** and variable resistance to trimethoprim-sulfamethoxazole (ranging from 3% to 6%)
- **Low** resistance to azithromycin **increased** between 2019 (1%) and 2022 (3%) and **decreased slightly** in 2023 (2%)



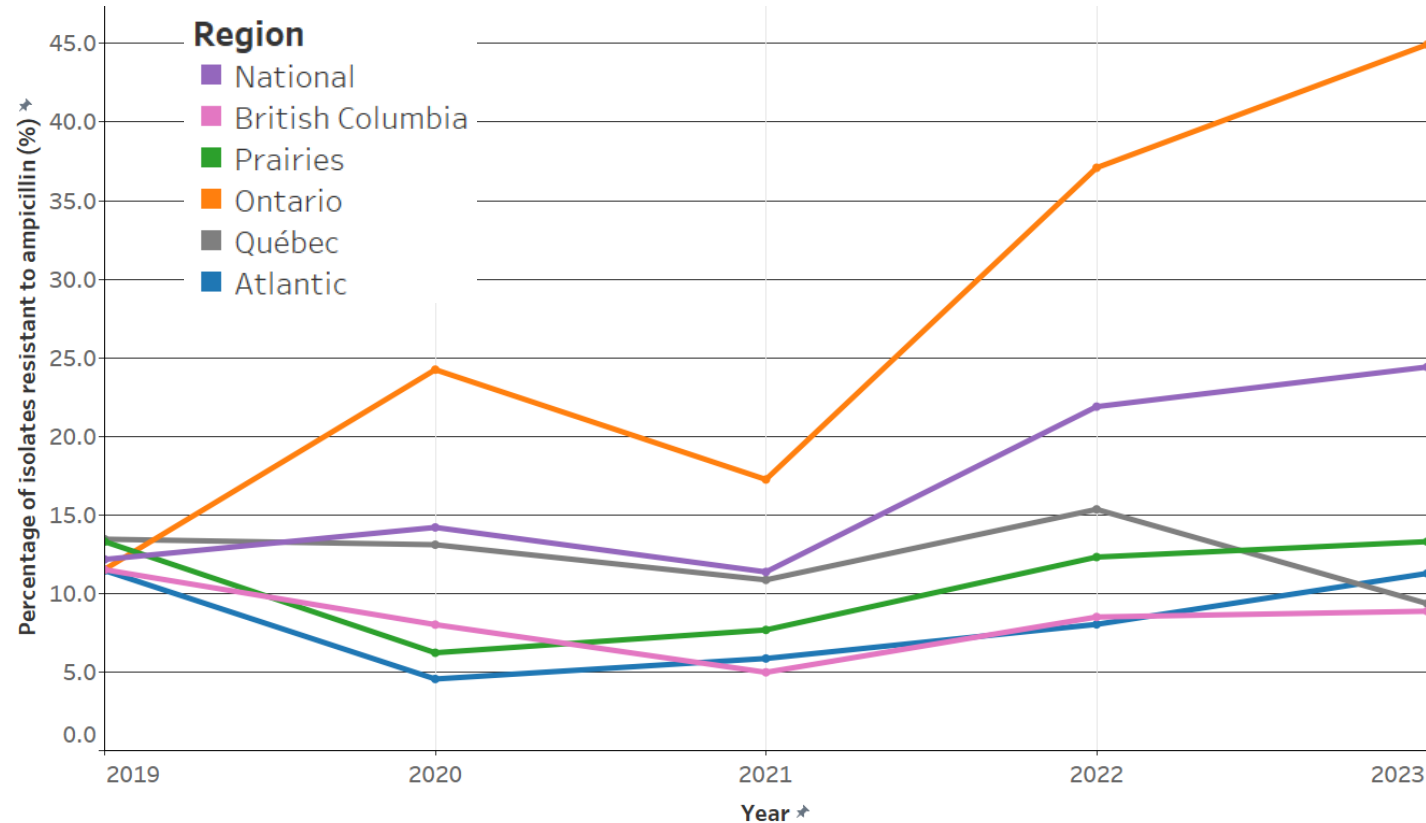
Substantial regional variation in non-susceptibility to ciprofloxacin

- Compared to the prevalence of non-susceptibility nationally
 - Atlantic provinces were **higher** since 2020
 - Ontario and Québec were **similar**
 - Prairies and British Columbia were **lower** and follow a similar trend



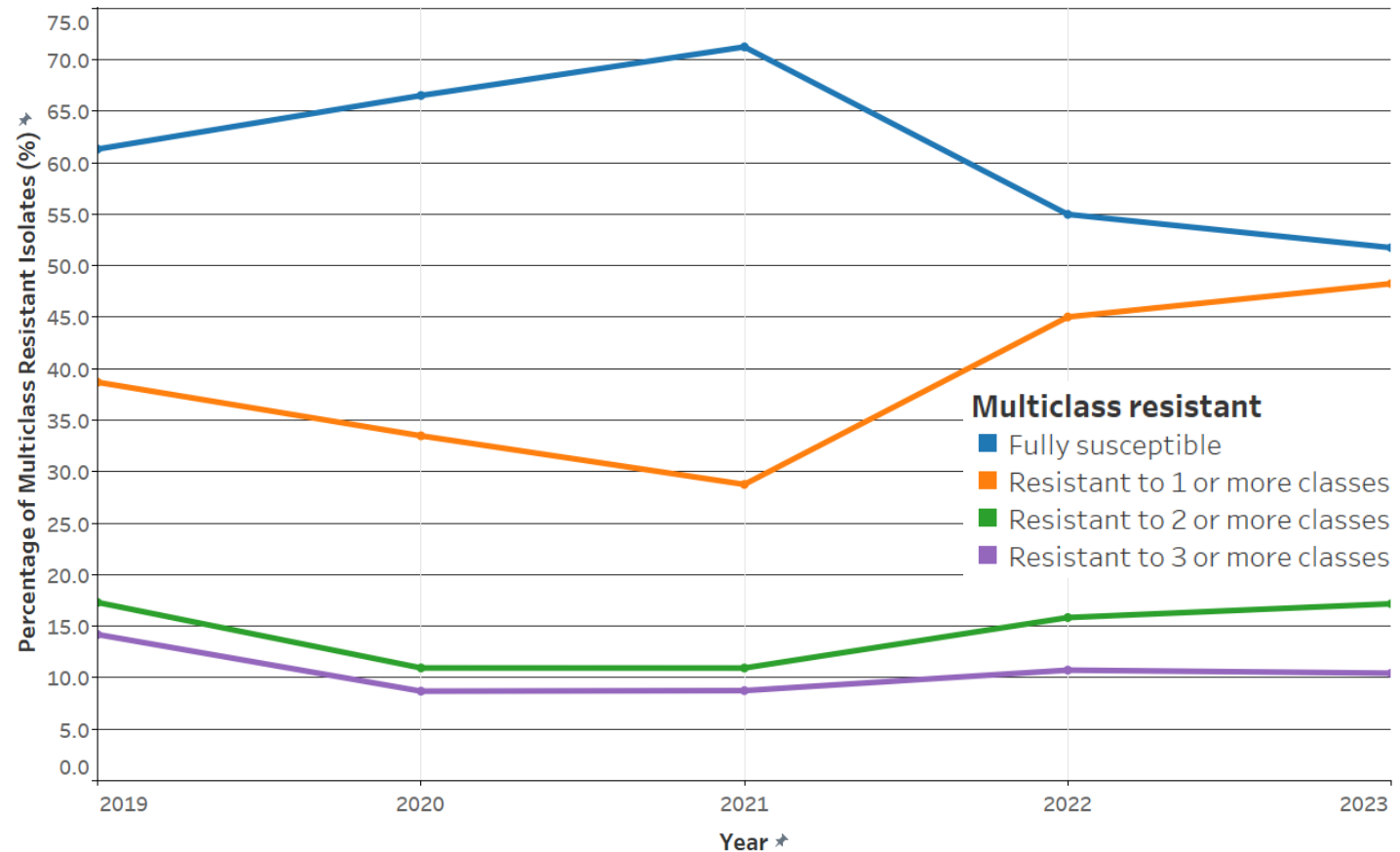
Substantial regional variation in ampicillin resistance

- Compared to the prevalence of resistance nationally
 - Ontario was **higher** since 2020
 - Québec was **similar** until 2021 and **lower** starting in 2022
 - Prairies, British Columbia and Atlantic provinces were **lower** since 2020



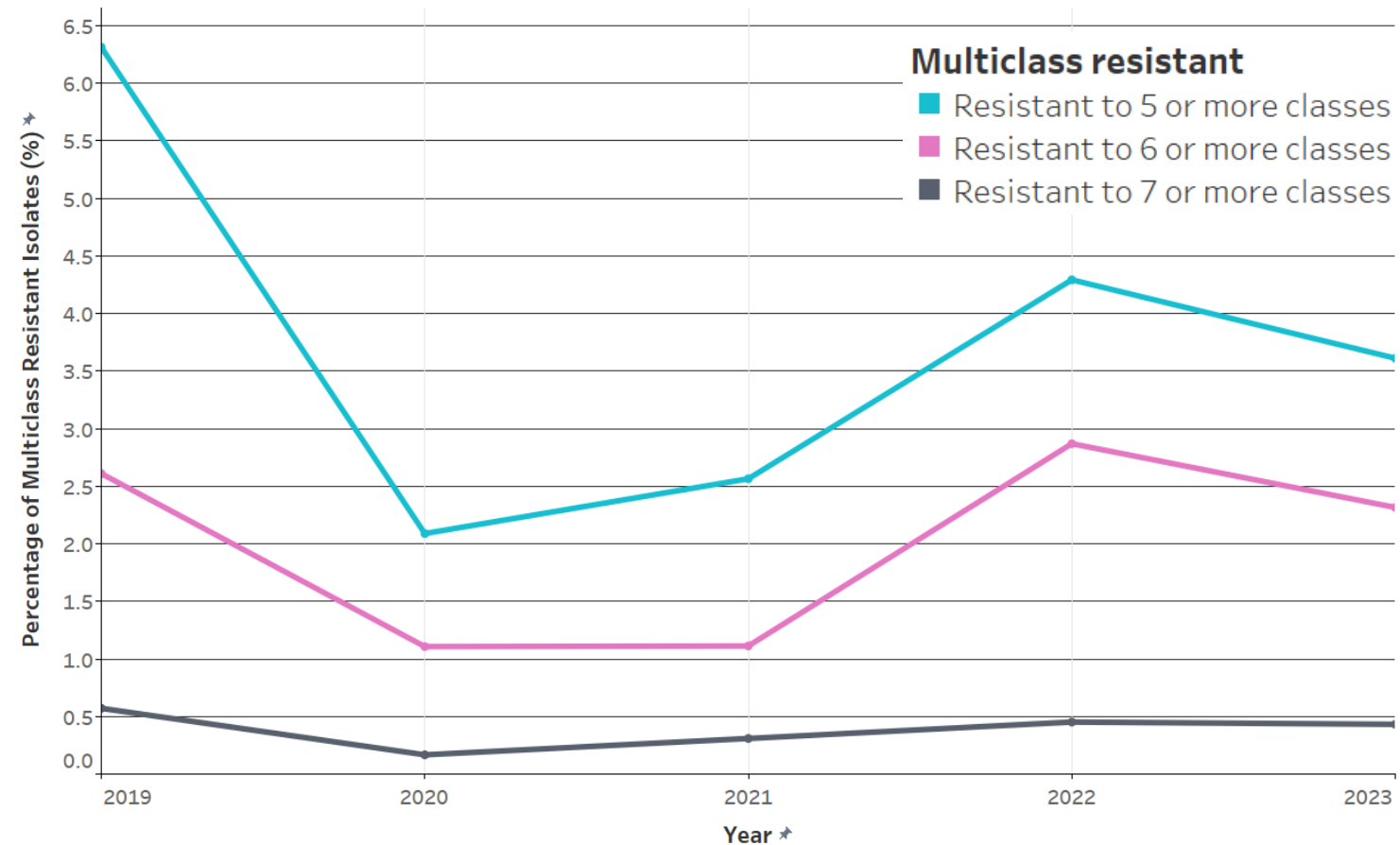
Increasing resistance to 2 or more classes and decreasing full susceptibility

- **Decreased** full susceptibility since 2021 (2021; 71% and 2023; 52%)
- **Moderate** resistance to 2 or more classes, **increased** since 2021 (2021; 11% and 2023; 17%)
- **Low to moderate** resistance to 3 or more classes, relatively **stable** since 2020 (2020; 9% and 2023; 10%)



Very low and stable resistance to 7 or more classes

- **Low** resistance to 5 or more classes, **decreased** between 2019 (6%) and 2023 (4%)
- **Low** and **variable** resistance to 6 or more classes (ranging from 1% to 3%)
- **Very low** and **stable** resistance to 7 or more classes (ranging from 0.2% to 0.6%)
- Since 2019, **no** resistance to 8 or more classes



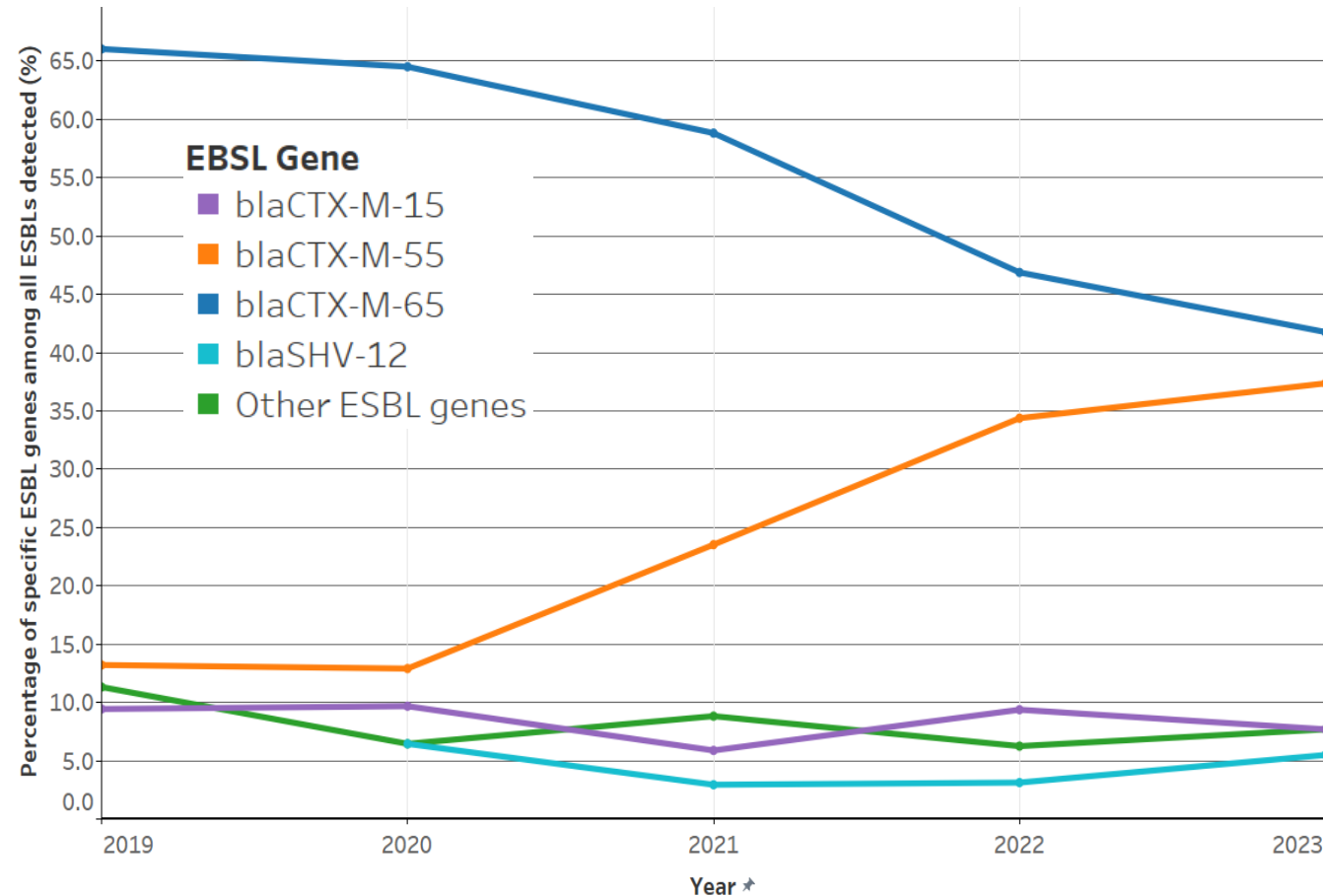
Overall ESBL genes in human non-typhoidal *Salmonella* are increasing with *bla*_{CTX-M-65} decreasing and *bla*_{CTX-M-55} increasing

- Top 4 ESBL genes among ESBLs detected

- *bla*_{CTX-M-65} **decreased** between 2019 (66%) and 2023 (42%)
- *bla*_{CTX-M-55} **increased** between 2019 (13%) and 2023 (37%)
- *bla*_{CTX-M-15} variable from 2019 to 2023 (ranging between 6% and 10%)
- *bla*_{SHV-12} variable from 2020 to 2023 (ranging between 3% and 7%)

- Other ESBL genes detected

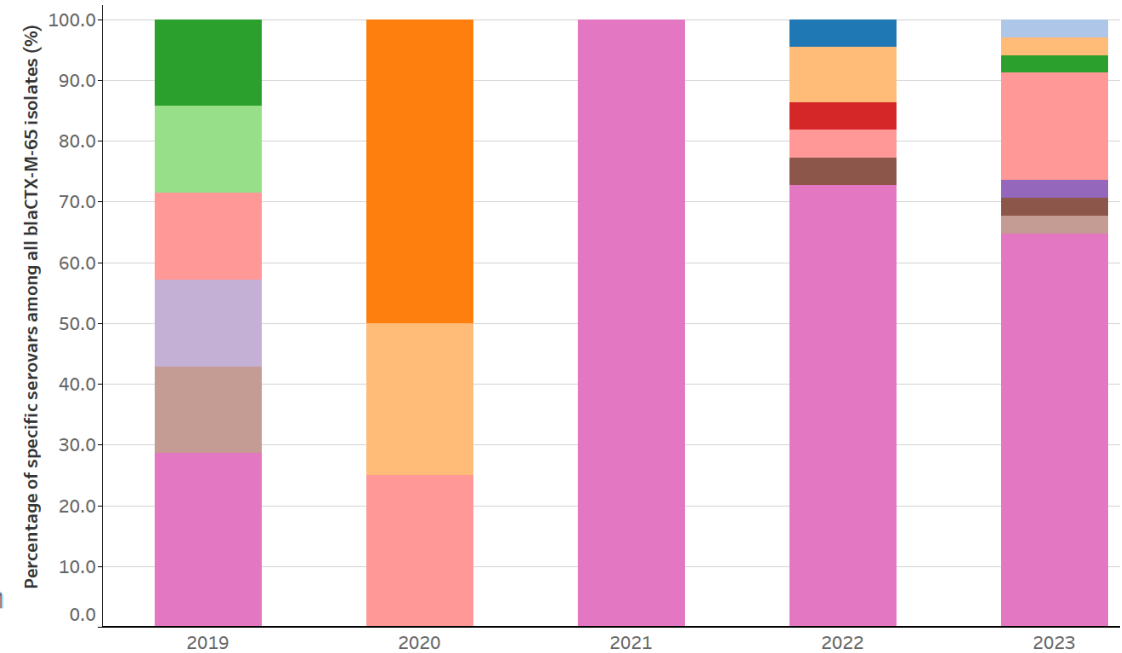
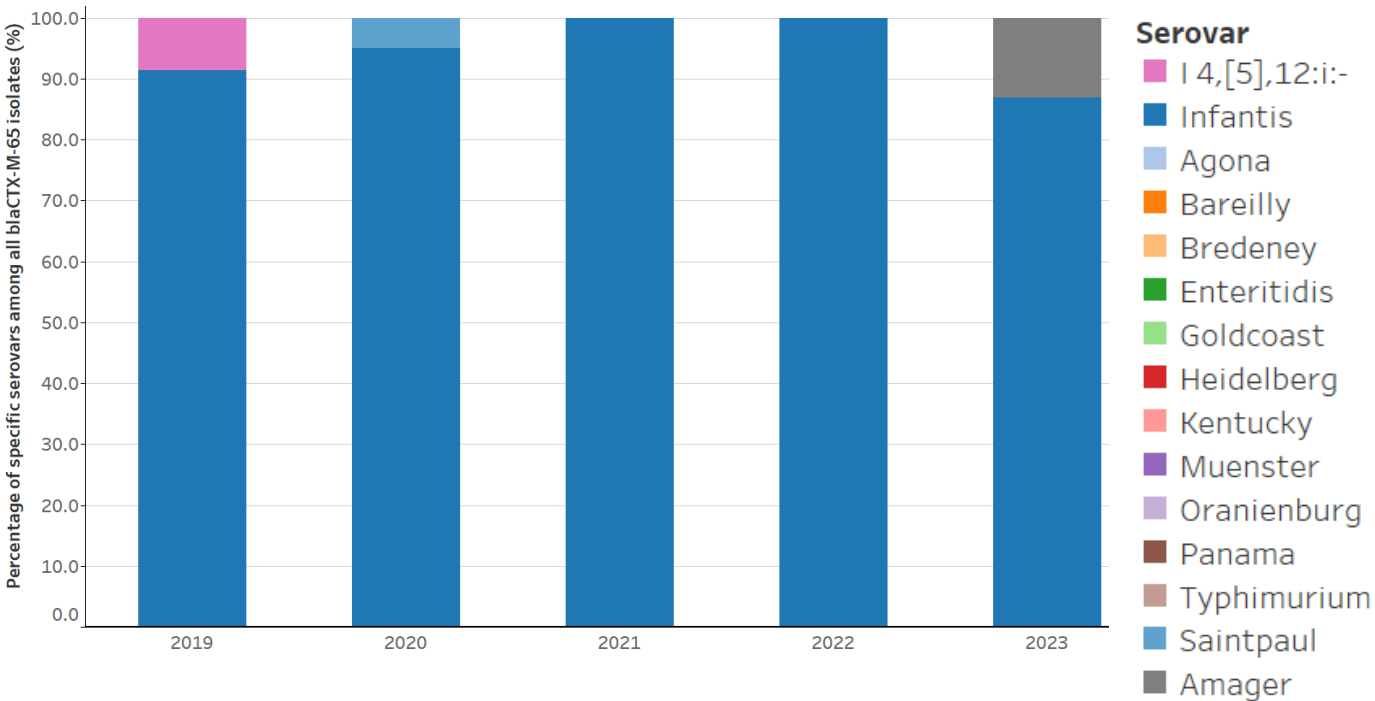
*bla*_{CTX-M-1} *bla*_{CTX-M-8} *bla*_{CTX-M-9} *bla*_{CTX-M-14}
*bla*_{CTX-M-14b} *bla*_{CTX-M-27} *bla*_{CTX-M-32} *bla*_{CTX-M-174}
*bla*_{SHV-2} *bla*_{SHV-30} *bla*_{TEM-15} *bla*_{TEM-52B} *bla*_{TEM-93}



bla*_{CTX-M-65} is mostly in *S. Infantis* and *bla*_{CTX-M-55} is mostly in *S. I 4,[5],12:i:-

- bla*_{CTX-M-65} predominately in *S. Infantis*

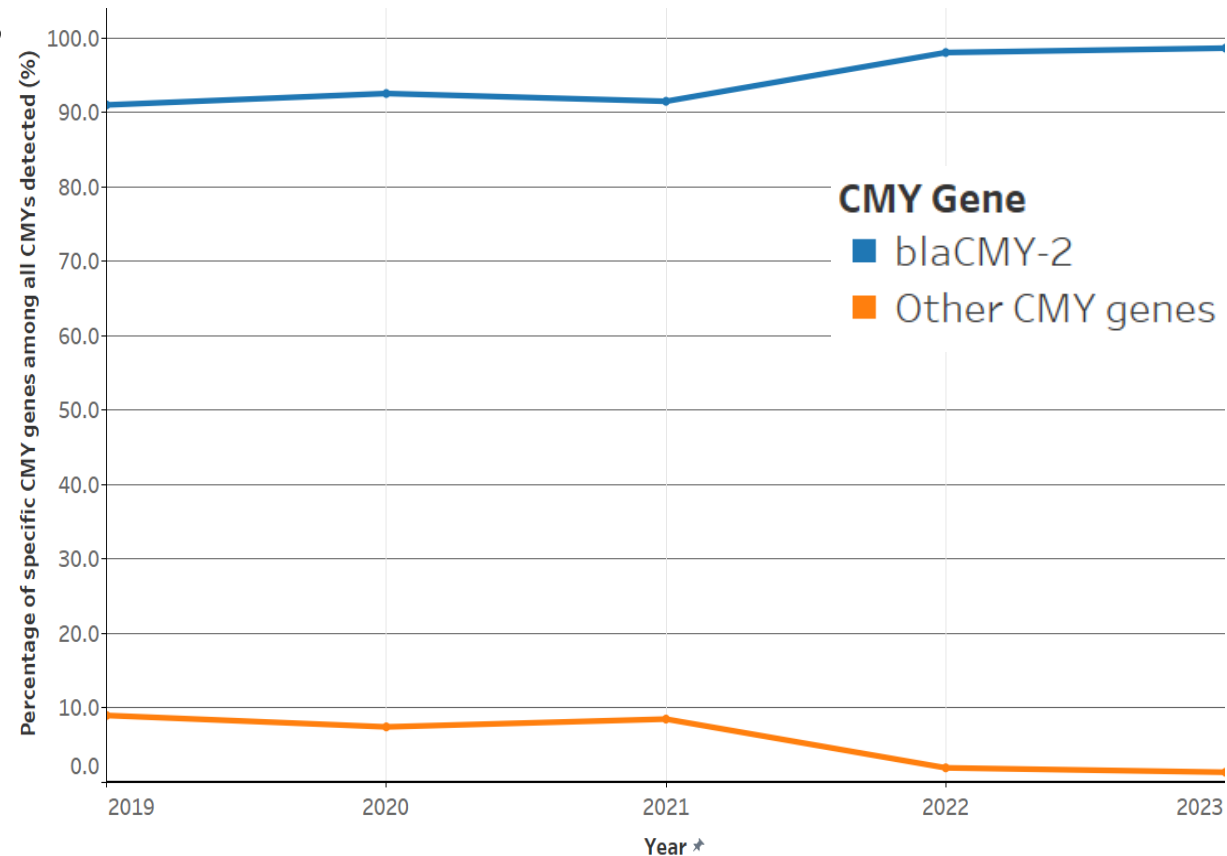
- bla*_{CTX-M-55} predominately in *S. I 4,[5],12:i:-*



Overall CMY genes in human non-typhoidal *Salmonella* are stable with *bla*_{CMY-2} increasing

- CMY genes stable between 2019 and 2023 (ranging between 1% and 2% of all isolates)
- *bla*_{CMY-2} predominate CMY gene **increased** between 2019 (91%) and 2023 (99%)
 - Mostly in *S. Dublin*, *S. Heidelberg* and *S. Typhimurium*
- Other CMY genes ranged between 0% and 6% each year

*bla*_{CMY-4} *bla*_{CMY-44} *bla*_{CMY-54} *bla*_{CMY-61}



XDR *Salmonella* I, 4 [5], 12:i:- continues to increase

- Extensively drug resistant (XDR) non-typhoidal *Salmonella* express resistance to **ampicillin, ceftriaxone, ciprofloxacin, azithromycin, trimethoprim, and sulfonamides**

Year	# of XDR	Ages 0-2yr	Ages 3-9yr	Ages 10-19yr	Adult 20+
2020	0	N/A	N/A	N/A	N/A
2021	8	5	0	0	3
2022	16	6	1	1	8
2023	19	2	4	0	13

- In 2021, **ONE** isolate from a child (0-2yr) was invasive (blood)
- In 2022 and 2023, **ALL** isolates from children were non-invasive (stool)
- In 2021 all isolates from adults were recovered from stool, 6 isolates from stool were recovered in 2022, and 10 in 2023; the remaining adult isolates were recovered from urine samples with the exception of an isolate of unknown sample origin in 2022

Human *Campylobacter*

Most *Campylobacter* infections do NOT require treatment with antimicrobials

- *Campylobacter* infections most commonly cause self-limiting diarrhea
 - Treatment with antimicrobials is not required or recommended
- Treatment with antimicrobials is considered:
 - When clinical signs are severe or prolonged
 - >6 diarrheal episodes/day, bloody diarrhea, diarrhea lasting >1 week, persistent fever
 - When patient is immunocompromised
 - Treatment options include azithromycin or ciprofloxacin (alternative)

***Campylobacter* has a high incidence rate in Canadians**

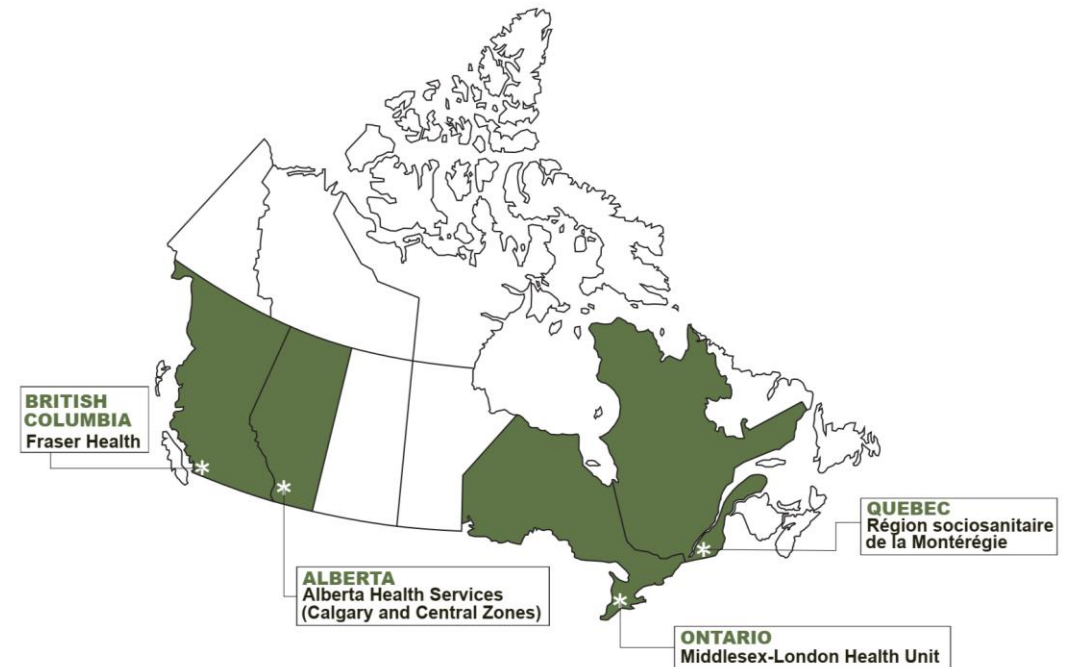
- Incidence rates of Canadians with *Campylobacter* in 2022

	2022 Incidence Rates (Cases/100,000 population)
<i>Campylobacter</i>	18.72

- Source of data – Canadian Notifiable Disease Surveillance System (CNDSS)
[Notifiable Diseases Online](#)

FoodNet Canada (FNC), the integrated sentinel site surveillance network for enteric disease in Canada

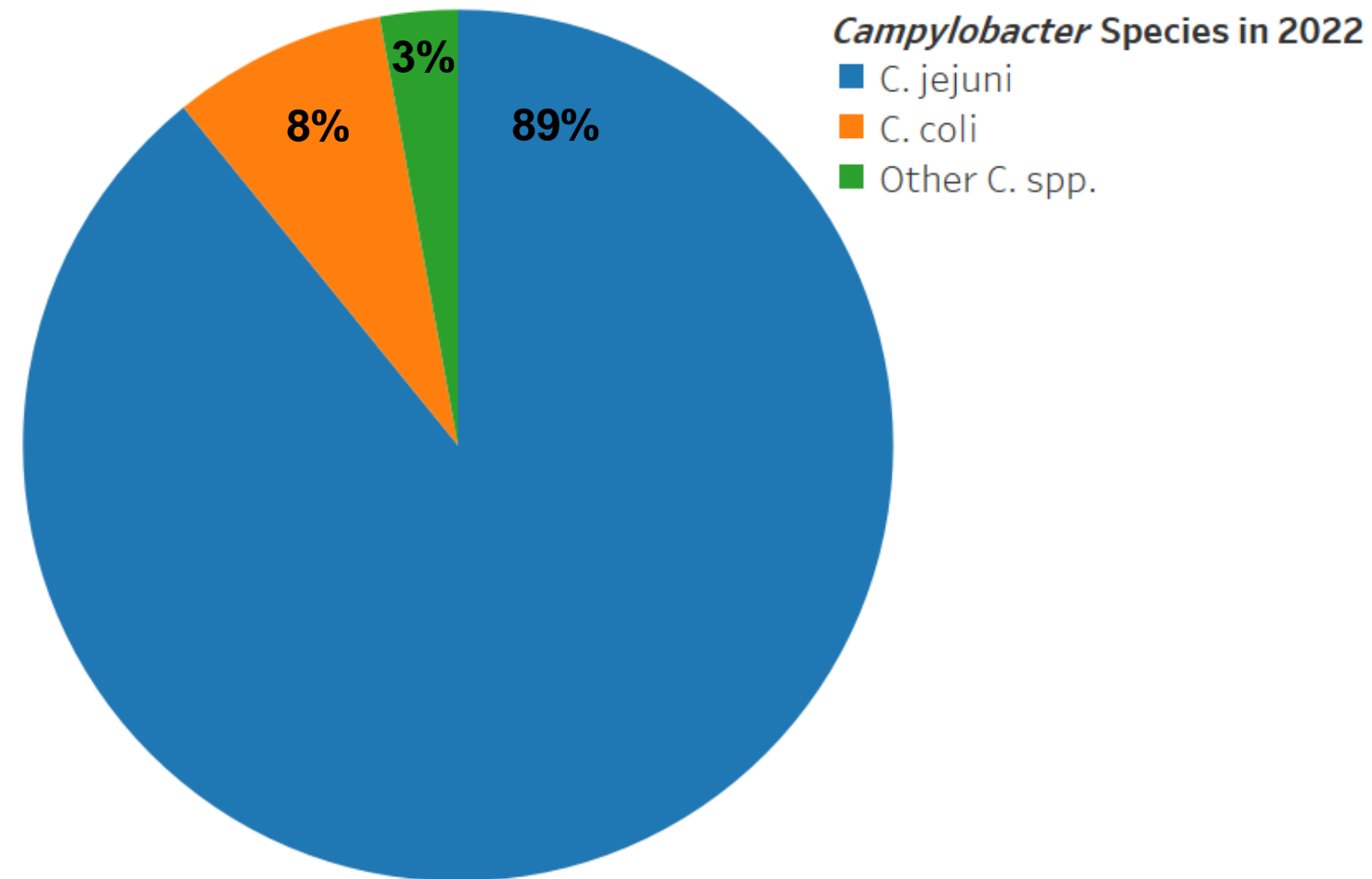
- *Campylobacter* isolates forwarded for antimicrobial susceptibility testing are a subset of all FNC *Campylobacter* cases
- Tested using broth microdilution for susceptibility to nine antimicrobials
 - For all antimicrobials including ciprofloxacin, only isolates classified as resistant are reported as resistant
- 3% of cases were excluded due to unresolved data discrepancies
- Data from 2017-2022 are presented with all sentinel sites combined



[About FoodNet Canada - Canada.ca](https://www.canada.ca/about-foodnet-canada)

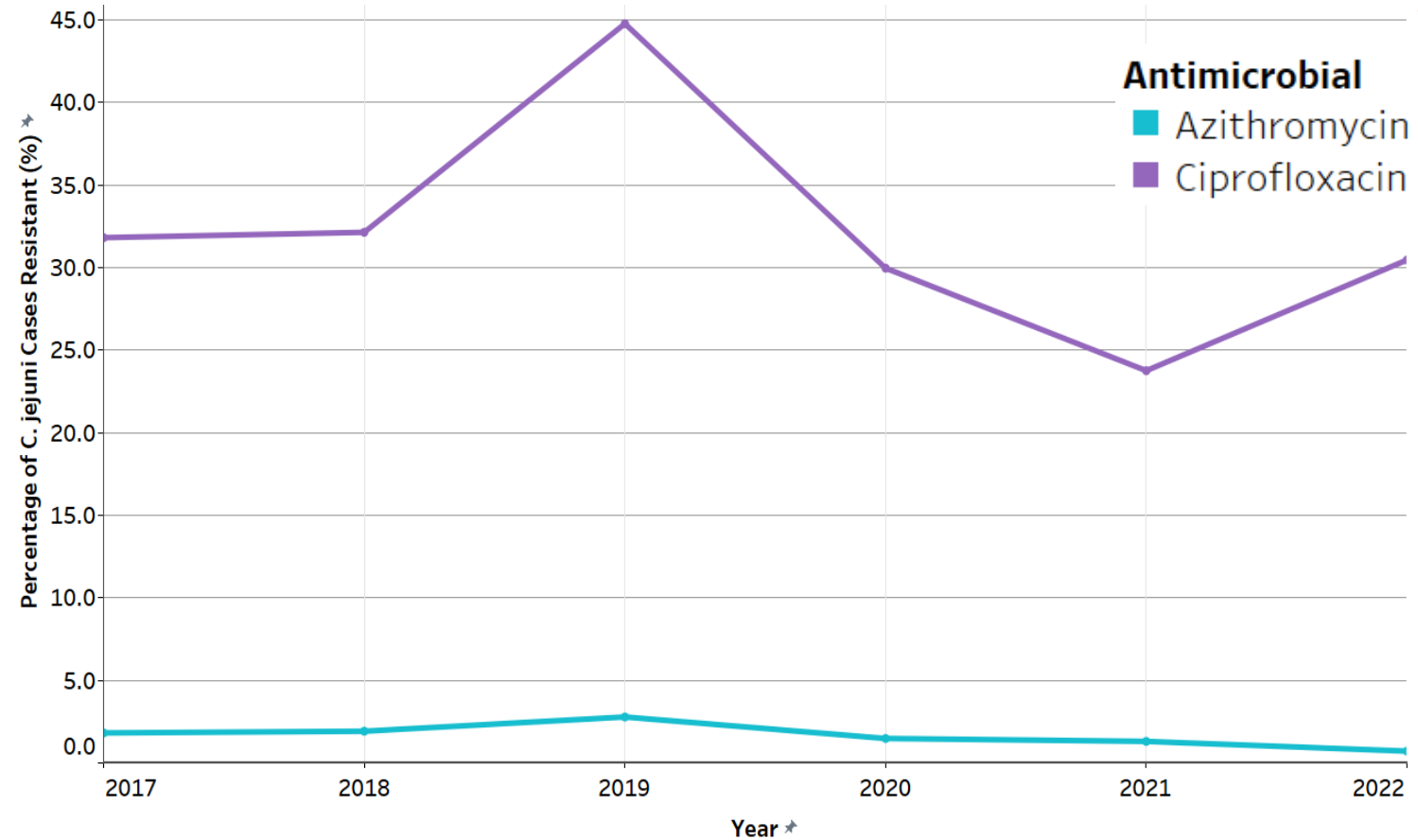
C. jejuni is the predominant *Campylobacter* species in humans

- In 2022, 89% of the cases were *C. jejuni*
- *Campylobacter* predominantly causes gastrointestinal infections (100% stool in 2022)



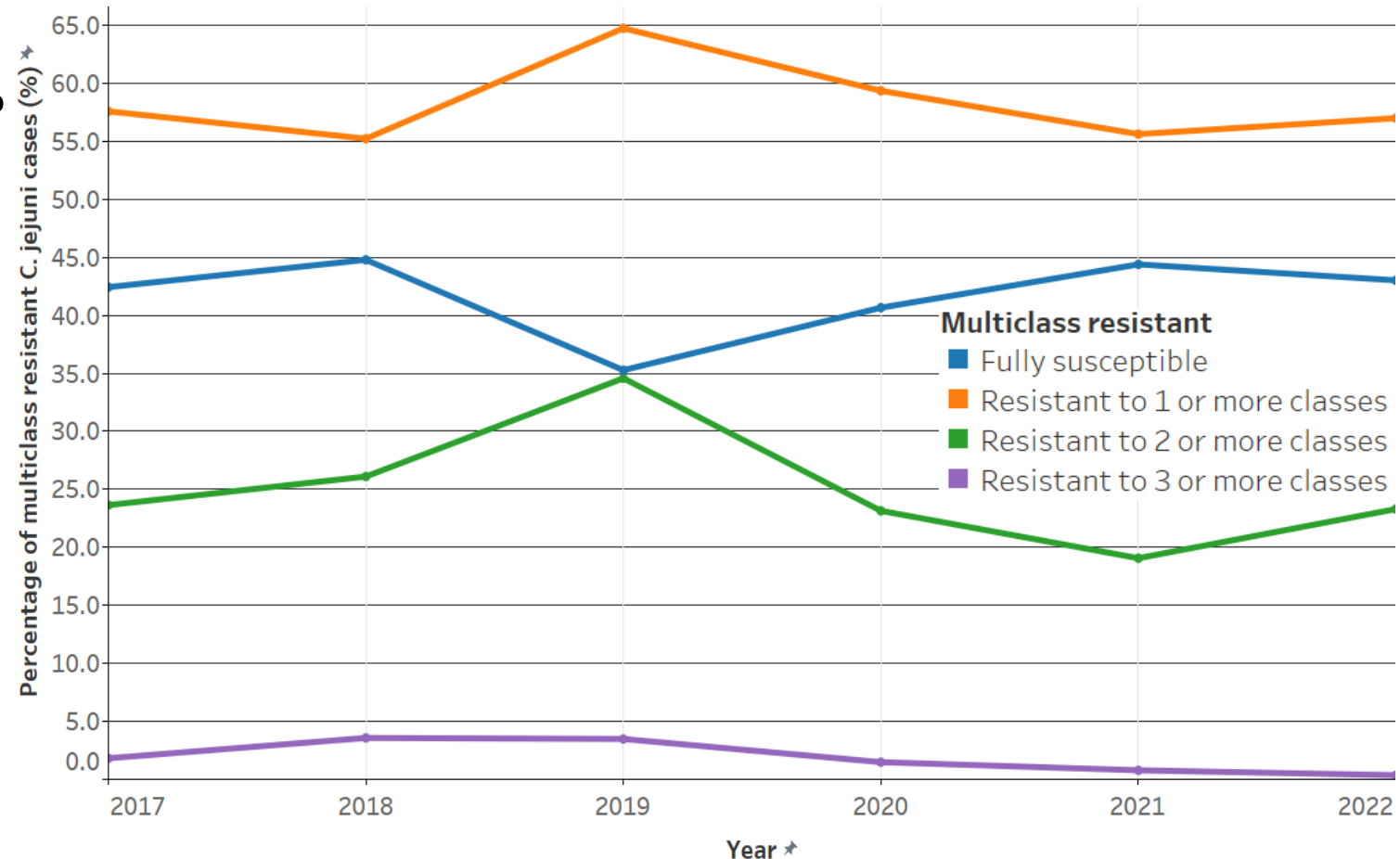
Lower resistance to azithromycin compared to ciprofloxacin

- *C. jejuni* (figure)
 - **Variable** and **high** resistance to ciprofloxacin, 31% in 2022
 - **Decreasing** and **low to very low** resistance to azithromycin, 0.7% in 2022
- *C. coli* (2017-2022 combined)
 - **High** resistance to ciprofloxacin (46%)
 - **Moderate** resistance to azithromycin (13%)



Resistance to 3 or more antimicrobial classes in *C. jejuni* was low to very low

- *C. jejuni* (figure)
 - **Variable** full susceptibility, 43% in 2022
 - **Decreasing** and **low to very low** resistance to 3 or more classes, 0.4% in 2022
- *C. coli* (2017-2022 combined)
 - **Lower** full susceptibility (36%)
 - **Moderate** resistance to 3 or more classes (13%)



Cases with resistance to 5 or more antimicrobial classes are infrequent; could complicate treatment, if required

Species	Year	Resistance Pattern	
		5 Antimicrobial Classes	6 Antimicrobial Classes
<i>C. jejuni</i>	2018	CIP-NAL-ERY-AZM-TEL-TET-CLI-FLO	
<i>C. jejuni</i>	2019	CIP-NAL-ERY-AZM-TET-CLI-GEN NAL-AZM-TET-CLI-GEN	CIP-NAL-ERY-AZM-TET-CLI-FLO-GEN
<i>C. coli</i>	2020		CIP-NAL-ERY-AZM-TET-CLI-FLO-GEN
<i>C. jejuni</i>	2021	CIP-NAL-ERY-AZM-TET-CLI-GEN	
<i>C. coli</i>	2022	CIP-NAL-ERY-AZM-TET-CLI-GEN CIP-NAL-ERY-AZM-TET-CLI-GEN	

Antimicrobial classes

Quinolones Macrolides/ketolides Tetracyclines Lincosamides Phenicols Aminoglycosides

Take Away Messages – Human *Campylobacter*

- *C. jejuni* is the predominant *Campylobacter* species in humans
- Lower resistance to azithromycin (2022; 0.7%) in *C. jejuni* compared to ciprofloxacin (2022; 31%)
- Resistance to 3 or more classes in *C. jejuni* was low to very low
- Cases with resistance to 5 or more antimicrobial classes are infrequent, however, they could complicate treatment, if required

Take Away Messages – Human *Salmonella*

- Extremely high non-susceptibility to ciprofloxacin in typhoidal *Salmonella*
- Increasing frequency of non-susceptibility to ciprofloxacin and resistance to ampicillin in non-typhoidal *Salmonella*
- Regional variation in *Salmonella* antimicrobial resistance is important to consider
- Overall ESBL genes in human non-typhoidal *Salmonella* are increasing with $bla_{\text{CTX-M-65}}$ decreasing and $bla_{\text{CTX-M-55}}$ increasing

Where can I find more information?

CIPARS Interactive data visualizations

<https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars/interactive-data.html>

CARSS Interactive data visualizations

Human *Salmonella*: <https://health-infobase.canada.ca/carss/amr/results.html?ind=13>

CIPARS website

<https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars.html>

FNC website

<https://www.canada.ca/en/public-health/services/surveillance/foodnet-canada.html>

Acknowledgements

- NML Division of Enteric Diseases and PulseNet Canada
- Provincial Public Health Laboratories
- FoodNet Canada (*Campylobacter*)
- FoodNet Canada Sentinel Sites (*Campylobacter*)
- National Enteric Surveillance Program (NESP)

Questions

Contact Information for CIPARS
Human Component

Dr. Melissa MacKinnon
melissa.mackinnon@phac-aspc.gc.ca

