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SURVEILLANCE REPORT

Carbapenem-resistant Enterobacterales in Ontario

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Background

Carbapenem-resistant Enterobacterales (CRE) represent a broad range of bacteria (including but not limited to, *Escherichia coli, Klebsiella, Proteus, Citrobacter,* and *Enterobacter* species) that are resistant to carbapenem antibiotics, one of the last options for therapy against multi-drug-resistant Gram-negative bacteria. Resistance to these agents can occur by a variety of mechanisms (e.g., porin channels, efflux pumps, beta-lactamase enzymes), but these organisms are typically divided into the categories of carbapenemase-producing Enterobacterales (CPE) and non-CPE. CPE are of particular public health concern given that resistance can be transferred between organisms via mobile genetic elements, hastening the spread of CPE and increasing the risk of outbreaks.

Compared to carbapenem-susceptible organisms, infections caused by CRE in hospitalized patients are associated with an over 3-fold increased odds of mortality.[1–3] Given the significant morbidity, mortality and economic burden of infections caused by CRE, the World Health Organization has designated these organisms as a critical priority pathogen for research, development and prevention strategies.[4]

In order to improve data collection and monitor the spread of CPE in healthcare settings in Ontario, the Health Protection and Promotion Act was updated May 2018 to include colonization or infection with CPE as a disease of public health significance (DOPHS).[5] Over the last decade, the Ontario Laboratories Information System (OLIS) has collected comprehensive microbiology data, including culture and susceptibility test results which can be used to monitor antimicrobial resistance including carbapenem resistant organisms. To provide recent data on these organisms, this report describes the epidemiology of both CRE and CPE in Ontario from 2017 to 2024. The CRE data is from OLIS and includes diagnostic isolates. The CPE data is from the Public Health Ontario Laboratory and includes both diagnostic and surveillance specimens. See technical notes for additional details.

Highlights

- Based on Ontario Laboratories Information System (OLIS) data from January 2017 to September 2024, 5,815 carbapenem resistant Enterobacterales cases were identified from diagnostic isolates. The incidence of CRE was low but more than doubled during the analysis period (3.3 per 100,000 population per year in 2017 to 6.9 per 100,000 population per year in 2024).
- CRE were more common among patients who were older, had higher comorbidity scores, and were hospitalized or in intensive care units. The distribution of CRE cases varies geographically, where Niagara, Hamilton, Peel, and Brant Public Health Unit have the highest rates.
- Based on Public Health Ontario data, among 3,386 confirmed cases of CPE (both infection and colonization) in Ontario from January 2017 to December 2024, carbapenemases were most often New Delhi metallo-β-lactamase (NDM) (n=1,883, 55.6%), oxacillinase-48 (OXA-48) (n=992, 29.3%), or *Klebsiella pneumoniae* carbapenemase (KPC) (n=542, 16.0%).

Results

Out of 3,061,743 Enterobacterales cases identified from diagnostic isolates, carbapenem resistance was identified in 5,815 (0.19%) patients during the period of January 2017 to September 2024 (Table 1).

Trends Over Time

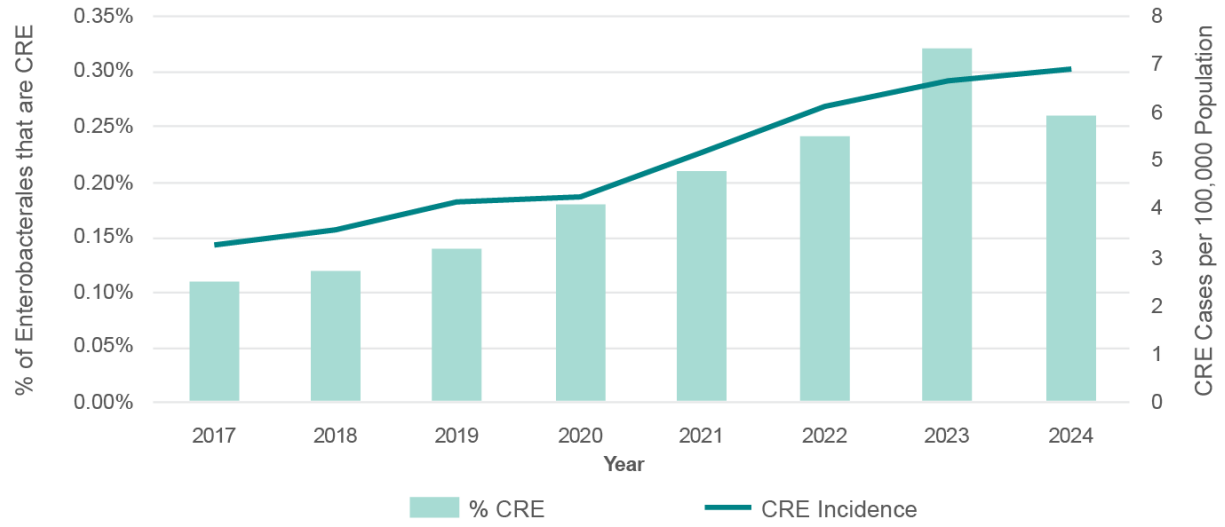
Between 2017 and 2024, the incidence was low but more than doubled (3.3 per 100,000 population per year in 2017 to 6.9 per 100,000 population per year in 2024). Similarly, the proportion of Enterobacterales cases that were CRE more than doubled during this period (0.11% in 2017 to 0.26% in 2024) (Figure 1).

Table 1: Cases of CRE from Diagnostic Isolates between January 2017 and September 2024

Year	Enterobacterales Cases	CRE Cases	% of Cases that are CRE	Cases Per 100,000 Population Per Year
2017	423,268	465	0.11%	3.3
2018	431,529	519	0.12%	3.6
2019	441,182	614	0.14%	4.2
2020	350,702	631	0.18%	4.3
2021	372,785	779	0.21%	5.2
2022	391,580	931	0.24%	6.1
2023	325,313	1,045	0.32%	6.7
2024	325,384	831	0.26%	6.9
Total Cases	**3,061,743**	**5,815**	**0.19%**	**5.0**

Data source: Ontario Laboratories Information System

Figure 1: CRE Cases Per Year in Ontario from Clinical/Diagnostic Isolates



Data source: Ontario Laboratories Information System

Microbiological Characteristics of CRE Cases

- Across genera, carbapenem resistance was relatively high in *Enterobacter* (n=3393/83,898; 4.04%), lower in *Serratia* (n=118/31,091; 0.38%), *Providencia* (n=39/11,648; 0.33%), *Citrobacter* (n=230/103,104; 0.22%), *Klebsiella* (992/468,219; 0.21%), and *Morganella* (n=51/38,581; 0.13%) and lowest in *Escherichia* (n=941/2,148,991; 0.04%) and *Proteus* (n=51/176,211; 0.03%) (Table 2).
- Most cases of CRE were identified in urine (n=3,680/5,815; 63%). However, the proportion of cases that were CRE was highest in respiratory specimens (n=492/24,559; 2.00%), followed by other specimen types (n=1,234/149,243; 0.83%), blood (n=409/91,852; 0.45%), and urine (n=3,680/2,796,089; 0.13%) (Table 2).

Table 2: Microbiological Characteristics of CRE from Diagnostic Isolates between January 2017 and September 2024

Characteristic	Enterobacterales Cases	CRE Cases	% of Cases that are CRE
Organism Genus			
Enterobacter	83,898	3,393	4.04%
Klebsiella	468,219	992	0.21%
Escherichia	2,148,991	941	0.04%
Citrobacter	103,104	230	0.22%
Serratia	31,091	118	0.38%
Morganella	38,581	51	0.13%
Proteus	176,211	51	0.03%
Providencia	11,648	39	0.33%
Specimen Site			
Blood	91,852	409	0.45%
Respiratory	24,559	492	2.00%
Urine	2,796,089	3,680	0.13%
Other	149,243	1,234	0.83%
Sterile Specimen			
No	2,949,047	5,091	0.17%
Yes	112,696	724	0.64%

Data source: Ontario Laboratories Information System
Notes: Organism genus is ordered in descending order, based on the absolute number of CRE cases.

Demographic Characteristics of CRE Cases

Age

CRE incidence in Ontario was higher with increasing age, 0.5 per 100,000 (proportion of Enterobacterales that are CRE: 0.07%) in those 0 to 17 years, 2.5 per 100,000 (proportion CRE: 0.13%) in 18 to 64 years, and 20.4 per 100,000 (proportion CRE: 0.26%) in patients 65 years and older (Table 3).

Sex

Although the proportion of Enterobacterales cases that were CRE was higher among men (0.48% in men compared to 0.12% in women), the incidence was similar between men and women (4.8 per 100,000 in men and 4.9 per 100,000 in women) (Table 3).

Association with Co-morbidities

Patients with a higher Charlson Comorbidity Index (CCI) had a higher incidence of CRE (CCI 0: 0.08% CRE compared to CCI five or greater at 0.57%). When stratified by healthcare setting, patients in the ICU had the highest proportion of CRE (1.2% in ICU compared to 0.1% in the community) (Table 3).

Table 3: Demographic Characteristics of Individuals with CRE from Diagnostic Isolates between January 2017 and September 2024

Characteristic	Enterobacterales Cases	CRE Cases	% of Cases that are CRE	Cases Per 100,000 Population Per Year
Age (years)				
0 to 17	160,468	119	0.07%	0.5
18 to 64	1,381,523	1,817	0.13%	2.5
65+	1,519,752	3,879	0.26%	20.4
Sex				
Female	2,469,855	2,962	0.12%	4.9
Male	591,888	2,853	0.48%	4.8
Setting				
Hospital (ICU)	52,239	655	1.25%	-
Hospital (non-ICU)	366,078	2,268	0.62%	-
Long-term Care	155,471	308	0.20%	-
Community	2,487,955	2,584	0.10%	-
Charlson Comorbidity Index				
No Hospitalization	329,108	79	0.02%	-
0	1,462,951	1,125	0.08%	-
1-2	648,511	1,558	0.24%	-
3-4	317,953	1,328	0.42%	-
5+	303,220	1,725	0.57%	-

Data source: Ontario Laboratories Information System

Notes: For incidence rates across all years, total cases from 2017 to 2024 were divided by the total number of inhabitant days across all of the included years combined. Census data are not available for setting or comorbidity index; hence incidence is not provided for these variables.

Geography and Marginalization

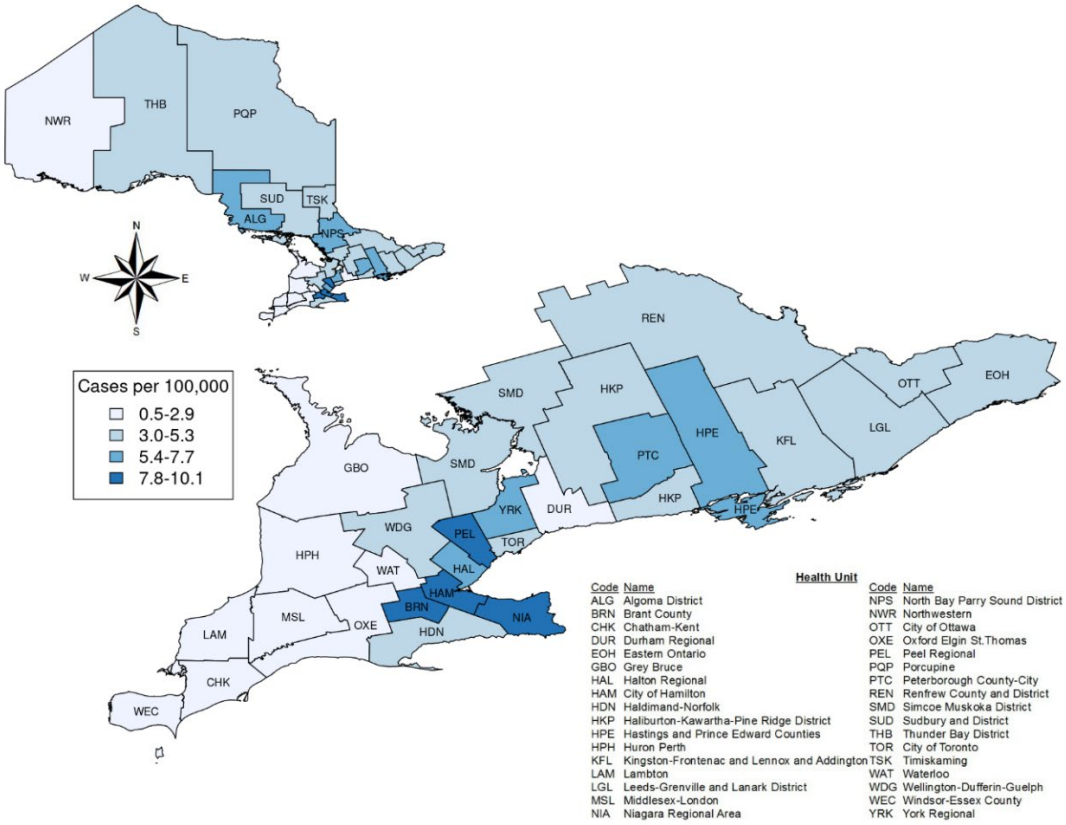
- Geographically, the proportion of Enterobacterales that were CRE was highest in Niagara (incidence 10.1 per 100,000, proportion CRE 0.35%), Hamilton (incidence 9.5 per 100,000, proportion CRE 0.32%), Peel (incidence 8.4 per 100,000, proportion CRE 0.34%), and Brant (incidence 8.3 per 100,000, proportion CRE: 0.26%) (Table 4, Figure 2).
- CRE prevalence was higher among regions with a greater proportion of marginalized populations for specific dimensions of the Ontario Marginalization Index.[6] CRE was more common in regions with a greater degree of marginalization for the Material Resources dimension (access to/attainment of basic material needs, lowest marginalization quintile 0.16% CRE; highest marginalization quintile 0.22% CRE) and Racialized and Newcomer Populations dimension (% recent immigrants and % who self-identify as a 'visible minority', lowest marginalization quintile 0.14% CRE; highest marginalization quintile 0.24% CRE) (Table 5).

Table 4: CRE Cases by Public Health Unit between January 2017 and September 2024

Public Health Unit	Enterobacterales Cases	CRE Cases	% of Cases that are CRE	Cases per 100,000 Population per Year
Algoma Public Health Unit	28,519	68	0.24%	7.4
Brant County Health Unit	39,699	102	0.26%	8.3
Chatham-Kent Public Health	19,517	14	0.07%	1.7
City of Hamilton Public Health Services	135,386	436	0.32%	9.5
Durham Region Health Department	149,270	156	0.10%	2.8
Eastern Ontario Health Unit	45,701	68	0.15%	4.0
Grey Bruce Health Unit	46,607	38	0.08%	2.7
Haldimand-Norfolk Health Unit	25,369	48	0.19%	5.1
Haliburton-Kawartha-Pine Ridge District Health Unit	48,548	77	0.16%	5.1
Halton Region Public Health	129,528	318	0.25%	6.7
Hastings & Prince Edward Counties Health Unit	43,128	81	0.19%	5.9
Huron Perth Public Health	10,258	6	0.06%	0.5
Kingston-Frontenac-Lennox and Addington Health Unit	49,973	55	0.11%	3.3
Lambton Public Health	23,000	22	0.10%	2.1

Public Health Unit	Enterobacterales Cases	CRE Cases	% of Cases that are CRE	Cases per 100,000 Population per Year
Leeds, Grenville, and Lanark District Health Unit	43,292	66	0.15%	4.6
Middlesex-London Health Unit	117,954	46	0.04%	1.1
Niagara Region Public Health	111,154	390	0.35%	10.1
North Bay Parry Sound District Health Unit	26,957	58	0.22%	5.5
Northwestern Health Unit	20,407	15	0.07%	2.3
Ottawa Public Health	185,351	260	0.14%	3.1
Peel Public Health	293,115	995	0.34%	8.4
Peterborough County-City Health Unit	35,784	66	0.18%	5.5
Porcupine Health Unit	24,466	22	0.09%	3.3
Public Health Sudbury & Districts	49,320	70	0.14%	4.3
Region of Waterloo Public Health and Emergency Services	89,682	117	0.13%	2.4
Renfrew County and District Health Unit	19,627	39	0.20%	4.5
Simcoe Muskoka District Health Unit	134,094	210	0.16%	4.4
Southwestern Public Health	54,190	30	0.06%	1.7
Thunder Bay District Health Unit	42,790	37	0.09%	3.0
Timiskaming Health Unit	7,502	10	0.13%	3.8
Toronto Public Health	573,749	1,130	0.20%	4.9
Wellington-Dufferin-Guelph	61,937	93	0.15%	3.8
Windsor-Essex County Health Unit	80,868	71	0.09%	2.1
York Region Public Health	257,857	555	0.22%	5.9

Figure 2: CRE Incidence by Public Health Unit, January 2017 to September 2024



Data source: Ontario Laboratories Information System

Table 5: CRE Cases by Ontario Marginalization Index Quintile between January 2017 and September 2024

Characteristic	Enterobacterales Cases	CRE Cases	% of Cases that are CRE
Household and Dwelling Quintile			
Not reported	37,510	55	0.15%
1 (low marginalization)	561,344	1101	0.20%
2	52,2544	834	0.16%
3	547,750	909	0.17%
4	598,733	1159	0.19%
5 (high marginalization)	793,862	1757	0.22%
Material Resources Quintile			
Not reported	37,510	55	0.15%
1 (low marginalization)	583,837	905	0.16%
2	632,042	1106	0.17%
3	609,965	1161	0.19%
4	578,418	1195	0.21%
5 (high marginalization)	619,971	1393	0.22%
Age and Labour Force Quintile			
Not reported	37,510	55	0.15%
1 (low marginalization)	647,772	1233	0.19%
2	540,612	1079	0.20%
3	508,689	987	0.19%
4	527,452	919	0.17%
5 (high marginalization)	799,708	1542	0.19%
Racialized and Newcomer Populations Quintile			
Not reported	37,510	55	0.15%
1 (low marginalization)	504,123	694	0.14%
2	549,518	954	0.17%
3	566,932	1043	0.18%
4	642,186	1274	0.20%
5 (high marginalization)	761,474	1795	0.24%

Data source: Ontario Laboratories Information System

Note: Forward sortation area (FSA) of patient address was used to assign Ontario Marginalization Index quintile for that area.[6]

Multi-drug Resistance Among CRE

CRE susceptibility data to alternative agents are shown below. Susceptibility to tigecycline, colistin and newer agents (e.g., ceftazidime-avibactam, cefiderocol) is not reported due to infrequent testing for these agents.

Cross-resistance with CRE was common to ciprofloxacin, trimethoprim-sulfamethoxazole, and amikacin. Of the reported drugs, amikacin retained the highest activity against CRE, but this varies across genus/species (Table 6).

Table 6: Percent Susceptibility to Other Antibiotics Among Cases of CRE

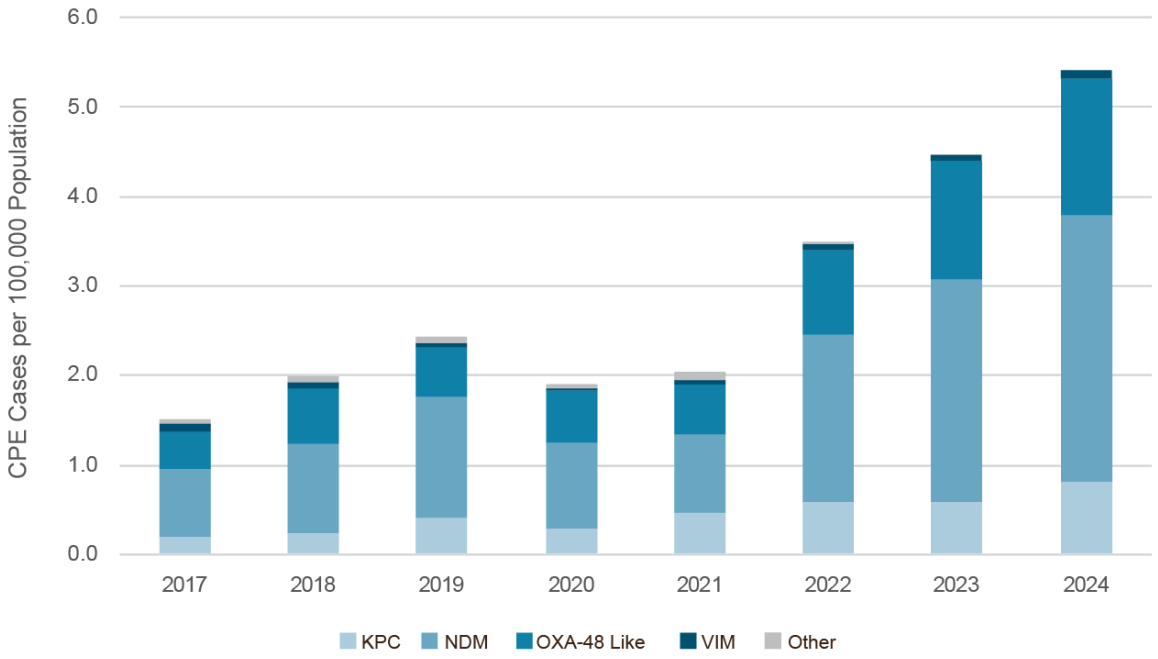
Characteristic	Ciprofloxacin	Gentamicin	Tobramycin	Amikacin	TMP-SMX
Year					
2017	71	83	74	91	72
2018	68	86	76	87	71
2019	62	82	72	88	68
2020	66	87	80	90	77
2021	69	91	84	93	78
2022	66	87	80	94	73
2023	69	90	82	92	79
2024	63	88	77	90	72
Organism					
Citrobacter	62	80	77	92	73
Enterobacter	85	96	92	98	87
Escherichia	28	74	59	71	47
Klebsiella	39	73	55	86	54
Morganella	73	78	88	94	75
Proteus	75	84	76	86	61
Providencia	72	56	51	90	82
Serratia	78	94	80	90	92
Age (years)					
0-17	93	97	80	91	84
18-64	62	85	76	92	70
65+	68	88	80	91	76
Sex					
Female	70	88	82	93	76
Male	64	86	76	89	72
Specimen Site					
Blood	70	89	80	89	78
Respiratory	68	88	79	90	75
Urine	65	87	79	91	73
Other	69	88	79	91	76
Setting					
Hospital (ICU)	68	87	76	84	75
Hospital (non-ICU)	69	87	79	93	75
Long-term care	57	85	76	94	73
Community	66	88	80	91	74

Data source: Ontario Laboratories Information System
TMP-SMX – trimethoprim-sulfamethoxazole
Notes: Percent susceptibility was based on actual percent susceptibility among documented cases of CRE, with imputation for missing results using rule and model-based imputation (see Technical Notes for further details); Nomenclature changed for *Enterobacter aerogenes* in 2017 to *Klebsiella aerogenes* hence this species may be captured under Enterobacter or Klebsiella Genus depending on the date of laboratory adoption of new nomenclature.[8]; Colour coding was applied to indicate degree of susceptibility (orange/red less than 60%; yellow 60 to 79%; green: 80% or higher)[9]

Carbapenemase-Producing Enterobacterales

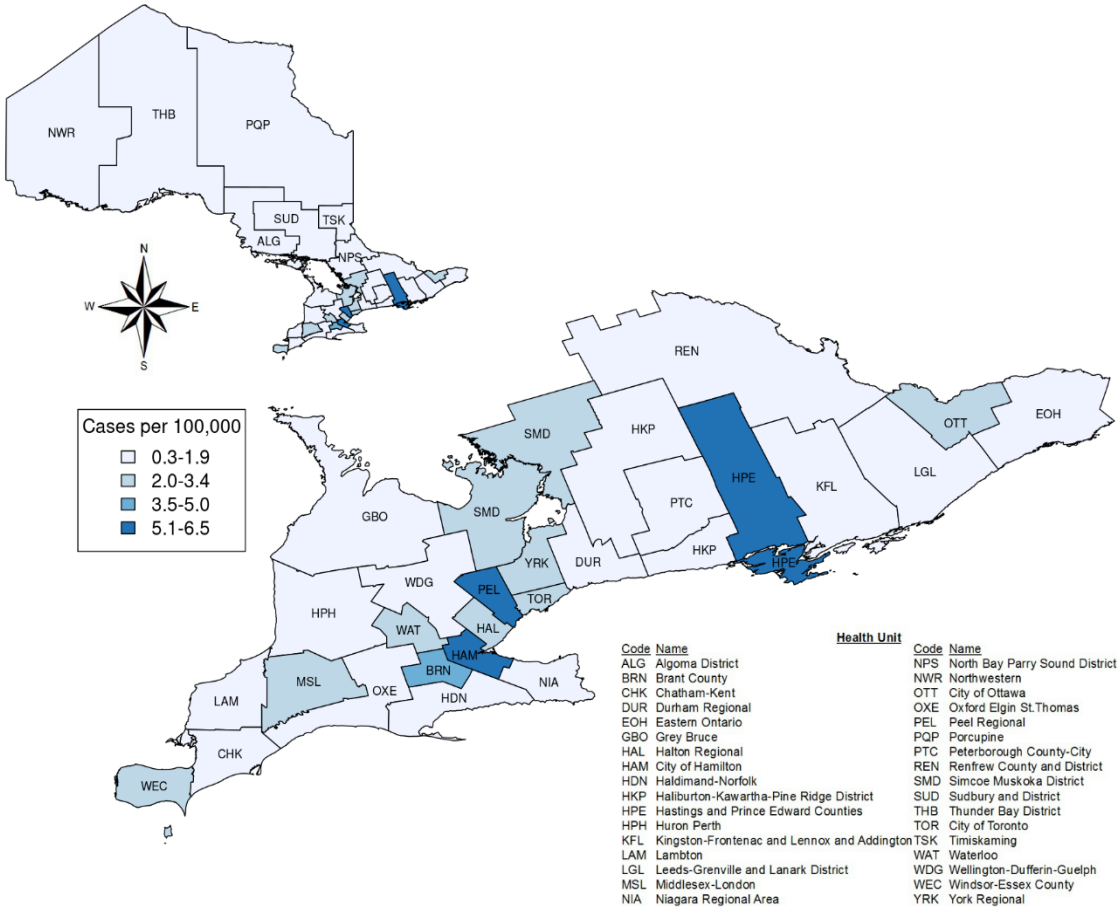
- 3,386 unique cases of carbapenemase-producing Enterobacterales (CPE) (both diagnostic and surveillance specimens) identified from the Public Health Ontario from January 2017 to December 2024 were evaluated. The most common specimen source was rectal (n=1,448, 42.8%), followed by urine (1,197, 35.4%), and other (530, 15.7%).
- Among all 3,386 confirmed cases of CPE in Ontario, carbapenemases were most often New Delhi metallo-β-lactamase (NDM) (n=1,883, 55.6%) followed by oxacillinase-48 (OXA-48) (n=992, 29.3%), and *Klebsiella pneumoniae* carbapenemase (KPC) (n=542, 16.0%).
- CPE cases increased from 1.4 per 100,000 per year in 2017 to 5.1 per 100,000 in 2024. (Figure 3)
- Distribution of CPE cases varied across Public Health Units, with overall rates highest in Peel (6.5 per 100,000), Hamilton (5.9 per 100,000) and Hastings Prince Edward (5.2 per 100,000). The incidence of all CPE and KPC, NDM, and OXA-48 is provided in Figures 4, 5, 6, and 7).

Figure 3: CPE Cases Detected Per Year in Ontario



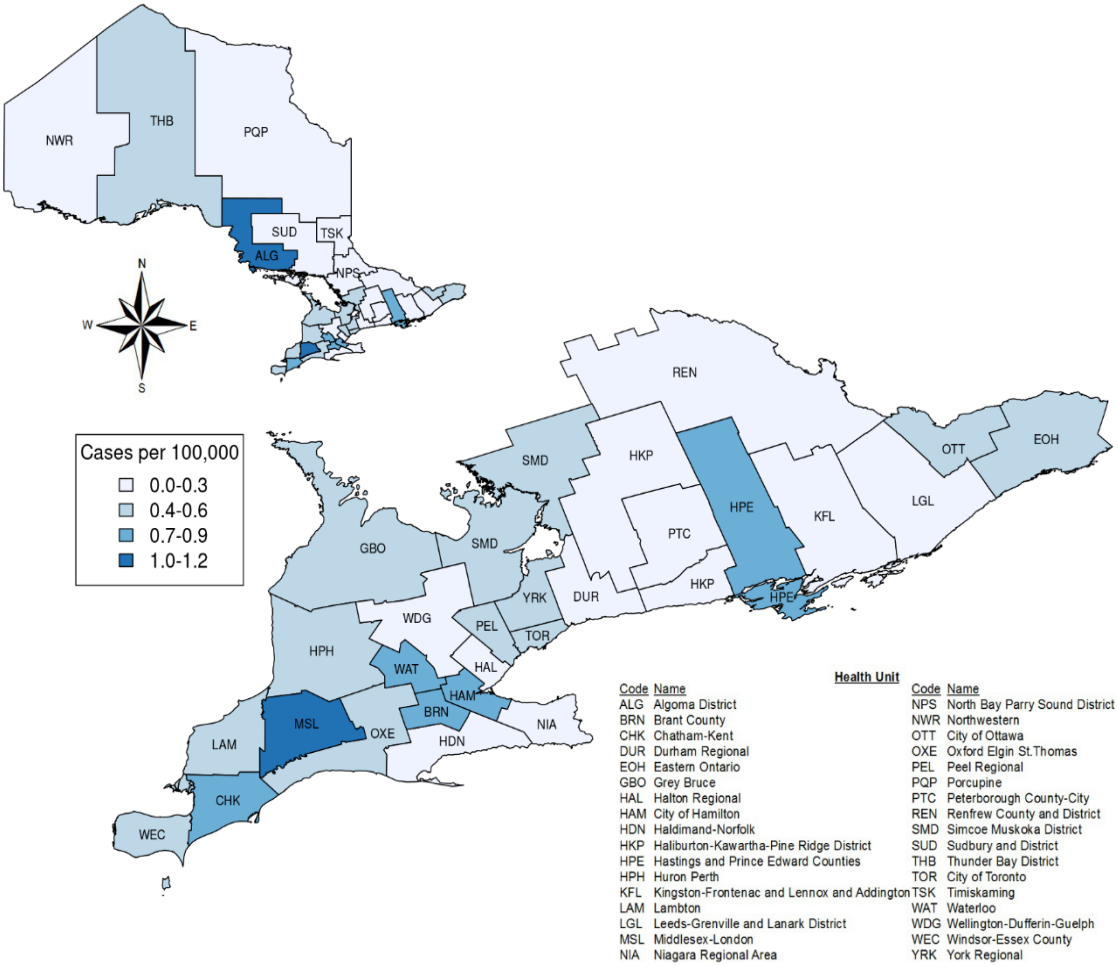
Data source: Public Health Ontario Laboratory Information Management System
Notes: KPC: *Klebsiella pneumoniae* carbapenemase; NDM: New Delhi metallo-β-lactamase (NDM); OXA-48 Like: Oxacillinase-48 Like; VIM: Verona integron-encoded metallo-β-lactamase.

Figure 4: CPE Incidence (Overall) by Public Health Unit, January 2017 to December 2024



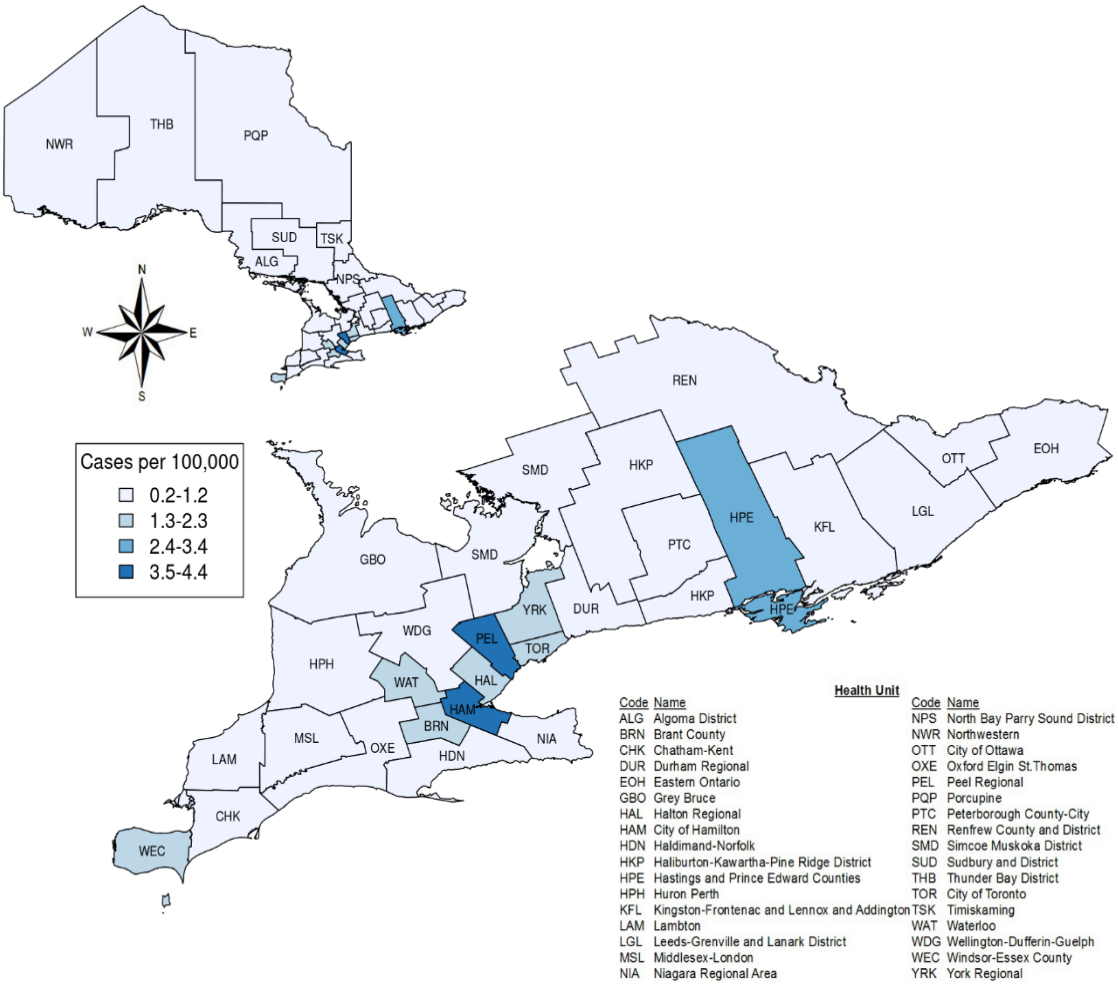
Data source: Public Health Ontario Laboratory Information Management System

Figure 5: Klebsiella pneumoniae carbapenemase (KPC) Incidence by Public Health Unit, January 2017 to December 2024



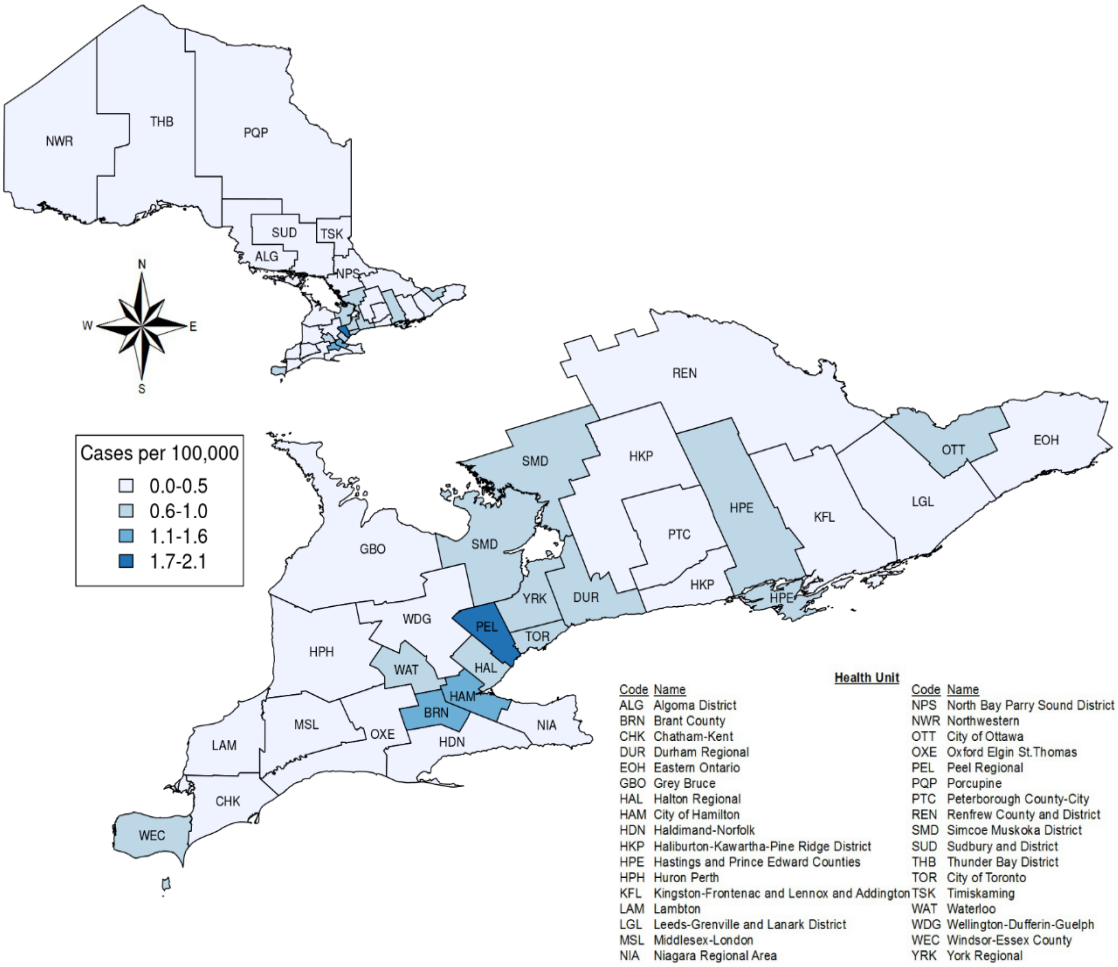
Data source: Public Health Ontario Laboratory Information Management System

Figure 6: New Delhi metallo-β-lactamase (NDM) Carbapenemase Incidence by Public Health Unit, January 2017 to December 2024



Data source: Public Health Ontario Laboratory Information Management System

Figure 7: Oxacillinase-48 (OXA-48) Carbapenemase Incidence by Public Health Unit, January 2017 to December 2024



Data source: Public Health Ontario Laboratory Information Management System

Technical Notes

Data Sources

CRE Case Data

- Data for CRE and associated demographics were extracted from the Ontario Laboratories Information System (OLIS) for culture and susceptibility results from January 1, 2017 to September 30, 2024. OLIS is housed within ICES. ICES is an independent, non-profit research institute funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). As a prescribed entity under Ontario's privacy legislation, ICES is authorized to collect and use health care data for the purposes of health system analysis, evaluation and decision support. Secure access to these data is governed by policies and procedures that are approved by the Information and Privacy Commissioner of Ontario.
- Carbapenem resistant Enterobacterales (CRE) were defined as Enterobacterales (*Escherichia, Klebsiella, Enterobacter, Citrobacter, Morganella, Providencia, Proteus, Serratia* species) that were resistant to at least one carpabenem (ertapenem, imipenem, meropenem). Due to decreased intrinsic susceptibility of *Proteus* species to imipenem,[10] resistance in this situation was not counted as CRE.
- Only the first isolate per patient per organism per year was reported.
- Only diagnostic specimens with antimicrobial susceptibility data were included (no CPE surveillance screening specimens included).
- CRE data were stratified broadly by specimen source (respiratory, blood, urine, and other). Specimen source was also categorized into whether it is expected to be a sterile (e.g., blood, joint fluid) vs. non-sterile specimen (e.g., urine, sputum).
- Data were based on reported results, as OLIS does not include suppressed/masked susceptibility data. CRE cases are only based on reported resistance to carbapenems. When evaluating co-resistance, since susceptibility data may be incomplete due to 1) variation in culture and susceptibility testing and reporting practices among laboratories and 2) lack of access to suppressed non-reported susceptibility results, we used a two-step imputation method to reduce missingness. The first step was rule-based imputation based on known intrinsic resistance or susceptibility as well as expected cross-resistance. The second step was model-based imputation to predict susceptibility where data were still missing after rule-based imputation. This approach used logistic regression models including the age, sex, organism and region.[11]

Regional Data

- Data were presented regionally by Public Health Unit based on the patient's Forward Sortation Area (FSA).
- Effective January 1, 2025, the Ontario Ministry of Health approved the voluntary merger of nine local health units into four entities. Since the time-period of data collection was prior to the merger, we reported the 34 pre-merger Public Health Units above.

Marginalization

- To evaluate social determinants of health, the Ontario Marginalization (ON-Marg) Index was used to stratify by various facets of marginalization in Ontario, including economic, ethno-racial, age-based and social marginalization.[6] This index includes four dimensions based on data from Statistics Canada (2021 census year):
    - Households and dwellings includes indicators that measure types and density of residential accommodations, and certain family structure characteristics (e.g., % living alone and % dwellings not owned)
    - Material resources: includes indicators that measure access to/attainment of basic material needs (e.g., % unemployment and % without a high school degree)
    - Age and labour force includes indicators to describe % seniors (65+), the dependency ratio (the ratio of seniors and children to the population 15-64) and % not participating in the labour force.
    - Racialized and newcomer populations includes indicators to describe % recent immigrants and % who self-identify as a 'visible minority'.
- Forward sortation area (FSA) of patient address was used to assign marginalization index quintile.

Patient Characteristics

Patient characteristics were identified from several databases in ICES including the Registered Persons DataBase (RPDB) for age, sex and location, Canadian Institute for Health Information Discharge Abstract Database (CIHI DAD) to identify hospitalizations and comorbidities and comorbidity index, the National Ambulatory Care Reporting System (NACRS) to identify emergency department visits, the Continuing Care Reporting System (CCRS) to identify long-term care residence. Patients not in hospital or long-term care at the time of sample collection were considered to be in the community. These datasets were linked using unique encoded identifiers and analyzed at ICES.

CPE Case Data

- Data for CPE were extracted from Public Health Ontario Laboratory Information Management System for specimens logged from January 1, 2017 to December 31, 2024.
- Only the first CPE sample per patient per year was reported.
- Diagnostic and surveillance specimens were included.
- Public health unit was assigned using patient postal code or ordering provider postal code if patient postal code was missing.

Census Data

Data for the denominator of incidence rates of CRE and CPE were extracted from the Canadian Census.[12] For CRE and CPE incidence rate, in 2024 data up to September 30, 2024 were included, hence the census count for that year was multiplied by 0.745 (272 days/365 days).

Data Caveats

- Data should be interpreted with caution. While the vast majority (over 90%) of Ontario hospitals report microbiology laboratory data into OLIS, the data may be incomplete for those hospitals not captured in OLIS. Non-Ontario residents are not included.
- CRE may be underestimated in cases where laboratories do not report/suppress susceptibility data when the isolate is resistant to carbapenems. However, this practice is relatively uncommon and is best practice to report unexpected resistance when it is identified. [13]
- Susceptibility data for other agents may be biased by laboratory testing and reporting practices. Some agents will be selectively reported, and as such resistance may appear elevated if reporting of these drugs is reserved for more difficult to treat cases. Susceptibility to novel agents with activity against CRE were not reported given the low rate of susceptibility testing.
- CRE data in OLIS were not subdivided by resistance mechanism (e.g., CPE and non-CPE) and genotypes for CRE were not retrievable in this dataset.
- CRE and CPE data may not be directly comparable as they represent different data sources with different eligibility criteria (i.e., CRE data from OLIS represent diagnostic specimens whereas CPE data from PHO represent both diagnostic and surveillance/screening specimens).
- Not all samples submitted for carbapenemase testing underwent organism identification at PHO. Fewer than 1% of samples had additional CPE testing performed outside of PHO; these results were not included.
- All samples from the same patient may not have been identified due to potential discrepancies in patient information used for patient linkage, i.e. health card number, and/or the patient's first name, last name, and date of birth.

References

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