

Carbapenemase-producing Organisms: Five-Year Surveillance Report, 2018–2022

**Bureau of Epidemiology
Division of Healthcare
Associated Infection
Prevention**

Published: April 2024



pennsylvania
DEPARTMENT OF HEALTH

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Introduction

Carbapenemase-producing organisms (CPOs) are a group of multidrug-resistant pathogens classified as an urgent threat to public health by the Centers for Disease Control and Prevention (CDC).¹ These organisms are resistant to carbapenem antibiotics via the production of carbapenemase, an enzyme that confers resistance to carbapenem antibiotics. Since the first detection of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella pneumoniae* in Pennsylvania in 2018, CPOs have spread throughout the state and include many carbapenemase-organism combinations. Carbapenemases are especially concerning because they can be transferred between organisms because their genetic material is located within mobile genetic elements called plasmids. There are many different types of carbapenemase genes, the most common of which include: KPC, New Delhi metallo- β -lactamase (NDM), Verona integron-mediated metallo- β -lactamase (VIM), imipenemase metallo- β -lactamase (IMP), and oxacillinase-type carbapenemase (e.g., OXA-23, OXA-24/40, OXA-48-like). Infections caused by CPOs are difficult to treat because carbapenems are often the last line of treatment in patients with multidrug-resistant pathogens. Due to their resistance, ability to spread rapidly in healthcare settings, and high mortality rate, public health efforts are needed to prevent and contain CPOs.² In Pennsylvania, CPOs are currently not reportable by law except in Allegheny County; carbapenem-resistant Enterobacteriaceae are reportable in Philadelphia County. During 2018–2022, the Bureau of Epidemiology, Division of Healthcare Associated Infection Prevention (HAIP) received CPO reports through voluntary reporting for all PA counties except Philadelphia.

Methods

The CPO 2023 Case Definition published by CDC was used to identify confirmed cases. A confirmed case of CPO includes laboratory confirmed evidence of carbapenemase production by a phenotypic method (e.g., modified carbapenemase inactivation method, also known as mCIM) or detection of a carbapenemase gene by a recognized molecular test (e.g., validated laboratory-developed nucleic acid amplification test; Cepheid Xpert Carba-R) or next generation sequencing.³ Each confirmed CPO case is further characterized as a *clinical* (i.e., collected for the purpose of diagnosing or treating disease in the course of normal care) or a *screening* (i.e., collected for the detection of colonization and not for the purpose of diagnosing or treating disease) case.

CPO reports with specimen collection dates January 1, 2018, through December 31, 2022, were collected using Pennsylvania's National Electronic Disease Surveillance System (PA-NEDSS) and analyzed using SAS Enterprise Guide (version 7.1) and R Statistical Software (version 4.2.3; R Core Team 2023). Reports were entered into PA-NEDSS by submitting laboratories or healthcare providers and investigated by public health staff to determine patient healthcare history and risk factors and laboratory test methods. Public health jurisdictions conducted investigations based on the location of the submitting healthcare facility and expanded the investigation as needed, to include additional affected healthcare facilities. Most screening cases detected during point-prevalence screenings were not entered as reports into PA-NEDSS; these data were obtained from the Maryland Laboratory Web

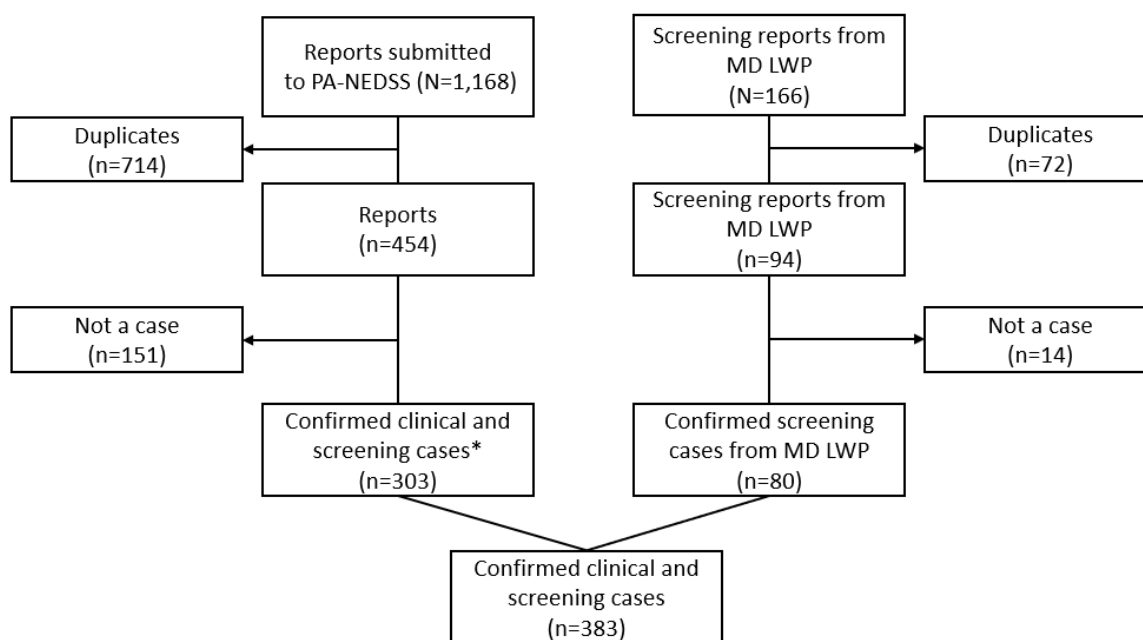
Portal (MD LWP) operated by the Maryland Department of Health Public Health Laboratory (MDH PHL). The MD PHL is a designated Regional Antimicrobial Resistance Laboratory and provides select testing for the Pennsylvania Department of Health through funding provided by CDC. Isolates from the same patient with the same organism and carbapenemase mechanism were considered duplicates and removed, according to the CDC case definition. Cases were also excluded if the jurisdiction of investigation was Philadelphia or out of state.

Results & Discussion

Case Identification & Case-Patient Characteristics

During 2018 through 2022, the HAIP division received 1,168 CPO reports (including non-confirmed and confirmed CPO cases) in PA-NEDSS from laboratories across PA, excluding Philadelphia. An additional 166 CPO reports were identified within the MD LWP, for a total of 1,334 reports. Of these, 786 were duplicates and an additional 165 did not meet case criteria, resulting in 383 confirmed CPO cases (Figure 1).

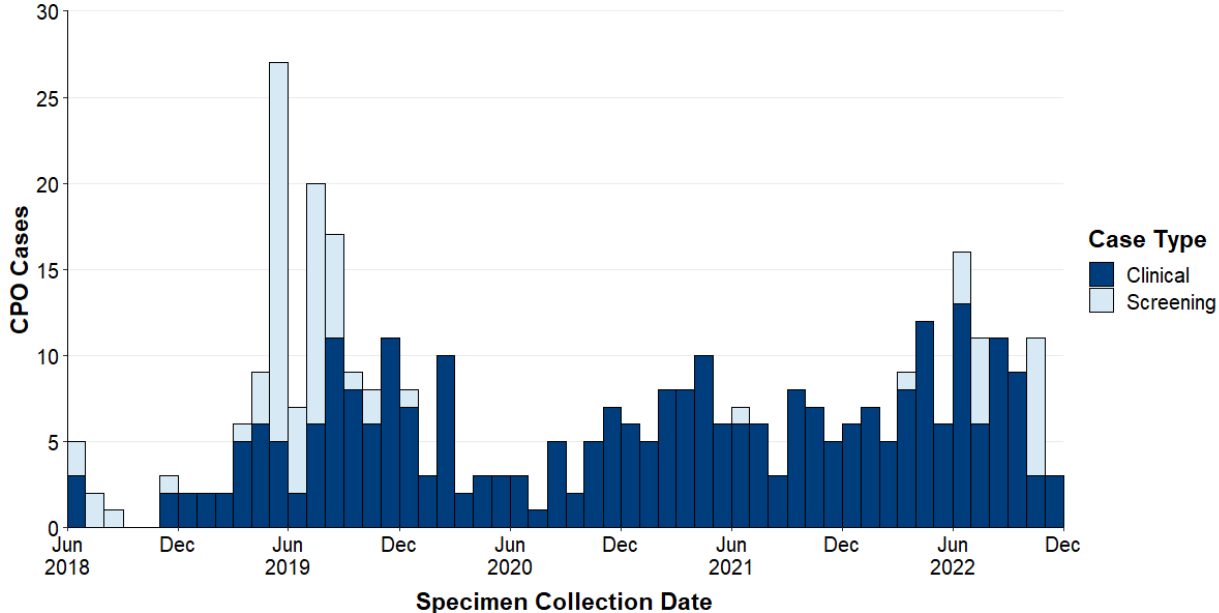
Figure 1. Flow chart of CPO reports submitted to PA-NEDSS, PA (excl. Philadelphia), 2018–2022



*Includes 294 clinical cases and 9 screening cases

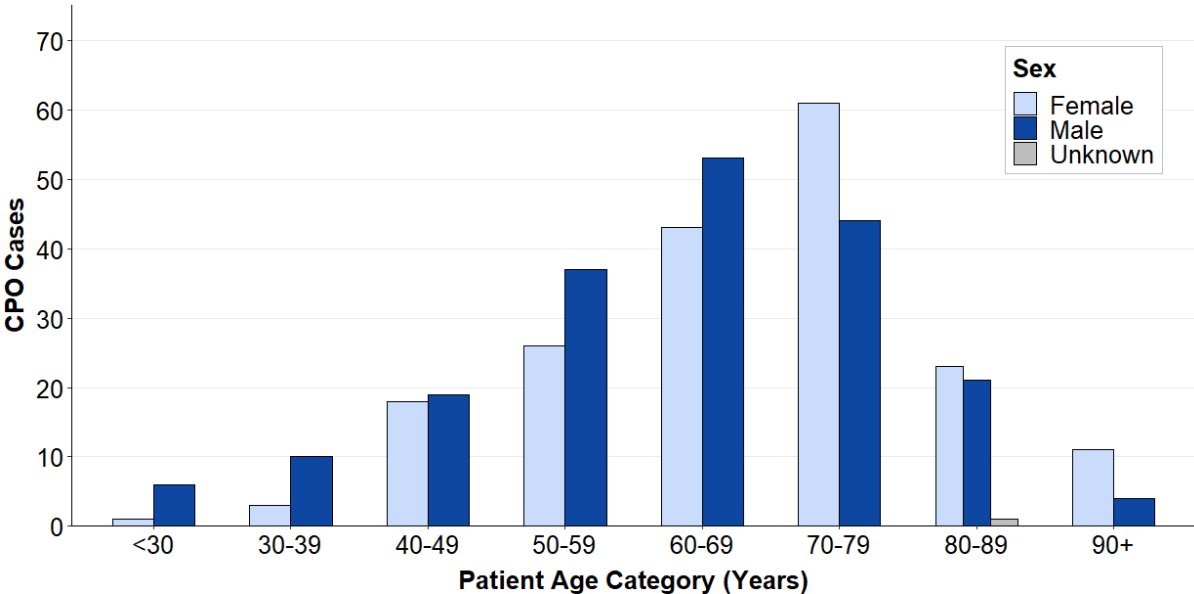
Clinical and screening case counts increased in 2019 and saw a decrease in 2020 (Figure 2). More screening cases were detected in 2019 likely due to increased testing. Both clinical and screening cases decreased in 2020 which was likely due to decreased reporting and testing during the COVID-19 pandemic. We observed a modest increase in both clinical and screening CPO cases during 2021–2022. Nationwide, studies have reported that increases in clinical and screening cases in 2021 and 2022 were related to increased transmission due to deviations in infection prevention and control practices during the surges of COVID-19. An increase in testing could also be a contributing factor.^{4,5}

Figure 2. Epidemic curve of confirmed screening and clinical CPO cases by specimen collection date, PA (excl. Philadelphia), 2018–2022 (N=383)



For each confirmed case, public health investigators identified select characteristics of the patient that was the source of the specimen (i.e., case-patient). While the age of case-patients ranged from 0 to 101 years, the median age was 67 and 68% (261/383) were in persons aged ≥ 60 years (Figure 3; Table 1). Overall, case-patients were equally distributed by sex; however, there were more female case-patients in age groups over 60 years (Figure 3).

Figure 3. Age and sex distribution of confirmed clinical and screening CPO case-patients, PA (excl. Philadelphia), 2018–2022 (N=383)



For each confirmed case, public health investigators also identified certain risk factors for each case-patient including if the person was hospitalized, a resident of a long-term care facility (LTCF), had history of international travel, had indwelling medical devices, or had any wounds (Table 1). These data were limited for screening cases so the following results include only clinical cases.

Most case-patients had been hospitalized in the 30 days prior to positive culture. While 30% of clinical cases had been a resident of a LTCF in the 30 days prior to positive culture, 30% also had missing data for this variable. Only 4 cases had a history of international travel which included travel to Pakistan, Mexico, Egypt, and Italy; two of these cases had an overnight stay in a hospital abroad. Most clinical case-patients had indwelling devices and nearly 30% had wounds; however, missing variables were common among this and all other patient risk factors.

Table 1. Case-patient risk factors of confirmed clinical CPO cases by specimen collection year, PA (excluding Philadelphia), 2018–2022 (N=294)

Case-Patient Risk Factors	Total (N=294)	2018 (n=7)	2019 (n=71)	2020 (n=50)	2021 (n=78)	2022 (n=88)
Hospitalized* (n (%))						
Yes	172 (59)	7 (100)	33 (46)	28 (56)	48 (62)	56 (64)
No	68 (23)	0 (0)	21 (30)	11 (22)	14 (18)	22 (25)
Unknown	54 (18)	0 (0)	17 (24)	11 (22)	16 (21)	10 (11)
LTCF resident† (n (%))						
Yes	89 (30)	0 (0)	1 (1)	14 (28)	32 (41)	42 (48)
No	121 (41)	0 (0)	1 (1)	32 (64)	42 (54)	46 (52)
Unknown	84 (29)	7 (100)	69 (97)	4 (8)	4 (5)	0 (0)
Travel outside US or Canada (n (%))						
Yes	4 (1)	0 (0)	0 (0)	2 (4)	0 (0)	2 (2)
No	105 (36)	0 (0)	1 (1)	22 (44)	34 (44)	48 (55)
Unknown	185 (63)	7 (100)	70 (99)	26 (52)	44 (56)	38 (43)
Indwelling device‡ (n (%))						
Yes	106 (36)	0 (0)	2 (3)	18 (36)	32 (41)	54 (61)
No	88 (30)	0 (0)	0 (0)	24 (48)	33 (42)	31 (35)
Unknown	100 (34)	7 (100)	69 (97)	8 (16)	13 (17)	3 (3)
Wound (n (%))						
Yes	84 (29)	0 (0)	2 (3)	15 (30)	25 (32)	42 (48)
No	104 (35)	0 (0)	0 (0)	26 (52)	35 (45)	43 (49)
Unknown	106 (36)	7 (100)	69 (97)	9 (18)	18 (23)	3 (3)

*PA-NEDSS Question: “In the 30 days prior to positive culture, was the patient hospitalized?”

† PA-NEDSS Question: “In the 30 days prior to positive culture, was the patient a resident of a nursing home or other long-term care facility (LTCF), or was he/she recently transferred from such a facility?”

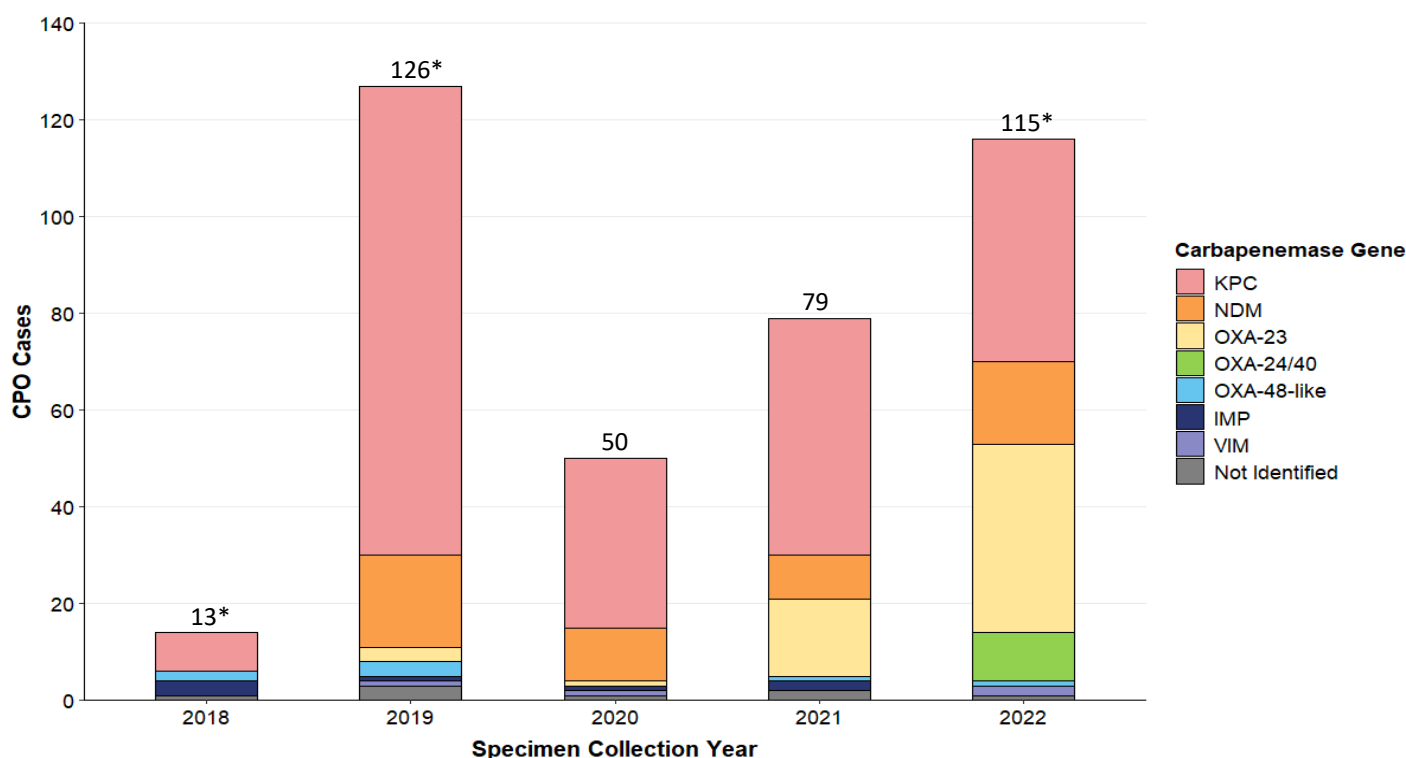
‡ PA-NEDSS Question: “Did the patient have indwelling / invasive devices (e.g., central IV line, ventilator)?”

CPO Isolate Characteristics

For all case isolates (i.e., clinical and screening), KPC was the leading carbapenemase detected in PA during 2018 to 2022 (Figure 4). During 2021 and 2022, there was an increase in OXA-23 detection;

testing for this mechanism at the MDH PHL began in early 2019. Corresponding with increased OXA-23 and OXA-24/40 rates in 2021-2022 were an increased volume of carbapenem-resistant *A. baumannii* (CRAB) isolates submitted from clinical labs. In Pennsylvania, OXA-23 and OXA-24/40 have only been found in *Acinetobacter baumannii*. OXA-48-like carbapenemase, IMP, and VIM were the least detected carbapenemases in PA.

Figure 4. Confirmed CPO clinical and screening cases per specimen collection year, stratified by carbapenemase gene, PA (excluding Philadelphia), 2018–2022 (N=383)

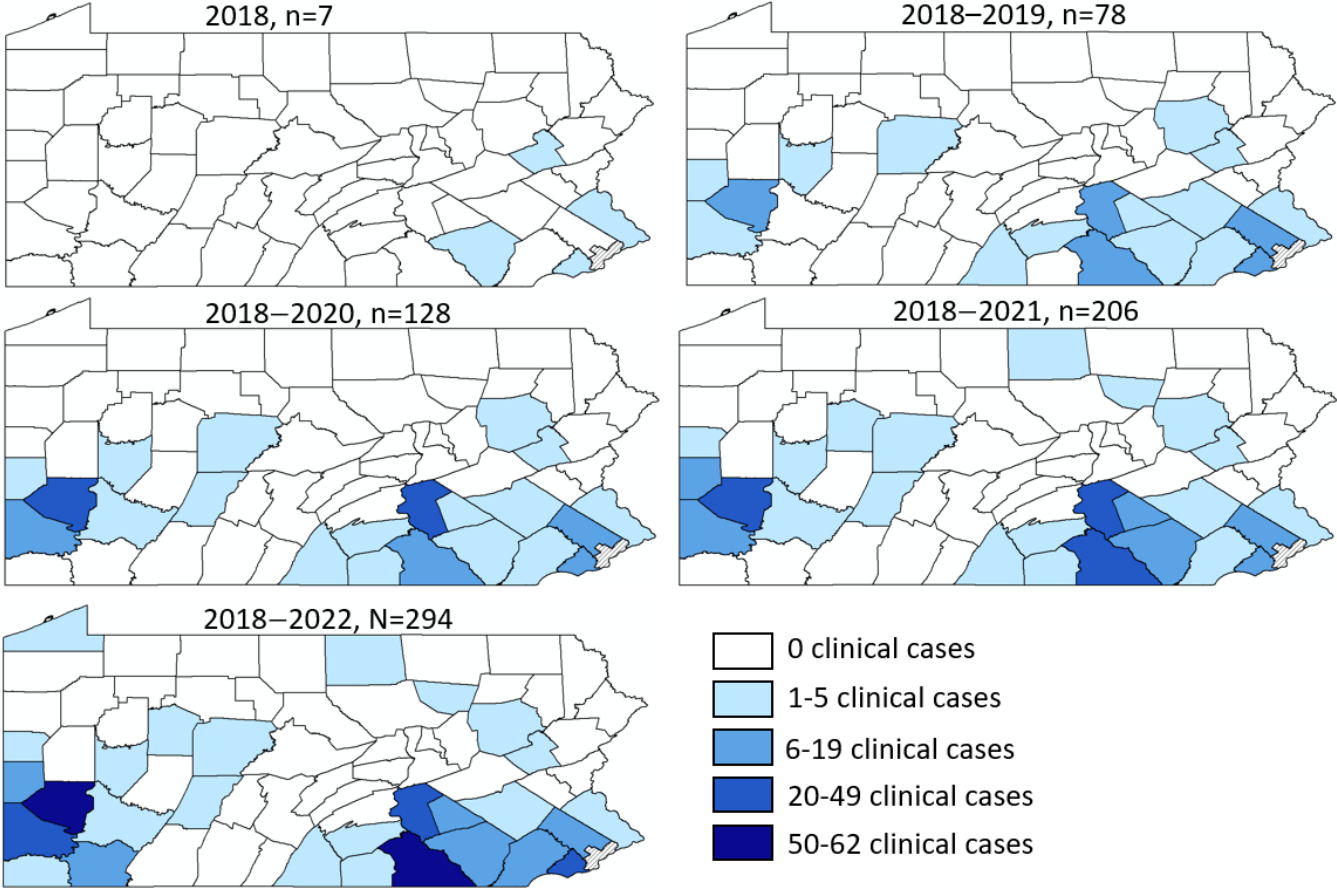


*Three cases had two mechanisms detected

The data that follow include only clinical CPO cases. Screening cases were excluded from analysis of isolate submission by laboratory (Figures 5 and 6) because most screening swabs were processed at the MDH PHL. Screening swabs typically are not tested for organism identification, and thus are also excluded from the breakdown by organism in Figure 7.

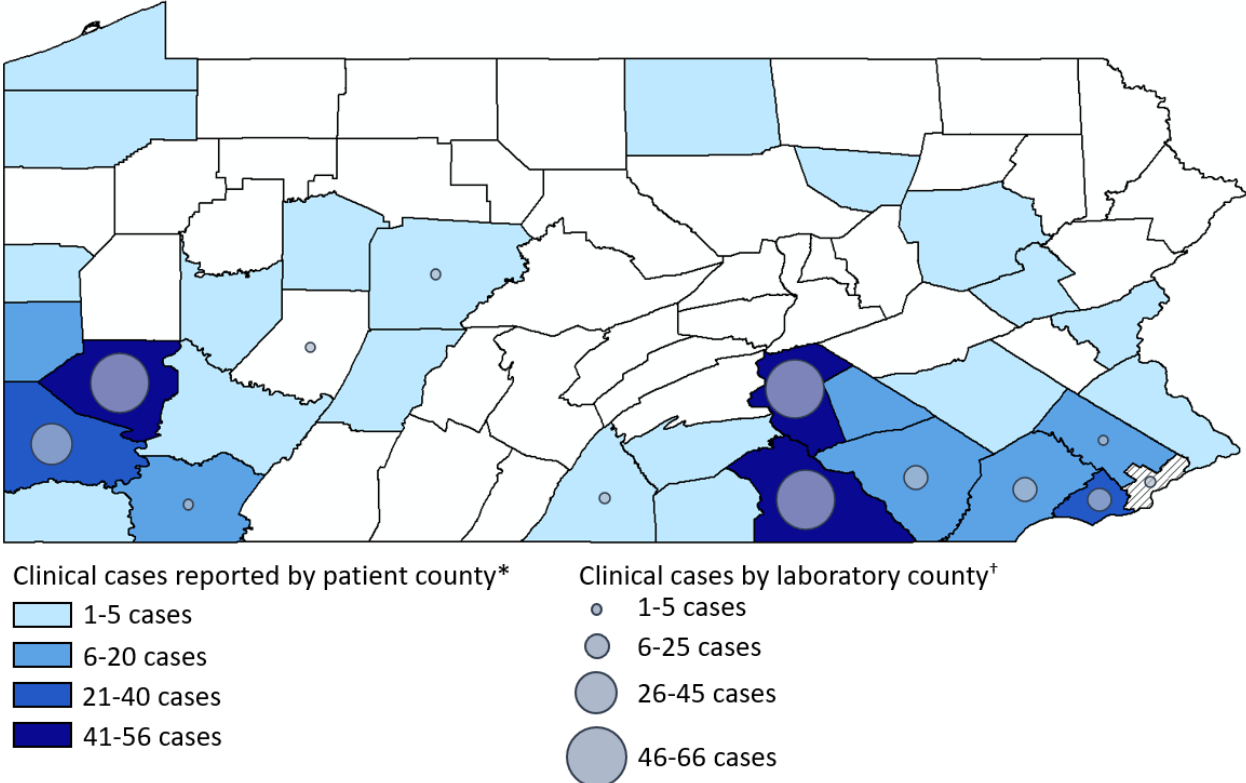
During 2018 through 2022, most clinical cases were identified from isolates sent by facilities in the southeast, southcentral, and southwest parts of the state, with fewer identified in the north (Figure 5). Allegheny County and York County had the most clinical cases identified (50–63 cases), followed by Washington, Dauphin, and Delaware counties with 20–49 clinical cases each.

Figure 5. Five-year progression of confirmed clinical CPO cases by county of healthcare facility where identified, PA (excl. Philadelphia), 2018–2022



Not all clinical laboratories have testing capability for carbapenemase detection, so many isolates are sent to the PA Bureau of Laboratories or the MDH PHL after carbapenem resistance is identified. Figure 6 shows the total number of isolates by the county of the laboratory where carbapenem resistance was first detected. It also shows the total number of confirmed clinical CPO cases by county of the case-patient’s address of permanent residence.

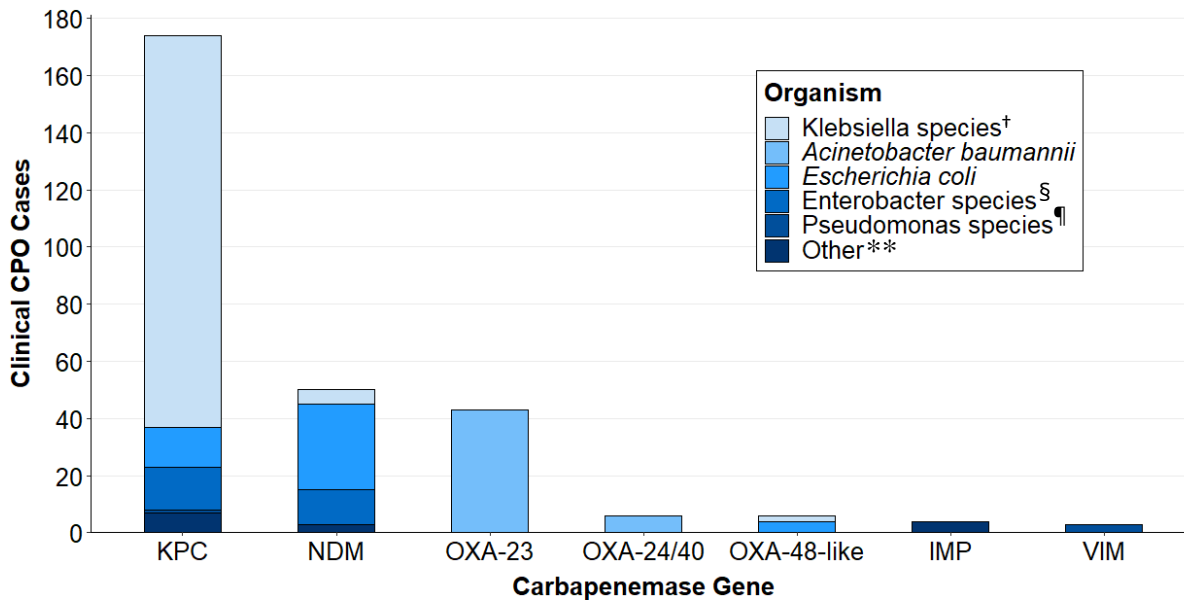
Figure 6. Two data points are superimposed in this figure: 1) Number of confirmed clinical cases by the county of the laboratory where carbapenem resistance was first detected; and 2) Number of confirmed CPO clinical cases by case-patient county of residence, PA (excluding Philadelphia), 2018–2022



*Cases with patient address outside PA not included (n=3)

† Laboratories outside PA not included (n=40)

Figure 7. Confirmed clinical CPO cases by carbapenemase gene and stratified by organism, PA (excluding Philadelphia), 2018–2022, (N=286*)



* Cases with no mechanism result were not included (n=8)

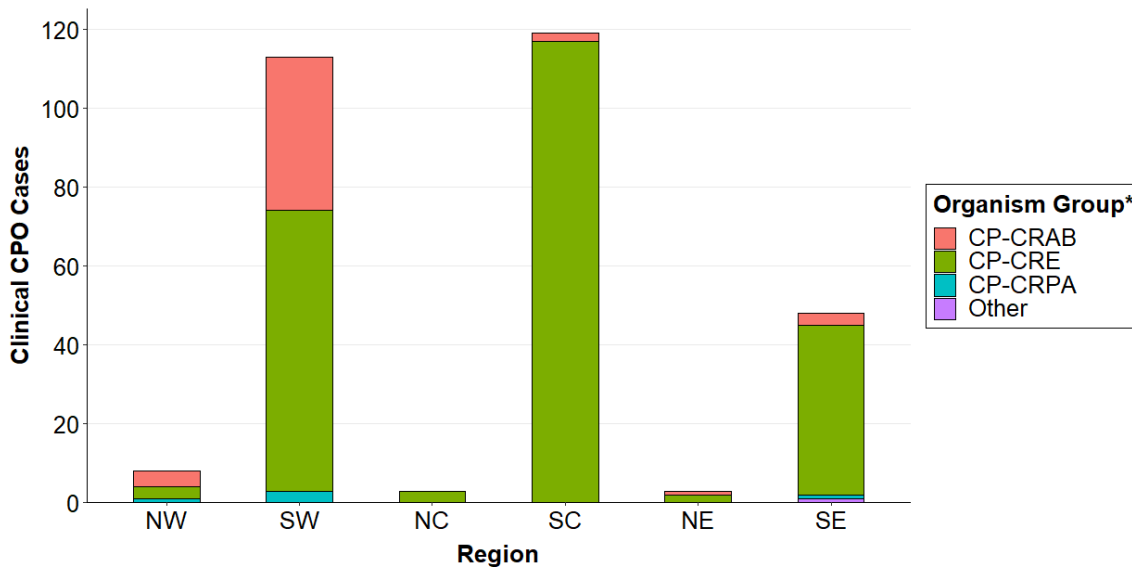
[†] Includes *Klebsiella pneumoniae* (n=104), un-specified *Klebsiella* (n=30), *Klebsiella oxytoca* (n=8), *Klebsiella aerogenes* (n=1), and *Klebsiella variicola* (n=1)

[§] Includes *Enterobacter cloacae* complex (n=16) and un-specified *Enterobacter* (n=12)

[¶] Includes *Pseudomonas aeruginosa* (n=3) and un-specified *Pseudomonas* (n=1)

^{**} Includes *Serratia* species (n=1), *Citrobacter freundii* (n=3), *Morganella morganii* (n=2), *Providencia* species (n=4), *Proteus mirabilis* (n=2), and *Raoultella planticola* (n=1)

Figure 8. Confirmed clinical CPO cases by region and stratified by organism grouping, PA (excluding Philadelphia), 2018–2022, (N=294)



* Carbapenemase-producing = CP; carbapenem-resistant *Acinetobacter baumannii* = CRAB; carbapenem-resistant Enterobacterales = CRE; carbapenem-resistant *Pseudomonas aeruginosa* = CRPA

Conclusions

Since CPOs are not reportable in PA, our understanding of CPO epidemiology is highly dependent on the ability of clinical and reference laboratories to conduct this testing, and their willingness to voluntarily report positive results. Furthermore, these data were susceptible to changes in reporting that may occur subsequent to staffing shortages or demands for other testing as occurred during the COVID-19 pandemic. In fact, some regularly reporting laboratories in western and southeastern PA temporarily halted reporting during the pandemic until March 2022, which may explain the decrease in cases observed in 2020 and a moderate number of cases in 2021.

During the five-year period, carbapenemase genes KPC and NDM were detected more in the central and eastern regions of PA. Laboratory capability to detect KPC and NDM in Enterobacterales is thought to be similar across the state, providing support for the conclusion that epidemiology of these carbapenemases may differ across regions. Detection of OXA-23 and OXA-24/40 were limited to *A. baumannii* and were detected much more frequently in the western region. While the laboratory capacity and frequency to detect carbapenemases in carbapenemase producing CRAB is not well known, targeted surveillance and outbreak response in the eastern region have not yielded the volume of case detection occurring in western PA. This provides support for the conclusion that epidemiology of carbapenemase producing CRAB may also differ across regions.

Notably, while global concern for NDM-producing *A. baumannii* is increasing,⁶⁻⁷ PA did not detect these organisms among healthcare-associated infections reported to the CDC's National Healthcare Safety Network by hospitals in 2022. The detection of carbapenemase production in *Pseudomonas* species was also rare, with a total of only 5 isolates reported during the five-year period. Likewise, although pediatric cases of CPO are increasing nationwide, they remain rare in PA. Public health maintains heightened concern for the future impact of CPOs in PA pediatric healthcare settings.

Public health efforts to increase volume of testing and the consistency of reporting are crucial to the understanding of the epidemiology of CPOs in PA in the next five-year period. The Division of HAIP is currently working with laboratories to increase CPO reporting and isolated submission across the state. Although some geographic areas are not yet reporting cases, the Division is also actively providing education and training to ensure healthcare facilities across PA are aware of infection control measures to prevent and contain CPOs.

Citations

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