Supplementary ~~Appendix~~

Table S1. State CRE Isolate Submission Reporting Mandates Across an Open Cohort of 29 U.S. States

State	State Administrative Code/Statute
AZ	1. Arizona Department of Health Services. Arizona Laboratory Reporting Requirements. 2018. https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/communicable-disease-reporting/lab-reporting-requirements.pdf 2. Arizona Administrative Code. Clinical Laboratory Director Reporting Requirements. A.A.C. § R9-6-204, Table 2.3. 2023. https://apps.azsos.gov/public_services/title_09/9-06.pdf
CO	1. Colorado Department of Public Health and Environment. Communicable Reporting Conditions. 2018. https://spl.cde.state.co.us/artemis/heserials/he1940018internet/he19400182018internet.pdf 2. Code of Colorado Regulations. Rules and Regulations Pertaining to Epidemic and Communicable Disease Control. 6 C.C.R. § 1009-1, Appendix A. 2015. https://www.sos.state.co.us/CCR/GenerateRulePdf.do?ruleVersionId=6495&fileName=6%20CCR%201009-1
CT	1. Cartter ML. Connecticut Epidemiologist, Vol. 37 No. 1, 2017. https://portal.ct.gov/-/media/departments-and-agencies/dph/dph/infectious_diseases/ctepinews/vol37no1pdf.pdf?rev=f27f07e7010b4c7bb77d451e31f14582&hash=6C24F99821C8BC6ADF424274B55326DD 2. Connecticut Agencies Regulations. List of reportable diseases and laboratory findings. Conn. Agencies Regs. § 19a-36-A2. 2015. https://eregulations.ct.gov/eRegsPortal/Browse/RCSA/Title_19aSubtitle_19a-36Section_19a-36-a2/
GA	1. Georgia Department of Public Health. Notifiable Disease/Condition Reporting. July 2018. https://www.gnrhealth.com/wp-content/uploads/2018/08/Georgia.DPH_.Notifiable.Disease.Poster.FINAL_.pdf 2. Georgia Code. Title 31 Health Chapter 12. Control of Hazardous Conditions, Preventable Diseases, and Metabolic Disorders. O.C.G.A. § 31-12-2. 2017. O.C.G.A. § 31-12-2_2 (1).pdf 3. Drenzek CL. Letter to Laboratories. 2018. https://dph.georgia.gov/document/publication/cre-letter-laboratories10-5-2018pdf
KS	1. Kansas Department of Health and Environment. Reportable Diseases in Kansas. 2018. https://www.kdhe.ks.gov/DocumentCenter/View/13900/Kansas-Notifiable-Disease-List-PDF 2. Kansas Administrative Regulations. Reporting and Submission Requirements for Laboratories. K.A.R. § 28-1-18. 2018. https://www.kdhe.ks.gov/DocumentCenter/View/14424/28-1-18-Reporting-and-Submission-Requirements-for-Laboratories-PDF
KY	1. Kentucky Administrative Regulations. Reporting and Submission Requirements for Laboratories. 902 K.A.R. 2:020. 2018. https://apps.legislature.ky.gov/law/kar/titles/902/002/020/8660/
LA	1. Louisiana Department of Health. Reportable Diseases and Conditions. L.A.C 51:II § 105. 2021. https://ldh.la.gov/assets/oph/Center-PHCH/Center-CH/infectious-epi/Surveillance/sanitarycode_06_21_Revision_final_1.pdf 2. Louisiana Administrative Code. Laboratory and Healthcare Facility Reporting Requirements. L.A.C 51:II § 107. 2019. https://www.doa.la.gov/media/j3hnpfdy/51.pdf
MA	1. Code of Massachusetts Regulations. Reporting of Antimicrobial Resistant Organisms and Cumulative Antibiotic Susceptibility Test Results (Antibiograms). 105 CMR § 300.171. https://www.law.cornell.edu/regulations/massachusetts/105-CMR-300-171 2. Code of Massachusetts Regulations. Submission of Selected Isolates and Diagnostic Specimens to the State Public Health Laboratory. 105 CMR § 300.172. https://www.law.cornell.edu/regulations/massachusetts/105-CMR-300-172 3. Secretary of the Commonwealth of Massachusetts. The Massachusetts Register 2017 Jan 27; (S1331):1311-1312. https://archives.lib.state.ma.us/server/api/core/bitstreams/3c8c25f4-19fe-4691-a5e8-623611012a28/content.
MD	1. Maryland Department of Health. CRE Reporting in Maryland: Frequently Asked Questions. 2015. https://health.maryland.gov/phpa/IDEHASharedDocuments/CRE%20FAQ_Revised2015.pdf

MN	1. Minnesota Department of Health. Diseases Reportable to the Minnesota Department of Health. 2017. https://www.hco.org/wp-content/uploads/2017/08/05-MN-Dept-of-Health-Diseases-Reportable-to-MN-Dept-of-Health.pdf 2. Minnesota Rules. Disease and Reports; Clinical Materials Submissions. MINN. R. 4605.7040 (2017). https://www.revisor.mn.gov/rules/4605.7040/version/2017-01-18%2011:45:42+00:00
MS	1. Mississippi State Department of Health. List of Reportable Diseases and Conditions. 2023. https://msdh.ms.gov/msdhsite/_static/resources/877.pdf 2. Mississippi Code. Laboratory Results that Must be Reported to the Mississippi State Department of Health. Miss. Code. § 15-2-11-1-19-B. 2015. https://msdh.ms.gov/page/resources/1719.pdf 3. Mississippi State Department of Health. Updates to the Mississippi State Department of Health List of Reportable Diseases and Conditions. Mississippi Morbidity Report, August 2015; 31(No. 5): 1-2. https://msdh.ms.gov/page/resources/6354.pdf
ND	1. North Dakota Health. Mandatory Reportable Infectious Conditions. North Dakota Administrative Code. 33-06-01. 2019. 10Reportable Conditions Laminated Sheet Three Columns_updated.pdf 2. North Dakota. North Dakota Administrative Code. arc201101339v1.pdf
NE	1. Nebraska Department of Health and Human Services. Nebraska Reportable Diseases Title 173 Regulations. 2017. https://dhhs.ne.gov/epi%20docs/ReportableDiseaseChart.pdf 2. Nebraska Administrative Code. Reportable Diseases, Poisonings, and Organisms: Lists and Frequency of Reports. 173 NAC 1-004.01. 2017. https://rules.nebraska.gov/rules?agencyId=37&titleId=102
NH	1. New Hampshire Division of Public Health Services. State of New Hampshire Reportable Infectious Diseases. 2022. https://www.dhhs.nh.gov/sites/g/files/ehbemt476/files/documents/2021-12/reportablediseases.pdf 2. New Hampshire Administrative Code. Reportable Diseases. He-P 301.02. 2016. https://gc.nh.gov/rules/state_agencies/he-p300.html
NM	1. New Mexico Department of Health. Notifiable Diseases or Conditions in New Mexico. 2016. https://www.nmhealth.org/publication/view/policy/372/ 2. New Mexico Administrative Code. Notifiable Diseases or Conditions in New Mexico. 7.4.3.13 NMAC. 2016. https://www.srca.nm.gov/parts/title07/07.004.0003.html
NV	1. Nevada Department of Health and Human Services. Clinical Laboratory Submissions to State and Local Public Health Laboratories. 2021. https://dpbh.nv.gov/uploadedFiles/dpbhnvgov/content/Programs/OPHIE/Docs/Specimen-Submission-to-Public-Health-Laboratories.pdf 2. Nevada Administrative Code. "Communicable disease" defined. NAC 441A.040. 2019. https://www.leg.state.nv.us/nac/NAC-441A.html#NAC441ASec040 3. Nevada Administrative Code. Duty of director or other person in charge of medical laboratory to report findings of communicable disease, causative agent of communicable disease or immune response to causative agent; contents of report; submission of certain microbiologic cultures, subcultures, culture-independent diagnostic tests or other specimen or clinical material; required reporting of results of certain tests relating to human immunodeficiency virus. NAC 441A.235. 2019. https://www.leg.state.nv.us/nac/NAC-441A.html#NAC441ASec235 4. Nevada Administrative Code. Carbapenem-resistant Enterobacteriaceae. NAC 441A.482. 2019. https://www.leg.state.nv.us/nac/NAC-441A.html#NAC441ASec482
OK	1. Oklahoma State Department of Health. Title 310. Oklahoma State Department of Health Chapter 515. Communicable Disease and Injury Reporting. 2017. chapter-515-final-rules-2017-distribution-copy.pdf
OR	1. Oregon Health Authority. Carbapenem-Resistant Enterobacterales (CRE). Oregon Health Authority : Carbapenem-Resistant Enterobacterales (CRE) : Diseases A to Z : State of Oregon
RI	1. Rhode Island Department of Health. 2016-RICR-30-05-1 Title 216- Department of Health Reporting and Testing of Infectious, Environmental, and Occupational Diseases. 2018. https://risos-apa-production-public.s3.amazonaws.com/DOH/REG_8910_20180806190715.pdf

SC	1. South Carolina Department of Health. South Carolina 2017 List of Reportable Conditions. 2017. https://dc.statelibrary.sc.gov/server/api/core/bitstreams/d19f5037-6163-45e0-ac48-6ae31acab9cc/content 2. South Carolina Department of Health. South Carolina 2019 List of Reportable Conditions. 2019. https://dc.statelibrary.sc.gov/server/api/core/bitstreams/1d22fa04-7278-4c17-9a80-c2dfb297940c/content
SD	1. South Dakota Department of Health. Healthcare Associated Infections. https://doh.sd.gov/topics/healthcare-associated-infections/carbapenemase-producing-organism-cpo/ 2. South Dakota Department Of Health. Reportable Diseases—South Dakota. 2024. https://doh.sd.gov/media/sjlbund5/reportable-disease-poster-2024.pdf
TN	1. Tennessee Department of Health. 2019 Tennessee Reportable Disease List for Healthcare Providers. 2019. https://www.tn.gov/content/dam/tn/health/documents/reportable-diseases/2019_List_For_Healthcare_Providers.pdf 2. Tennessee Department of Health. 2019 Tennessee Reportable Disease List for Laboratories. 2019. https://www.tn.gov/content/dam/tn/health/documents/reportable-diseases/2019_List_For_Laboratories.pdf
UT	1. Utah Department of Health and Human Services. Utah Reportable Diseases. 2018. https://epi.utah.gov/wp-content/uploads/Rpt_Disease_List.pdf
VA	1. Virginia Department of Health. Carbapenem-Resistant Organisms (CRO), Data and Reporting. Virginia Regulations for Disease Reporting and Control (12 VAC 5-90-80). 2018. https://www.vdh.virginia.gov/haiar/cro/ 2. Virginia Department of Health. Virginia Reportable Disease Condition List. 2023. https://www.vdh.virginia.gov/content/uploads/sites/134/2023/03/VIRGINIA-REPORTABLE-DISEASE-LIST.pdf
VT	1. Vermont Department of Health. Guidelines for Carbapenem-Resistant Organisms: Laboratory Testing and Infection Prevention. 2019. https://www.healthvermont.gov/sites/default/files/documents/pdf/hs_id_hai_CRO-Guidelines-June-2019.pdf
WA	1. Washington State Department of Health. Highly Antibiotic Resistant Organisms: Reporting and Specimen Submission Requirements for Healthcare Facilities, Healthcare Providers and Laboratories in Washington State. 2012. Reporting and Specimen Submission Requirements for Healthcare Facilities, Healthcare Providers and Laboratories in Washington State - October 23 2012 2. Washington State. WAC 246-101-101 Notifiable Conditions—Health Care Providers and Health Care Facilities. https://app.leg.wa.gov/WAC/default.aspx?cite=246-101-101
WV	1. West Virginia. West Virginia Title 64 Legislative Rule Bureau for Public Health Series 7, Reportable Diseases, Events, and Conditions. § 64-7-3. https://oeps.wv.gov/reporting/documents/laws/WV_Reportable_Disease_Rule.pdf
WY	1. Wyoming Department of Health. Wyoming Department of Health Reportable Diseases and Conditions. State Statute § 35-4-107. https://health.wyo.gov/wp-content/uploads/2025/01/2025ReportableListFinal.pdf 2. State of Wyoming Department of Health. Summary of Reportable Disease 2017 Annual Report. 2017. https://health.wyo.gov/wp-content/uploads/2018/05/2017-Annual-Report_Draft_V1.3_Combined.pdf

File S1. Methods Describing Definitions and Analytic Limitations

Definitions

We defined CRE as *Klebsiella spp., Enterobacter spp., or E. coli* isolated from a clinical culture from a patient in a U.S. healthcare facility that was resistant to one or more carbapenems at a public health laboratory using Clinical and Laboratory Standards Institute interpretive criteria (minimum inhibitory concentrations of ≥4 μg/ml for imipenem, meropenem, and doripenem or ≥2 μg/ml for ertapenem).[13] Carbapenemase-producing CRE (CP-CRE) were defined as a CRE with at least one carbapenemase (KPC, NDM, VIM, IMP, and OXA-48-like) detected or demonstrated carbapenemase production but no carbapenemase identified by PCR or lateral flow assay. Isolates were assigned to the state where the specimen was collected. Each carbapenemase detected was counted separately, irrespective of whether multiple carbapenemases were detected from the same isolate.

Limitations

Our analysis has several limitations in addition to those already mentioned. First, our analysis excluded some of the most populous states, including California, Florida, Texas, and New York, because they do not meet cohort requirements for CRE isolate submission. While our cohort incidence rates may not be generalizable to the national burden of CP-CRE, similar trends across all 50 U.S. states and the District of Columbia suggest national shifts in the underlying epidemiology of CP-CRE during the analysis period. Second, we were not able to identify patients that contributed multiple isolates. While this could inflate incidence estimates, it is unlikely to be differential by carbapenemase and therefore the relative changes in incidence among different mechanisms should be unaffected. Third, we calculated incidence rates using the state population from where the isolate was collected as a proxy for the target population; however, this approach does not account for out-of-state residents. To assess how this limitation might bias our estimates, we queried health departments with the highest CP-CRE burden about the frequency

of isolates originating from out-of-state patients; estimates ranged from 3% to 10% of isolates. While the inclusion of out-of-state patients could potentially inflate our estimates, these isolates nonetheless contribute to the overall burden of CP-CRE in the United States and are unlikely to substantially alter the observed trends. Fourth, we classified clinical CRE isolates based on specimen source, which may result in the misclassification of surveillance cultures as clinical cultures; additionally, not all clinical cultures represent infections. Finally, isolate submission to states is passive, as it relies on healthcare providers and laboratorians to report and submit CRE isolates to their public health laboratories, thus some isolates may not be submitted for testing at the PHL.

File S2. Statistical Analysis Plan for Open Cohort and Calculating Incidence Rates

Original Statistical Analysis Plan—Developed 11/15/2024

Objective: Evaluate epidemiologic changes of carbapenemase-producing carbapenem-resistant Enterobacterales (CP-CRE) clinical isolates reported to the CDC Antimicrobial Resistance Laboratory Network from January 2019-December 2023.

Methods

Open Cohort:

- Developed a left-sided open cohort of U.S. states where the submission of carbapenem-resistant *Klebsiella* spp., *Escherichia coli*, and *Enterobacter* spp. isolates are mandated before July 1, 2020, and contributed a minimum of 36 consecutive months of data.
    - All state mandates were determined based on state legislature and confirmed by state Healthcare-Associated Infections/Antimicrobial Resistance programs.
- States were admitted into the cohort in the calendar year following the implementation of their reporting mandate. For states entering the cohort in 2019, all states were required to have a mandate in 2018 or earlier.

Inclusion Criteria:

We included carbapenem-resistant *Klebsiella* spp.*, Enterobacter* spp.*,* and *E. coli* isolates with public health laboratory testing for modified carbapenem inactivation method (mCIM) and real-time polymerase-chain reaction (PCR) or lateral flow assay to identify the presence of the carbapenemase genes bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{IMP}, and $bla_{OXA\text{-}48\text{-}like}$ or their gene products, respectively.

Exclusion Criteria:

- Isolates collected from specimen sources associated with colonization screening (e.g., rectal, axilla/groin).

Incidence Rates Methodology

We calculated annual aggregate and state-specific incidence rates for CRE, CP-CRE, and by carbapenemase using the mathematical equations below (**Equations S1-S2**). All incidence rates were expressed per 100,000 persons. 95% confidence intervals (95% CIs) were derived using the delta method. Age-adjusted incidence rates were standardized to the 2010 U.S. population across four age groups: 0-18 years; 19-64 years; 65-79 years; ≥80 years. We performed single imputation for instances where age was missing (9% of isolates) using the median age of patients with CP-CRE for each respective state.

1. ***Unadjusted Incidence Rates***

$$\frac{CRE, CP\ CRE,\ \&\ carbapenemase\ isolate\ counts}{U.S.\ Census\ population\ for\ each\ given\ year} * 100{,}000$$

2. ***Age-Adjusted (Direct Standardized) Incidence Rates***

Age Groups: 0-18 years; 19-64 years; 65-79 years; ≥80 years

$$\frac{CP\ CRE\ \&\ carbapenemase\ isolate\ counts\ for\ each\ age\ group}{2010\ U.S.\ Census\ population\ for\ each\ age\ group} * 100{,}000$$

$$Age - Adjusted\ Incidence\ Rate = IR_{0-18\ yrs} + IR_{19-64 yrs} + IR_{65-79\ yrs} + IR_{\geq 80\ yrs}$$

Temporal Trends

We assessed temporal trend models using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. We modeled year using four indicator variables, representing each specific year. State-specific results with fewer than five isolates reported in any category were suppressed to protect patient confidentiality. We calculated the percent change from the incidence rate ratio comparing 2023 to 2019. All analyses will be performed in R, version 4.4.0 (R Foundation for Statistical Computing).

Sensitivity Analyses

We conducted a sensitivity analysis to determine the unadjusted incidence rates of CP-CRE and carbapenemase genes in all 50 U.S. States and the District of Columbia, and in a stable cohort of 24 states where CRE reporting was mandated for all 5 years (2019-2023). The findings were compared to estimates derived from our open cohort. Furthermore, to assess the impact of outliers we evaluated the influence of states with extreme effect estimates—identified using the interquartile range method (i.e., Quartile 3 + 1.5[interquartile range])—and compared the incidence rates of our open cohort with and without the outlier states.

Table S2. States Included in Open Cohort, by Year

Year	No. of States	States
2019	24	AZ, CO, CT, GA, KS, KY, MA, MD, MN, MS, ND, NE, NH, NM, OR, RI, SC, SD, TN, UT, VA, WA, WV, WY
2020	28	AZ, CO, CT, GA, KS, KY, **LA**, MA, MD, MN, MS, ND, NE, NH, NM, **NV**, **OK**, OR, RI, SC, SD, TN, UT, VA, **VT**, WA, WV, WY
2021	29	AZ, CO, CT, GA, KS, KY, LA, MA, MD, MN, MS, **MT**, ND, NE, NH, NM, NV, OK, OR, RI, SC, SD, TN, UT, VA, VT, WA, WV, WY
2022	29	AZ, CO, CT, GA, KS, KY, LA, MA, MD, MN, MS, MT, ND, NE, NH, NM, NV, OK, OR, RI, SC, SD, TN, UT, VA, VT, WA, WV, WY
2023	29	AZ, CO, CT, GA, KS, KY, LA, MA, MD, MN, MS, MT, ND, NE, NH, NM, NV, OK, OR, RI, SC, SD, TN, UT, VA, VT, WA, WV, WY

Footnote: States are bolded and underlined in the year they entered the cohort. No states exited the cohort.

Table S3. Trend Analysis of Age-Adjusted Incidence Rates/100,000 Persons Across an Open Cohort of U.S. States with Required CRE Isolate Submission, 2019-2023

	Indicator Year Incidence Rate Ratio[a] 2023 vs. 2019 (95% CI)	Cumulative 5-Year % Change[b] (95% CI)
All CP-CRE	1.69 (1.61, 1.78)	69 (61, 78)
KPC	0.96 (0.90, 1.03)	-4 (-10, 3)
NDM	5.61 (4.96, 6.36)	461 (396, 536)

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. Each carbapenemase gene (i.e., KPC and NDM) was counted within its respective category, irrespective of whether multiple carbapenemase genes were detected in a single isolate.

[a]Incidence Rate Ratio= e^p, where p is the modeled parameter estimate for the variable year

[b]Percent Change= $(e^p-1)*100$, where p is the modeled parameter estimate for the variable year

Table S4. Unadjusted and Age-Adjusted CP-CRE, KPC-CRE, and NDM-CRE Incidence Rates, Overall and by Age Group Across an Open Cohort of U.S. States with Required CRE Isolate Submission, 2019-2023

				CP-CRE[a]			KPC-CRE			NDM-CRE		
Year	No. of States	Age-Group	U.S. Census Population[b]	No. of Cases	Unadjusted Incidence/ 100,000 Persons (95% CI)	Age-Adjusted[c,d] Incidence/ 100,000 Persons (95% CI)	No. of Cases	Unadjusted Incidence/ 100,000 Persons (95% CI)	Age-Adjusted[c,d] Incidence/ 100,000 Persons (95% CI)	No. of Cases	Unadjusted Incidence/ 100,000 Persons (95% CI)	Age-Adjusted[c,d] Incidence/ 100,000 Persons (95% CI)
2019	24	Overall	102,253,036	2,267	**2.22 (2.13, 2.31)**	**1.98 (1.90, 2.07)**	1,749	**1.71 (1.63, 1.79)**	**1.53 (1.46, 1.61)**	288	**0.28 (0.25, 0.32)**	**0.25 (0.22, 0.28)**
		0-18	24,125,840	43	0.14 (0.12, 0.16)		26	0.07 (0.05, 0.08)		13	0.03 (0.02, 0.03)	
		19-64	61,412,713	970	1.57 (1.50, 1.64)		775	1.25 (1.19, 1.32)		108	0.19 (0.17, 0.22)	
		65-80	13,328,052	996	7.37 (7.05, 7.71)		756	5.75 (5.46, 6.07)		132	0.89 (0.79, 1.01)	
		81+	3,386,431	258	8.52 (8.02, 9.05)		192	5.84 (5.40, 6.30)		35	1.28 (1.12, 1.47)	
2020	28	Overall	115,487,153	1,903	**1.65 (1.58, 1.72)**	**1.48 (1.41, 1.54)**	1,475	**1.28 (1.21, 1.34)**	**1.15 (1.09, 1.21)**	259	**0.22 (0.20, 0.25)**	**0.20 (0.17, 0.22)**
		0-18	27,508,789	16	0.10 (0.09, 0.12)		11	0.05 (0.04, 0.06)		2	0.02 (0.02, 0.03)	
		19-64	69,136,236	832	1.17 (1.11, 1.23)		686	0.94 (0.89, 0.99)		98	0.16 (0.14, 0.18)	
		65-80	15,279,354	847	5.50 (5.24, 5.77)		622	4.31 (4.07, 4.56)		123	0.71 (0.63, 0.81)	
		81+	3,562,774	208	6.35 (5.96, 6.77)		156	4.37 (4.03, 4.73)		36	1.02 (0.89, 1.18)	
2021	29	Overall	117,033,977	2,534	**2.17 (2.08, 2.25)**	**1.91 (1.84, 1.99)**	1,676	**1.43 (1.37, 1.50)**	**1.26 (1.20, 1.33)**	593	**0.51 (0.47, 0.55)**	**0.45 (0.42, 0.49)**
		0-18	27,595,613	29	0.14 (0.12, 0.16)		9	0.05 (0.04, 0.07)		14	0.05 (0.04, 0.06)	
		19-64	69,848,395	1,069	1.52 (1.45, 1.58)		739	1.04 (0.98, 1.09)		238	0.35 (0.32, 0.38)	
		65-80	15,954,476	1,163	7.13 (6.83, 7.45)		773	4.77 (4.52, 5.03)		255	1.59 (1.46, 1.74)	
		81+	3,635,493	273	8.24 (7.77, 8.74)		155	4.84 (4.47, 5.23)		86	2.29 (2.05, 2.55)	
2022	29	Overall	117,566,458	3,137	**2.67 (2.58, 2.76)**	**2.35 (2.27, 2.44)**	1,679	**1.43 (1.36, 1.50)**	**1.25 (1.19, 1.31)**	1,200	**1.02 (0.97, 1.08)**	**0.91 (0.86, 0.96)**
		0-18	27,485,907	53	0.16 (0.14, 0.19)		17	0.05 (0.04, 0.07)		25	0.09 (0.08, 0.12)	
		19-64	69,914,542	1,311	1.85 (1.77, 1.92)		692	1.02 (0.97, 1.08)		516	0.69 (0.65, 0.74)	
		65-80	16,466,165	1,370	8.69 (8.35, 9.03)		768	4.70 (4.46, 4.95)		419	3.17 (2.97, 3.39)	
		81+	3,699,844	403	10.03 (9.48, 10.62)		202	4.77 (4.41, 5.15)		168	4.55 (4.14, 5.00)	
2023	29	Overall	118,211,191	4,341	**3.67 (3.56, 3.78)**	**3.16 (3.07, 3.26)**	1,908	**1.61 (1.54, 1.69)**	**1.38 (1.32, 1.44)**	1,831	**1.55 (1.48, 1.62)**	**1.34 (1.28, 1.41)**
		0-18	27,350,075	64	0.22 (0.19, 0.26)		13	0.06 (0.05, 0.08)		36	0.14 (0.11, 0.17)	
		19-64	70,058,521	1,695	2.51 (2.42, 2.60)		761	1.14 (1.08, 1.20)		718	1.04 (0.98, 1.10)	
		65-80	16,973,914	2,017	11.80 (11.39, 12.21)		930	5.24 (4.98, 5.51)		810	4.75 (4.49, 5.03)	
		81+	3,828,681	565	13.62 (12.91, 14.37)		204	5.32 (4.93, 5.74)		267	6.81 (6.24, 7.43)	

Footnote: VIM- and IMP-CRE are not shown due to the number of isolates representing <1% of all CP-CRE. [a]CP-CRE, includes *Klebsiella* spp., *Enterobacter* spp., and *Escherichia coli* with the presence of mCIM+/PCR-, bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{IMP}, and $bla_{OXA\text{-}48\text{-}like}$ carbapenemase gene; [b]U.S. 2019-2023 Census Population Estimates; [c]Age-adjusted rates were standardized to the U.S. 2010 Census Population Estimates[16]; [d]Age weights: 0-18 years weight= 0.25; 19-64 years weight= 0.62; 65-80 years weight=0.10; 81+ years weight=0.03

Table S5. Unadjusted CP-CRE Incidence Rates per 100,000 Persons Across an Open Cohort of U.S. States with Required CRE Isolate Submission, by Carbapenemase, 2019-2023

Year	Total Population	Total No. of CP-CRE Clinical Cases					Unadjusted Incidence Rate/100,000 Persons				
		KPC	NDM	OXA-48-like	VIM	IMP	KPC (95% CI)	NDM (95% CI)	OXA-48-like (95% CI)	VIM (95% CI)	IMP (95% CI)
2019[a]	102,253,036	1,749	288	96	24	1	1.71 (1.63, 1.79)	0.28 (0.25, 0.32)	0.09 (0.08, 0.11)	0.023 (0.016, 0.035)	0.0010 (0.0001, 0.0069)
2020[b]	115,487,153	1,475	259	82	19	6	1.28 (1.21, 1.34)	0.22 (0.20, 0.25)	0.07 (0.06, 0.09)	0.016 (0.011, 0.026)	0.0052 (0.0023, 0.0116)
2021[c]	117,033,977	1,676	593	89	29	11	1.43 (1.37, 1.50)	0.51 (0.47, 0.55)	0.08 (0.06, 0.09)	0.025 (0.017, 0.036)	0.0094 (0.0052, 0.0170)
2022[c]	117,566,458	1,679	1,200	123	49	5	1.43 (1.36, 1.50)	1.02 (0.97, 1.08)	0.10 (0.09, 0.12)	0.042 (0.032, 0.055)	0.0043 (0.0018, 0.0102)
2023[c]	118,211,191	1,908	1,831	167	31	7	1.61 (1.54, 1.69)	1.55 (1.48, 1.62)	0.14 (0.12, 0.16)	0.026 (0.018, 0.037)	0.0059 0.0028, 0.0124)

Footnote: Each carbapenemase gene were counted within its respective category, irrespective of whether multiple carbapenemase genes were detected.

[a]24 total U.S. States; [b]28 total U.S. States; [c]29 total U.S. States; Abbreviations: CP-CRE, carbapenemase-producing carbapenem-resistant Enterobacterales

Table S6. Unadjusted CP-CRE, KPC-CRE, and NDM-CRE Incidence Rates by State, Across an Open Cohort of 29 U.S. States with Required CRE Isolate Submission, 2019-2023, by State

State	Mechanism	Age-Adjusted[a] Incidence Rates/100,000 Persons					Trend
		2019	2020	2021	2022	2023	% Change[b] (95% CI)
AZ	All CP-CRE	1.50 (1.25, 1.80)	1.91 (1.61, 2.24)	3.76 (3.35, 4.21)	9.25 (8.60, 9.94)	14.28 (13.48, 15.11)	917 (749, 1130)
	KPC-CRE	1.19 (0.97, 1.46)	1.20 (0.96, 1.47)	1.28 (1.04, 1.56)	1.48 (1.23, 1.78)	1.03 (0.83, 1.28)	No change
	NDM-CRE	0.18 (0.10, 0.31)	0.54 (0.39, 0.74)	2.26 (1.95, 2.62)	7.46 (6.88, 8.08)	10.96 (10.27, 11.69)	**6353 (3928, 11152)**
CO	All CP-CRE	0.59 (0.43, 0.80)	0.52 (0.38, 0.72)	0.08 (0.03, 0.20)	0.90 (0.68, 1.17)	0.92 (0.69, 1.19)	No change
	KPC-CRE	0.25 (0.15, 0.39)	0.10 (0.04, 0.20)	--	0.20 (0.10, 0.34)	0.18 (0.09, 0.32)	No change
	NDM-CRE	0.17 (0.09, 0.31)	--	--	0.08 (0.03, 0.20)	0.19 (0.10, 0.34)	No change
CT	All CP-CRE	2.11 (1.67, 2.63)	1.77 (1.37, 2.25)	2.82 (2.31, 3.41)	1.74 (1.35, 2.22)	3.13 (2.60, 3.74)	56 (19, 107)
	KPC-CRE	1.51 (1.14, 1.96)	1.42 (1.07, 1.87)	1.67 (1.29, 2.14)	1.05 (0.76, 1.43)	1.62 (1.25, 2.07)	No change
	NDM-CRE	0.47 (0.28, 0.75)	0.23 (0.10, 0.44)	1.00 (0.71, 1.36)	0.52 (0.32, 0.80)	1.14 (0.83, 1.54)	**150 (47, 343)**
GA	All CP-CRE	3.01 (2.71, 3.34)	0.36 (0.26, 0.49)	2.92 (2.62, 3.24)	2.13 (1.88, 2.41)	2.01 (1.79, 2.25)	-15 (-27, -2)
	KPC-CRE	2.22 (1.96, 2.51)	0.27 (0.18, 0.39)	1.97 (1.73, 2.24)	1.34 (1.14, 1.57)	1.29 (1.11, 1.49)	-27 (-40, -13)
	NDM-CRE	0.28 (0.19, 0.39)	--	0.37 (0.27, 0.49)	0.45 (0.34, 0.59)	0.32 (0.24, 0.43)	No change
KS	All CP-CRE	0.58 (0.34, 0.92)	0.53 (0.30, 0.86)	0.40 (0.21, 0.71)	0.59 (0.35, 0.94)	0.81 (0.53, 1.21)	No change
	KPC-CRE	0.29 (0.13, 0.56)	0.27 (0.12, 0.54)	0.27 (0.12, 0.54)	0.21 (0.08, 0.46)	0.20 (0.07, 0.44)	No change
	NDM-CRE	--	--	--	0.22 (0.09, 0.47)	0.40 (0.21, 0.70)	**550 (401, 699)**
KY	All CP-CRE	2.21 (1.81, 2.67)	1.91 (1.55, 2.34)	3.98 (3.45, 4.59)	2.78 (2.32, 3.28)	4.46 (3.89, 5.10)	102 (61, 154)
	KPC-CRE	1.62 (1.28, 2.02)	1.44 (1.13, 1.81)	3.58 (3.07, 4.16)	2.09 (1.71, 2.54)	2.78 (2.33, 3.29)	73 (32, 128)
	NDM-CRE	0.10 (0.03, 0.25)	0.19 (0.09, 0.37)	0.15 (0.06, 0.30)	0.28 (0.15, 0.30)	0.46 (0.29, 0.71)	**340 (243, 437)**
LA	All CP-CRE	*	0.61 (0.41, 0.87)	0.46 (0.29, 0.69)	1.13 (0.73, 1.30)	0.98 (0.73, 1.30)	64 (6, 160)[c]
	KPC-CRE	*	0.59 (0.39, 0.84)	0.27 (0.15, 0.45)	0.83 (0.60, 1.13)	0.71 (0.51, 0.98)	No change[c]
	NDM-CRE	*	--	--	0.18 (0.09, 0.35)	0.21 (0.10, 0.39)	No change[c]
MA	All CP-CRE	1.84 (1.54, 2.17)	1.40 (1.14, 1.69)	2.36 (2.02, 2.74)	1.18 (0.95, 1.46)	2.19 (1.86, 2.55)	No change
	KPC-CRE	0.86 (0.67, 1.10)	0.79 (0.60, 1.02)	1.11 (0.89, 1.37)	0.40 (0.27, 0.58)	0.96 (0.75, 1.22)	No change
	NDM-CRE	0.85 (0.65, 1.09)	0.56 (0.41, 0.76)	1.15 (0.91, 1.42)	0.66 (0.49, 0.87)	1.10 (0.88, 1.37)	No change
MD	All CP-CRE	5.34 (4.79, 5.94)	3.92 (3.45, 4.44)	4.86 (4.35, 5.43)	5.49 (4.95, 6.09)	6.74 (6.14, 7.39)	36 (19, 56)
	KPC-CRE	4.83 (4.31, 5.40)	3.22 (2.80, 3.69)	3.94 (3.48, 4.45)	3.65 (3.20, 4.13)	4.50 (4.00, 5.03)	No change
	NDM-CRE	0.36 (0.23, 0.54)	0.61 (0.44, 0.82)	0.90 (0.68, 1.16)	1.66 (1.37, 2.00)	1.96 (1.64, 2.33)	**456 (270, 771)**

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. [a]Age-adjusted rates were standardized to the U.S. 2010 Census Population Estimates; [b]Percent change from 2019-2023; [c]Percent change from 2020-2023; [d]Percent change from 2021-2023; --, represents instances when <5 cases were observed; *, represents years where a state had not yet entered the cohort.

State	Mechanism	Age-Adjusted[a] Incidence Rates/100,000 Persons					Trend
		2019	2020	2021	2022	2023	% Change[b] (95% CI)
MN	All CP-CRE	0.61 (0.43, 0.83)	0.47 (0.32, 0.67)	0.61 (0.44, 0.82)	0.69 (0.53, 0.90)	1.03 (0.80, 1.32)	66 (13, 146)
	KPC-CRE	0.29 (0.18, 0.46)	0.18 (0.10, 0.32)	0.27 (0.16, 0.43)	0.32 (0.21, 0.48)	0.24 (0.13, 0.41)	No change
	NDM-CRE	0.24 (0.14, 0.40)	0.14 (0.07, 0.26)	0.20 (0.11, 0.34)	0.25 (0.15, 0.39)	0.46 (0.31, 0.66)	**94 (8, 263)**
MS	All CP-CRE	1.57 (1.17, 2.08)	0.26 (0.13, 0.50)	2.89 (2.33, 3.55)	3.70 (3.07, 4.43)	4.23 (3.55, 5.01)	176 (102, 284)
	KPC-CRE	1.47 (1.08, 1.96)	0.13 (0.04, 0.32)	2.44 (1.93, 3.05)	2.76 (2.22, 3.40)	2.40 (1.89, 3.01)	63 (14, 134)
	NDM-CRE	--	--	0.22 (0.09, 0.47)	1.01 (0.69, 1.42)	1.70 (1.28, 2.21)	**1800 (603, 7691)**
MT	All CP-CRE	*	*	0.32 (0.08, 0.86)	0.49 (0.18, 1.11)	0.52 (0.20, 1.12)	No change[d]
	KPC-CRE	*	*	--	--	--	No change[d]
	NDM-CRE	*	*	--	--	--	No change[d]
ND	All CP-CRE	1.46 (0.73, 2.63)	1.29 (0.62, 2.41)	1.98 (1.15, 3.24)	1.36 (0.67, 2.48)	0.79 (0.29, 1.76)	No change
	KPC-CRE	1.21 (0.55, 2.31)	1.16 (0.53, 2.23)	1.62 (0.88, 2.78)	0.95 (0.40, 1.94)	--	No change
	NDM-CRE	--	--	--	--	--	No change
NE	All CP-CRE	0.69 (0.40, 1.13)	--	--	--	0.80 (0.49, 1.27)	No change
	KPC-CRE	0.41 (0.20, 0.77)	--	--	--	0.14 (0.04, 0.41)	No change
	NDM-CRE	0.24 (0.09, 0.56)	--	--	--	0.34 (0.14, 0.70)	No change
NH	All CP-CRE	0.41 (0.18, 0.87)	0.44 (0.20, 0.90)	0.37 (0.16, 0.81)	--	0.16 (0.03, 0.56)	No change
	KPC-CRE	--	0.24 (0.08, 0.65)	--	--	--	No change
	NDM-CRE	--	--	--	--	--	No change
NM	All CP-CRE	1.13 (0.76, 1.65)	0.90 (0.59, 1.35)	0.97 (0.64, 1.45)	1.05 (0.69, 1.55)	2.08 (1.54, 2.75)	77 (32, 121)
	KPC-CRE	0.78 (0.48, 1.22)	0.65 (0.39, 1.04)	0.73 (0.44, 1.17)	0.44 (0.22, 0.82)	0.89 (0.56, 1.38)	No change
	NDM-CRE	--	--	0.21 (0.07, 0.50)	0.33 (0.15, 0.67)	0.73 (0.43, 1.18)	**850 (704, 996)**
NV	All CP-CRE	*	4.86 (4.15, 5.66)	3.56 (2.96, 4.25)	1.83 (1.40, 2.35)	2.27(1.81, 2.81)	-49 (-60, -34)[c]
	KPC-CRE	*	4.60 (3.91, 5.38)	3.19 (2.63, 3.85)	1.56 (1.17, 2.05)	1.73 (1.33, 2.21)	-59 (-69, -45)[c]
	NDM-CRE	*	0.34 (0.17, 0.61)	0.40 (0.22, 0.68)	0.21 (0.09, 0.43)	0.46 (0.27, 0.75)	No change[c]
OK	All CP-CRE	*	3.73 (3.16, 4.37)	3.18 (2.68, 3.75)	2.85 (2.39, 3.38)	2.71 (2.24, 3.25)	-23 (-39, -2)[c]
	KPC-CRE	*	3.63 (3.07, 4.26)	2.26 (1.85, 2.77)	2.63 (2.19, 3.13)	2.08 (1.67, 2.56)	(-39, -53, -21)[c]
	NDM-CRE	*	--	0.22 (0.10, 0.41)	0.24 (0.12, 0.43)	0.35 (0.19, 0.58)	**650 (502, 798)[c]**

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. [a]Age-adjusted rates were standardized to the U.S. 2010 Census Population Estimates; [b]Percent change from 2019-2023; [c]Percent change from 2020-2023; [d]Percent change from 2021-2023; --, represents instances when <5 cases were observed; *, represents years where a state had not yet entered the cohort.

State	Mechanism	Age-Adjusted[a] Incidence Rate/100,000 Persons (95% CI)					Trend
		2019	2020	2021	2022	2023	% Change[b] (95% CI)
OR	All CP-CRE	0.51 (0.32, 0.77)	0.16 (0.07, 0.33)	0.48 (0.30, 0.75)	0.50 (0.33, 0.76)	0.25 (0.13, 0.45)	No change
	KPC-CRE	0.11 (0.04, 0.28)	--	--	--	--	No change
	NDM-CRE	0.30 (0.16, 0.51)	0.10 (0.03, 0.24)	0.21 (0.09, 0.40)	0.14 (0.05, 0.30)	0.18 (0.08, 0.36)	No change
RI	All CP-CRE	3.49 (2.46, 4.81)	2.96 (2.02, 4.21)	1.16 (0.64, 1.97)	2.76 (1.89, 3.96)	4.49 (3.35, 5.92)	No change
	KPC-CRE	3.25 (2.26, 4.54)	2.66 (1.77, 3.85)	0.83 (0.41, 1.55)	1.70 (1.04, 2.67)	2.44 (1.61, 3.56)	No change
	NDM-CRE	--	--	--	1.00 (0.47, 1.85)	1.41 (0.82, 2.30)	**500 (378, 622)**
SC	All CP-CRE	1.53 (1.25, 1.87)	1.56 (1.28, 1.89)	1.38 (1.12, 1.69)	1.52 (1.22, 1.87)	3.02 (2.59, 3.50)	79 (41, 128)
	KPC-CRE	1.36 (1.09, 1.67)	1.31 (1.06, 1.62)	0.94 (0.73, 1.20)	0.98 (0.75, 1.26)	1.68 (1.36, 2.05)	No change
	NDM-CRE	0.11 (0.05, 0.25)	0.16 (0.07, 0.30)	0.29 (0.17, 0.46)	0.29 (0.17, 0.47)	0.82 (0.61, 1.09)	**629 (254, 1661)**
SD	All CP-CRE	0.96 (0.44, 1.86)	--	0.56 (0.18, 1.35)	0.69 (0.27, 1.49)	0.62 (0.24, 1.37)	No change
	KPC-CRE	0.88 (0.38, 1.75)	--	--	0.48 (0.15, 1.20)	0.47 (0.15, 1.18)	No change
	NDM-CRE	--	--	--	--	--	No change
TN	All CP-CRE	3.67 (3.25, 4.14)	3.41 (3.00, 3.86)	1.29 (1.04, 1.58)	4.36 (3.90, 4.86)	4.19 (3.75, 4.67)	23 (5, 44)
	KPC-CRE	3.11 (2.72, 3.54)	3.06 (2.67, 3.48)	0.94 (0.73, 1.19)	3.35 (2.95, 3.79)	3.07 (2.70, 3.49)	No change
	NDM-CRE	0.24 (0.14, 0.38)	0.13 (0.06, 0.25)	0.10 (0.04, 0.20)	0.66 (0.49, 0.88)	0.79 (0.61, 1.02)	**250 (112, 508)**
UT	All CP-CRE	0.86 (0.58, 1.23)	0.38 (0.21, 0.66)	0.92 (0.63, 1.29)	0.56 (0.34, 0.87)	1.15 (0.83, 1.57)	No change
	KPC-CRE	0.22 (0.09, 0.45)	0.08 (0.02, 0.26)	0.18 (0.07, 0.38)	0.27 (0.13, 0.51)	0.43 (0.25, 0.71)	No change
	NDM-CRE	--	--	0.31 (0.16, 0.57)	0.15 (0.05, 0.35)	0.17 (0.06, 0.38)	No change
VA	All CP-CRE	3.63 (3.25, 4.04)	2.09 (1.81, 2.41)	2.04 (1.76, 2.35)	2.47 (2.16, 2.81)	3.28 (2.93, 3.67)	No change
	KPC-CRE	3.27 (2.92, 3.67)	1.79 (1.53, 2.08)	1.68 (1.42, 1.96)	1.56 (1.32, 1.84)	1.76 (1.50, 2.05)	-44 (-54, -33)
	NDM-CRE	0.29 (0.20, 0.43)	0.20 (0.12, 0.31)	0.31 (0.21, 0.45)	0.86 (0.68, 1.07)	1.42 (1.19, 1.69)	**359 (212, 598)**
VT	All CP-CRE	*	--	0.57 (0.18, 1.49)	--	--	No change[c]
	KPC-CRE	*	--	--	--	--	No change[c]
	NDM-CRE	*	--	--	--	--	No change[c]
WA	All CP-CRE	0.46 (0.32, 0.63)	0.53 (0.38, 0.71)	0.40 (0.28, 0.57)	0.58 (0.43, 0.77)	0.93 (0.74, 1.15)	126 (56, 235)
	KPC-CRE	0.20 (0.12, 0.33)	0.13 (0.06, 0.24)	0.13 (0.06, 0.23)	0.20 (0.12, 0.33)	0.20 (0.12, 0.32)	No change
	NDM-CRE	0.15 (0.08, 0.26)	0.29 (0.19, 0.44)	0.22 (0.13, 0.36)	0.31 (0.20, 0.45)	0.46 (0.33, 0.63)	**250 (90, 595)**

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. [a]Age-adjusted rates were standardized to the U.S. 2010 Census Population Estimates; [b]Percent change from 2019-2023; [c]Percent change from 2020-2023; [d]Percent change from 2021-2023; --, represents instances when <5 cases were observed; *, represents years where a state had not yet entered the cohort.

State	Mechanism	Age-Adjusted[a] Incidence Rate/100,000 Persons (95% CI)					Trend
		2019	2020	2021	2022	2023	% Change[b] (95% CI)
WV	All CP-CRE	--	--	--	--	--	No change
	KPC-CRE	--	--	--	--	--	No change
	NDM-CRE	--	--	--	--	--	No change
WY	All CP-CRE	--	--	0.72 (0.23, 1.78)	--	--	No change
	KPC-CRE	--	--	--	--	--	No change
	NDM-CRE	--	--	--	--	--	No change

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. [a]Age-adjusted rates were standardized to the U.S. 2010 Census Population Estimates; [b]Percent change from 2019-2023; [c]Percent change from 2020-2023; [d]Percent change from 2021-2023; --, represents instances when <5 cases were observed; *, represents years where a state had not yet entered the cohort.

Table S7. Sensitivity Analysis of CP-CRE, KPC-CRE, NDM-CRE Trends across U.S. States with Varying CRE Reporting Requirements, 2019-2023

Year	Open Cohort of U.S. States w/CRE Isolate Submission Required for 36 consecutive months[a]	50 U.S. States, and the District of Columbia[b]	22 U.S. States, District of Columbia, and Puerto Rico w/o CRE Isolate Submission Required[c]	24 U.S. States w/ CRE Isolate Submission Required During Entire Study Period[d]
CP-CRE Unadjusted Incidence Rates/ 100,000 Persons (95% CI)				
2019	2.22 (2.13, 2.31)	1.73 (1.68, 1.77)	1.47 (1.43, 1.52)	2.22 (2.13, 2.31)
2020	1.65 (1.58, 1.72)	1.36 (1.33, 1.40)	1.22 (1.17, 1.27)	1.50 (1.43, 1.57)
2021	2.17 (2.08, 2.25)	1.68 (1.64, 1.73)	1.42 (1.37, 1.47)	2.15 (2.06, 2.24)
2022	2.67 (2.58, 2.76)	1.96 (1.91, 2.00)	1.57 (1.51, 1.62)	2.76 (2.66, 2.87)
2023	3.67 (3.56, 3.78)	2.64 (2.58, 2.69)	2.08 (2.02, 2.14)	3.89 (3.78, 4.01)
Cumulative % Change, 2019-2023	66 (57, 74)	53 (47, 57)	41 (35, 48)	76 (67, 85)
KPC-CRE Unadjusted Incidence Rates/ 100,000 Persons (95% CI)				
2019	1.71 (1.63, 1.79)	1.38 (1.34, 1.42)	1.20 (1.16, 1.25)	1.71 (1.63, 1.79)
2020	1.28 (1.21, 1.34)	1.06 (1.03, 1.10)	0.95 (0.91, 0.99)	1.10 (1.03, 1.16)
2021	1.43 1.37, 1.50)	1.18 (1.14, 1.21)	1.04 (1.00, 1.08)	1.39 (1.32, 1.46)
2022	1.43 (1.36, 1.47)	1.18 (1.15, 1.22)	1.05 (1.01, 1.10)	1.39 (1.32, 1.47)
2023	1.61 (1.54, 1.69)	1.32 (1.28, 1.36)	1.16 (1.12, 1.21)	1.63 (1.56, 1.71)
Cumulative % Change, 2019-2023	-6 (-12, 1)	-4 (-8, -0.3)	-3 (-8, 2)	-5 (-11, 2)
NDM-CRE Unadjusted Incidence Rates/ 100,000 Persons (95% CI)				
2019	0.28 (0.25, 0.32)	0.21 (0.20, 0.23)	0.18 (0.16, 0.20)	0.28 (0.25, 0.32)
2020	0.22 (0.20, 0.25)	0.19 (0.18, 0.20)	0.17 (0.15, 0.19)	0.24 (0.21, 0.27)
2021	0.51 (0.47, 0.55)	0.35 (0.33, 0.37)	0.26 (0.24, 0.29)	0.54 (0.50, 0.59)
2022	1.02 (0.97, 1.08)	0.63 (0.60, 0.65)	0.41 (0.39, 0.44)	1.12 (1.06, 1.19)
2023	1.55 (1.48, 1.62)	1.03 (1.00, 1.07)	0.75 (0.71, 0.79)	1.71 (1.63, 1.79)
Cumulative % Change, 2019-2023	500 (387, 524)	390 (352, 432)	318 (274, 368)	506 (436, 587)

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group. [a] Includes 29 U.S. states with required CRE isolates submission by July 1, 2020; [b] Includes all 50 U.S. states and the District of Columbia; [c] Includes 22 U.S. states, District of Columbia, and Puerto Rico without CRE isolates reporting requirements by July 1, 2020; [d] Includes 24 U.S. states with CRE isolate submission before July 1, 2018.

Table ~~S~~8. Trend Analysis of CP-CRE Incidence Rates of Genera Across an Open Cohort of U.S. States with Required CRE Isolate Submission, 2019-2023

Group	CP-CRE Cumulative 5-Year % Change[a] (95% CI)	KPC Cumulative 5-Year % Change[a] (95% CI)	NDM Cumulative 5-Year % Change[a] (95% CI)	OXA-48-like Cumulative 5-Year % Change[a] (95% CI)
Genus				
Klebsiella spp.	71 (61, 82)	-9 (-15, -1)	909 (730, 1140)	151 (70, 281)
Enterobacter spp.	48 (32, 67)	4 (-11,20)	283 (180, 435)	--
E. coli	65 (45, 87)	0.1 (-19, 23)	161 (116, 217)	-9 (-36, 28)

Footnote: Trends were assessed using a Poisson generalized linear model with robust sandwich estimators and log-link adjusting for age group.

-- model wouldn't converge due to small N's

[a]Percent Change= $(e^{p}-1)*100$, where p is the modeled parameter estimate for the variable year

Figure S1. Sensitivity Analysis of Unadjusted CP-CRE, KPC-CRE, and NDM-CRE Incidence Rates in an Open Cohort with and without Outlier States. Footnote: Open cohort includes 29 U.S. states with required CRE isolates submission by July 1, 2020; w/o outlier states include all states from the Open cohort except for those states with extreme effect estimates.

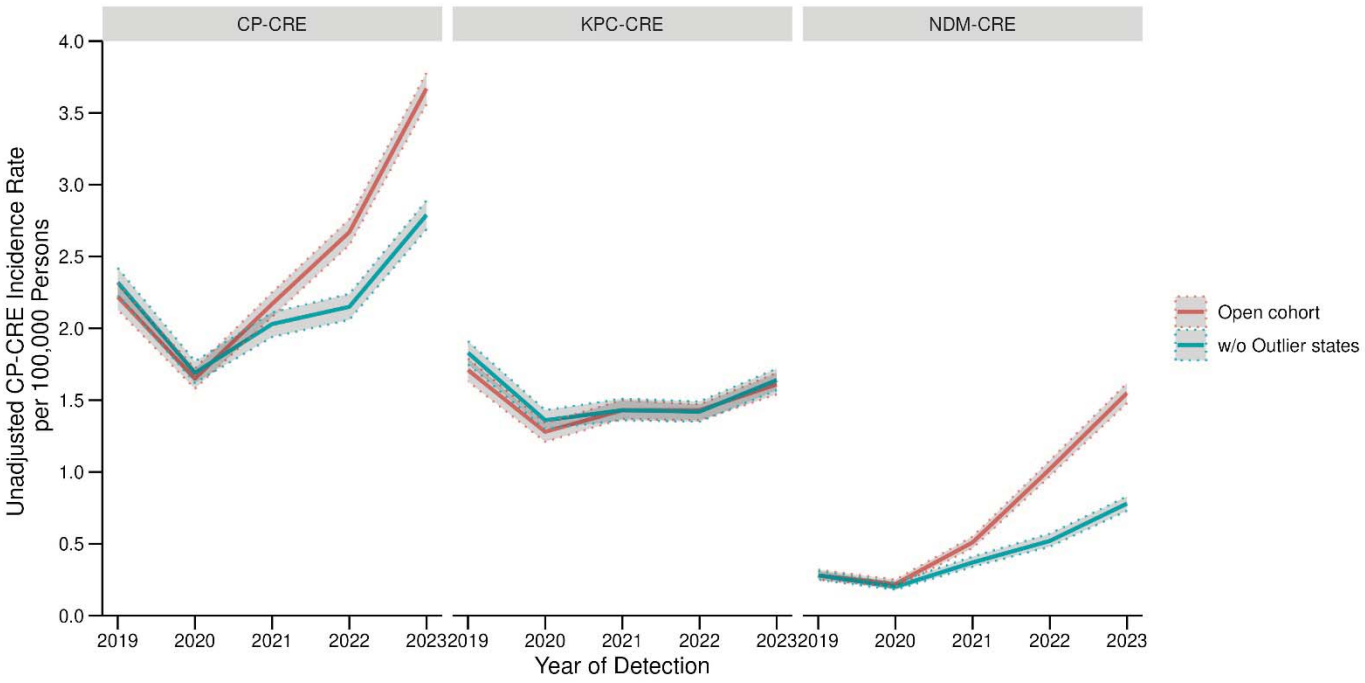

Figure S2. Percent of Isolates with Carbapenemase Detected from Carbapenem-Resistant (A) *Klebsiella spp.*, (B) *Escherichia coli*, and (C) *Enterobacter spp.* Clinical Isolates among an Open Cohort of U.S. States with Required CRE Isolate Submission, 2019-2023. Footnote: CP-CRE, includes Klebsiella spp., Enterobacter spp., and Escherichia coli with the presence of mCIM+/PCR-, blaKPC, blaNDM, blaVIM, blaIMP, and blaOXA-48-like carbapenemase gene. VIM- and IMP-CRE are not shown due to the number of isolates representing <1% of all CP-CRE. Abbreviations: CP-CRE, carbapenemase-producing carbapenem-resistant Enterobacterales.