

## INTRODUCTION

Carbapenem-resistant Enterobacterales (CRE) are considered an urgent threat to human health by the CDC<sup>1,2</sup>. Tracking resistance over time is important to understand trends and patterns. Tracking carbapenem resistance is complicated by definitions which include resistance to ertapenem only which can differ in epidemiology, mechanism, and treatment options<sup>3</sup>. This study examines trends of CRE from 2015 to 2019 and the impact of carbapenem resistance on outcomes.

## OBJECTIVES

1. Describe the characteristics and hospitalization outcomes of the two classes of CRE: CR-1/2 (resistant to both classes of carbapenems and Erta-R (resistant to class 1 carbapenems only).
2. Examine the trends of CRE by the common pathogens for these two classes from 2015 through 2019.

## METHODS

## Data source

The Premier HealthCare Database collects anonymised patient-level clinical data from over 700 US hospitals annually, with a subset of 312 providing microbiological details for Gram-negative pathogens, including specimen site, pathogen and antibiotic susceptibility.

## Study design, population and setting

- Retrospective cohort
- Enterobacterales infections identified in the Premier database from 2015 to 2019 categorized into 3 groups: ertapenem only resistant (Erta-R); isolates resistant to ertapenem and class 2 carbapenems (CR-1/2); and carbapenem susceptible (CS). Enterobacterales included E. coli, Klebsiella pneumoniae and oxytoca, Proteus mirabilis, Enterobacter cloacae and aerogenes, Serratia marcescens, Morganella morganii, Providentia, and Citrobacter (all spp).

## Inclusion/exclusion criteria:

- Patients with microbiology testing of Gram-negative infection (GNI) at any site in an inpatient setting from 2015 -2019 Q2.
- Excluded patients without antibiotic susceptibility testing or interpretable CR/CS results, pathogen species with < 100 patients, polymicrobial infections, those with multiple infection sites or multiple pathogens on the same index day, and if hospitalized < 48 hours.

## Outcomes

- Discharge status, length of stay (LOS), infection associated charges by CR status
- Proportion of CR among top pathogens
- CR trends by year for selected pathogens

## Statistical analysis

- Outcomes were tabulated and compared between the 2 groups of resistance and CS.
- Statistical significance of difference between proportions was tested with chi square for categorical data, Kruskal-Wallis test for differences between group medians. Significance level was set at 0.05.

## RESULTS

Table 1 Baseline characteristics of CRE patients

Variable	Erta-R (N=692)		CR-1/2 (N= 2,397)		CS (N= 222,368)		P-value*
	N	%	N	%	N	%	
Sex (female)	354	51	1,236	41	148,489	67	<0.01
Age, median (IQR)	68	(57-79)	68	(57-78)	70	(57-82)	<0.01
Race							
White	557	81	1729	72	166,231	75	<0.01
Black	88	13	463	19	30,106	14	<0.01
Admission source							
Nonhealthcare facility	505	73	1,672	70	167,182	75	<0.01
Transfer –any facility	170	25	633	26	49,584	22	<0.01
Hospital type							
Urban (vs. rural)	663	96	2,252	94	194,452	88	<0.01
Teaching (vs. non)	447	65	1,456	61	109,578	49	<0.01
CCI score median (IQR)	4	(2-5)	3	(2-5)	2	(1-4)	
Diabetes	374	46	1,331	56	102,257	46	<0.01
Congestive heart failure	249	36	870	36	59,857	27	<0.01
Renal insufficiency	281	41	1,077	45	68,511	31	<0.01
COPD	220	32	797	33	61,934	28	<0.01
Infection Type							
BSI	59	9	162	7	15,537	7	0.26
Respiratory	118	17	455	19	14,903	7	<0.01
UTI	343	50	1293	54	160,338	72	<0.01
Other	172	25	487	20	31,590	14	<0.01

\* P-values should be regarded with caution due to large sample size

Table 2 Outcomes

Variable	Erta-R (N=692)		CR-1/2 (N= 2,397)		CS (N=222,368)		P-value
	N	%	N	%	N	%	
Discharge status							
Death	61	9	237	10	8,986	4	<0.01
Home	254	37	725	30	121,313	55	<0.01
Other	377	54	1435	60	92,069	41	<0.01
LOS, median (IQR)	10	(6-22)	10	(6-19)	6	(4-11)	<0.01
Post-inf. LOS, median (IQR)	8	(5-14)	8	(5-13)	6	(4-9)	<0.01
Post-inf. charges, median (IQR)	48,814	23,579 – 105,025	53,695	26,619 – 111,779	30,887	17,178- 59,915	<0.01
Readmissions within 30 d	46	7	181	8	7,206	3	<0.01

Fig 1. ERTA-R (CR to class 1 only), total from 2015 -2019 and by year

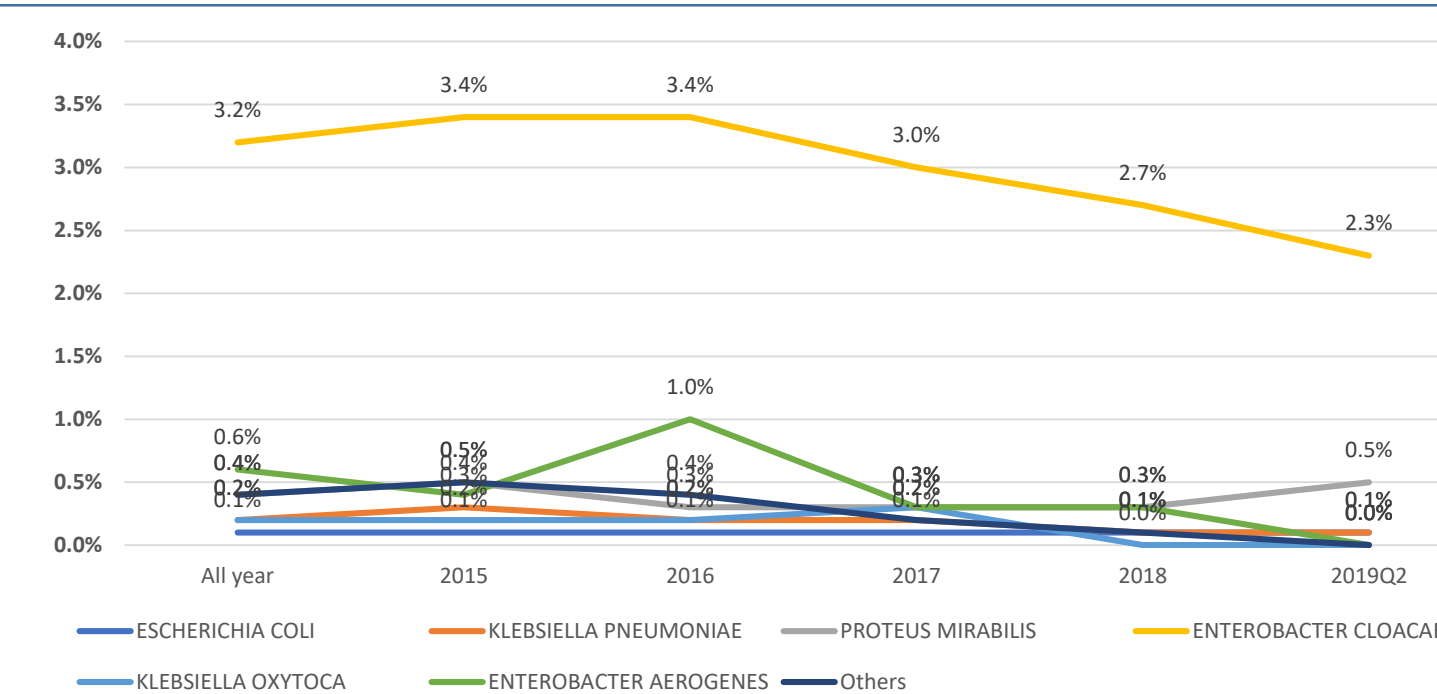


Fig 2. CR-1/2 (CR to both classes), total from 2015 -2019 and by year

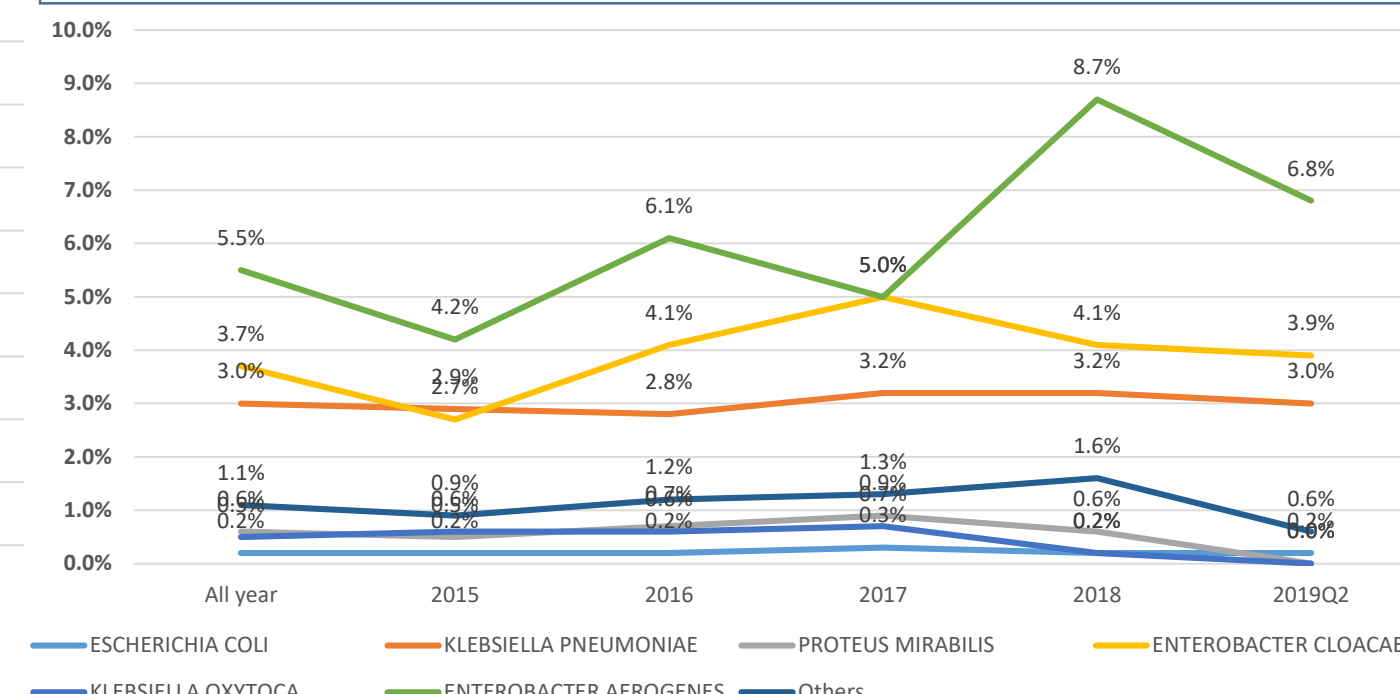


Fig 4. ERTA-R (class 1 only), proportions of top pathogens

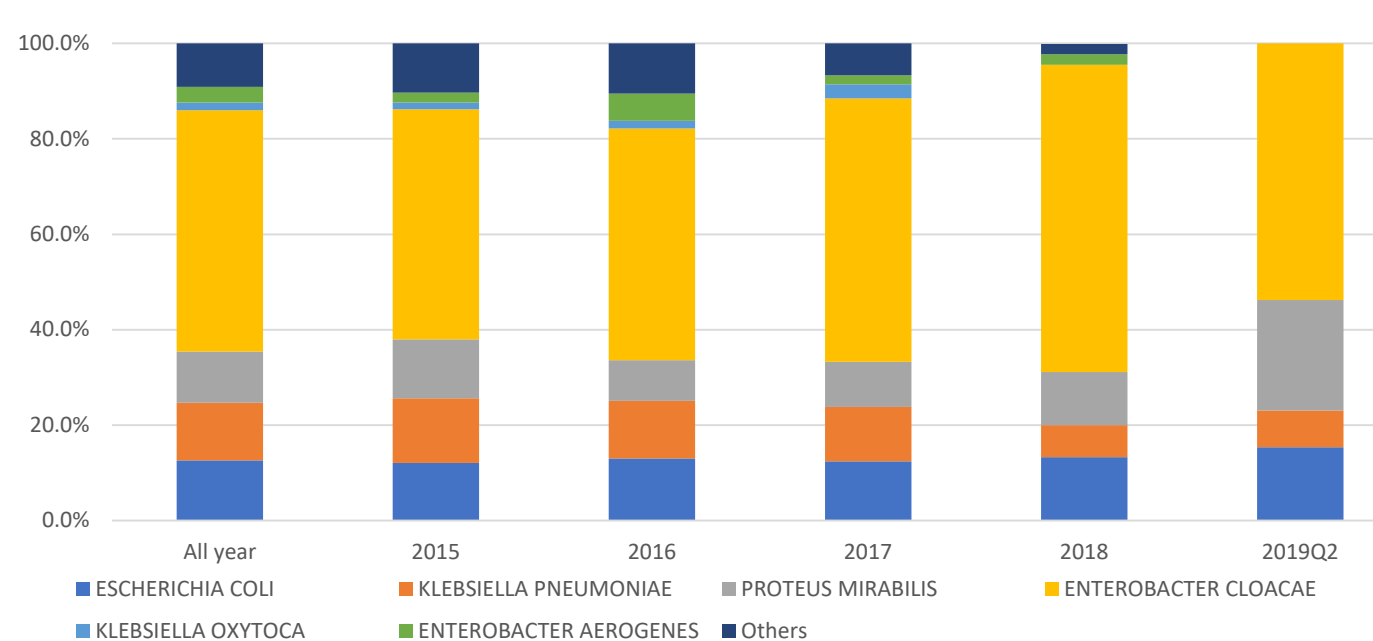
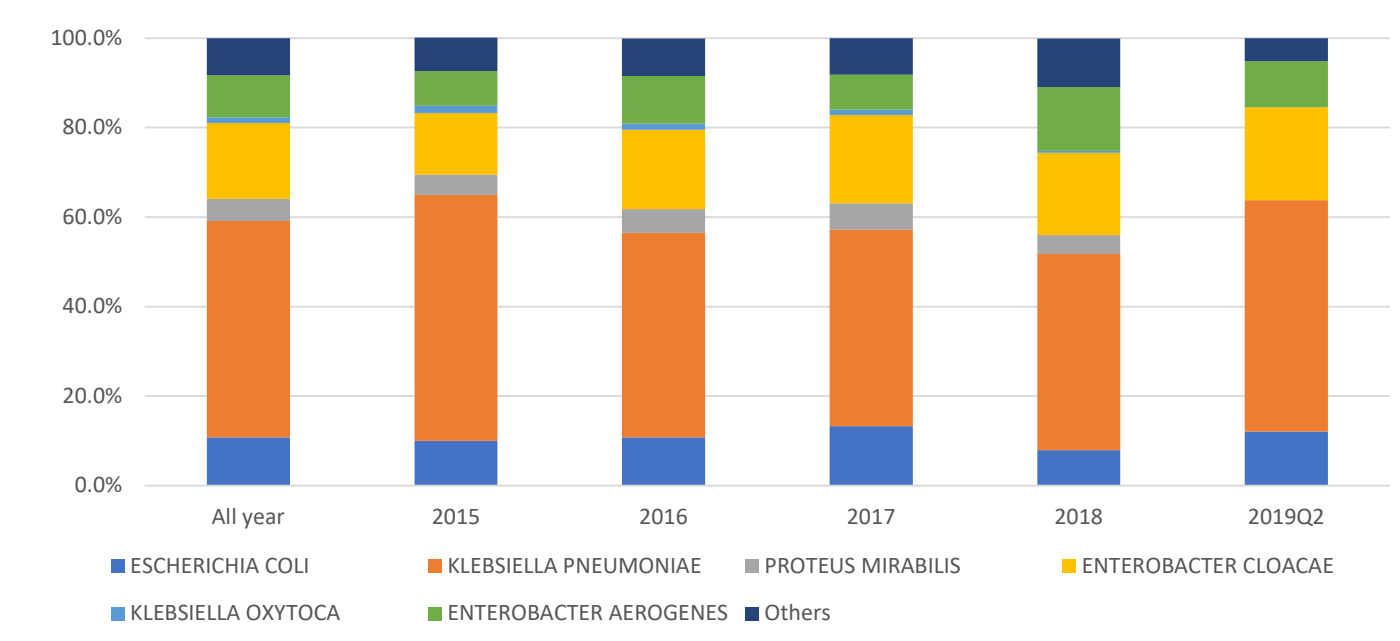


Fig 3. CR-1/2 (both classes), proportions of top pathogens



- The overall rate of CR among the Enterobacterales tested from 2015 to 2019 has been stable changing from 0.9% to 0.8%.

## CONCLUSIONS

- The overall CR rate in the US for Enterobacterales has been relatively stable from 2015-2019 in both CR categories.
- There is an increased frequency of Black race and diabetes in the CR-1/2 class compared to both Erta-R and CS; White race was more common in the Erta-R group. Urban and teaching hospitals were more common in both Erta-R and CR-1/2 and had greater median CCI.
- Respiratory infections accounted for almost three times as much of total infections in both CR groups compared to CS. In contrast, UTI's accounted for 50% more infections in the CS group than either CR group.
- Mortality was more than twice as great in both CR groups compared to CS and median post-infection LOS was 2 days longer for both as well. Median post-infection associated charges were similarly greater in CR groups by more than 50%. Readmissions were more than twice as likely. The only substantial difference in outcomes between the CR-1/2 and Erta-R groups was a slightly greater median for post-infection charges but the variation in charges was large as reflected in the IQR.

- Trends of CR by pathogen demonstrate a decrease in Erta-R among Enterobacter cloacae especially from 2016-19 while an increase in CR-1/2 is seen among Enterobacter aerogenes from 2017 thru 2019.
- Proportions of the top six CRE pathogens have changed slightly but in general, Enterobacter cloacae and Klebsiella pneumoniae make up the largest proportions of Erta-R and CR-1/2, respectively for all years.

## REFERENCES

1. More People in the United States Dying from Antibiotic-Resistant Infections than Previously Estimate; <https://www.cdc.gov/media/releases/2019/p1113-antibiotic-resistant.html>
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3. Papp-Wallace KM, Endimiani A, Taracila MA, Bonomo RA. Carbapenems: past, present, and future. Antimicrob Agents Chemother. 2011;55(11):4943-4960. doi:10.1128/AAC.00296-11

