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# Efficacy of Antibiotic Treatments for Klebsiella and ESBL pneumonia

## Introduction

- There is a dearth of knowledge and studies about empiric antibiotic treatment for Extended Spectrum-β-Lactamase (ESBL) bacterial pneumonia.<sup>1</sup>
- This study is meant to improve quality of evidence to “medium” levels from the current level of “very-low” quality.<sup>1</sup>
- Improved methods for treating Klebsiella Pneumoniae infection.
- Primary outcome:** Mortality
- Aim:** To assess differences in patient survival probability due to different antibiotic regimens, considering all classes of antibiotics.

## Methods

- Population:** People hospitalized with Klebsiella Pneumoniae or ESBL-type antibiotic resistant gram-negative bacterial pneumonia.
- Data source:** Electronic medical record data from the HealthFacts database (de-identified data from 700 Cerner hospitals).
- Statistical Analysis:**
  - Forward/backward model selection were used to find statistically significant factors.
  - Cox Proportional Hazard Models were used to determine the Hazard Ratios of Klebsiella and ESBL Pneumonia and their survival probability.
  - We adjusted for the effects of antibiotic resistance(s), antibiotic allergies, age, organ failure, severity of illness, mechanical ventilation, sepsis, and previous aminoglycoside use.

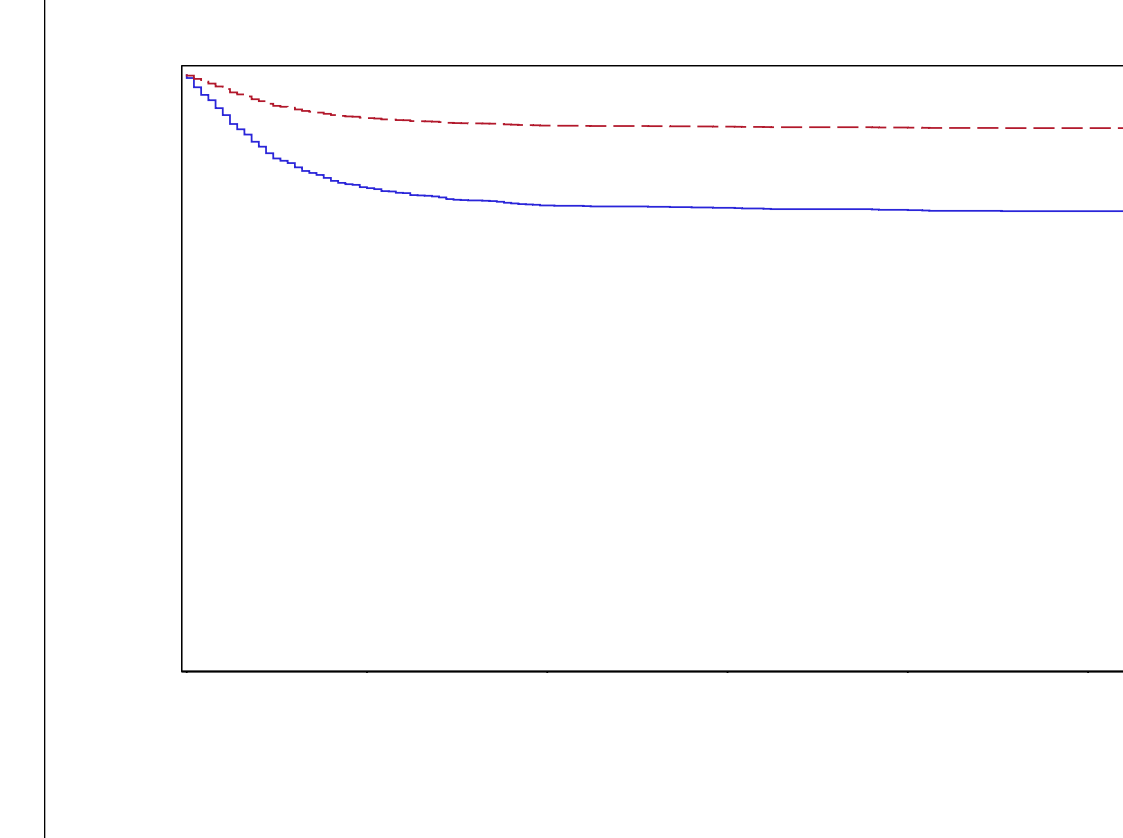
## Results

**Table 1: Effect of classes of antibiotics on patient survival from ESBL Pneumonia**

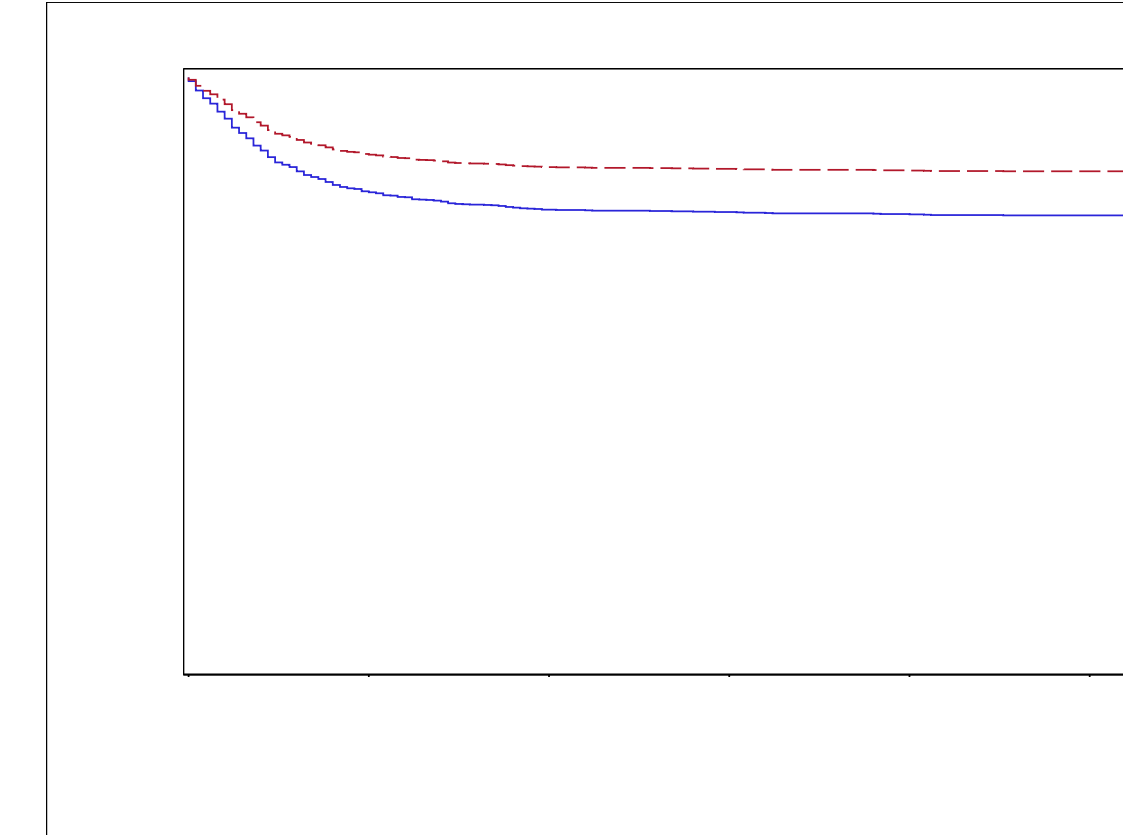
Associated with Increased Survival	No Association with Survival
Nitrofurans Polypeptides Tetracyclines*	Aminoglycosides Aminopenicillins Ansamycins Carbapenems Cephalosporins-1 <sup>st</sup> Cephalosporins-2 <sup>nd</sup> Cephalosporins-3 <sup>rd</sup> Cephalosporins-4 <sup>th</sup> Lincosamides Macrolides Miscellaneous antibiotics Monobactams Natural penicillins Quinolones Oxazolidinones
Associated with Decreased Survival	Insufficient data
Glycopeptides Rifamycin derivatives*	Antipseudomonal penicillins Beta lactamase inhibitors Carbacephem Cephalosporins-5 <sup>th</sup> Fosfomicin Ketolide Leprostatics Lipopeptides Nicotinic acid derivative Penicillin combo Streptomyces derivatives Anti-mycobacterials

(\*on the boundary of significance)

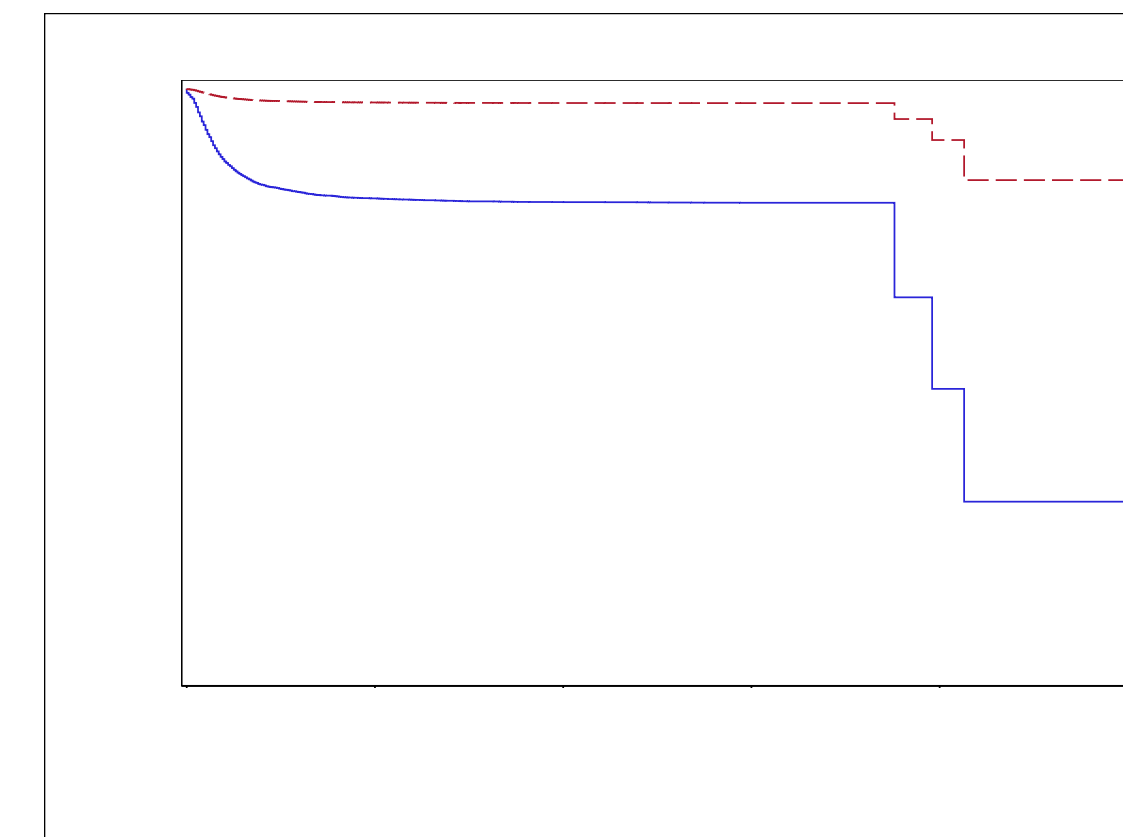
**Figure 1: Nitrofurans are associated with a large significant reduction in mortality from ESBL pneumonia**



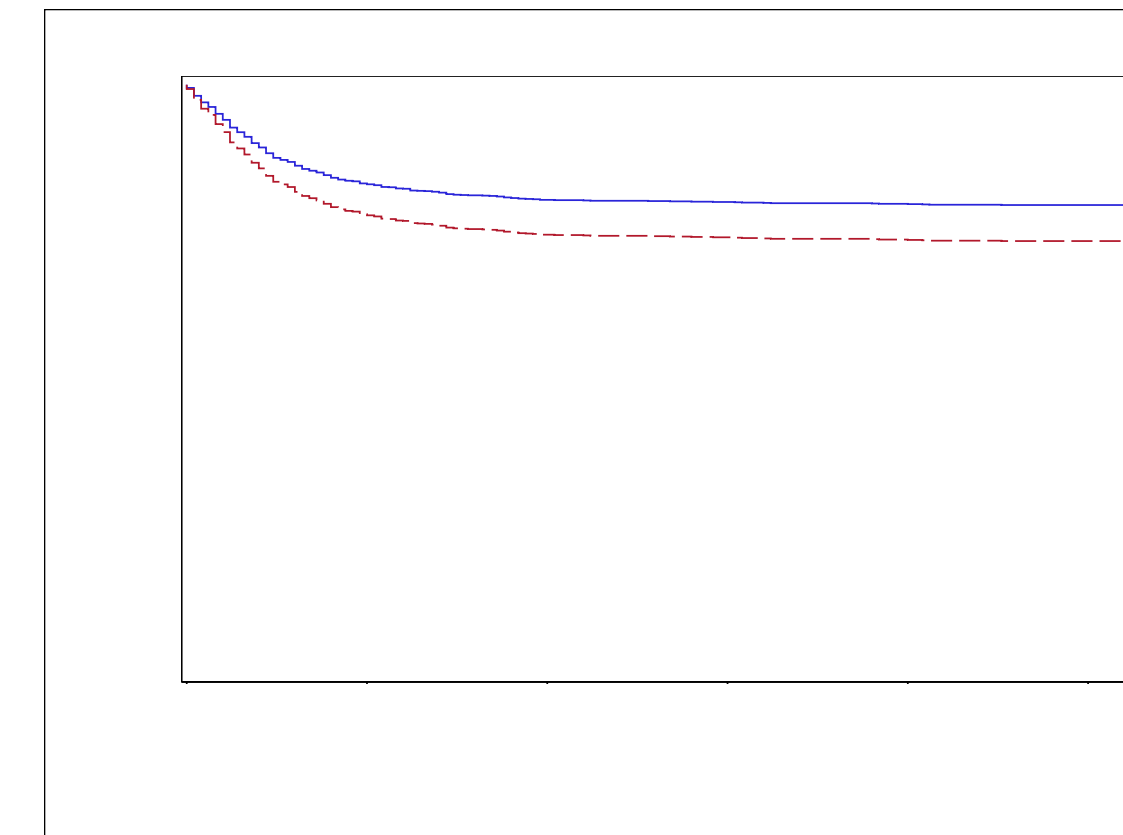
**Figure 2: Polypeptide antibiotics (e.g. Polymyxins/Colistin) are associated with a smaller reduction in mortality from ESBL Pneumonia infections**



**Figure 3: Prior aminoglycoside use has a strong protective effect on patient mortality from K. Pneumoniae infection**



**Figure 4: Glycopeptide antibiotics are associated with a significant increase in patient mortality from ESBL pneumonia**



**Table 2: Effect of classes of antibiotics on patient survival from K. Pneumoniae infection**

Associated with Increased Survival	No Association with Survival
Carbapenems Polypeptides	Aminopenicillins Ansamycins Antipseudomonal penicillins Cephalosporins-1 <sup>st</sup> Cephalosporins-2 <sup>nd</sup> Cephalosporins-3 <sup>rd</sup> Cephalosporins-4 <sup>th</sup> Lincosamides Lipopeptides Macrolides Miscellaneous antibiotics Monobactams Nitrofurans Nicotinic acid derivative Quinolones Oxazolidinones Rifamycin derivatives Streptomyces derivatives Tetracyclines
Associated with Decreased Survival	Insufficient data
Anti-mycobacterials Glycopeptides Aminoglycosides	Beta lactamase inhibitors Carbacephem Cephalosporins-5 <sup>th</sup> Ketolide Leprostatics Natural penicillins Penicillin combo Streptomyces derivatives

**Table 3: ESBL among Pneumonia cases by Census Division (Overall and for Klebsiella Pneumoniae)**

Census Division	Pneumonia	ESBL	%ESBL	Census Division	K. Pneumoniae	ESBL	Carb_res	%ESBL	%Carb_res
1	82668	54	0.07	1	573				
2	245721	102	0.04	2	1311				
3	80747	21	0.03	3	443				
4	151255	230	0.15	4	1334	2		0.15	
5	96526	332	0.34	5	400	37	1	9.25	0.25
6	251687	217	0.09	6	2535	13	2	0.51	0.08
7	98559	127	0.13	7	558				
8	44061	4	0.01	8	237				
9	162913	905	0.56	9	1242	29	4	2.33	0.32

## Discussion

- For Klebsiella Pneumoniae infections prior treatment with aminoglycosides improves patient survival by ≈14% suggesting that aminoglycosides are a potential empiric therapy for Klebsiella Pneumoniae.
- For ESBL resistance, nitrofurans such as nitrofurantoin are associated with ≈12% increase in survival. There was insufficient data to evaluate Fosfomicin and beta-lactamase inhibitor + antibiotic combinations.
- Our analysis has yielded evidence of moderate quality for inclusion into treatment guidelines.

## Acknowledgements

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