

Clinical outcomes of patients in the intensive care unit with infections caused by multiresistant gram-negative bacteria in colombian patients

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BACKGROUND

- Over the last decade, a steady increase in the percentage of gram-negative bacteria has been reported worldwide^{1,2}. These bacteria are resistant to all families of antibiotics, specifically to carbapenems¹.
- In Colombia, official reports suggest that within isolated *K. pneumoniae* at intensive care unit (ICU), between 9,3% and 14,6% have shown resistance to carbapenems and in hospitalized cases it has been around 8,8% - 12,7%².
- Gram-negative bacterial resistance is a relevant problem for the ICU. It has been associated to increase the mortality, prolonged hospital length of stay (LOS) and increased the cost of attention⁴.

OBJECTIVE

- To describe the clinical outcomes in patients in the intensive care unit (ICU) with infections caused by multiresistant Gram-negative bacteria.

METHODS

- This study is an observational, retrospective study in Colombian ICU patients from two hospitals between 2018 to 2021.
- All patients were above 18 years of age, admitted in the ICU, had antibiotic treatment for more than 48 hours, had microbiological isolation culture by multiresistant gram negatives, and with hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), intra-abdominal infection (IAI), urinary tract infection (UTI) including pyelonephritis and bacteremia diagnosis, were included in the study.
- The index date was the date of diagnosis with an infection reported in the medical records. Patients were followed up until 30 days in the hospital, discharge, or death.
- Clinical outcomes included were in-hospital mortality, length-of-stay (LoS) in ICU and mechanical ventilation (MV).
- The demographic and clinical characteristics, which included the date and site of infection, data on the isolated pathogens and their susceptibility testing to antimicrobial agents, were collected.
- The statistical analyses were performed using R software (version 4.2.1; R Foundation for Statistical Computing). Descriptive and stratified analyses were performed to examine important demographic and clinical characteristics of patients.
- Multivariable regression analysis was performed to evaluate the relationships between demographic, clinical and treatment characteristics.

RESULTS

- One hundred sixty-two patients were included in the study but only 152 patients had information about treatments used. Included patients tended to be older adults, the mean age was 59.1 (Standard deviation (SD) 16.1) and they were mainly men (59.9%).
- The main first diagnoses in ICU were community-acquired pneumonia (n=18 patients), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (n=21), HAP (n=14), IAI (n=13), primary bacteremia (n=15).
- The mean APACHE II score at the admission in ICU was 40.8 (SD 23.86). The main etiological causes of infection were *K. pneumoniae* (45.0%), *E. coli* (13.6%), *P. aeruginosa* (12.3%), and *Enterobacter* spp. (9.8%).
- Carbapenemases were reported in 83.3% of cases while extended spectrum beta lactamase (ESBL)/AmpC resistance was 7.40% and inhibitor resistant beta-lactamases was 6.2%.
- The frequency of death in patients with multiresistant gram negative in ICU was 40.7%. The median time to death was 37 (Confidence interval 95% 31 – NA) days. (Figure 1). The frequency of death was similar for all the types of resistance (Table 1). The clinical and demographic variables associated to death were Sofa score, previous hospitalization in ICU, use of central venous catheter, and infectious by *Klebsiella* spp and use of combine treatment (Figure 2).
- The mean time in ICU was 27.6±33.5 days. In patients with carbapenemases was higher compared to other resistance. The variables associated to increase the number days of ICU was score Pitt while chemotherapy reduces the time of ICU (Figure 3).
- MV was required in 132 patients and the mean time in MV was 23.8±32.6 days. Age, Apache score, and previous surgery were associated to increase the MV days. (Figure 4)
- The use of empiric treatment increased the mortality risk and decreased the LoS of UCI, but it was not statistically significant on either.

Table 1. Clinical Outcomes of multiresistant gram negative patients in ICU

Type of resistance	Death (%)	ICU days mean (SD)	Mechanical ventilation Days mean (SD)	Hospital days mean (SD)
Carbapenemases	56 (41.0)	30.4 (35.3)	26.0 (34.2)	75.3 (315)
ESBL/AmpC	6 (40.0)	12.1 (9.5)	8.8 (12.1)	26.7 (14.3)
Resistance inhibitors	4 (40.0)	12.7 (18.1)	11.6 (14.1)	15.2 (16.7)
<i>Klebsiella pneumoniae</i>	35 (47.9)	27.5 (38.2)	21.1 (35.6)	94.2 (429.5)
<i>Acinetobacter baumanni</i>	1 (25.0)	57.5 (33.8)	49 (25.2)	81 (120.5)

* The upper CI for this specie was 989.2, and the coefficient value was 71.4

RESULTS (cont)

Type of resistance	Death (%)	ICU days mean (SD)	Mechanical ventilation Days mean (SD)	Hospital days mean (SD)
<i>Aeromonas Sobria</i>	0 (0.0)	3 (NA)	NA	13 (NA)
<i>Burkholderia cepacia</i>	0 (0.0)	18 (12.7)	24 (NA)	31 (5.7)
<i>Chryseobacterium indologenes</i>	0 (0.0)	70.3 (10.1)	63.3 (6.0)	96.0 (12.1)
<i>Citrobacter freundii</i>	0 (0.0)	5 (NA)	NA	36 (NA)
<i>Enterobacter aerogenes</i>	3 (33.3)	27.2 (15.0)	14.4 (16.0)	35.1 (13.0)
<i>Enterobacter cloacae</i>	1 (14.3)	22.4 (28.5)	18.3 (21.7)	45.2 (48.3)
<i>Escherichia Coli</i>	5 (22.7)	10 (12.5)	7.7 (12.3)	21.1 (13.0)
<i>Klebsiella oxytoca</i>	9 (75.0)	37.2 (42.2)	36.5 (45.7)	50.2 (45.4)
<i>Pseudomonas aeruginosa</i>	7 (46.6)	29.9 (23.1)	24.7 (21.9)	55 (32.7)
<i>Serratia Fonticola</i>	0 (0.0)	7 (NA)	NA	29 (NA)
<i>Serratia marcescens</i>	5 (71.4)	44.7 (42.7)	34.7 (37.1)	61.6 (58.3)

Figure 1. Survival analysis in patients with multiresistant gram negative

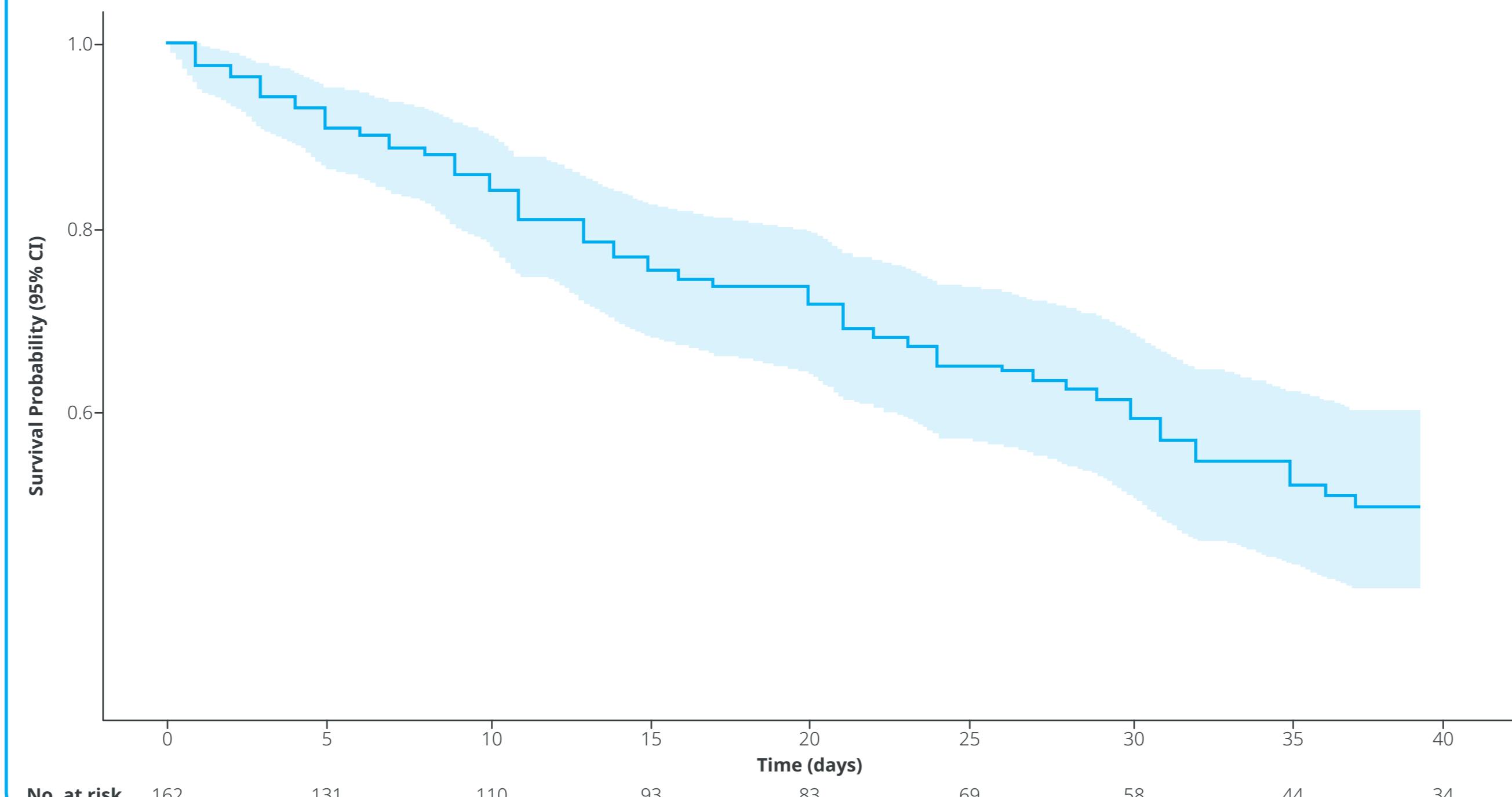


Figure 2. Multivariable analysis of clinical and demographic characteristics associated to death

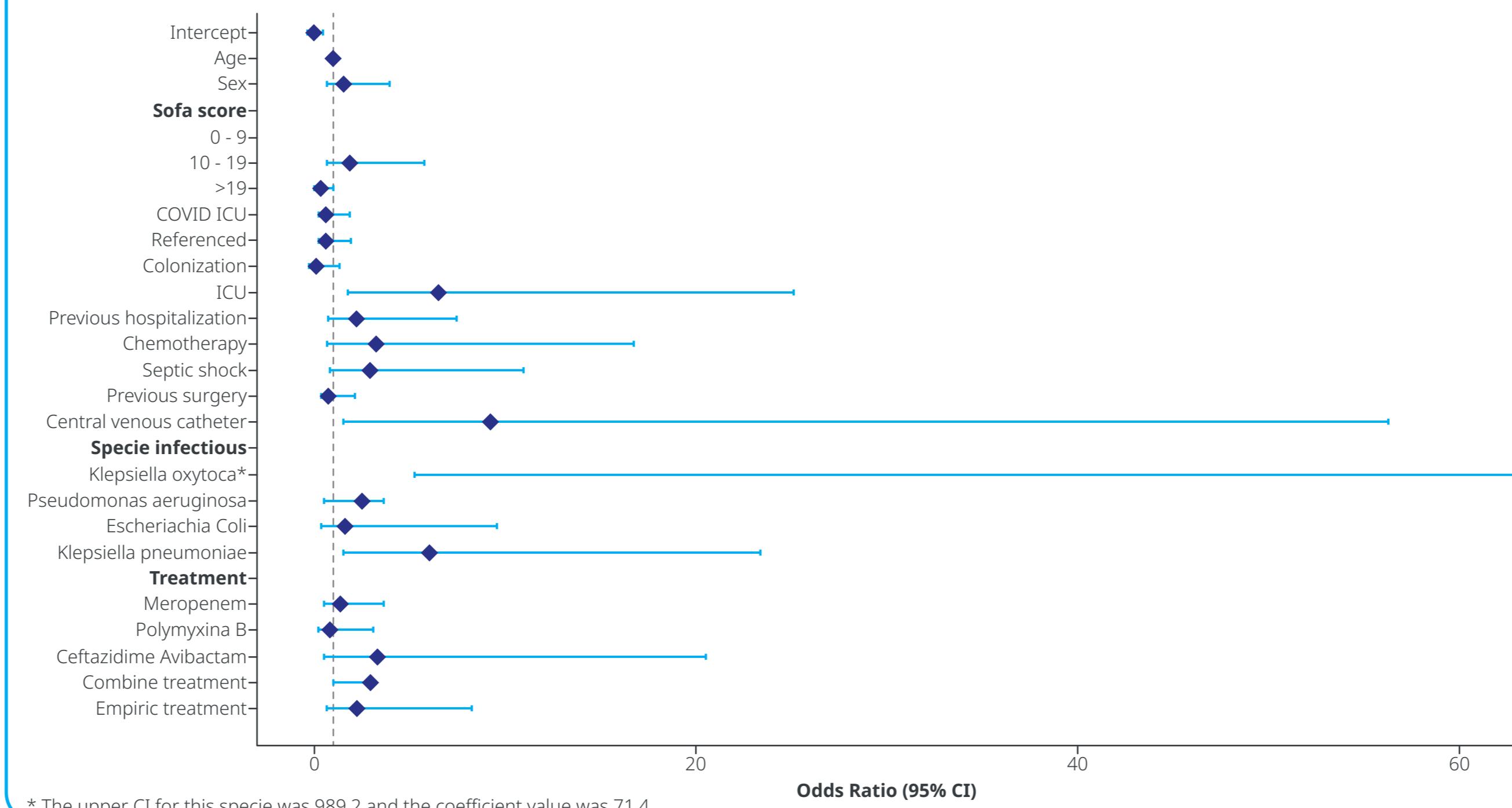


Figure 3. Multivariable analysis of clinical and demographic characteristics associated to Length of stay in Intensive Care Unit

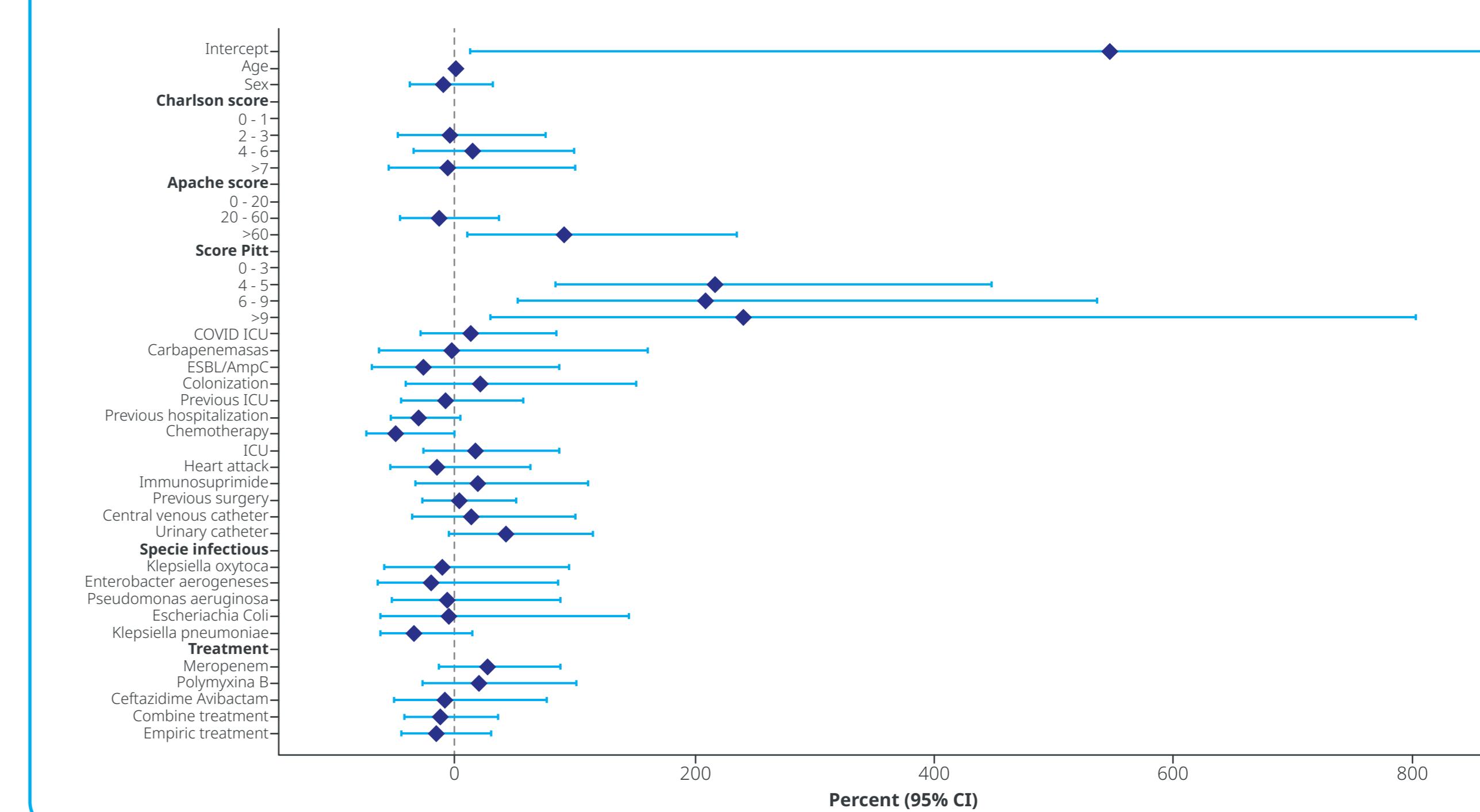
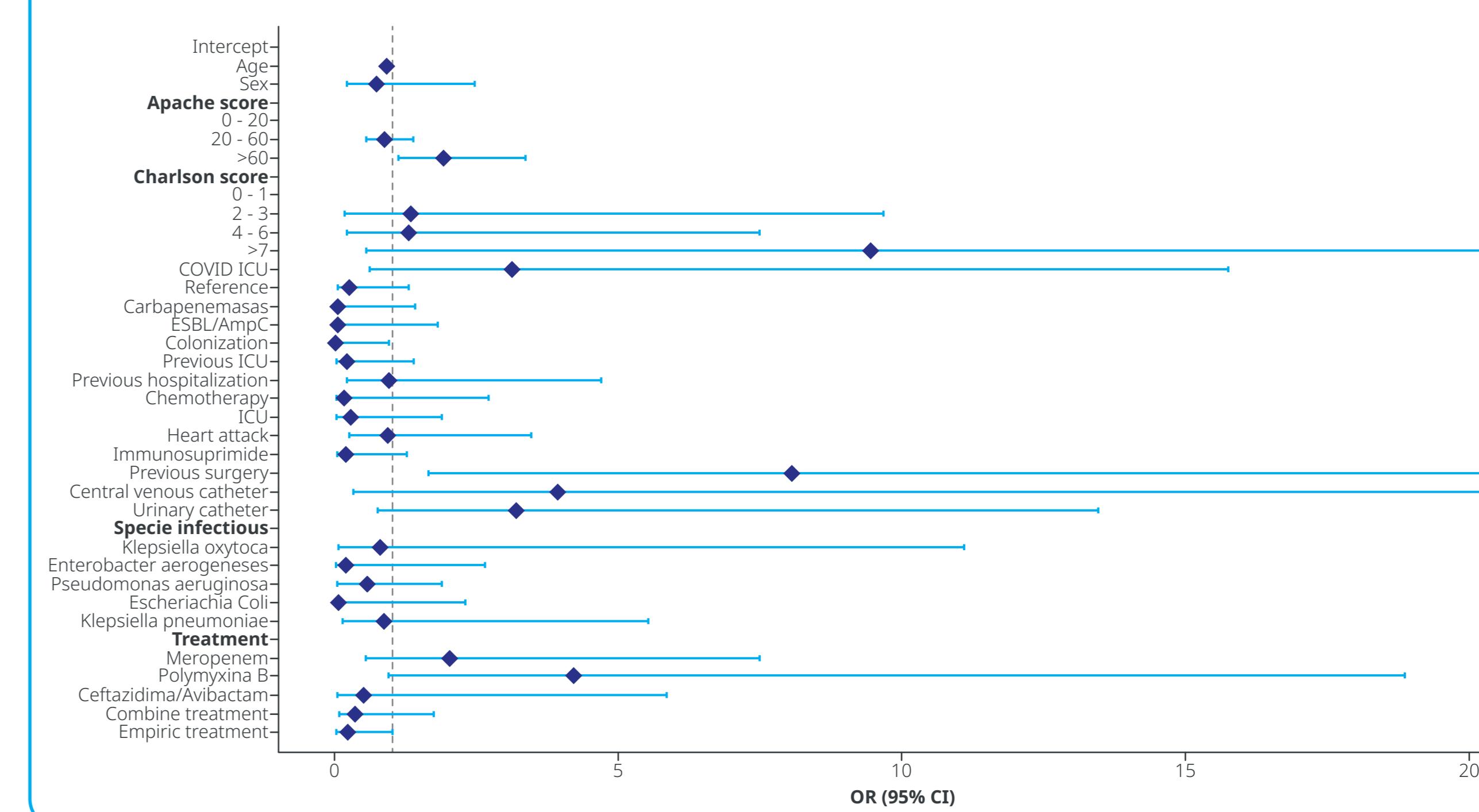


Figure 4. Multivariable analysis of clinical and demographic characteristics associated to ventilation mecanical more than 14 days.



CONCLUSION

- The mortality of ICU patients with infections caused by multiresistant Gram-negative bacteria reported high frequency and long LoS of ICU and VM, however, clinical and treatment characteristics can modify these outcomes.

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