GRUPPO ITALIANO PER LA VALUTAZIONE DEGLI INTERVENTI IN TERAPIA INTENSIVA

UNIVERSITÀ DEGLI STUDI DI BARI ALDO MORO

The burden of Ventilator-associated pneumonia by Pseudomonas Aeruginosa – a five-year retrospective registry-based study in 155 Italian ICUs

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BACKGROUND

Ventilator associated pneumonia

- First cause of heathcare-associated infections
- Associated with prolonged hospitalization and increasing patient morbidity, mortality and costs*

P. aeruginosa

- associated with **MDR** & **XDR**
- Carbapenems-R PA ranked as high priority pathogen in the 2024 WHO list**
- Reason for inappropriate initial antimicrobial therapy ***

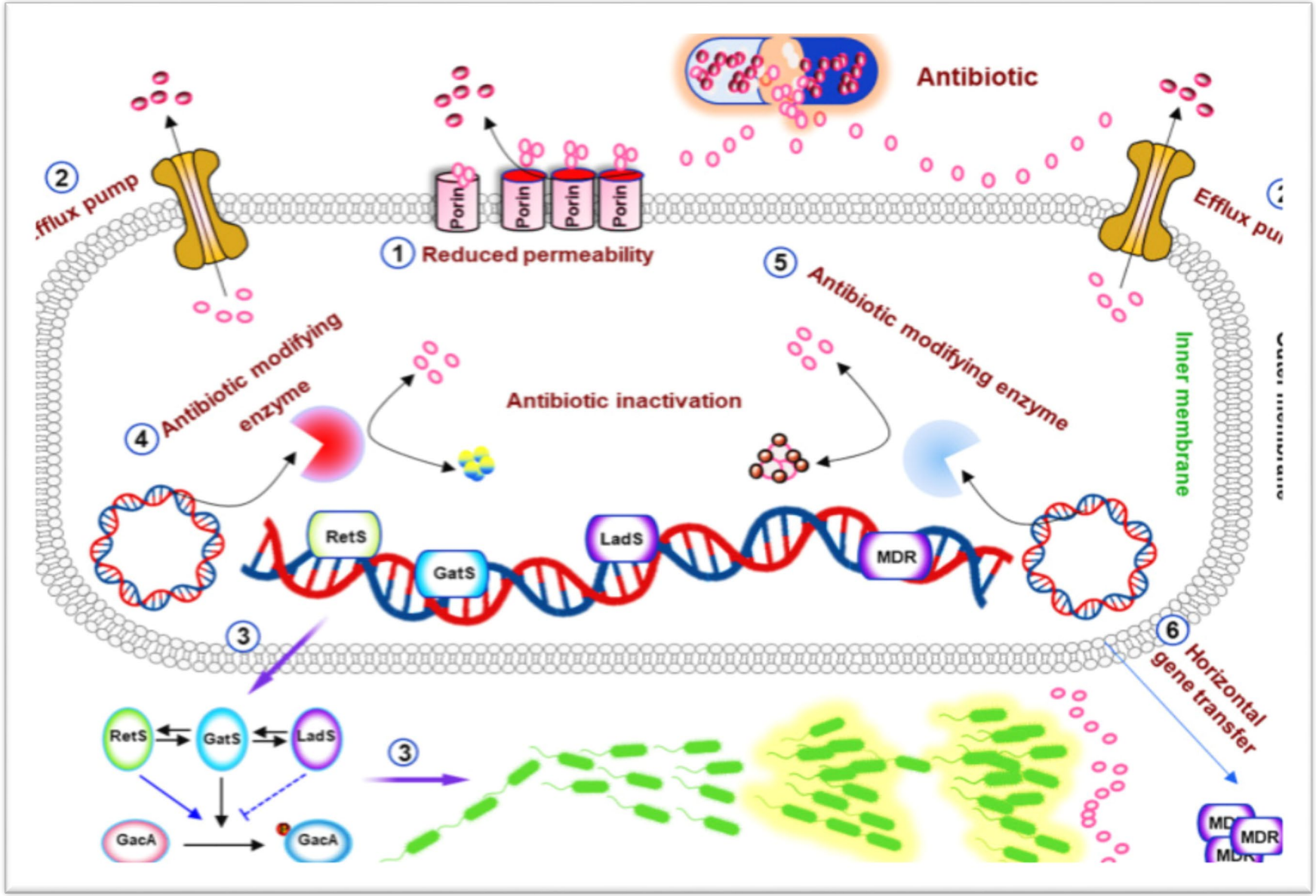
*LW Xing R, Wang C. The effect of ventilator- associated pneumonia on the prognosis of intensive care unit patients within 90 days and 180 days. BMC Infect Dis. 2021;21(1):684.

**https://www.who.int/publications/i/item/9789240093461

***ZM Nathanson BH, Puzniak LA, Dillon RJ, Shorr AF. The risk of inappropriate empiric treatment and its outcomes based on pathogens in non-ventilated (nvHABP), ventilated (vHABP) hospital-acquired and ventilator-associated (VABP) bacterial pneumonia in the US, 2012-2019. BMC Infect Dis. 2022 Oct 5;22(1):775. doi: 10.1186/s12879-022-07755-y. PMID: 36199012; PMCID: PMC9533487.

BACKGROUND

P. aeruginosa virulence



*Signal Transduct Target Ther . 2022 Jun 25; Pseudomonas aeruginosa: pathogenesis, virulence factors, antibiotic resistance, interaction with host, technology advances and emerging therapeutics Shugang Qin et al.

RESEARCH Open Access

Incidence of hospital-acquired infections due to carbapenem-resistant *Enterobacterales* and *Pseudomonas aeruginosa* in critically ill patients in Italy: a multicentre prospective cohort study

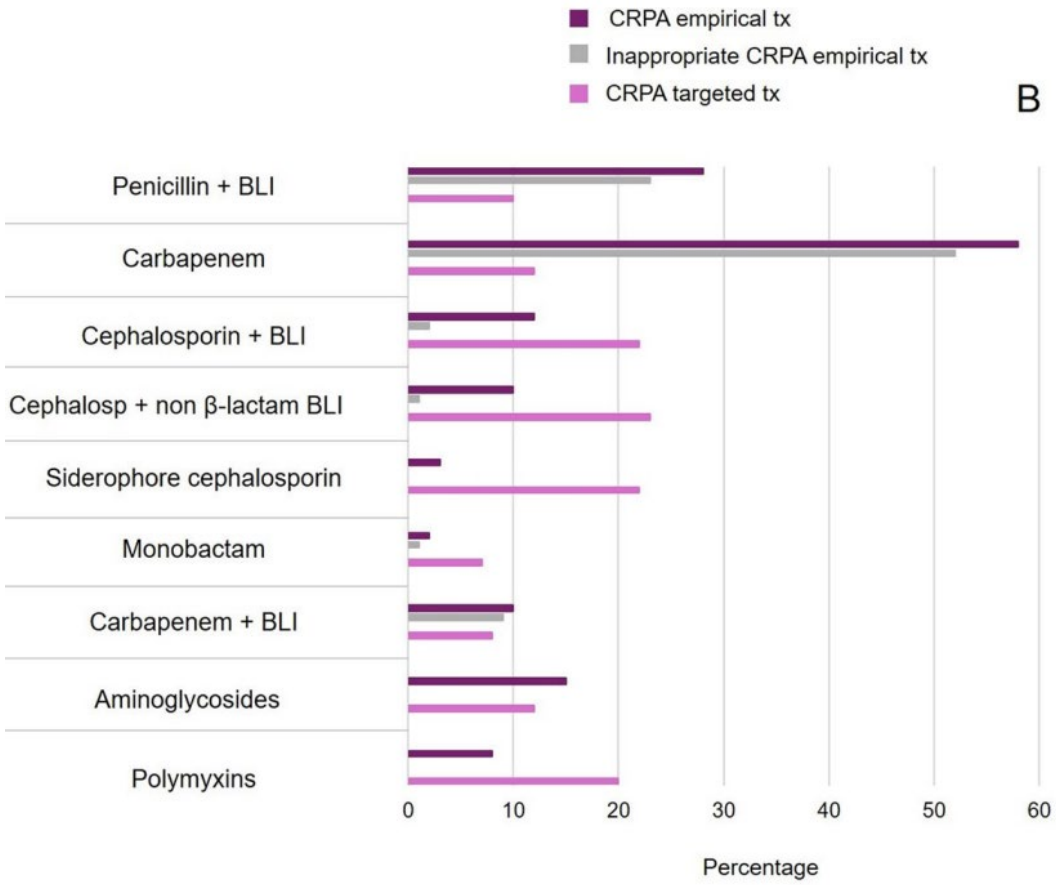
Gennaro De Pascale[1,2†], Andrea Cortegiani[3,4*†], Matteo Rinaldi[5,6], Massimo Antonelli[1,2], Sergio Cattaneo[7], Maurizio Cecconi[8,9], Raffaele Cuffaro[10], Lidia Dalfino[11], Filomena Di Biase[12], Abele Donati[13,14], Francesca Romana Fasano[15], Teresa Fasciana[16], Giuseppe Foti[17,18], Antonella Frattari[19], Roberto Fumagalli[20,21], Massimo Girardis[22], Leonardo Gottin[23], Alessia Mattei[24], Marta Milazzo[3], Giorgia Montrucchio[25,26], Daniela Pasero[27,28], Fabio Picciafuochi[29], Emanuela Sensi[30], Giuseppe Servillo[31], Maria Alejandra Vidal Pereira[15], Teresa Spanu[32†], Pierluigi Viale[5,6†] and on behalf of the INCREASE-IT Study Group

Mortality was significantly higher in patients with CRE (36.7%) compared to those with CRPA (20.0%)

13,088 patients admitted with hospital-acquired infections due to CRE and CRPA treated in 20 ICUs from June 2021 to February 2023. Prospective, multicenter, non-interventional cohort study

158 patients. Full analysis was conducted in 98 CRE and 60 CPRA **The incidence of CRPA infections was 1.74** per 1000 patient days; **CRPA** accounted for **26.8% of P. aeruginosa** infections. **VAP** occurred **in 50% of CRPA**

Higher rates of inappropriate antibiotic treatment were observed for CRE (74%), in particular, 73.1% for KPC-producing CRE and 80% for MBL-CRE, than CRPA (37.7%)



STUDY PURPOSE

PRIMARY ENDPOINT

The **annual proportion of PaVAP** among all Gram negatives VAP for the five years between 2020 and 2024

SECONDARY ENDPOINT

- Relative proportions of CS, CR non-DTR and DTR strains
- Observed in-ICU and in-hospital mortality
- Standardized Mortality Ratio (SMR)
- Length of ICU and hospital stay
- Duration of mechanical ventilation
- Length of stay after a VAP episode in ICU

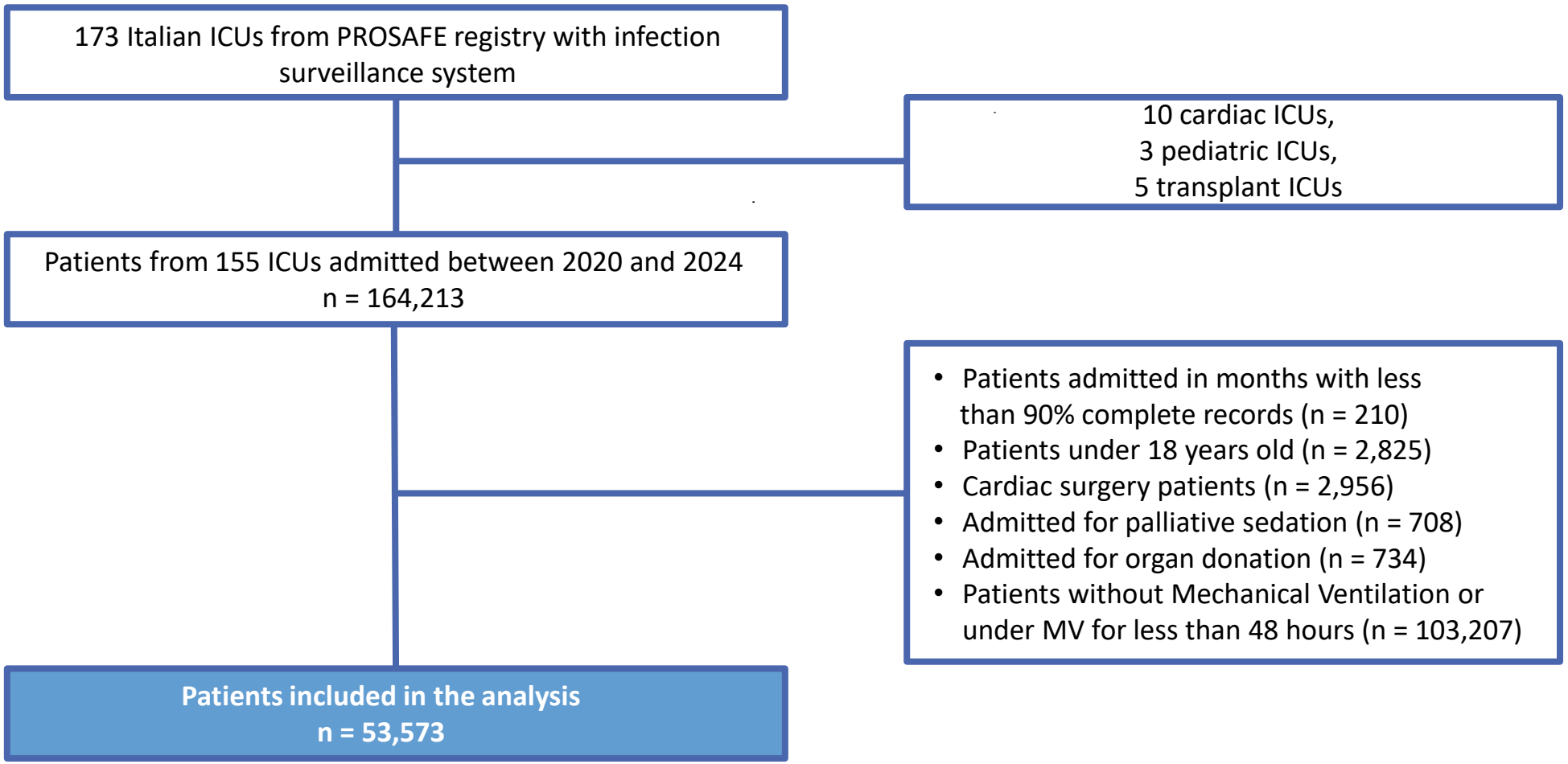
HYPOTHESIS

There is a worsening incidence in P. *aeruginosa* VAP in Italian ICUs

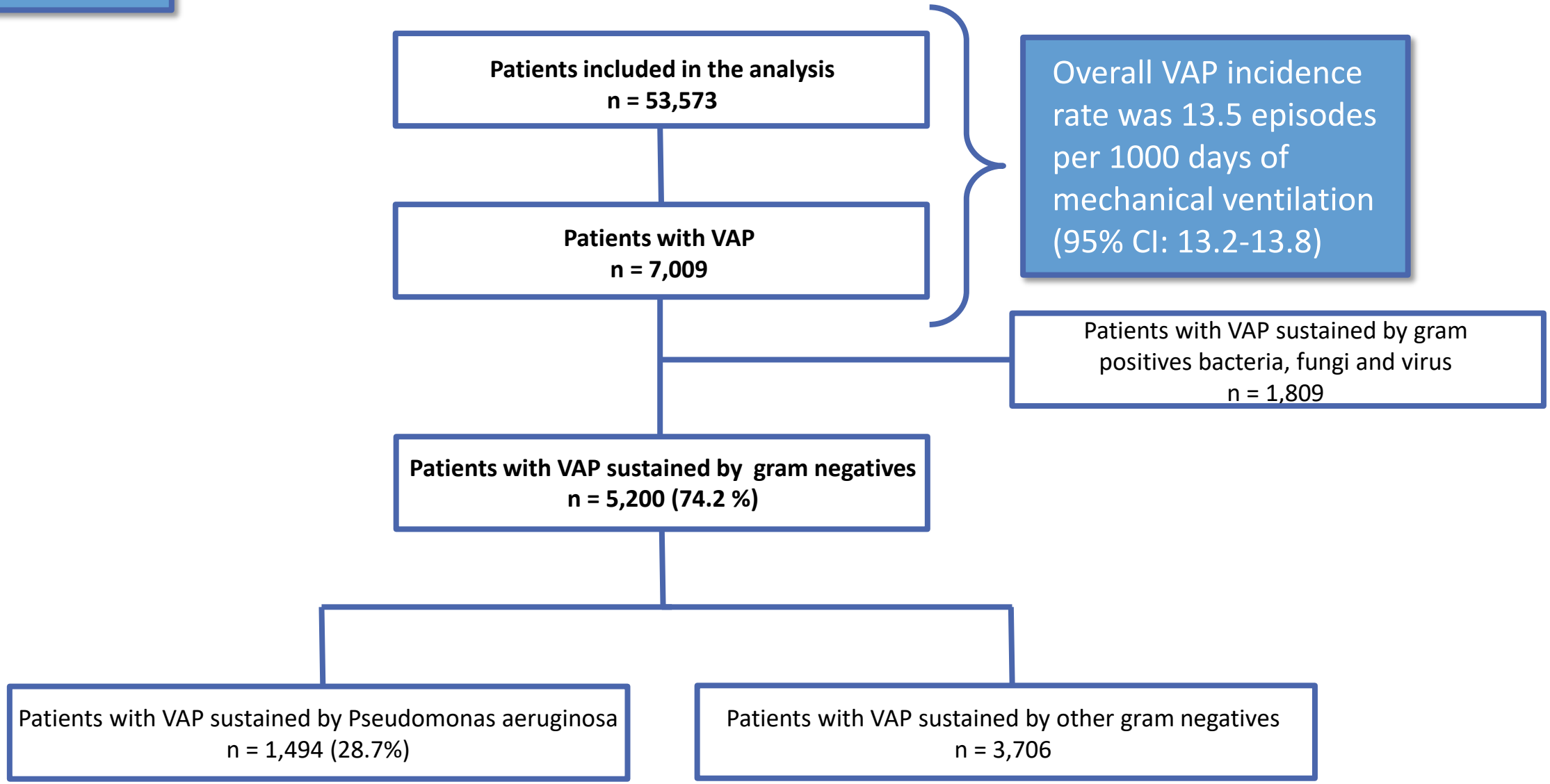
Outcomes of PaVAP patients are worse than those of VAP sustained by other gram negatives pathogens

The PaVAP carbapenem-resistant not-DTR and with difficult to treat resistance (DTR) have significantly worse outcomes as compared to multi-susceptible strains.

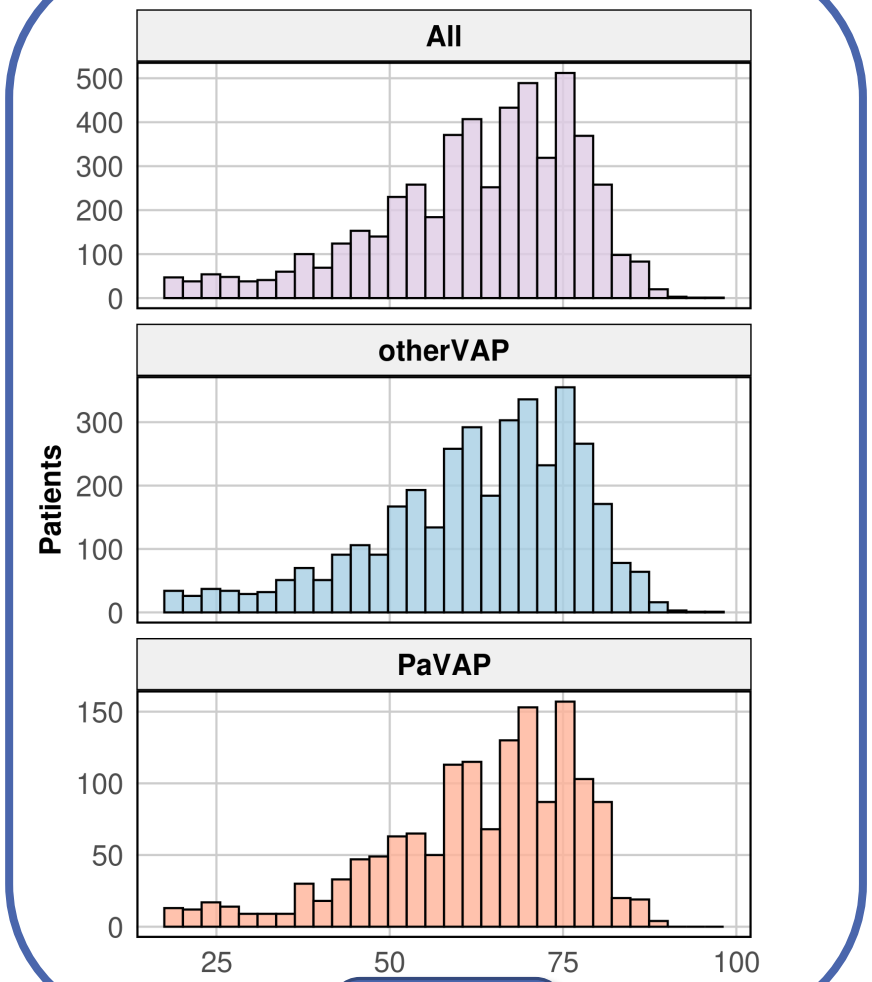
POPULATION


173 Italian ICUs from PROSAFE registry with infection surveillance system
10 cardiac ICUs,
3 pediatric ICUs,
5 transplant ICUs
Patients from 155 ICUs admitted between 2020 and 2024
n = 164,213
• Patients admitted in months with less than 90% complete records (n = 210)
• Patients under 18 years old (n = 2,825)
• Cardiac surgery patients (n = 2,956)
• Admitted for palliative sedation (n = 708)
• Admitted for organ donation (n = 734)
• Patients without Mechanical Ventilation or under MV for less than 48 hours (n = 103,207)
Patients included in the analysis
n = 53,573

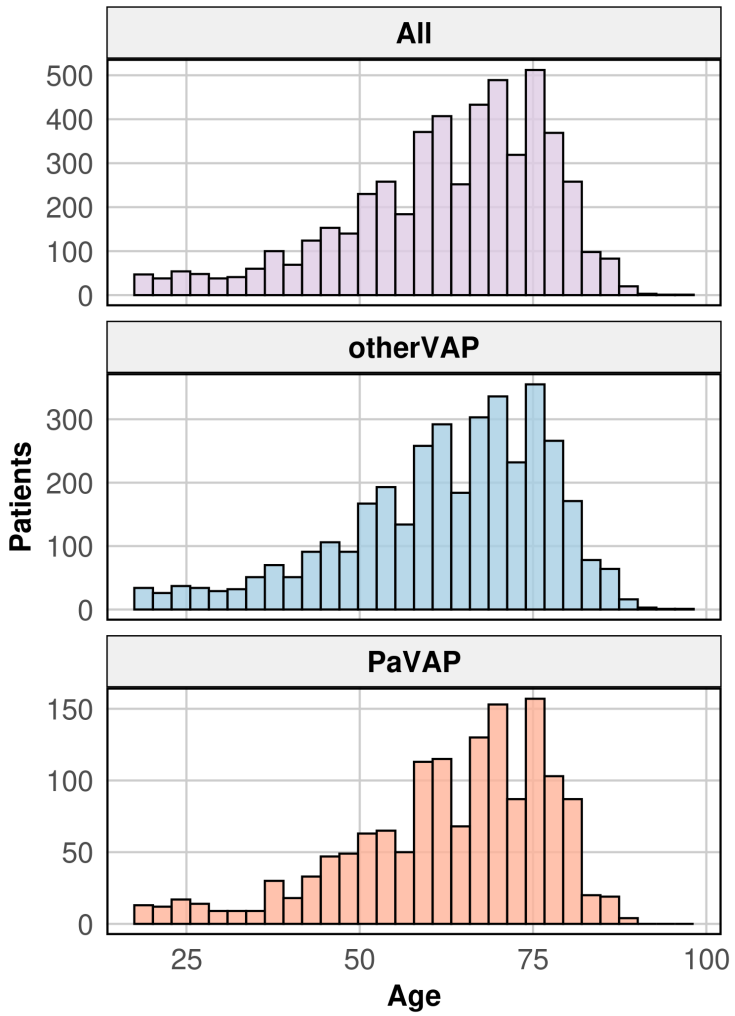
POPULATION


Patients included in the analysis
n = 53,573
Patients with VAP
n = 7,009
Overall VAP incidence rate was 13.5 episodes per 1000 days of mechanical ventilation (95% CI: 13.2-13.8)
Patients with VAP sustained by gram positives bacteria, fungi and virus
n = 1,809
Patients with VAP sustained by gram negatives
n = 5,200 (74.2 %)
Patients with VAP sustained by Pseudomonas aeruginosa
n = 1,494 (28.7%)
Patients with VAP sustained by other gram negatives
n = 3,706

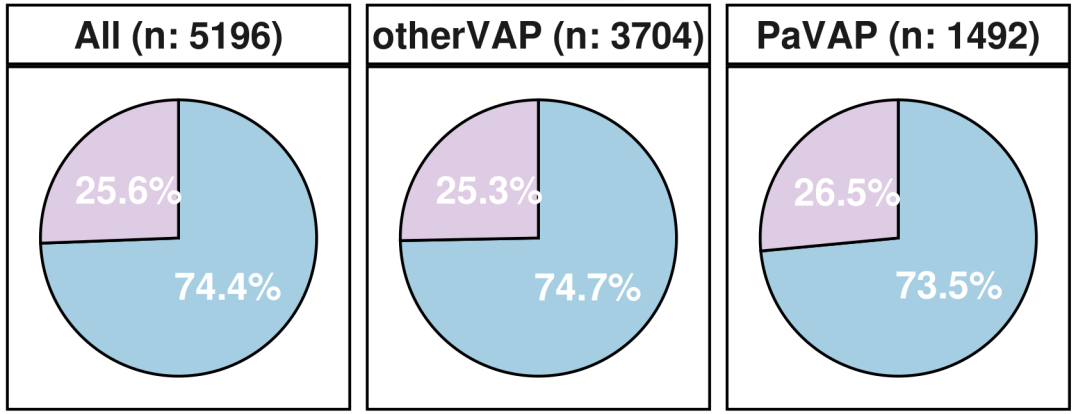
DEMOGRAPHICS AND CLINICAL CHARACTERISTICS



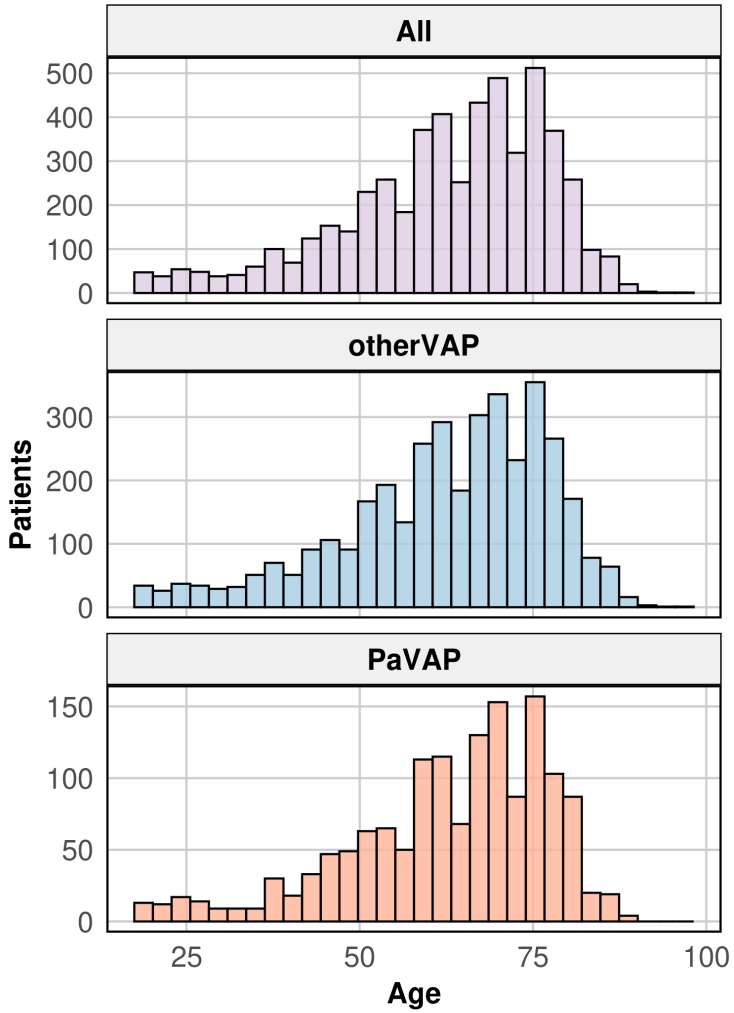
DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

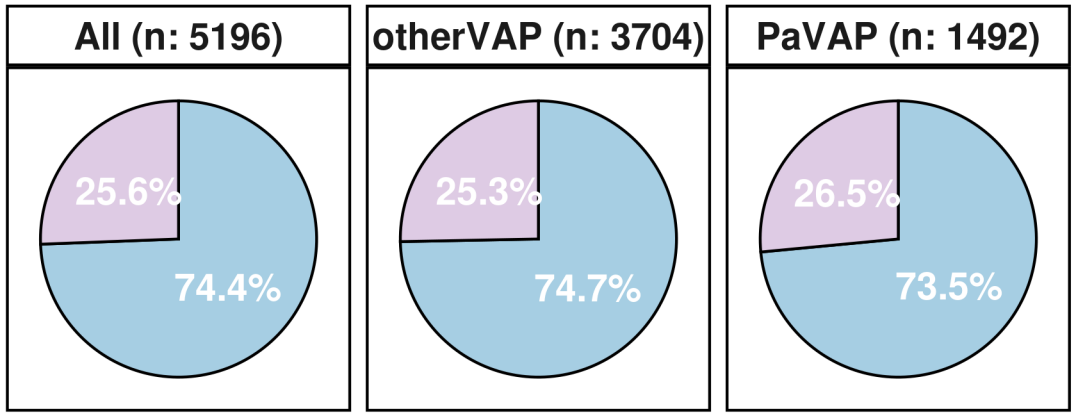


Sex

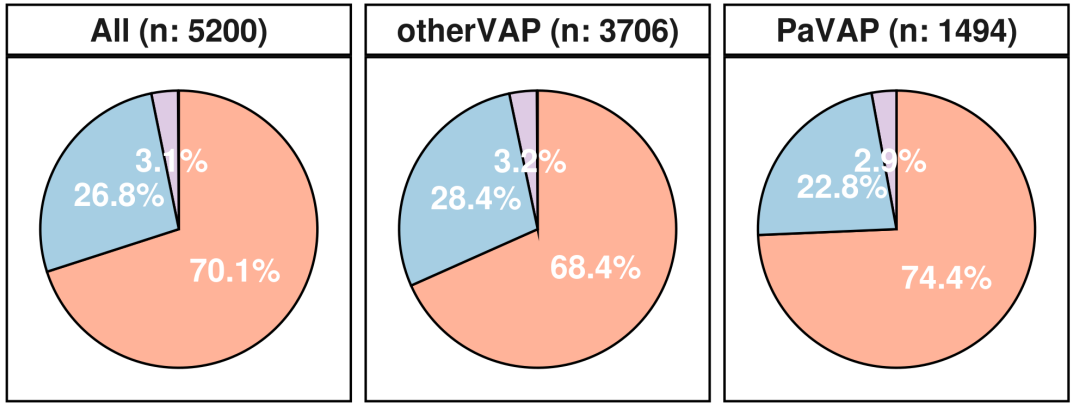


DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

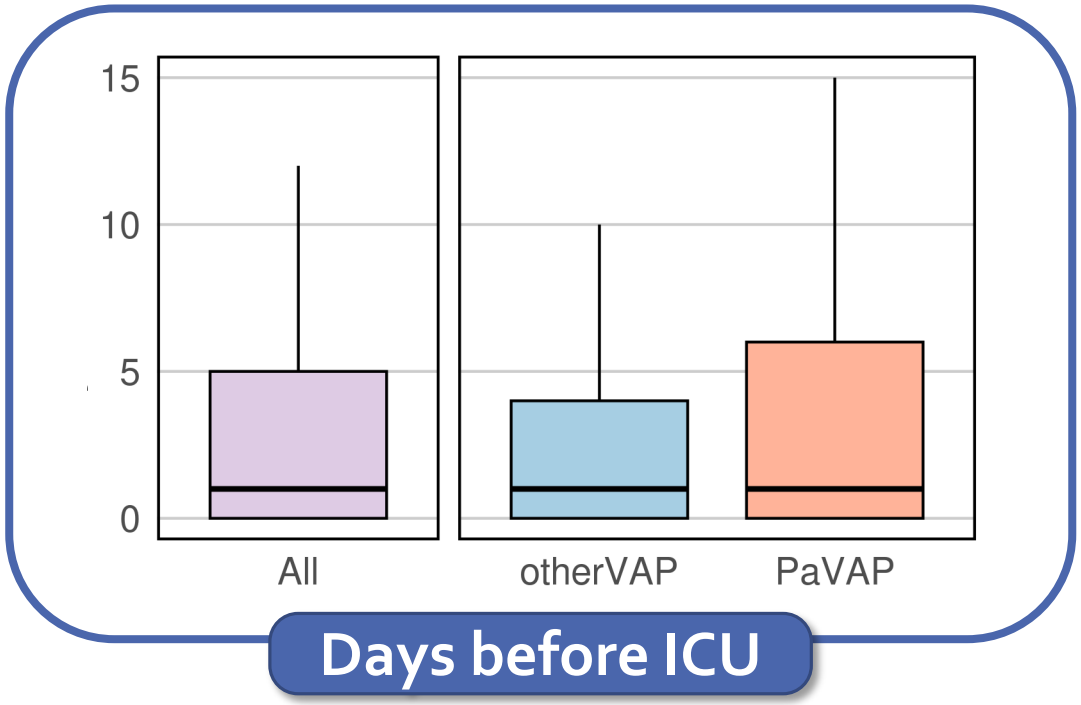




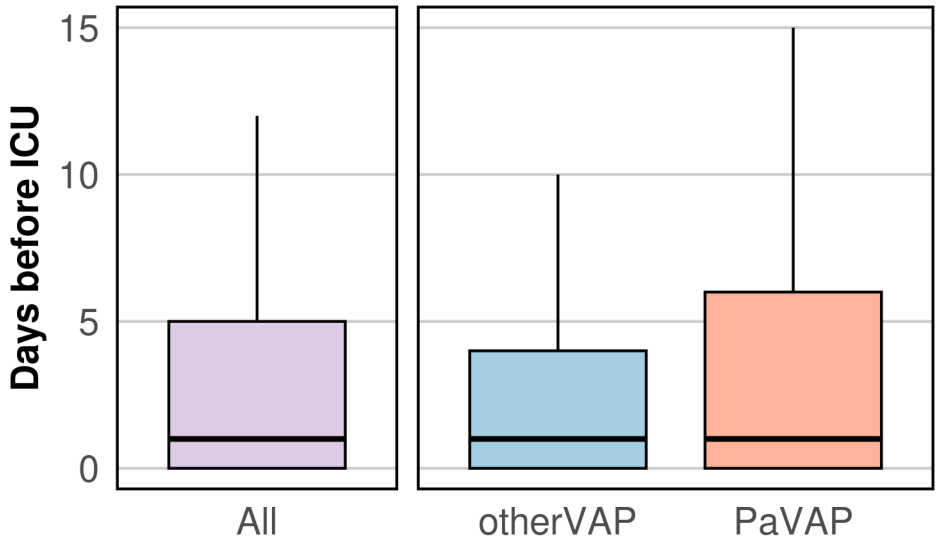
Type of surgery

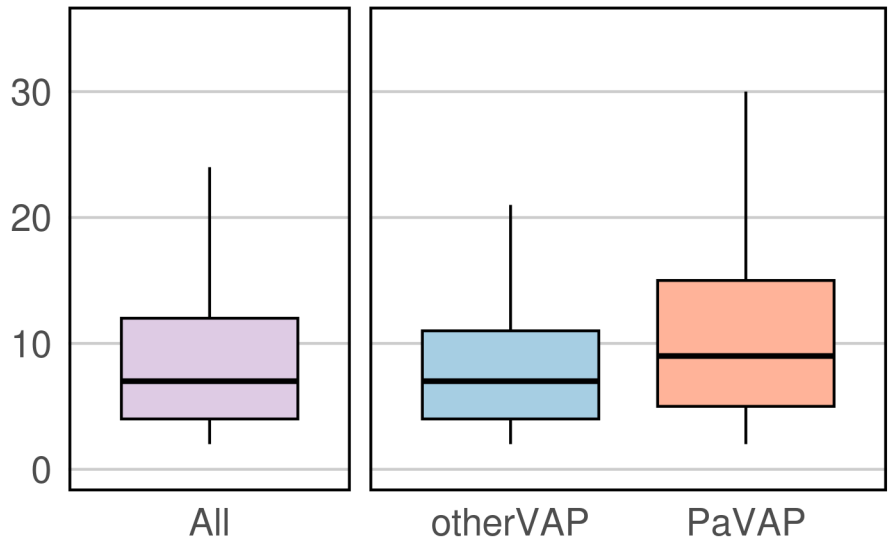


DEMOGRAPHICS AND CLINICAL CHARACTERISTICS



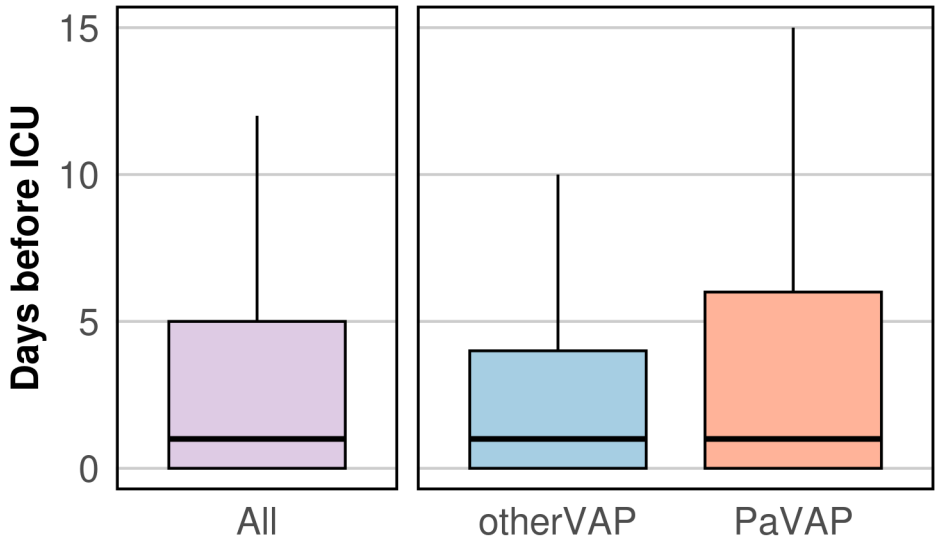
DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

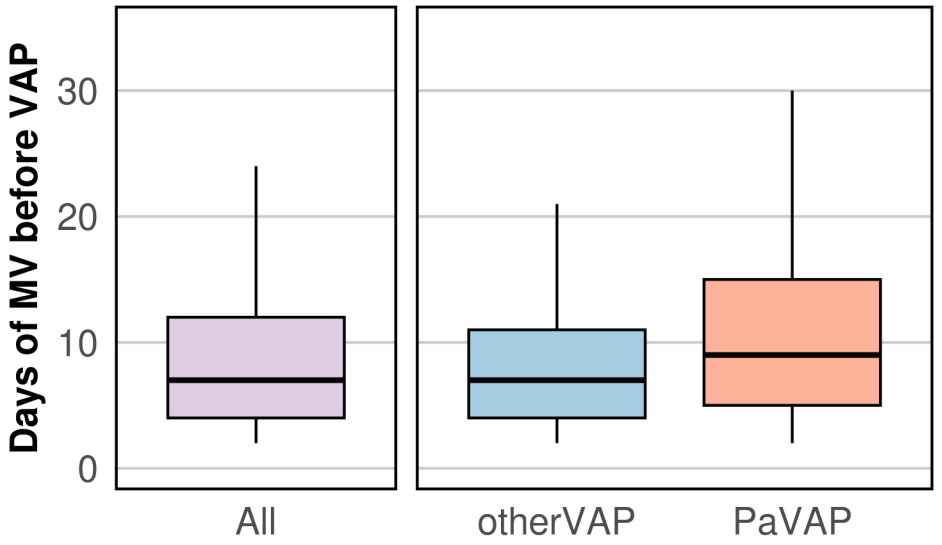




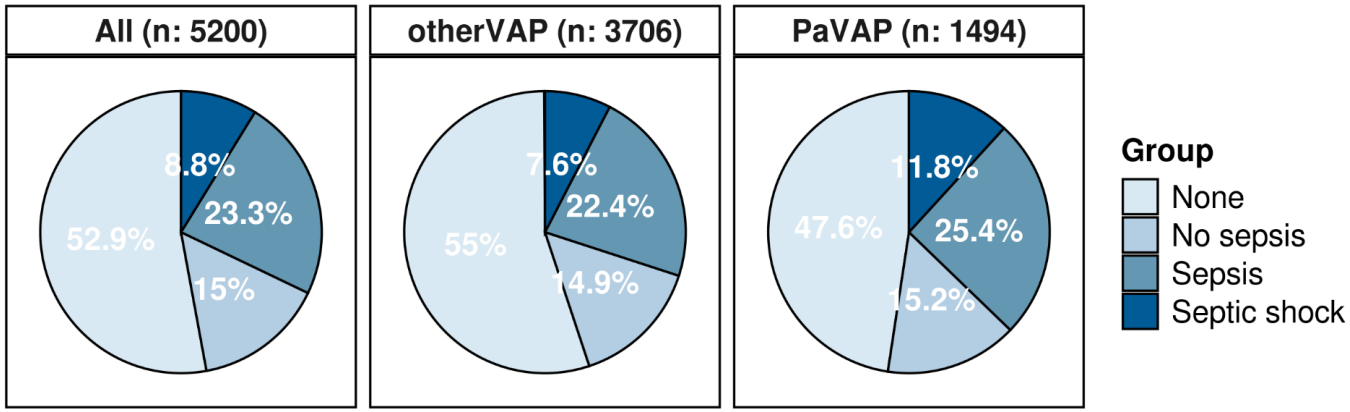
Days on MV before VAP

DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

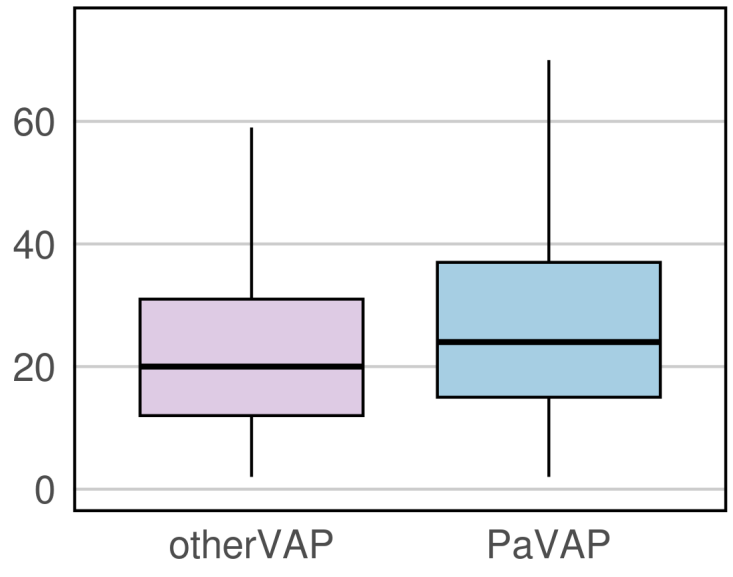




Severity of infection at admission

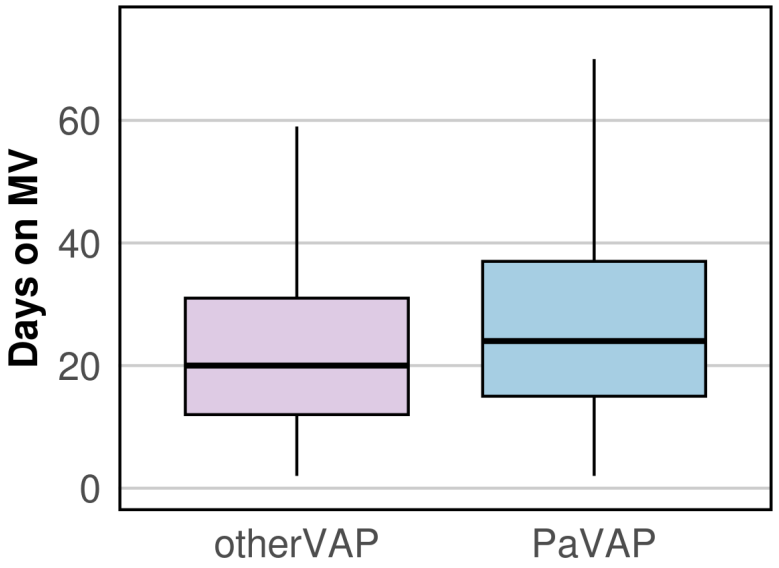


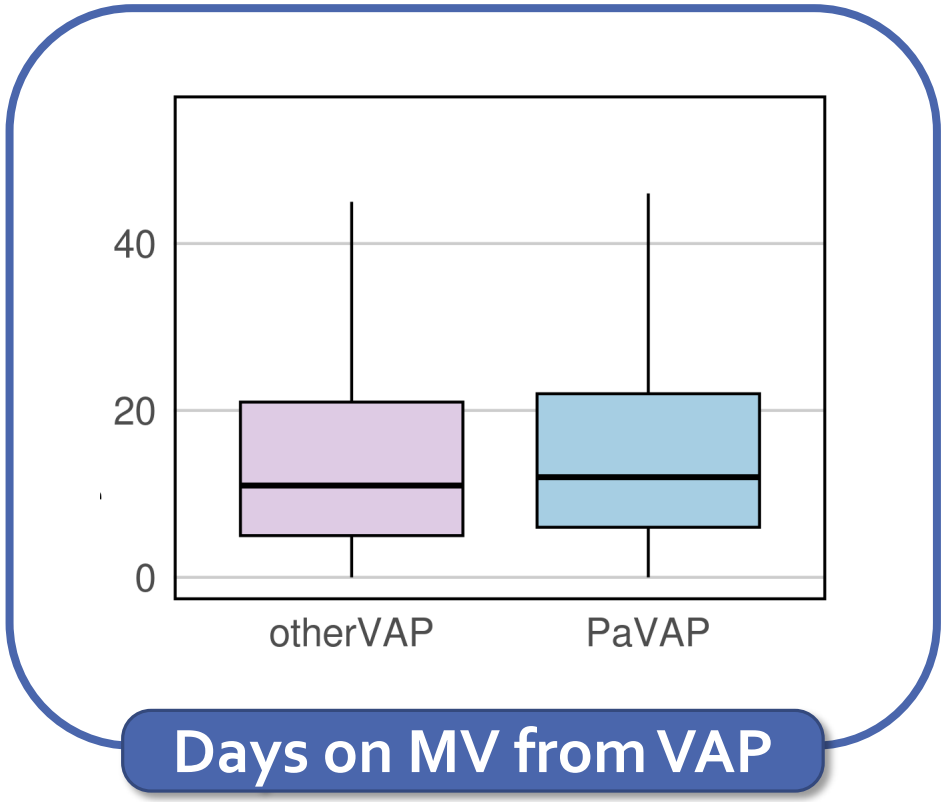
CLINICAL OUTCOMES



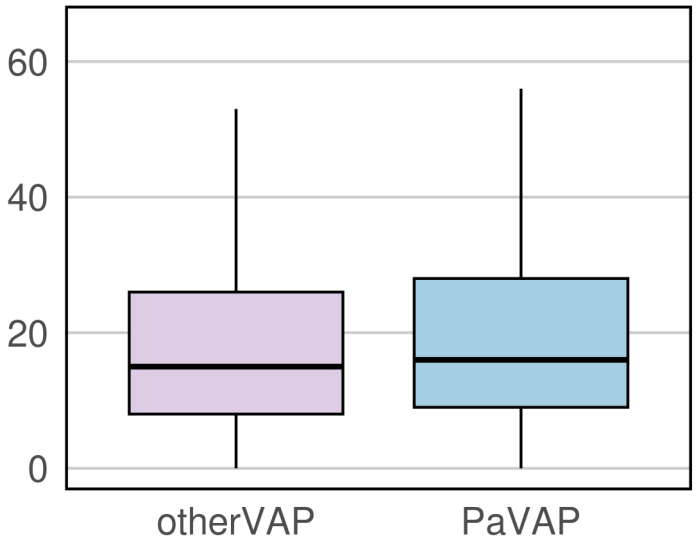
Days on MV

CLINICAL OUTCOMES



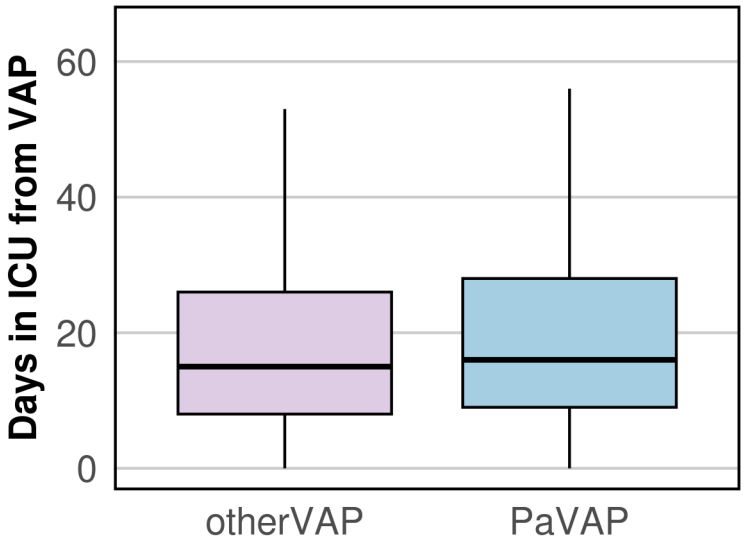


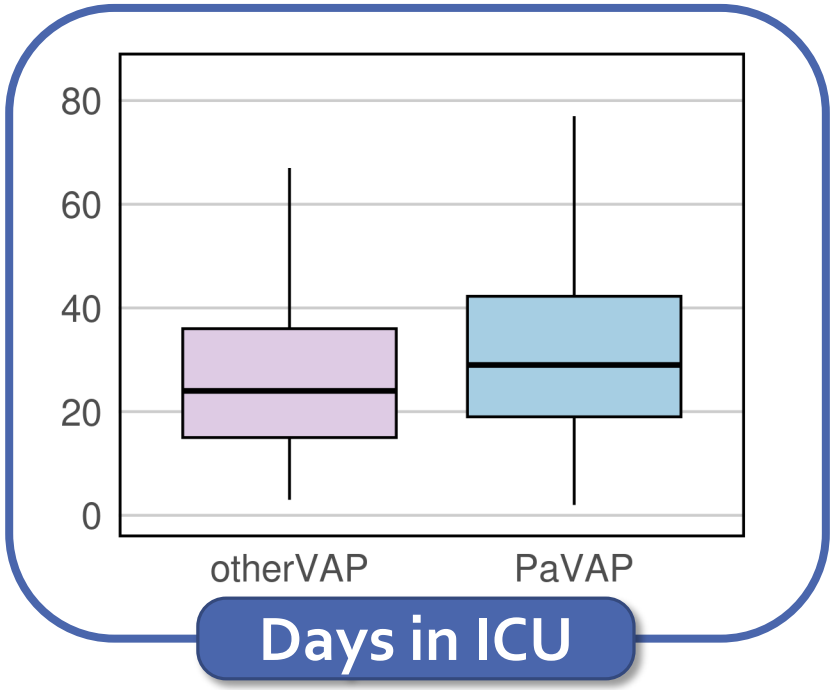
CLINICAL OUTCOMES



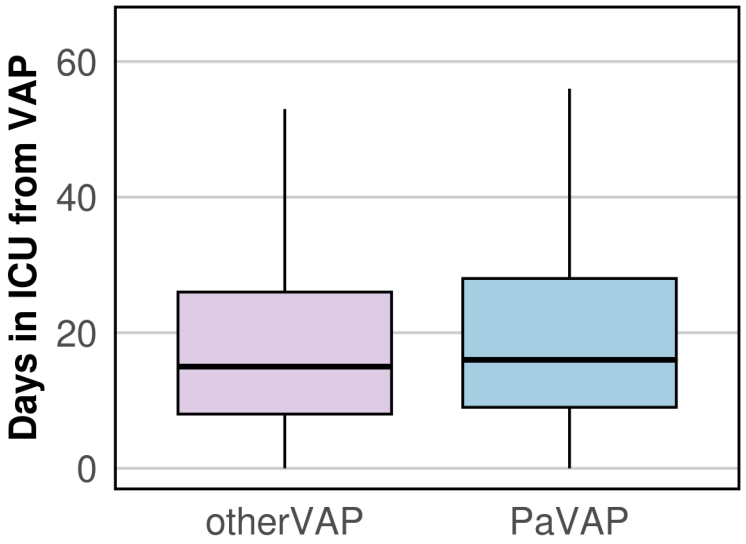
Days in ICU from VAP

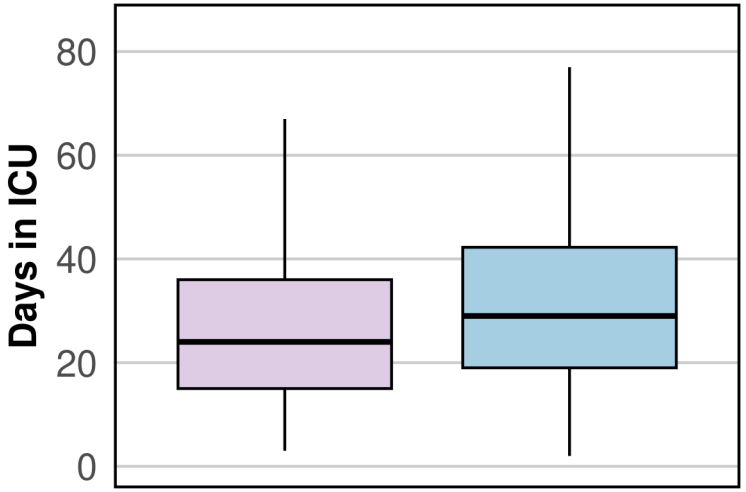
CLINICAL OUTCOMES



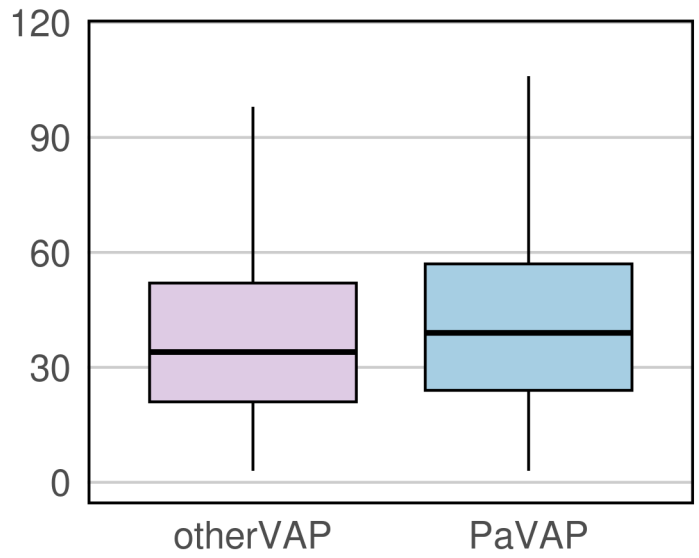


CLINICAL OUTCOMES

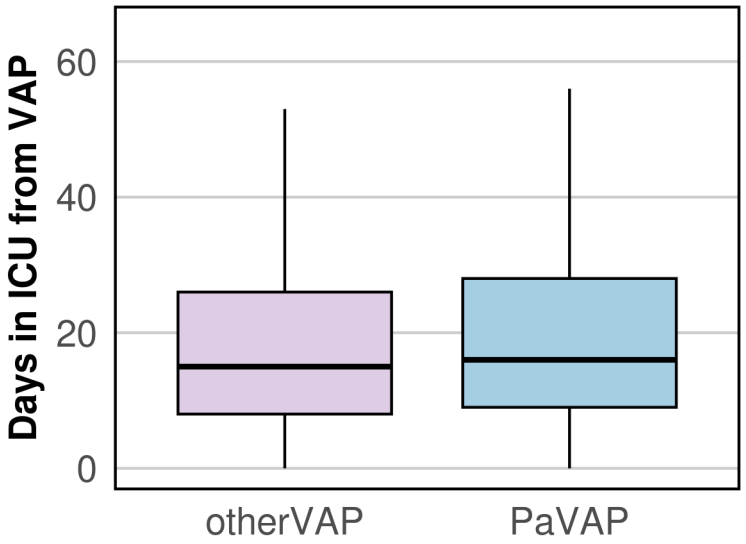


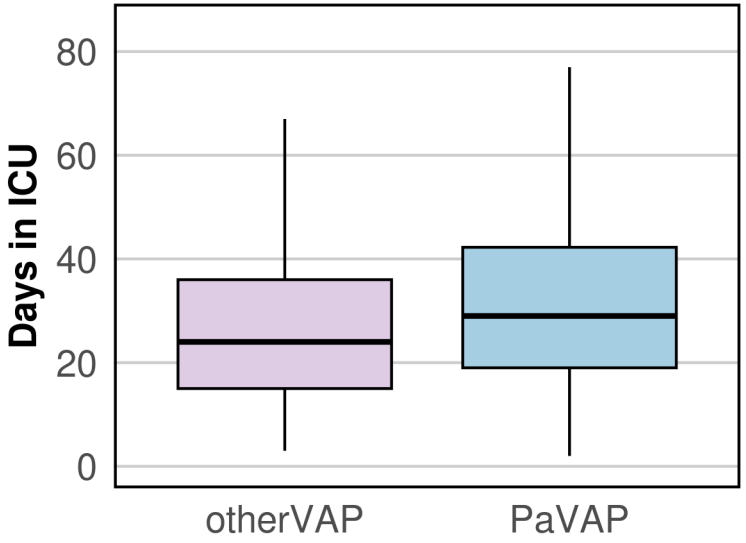


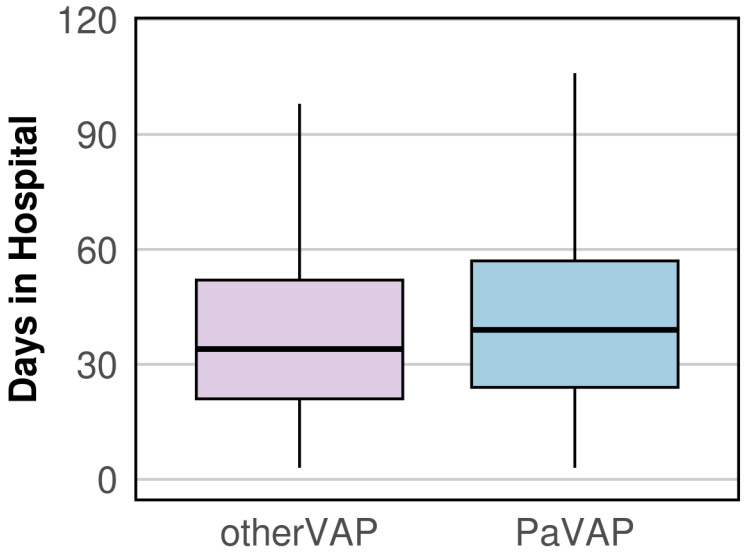
Days in Hospital



CLINICAL OUTCOMES



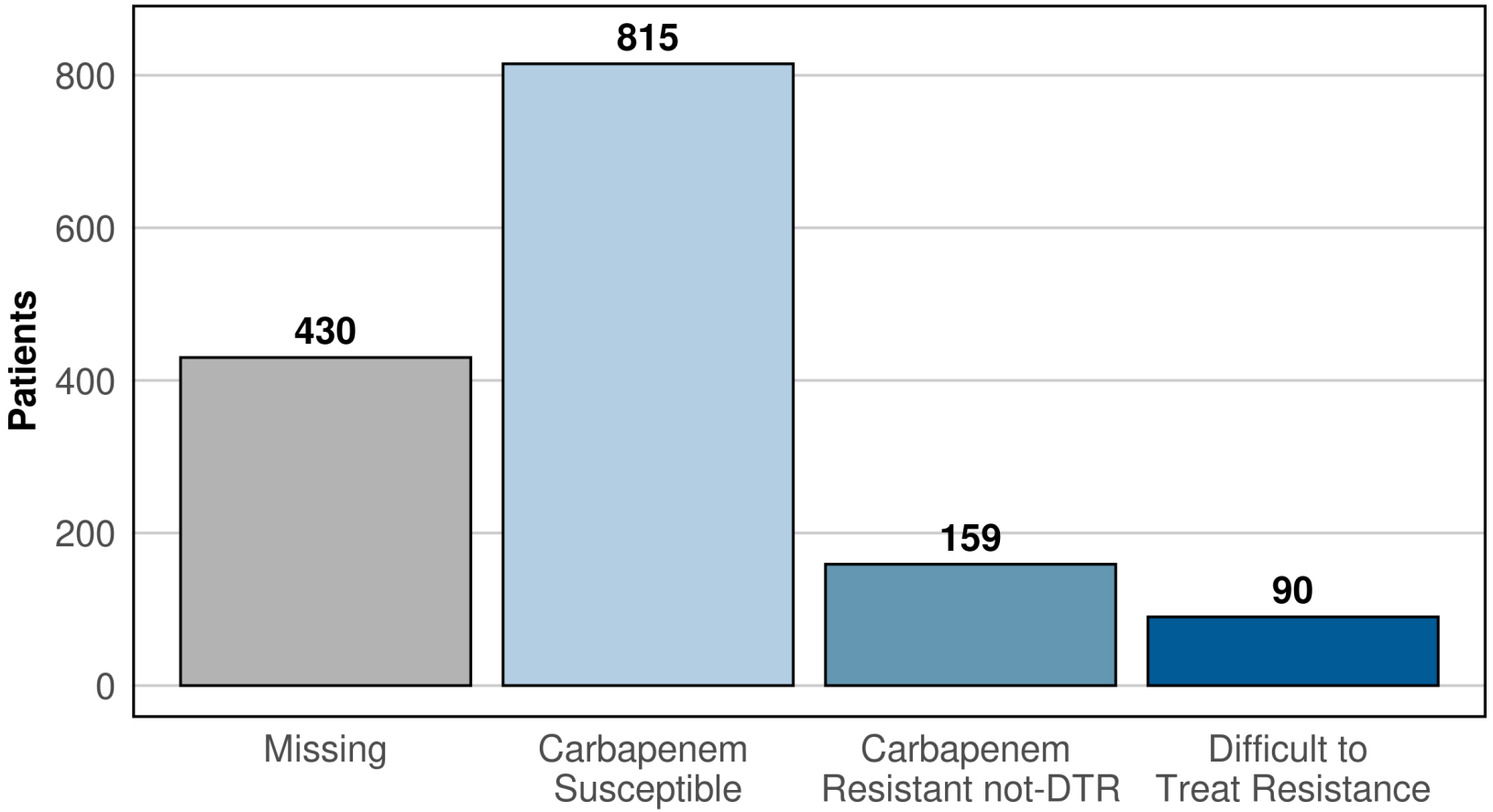




No difference in terms of mortality

CLINICAL OUTCOMES

Stratified by resistance profile



CLINICAL OUTCOMES Stratified by resistance profile

Observed mortality

Carbapenem Susceptible (CS)	Carbapenem Resistant not-DTR (CR not-DTR)	Difficult to Treat Resistance (DTR)
301 (37.6%)	60 (38.5%)	46 (51.7%)

*

CLINICAL OUTCOMES Stratified by resistance profile

Observed mortality

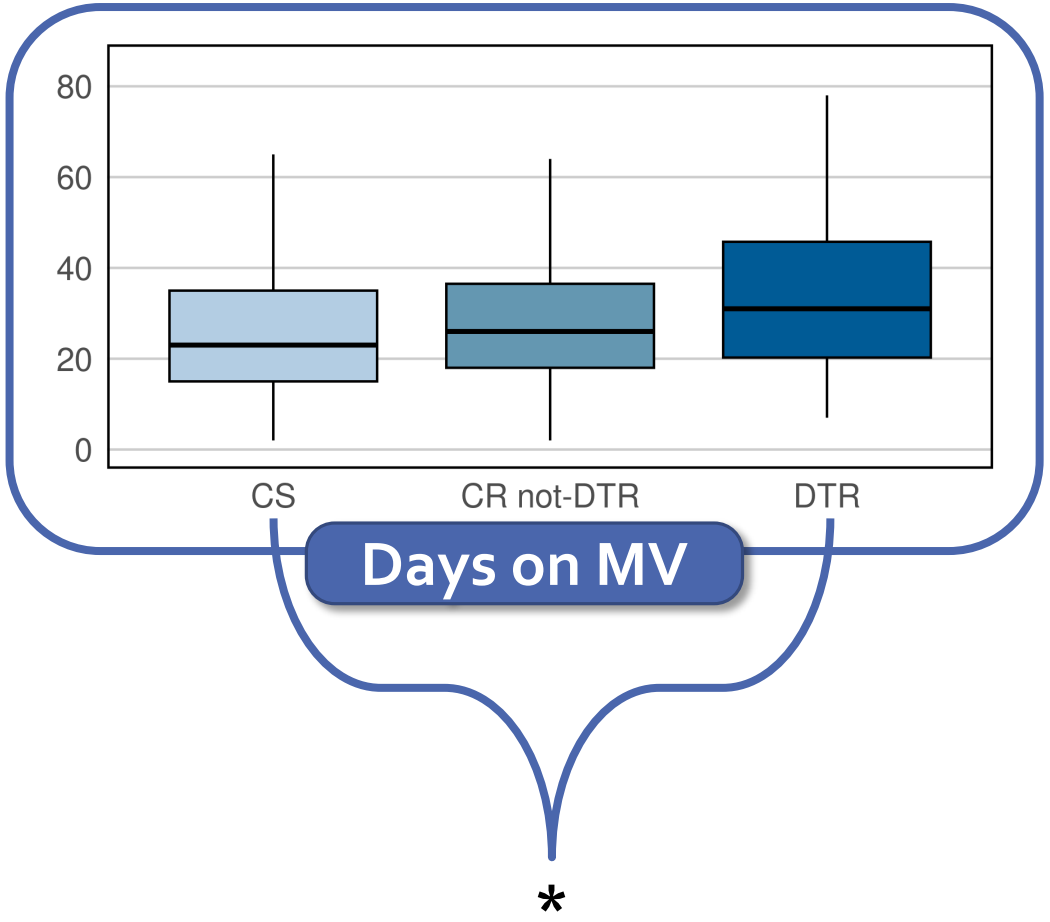
Carbapenem Susceptible (CS)	Carbapenem Resistant not-DTR (CR not-DTR)	Difficult to Treat Resistance (DTR)
301 (37.6%)	60 (38.5%)	46 (51.7%)

Standardized Mortality Ratio (SMR)

Carbapenem Susceptible (CS)	Carbapenem Resistant not-DTR (CR not-DTR)	Difficult to Treat Resistance (DTR)
1.02 (0.94-1.10)	1.11 (0.93-1.29)	1.48 (1.23-1.74)

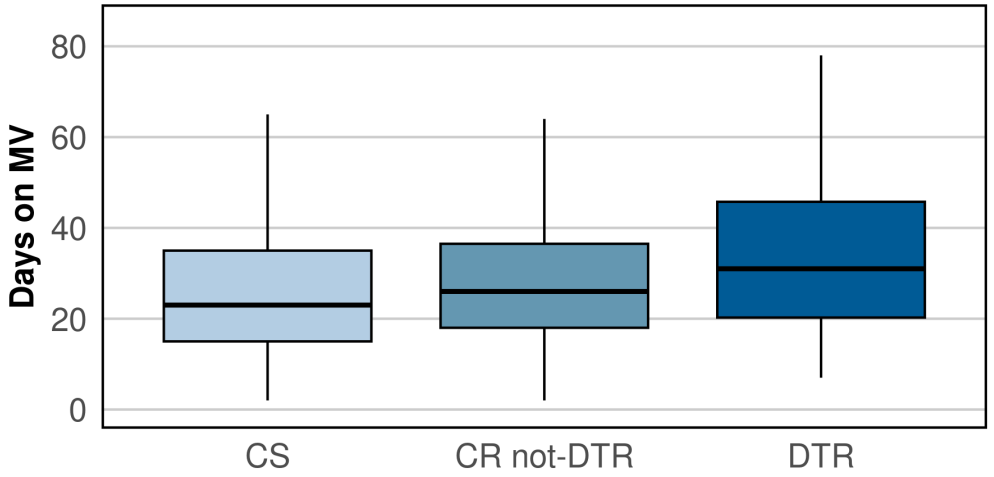
*

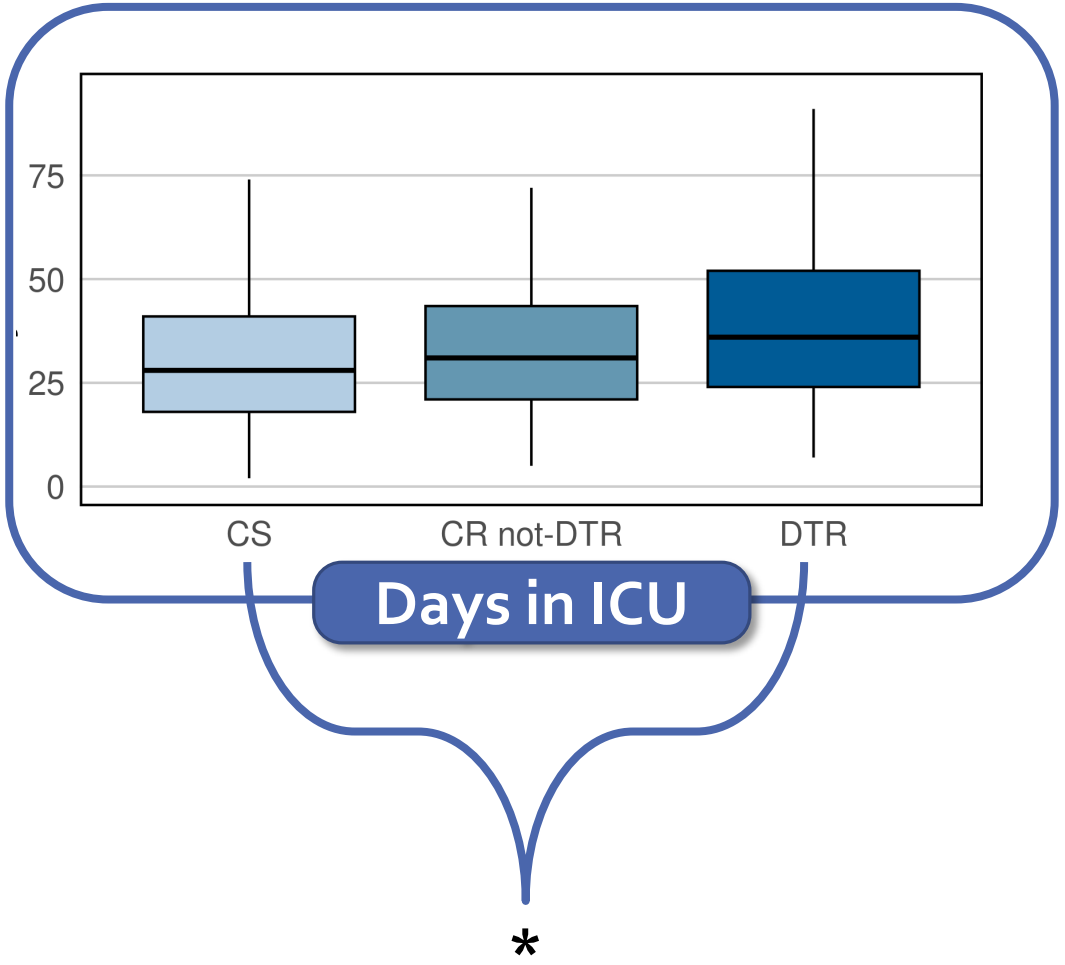
CLINICAL OUTCOMES Stratified by resistance profile



CLINICAL OUTCOMES

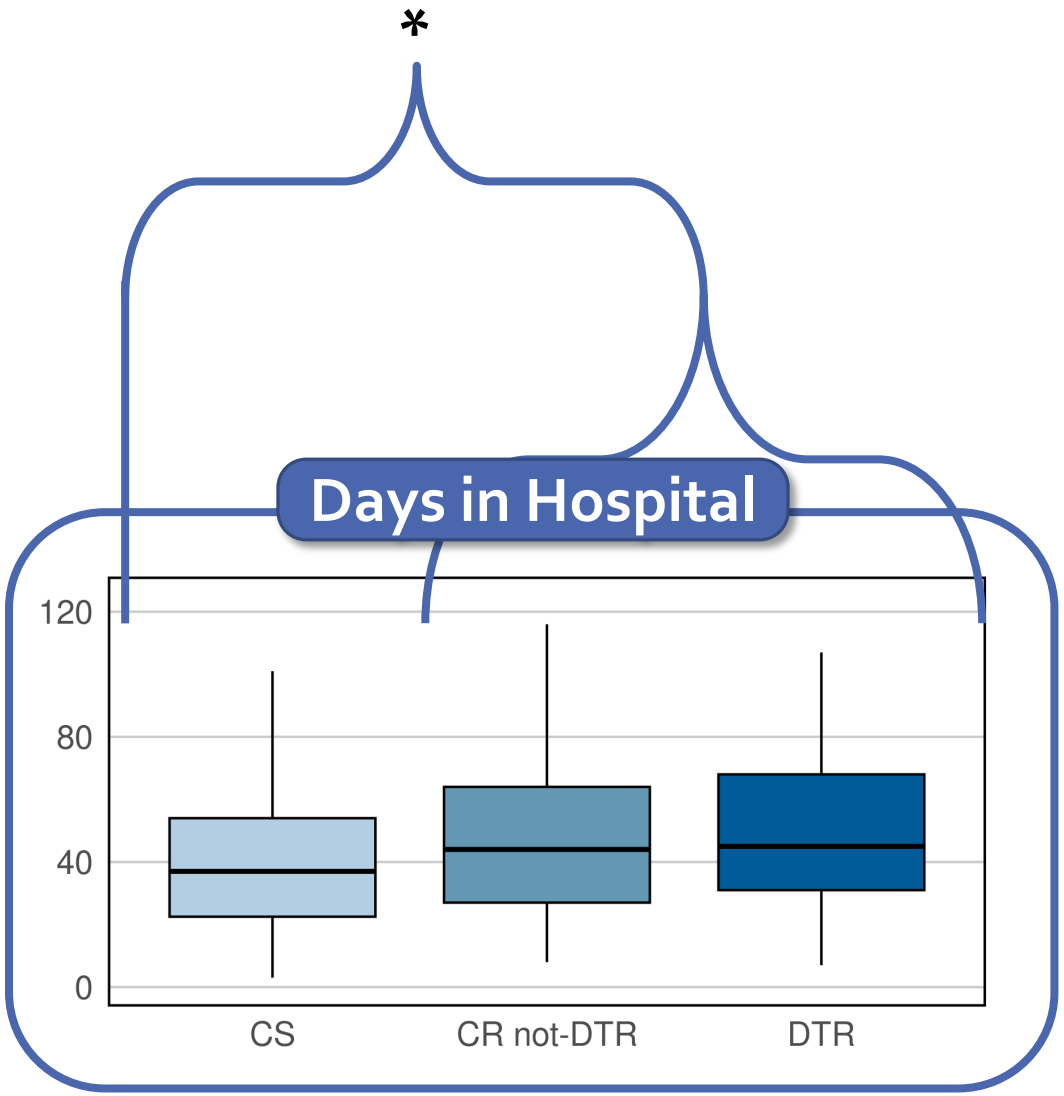
Stratified by resistance profile



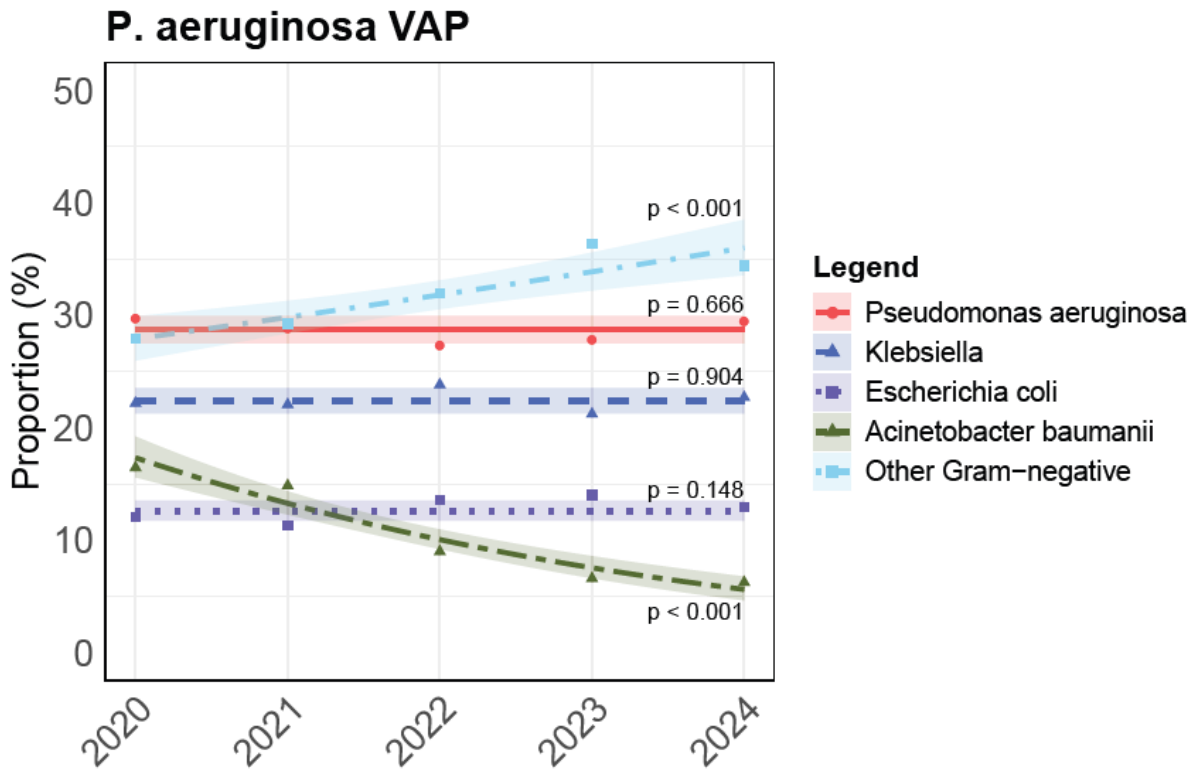


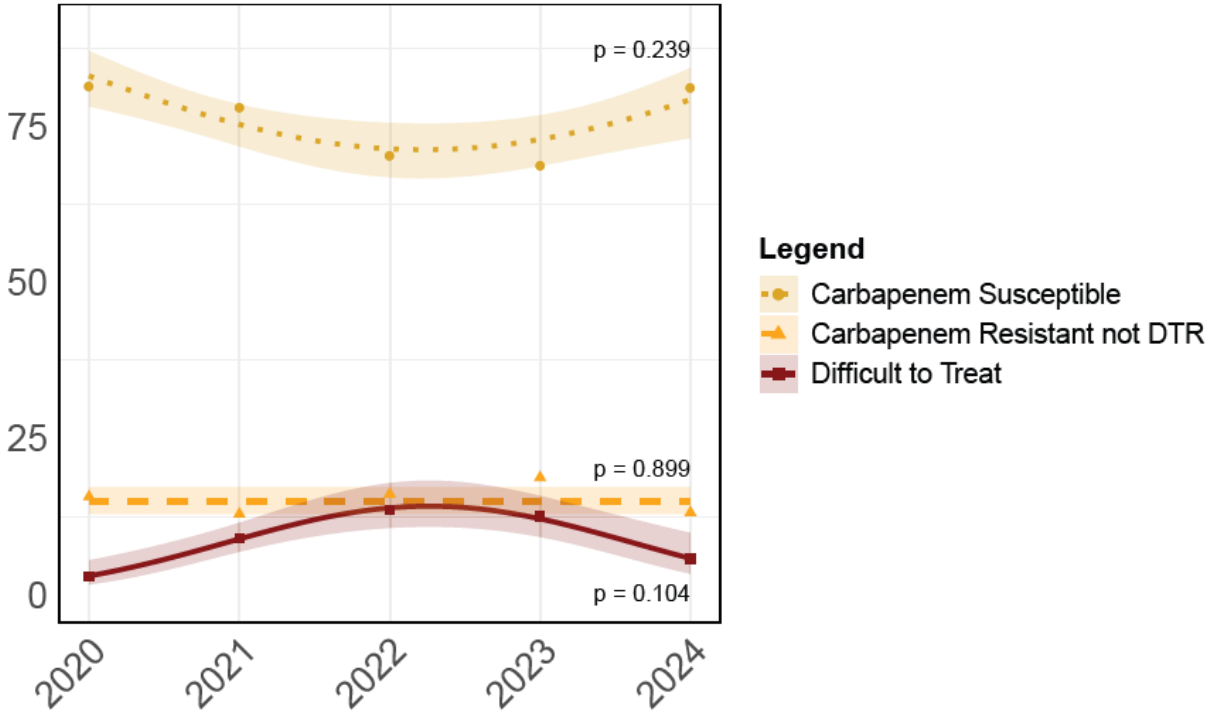
CLINICAL OUTCOMES

Stratified by resistance profile

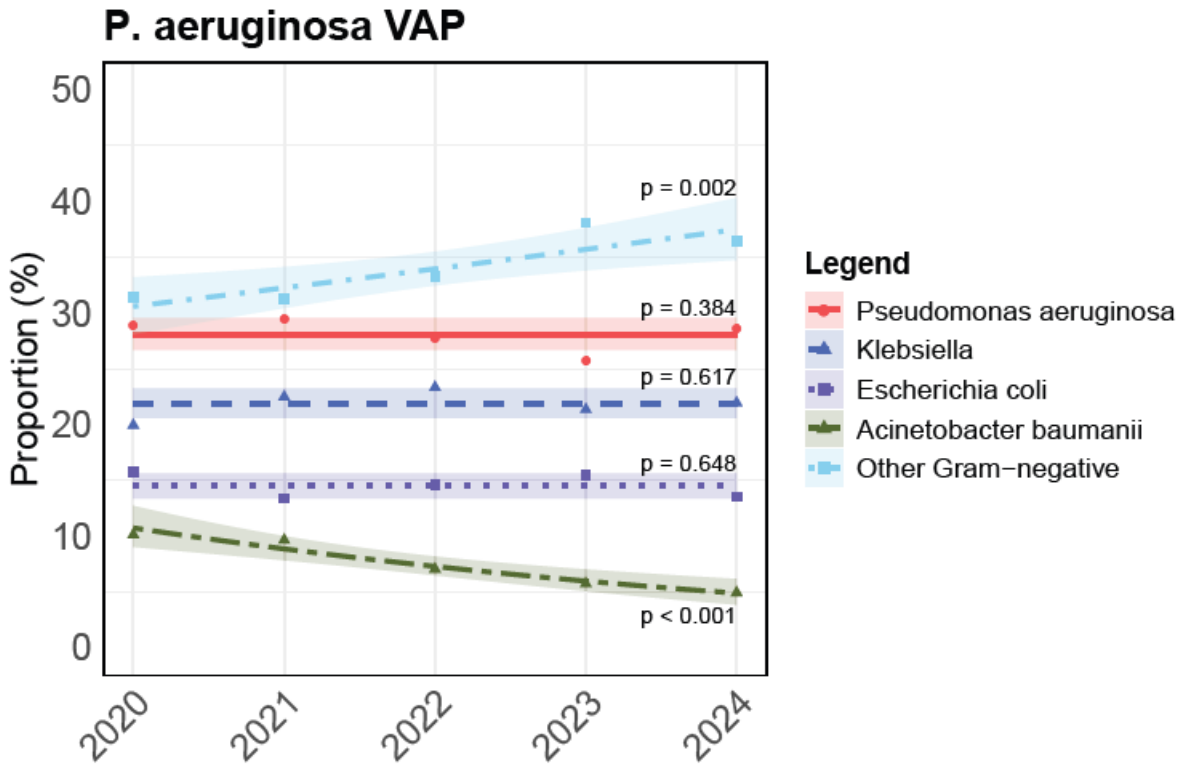


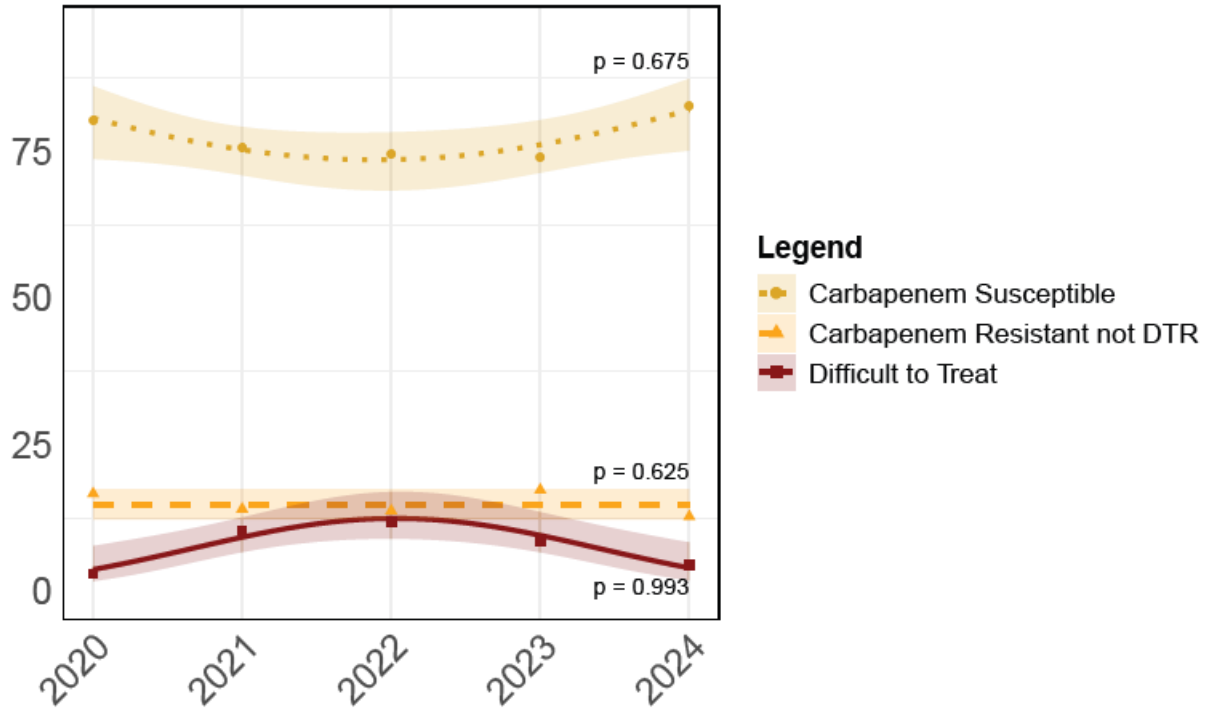
TREND ANALYSIS





SENSITIVITY ANALYSIS





DISCUSSION

Stable trend in the overall proportion of PaVAP

The **relative burden of DTR PaVAP** increased till 2022, reaching a plateau in 2023 and declining in 2024

?

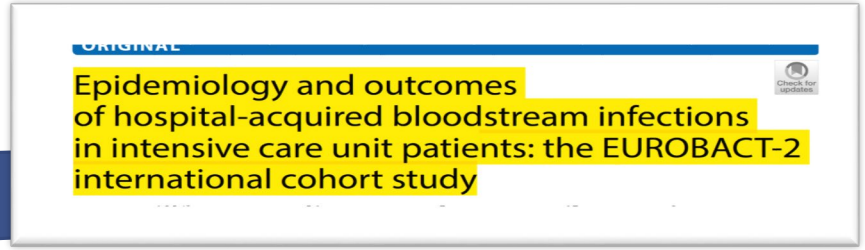
- Inappropriate utilization of antibiotics during the COVID-19 pandemic*
- High patient volume, even without exceeding capacity, affects patient care, and this could have compromised certain infection control practices in the hospitals**
- The lack of reporting of enhanced IPAC and/or ASP was significantly associated with an increase in gram-negative AMR***

*Impact of the COVID-19 pandemic on the epidemiology and molecular features of *Pseudomonas aeruginosa* bloodstream infections, María López et al.
**Trends in Pseudomonas aeruginosa (P. aeruginosa) Bacteremia during the COVID-19 Pandemic: A Systematic Review. Qin Xiang Ng et al.
***Antibiotic resistance associated with the COVID-19 pandemic: a systematic review and meta-analysis. Bradley J. Langford et al

DISCUSSION

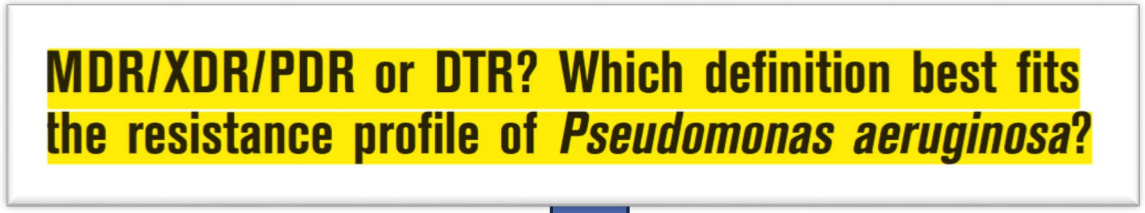
DTR PaVAP patients had worse SMR and longer mechanical ventilation and ICU stays compared to CS PaVAP patients.

Longer delays to adequate antimicrobial therapy due to resistance to all first line agents → **prognostic weight of DTR in GNBs infections** *


ORIGINAL

Epidemiology and outcomes of hospital-acquired bloodstream infections in intensive care unit patients: the EUROBACT-2 international cohort study

Higher mortality: comorbidities, medical and COVID-19 admissions, higher severity of illness, ICU-acquired HA-BSI, respiratory sources, **DTR Gram-negative bacteria** or fungus, patients who did not receive adequate antimicrobials or for whom source control was required but not achieved.


MDR/XDR/PDR or DTR? Which definition best fits the resistance profile of *Pseudomonas aeruginosa*?

-DTR seemed to identify better than CR and XDR categories the cases of P. aeruginosa with limited treatment options

-the DTR definition should be continuously updated

CONCLUDING REMARKS

- First large-scale analysis using the **GiViTI clinical quality database** focused on VAP
- In critically ill Italian patients ***P. aeruginosa*** caused **28.7% of VAP** cases
- **DTR strains** are associated with **higher mortality** and require urgent acknowledgement and mitigation actions
- **PaVAP** was also associated with **poor patient outcomes** and **increase resources use**, requiring longer mechanical ventilation, ICU and hospital stays

WE NEVER WORK ALONE!

Study group→ Adalgisa Caracciolo, Lidia Dalfino, Monica Stufano, Bruno Viaggi, Stefano Finazzi, Luigi Pisani, Sara Bettoni, Ivana Magnesa

Thanks!