

**Supplementary material. Impact of empirical antibiotic regimens on mortality in neutropenic patients with bloodstream infection presenting with septic shock.**

**Table S1. Risk factors for receiving inappropriate empirical antibiotic therapy in Gram-negative bacilli BSI and candidemia. Univariate and multivariate analysis.**

Risk Factor	AEAT n=169 (%)	IEAT n=32 (%)	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Age ≥70 years	40 (23.7)	8 (25.0)	1.08 (0.45-2.58)	0.871	-	-
Male sex	99 (58.6)	20 (62.5)	0.85 (0.39-1.85)	0.679	-	-
Acute leukemia	49 (29.0)	7 (21.9)	0.69 (0.28-1.69)	0.410	-	-
Non-Hodgkin lymphoma	31 (18.3)	7 (21.9)	1.25 (0.50-3.14)	0.640	-	-
Multiple myeloma	11 (6.5)	4 (12.5)	2.05 (0.61-6.90)	0.267	-	-
Chronic leukemia	5 (3.0)	2 (6.3)	2.19 (0.41-11.80)	0.309	-	-
Solid Neoplasia	58 (34.3)	8 (25.0)	0.64 (0.27-1.51)	0.412	-	-
Hematopoietic stem cell transplantation	22 (13.0)	7 (21.9)	1.87 (0.72-4.84)	0.191	-	-
Any comorbidity	54 (32.0)	13 (40.6)	1.46 (0.67-3.17)	0.340	-	-
Corticosteroid therapy	78 (46.2)	19 (59.4)	1.71 (0.79-3.67)	0.170	-	-

Nosocomial acquisition	61 (36.1)	21 (65.6)	3.38 (1.53-7.48)	<b>0.002</b>	0.67 (0.18-2.40)	0.533
Previous antibiotic therapy	82 (48.5)	24 (75.0)	3.18 (1.35-7.49)	<b>0.006</b>	2.32 (0.84-6.43)	0.106
Pulmonary source	33 (19.5)	8 (25.0)	1.37 (0.57-3.33)	0.481	-	-
Endogenous/unknown source	80 (47.3)	13 (40.6)	0.76 (0.35-1.64)	0.485	-	-
Catheter-related BSI	9 (5.3)	3 (9.4)	1.84 (0.47-7.20)	0.411	-	-
Acute kidney injury	117 (71.3)	22 (71.0)	0.98 (0.42-2.29)	0.966	-	-
Empirical $\beta$ -lactam plus aminoglycoside	111 (65.7)	5 (15.6)	0.10 (0.04-0.27)	<b>&lt;0.001</b>	0.10 (0.03-0.32)	<b>&lt;0.001</b>
Empirical $\beta$ -lactam plus specific gram-positive coverage	51 (30.2)	10 (31.3)	1.05 (0.47-2.38)	0.904	-	-
<i>E. coli</i>	79 (46.7)	4 (12.5)	0.16 (0.06-0.48)	<b>&lt;0.001</b>	0.30 (0.09-1.02)	0.053
<i>Klebsiella</i> spp.	31 (18.3)	1 (2.2)	0.14 (0.02-1.09)	<b>0.033</b>	0.20 (0.02-1.68)	0.138
<i>Pseudomonas aeruginosa</i>	50 (29.6)	13 (40.6)	1.63 (0.75-3.55)	0.217	-	-
MDR- <i>P. aeruginosa</i>	7 (4.1)	6 (18.8)	5.34 (1.66-17.15)	<b>0.002</b>	7.83 (1.80-34.12)	<b>0.006</b>
Candidemia	3 (1.8)	10 (31.3)	25.15 (6.43-98.46)	<b>&lt;0.001</b>	14.20 (3.00-67.27)	<b>0.001</b>
Polymicrobial	13 (7.7)	2 (6.3)	0.80 (0.17-3.73)	1.000	-	-

Abbreviations. AEAT: appropriate empirical antibiotic therapy; IEAT: inappropriate empirical antibiotic therapy; BSI: bloodstream infection; MDR: multidrug resistant.

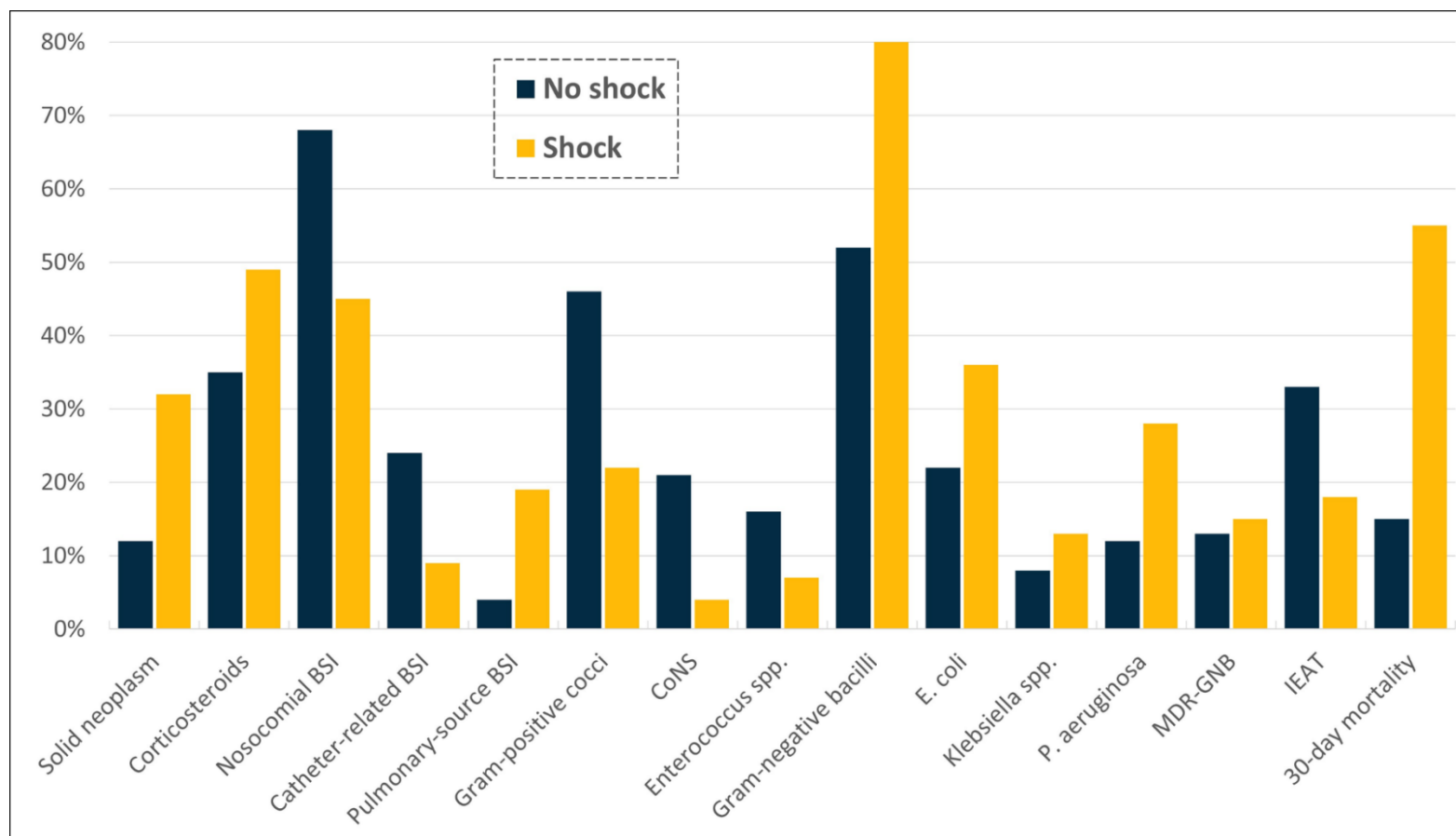
**Table S2. Additional clinical and demographic characteristics of patients with BSI episodes presenting with and without septic shock.**

	<b>ALL EPISODES</b> <b>N=1563 (%)</b>	<b>NO SEPTIC SHOCK</b> <b>n=1306 (%)</b>	<b>SEPTIC SHOCK</b> <b>n=257 (%)</b>	<b>p-value</b>
<b>Hematological malignancy</b>				
<b>Acute leukemia</b>	707 (45)	635 (49)	72 (28)	<0.001
<b>Non-Hodgkin's lymphoma</b>	267 (17)	213 (16)	54 (21)	0.067
<b>Multiple myeloma</b>	122 (8)	101 (8)	21 (8)	0.811
<b>Chronic leukemia</b>	74 (5)	63 (5)	11 (4)	0.708
<b>Myelodysplastic syndrome</b>	72 (5)	64 (5)	8 (3)	0.211
<b>Comorbidities</b>				
<b>Diabetes mellitus</b>	163 (10)	131 (10)	32 (13)	0.246
<b>COPD</b>	100 (6)	76 (6)	24 (9)	0.035

<b>Chronic cardiopathy</b>	107 (7)	87 (7)	20 (8)	0.516
<b>Chronic kidney disease</b>	41 (3)	34 (3)	7 (3)	0.912
<b>Chronic liver disease</b>	42 (3)	30 (2)	12 (5)	0.032
<b>Clinical conditions</b>				
<b>Central venous catheter</b>	1146 (73)	1000 (77)	146 (57)	<0.001
<b>Urinary catheter</b>	125 (8)	86 (7)	39 (15)	<0.001
<b>Prior antibiotic therapy</b>	926 (59)	785 (60)	141 (55)	0.118
<b>Quinolone prophylaxis</b>	303 (19)	274 (21)	29 (11)	<0.001

Abbreviations. COPD: chronic obstructive pulmonary disease.

**Figure S1. The most significant differences in baseline characteristics, epidemiology, and outcomes between patients with and without septic shock.**



Abbreviations. BSI: bloodstream infection, CoNS: coagulase-negative staphylococci, MDR-GNB: multidrug-resistant gram-negative bacilli, IEAT: inappropriate empirical antibiotic therapy.

**Table S3. Empirical treatments and outcomes of patients with BSI episodes presenting with and without septic shock.**

	<b>ALL EPISODES</b> N=1563 (%)	<b>NO SEPTIC SHOCK</b> n=1306 (%)	<b>SEPTIC SHOCK</b> n=257 (%)	<b>p-value</b>
<b>Empirical treatment</b>				
<b>β-lactam</b>	1384 (88.5)	1143 (87.5)	241 (93.8)	0.004
<b>Carbapenem</b>	601 (38.5)	459 (35.1)	142 (55.3)	<0.001
<b>Piperacillin-Tazobactam</b>	239 (15.3)	189 (14.5)	50 (19.5)	0.042
<b>Cefepime</b>	490 (31.3)	430 (32.9)	60 (23.3)	0.002
<b>Aminoglycoside</b>	626 (40)	489 (37.4)	137 (53)	<0.001
<b>Combined with a β-lactam</b>	615 (98.2)	480 (98.2)	135 (98.5)	0.764
<b>Quinolone</b>	101 (6.5)	86 (6.6)	15 (5.8)	0.656
<b>Specific gram-positive coverage*</b>				
<b>Combined with a β-lactam</b>	351 (82.9)	268 (79.8)	83 (95.4)	<0.001

\* Including glycopeptides (vancomycin and teicoplanin), daptomycin and linezolid.

**Table S4. Causative agents in episodes with septic shock receiving inappropriate empirical antibiotic therapy.**

Microorganisms	Inappropriate empirical antibiotic therapy n= 45 (%) *
<i>Pseudomonas aeruginosa</i>	15 (33.3)
MDR <i>P. aeruginosa</i>	7 (15.6)
<i>Escherichia coli</i>	4 (8.9)
ESBL <i>E. coli</i>	1 (2.2)
<i>Stenotrophomonas maltophilia</i>	2 (4.4)
<i>Acinetobacter baumannii</i>	2 (4.4)
<i>Klebsiella pneumoniae</i>	1 (2.2)
<i>Enterobacter cloacae</i>	1 (2.2)
<i>Clostridium septicum</i>	1 (2.2)
<i>Enterococcus</i> spp.	6 (13.3)
<i>E. faecium</i>	4 (8.9)
<i>E. faecalis</i>	2 (4.4)
Coagulase-negative staphylococci	4 (8.9)
<i>Staphylococcus aureus</i>	1 (2.2)
<i>Candida</i> spp.	10 (22.2)

<b><i>Candida albicans</i></b>	3 (6.7)
<b><i>Non-albicans Candida</i></b>	7 (15.6)

\*Including 2 polymicrobial episodes

Abbreviations. MDR: multidrug resistant; ESBL: extended-spectrum beta-lactamase.