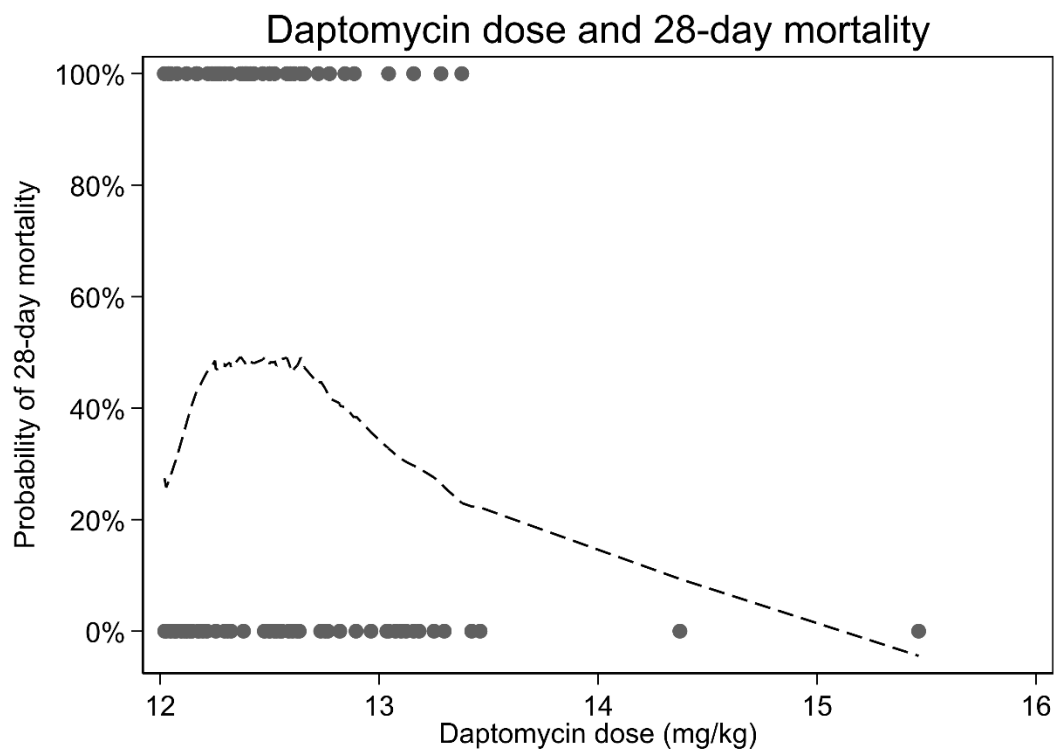


Supplementary Material

Outcomes and Adverse Events Among Patients With Vancomycin-Resistant Enterococcal Bloodstream Infection Treated With Daptomycin Doses Greater Than 12 mg/kg

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Figure S1. Exploratory locally-weighted scatterplot smoothing plot showing the smoothed probability of 28-day mortality across daptomycin doses. Individual points represent observed outcomes (death or survival). The curve is shown only for visualization and was not adjusted for covariates.



Supplementary Table 1. Sex-stratified baseline characteristics of patients with a vancomycin-resistant enterococcal bloodstream infection treated with daptomycin

Variable	Total (n=101)	Male (n=52)	Female (n=49)	p
Demographics				
Age, years	70.2 (62.3–78.6)	70.3 (62.6–79.2)	70.2 (60.0–78.2)	0.61
Body mass index, kg/m ²	21.6 (18.5–24.2)	21.1 (18.8–23.6)	21.9 (17.5–25.0)	0.65
Duration of hospitalization before onset of BSI, days	14 (6–35)	14.5 (5.5–37)	11 (6–32)	0.79
Comorbidity and host factors				
Charlson comorbidity index	5 (3–6)	5 (3–6.5)	4 (2–6)	0.31
Diabetes mellitus	40 (39.6)	24 (46.2)	16 (32.7)	0.17
Chronic kidney disease	30 (29.7)	17 (32.7)	13 (26.5)	0.50
Baseline renal replacement therapy	11 (10.9)	6 (11.5)	5 (10.2)	0.83
Underlying malignancy	68 (67.3)	35 (67.3)	33 (67.4)	1.00
Immunosuppressant use	34 (33.7)	20 (38.5)	14 (28.6)	0.29
Statin use	6 (5.9)	2 (3.9)	4 (8.2)	0.43
Infection source				
Primary bacteremia	44 (43.6)	30 (57.7)	14 (28.6)	0.003
Urinary tract infection	45 (44.6)	15 (28.9)	30 (61.2)	0.001

Intra-abdominal infection	15 (14.9)	6 (11.5)	9 (18.4)	0.34
Clinical characteristics at presentation				
Neutropenia (<500 cells/ μ L)	21 (21.2)	9 (18.0)	12 (24.5)	0.43
Platelet count ($\times 10^4/\mu$ L)	9.5 (2.6–21.7)	9.9 (2.3–22.3)	9.5 (3.4–20.8)	0.87
Total bilirubin (mg/dL)	0.9 (0.5–2.6)	0.9 (0.5–4.2)	1.0 (0.6–2.1)	0.73
Mechanical ventilation at onset of BSI	23 (22.8)	15 (28.9)	8 (16.3)	0.13
Pitt bacteremia score	2 (0–3)	2 (0–3.5)	1 (0–3)	0.25
Treatment characteristics				
Time to initiation of daptomycin, days	2 (1–3)	2 (2–3)	2 (1–3)	0.26
Daptomycin dose, mg/kg	12.5 (12.2–12.8)	12.5 (12.1–12.8)	12.5 (12.2–12.7)	0.84
Daptomycin dose 12–13 mg/kg	84 (83.2)	44 (84.6)	40 (81.6)	0.69

Data are presented as median (interquartile range) unless otherwise indicated, or as number (%).

Abbreviation: BSI, bloodstream infection

Supplementary Table 2. Estimated daptomycin exposure metrics by 28-day mortality status and by dose stratum in patients with a vancomycin-resistant enterococcal bloodstream infection

Exposure metric (Estimated)	Survivors (n=59)	Non- survivors (n=42)	<i>P</i>	12-13 mg/kg (n=84)	>13 mg/kg (n=17)	<i>P</i>
C_{min} , mg/L	8.2 (4.6— 10.9)	10.5 (3.8— 21.7)	0.08	8.9 (4.1— 15.8)	9.2 (5.4— 11.1)	0.68
fAUC, mg.h/L	121.7 (98.3— 177.9)	139.4 (117.1— 167.9)	0.26	127.1 (104.4— 166.6)	132.6 (102.9— 227.7)	0.55
fAUC/MIC	61.1 (43.5— 92.9)	62.5 (42.3— 73.7)	0.85	61.1 (42.3— 78.5)	64.9 (41.4— 92.9)	0.83

Data are presented as median (interquartile range) unless otherwise indicated, or as number (%).

Abbreviation: fAUC, free area under the concentration-time curve; MIC, minimum inhibitory concentration

Supplementary Table 3. Baseline characteristics of patients with a vancomycin-resistant enterococcal bloodstream infection treated with daptomycin, stratified by an elevated creatine kinase (CK) level

Variable	Elevated CK (n = 14)	Non-elevated CK (n = 87)	p
Demographics			
Age, years	71.0 (66.8–77.8)	69.4 (60.2–78.7)	0.44
Male sex	6 (42.9)	46 (52.9)	0.49
Body mass index, kg/m ²	22.6 (19.6–25.2)	21.2 (17.9–24.0)	0.17
Duration of hospitalization before onset of BSI, days	8.5 (1.0–19.0)	15.0 (6.0–37.0)	0.12
Comorbidity and host factors			
Charlson comorbidity index	3.0 (2.0–6.0)	5.0 (3.0–7.0)	0.28
Diabetes mellitus	9 (64.3)	31 (35.6)	0.04
Chronic kidney disease	4 (28.6)	26 (29.9)	0.92
Baseline renal replacement therapy	3 (21.4)	8 (9.2)	0.17
Underlying malignancy	7 (50.0)	61 (70.1)	0.13
Immunosuppressant use	5 (35.7)	29 (33.3)	0.86
Statin use	1 (7.1)	5 (5.7)	0.60
Infection source			
Primary bacteremia	7 (50.0)	37 (42.5)	0.60
Urinary tract infection	7 (50.0)	38 (43.7)	0.66
Intra-abdominal infection	0 (0.0)	15 (17.2)	0.09

Clinical characteristics at presentation			
Neutropenia (<500 cells/ μ L)	4 (28.6)	17 (20.0)	0.47
Platelet count ($\times 10^4/\mu$ L)	7.6 (1.8–17.1)	10.1 (3.4–21.8)	0.56
Total bilirubin (mg/dL)	1.1 (0.5–6.6)	0.9 (0.5–2.6)	0.44
Mechanical ventilation at onset of BSI	6 (42.9)	17 (19.5)	0.05
Pitt bacteremia score	3.0 (1.0–5.0)	1.0 (0.0–3.0)	0.04
Treatment characteristics			
Time to initiation of daptomycin, days	2.0 (2.0–3.0)	2.0 (1.0–3.0)	0.75
Daptomycin dose, mg/kg	12.5 (12.3–13.3)	12.4 (12.2–12.7)	0.30
Daptomycin dose >13 mg/kg	4 (28.6)	13 (14.9)	0.21
Pharmacokinetic parameters			
Estimated C_{min} , mg/L	10.3 (5.2–19.8)	8.7 (4.2–14.1)	0.11
Estimated $C_{min} > 24.3$ mg/L	2 (14.3)	7 (9.0)	0.54

Data are presented as median (interquartile range) unless otherwise indicated, or as number (%). C_{min} values are model-based estimates (see Methods); they are not directly measured. Estimated C_{min} was available for 92 of 101 patients.

Abbreviations: BSI, bloodstream infection; CK, creatine kinase; C_{min} , estimated trough concentration