

## **Supplementary Information:**

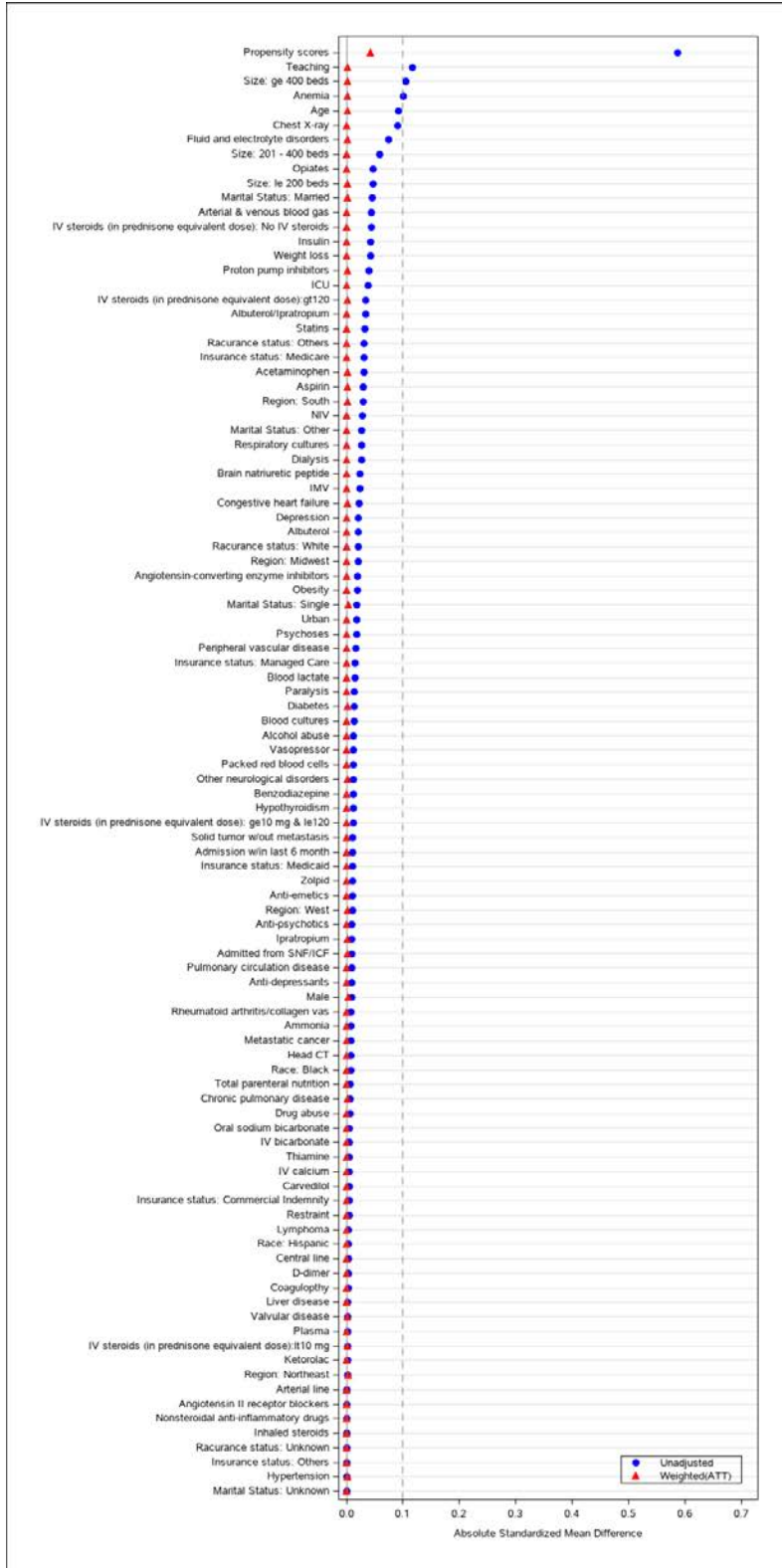
### **Premier Healthcare Database:**

The Premier database is an inpatient data service developed for measuring quality and healthcare utilization. The participating hospitals are drawn from all regions of the United States and are representative of US acute care hospitals, with some overrepresentation of larger hospitals, the southern region, and urban facilities. The Premier database contains socio-demographic information, ICD-9-CM (*International Classification of Diseases, Ninth Revision, Clinical Modification*) diagnosis codes, hospital and physician information and date-stamped hospital charge codes for all items charged to the patient or insurer including medications, laboratory/diagnostic tests and procedures. The charge data are collected electronically from each of the participating hospitals and audited frequently to ensure data validity. Approximately 75% of the participating hospitals provide information on actual hospital costs and the remaining hospitals provide cost estimates based on the Medicare cost to charge ratios. Data elements also included microbiology laboratory data, including culture results and antibiotic sensitivity results through SafetySurveillor® (an infection tracking tool).

### **Antimicrobial treatment definitions:**

- Anti-MRSA antibiotics were defined as vancomycin, linezolid, tigecycline and ceftaroline.
- Antipseudomonal antibiotics were defined as amikacin, gentamicin, tobramycin, cefepime, ceftazidime, cefoperazone, doripenem, imipenem, meropenem, aztreonam and piperacillin-tazobactam.

# Supplementary Figure 1: De-escalation among patients with negative cultures: before and after propensity adjustment



**Supplementary Table 1: Characteristics of patients with de-escalation by day 4 based on the hospital rates of de-escalation (quartiles of de-escalation)**

Factor	Hospital rate of de-escalation				p-value
	≥2.4% and < 8% (N=116)	≥8% and < 13% (N=224)	≥13% and < 18% (N=253)	≥18% and < 36% (N=464)	
Age, median [Q1, Q3]	75.0[65.0,86.5]	74.0[62.0,83.5]	68.0[55.0,81.0]	74.0[60.5,85.0]	<0.001 <sup>b</sup>
Gender, No. (%)					0.89 <sup>c</sup>
. Female	55(47.4)	116(51.8)	125(49.4)	232(50.0)	
. Male	61(52.6)	108(48.2)	128(50.6)	232(50.0)	
Race, No. (%)					<0.001 <sup>c</sup>
. White	95(81.9)	174(77.7)	160(63.2)	330(71.1)	
. Black	11(9.5)	43(19.2)	86(34.0)	58(12.5)	
. Hispanic	0(0.0)	1(0.45)	0(0.0)	2(0.43)	
. Others	10(8.6)	6(2.7)	7(2.8)	72(15.5)	
. Unknown	0(0.0)	0(0.0)	0(0.0)	2(0.43)	
Marital Status, No. (%)					<0.001 <sup>c</sup>
. Married	49(42.2)	78(34.8)	89(35.2)	147(31.7)	
. Single	67(57.8)	127(56.7)	157(62.1)	244(52.6)	
. Other	0(0.0)	18(8.0)	7(2.8)	73(15.7)	
Admission Source, No. (%)					<0.001 <sup>c</sup>
. Emergency Room	102(87.9)	192(85.7)	238(94.1)	397(85.6)	
. SNF/ICF	8(6.9)	32(14.3)	10(4.0)	55(11.9)	
. Clinic	6(5.2)	0(0.0)	4(1.6)	12(2.6)	
. Others	0(0.0)	0(0.0)	1(0.40)	0(0.0)	
Discharge Disposition, No. (%)					0.035 <sup>c</sup>
. Home	33(28.4)	87(38.8)	114(45.1)	198(42.7)	
. Home Health	27(23.3)	31(13.8)	45(17.8)	55(11.9)	
. Hospice	5(4.3)	15(6.7)	8(3.2)	25(5.4)	
. Expired	5(4.3)	7(3.1)	6(2.4)	14(3.0)	
. Others	46(39.7)	84(37.5)	80(31.6)	172(37.1)	
Insurance Payer, No. (%)					0.008 <sup>c</sup>
. Medicare	90(77.6)	174(77.7)	171(67.6)	357(76.9)	
. Medicaid	9(7.8)	13(5.8)	30(11.9)	42(9.1)	
. Managed Care	11(9.5)	20(8.9)	29(11.5)	36(7.8)	
. Commercial Indemnity	1(0.86)	12(5.4)	9(3.6)	5(1.1)	
. Others	5(4.3)	5(2.2)	14(5.5)	24(5.2)	

Principal Diagnosis, No. (%)					<i>&lt;0.001<sup>c</sup></i>
. Pneumonia	61(52.6)	130(58.0)	115(45.5)	195(42.0)	
. Aspiration Pneumonia	10(8.6)	33(14.7)	36(14.2)	53(11.4)	
. Sepsis	44(37.9)	53(23.7)	93(36.8)	204(44.0)	
. Respiratory Failure	1(0.86)	8(3.6)	9(3.6)	12(2.6)	
Admission w/in last 6 month, No. (%)	26(22.4)	26(11.6)	30(11.9)	87(18.8)	<i>0.006<sup>c</sup></i>
Dialysis, No. (%)	6(5.2)	11(4.9)	17(6.7)	17(3.7)	0.34 <sup>c</sup>
Admitted from SNF/ICF, No. (%)	8(6.9)	32(14.3)	10(4.0)	55(11.9)	<i>&lt;0.001<sup>c</sup></i>
<b>Comorbidities</b>					
Combined comorbidity scores, Median [Q1, Q3]	4.0[2.0,5.0]	3.0[1.00,5.0]	3.0[1.00,5.0]	3.0[1.00,5.0]	0.32 <sup>b</sup>
Hypertension, No. (%)	83(71.6)	165(73.7)	182(71.9)	330(71.1)	0.92 <sup>c</sup>
Chronic pulmonary disease, No. (%)	56(48.3)	104(46.4)	108(42.7)	196(42.2)	0.54 <sup>c</sup>
Anemia, No. (%)	40(34.5)	79(35.3)	95(37.5)	132(28.4)	0.062 <sup>c</sup>
Diabetes, No. (%)	37(31.9)	82(36.6)	93(36.8)	161(34.7)	0.79 <sup>c</sup>
Congestive heart failure, No. (%)	35(30.2)	64(28.6)	71(28.1)	147(31.7)	0.73 <sup>c</sup>
<b>Treatment/ test on day 0/1</b>					
Blood cultures, n (%)	113(97.4)	219(97.8)	251(99.2)	461(99.4)	0.13 <sup>d</sup>
Respiratory cultures, n (%)	12(10.3)	30(13.4)	27(10.7)	57(12.3)	0.76 <sup>c</sup>
NIV, No. (%)	11(9.5)	10(4.5)	22(8.7)	27(5.8)	0.14 <sup>c</sup>
Blood lactate, No. (%)	68(58.6)	107(47.8)	142(56.1)	333(71.8)	<i>&lt;0.001<sup>c</sup></i>
Arterial & venous blood gas, No. (%)	33(28.4)	68(30.4)	85(33.6)	159(34.3)	0.55 <sup>c</sup>
Influenza test, No. (%)	11(9.5)	39(17.4)	61(24.1)	61(13.1)	<i>&lt;0.001<sup>c</sup></i>
Positive influenza test, No. (%)	0(0.0)	3(1.3)	0(0.0)	1(0.22)	0.16 <sup>d</sup>
<b>Treatment/test on day 4</b>					
Arterial & venous blood gas, No. (%)	5(4.3)	8(3.6)	13(5.1)	15(3.2)	0.63 <sup>c</sup>
Brain natriuretic peptide, No. (%)	4(3.4)	3(1.3)	4(1.6)	13(2.8)	0.43 <sup>c</sup>

Blood lactate, No. (%)	1(0.86)	0(0.0)	4(1.6)	10(2.2)	0.15 <sup>c</sup>
ICU, No. (%)	2(1.7)	5(2.2)	6(2.4)	12(2.6)	0.96 <sup>c</sup>
IMV, No. (%)	2(1.7)	2(0.89)	5(2.0)	7(1.5)	0.81 <sup>d</sup>
NIV, No. (%)	3(2.6)	5(2.2)	9(3.6)	20(4.3)	0.52 <sup>c</sup>
Vasopressor, No. (%)	0(0.0)	0(0.0)	1(0.40)	5(1.1)	0.41 <sup>d</sup>
Chest xray, No. (%)	15(12.9)	35(15.6)	37(14.6)	59(12.7)	0.73 <sup>c</sup>
Blood culture, No. (%)	2(1.7)	3(1.3)	2(0.79)	4(0.86)	0.73 <sup>d</sup>
Respiratory culture, No. (%)	2(1.7)	8(3.6)	11(4.3)	12(2.6)	0.46 <sup>c</sup>
Proton pump inhibitors, No. (%)	57(49.1)	85(37.9)	117(46.2)	188(40.5)	0.10 <sup>c</sup>
<b>Outcomes</b>					
14-day mortality, No. (%)	4(3.4)	6(2.7)	4(1.6)	12(2.6)	0.71 <sup>d</sup>
Late ICU (day5+), No. (%)	2/111(1.8)	1/214(0.47)	4/243(1.7)	2/446(0.45)	0.26 <sup>c</sup>
Length of Stay, median[q1, q3]	4.0[3.0,6.0]	4.0[3.0,6.0]	4.0[3.0,7.0]	4.0[3.0,6.0]	0.053 <sup>b</sup>
Costs, median[q1, q3]	6087.9[4361.6,10846.9]	6778.3[4918.6,9316.2]	7944.7[5491.9,1853.9]	7538.4[5558.2,10759.9]	<b>&lt;0.001<sup>b</sup></b>

p-values: a=ANOVA, b=Kruskal-Wallis test, c=Pearson's chi-square test, d=Fisher's Exact test.

### Hospital level outcomes

There were no discernible trends in 14-day mortality, late ICU transfer or median length of stay across the four quartiles of de-escalation to suggest increased use of de-escalation had compromised patient outcomes. In-hospital 14-day mortality was 3.4% in hospitals in the first quartile, 2.7% in second quartile and 1.6% in the third and 2.6% in the highest quartiles of de-escalation. However, the hospital median costs were significantly different across the quartiles with median of USD 6087 for hospitals in the first quartile, USD 7538 in the highest quartile of de-escalation.