

**Table S1: Variables considered for confounding or effect modification of the relationship between hospital mortality and antibiotic timing**

Variables considered for adjustment in the generalized estimating equation population averaged logistic regression model <sup>1</sup>	
1. Nosocomial	27. Meningitis
2. Number of antibiotics given	28. Catheter
3. Ward	29. Device
4. ICU	30. Other infection
5. Europe	31. Renal organ failure
6. South America	32. Hepatic organ failure
7. Ward/Europe interaction	33. Hematologic organ failure
8. Ward/South America interaction	34. Pulmonary organ failure
9. ICU/Europe interaction	35. Mechanical ventilation (MV)
10. ICU/South America interaction	36. Pulmonary organ failure/MV interaction
11. Cardiovascular organ fail, yes	37. 2 baseline organ failures
12. Lactate >4 in 6 hours	38. 3 baseline organ failures
13. Map $\geq$ 65 mm Hg with pressors	39. 4 baseline organ failures
14. Map $\geq$ 65 mm Hg not applicable	40. 5 baseline organ failures
15. Received rhAPC	41. Hyperthermia
16. rhAPC not applicable	42. Hypothermia
17. Received low dose steroids	43. Chills with rigors
18. Low dose steroids not applicable	44. Tachycardia
19. CVP > 8 mm Hg	45. Tachypnea
20. ScvO <sub>2</sub> $\geq$ 70%	46. Leukopenia
21. Hypotensive, only	47. Hyperglycemia
22. Lactate > 4 hours and hypotensive	48. Measure lactate with 6 hours
23. Median glucose	49. Blood cultures before ABX
24. Pneumonia	50. Broad spectrum antibiotic
25. UTI	51. Glucose control
26. Abdominal	52. Septic shock vs. severe sepsis

<sup>1</sup> If a particular value of a variable is not mentioned in the table it is due to it being the referent group. For example the referent group for nosocomial infection is community acquired infection.