Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Pairwise Correlation Between Individual SEP-1 Sepsis Bundle Components for Patients with Community-onset Sepsis and Hospital-onset Sepsis

Community-Onset Sepsis					
	Blood cultures	Lactate	Antibiotics	IV Fluids	2 nd Lactate
Lactate	0.57				
Antibiotics	0.61	0.42			
IV Fluids	-0.037	-0.045	-0.022		
2 nd Lactate	0.065	0.045	0.029	-0.12	
Vasopressors	0.01	0.012	-0.015	0.012	0.024
		Hospital-C	Onset Sepsis		
	Blood cultures	Lactate	Antibiotics	IV Fluids	2 nd Lactate
Lactate	0.33				
Antibiotics	0.66	0.28			
IV Fluids	-0.038	-0.10	-0.0396		
2 nd Lactate	0.068	0.036	0.098	-0.031	
Vasopressors	0.005	0.015	0.082	0.082	-0.001

Legend: Community-onset sepsis was defined by time zero of sepsis occurring in the emergency department. Hospital-onset sepsis was defined by time zero of sepsis occurring on an inpatient

unit even if signs or symptoms of sepsis preceded admission.

eTable 2. Relative Risk of In-hospital Mortality Associated with Clinical Variables in the Raw Cohorts with Community-onset and Hospital-onset Sepsis

	Community-	Onset Sepsis	Hospital-O	nset Sepsis
	n = 4	1108	n=2	296
	Relative Risk	p-value	Relative Risk	p-value
Age in years	1.01	< 0.001	1.01	0.001
ECI	1.06	< 0.001	1.08	< 0.001
Female	1.03	0.60	1.08	0.36
Postoperative	1.21	0.35	1.05	0.69
Pneumonia POA	1.41	< 0.001	1.19	0.09
UTI POA	0.66	< 0.001	0.68	0.002
SSTI POA	0.83	0.21	0.93	0.70
New Bacteremia	1.04	0.66	1.28	0.032
Immunosuppressed	1.25	0.005	1.26	0.008
Fever	0.47	< 0.001	0.64	< 0.001
Septic Shock	1.84	< 0.001	1.27	0.005
- Hypotension	0.92	0.26	0.97	0.73
- Elevated Lactate	0.83	0.033	1.25	0.10

Legend: POA, present on admission. UTI, urinary tract infection. SSTI, skin and/or soft tissue infection. Bold font denotes a statistically significant standardized difference for an $\alpha = 0.05$.

eTable 3. Characteristics of the Total Sample Before and After Being Rebalanced on Propensity for Treatment and Observable Characteristics

	Raw Total Sample			Rebala	nced Total S	ample
	Treated	Untreated	SD	Treated	Untreated	SD
Time Zero of Sepsis (Hours*)	8.97	34.3	-0.33	6.55	8.45	-0.025
Age	65.6	63.3	0.13	65.9	66.1	-0.011
Female (%)	43.7	45.3	-0.033	43.6	44.68	-0.003
Elixhauser Comorbidities	4.91	5.14	-0.076	4.84	4.85	-0.003
Postoperative (%)	3.01	9.67	-0.28	1.98	1.98	0
Pneumonia POA† (%)	34.0	25.3	0.19	34.0	34.0	0
Urinary tract infection (%)	25.4	21.2	0.10	26.0	26.0	0
Skin / soft tissue infection (%)	7.99	6.03	0.077	7.88	6.53	0.053
New Bacteremia‡ (%)	14.6	14.5	0.003	14.6	15.8	-0.033
Immunosuppressed (%)	19.2	24.7	-0.13	18.3	18.3	0
Fever (%)	36.8	22.7	0.31	35.5	35.5	0
Septic Shock (%)	27.5	42.7	-0.32	27.2	27.2	0
- Hypotension	35.5	55.0	-0.40	35.8	35.8	0
- Elevated Serum Lactate***	28.7	17.2	0.28	29.1	27.8	0.029
Hospital 1 (%)	9.85	11.6	-0.055	9.49	9.49	0
Hospital 2 (%)	13.5	17.3	-0.10	13.2	13.2	0
Hospital 3 (%)	32.7	41.3	-0.18	32.9	32.9	0
Hospital 4 (%)	43.9	29.9	0.29	44.5	44.5	0

 Legend: SD, standardized difference. POA, present on admission. Bold font denotes a statistically significant standardized difference for an $\alpha=0.05$. * Hours from admission. † Pneumonia POA was determined by diagnosis codes. ‡ New bacteremia was defined by positive blood culture after time zero of sepsis in a patient who did not have a positive blood culture in the preceding week. Possible skin contaminants were excluded. *** Elevated serum lactate was defined as a value of >20 mmol/L at time of onset of sepsis or in the preceding 6 hours. To meet the definition of shock, serum lactate needed to be 4 mmol/L or greater.

eTable 4. Relative Risk of In-hospital Mortality Associated with Clinical Variables in the Raw Total Sample

	Relative Risk	95% Confidence Interval	p-value
SEP-1 Sepsis Bundle	0.99	(0.88, 1.12)	0.88
Hospital-Onset of Sepsis	1.05	(0.94, 1.17)	0.381
Age in years*	1.01	(1.01, 1.01)	< 0.001
Female	1.06	(0.96, 1.17)	0.28
Elixhauser Comorbidities*	1.07	(1.05, 1.08)	< 0.001
Postoperative	1.35	(0.88, 1.30)	0.48
Pneumonia POA	1.35	(1.21, 1.50)	< 0.001
Urinary Tract infection POA	0.67	(0.58, 0.77)	< 0.001
Skin / soft tissue infection POA	0.85	(0.68, 1.06)	0.16
New Bacteremia	1.12	(0.98, 1.28)	0.10
Immunosuppressed	1.25	(1.11, 1.40)	< 0.001
Fever	0.51	(0.44, 0.59)	< 0.001
Septic Shock	1.55	(1.40, 1.72)	< 0.001

Legend: POA, present on admission. * Relative risk is reported for incremental increase in 1 year of age or 1 additional Elixhauser comorbidity.

eTable 5. Results from Endogenous Treatment Effects Models Compared with Unweighted/Unbalanced Regression

Treatment		ATET	NATE
SEP-1	MD	+0.10	-0.23
	VD	+0.26	-0.60
Blood Cultures	MD	-5.01	+0.97
	VD	-0.44	-0.28
Serum Lactate	MD	-2.68	+1.26
	VD	-0.004	+0.28
Antibiotics	MD	-3.83	-1.03
	VD	-0.45	-0.27
IV Fluids	MD	-0.57	+2.64
	VD	-0.23	-010

Legend: ATET, average treatment effect on the treated. NATE, naïve (i.e., unweighted / unbalanced) treatment effect. MD, Mortality difference calculated as the average difference in probabilities between the treated and untreated (unit is percentage points); VD, vasopressor days; IV, intravenous.

eTable 6. Prespecified Sensitivity Analyses Evaluating Treatment Effect of the Complete SEP-1 Bundle in Different Cohorts*

Subgroup	Mortality Difference†	Vasopressor Days
$Age \ge 65$	-0.01% (-3.88, 3.86)	+0.37 (0.14, 0.60)
Age < 65	+1.94% (-1.37, 5.26)	+0.48 (0.21, 0.75)
Pneumonia POA	-0.96% (-6.70, 4.77)	+0.59 (0.26, 0.92)
No Pneumonia POA	+1.30% (-1.40, 4.00)	+0.32 (0.11, 0.52)
Immunosuppressed	+4.63% (-1.53, 10.8)	+0.86 (0.45, 1.28)
Not Immunosuppressed	-0.61% (-3.42, 2.21)	+0.26 (0.07, 0.45)
New Bacteremia	+1.35% (-5.03, 7.72)	+0.45 (-0.09, 0.99)
No New Bacteremia	+0.23% (-2.62, 3.07)	+0.38 (0.20, 0.57)
Fever	+2.30% (-0.97, 5.56)	+0.33 (0.07, 0.59)
Afebrile	+0.53% (-2.93, 3.99)	+0.40 (0.18, 0.62)
Septic Shock	+2.19% (-3.05, 743)	+0.55 (0.14, 0.97)
Sepsis without Shock	-0.38% (-3.58, 2.82)	0.01 (-0.16, 0.19)

Legend: SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Dedicated propensity and outcomes models were run within the subgroup of interest. Subgroup analyses excluded all encounters from outside the subgroup. † Difference in probability of in-hospital death was estimated as the average treatment effect on the treated and is expressed in percentage points.

eTable 7. Treatment Effects of SEP-1 Bundle Components in Different Cohorts*

		Blood Cultures	Lactate	Antibiotics	IV Fluids†
Age ≥ 65	MD	-9.58 (-200, 0.86)	-3.51 (-9.06, 2.03)	-3.84 (-8.81, 1.14)	-3.83 (-12.2, 4.51)
n = 2459	VD	-0.88 (-1.69, -0.07)	0.15 (-0.28, 0.59)	-0.42 (-0.82, -0.01)	-0.18 (-0.86, 0.49)
Age < 65	MD	-2.37 (-8.19, 3.45)	-1.18 (-5.73, 3.38)	1.40 (-2.60, 5.40)	5.61 (-1.02, 12.2)
n = 2854	VD	-0.48 (-1.00, 0.04)	-0.06 (-0.47, 0.35)	-0.18 (-0.54, 0.18)	-0.13 (-0.83, 0.57)
Pneumonia POA	MD	-10.3 (-25.5, 4.91)	-2.41 (-11.0, 6.18)	-3.38 (-10.9, 4.13)	1.95 (-15.9, 19.8)
n = 1613	VD	-0.26 (-0.90, 0.85)	0.31 (-0.31, 0.94)	-0.08 (-0.63, 0.46)	-0.14 (-1.72, 1.44)
No Pneumonia POA	MD	-2.75 (-8.01, 2.50)	-2.27 (-6.43, 1.88)	-3.60 (-8.00, 0.82)	-2.61 (-8.83, 3.62)
n = 3975	VD	-0.58 (-1.08, -0.07)	-0.09 (-0.44, 0.27)	-0.61 (-0.99, -0.22)	-0.35 (-0.90, 0.21)
Immunosuppressed	MD	-3.60 (-14.7, 7.50)	-1.21 (-10.3, 7,85)	0.08 (-8.32, 8.47)	12.4 (-3.59, 28.4)
n = 1376	VD	-0.24 (-0.99, 0.50)	0.25 (-0.40, 0.89)	-0.75 (-1.50, -0.001)	0.22 (-1.46, 1.91)
Non-	MD	-5.76 (-13.0, 1.47)	-3.01 (-7.39, 1.36)	-4.01 (-8.02, 0.01)	-1.97 (-8.18, 4.24)
immunosuppressed n = 4352	VD	-0.79 (-1.42, -0.16)	-0.03 (-0.38, 0.31)	-0.38 (-0.70, -0.06)	-0.43 (-0.97, 0.11)
New Bacteremia	MD	-13.9 (-28.4, 0.53)	-4.98 (-18.1, 8.12)	-4.33 (-12.5, 3.81)	-1.43 (-19.5, 16.6)
n = 738	VD	-2.11 (-3.53, -0.69)	-0.24 (-1.22, 0.74)	-1.34 (-2.08, -0.60)	-0.07 (-1.71, 1.58)
No New Bacteremia	MD	-2.34 (-8.40, 3.73)	-2.11 (-6.13, 1.92)	-2.80 (-6.38, 0.77)	-0.04 (-6.22, 6.14)
n = 5476	VD	-0.28 (-0.76, 0.21)	0.18 (-0.15, 0.51)	-0.20 (-0.49, 0.09)	-0.16 (-0.71, 0.39)
Fever	MD	0.23 (-17.3, 17.7)	-4.62 (-14.0, 4.72)	-2.03 (-8.54, 4.48)	3.60 (-3.70, 10.9)
n = 1722	VD	0.81 (-0.26, 1.87)	0.02 (-0.66, 0.69)	-0.25 (-0.77, 0.28)	0.28 (-0.68, 1.24)
Afebrile	MD	-5.22 (-11.1, 0.64)	-3.47 (-7.92, 0.98)	-2.77 (-6.69, 1.14)	0.47 (-7.05, 7.98)
n = 4225	VD	-0.61 (-1.08, -0.15)	0.01 (-0.31, 0.34)	-0.38 (-0.69, -0.06)	-0.36 (-1.03, 0.32)
Septic Shock	MD	-4.58 (-14.5, 5.29)	-3.39 (-12.9, 6.20)	-6.54 (-13.7, 0.61)	-6.30 (-14.5, 1.94)
n = 2248	VD	-0.55 (-1.50, 0.40)	0.11 (-0.62, 0.83)	-0.45 (-1.00, 0.10)	-0.61 (-1.32, 0.11)
Sepsis without Shock	MD	-6.42 (-13.0, 0.11)	-3.63 (-7.95, 0.68)	-2.45 (-5.99, 1.10)	2.66 (-6.58, 11.9)
n = 3164	VD	-0.36 (-0.71, -0.003)	-0.17 (-0.47, 0.13)	-0.11 (-0.31, 0.08)	0.19 (-0.40, 0.79)

Legend: MD, Mortality difference calculated as the average difference in probabilities between the treated and untreated (unit is percentage points); VD, vasopressor days; 95% CI, 95% confidence interval. POA, present on admission. * Dedicated propensity and outcomes models were run within the subgroup of interest. Subgroup analyses excluded all encounters from outside the subgroup. † Only measured among individuals in whom intravenous fluids were indicated based on SEP-1 guidance

eTable 8. Treatment Effects of SEP-1 Sepsis Bundle and Components on 30-day In-hospital Mortality in Total Sample and Rebalanced Cohorts with Community-onset & Hospital-onset Sepsis

	Total Sample	Community-Onset Sepsis	Hospital-Onset Sepsis
Risk Difference		Risk Difference*	Risk Difference*
	(95% CI)	(95% CI)	(95% CI)
SEP-1 Bundle	+0.49 (-1.93, 2.90)	+0.67 (-2.16, 3.49)	+0.91 (-5.29, 7.11)
Blood cultures	-5.13 (-11.0, 0.74)	-5.98 (-15.2, 3.25)	-2.43 (-8.31, 3.45)
Serum Lactate	-1.86 (-5.63, 1.92)	-5.76 (-12.4, 0.88)	+0.44 (-4.94, 4.06)
Antibiotics	-3.78 (-7.67, 0.11)	-3.72 -8.90, 1.47)	-4.12 (-8.99, 0.74)
Intravenous Crystalloid	+1.14 (-4.07, 6.36)	+0.84 (-5.91, 7.59)	-4.63 (-15.1, 5.84)

Legend: 95% CI, 95% confidence interval. SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Mortality is expressed as an absolute probability difference between the average of the treated and the average of the untreated, expressed in terms of percentage points.

eTable 9. Treatment Effects of SEP-1 Sepsis Bundle and Components on Hospital Length of Stay (Measured from Time Zero of Sepsis Until Discharge)

	Total Sample	Community-Onset Sepsis	Hospital-Onset Sepsis
	Length of Stay*	Length of Stay*	Length of Stay*
	(95% CI)	(95% CI)	(95% CI)
SEP-1 Bundle	-0.54 (-1.41, 0.33)	-0.79 (-1.93, 0.35)	-1.08 (-3.42, 1.27)
Blood cultures	-0.05 (-1.78, 1.69)	+1.43 (-0.72, 3.58)	-1.35 (-3.99, 1.28)
Serum Lactate	-0.28 (-1.43, 0.87)	-0.47 (-2.63, 1.69)	-0.99 (-2.84, 0.85)
Antibiotics	+0.26 (-0.65, 1.17)	+0.78 (-0.38, 1.93)	+0.42 (-1.28, 2.12)
Intravenous Crystalloid	-1.15 (-2.86, 0.55)	-0.71 (-2.73, 1.30)	+1.49 (-1.41, 4.38)

Legend: 95% CI, 95% confidence interval. SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Length of stay is expressed in days from time zero of sepsis until discharge.

eTable 10. Treatment Effects of SEP-1 Sepsis Bundle and Components on Composite Outcome of In-hospital Mortality or Discharge to Hospice

	Total Sample	Community-Onset Sepsis	Hospital-Onset Sepsis
	Risk Difference*	Risk Difference*	Risk Difference*
	(95% CI)	(95% CI)	(95% CI)
SEP-1 Bundle	-0.43 (-3.37, 2.52)	+0.08 (-3.39, 3.23)	-2.97% (-9.91, 3.96)
Blood cultures	-5.00 (-11.0, 1.04)	-10.2% (-19.3, -1.01)	+0.31% (-5.88, 6.49)
Serum Lactate	-1.35 (-5.28, 2.58)	-6.14 (-13.3, 1.01)	-1.01% (-5.96, 3.94)
Antibiotics	-3.58 (-7.52, 0.36)	-3.16 (-8.40, 2.08)	-4.78% (-9.70, 0.14)
Intravenous Crystalloid	-2.18 (-7.74, 3.38)	-4.23 (-11.6, 3.10)	-6.08 (-17.4, 5.25)

Legend: 95% CI, 95% confidence interval. SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Risk differences were estimated as the average treatment effect on the treated and are expressed in terms of percentage points.

eTable 11. Treatment Effects of SEP-1 Sepsis Bundle and Components in Rebalanced Cohorts with Sepsis Presenting on the Inpatient Ward or Intensive Care Unit

	Ward-Onset Sepsis		ICU-Onse	et Sepsis
	(n = 9)	87)	(n = 1,128)	
	Mortality Risk Difference*	95% CI	Mortality Risk Difference*	95% CI
SEP-1 Bundle	+1.70	(-15.2, 18.6)	-0.50	(-11.2, 10.2)
Blood cultures	-8.11	(-19.3, 3.04)	-1.78	(-12.6, 9.11)
Serum Lactate	+3.45	(-5.75, 12.6)	-1.30	(-10.2, 7.5)
Antibiotics	-5.79	(-14.1, 2.54)	-5.81	(-14.4, 2.83)
Intravenous Crystalloid	Utd	Utd	-4.76	(-21.6, 12.1)
	Vasopressor Days*	95% CI	Vasopressor Days*	95% CI
SEP-1 Bundle	+0.53	(-0.16, 1.22)	1.07	(0.14, 2.00)
Blood cultures	+0.29	(-0.22, 0.81)	-0.33	(-1.23, 0.57)
Serum Lactate	+0.70	(0.01, 1.40)	+0.34	(-0.34, 1.02)
Antibiotics	+0.29	(-0.11, 0.70)	-0.22	(-0.93, 0.49)
Intravenous Crystalloid	Utd	Utd	+0.35	(-0.93, 1.63)

Legend: ICU, intensive care unit. Utd, unable to determine. 95% CI, 95% confidence interval. SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Differences in probability of in-hospital mortality and days spent on vasopressors were estimated as the average treatment effect on the treated. Mortality risk difference was expressed in terms of percentage points.

eTable 12. Treatment Effects of SEP-1 Sepsis Bundle and Components in Rebalanced Cohorts with Time Zero of Sepsis <48 or >48 Hours After Arrival

	Time Zero < 48 Hours		Time Zero >	48 Hours
	After Arrival		After Arrival	
	Mortality Risk Difference*	95% CI	Mortality Risk Difference*	95% CI
SEP-1 Bundle	+0.16	(-2.39, 2.72)	1.26	(-22.3, 24.8)
Blood cultures	-6.08	(-13.0, 0.85)	-4.16	(-15.1, 6.81)
Serum Lactate	-5.26	(-9.82, -0.70)	+7.77	(-4.80, 20.3)
Antibiotics	-4.33	(-8.33, -0.32)	-5.67	(-16.1, 4.79)
Intravenous Crystalloid	-0.92	(-7.29, 5.46)	+34.2	(-15.2, 84.4)
	Vasopressor Days*	95% CI	Vasopressor Days*	95% CI
SEP-1 Bundle	+0.37	(-0.02, 0.03)	0.13	(-1.38, 1.64)
Blood cultures	-0.64	(-1.19, -0.09)	-0.28	(-1.20, 0.64)
Serum Lactate	-0.10	(-0.45, 0.25)	0.82	(-0.04, 1.69)
Antibiotics	-0.45	(-0.77, -0.12)	-0.48	(-1.44, 0.48)
Intravenous Crystalloid	-0.48	(-1.00, 0.05)	0	(0, 0)

Legend: 95% CI, 95% confidence interval. SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Differences in probability of inhospital mortality and days spent on vasopressors were estimated as the average treatment effect on the treated. Mortality risk difference was expressed in terms of percentage points.

eTable 13. Post Hoc Sensitivity Analyses

	Admitted from Home (n = 3732 matched)		Source Other than Home (n = 2077 matched)	
	Mortality Risk Difference*	95% CI	Mortality Risk Difference*	95% CI
SEP-1 Bundle	-0.04	(-3.13, 3.05)	1.33	(-3.31, 5.97)
Blood cultures	-0.59	(-5.99, 4.82)	-7.63	(-16.4, 1.14)
Serum Lactate	-4.27	(-9.70, 1.17)	-4.46	(-11.6, 2.68)
Antibiotics	-2.66	(-6.93, 1.62)	-5.28	(-11.5, 0.91)
Intravenous Crystalloid	-3.02	(-10.2, 4.21)	0.32	(-6.23, 6.87)
	Vasopressor Days	95% CI	Vasopressor Days	95% CI
SEP-1 Bundle	0.33	(0.13, 0.54)	0.59	(0.27, 0.90)
Blood cultures	-0.54	(-1.12, 0.04)	-0.40	(-1.03. 0.23)
Serum Lactate	0.02	(-0.38, 0.41)	0.01	(-0.55, 0.58)
Antibiotics	-0.45	(-0.79, -0.10)	-0.09	(-0.51, 0.33)
Intravenous Crystalloid	-0.51	(-1.15, 0.14)	-0.10	(-0.65, 0.45)
		. , , ,	0.1-0	(0.00, 0.10)
	Malignand	y Absent	Malignand	y Present
	Malignano (n = 4521 1	y Absent	Malignand (n = 978 r	y Present
	Malignand	y Absent	Malignand	y Present
SEP-1 Bundle	Malignano (n = 4521 1 Mortality Risk	ey Absent matched)	Malignand (n = 978 r Mortality Risk	y Present natched)
	Malignand (n = 4521 material Mortality Risk Difference*	y Absent matched) 95% CI	Malignand (n = 978 r Mortality Risk Difference*	y Present natched) 95% CI
SEP-1 Bundle	Malignand (n = 4521 mag) Mortality Risk Difference*	y Absent matched) 95% CI (-1.60, 3.83)	Malignand (n = 978 r Mortality Risk Difference* -1.23	y Present natched) 95% CI (-8.81, 6.35)
SEP-1 Bundle Blood cultures	Malignand (n = 4521 mag) Mortality Risk Difference* 1.11 -6.01	95% CI (-1.60, 3.83) (-12.6, 0.60)	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46	y Present natched) 95% CI (-8.81, 6.35) (-21.8, 4.92)
SEP-1 Bundle Blood cultures Serum Lactate	Malignand (n = 4521 i Mortality Risk Difference* 1.11 -6.01 -0.66	95% CI (-1.60, 3.83) (-12.6, 0.60) (-4.59, 3.28)	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46 -10.0	95% CI (-8.81, 6.35) (-21.8, 4.92) (-22.0, 0.10)
SEP-1 Bundle Blood cultures Serum Lactate Antibiotics	Malignano (n = 4521 magnetics) Mortality Risk Difference* 1.11 -6.01 -0.66 -3.89	95% CI (-1.60, 3.83) (-12.6, 0.60) (-4.59, 3.28) (-8.04, 0.26)	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46 -10.0 0.69	y Present natched) 95% CI (-8.81, 6.35) (-21.8, 4.92) (-22.0, 0.10) (-8.58, 9.96)
SEP-1 Bundle Blood cultures Serum Lactate Antibiotics	Malignand (n = 4521 i Mortality Risk Difference* 1.11 -6.01 -0.66 -3.89 0.32 Vasopressor	y Absent matched) 95% CI (-1.60, 3.83) (-12.6, 0.60) (-4.59, 3.28) (-8.04, 0.26) (-6.23, 6.87)	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46 -10.0 0.69 -2.01 Vasopressor	y Present natched) 95% CI (-8.81, 6.35) (-21.8, 4.92) (-22.0, 0.10) (-8.58, 9.96) (-16.1, 12.0)
SEP-1 Bundle Blood cultures Serum Lactate Antibiotics Intravenous Crystalloid	Malignand (n = 4521 i Mortality Risk Difference* 1.11 -6.01 -0.66 -3.89 0.32 Vasopressor Days*	y Absent matched) 95% CI (-1.60, 3.83) (-12.6, 0.60) (-4.59, 3.28) (-8.04, 0.26) (-6.23, 6.87) 95% CI	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46 -10.0 0.69 -2.01 Vasopressor Days*	y Present natched) 95% CI (-8.81, 6.35) (-21.8, 4.92) (-22.0, 0.10) (-8.58, 9.96) (-16.1, 12.0) 95% CI
SEP-1 Bundle Blood cultures Serum Lactate Antibiotics Intravenous Crystalloid SEP-1 Bundle	Malignand (n = 4521 i Mortality Risk Difference* 1.11 -6.01 -0.66 -3.89 0.32 Vasopressor Days* 0.46	95% CI (-1.60, 3.83) (-12.6, 0.60) (-4.59, 3.28) (-8.04, 0.26) (-6.23, 6.87) 95% CI (0.27, 0.65)	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46 -10.0 0.69 -2.01 Vasopressor Days* 0.17	y Present natched) 95% CI (-8.81, 6.35) (-21.8, 4.92) (-22.0, 0.10) (-8.58, 9.96) (-16.1, 12.0) 95% CI (-0.32, 0.66)
SEP-1 Bundle Blood cultures Serum Lactate Antibiotics Intravenous Crystalloid SEP-1 Bundle Blood cultures	Malignand (n = 4521 i Mortality Risk Difference* 1.11 -6.01 -0.66 -3.89 0.32 Vasopressor Days* 0.46 -0.40	y Absent matched) 95% CI (-1.60, 3.83) (-12.6, 0.60) (-4.59, 3.28) (-8.04, 0.26) (-6.23, 6.87) 95% CI (0.27, 0.65) (-0.86, 0.06)	Malignand (n = 978 r Mortality Risk Difference* -1.23 -8.46 -10.0 0.69 -2.01 Vasopressor Days* 0.17 -0.78	y Present natched) 95% CI (-8.81, 6.35) (-21.8, 4.92) (-22.0, 0.10) (-8.58, 9.96) (-16.1, 12.0) 95% CI (-0.32, 0.66) (-1.84, 0.29)

Legend: 95% CI, 95% confidence interval. SEP-1 refers to the Early Management Bundle for Severe Sepsis / Septic Shock (National Quality Forum #0500). * Differences in probability of inhospital mortality and days spent on vasopressors were estimated as the average treatment effect on the treated. Mortality risk difference was expressed in terms of percentage points.