

Three-Hour Bundle Compliance and Outcomes in Patients With Undiagnosed Severe Sepsis

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e-Table 1: Infection ICD-9 diagnosis codes

To define severe sepsis criteria, we followed a modified Angus method requiring a diagnosed infection + ≥ 2 sites of acute organ dysfunction. The ICD-9 diagnosis codes for infection listed below are based on definitions set forth by the American College of CHEST Physicians/Society of Critical Care Medicine Consensus definitions.

ICD9 Codes	ICD-9 Code Description
001.0 - 139.99	Infectious & parasitic Infections
320.0 - 326.99	Meningitis, encephalitis, abscess, phlebitis and thrombophlebitis
038.0 - 038.9	Septicemia*
420.0 - 421.9	Acute pericarditis and endocarditis
451.0 - 451.9	Phlebitis and thrombophlebitis
461.0 - 465.9	Sinusitis, pharyngitis, tonsillitis, URI's, laryngitis, bronchitis, and bronchiolitis
481 - 482.9 485 - 486	Pneumonia and bronchopneumonia
491.21	Obstructive chronic bronchitis with (acute) exacerbation
494.0 - 494.1	Bronchiectasis
510 - 510.9	Empyema
513 - 513.1	Abscess of lung or mediastinum
540.0, 540.1, 540.9 - 542, 566	Appendicitis
562.01-562.11	Diverticulitis of small intestine (without hemorrhage)
562.13	Changes in vascular appearance of retina
567.0 - 567.9	Peritonitis
569.5 - 569.83	Abscess or perforation of intestine
572.0 - 572.1	Abscess of liver
575	Cholecystitis
590.0 - 590.9	Chronic pyelonephritis
599	UTI/Urethral infection
601 - 601.9	Prostatitis
614	Acute salpingitis and oophoritis
616.9	Unspecified inflammatory disease of cervix vagina and vulva
670.00- 670.04	Major puerperal infection
681 - 681.9	Cellulitis, abscess, onychia, and paronychia of digits
686 - 686.1	Pyoderma
686.8 - 686.9	Other local infections, skin & subcutaneous
711.00- 711.99	Arthritis
730.00 -730.99	Osteomyelitis
790.7	Bacteremia
996.6 - 996.69	Infection and inflammatory reaction due to device implant and graft
998.51	Infected post-operative seroma
998.59	Acute reaction to foreign substance accidentally left during a procedure
999.3	Infection due to central venous catheter

*According to ICD-9: "Septicemia, assigned code 038.x, is a systemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood, which can include bacteria, viruses, fungi or other organisms. Effective with discharges of December 15, 2003, per Coding Clinic, fourth quarter 2003, septicemia no longer equates with sepsis."

e-Table 2: Criteria for Acute Organ Dysfunctions

To define severe sepsis, we followed a modified Angus method requiring a diagnosed infection + ≥ 2 sites of acute organ dysfunction. The ICD-9 diagnosis codes for acute organ dysfunction, as well as acute dysfunction identified by abnormal first laboratory data (listed below) are based on definitions set forth by the American College of CHEST Physicians/Society of Critical Care Medicine Consensus definitions.

Organ System*	Physiological/Lab Markers	Threshold Value	ICD-9 Description & Code
Neurological	Glasgow Coma Scale	< 15	Encephalopathy Unspecified 384.30 Metabolic Encephalopathy, 348.31 Other Encephalopathy 348.30 Transient Mental Disorder 293.9 Anoxic Brain Damage, 348.1
Hematological	Partial Thromboplastin Time Platelet Count INR D-dimer	> 60 sec < 100,000/ μ L > 1.5 > 230	Defibrination Syndrome, 286.6 Thrombocytopenia, 287.5 Secondary Thrombocytopenia, 287.4 Other and unspecified coagulation defects, 286.9
Respiratory	Arterial O ₂ saturation PaO ₂	< 90% < 70%	Acute respiratory failure 518.81
Cardiovascular	Systolic Blood pressure MAP Received a vasopressor**	< 90 mmHg < 65 mmHg	Hypotension 458.0 Shock w/o trauma 785.5 Septic Shock 785.52 Other shock, no trauma 785.59
Hepatic	Bilirubin, total ALT AST	> 2 mg/dL > 90 U/L > 90 U/L	Acute and subacute necrosis of the liver, 570 Hepatic infarction 573.4
Renal	Creatinine	>2 mg/dL	Oliguria and anuria, 788.5 Acute Kidney Failure, 584
Lactic acidosis	Lactate	>2mmol/L	

*Required 2 or more different organ systems be compromised, from any combination of the 7 systems listed, plus one ICD-9 infection code to meet criteria for severe sepsis. All lab values were sorted by first measurement date and only included as an acute organ dysfunction if it met threshold.

**Vasopressor types for cardiovascular dysfunction included dobutamine, dopamine, norepinephrine, epinephrine, vasopressin, or phenylephrine.

e-Table 3: Surviving Sepsis Campaign 3-hour treatment completion rates for patients with severe sepsis.

Bundle Protocol Component	Overall Cohort	Patients with sepsis specific ICD-9 code 995.92	Patients without sepsis specific ICD-9 code 995.92	P value*
	n=5631	n=1847 (32.8%)	n=3784 (67.2%)	
All 4 components	491 (8.72%)	189 (10.2%)	302 (7.98%)	p<0.005
Therapeutic Components*	1764 (31.3%)	665 (36.0%)	1099 (29.0%)	p<0.001
Blood culture	3483 (61.9%)	1411 (76.3%)	2072 (54.8%)	p<0.001
Lactate measured within 3 hours	1589 (28.2%)	541 (29.3%)	1048 (27.7%)	p=0.23
Broad spectrum given under three hours	2087 (37.1%)	801 (43.4%)	1286 (34.0%)	p<0.001
Antimicrobial given under three hours	2593 (46.1%)	1010 (54.7%)	1583 (41.8%)	p<0.001
First antimicrobial given was broad spectrum	4271 (75.8%)	1402 (75.9%)	2869 (75.8%)	p=0.97
Time to antimicrobial (mean hours ± SD)	3.70 ± 1.96	3.27 ± 1.87	3.91 ± 1.96	p<0.001
Appropriate Fluids *	4825 (85.7%)	1549 (83.9%)	3276 (86.6%)	p<0.001
Patients with a need for fluids*	928 (16.5%)	371 (20.1%)	557 (14.8%)	p<0.001
Fluids given at 30mL/Kg among those only with a need	133(14.3%)	74 (19.6%)	59 (10.6%)	p<0.001

*All p values less than 0.001 were rounded and reported p<0.001.

*Therapeutic components were defined as receiving both a broad spectrum antibiotic and appropriate IV fluid within 3 hours of triage. Appropriate fluid was defined as crystalloid IV fluids given at a rate of 30mL/kg, within 2.5 hours of triage if the patient was hypotensive or had a lactate >4, or appropriately not given if the patient had no need for fluids based on MAP and lactate values. Following the SCCM definitions, a need for fluids was met if the first MAP was < 70mmHg or the first serum lactate ≥ 4 mmol/L.

e-Table 4: Multivariate logistic regression model of adjusted odds ratios for receiving therapeutic components of the bundle protocol.

Overall model choice was based on using Hosmer and Lemeshow Goodness-of-Fit Test where a higher p value indicates significance, (Chi-squared value, 8.24, p=0.410).

Predictors of receiving therapeutic components of treatment in final model	Adjusted Odds Ratios	95% Confidence Interval
Age	1.01	1.00-1.01
Sepsis specific ICD-9 diagnosis code 995.52	1.22	1.10 – 1.36
Respiratory Infections	1.60	1.42 – 1.78
Respiratory Dysfunction	1.25	1.12 – 1.40

e-Table 5: Multivariate logistic regression model of adjusted odds ratios for 30-day mortality.

Overall model choice was based on using Hosmer and Lemeshow Goodness-of-Fit Test where a higher p value indicates significance, (Chi-squared value, 7.14, p=0.41).

Predictors of Mortality	Adjusted Odds Ratios	95% Confidence Interval
Organ Dysfunction Score	1.85	1.66-2.08
Presence of Sepsis specific ICD-9 diagnosis code 995.52	2.53	1.89-3.39
3-Hour Bundle Completed	0.42	0.22-0.80
Broad Spectrum antibiotic given within 3 hours of triage	1.39	1.03-1.86

e-Figure 1: Treatment completion rates for ICD-9 (+) and ICD-9 (-) patients when controlling for the presence of a respiratory infection, n=2516.

