Sepsis Bundle Protocol for the University of California, San Francisco

The sepsis bundle follows five ordered steps:

1. Drawing lactate blood samples within six hours of sepsis onset (if not already done by the bedside nurse)

2. Drawing blood cultures

3. Administering antibiotics within 3 hours of sepsis onset (most common antibiotics include linezolid, meropenem, piperacillin-tazobactan, vancomycin, and cefepime)

4. Administering 30 mL/kg of crystalloid or a colloid equivalent fluid bolus for hypotensive patients or for patients with a lactate level higher than 4 mmol/L

5. Administering a predetermined dose of one or more vasopressors (norepinephrine, dopamine, dobutamine, epinephrine, or vasopressin) to maintain a mean arterial pressure of more than 65 mmHg, if the patient is unresponsive to fluid resuscitation

Table 1. Variables collected by the MLA. Variables in categories (1) and (2) were used to generate an MLA score, and variables in category (3) were used to assess patient outcomes. BUN = Blood Urea Nitrogen, WBC = White Blood Cell, INR = International Normalized Ratio, FiO_2 = Fraction of inspired oxygen.

(1) Data required for prediction	(2) Optional data, used if available	(3) Outcome-related measurements
- Systolic blood pressure - Diastolic blood pressure - Heart rate - Temperature - Respiratory rate SpO_2 - Age	- Glucose - BUN - pH - Creatinine - Lactate FiO_2 - WBC count - INR - Platelets - Bilirubin	- Hospital admission time - Hospital discharge time - ICU admission time - ICU discharge time - In-hospital death indication

Severe Sepsis Gold Standard for Retrospective Identification:

We retrospectively defined a patient as severe septic if they met two of the following SIRS criteria and two of the following organ dysfunction criteria within the same hour.

SIRS criteria are defined as:
1. Heart rate > 90 beats/ min,
2. body temperature > 38 °C or < 36 °C,
3. respiratory rate >20 breaths/min
4. white blood cell count > 12,000 cells/μL or < 4,000 cells/μL.

Organ dysfunction criteria are defined as:
1. Lactate > 2 mmol/L
2. Systolic blood pressure < 90 mmHg
3. Urine output < 0.5 mL/kg, over two hours
4. Creatinine > 2 mg/dL
5. Bilirubin > 2 mg/dL
6. Platelet count < 100,000 μL
7. International normalized ratio > 1.5
8. PaO2 > 0.5

Table 2: ICD-10 codes searched for in the patient EHR to retrospectively determine comorbidities of patients enrolled in the trial. Each terms in quotation marks was independently searched for in the patient record to determine the presence or absence of each comorbidity.

Condition	ICD-10 Search Terms
Sepsis	"R65"
Severe Sepsis	"R652"
Septic Shock	"R6521"
Cardiovascular	"I"
Renal	"N2"
Liver	"K70" through "K77"
Organ Transplant	"Z94"
HIV	"Z21, B20"
Mental Health Disorder	"F1" through "F98"
Diabetes	"E08", "E09", "E10", "E11", "E13"
COPD	"J44"
Cancer	"C" and "D1" through "D49"
Alcohol Abuse	"F10"
Pneumonia	"J12" through "J19"

Table 3: Comparison of sepsis monitoring system study designs and outcomes. The present trial is described in the first row, and is the first RCT to demonstrate statistically significant reductions for in-hospital mortality and length of stay, which are italicized throughout.

| Study | Outcomes Assessed | | Study Design | Algorithm Type | Sepsis Prediction or Detection |
	Statistically Significant (P < .05)	*Not Statistically Significant*			
Shimabukuro et al. (2017), this study	* *Length of stay* * *In-hospital mortality*		Randomized controlled trial	Machine learning-based	Prediction
Semler et al. (2015)		* *In-hospital mortality* * Time to sepsis bundle completion * Days out of ICU * Days off of ventilator	Randomized controlled trial	Rules-based	Detection only
Hooper et al. (2012)		* *Length of stay* * *In-hospital mortality* * Time to antibiotic administration * Amount of fluids administered	Randomized controlled trial	Rules-based	Detection only
Sawyer et al. (2011)	* Intervention within 12 hours * Antibiotic escalation * Fluid administration * Oxygen therapy	* *Length of stay* * *In-hospital mortality*	Observational pilot study	Machine learning-based	Prediction and detection
Berger et al. (2010)	Lactate testing	*In-hospital mortality*	Before-and-after study	Rules-based	Detection only