

# Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock

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**IMPORTANCE** Drug shortages in the United States are common, but their effect on patient care and outcomes has rarely been reported.

**OBJECTIVE** To assess changes to patient care and outcomes associated with a 2011 national shortage of norepinephrine, the first-line vasopressor for septic shock.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective cohort study of 26 US hospitals in the Premier Healthcare Database with a baseline rate of norepinephrine use of at least 60% for patients with septic shock. The cohort included adults with septic shock admitted to study hospitals between July 1, 2008, and June 30, 2013 (n = 27 835).

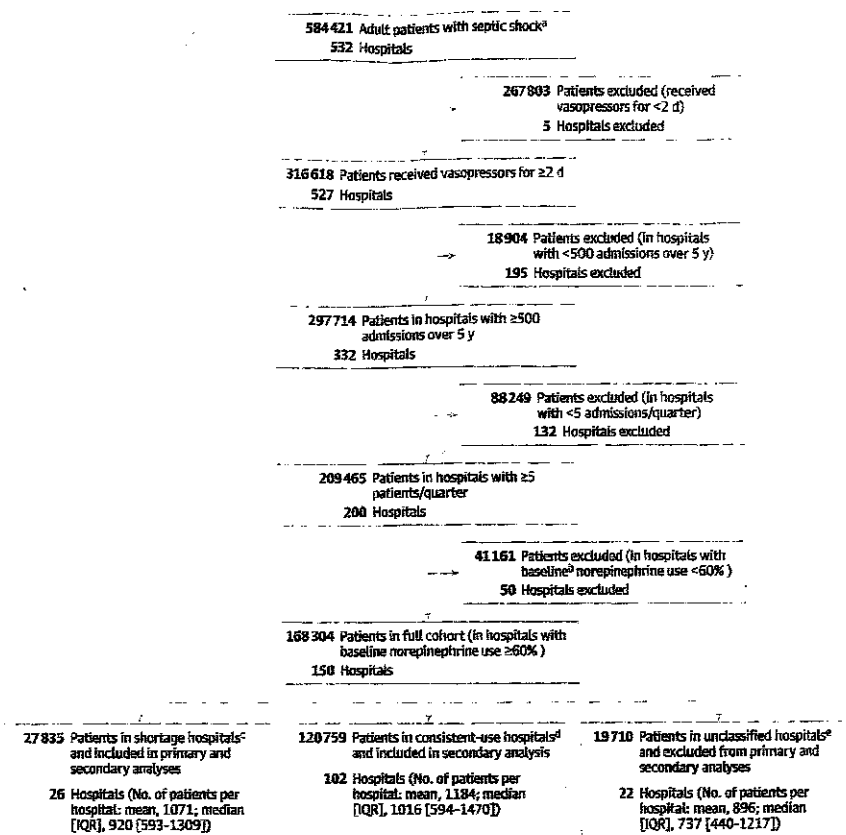
**EXPOSURES** Hospital-level norepinephrine shortage was defined as any quarterly (3-month) interval in 2011 during which the hospital rate of norepinephrine use decreased by more than 20% from baseline.

**MAIN OUTCOMES AND MEASURES** Use of alternative vasopressors was assessed and a multilevel mixed-effects logistic regression model was used to evaluate the association between admission to a hospital during a norepinephrine shortage quarter and in-hospital mortality.

**RESULTS** Among 27 835 patients (median age, 69 years [interquartile range, 57-79 years]; 47.0% women) with septic shock in 26 hospitals that demonstrated at least 1 quarter of norepinephrine shortage in 2011, norepinephrine use among cohort patients declined from 77.0% (95% CI, 76.2%-77.8%) of patients before the shortage to a low of 55.7% (95% CI, 52.0%-58.4%) in the second quarter of 2011; phenylephrine was the most frequently used alternative vasopressor during this time (baseline, 36.2% [95% CI, 35.3%-37.1%]; maximum, 54.4% [95% CI, 51.8%-57.2%]). Compared with hospital admission with septic shock during quarters of normal use, hospital admission during quarters of shortage was associated with an increased rate of in-hospital mortality (9283 of 25 874 patients [35.9%] vs 777 of 1961 patients [39.6%], respectively; absolute risk increase = 3.7% [95% CI, 1.5%-6.0%]; adjusted odds ratio = 1.15 [95% CI, 1.01-1.30]; P = .03).

**CONCLUSIONS AND RELEVANCE** Among patients with septic shock in US hospitals affected by the 2011 norepinephrine shortage, the most commonly administered alternative vasopressor was phenylephrine. Patients admitted to these hospitals during times of shortage had higher in-hospital mortality.

Figure 1. Cohort Creation Diagram for the Study of Norepinephrine Shortage and Septic Shock



IQR indicates interquartile range.

<sup>a</sup> Patients meeting the criteria by Angus and colleagues<sup>13</sup> for severe sepsis and receiving 1 or more vasopressor during hospitalization.

<sup>b</sup> Defined as mean use over the first 8 quarters of the study period.

<sup>c</sup> Hospitals meeting 3 criteria for norepinephrine use patterns consistent with shortage: (1) more than 20% relative decrease in norepinephrine use from baseline in at least 1 quarter of 2011; (2) return to norepinephrine use rates within 10% relative to the baseline rate by the second quarter of 2012; and

(3) no more than 1 quarter of norepinephrine use more than 20% below baseline before or after 2011.

<sup>d</sup> Hospitals with use of norepinephrine that did not decrease by more than 20% in any study quarter of 2011.

<sup>e</sup> Hospitals that did not meet either set of inclusion criteria (ie, had decrease in norepinephrine use during ≥1 quarter of the shortage year, but also had decreases of >20% in norepinephrine use in ≥2 other quarters).