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Cost-Effectiveness Analysis of Early Point-of-Care Lactate Testing in the Emergency Department

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Abstract

Objectives—To determine the cost-effectiveness of implementing a Point-of-Care (POC) Lactate program in the ED for patients with suspected sepsis to identify patients with occult hypoperfusion.

Methods—We constructed a cost-effectiveness model to examine an ED with an average volume of 30,000 patients annually. We evaluated a POC Lactate Program in which patients with SIRS and suspected infection are screened for an elevated lactate ≥ 4 mmol/L. Using the POC program, those with severe sepsis and elevated lactate levels are resuscitated and their lactate clearance is evaluated by serial POC lactate measurements. Patients with adequate lactate clearance are admitted to the general medical floor, whereas those without adequate clearance are admitted to the intensive care unit (ICU). In the base-case we assumed 68% of patients with severe sepsis and an elevated lactate identified in the ED would have adequate lactate clearance to allow for medical floor admission with a 2% overall mortality reduction. The POC Lactate Program was compared with a Usual Care Strategy in which all patients with severe sepsis and an elevated lactate are admitted to the ICU. Costs were estimated from the 2014 Medicare Inpatient and National Physician Fee schedules, and hospital and industry estimates. We conducted one- and two-way sensitivity analyses across pre-determined ranges for each variable.

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Results—In the base-case, an ED with 30,000 visits per year had 5,340 patients with suspected sepsis, of which 207 had severe sepsis and 44 with a lactate ≥ 4 mmol/L. The POC Lactate Program cost \$39.53 to screen each ED patient with suspected sepsis, perform serial lactate testing on those with an elevated lactate, and to admit those with their subsequent admission costs. This was compared with the Usual Care Strategy which had a cost of \$33.20 per patient for lactate testing. In the POC arm, 14 of the 44 patients had inadequate lactate clearance and were admitted to the ICU, and the remaining 30 patients were admitted to a medical floor after adequate lactate clearance. In one year, the POC Program cost an additional \$33,802 and resulted in a total of 1.07 additional quality-adjusted life years (QALYs) spread out over 5,340 patients with suspected sepsis who had lactate measured in the ED. The POC arm had an incremental cost-effectiveness ratio of \$31,590 per QALY gained, well below accepted willingness-to-pay-thresholds.

Conclusions—Implementing a POC Lactate Program for screening ED patients with suspected sepsis is a cost-effective intervention for ED patients to identify severe sepsis responsive to early resuscitation.

INTRODUCTION

Patients commonly present to hospital-based emergency departments (ED) with severe sepsis, with nearly 600,000 cases treated annually in U.S. hospitals, accounting for 1 in 10 admissions to intensive care units (ICU).¹ The term “severe sepsis” applies to patients with a systematic inflammatory response syndrome (SIRS) caused by infection and associated with acute organ dysfunction.² Over the past decade, the ED treatment for severe sepsis has changed dramatically, with greater focus on early identification and early treatment with antibiotics, aggressive fluid resuscitation, use of vasopressors, and frequent re-evaluation.

Because of the time-sensitive nature of severe sepsis, early recognition is central to effective resuscitation. While some cases of severe sepsis are clinically apparent upon ED arrival, others cases are clinically occult and associated with delayed recognition.³ One of the key ways to identify patients with occult severe sepsis is the use of blood lactate testing.^{4–6} A high blood lactate can indicate tissue hypoperfusion, and the need for more urgent interventions.^{4–6} Further, serial lactate testing can risk-stratify patients based on initial response to resuscitation efforts as measured by a patient’s lactate clearance.^{7–10} Lactate clearance is defined as the percent decrease in lactate between initial and subsequent measures.⁹ For patients with severe sepsis and septic shock with adequate lactate clearance, decreases in in-hospital, 28-day, and 30-day mortality of between 10 and 40% have been reported.^{8–10}

Point-of-care (POC) laboratory testing (i.e., testing performed in close proximity to the patient), facilitates early detection of elevated lactate and may hasten treatment of severe sepsis.^{11,12} POC testing also facilitates the use of serial testing by providing near real-time data on lactate clearance. POC lactate measurements offer two potential benefits for the management of severe sepsis in the ED: (1) earlier recognition of hypoperfusion, leading to more timely treatment and improved patient outcomes; and (2) rapid serial measurements demonstrating lactate clearance, facilitating de-escalation of critical care in the ED and avoidance of an otherwise unnecessary ICU admission.

In this paper, we used computer-based modeling to estimate the cost-effectiveness of implementing a POC serial lactate screening program to rapidly identify occult hypoperfusion in patients presenting to the ED with suspected sepsis.

METHODS

Overview

Our model examined the cost-effectiveness of strategies to evaluate patients presenting to the ED with SIRS and the clinical suspicion for an infectious etiology (suspected sepsis).^{13–16} Our average patient was assumed to be 76 years-old because that is the mean age of patients presenting to the ED with severe sepsis.^{12,17,18} Our model assumed that the ED treats an average of 30,000 patients per year. We evaluated two possible scenarios: a point-of-care lactate program (POC Lactate Program) that measures lactate with a bedside device in the ED and a Usual Care Strategy in which a single lactate level was measured on ED patients in the hospital laboratory.

In the POC strategy, patients with severe sepsis and a lactate ≥ 4 mmol/L are resuscitated with a subsequent lactate measured to evaluate lactate clearance. Those with adequate lactate clearance are admitted to a medical floor and the remaining patients are admitted to the intensive care unit (ICU).

Alternatively, patients in the Usual Care Strategy were assumed to have no POC lactate testing and traditional laboratory lactates were obtained within 3 hours as recommended by the Surviving Sepsis Guidelines.² We assumed no serial lactate testing in the Usual Care strategy due to the long turn-around time for results using standard laboratory testing. All patients in the Usual Care Strategy with severe sepsis and a lactate greater than 4 mmol/L were assumed to be admitted to an ICU. We dichotomized clinical outcomes into those who survived and those who died based on epidemiological data for these populations.

Model Structure—We constructed our models using software (TreeAge 2015, Williamstown, MA) commonly used to evaluate decision models and perform sensitivity analyses (Figure 1). We constructed a cost-effectiveness model in which long-term patient outcomes differed between the POC Lactate Program and Usual Care Strategy. The models estimated costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs). A QALY is a year of life lived in perfect health.¹⁹ An ICER is used to estimate the cost necessary to achieve one additional QALY. The standard threshold, considered the maximum dollar amount society should pay for a single QALY, was conservatively assumed to be \$50,000 in this study. Recent papers suggest potentially higher thresholds (i.e., \$100,000 to \$200,000/QALY),²⁰ which were evaluated in sensitivity analyses. This study was approved as exempt from institutional review board review as non-human subjects research.

Model Parameters/Input Parameters

Clinical Probabilities—Clinical probabilities were obtained from published, peer-reviewed research (Table 1). When available, multiple studies were combined to determine mean probabilities for particular events and their accompanying ranges. If no data were

available, we used expert opinion from the investigators for the base-case and range values. In the base-case scenario, we assumed that among our annual ED patient volume, 17.8% of ED patients had SIRS,²¹ and 0.7% of all ED patients had severe sepsis.¹ Further, we assumed that among these patients with severe sepsis, 21% had an initial lactate ≥ 4 mmol/L.^{3,12,22} Among the patients in the POC Lactate Program with an elevated lactate who were resuscitated and had a second lactate checked in the ED, 68% of patients would demonstrate an adequate lactate clearance of at least 10%, with an associated in-hospital mortality of 19.2%.^{8–10,23} On the other hand, patients with an inadequate lactate clearance had an in-hospital mortality rate of 61.4%.^{8–10,23} For patients in the Usual Care Strategy, we assumed that the overall mortality was a weighted average of those with both adequate and inadequate lactate clearance. Thus, for both strategies in the decision model, if the ED population had an increased prevalence of adequate lactate clearance, the collective population would have a lower mortality rate. Further, we estimated that earlier recognition of occult severe sepsis and the accompanying resuscitation facilitated by the POC Lactate Program would confer an in-hospital mortality benefit above and beyond typical ED resuscitation of 2% combined for both the responders and non-responders resuscitated in the ED. This estimate is conservative compared with the 13% absolute reduction in mortality found by Singer et al,¹² and is explored by sensitivity analyses in the model.

For the Usual Care Strategy, we assumed that a patient's ability to clear lactate was unknown in the ED because only a single value was obtained to guide initial resuscitative efforts. We assumed that only this single lactate value would influence the care they received in the ED and the disposition location (i.e., medical floor versus ICU).

Costs—We modeled three sources of costs in our decision tree (Table 2): 1) physician costs; 2) hospital costs; and 3) fixed and variable costs of the iSTAT laboratory equipment commonly used for POC testing. We used 2014 Centers for Medicare and Medicaid data for diagnosis related groups (DRGs) and relative value units (RVUs) as surrogates for charges.¹⁹ Hospital charges were calculated using DRGs 871 and 872 (septicemia or severe sepsis with major critical care and with/without mechanical ventilation) from the CMS inpatient files.²⁴ Consistent with prior analyses, we assumed that deaths would result in charges that were two standard deviations beyond the mean charges for DRG 871, and 872.²⁵ Professional charges were based on the 2014 National Physician Fee Schedule for outpatient treatment as well as the mean length of stay for inpatient treatment.²⁶ Current Procedural Terminology (CPT) code 99222 (initial hospital care) was used for hospital day one and CPT code 99231 (subsequent hospital care) was used for each subsequent complete or partial hospital day.²⁶ Finally, we used a cost-to-charge ratio of 30% to adjust charges to costs.¹⁹

Equipment costs were based upon both fixed and variable costs for both the setup and ongoing use of the equipment. We assumed that the facility did not have the iSTAT equipment prior to implementation. Fixed costs include the purchase of the equipment, initial iSTAT cartridges, maintenance service contract, and estimated information technology costs to integrate with an existing electronic health record. We also included an estimated one-time set-up cost for staff time to train both ED clinical technicians (i.e., paramedics) and nurses to use the equipment. We estimated that training would take one hour per staff member and that the entire ED staff would be trained. Further, we estimated variable costs

using the cost per iSTAT cartridge purchase, and an estimated staffing cost to conduct each test. We estimated that each test would take 10 minutes to conduct. For all costs, we evaluated the sensitivity of model results using plausible ranges of each variable's value.

Life Expectancy and Disutilities—To determine QALYs, life expectancies and utilities were input into the model (Table 3). The initial life expectancy estimate was obtained from the National Vital Statistics report for 76 year-old patients across all races, ethnicities and genders.²⁷ Since life expectancy represents years that have not yet been lived and exist only in the future, we employed a standard discounting rate of 3% to account for the present value of the remaining life years.²⁸

Survival was assigned a value of 1 while death was assigned a value of 0. Disease states ranged in value between 0 and 1 depending upon qualities of life and could either temporarily or permanently reduce quality of life. We assumed that disabilities were permanent and affected the remainders of the patients' life expectancies. To account for this, utilities were multiplied by life expectancies to determine quality adjusted life expectancies. We also examined whether a short-term disutility associated with being in the ICU or a short-term utility from being resuscitated earlier, would influence the model. In the base-case, we assumed that there was no difference.

Sensitivity Analyses—We performed one-way sensitivity analyses using ICERs for all variables in the model in order to evaluate their effect on the decision strategy. Using the parameters that had the largest effect on ICERs, two-way sensitivity analyses were conducted to evaluate for potential interaction amongst the variables. Both cost-effective and dominant strategies are reported. A "cost-effective" strategy is one in which there is a positive ICER when compared with another strategy. This can be accomplished through either a higher cost, yet higher number of QALYs or a lower cost, yet lower number of QALYs, provided the reduced cost justified the loss in effectiveness. A dominant strategy is both less costly and leads to a gain of QALYs (i.e., more effective). To determine how much cost is tolerable, we used a willingness-to-pay threshold of \$50,000/QALY in our base-case. However, there are arguments to potentially change this threshold to higher values (e.g., \$100,000 or \$200,000).²⁰ Therefore, we examined how a change in this threshold might influence our results.

RESULTS

Main Results

In the base-case, an ED with 30,000 visits per year had 5,340 patients present with suspected sepsis and a lactate measured, of which 207 had severe sepsis and 44 had a lactate ≥ 4 mmol/L. In this case, the POC Lactate Program was the preferred strategy with a cost of \$39.53 per patient with suspected sepsis who had a lactate measured and an effectiveness of 9.7384 QALYs (Table 4). The Usual Care Strategy had a cost of \$33.20 per patient and an effectiveness of 9.7382 QALYs. Thus, the POC Lactate Program cost an additional \$6.33 per patient with suspected sepsis and resulted in an additional effectiveness benefit of 0.0002 QALYs per patient. Extrapolated to an ED with 30,000 annual patient visits, the POC Program would cost an additional \$33,802 and result in a total of 1.07 additional QALYs per

year the program is in use spread out over 5,340 patients with suspected sepsis who had lactate measured in the ED. This equates to \$33,318 paid per additional QALY gained, which is below the willingness-to-pay threshold of \$50,000/QALY.

Sensitivity Analyses

One-way sensitivity analyses were performed across all input variables to evaluate their direct effects on the selection of the decision strategy. Using a willingness-to-pay threshold of \$50,000/QALY, the following clinical variables influenced the decision strategy: the percentage of severe sepsis patients with an elevated lactate, the percentage of patients presenting to the ED who had severe sepsis, the number of annual ED visits, mortality reduction from the POC Lactate Program, both fixed and variable costs of the POC Lactate Program, patient age, percentage of patients with adequate lactate clearance, and cost of an ICU admission. The effect of varying each of these variables can be seen in the tornado diagram in Figure 2. Among these variables, when an ED had at least 25,000 patient visits annually, 0.6% of ED patients had severe sepsis, and at least 17.2% of severely septic patients had an elevated lactate, the POC program was cost-effective. If any of these variables fell below the stated thresholds, the POC program was not cost-effective, and the Usual Care strategy was preferred. Varying the remainder of the variables across their ranges (Tables 1–3) did not affect the decision strategy, with the POC program being preferred across all these ranges. Threshold values for each variable that influence the decision strategy are provided in Table 5.

Evaluating the one-way sensitivities, none of the threshold values that changed the preference from POC Lactate Program to the Usual Care Strategy were within 10% of the base-case estimate used in the decision model. Four variables were between 10% and 20% of the base-case values (percentage of severe sepsis patients with an elevated lactate, percentage of ED patients with severe sepsis, number of annual ED patients, and patient age). The base-case willingness-to-pay threshold of \$50,000/QALY also influenced the selection of the preferred strategy. Increasing the willingness-to-pay threshold to \$100,000/QALY made the POC Lactate Program the preferred strategy for all variables examined except for the following three: 1) the percentage of ED severe sepsis patients with lactates 4 mmol/L 2) the percentage of ED patients with severe sepsis; and 3) the number of annual ED visits. Among these three variables, the POC Lactate Program was cost-effective over an extended range of the variable. Similarly, if the willingness-to-pay threshold were increased to \$200,000/QALY, the POC Lactate Program would be cost-effective across the entire range of annual ED visits and would make the POC strategy cost-effective at lower probabilities of severe sepsis and for those patients with an elevated lactate.

Considering that variables in cost-effectiveness analyses can be interdependent,¹⁹ we performed two-way sensitivity analyses on following the variables with the largest effect on ICER values: 1) percentage of severe sepsis patients with a lactate 4 mmol/L; 2) the probability of severe sepsis; 3) annual ED visits; 4) mortality reduction from the POC Lactate Program; and 5) fixed costs of the POC Lactate Program. An example plot of the two-way sensitivity results can be seen in Figure 3. Across all five variables, as the frequency of patients with elevated lactates, severe sepsis, annual ED visits, and patients

who survive increase, along with fixed costs from the POC Lactate Program decreasing, the POC Lactate Program was more likely to be the preferred strategy.

DISCUSSION

The POC Lactate Program for screening ED patients with suspected sepsis for occult hypoperfusion can be a cost-effective strategy in the ED. In an ED with 30,000 annual visits, the cost of implementing a POC program would be \$33,802; however, this additional cost would be offset by improvements in mortality and lowering ICU admissions, such that each additional QALY gained would cost \$33,318, which is well below current willingness-to-pay thresholds to define a cost-effective intervention. Sensitivity analyses found that the cost-effectiveness of this screening program is dependent on a number of conditions, including the number of severely septic patients ultimately found to have elevated lactates, the number who demonstrate adequate lactate clearance in the ED to allow for general floor admissions, and the costs of executing the program. The primary benefit of this program is by taking patients who would have otherwise been cared for in an ICU setting, and instead resuscitating them in the ED. While these patients are still admitted to the hospital, they are cared for in a lower cost setting on the medical floor. Considering this is a screening program conducted among thousands of ED patients with suspected sepsis, the primary benefit of this program is a reduction in costs through improved resuscitation and more efficient use of ICU beds, with a small improvement in mortality.

One of our assumptions in the base-case is that earlier identification of elevated lactate in the POC program would lead to more aggressive ED-based resuscitation and results in a mortality benefit of 2%. This variable was a key driver of the decision model. If the mortality benefit of the POC program dropped below 1.4%, the Usual Care Strategy was preferred at a \$50,000/QALY willingness-to-pay threshold. At a threshold of \$100,000/QALY, the POC Lactate Program was preferred until there was no difference in mortality. However, this can be offset with an accompanying increase in the percentage of patients with severe sepsis and an elevated lactate. Thus, while there is debate on the appropriate value for the willingness-to-pay,²⁰ we used a more conservative willingness-to-pay threshold in our base-case analyses. Future studies should focus on better defining actual improvements in ICU admission rates and mortality from similar programs.

Limitations

The results of this cost-effectiveness analysis are subject to several limitations. First, while neurological functioning is an important indicator of cost and outcomes following sepsis, sufficient data on the multiple possible outcomes and their originating state are not available to justify separating up these possible outcomes. Therefore, we simplified clinical outcomes to death and survival. Understanding whether more aggressive resuscitation may result in patients who live longer, yet require long-term, higher cost care would have important implications for the results of this study. Second, our model uses a societal perspective and did not take the perspective of maximizing hospital revenues which would be affected by a patient who otherwise would have been admitted to the ICU and instead will be admitted to the floor. However, ICUs frequently operate at near full capacity.²⁹ Therefore, any loss in

revenue from decreased ICU use by septic patients from the ED is likely to be offset by ICU use from another patient. With sepsis now included in value-based purchasing, this may change with a greater focus on prevention through capitation, where systems may benefit from lower intensity care..³⁰ Third, due to the multitude of potential paths patients can take following admission from the ED, we made the simplifying assumption in our model that patients were admitted to either the ICU or a medical floor. However, other possibilities exist such as admission to a step-down unit, and the possibility that patients can switch between levels of care during the course of their stay altering the degree of cost. We reflected these potential scenarios in our cost-effectiveness analysis and the plausible ranges evaluated as the costs associated with each setting. Only ICU admission costs for survivors influenced our decision strategy, and this occurred when ICU costs decreased towards \$33,000, a nearly 30% reduction from the average ICU admission for severe sepsis in 2014. This finding likely occurred because it minimized the difference between the ICU and medical floor cost. Considering medical costs have not seen a reduction since 1940,³¹ achieving such a widespread reduction is an unlikely event. Finally, reductions in ICU admissions came from identifying patients with an adequate lactate clearance which is associated with lower mortality. This analysis assumes that a clinician will place a patient with adequate lactate clearance on the floor. However, some providers may be reluctant to do so, or have varying thresholds for use of the ICU.

CONCLUSION

In this cost-effectiveness model, we found a POC Lactate Program is likely to be cost-effective for EDs with at least 25,000 patient visits per year and 0.6% of their patients having severe sepsis at a standard willingness-pay-threshold of \$50,000/QALY.

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Figure 1.
Decision tree depicting the POC Lactate Program and Usual Care Strategy.

Figure 2.

Tornado diagram of one-way sensitivity analyses. This figure plots each variable's incremental cost-effectiveness ratio (ICER), or cost to achieve one additional quality adjusted life year (QALY), across the range of each variable's values examined in the model. Ranges for each variable are reported and the direction of their influence on the ICER. The center line at an ICER of \$32,483 represents the average ICER of all variables. Negative ICERs indicate that the POC Lactate Program is dominant when compared with the Usual Care Strategy at that particular value.

Note: CE, cost-effectiveness; ICU, intensive care unit; POC, point-of-care; QALY, quality-adjusted life year

Figure 3.

Example two-way sensitivity analysis for the decision model depicting the percentage of ED patients with severe sepsis versus the annual number of ED visits. The shading indicates whether the POC Lactate Program (dark gray), or the Usual Care Strategy (light gray) is the preferred strategy at a willingness-to-pay threshold of \$50,000/QALY.

Table 1

Clinical Probabilities and ranges of values for each variable used in the decision model.

Variable	Base-case	Range		Reference(s)
		Low	High	
Age, y	76	40	90	12,17,18
Annual ED Visits	30,000	10,000	100,000	Estimate
Percentage of ED Patients with Suspected Sepsis	17.8%	10%	25%	21
Percentage of ED Patients with Severe Sepsis	0.7%	0	2%	1
Percentage of Severe Sepsis Patients with Elevated Lactates ≥ 4 mmol/L	21%	6%	36%	3,12,22
Patients with Adequate Lactate Clearance (%)	68%	46%	90%	8–10,23
Absolute In-Hospital Mortality Reduction due to POC Lactate Program	2%	0%	10%	Estimate
In-Hospital Mortality Among Patients with Adequate Lactate Clearance (%)	19.2%	5%	40%	8–10,23
In-Hospital Mortality Among Patients with Inadequate Lactate Clearance (%)	61.4%	50%	80%	8–10,23

Table 2

Costs and ranges of values for each variable used in the decision model.

Variable	Basecase	Range		Reference(s)
		Low	High	
Discount Rate	3%	0	6%	28
Cost-to-charge Ratio	0.3	0.2	0.4	19
<i>POC Lactate Program</i>				
Equipment and Training Costs (fixed)	\$34,909	\$20,000	\$50,000	Industry and Facility Estimates
Equipment Costs per patient (variable)	\$5	\$4	\$6	Industry Estimate
Staffing costs per patient (variable)	\$8	\$4	\$12	Facility Estimate
<i>Hospital and Physician Costs</i>				
Floor Admission	\$27,323	\$10,000	\$40,000	24,26
Floor Admission and Death	\$72,417	\$50,000	\$90,000	24,26
ICU Admission	\$47,030	\$30,000	\$60,000	24,26
ICU Admission and Death	\$136,744	\$100,000	\$200,000	24,26

Note: Discount rate is the rate that future life expectancy can be brought back to the present.

Table 3

Clinical utilities and ranges of values for each variable used in the decision model.

Variable	Basecase	Range		Reference(s)
		Low	High	
Sepsis	0.69	0.6	0.8	³²
Sepsis Quality of Life Benefit from POC Lactate Program	0	0	0.1	Estimate
ICU Admission Short-Term Disutility	0	0	0.1	Estimate
Death	0	-	-	

Table 4

Base-case results for the decision model by strategy.

	Cost (\$ per patient)	Incremental Cost (\$ per patient)	Effectiveness (QALYs per patient)	Incremental Effectiveness (QALYs per patient)
Usual Care Strategy	\$33.20	-	9.7382	
POC Lactate Program	\$39.53	\$6.33	9.7384	0.0002

Table 5

One-way sensitivity results for POC Lactate Program compared with Usual Care Strategy with a willingness-to-pay threshold of \$50,000/QALY.

Variable	Usual Care Strategy Preferred	POC Lactate Preferred	
		Cost-Effective Range of POC Lactate Program	Dominance Range of POC Lactate Program
Percentage of Severe Sepsis Patients who have Lactate 4mmol/L (%)	< 17.2%	17.2%–36.0%	> 36%
Percentage of ED patients who have Severe Sepsis (%)	< 0.6%	0.6%–1.2%	> 1.2%
Number of Annual ED Visits	< 25,000	25,000 – 51,000	> 51,000
In-Hospital Mortality Reduction from POC Lactate Program	< 1.4%	1.4% – 10%	-
Fixed Costs POC of Lactate Program (one time cost)	> \$42,000	\$21,000 – \$42,000	< \$21,000
Variable Costs of POC Lactate Program (cost of lactate measurement for individual patient)	> \$16	\$8-\$16	-
Mean patient age among ED patients with suspected sepsis	> 84 yo	40 – 84 yo	-
Percentage of ED Patients with Severe Sepsis who have adequate Lactate Clearance for floor admission (%)	< 40%	40–90%	-
Cost of Admission to ICU with Survival	< \$33,000	\$33,000 – \$60,000	-