

Potential mortality and cost reduction in adult severe sepsis and septic shock through the use of an innovative fluid delivery device

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Background: While early fluid resuscitation has been shown to significantly improve health and economic metrics in septic shock, providers are often unable to achieve fluid delivery guidelines using current techniques.

Purpose: To examine expected clinical and economic consequences of more consistent achievement of fluid resuscitation guidelines through use of a novel fluid delivery technology.

Patients and methods: A decision analytic model was developed to compare expected costs and outcomes associated with the standard technique vs a novel, faster technique for rapid fluid resuscitation in adult patients with severe sepsis or septic shock.

Results: Use of an innovative fluid delivery device (LifeFlow) resulted in lower expected mortality compared to standard intravenous fluid delivery methods (reduction of 10 fewer deaths per 500 cases). Compared to standard methods, use of the innovative rapid fluid delivery device also resulted in lower expected hospital costs (US\$1,569,131 cost reduction per 500 cases), a lower required use of mechanical ventilation (24% vs 31%), decreased average length of stay (11 vs 13 days), decreased average intensive care unit length of stay (2 vs 3 days), and decreased use of vasopressors (17% vs 21%). A sensitivity analysis showed that utilization of the rapid fluid delivery device is more cost-effective than standard methods, even under the most conservative assumptions.

Conclusion: Based on existing data supporting the importance of early, controlled fluid resuscitation in septic shock patients, the analytical model developed in this study demonstrated the benefit of a novel device that facilitates earlier fluid bolus completion and better adherence to sepsis bundles.

Keywords: sepsis syndrome, sepsis bundles, fluid administration, surviving sepsis campaign, resuscitation

Introduction

Early fluid resuscitation targeted at reversal of shock has been shown to significantly improve mortality, length of hospital stay, and cost in patients with septic shock (SS).^{1,2} However, numerous barriers to effective fluid delivery exist, including poor understanding of guidelines, fear of the adverse effects of fluid overload, and inherent limitations of current fluid delivery techniques. As a result, clinicians often do not achieve published fluid delivery guidelines.³⁻⁵

The majority of SS patients are fluid-responders and Surviving Sepsis Campaign (SSC) guidelines have specified a 3-hour target time window for initial fluid resuscitation.⁶ There is strong evidence that bundle compliance and adherence to time-sensitive elements of sepsis treatment, including early fluid management, improves patient outcomes.^{1,4,6-13} However, there is no evidence that 3 hours is the optimal resuscitation window. Three hours may not be fast enough in some patients since even short delays in bundle initiation

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can negatively impact outcomes.¹⁴ The recently proposed SSC Hour-1 bundle¹⁵ and the surrounding debate highlight the need for more rigorous additional data before developing and implementing broad new clinical guidelines as well as the critical role early fluids can have in some patients. One recent study has demonstrated that initiation of fluid resuscitation in the first 30 minutes of care improves mortality in SS patients.¹⁶

Current methods of fluid resuscitation include gravity infusion, intravenous (IV) infusion pumps, pressure bags (PBs), manual syringes (the “push-pull” technique, or PPT), and mechanical rapid infusers such as the Level 1® and Belmont® Rapid Infuser. All of these techniques have drawbacks that limit the ability of providers to achieve early fluid delivery in SS. Infusion pumps deliver a maximum rate of 1,000 mL/hr, gravity flow is similarly slow, and while the addition of a pressure bag may speed up the infusion, this technique requires constant re-inflation to achieve adequate flow. With PPT, providers may be able to achieve the bundle guidelines, but this complex and labor-intensive technique may be associated with increased risk of nosocomial infection and is rarely used with adult patients.^{17,18} Mechanical rapid infusers are typically only available in large trauma centers, require significant training for proper use, work best with large-bore IV access, and are frequently unavailable in the hospital outside of the emergency department.¹⁹

A novel, hand-operated device (LifeFlow®; 410 Medical, Durham, NC, USA) is now available that enables health care providers to rapidly deliver IV fluids to critically ill patients. Simulation and post-market clinical analyses comparing this novel device to other fluid delivery alternatives, specifically pressure bags and PPT, have demonstrated that this new device provides fluid volumes faster than current techniques, likely enabling routine achievement of bundle guidelines. In one such study, clinicians using the novel device were able to complete a SS clinical scenario in approximately half the

time as clinicians using pressure bags.²⁰ The novel device has also been shown to improve the control and accuracy of fluid bolus size administered compared to standard techniques.²⁰

Because adherence to fluid delivery guidelines is associated with improved health outcomes in adult SS, it is important for health care facilities to understand the clinical and economic implications associated with new rapid fluid delivery methods compared to standard techniques. This analysis examines expected clinical and economic consequences which may be associated with more consistent achievement of fluid resuscitation guidelines through the use of a novel, more rapid fluid delivery technique in adult SS.

Materials and methods

A decision analytic model (Figure 1) was developed to compare expected costs and outcomes associated with the standard techniques vs a novel, faster technique for rapid fluid resuscitation in adult patients with severe sepsis or SS. The analysis was conducted from the perspective of a facility operating within a traditional fee-for-service reimbursement environment where the facility is not accountable for reducing longer-term costs of patient care.

The model relies primarily on the findings of Leisman et al which describe the costs and outcomes associated with patients who are managed in compliance vs in non-compliance with established sepsis bundles for patients presenting with SS.¹ The Leisman study was utilized as the primary study informing the model for the following reasons: 1) it provided consistent data collection and outcomes from three separate facilities and patient cohorts; 2) it provided the most comprehensive information regarding costs and outcomes associated with patients managed in compliance vs non-compliance with established sepsis bundles; and 3) the publication included data regarding the percentage of time that non-compliance with fluid delivery was the only

Decision tree

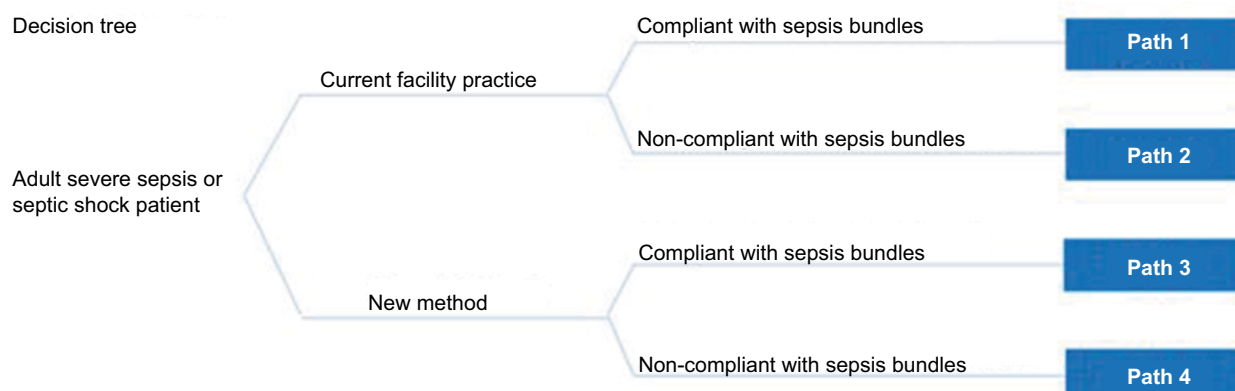


Figure 1 Decision tree model structure.

component preventing compliance with the sepsis bundles, enabling estimation of the impact of improved fluid resuscitation on compliance with the bundle as a whole.

The model examined probable outcomes and costs based on existing literature on adult patients with SS,^{7–10} covering the time from presentation to hospital discharge or death (but not subsequent phases of care). Patient mortality, hospital length of stay (LOS), the occurrence of bundle compliant fluid delivery (30 mL/kg within 3 hours), intensive care unit (ICU) LOS, use of vasopressors, mechanical ventilation and facility costs associated with SS diagnosis, vascular access, and IV fluid delivery were tracked. Paths 1 and 2 modeled patients treated with standard methods. Paths 3 and 4 modeled patients treated in an identical manner but assuming a novel, faster technique was used for fluid resuscitation. Paths 1 and 3 model those patients who receive protocol compliant care, whereas Paths 2 and 4 model those patients who receive protocol non-compliant care. It was conservatively assumed that the availability of the novel, faster technique would not influence the timeliness of SS diagnosis or the timeliness of vascular access.

Movement through the decision tree was governed by the likelihood of sepsis bundle compliance. For standard techniques (eg, pressure bag; Paths 1 and 2), transition probabilities dictating patient movement through the model were drawn from the peer-reviewed literature.^{1,5} For the novel fluid delivery technique (Paths 3 and 4), transition probabilities were assigned based on data collected in a single-center study.²⁰ Briefly, four critical care clinicians, each with more than 5 years of experience, participated in the 2-day study. All clinicians had prior experience with the novel fluid delivery technology as well as with PPT and PB fluid delivery methods. In each case, the participant was asked to follow hospital or manufacturer protocol to set up and deliver 1 L of saline as quickly as possible to a simulated patient using each of the three different fluid delivery methods. Setup and

infusion times were recorded for each infusion method and corresponding IV gauge. Flow rates of the three techniques were compared using ANOVA (Table S1). With 18-gauge catheters, a size commonly used in adult patients, the novel technology was two-fold faster than pressure bags for delivering a 1 L fluid bolus; these data informed our base case model assumptions of more favorable bundle compliance for the novel technology.

Model assumptions (Table 1) related to patient mortality and facility costs incurred for compliance vs non-compliance with sepsis bundles were drawn from peer-reviewed literature.^{1,21} All costs were updated to 2017 USD utilizing the Consumer Price Index for health care services. Costs associated with analogous standard methods and new method pathways (eg, Path 1 and Path 3; Path 2 and Path 4) were assumed to be identical except for the additional cost of the new method, estimated to be US\$250 per patient. Otherwise, the cost of care on each analogous model pathway was similar for patients managed with standard IV fluid delivery methods vs the new method. Mortality rates for standard IV fluid delivery methods vs the new method were identical across analogous model pathways; ie, mortality depends on time-sensitive patient outcomes (ie, sepsis diagnosis, vascular access, IV fluid receipt), but not on the means to achieve those outcomes.

In order to demonstrate the robustness of the results, a series of one-way sensitivity analyses were performed using TreeAge Pro (TreeAge Software, Inc., Williamstown, MA, USA). One-way sensitivity analyses consisted of the manipulation of key variables one at a time by increasing or decreasing values across a range that is supported from the peer-reviewed literature, or by 30% for cost estimates (per standard health economics practice), to determine the impact these changes may have upon the cost-effectiveness findings. Additionally, we conducted a “worst case” sensitivity

Table 1 Costs and outcome assumptions for bundle compliance vs non-compliance

	Bundle compliant (Paths 1 and 3)	Bundle non-compliant (Paths 2 and 4)
Standard method compliance rate	26%	74%
New method compliance rate	75%	25%
Total direct mean hospital costs	\$29,363	\$36,808
Average daily hospital costs	\$2,669	\$2,831
Probability of mechanical ventilation	24%	31%
Probability of patient mortality	18%	23%
Probability of intensive care unit admission	40%	42%
Average intensive care unit length of stay (days)	2	3
Average hospital length of stay (days)	11	13
Probability of vasopressor use	17%	21%
Additional per patient new method cost	\$250	\$250

Note: All costs are expressed in US\$.

analysis in which the least favorable value (with respect to LifeFlow) was adopted for each variable. The findings from this analysis would determine if a new, faster fluid resuscitation method would be cost-effective even under the least favorable conditions.

Results

The decision to utilize a new, faster fluid delivery method resulted in decreased costs when compared to standard fluid delivery methods (\$1,569,131 cost reduction per 500 patients) as well as decreased mortality (10 fewer patient deaths per 500 patients). Additionally, as shown in Table 2, the use of a new method resulted in reductions in total hospital days, number of ICU admissions, number of ICU days, number of patients requiring vasopressors, and number of patients requiring mechanical ventilation.

To determine if model findings were robust to reasonable changes in assumptions, one-way sensitivity and threshold analyses were performed. In all sensitivity analyses, a new, faster fluid delivery method was associated with improved

outcomes (including reduced mortality) and lower costs as compared to standard fluid delivery procedures, demonstrating the stability of modeled results (Table 3). Additionally, we conducted a “worst case” sensitivity analysis in which the least favorable value (with respect to a new fluid delivery method) was adopted for each variable. The findings from this analysis confirmed that utilization of a new, faster fluid resuscitation method would be cost-effective even under the most conservative assumptions.

Conclusion

Early fluid resuscitation has been demonstrated to have many significant benefits in the treatment of adult SS.^{1,3,9,10,13,16} However, standard fluid delivery techniques have drawbacks that limit the ability of providers to consistently achieve fluid resuscitation goals. The ideal fluid delivery technique would enable more rapid diagnosis and treatment, and would potentially allow clinicians to intervene earlier in the disease process. An innovative, rapid fluid delivery device may offer clinicians greater control and speed in resuscitating critically ill patients. The purpose of this analysis was to evaluate, through an analytical model, the impact of a new, more rapid fluid resuscitation technique on overall bundle compliance and ultimately on patient and economic outcomes.

Our model indicated that the use of a more rapid fluid resuscitation technique may offer a significant cost benefit and mortality reduction compared to standard fluid delivery methods for adult SS presenting in the hospital. Cost savings are primarily due to the shorter inpatient hospital stay, reduced ICU admissions, and other associated costs influenced by increased protocol compliance associated with early, rapid fluid delivery.

Additionally, for the range of values investigated and across all parameters allowed to vary, the new fluid delivery

Table 2 Expected benefits of new, faster fluid delivery method per 500 patients

Variable	Expected benefit
Reduction in expected facility costs	US \$1,569,131
Reduction in patient deaths	10
Reduction in total hospital days	455
Reduction in number of patients admitted to intensive care unit	5
Reduction in total intensive care unit days	121
Reduction in number of patients requiring vasopressors	11
Reduction in number of patients requiring mechanical ventilation	17

Table 3 One-way sensitivity analysis

Model variable	Range	Base case assumption	Conservative assumption	New method cost saving with conservative assumption?
Average LOS for patient not receiving bundle compliant care	8–18 days	13 days	8 days	Yes
Average reduction in LOS for patient receiving bundle compliant care	1–4 days	2 days	1 day	Yes
Under current practices, % of time facility achieves bundle compliant care	26%–53%	26%	53%	Yes
% of time that non-compliance with fluid delivery is the cause of bundle non-compliant care	65%–98%	82%	65%	Yes
% of time that new method use will change bundle non-compliant fluid delivery to bundle compliant	50%–90%	75%	50%	Yes
Mean per-patient cost savings enabled by bundle compliant care	\$6,328–\$8,562	\$7,445	\$6,328	Yes

Note: All costs are expressed in US\$.

Abbreviation: LOS, length of stay.

method was the most cost-effective fluid delivery method, even modeling the most conservative assumptions, proving the robustness of the model results. This analysis adds to the knowledge base regarding the outcomes and related facility costs of alternative fluid resuscitation treatments in SS. When compared to standard fluid delivery methods, this new fluid delivery method offers faster, more efficient, and more controlled fluid resuscitation resulting in improved patient health and economic outcomes vs standard fluid delivery methods. Finally, costs included in this model are from the index SS hospitalization only and do not include costs of subsequent re-admissions. This likely underestimates the cost benefits of improved fluid resuscitation, as poor health outcomes associated with bundle non-compliance are likely to result in increased re-admission rates.

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Disclosure

Dr. Piehl is co-founder and Chief Medical Officer of 410 Medical. The authors report no other conflicts of interest in this work.

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Supplementary material

Table S1 Fluid delivery flow rates

Gauge	mL/min			P-value
	Pressure bag	Push-pull	New method	
16	120	125	218	0.003
18	96	110	192	<0.001
20	80	101	223	<0.001
22	46	84	193	<0.001
CVC	47	72	126	<0.001

Abbreviation: CVC, central venous catheter.

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