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Cost-effectiveness of rapid diagnostic assays that perform directly on blood samples for the diagnosis of septic shock☆

Fadi Shehadeh, Ioannis M. Zacharioudakis, Fainareti N. Zervou, Eleftherios Mylonakis *

Infectious Diseases Division, Warren Alpert Medical School of Brown University, Rhode Island Hospital, Providence, RI, United States

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ABSTRACT

Molecular diagnostic assays that test directly whole blood provide the ability to decrease inappropriate antimicrobial therapy and improve survival in patients with septic shock. We developed a decision analysis model to evaluate the cost-effectiveness of the addition of molecular assays to blood cultures in adults admitted to medical ICUs with septic shock. Under baseline assumptions, the use of molecular diagnostic methods was cost-saving in all cases that the length of hospital stay differed by 2 and 4 days between patients receiving appropriate and inappropriate antimicrobial therapy. In the case that the length of stay was the same, the use of molecular methods was cost-effective with an estimated incremental cost-effectiveness ratio (ICER) < $3000 per death averted. In the extreme that the length of stay between the 2 groups was the same, the highest cost reached was when the cost of the assay was $1000, with the estimated ICER being < $20,000 per death averted.

1. Introduction

Sepsis is associated with about 6% of hospital admissions (Rhee et al., 2017), and septic shock has a mortality that can exceeds 40% (Singer et al., 2016) with a total annual hospitalization cost for patients with severe sepsis in the United States estimated at $24.3 billion (Lagu et al., 2012). The management of patients with sepsis relies mainly on early identification of the source of sepsis and initiation of appropriate antimicrobial therapy (Cohen et al., 2015) (AAT). Inappropriate antimicrobial therapy (IAAT) for severe infections increases 30-day mortality by 71% and in-hospital mortality by 67% (Marquet et al., 2015). Moreover, IAAT increases hospital length of stay (LOS) and costs (Abraham et al., 2016; Kumar et al., 2009; Marquet et al., 2015; Shorr et al., 2011) by >$10,000 (Shorr et al., 2008). It is therefore apparent that the rapid identification of pathogens and their antimicrobial resistance profile can play a key role in minimizing the instances of IAAT in sepsis and may decrease the mortality rates, hospital LOS, and subsequently costs. Although blood cultures remain the gold standard for microbiological diagnosis of sepsis, they can have long time to pathogen detection and turnaround times (Riedel and Carroll, 2016) and often take 48–72 h from sample acquisition to microbiologic diagnosis (Kothari et al., 2014).

The need for timely diagnosis has led to the development of several rapid diagnostic techniques and systems for the identification of bloodstream pathogens. These fall into 2 main categories: those that use a positive blood culture as a sample and those that perform direct diagnosis from blood (Kothari et al., 2014; Marco, 2017; Opota et al., 2015; Peker et al., 2018; Pfaller et al., 2016; Riedel and Carroll, 2016; Vutukuru et al., 2016). Assays from the first category have been widely used and have been shown to reduce sepsis-related mortality (Kothari et al., 2014). Molecular methods with direct pathogen identification from whole blood specimens are emerging (Opota et al., 2015) and have the potential of pathogen isolation in 2–7 h. The use of molecular methods is appealing due to their rapid turnaround time and thus their potential to significantly decrease the empirical IAAT. However, as these assays are moving through development and regulatory evaluation, their adoption in daily clinical practice is highly dependent on their cost-efficiency profile.

Parameters that influence the cost-effectiveness of such assays are expected to vary widely between different clinical settings, and they are dependent on the cost and performance of the assay as well as on the patient population and local microbiology. The purpose of this study is to examine the cost-effectiveness of these assays over a wide range of parameters in order to aid clinical centers reaching a decision on their potential adoption.

2. Materials and methods

We constructed a decision analytic model to examine the cost-effectiveness of the adjunct use of rapid diagnostic molecular tests performed directly in blood samples to the current standard of care in

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* Corresponding author. Tel.:+1-401-444-7856; fax: +1-401-444-8179.
E-mail address: emylonakis@lifespan.org (E. Mylonakis).

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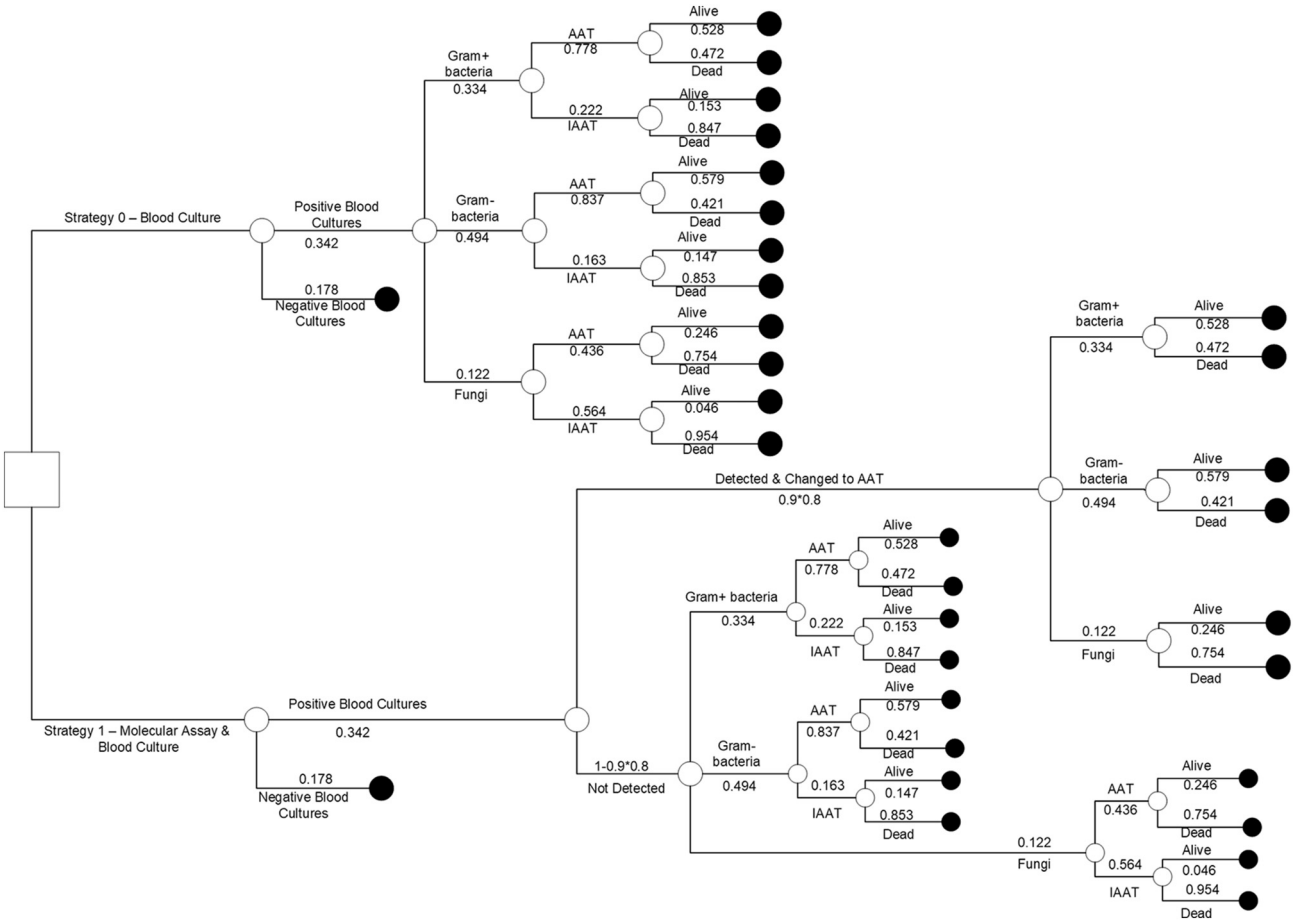

Fig. 1. Decision tree with base case input values. The decision tree is a graphical display of a logical sequence of events in the 2 study arms. The *square* represents the decision node from which the 2 competing strategies (molecular method plus blood cultures vs. blood cultures alone) originate. The *circles* are chance nodes that lead to a particular outcome (e.g. survival or death) beyond the control of our decision. The probabilities assigned to the decision tree are for baseline analysis and are listed in Table 1.

adult patients hospitalized with septic shock (Fig. 1). Septic shock was defined as documented or suspected infection with persistent hypotension requiring therapy with vasopressors and 2 of the following 4 elements: a heart rate of >90 beats/min; a respiratory rate of >20 breaths/min or pCO_2 of <32 mmHg; a core temperature of <36 °C or > 38 °C; and a WBC count of <4000/μL or > 12,000/μL, or >10% immature forms (bands) (Kumar et al., 2009).

2.1. Model structure

In the baseline arm, patients admitted with septic shock had only blood cultures collected. In the interventional arm, patients had molecular testing performed at the time of diagnosis of septic shock as an adjunct to blood cultures. After the diagnosis of septic shock was established, a patient could receive AAT or IAAT. Appropriate antimicrobial therapy was considered the therapy that had in vitro activity against the isolated pathogenic organisms, and was initiated within 6 h of hypotension. The decision tree with the base case input values is presented in Fig. 1.

2.2. Assigning probabilities and costs

The assigned probabilities and costs are displayed in Table 1. Probabilities were derived from Kumar et al. (2009), while costs were derived from Paoli et al. (2018) and local costs. Based on the study of Kumar et al. (2009), a retrospective multicenter study of adult patients with septic shock in 22 medical intensive care units in Canada, the United States, and Saudi Arabia between 1996 and 2005, 33.4% of infections were caused by Gram-positive organisms, 49.41% by Gram-negative organisms, and 12.21% by fungi. Based on the results of the same study, 80.1% of patients that were tested only with blood cultures received AAT, with the percentages being 77.8% for Gram-positive organisms, 83.7% for Gram-negative organisms, and 43.6% for fungi. Moreover, patients who were treated with appropriate antimicrobial treatment had a 52% chance of survival to hospital discharge compared to 10.3% for those with initially inappropriate antimicrobial treatment (Kumar et al., 2009). Specifically, patients with Gram-positive infection had a survival rate of 52.8% with appropriate therapy vs. 15.3% with inappropriate therapy, with the relevant numbers being 57.9% vs. 14.7% for patients with Gram-negative infection and 24.6% vs. 4.6% for patients with fungal infection (Kumar et al., 2009).

The average hospital LOS for subjects treated with inappropriate or appropriate therapy varies among individual studies (Marquet et al., 2015; Raman et al., 2015). For example, in the study by Shorr et al. (2011), a retrospective review of all patients with Gram-negative severe sepsis or septic shock at the Barnes-Jewish Hospital between January 2002 and December 2007, patients receiving AAT had a hospital stay of 9 vs. 11 days of those who received IAAT. This difference in hospital LOS varied from 0 to 4 days in other studies (Battle et al., 2017; Marschall et al., 2008; Shorr et al., 2011). To minimize inconsistencies between studies, we described 4 base case scenarios with 0, 1, 2, or 4 days of hospital LOS difference between patients receiving AAT and IAAT.

On the base case analysis, the molecular test results led to a change of therapy in 80% of cases that were detected by the assay and were initially on IAAT. This was achieved by the ability of the test to detect

Table 1
Model inputs and baseline estimates.

Model variable	Value	Source
Percentage of positive blood cultures	0.342	Kumar et al. (2009)
Percentage of isolated gram-positive bacteria	0.334	Kumar et al. (2009)
Percentage of isolated gram-negative bacteria	0.494	Kumar et al. (2009)
Percentage of isolated fungi	0.122	Kumar et al. (2009)
Percentage of AAT for gram-positive bacteria	0.778	Kumar et al. (2009)
Percentage of AAT for gram-negative bacteria	0.837	Kumar et al. (2009)
Percentage of AAT for fungi	0.436	Kumar et al. (2009)
Overall percentage of AAT	0.801	Kumar et al. (2009)
Sensitivity of molecular assay	0.90 [0.5–0.95]	Mylonakis et al. (2015)
Panel efficiency of molecular assay	0.80 [0.3–0.9]	Kumar et al. (2009)
Survival rate of AAT for gram-positive bacteria	0.528	Kumar et al. (2009)
Survival rate of IAAT for gram-positive bacteria	0.153	Kumar et al. (2009)
Survival rate of AAT for gram-negative bacteria	0.579	Kumar et al. (2009)
Survival rate of IAAT for gram-negative bacteria	0.147	Kumar et al. (2009)
Survival rate of AAT for fungi	0.246	Kumar et al. (2009)
Survival rate of IAAT for fungi	0.046	Kumar et al. (2009)
Difference in LOS in AAT and IAAT	[0–4]	Shorr et al. (2011), Battle et al. (2017), Marschall et al. (2008)
Cost of molecular assay	155 [100–1000]	Khare et al. (2014)
Hospitalization cost per day	$3040	Paoli et al. (2018)

microbes that were either not covered by the initial empiric treatment (i.e., fungal infections) or had resistance to the empiric therapy based on the hospital antimicrobial resistance profile, inherently or based on their resistance genes. Based on the study of Kumar et al. (2009), 5 *Candida* spp. are responsible for 24.9% of cases of IAAT; *Staphylococcus aureus*, *Enterococcus faecalis*, and *Enterococcus faecium* for 27.5%; and 6 common Gram-negative bacteria for 30.2%. The addition of an echinocandin to the initial therapy based on the results of the molecular study and the broadening of the initial empiric therapy when resistance genes like *mec*, *vanA*, and *vanB* or extended-spectrum beta-lactamase (ESBL)–related gene mutations were detected would change the IAAT to AAT. Finally, identification of *Stenotrophomonas maltophila* is responsible for 1.7% of cases of IAAT, and identification will change IAAT to AAT driven by its unique antimicrobial resistance profile. The results of the molecular testing were provided within 6 h of testing, allowing treatment to be adjusted accordingly. We assumed that the patient that was eventually treated appropriately adopted the survival rate and the hospital LOS of patients treated with AAT.

On the base case scenario, the molecular method had a 90% sensitivity of detecting the pathogen that would eventually grow in the blood culture, similar to the sensitivity of FDA-approved molecular assays (Mylonakis et al., 2015). Blood culture, the gold standard reference test for the purposes of this analysis, had a 100% sensitivity and specificity. In 34.2% of cases, a pathogen was isolated from blood (Kumar et al., 2006). In blood cultures that finalized negative, antimicrobial therapy was considered neither appropriate nor inappropriate. In these cases, the adjunct molecular testing was also assumed to be negative.

To be able to examine the cost-effectiveness of these techniques, we used an average estimate of septic shock hospitalization cost in the US provided by Paoli et al. ($3040/day) (Paoli et al., 2018). The cost of the molecular test at the base case scenario was assumed to be $155. This number was extrapolated from the reported cost of consumables of The FilmArray® Gastrointestinal (GI) Panel test (BioFire Diagnostics, Salt Lake City, UT, USA) (Khare et al., 2014), which is an FDA-approved test that detects 22 gastrointestinal pathogens involved in gastrointestinal infections. For the patients that did not grow microbe on their blood cultures, the cost of molecular testing was added in the intervention arm with no effect on efficacy or hospital LOS.

2.3. Outcomes and data analysis

To compare the 2 competing strategies, the incremental cost-effectiveness ratio (ICER) was used to express the result. The ICER was measured as the difference in costs of the competing strategies divided by the difference in health effects (survival). ICERs can be compared to budget thresholds, and an intervention with an ICER that is smaller than the willingness to pay of the decision maker is considered cost-effective. To account for uncertainty, we used deterministic methods by adjusting point estimates regarding the sensitivity of the molecular method, the cost of the molecular method, and the panel efficiency to predefined extremes as presented in Table 1.

In the baseline arm, blood cultures were used, and a combined survival rate was computed based on the percentage of AAT and the survival rates of AAT and IAAT for each organism type.

$$s_{o,gram+} = Perc_{AAT,gram+} \cdot Surv_{AAT,gram+} + \left(1 - Perc_{AAT,gram+}\right) \cdot Surv_{IAAT,gram+}$$

$$s_{o,gram-} = Perc_{AAT,gram-} \cdot Surv_{AAT,gram-} + \left(1 - Perc_{AAT,gram-}\right) \cdot Surv_{IAAT,gram-}$$

$$s_{o,fungi} = Perc_{AAT,fungi} \cdot Surv_{AAT,fungi} + \left(1 - Perc_{AAT,fungi}\right) \cdot Surv_{IAAT,fungi}$$

The overall survival rate for this strategy was obtained by averaging the above survival rates, weighted by the percentage of infections caused by each organism group.

$$s_o = \frac{perc_{gram+} \cdot s_{o,gram+} + perc_{gram-} \cdot s_{o,gram-} + perc_{fungi} \cdot s_{o,fungi}}{perc_{gram+} + perc_{gram-} + perc_{fungi}}$$

The cost of this method was computed based on the combined probability of AAT, the hospital LOS for AAT and IAAT, and the hospitalization cost per day.

$$cost'_o = perc_{AAT} \cdot LOS_{AAT} \cdot cost_{hosp/day} + (1 - perc_{AAT}) \cdot LOS_{IAAT} \cdot cost_{hosp/day}$$

The final cost was computed by taking into account that a percentage of the initial blood cultures will finalize negative.

$$cost_o = perc_{pos} \cdot cost'_o$$

In the interventional arm, molecular testing was performed at the time of diagnosis of septic shock as an adjunct to blood cultures. The effectiveness of the strategy was defined based on the sensitivity of the assay and the panel efficiency. Panel efficiency was defined as the percentage of cases in which therapy was changed from IAAT to AAT based on the molecular test results.

$$eff = sensitivity \cdot panelEfficiency$$

The survival rate was presumed equal to the survival rate of AAT for every treatment change resulting from a detection of an organism, and equal to the baseline arm for those organisms not detected by the assay or those detected but not resulting in a treatment change.

$$s_{1,gram+} = eff \cdot Surv_{AAT,gram+} + (1 - eff) \cdot s_{o,gram+}$$

$$s_{1,gram-} = eff \cdot Surv_{AAT,gram-} + (1 - eff) \cdot s_{o,gram-}$$

$$s_{1,fungi} = eff \cdot Surv_{AAT,fungi} + (1 - eff) \cdot s_{o,fungi}$$

The overall survival rate for this strategy was obtained by averaging the above survival rates, weighted by the percentage of infections caused by each organism group.

$$s_1 = \frac{perc_{gram+} \cdot s_{1,\,gram+} + perc_{gram-} \cdot s_{1,\,gram-} + perc_{fungi} \cdot s_{1,\,fungi}}{perc_{gram+} + perc_{gram-} + perc_{fungi}}$$

Cost of this method was computed based on the hospital LOS for AAT, the effectiveness of the strategy, the hospitalization cost per day and the cost of the assay.

$$cost_1' = perc_{AAT} \cdot LOS_{AAT} \cdot cost_{hosp/day} +$$

$$+(1-perc_{AAT}) \cdot (LOS_{IAAT} \cdot (1-eff) + LOS_{AAT} \cdot eff) \cdot cost_{hosp/day} + cost_{assay}$$

The final cost was computed by taking into account that a percentage of the initial blood cultures will finalize negative.

$$cost_1 = perc_{pos} \cdot cost_1' + \left(1-perc_{pos}\right) \cdot cost_{assay}$$

Finally, the ICER was computed.

$$ICER = \frac{cost_1 - cost_o}{s_1 - s_o}$$

Matlab R2017a (The MathWorks, Inc., Natick, Massachusetts, United States) was used for the design and the analysis of the cost-effectiveness model.

3. Results

We evaluated 4 base case scenarios for 4 studied differences in hospital LOS between patients receiving AAT and IAAT, that is, 0, 1, 2, and 4 days. In the base case scenarios, the use of blood culture had an average estimated cost per patient of $9357, $9564, $9771, and $10,185 for a difference in hospital LOS of 0, 1, 2, and 4 days, respectively. The respective values for the interventional arm when a molecular method was used as an adjunct to blood cultures were $9512, $9570, $9628, and $9744 per patient. The difference in cost per patient of the interventional arm to the baseline arm was $155, $6, −$143, and −$441 for a difference in hospital LOS of 0, 1, 2, and 4 days, respectively.

Under baseline assumptions, the use of the molecular diagnostic method was less costly and more effective in the cases that the length of hospital stay differed by 2 and 4 days between patients receiving AAT and IAAT (Table 2). In the case that the hospital LOS differed by 1 day or was the same, the use of the molecular method as an adjunct to the blood cultures was more effective but more costly (ICER: $2678/death averted and $104/death averted, respectively).

The dominance of the use of the molecular method was robust in all 1-way sensitivity analyses when the difference of the hospital LOS was 4 days and became more costly only when the cost of the assay reached $596, as shown in Figs. 2–4. On the other hand, in the extreme when patients receiving appropriate and inappropriate therapy had the same LOS, the use of the molecular method was more effective but more costly, with the highest cost reached when the cost of the assay was $1000 (ICER $17,281/death averted). When the difference at the LOS was 2 days, the molecular method remained more effective and less costly when the cost of the assay remained below $298 and the efficiency of the panel was above 42%, with the highest ICER being $12,132/death averted at an assay cost of $1000. Finally, in the case of 1-day difference in hospital LOS between patients receiving AAT and IAAT, the use of the molecular assay remained more effective and less costly when the cost of the assay remained below $149 and the efficiency of the assay was above 84%, with the highest ICER being $14,707/death averted at an assay cost of $1000.

Table 2
Model output.

Sensitivity analysis variable	LOS difference (days)	Assay cost	Sensitivity	Efficiency	ICER (USD/death averted)
Baseline	0	$155	90%	80%	$2678
	1	$155	90%	80%	$104
	2	$155	90%	80%	< 0
	4	$155	90%	80%	< 0
Assay Cost	0	$100	90%	80%	$1728
	0	$1000	90%	80%	$17,281
	1	< $149	90%	80%	< 0
	1	$1000	90%	80%	$14,707
	2	< $298	90%	80%	< 0
	2	$1000	90%	80%	$12,132
	4	< $596	90%	80%	< 0
	4	$1000	90%	80%	$6984
Assay Sensitivity	0	$155	50%	80%	$4821
	0	$155	95%	80%	$2538
	1	$155	50%	80%	$2247
	1	$155	> 94%	80%	< 0
	2	$155	> 50%	80%	< 0
	4	$155	> 50%	80%	< 0
Panel efficiency	0	$155	90%	30%	$7143
	0	$155	90%	95%	$2256
	1	$155	90%	30%	$4569
	1	$155	90%	> 84%	< 0
	2	$155	90%	30%	$1994
	2	$155	90%	> 42%	< 0
	4	$155	90%	> 30%	< 0

LOS difference: difference in hospital stay between patients receiving AAT and IAAT.

4. Discussion

In this study, we evaluated the implementation of a rapid molecular diagnostic test as an adjunct to the standard blood cultures in a high-risk setting, such as the medical intensive care unit, that has the potential to increase survival by increasing the rate of appropriate antimicrobial therapy. Under baseline assumptions, the use of a molecular diagnostic method was cost-saving in all cases that the length of hospital stay differed by 2 and 4 days between patients receiving AAT and IAAT. Even in the case that the length of hospital stay was the same between patients receiving AAT and IAAT, the use of the molecular method as an adjunct to the blood cultures was cost-effective for a willingness to pay <$3000 per death averted. Our results remained robust in all sensitivity analyses regarding the sensitivity and efficiency of the molecular method when the difference in hospital stay between patients receiving appropriate vs. inappropriate therapy was at least 4 days. In the extreme that the length of hospital stay between the 2 groups was the same, the highest cost reached was when the cost of the assay was $1000, with the estimated ICER being less than $20,000 per death averted.

This study focused on the cost-effectiveness of early identification of the etiology of septic shock. This cost-effectiveness mainly arises from identifying microbes or antimicrobial resistance genes that would guide a change in the initial empiric antimicrobial therapy, such as in cases of isolation of yeasts, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant Enterococci, multidrug-resistant Gram-negative bacteria, or organisms with unique antimicrobial resistance profiles, and subsequently affect the LOS and overall survival (Marquet et al., 2015; Raman et al., 2015). In our base case analysis, we assumed that the use of a molecular diagnostic method could lead to an 80% change from inappropriate to appropriate treatment based on the data by Kumar et al. (2009). However, this percentage is highly dependent on the individual hospital's antimicrobial resistance profile, with higher percentages expected in hospitals with high rates of antimicrobial resistant pathogens. For this reason, we performed a sensitivity analysis

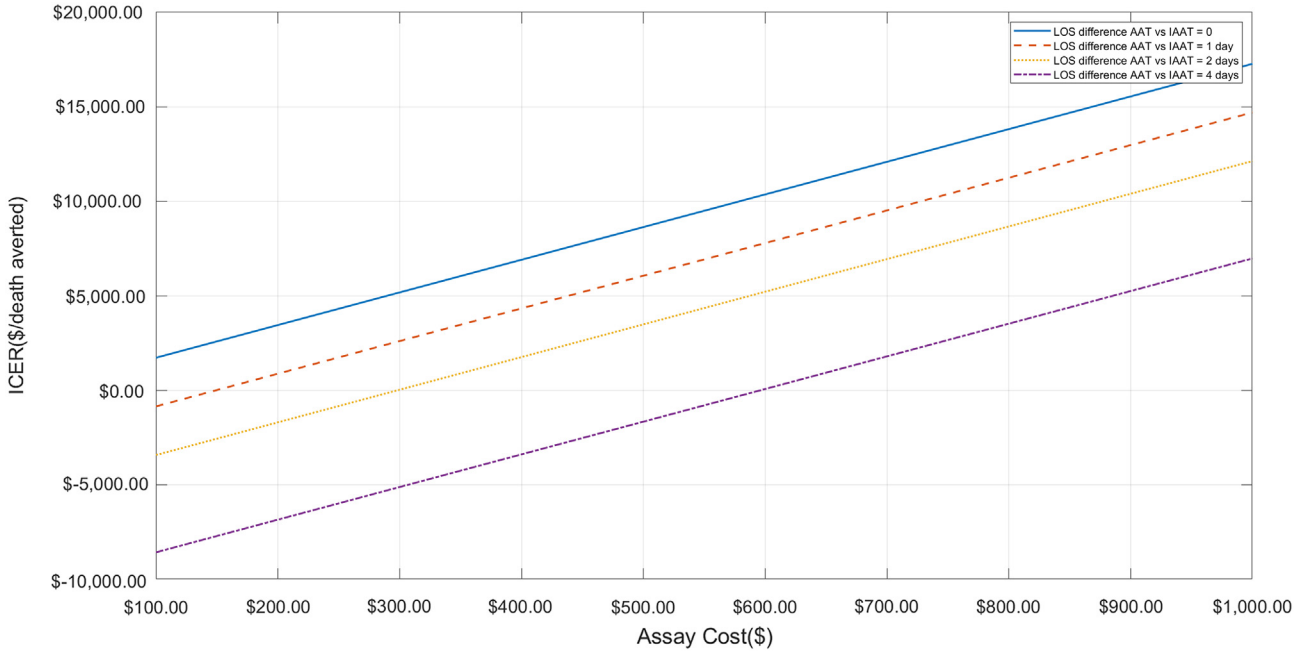

Fig. 2. One-way sensitivity analysis when assay cost ranges from $100 to $1000 for all 4 base case scenarios (i.e., when the difference in hospital LOS between patients receiving AAT and IAAT is 0, 1, 2, and 4 days).

that showed that our results were robust in a range of panel efficiency from 30% to 95% in the case that the expected difference in the hospital LOS between patients receiving appropriate vs. inappropriate therapy was at least 2 days.

Besides the decrease in length of hospital stay and improvement in survival, additional benefits are to be expected from early microbiological diagnosis. Those benefits could be early deescalation in broad-spectrum antimicrobial regimens, decrease in antimicrobial resistance rates, as well as guidance towards directed diagnostic and therapeutic methods for appropriate source identification and control. These benefits should increase even further the cost-effectiveness of an algorithm that combines a molecular diagnostic method with blood cultures, but these benefits are difficult to quantify and were not used in our analysis.

The economics and logistics of the molecular diagnostics such as the high costs of the assays and their reagents, the space requirements, the low system throughput, and the upfront expenses of these tests appear to play a significant role in the slow adaptation or even demise of such systems that might otherwise be precise at the study level (Ozenci et al., 2018). As such, studies that evaluate the cost-effectiveness of these techniques in different clinical settings become particularly important. Due to their high overall cost, these rapid molecular diagnostic tests may not be cost-effective in many clinical settings but could prove

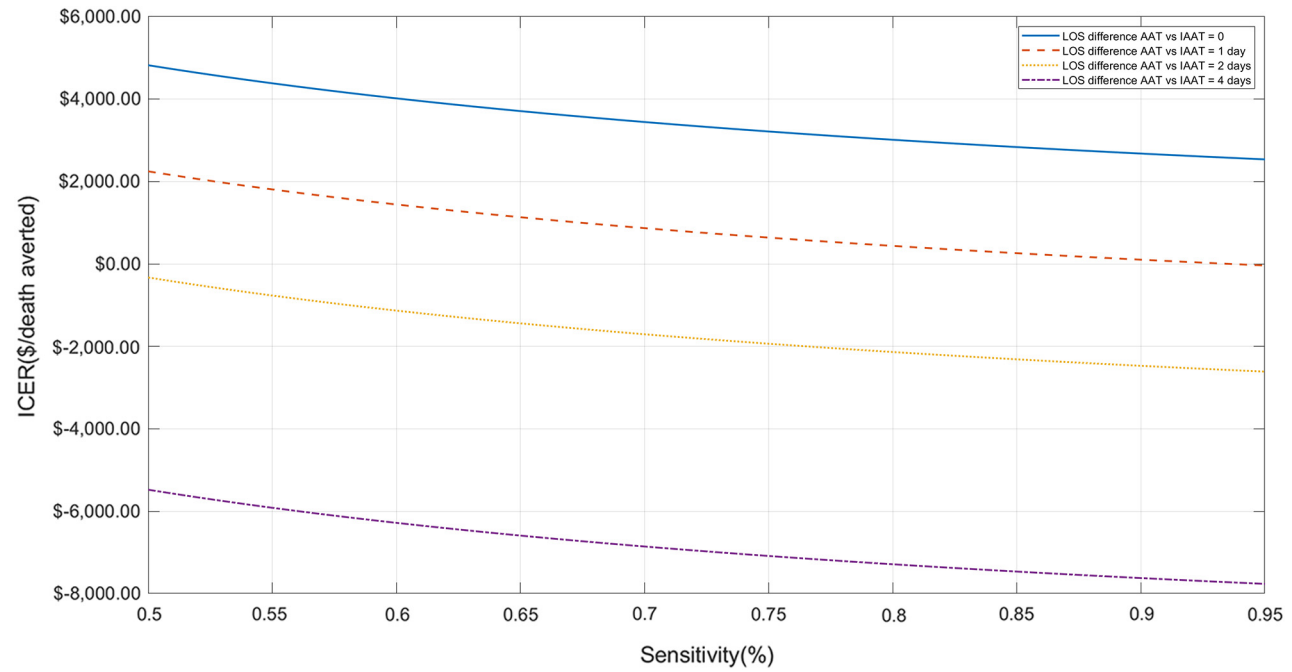

Fig. 3. One-way sensitivity analysis when the sensitivity of the assay ranges from 50% to 95% for all 4 base case scenarios (i.e., when the difference in hospital LOS between patients receiving AAT and IAAT is 0, 1, 2, and 4 days).

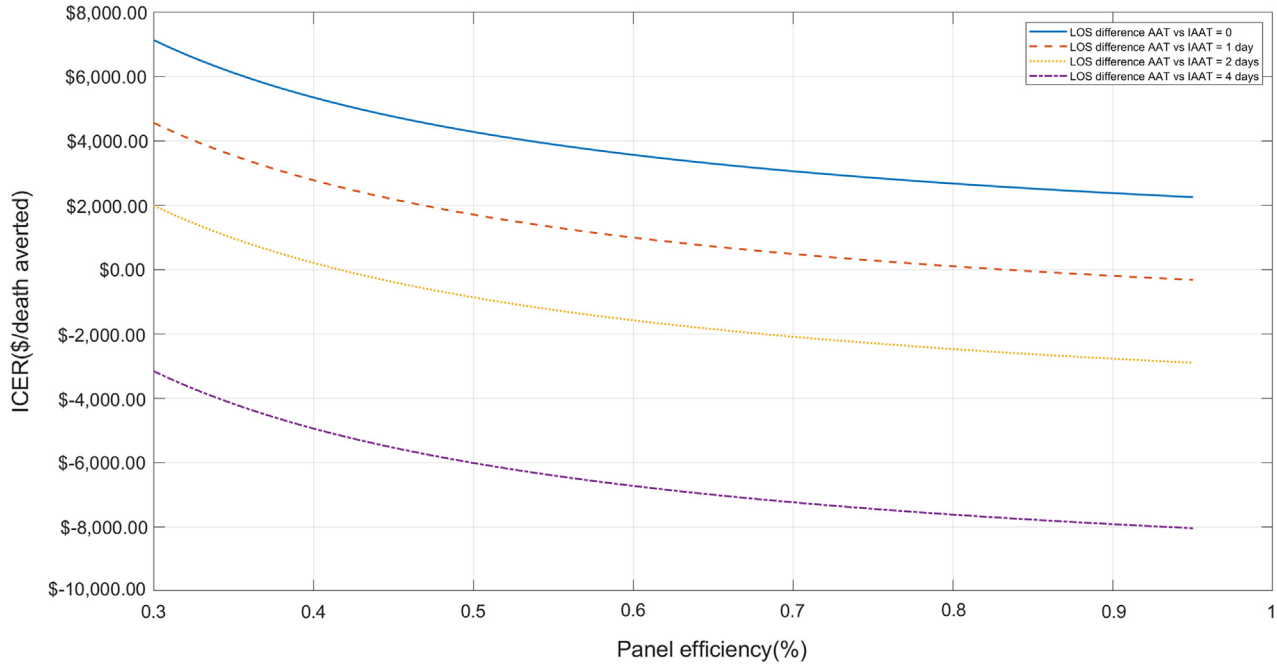

Fig. 4. One-way sensitivity analysis when the efficiency of the assay ranges from 30% to 95% for all 4 base case scenarios (i.e., when the difference in hospital LOS between patients receiving AAT and IAAT is 0, 1, 2, and 4 days).

very valuable and cost-effective in settings such as the ICU, where the early identification of pathogens and antimicrobial resistance genes can have a mortality benefit. Our model evaluates the cost-effectiveness of the scenario where the molecular testing is performed at the time of initial clinical diagnosis, thus enabling an early identification of the etiology of septic shock. It is possible that the testing will be performed more than once in clinical practice, but the cost of repeat testing has not been incorporated in our analysis. Furthermore, depending on hospital microbiology, a different percentage of IAAT is expected to change to AAT with the use of different molecular diagnostic methods. For example, in a hospital with a high prevalence of ESBL-producing organisms, the empiric therapy may be vastly different compared to a hospital with different epidemiology, and this may affect the expected panel efficiency and thus the cost-effectiveness of the assay. To address this issue, the cost-effectiveness results were presented over a wide range of panel efficiency.

It should be noted that our estimated survival outcomes in patients receiving AAT and IAAT were based on a retrospective observational study (Kumar et al., 2009) and not a randomized controlled trial. As such, baseline characteristics of patients that received AAT or IAAT might differ. As it is impossible to conduct a randomized trial comparing appropriate and inappropriate antimicrobial treatment, future randomized trials that will incorporate a molecular diagnostic method as an adjunct to blood cultures and examine the clinical outcomes are necessary to confirm the observations of this cost-effectiveness study. Similarly, the effect of initiation of appropriate antimicrobial therapy in the length of hospital stay differs in individual studies between 0 and 4 days (Battle et al., 2017; Marschall et al., 2008; Shorr et al., 2011). In an effort to overcome this, 4 different base case scenarios were run in which the hospital LOS differed by 0, 1, 2, and 4 days between patients receiving AAT vs. IAAT. Even in the case that the length of hospital stay was the same between patients receiving AAT and IAAT, the use of the molecular method as an adjunct to the blood cultures was cost-effective for a willingness to pay of less than $3000 per death averted, increasing the robustness of our results. Furthermore, in our base case analysis, we assumed a sensitivity of the molecular method of 90% as a reasonable target for the test to get FDA approval (Mylonakis et al., 2015). However, the adjunct use of a molecular method remained dominant in a range of sensitivities from 50% to 95% when there were at least 2 days of difference in the hospital LOS between patients who received AAT vs. IAAT. Finally, it should also be noted that the initial investment of the hospital and the maintenance costs required for the molecular techniques were not taken into consideration in our base case analyses.

5. Conclusions

Given the significant morbidity and mortality of septic shock, the standardization of molecular tests that are performed directly on blood samples and guide the antimicrobial therapy early in the disease course is appealing. However, the adaptation of those methods in daily clinical practice is highly dependent on their cost-efficiency profile. Our analysis provides an estimation of the economic perspective of a diagnostic algorithm that incorporates molecular tests based on the available data, and gives a projected estimate of what to expect in a wide range of sensitivity, cost, and efficiency of different methods. Blood culture remains the mainstay of the diagnostic algorithm since it is the only method that provides the resistant profile of the isolated organism. In this study, we demonstrated that, on baseline scenarios and provided thresholds for willingness to pay of less than $3000 per death averted, such diagnostic algorithms are cost-effective even when there is no difference in the length of hospital stay between patients on AAT and IAAT. However, the dominance of such a policy needs to be verified in clinical trials that will incorporate the sensitivity, cost, and efficiency of the specific molecular method.

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