White Paper

The Health and Economic Impact of Rapid AST in the Management of Bloodstream Infections

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Antimicrobial susceptibility testing (AST) is a core diagnostic tool for the appropriate and timely administration of antimicrobial therapies utilised to treat bloodstream infections (BSIs), which are a leading cause of sepsis. Implementation of rapid AST systems in critical points of patient care has demonstrated itself as a cost-effective strategy for the management of sepsis patients while concurrently enhancing the overall quality of care given to these patients. Rapid AST is associated with a reduction in the time to tailored therapies, shorter hospital length of stay, lower hospital readmission rates, and faster discontinuation of broad-spectrum and ineffective antimicrobials. These collective outcomes contribute to a favourable economic evaluation and compelling value proposition, particularly when navigating financial constraints within the healthcare sphere. Swift therapeutic and diagnostic protocols are essential in the treatment of sepsis patients.

Bloodstream infections and sepsis

Bloodstream infections (BSIs) are defined as the presence of viable bacterial, fungal, or viral microorganisms in the blood, and are associated with signs of systemic infection[1]. These infections can originate from various sources, including wounds, surgeries, intravenous (IV) lines, or various organ infections, and once these pathogens enter the bloodstream they can quickly spread throughout the body, leading to severe illness. BSIs are a leading cause of worldwide morbidity and mortality that requires immediate attention and administration of antibiotics[2]. Without prompt action, BSIs can quickly progress into severe infectious conditions such as sepsis[3].

Sepsis is a life-threatening condition of organ dysfunction caused by the dysregulation of a host's immune system in response to infection[4]. Affecting more than 50 million individuals worldwide per year – and causing around 11 million potentially avoidable deaths – sepsis cases represent a significant clinical and economic burden, where accurate diagnostics, rapid susceptibility testing, and optimal antimicrobial treatments are necessary in combating this time-sensitive condition[3].

The importance of rapid AST

Antimicrobial susceptibility testing (AST) stands as a fundamental pillar in the microbiological diagnosis and treatment of patients suffering from time-sensitive cases of infection such as sepsis. Any time bacterial infection is suspected, and prior to pathogen identification, patients are administered empiric broad-spectrum antimicrobial therapy based on their clinical presentation, clinical history, and the epidemiological setting[5]. Empiric therapy involves making a clinically educated judgement for the best course of treatment with limited knowledge at the time of patient presentation.

Quantitative determination of phenotypic AST provides the minimum inhibitory concentration (MIC) of a pathogen, thereby facilitating the revision and refinement of broad-spectrum antimicrobials into a personalised treatment regimen for each patient and infection[6]. Inadequate or suboptimal empiric therapy is associated with an increased risk of patient morbidity and mortality, and thus AST is a necessary step for antimicrobial adjustment[7].

The current gold standard for conventional in vitro AST includes broth microdilution, disk diffusion, and agar dilution[8]. However, these methods have a turn-around time of approximately 24 hours and require additional isolation steps prior to testing. In the context of time-dependent infections like sepsis, patient mortality increases for every hour in delay of administration of effective antibiotic therapy, meaning timely diagnosis and intervention are paramount[9]. Without prompt treatment, sepsis can very rapidly progress into septic shock, a subset of sepsis in which there are particularly profound circulatory, cellular, and metabolic abnormalities that are associated with a 50% risk of mortality[10]. Appropriate antimicrobial therapies have been shown to significantly improve patient outcomes when initiated at an early stage and without delay[11]. Expediting the AST process is therefore a vital aspect of improving patient outcomes and reducing morbidities associated with disease progression, prolonged hospital stay, and unnecessary exposure to antimicrobials. This imperative is particularly important for critically ill patients with altered and variable pharmacokinetics of antibiotics who require prompt, tailored antibiotic interventions[12]. In cases such as these, rapid AST systems that can support clinical decisions and assist in improving patient outcomes are crucial.

Rapid AST systems are defined as platforms capable of producing a comprehensive AST report within 8 hours from positive blood culture[13]. In practical terms, this means that treatment optimisation should all be achievable at least one day earlier than standard of care (SoC). Rapid AST is a welcome addition to the diagnostic workflow when restrictive opening hours and availability of clinical microbiologists are major limitations to processing of patient samples, where positive blood cultures are commonly left unprocessed for up to 70% of the working day[14].

Cost-effective, rapid AST is a necessity in streamlining procedures and reducing the hands-on time of hospital personnel, all the while providing actionable results that can promptly and accurately guide treatment decisions in time-sensitive cases of infection.

Clinical impact

Numerous studies have investigated the impact of rapid AST systems in experimental and quasi -experimental set-ups comparing rapid AST to conventional workflows. These investigations have encompassed retrospective and theoretical analyses, as well as intervention studies where rapid AST was run in real-time parallel to the conventional testing[15-20]. The collective findings indicate that rapid AST is a beneficial aid to all aspects of a BSI/sepsis patient's treatment, ranging from primary time-to-AST reporting to secondary outcomes such as treatment duration and length of hospital stay.

Implementation of rapid AST systems in hospitals is associated with a shortened time from initial diagnosis to the administration of optimal targeted therapies for patients and thereby mediates the total length of antibiotic treatment and time spent in the hospital or ICU. A retrospective analysis in the US reported that the median length of stay (LOS) for patients hospitalised with sepsis is 7.7 days[21], where several studies have demonstrated that rapid AST contributes to shortened LOS and the potential to discharge patients several days earlier, where some studies reported a reduced length of stay by nearly three days[15,17-19].

Reducing the time-to-result is one of the core necessities when implementing a rapid AST system; ideally, AST and MIC reports should be delivered in under 8 hours from positive blood culture. Several studies have demonstrated that rapid AST systems provide significant time savings and overall reduction time from blood collection to AST results[22-26]. This was reflected in a faster time for optimisation of targeted antibiotics – in some cases, this amounted to time savings of over 50 hours[15,19,20,22,27-29].

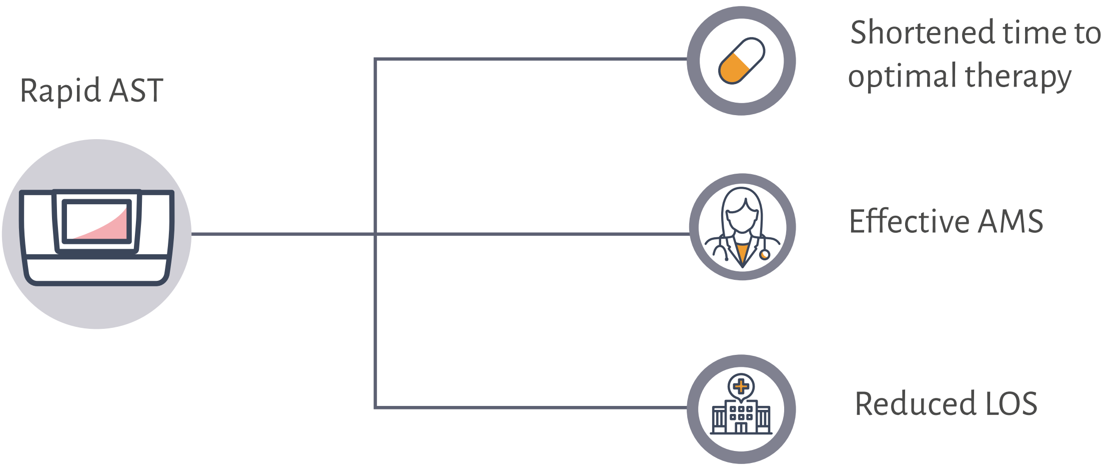

Figure 1. Rapid AST contributes to the core principles of clinical care.

Faster de-escalation of broad-spectrum antibiotic therapy and discontinuation of ineffective antimicrobials is of high importance to the patient, reducing the extent of antimicrobial exposure and the potential for toxicity or side effects associated with these treatments[20]; concurrently, this reduction in antimicrobial usage helps to limit the emergence of antimicrobial resistance in the patient and wider population, contributing to effective antimicrobial stewardship strategies (AMS)[17,20,22,28]. This is of critical importance when considering the increasing emergence of worldwide resistance. Healthcare professionals must be cognizant of the fact that current and future clinical outcomes of infection control and AMS are reliant on the extent to which we currently administer and use these broad collections of antibiotics[30]. Rapid AST can help to mitigate this problem through faster time to AST results and quicker antibiotic therapy modifications[20].

Furthermore, rapid AST can support clinical decision-making from a single AST report, reducing the amount of repeated testing that frequently occurs when using conventional AST methods[31].

Up to one-third of all sepsis survivors are re-hospitalised within 30 days of their initial discharge, and 90-day readmission rates can reach as high as 43%[32,33]. For many of these cases, this is the result of recurrent sepsis caused by a pathogen unrelated to the first instance of infection. In one retrospective study comparing pre- and post-intervention of rapid AST bundled with an effective AMS program, they found that rapid AST has the potential to decrease the rate of patient readmissions from 22% to 14%[18]. This would reduce the burden of sepsis not only the patient, but also for healthcare institutions and in the wider society.

It has been shown that there is a trend of reduction in patient mortality when rapid AST systems are implemented into the diagnostic workflow[17,34]. However, this has only been observed in large-scale meta-analyses, where single- or multi-centre investigations have been unable to show a perceived improvement in patient mortality following earlier antimicrobial de-escalation[35].

The importance of rapid AST in infection management is apparent and its clinical impact will only continue to rise.

Economic savings

With an estimated 50 million cases of sepsis per year, and a diminishing arsenal of effective antibiotics due to the rising prevalence of antibiotic resistance, sepsis management poses a growing and substantial financial burden to global healthcare systems[13,36]. Based on data and economic studies from high-income countries, the estimated cost of sepsis is around $32,000 per patient and accounts for nearly 9% of aggregated hospitalisation expenditure[37,38]. This is equivalent to over $50 billion in annual costs in US hospitals alone.

Rapid AST has demonstrated the potential to yield financial savings of over €3,000 per patient for only a moderate increase in testing costs when compared to conventional methods[24]. It is anticipated that implementation of rapid AST in the ICU would generate additional savings due to its greater clinical impact in the most severe patient cases. Moreover, when complemented by effective antimicrobial stewardship programs, these savings are further increased[17]. A decision-analytic model comparing conventional AST methods to rapid molecular testing across hospitalised patients in the United States suggested savings of up to $10,449 per patient when rapid AST is combined with an effective ASP and LOS exceeds 10 days[17].

Additional supplementary cost reductions are achieved due to clinical decisions being made earlier in a patient's clinical course and individualised therapies can be optimised sooner[24]. This encourages a more rapid de-escalation of the empiric antimicrobial spectrum and would be expected to generate savings through reduced antibiotic consumption[16].

These reports have been supported by several meta-analyses and valuation models that suggest that a significant proportion of these savings stem from the reduced time to appropriate treatments, coupled with the ensuing reduction in the length of hospital stays[16,17,24]. While the clinical benefits of de-escalation remain under discussion, it is generally accepted that earlier tailoring of antimicrobial therapy and reduced LOS are considered to be the key drivers to achieving savings[24]. These savings translate to a substantial $5.65 million for every 100,000 hospital admissions[16].

In summary, implementation of rapid AST systems has been shown to significantly impact healthcare economics by expediting the optimisation of treatment plans, shortening hospital stays, and improving utilisation of hospital resources, all of which can lower direct and indirect medical costs.

Table 1. Clinical and economic benefits from rapid AST implementation reported from several studies .

Clinical and Economic Reporting (Rapid AST vs Conventional)

Time to AST result
-50.2 hours (14.4 vs 64.5)[29]
-34.8 hours (48.3 vs 83.1)[22]
-31.4 hours (13.5 vs 44.9)[23]
-61.7 hours (27.8 vs 89.5)[24]

Time to antibiotic optimisation
-34.6 hours (38.2 vs .72.8)[22]
-19.5 hours (50 vs 69.5)[27]
-4 hours (7 vs 11)[28]
-5.4 hours (9 vs 14.4)[19]
-26.4 hours (31.2 vs 57.6)[15]
-15.9 hours (20.4 vs 36.6)[20]

Length of stay
-2.6 days (5.3 vs 7.9)[18]
-2 days (6 vs 8)[19]
-1.8 days (6.3 vs 8.1)[15]

Savings per patient
€3,074[24]
$1,642[16]

Rapid AST is central to core healthcare policies

Rapid AST systems alleviate many of the challenges faced by numerous healthcare institutions, at technical, clinical, and economic levels. Increased automation helps to effectively streamline the intensive workflow that many healthcare institutions are burdened by, increasing the number of available hands in the laboratories and wards, and permitting staff to focus their attention towards additional patients or other urgent matters. Simultaneously, these intervention studies have shown that rapid AST has the potential to improve patient care while concurrently generating increased savings through the overall reduction of hospital expenditure.

In the long run, sustained usage of rapid AST systems offsets the initial investment and maintenance costs as it drives savings through reduced antibiotic consumption and faster patient discharge[24].

In the backdrop of escalating global antimicrobial resistance rates, the necessity of adept and efficient systems to manage this growing challenge becomes even more pronounced. Rapid AST is a potent tool for swift antimicrobial dosage adjustments and the revision of empiric therapy, contributing to effective patient treatment and antimicrobial stewardship that can concurrently appraise and prevent misuse of antimicrobials that would otherwise lead to further emergence of antibiotic resistance in patients or the global population[20,28].

Beyond the scope of these individual studies, rapid AST would be expected to contribute significantly to the reduction in infection-associated societal costs. For example, indirect costs associated with severe sepsis account for 70-80% of costs and result mainly from productivity losses due to mortality[39]. Additionally, it is possible that infection outbreak caused by resistant bacteria would be contained at an earlier stage because of increased surveillance and quicker patient isolation. Furthermore, infections resulting from long-term use or overuse of antibiotics, like C. *difficile* infections, may be reduced or made more manageable. Preventable C. *difficile* infections are estimated to directly cost the United States over $6.3 billion every year and require nearly 2.4 million days of combined inpatient stay, a burden that could be significantly reduced[40].

At an institutional level, the time and monetary savings offered by rapid AST systems could be allocated to other systemic areas, potentially contributing to improved overall care and budgeting.

The critical role of ASTar

ASTar is a state-of-the-art rapid AST system from Q-linea that offers an unparalleled and extensive means of susceptibility testing and AST reporting when time matters most. Solving many of the issues faced in microbiology laboratories through extensive timesaving and the delivery of true MIC values in approximately six hours, ASTar represents a fully automated remedy requiring two-minutes hands-on time that markedly reduces the extent of technical handling required by hospital personnel[41].

ASTar can test directly from positive blood cultures and begin susceptibility testing prior to pathogen identification. The antimicrobial panel covers a broad range of pathogens and antimicrobial dilutions to generate extensive and reliable MIC values in a single run. This accelerates patient diagnosis and delivery of AST reports, and narrower, tailored therapy can begin sooner.

Furthermore, fixed dilution sample preparations are commonly used in rapid AST systems – preparations that are inadequate at accounting for the inoculum effect and can lead to administration of ineffective antimicrobial dosages. ASTar overcomes this issue by utilising a controlled inoculum during sample preparation that will consistently generate accurate MIC values during the testing period and can reliably work on blood culture samples up to 16 hours after signalling positive[42]. Accurate MIC determination provided by ASTar is vital for reliable AST reporting and treatment success.

The easy-to-follow workflow can be seamlessly integrated into hospital operations and offers an elegant solution to many of the prevailing AST challenges faced today[43].

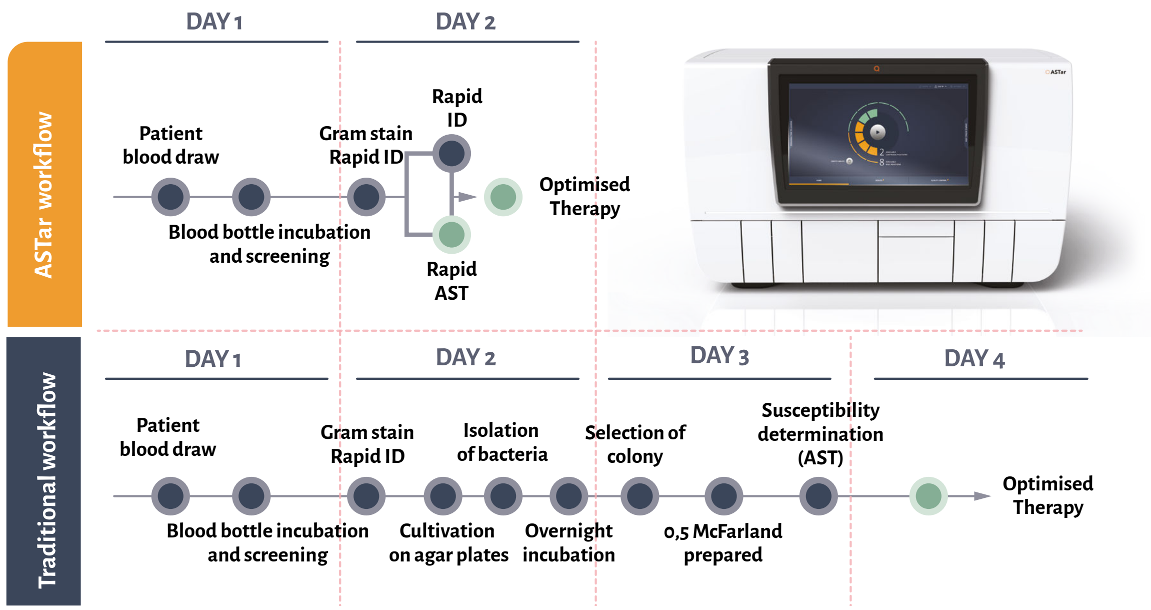

Figure 2. ASTar workflow. Fully automated rapid AST supported by ASTar can save up to 48 hours compared to the conventional workflow.

Conclusion

Rapid AST can already be considered an essential element within contemporary healthcare and its significance will only continue to grow.

With the advent of newer technologies and continued development of rapid AST systems, the demand of accompanying requirements for these systems also increases; where they need to offer increased automation with minimal handling, greater enrichment of the pathogen from background interferences, delivery of broad-species and broad-antimicrobial results, and timely MIC reporting that matches the most critical timepoints in clinical decision making[44]; all the while remaining a cost-effective solution that allows for easier adoption of these new technologies and devices[45].

In summary, the significance of rapid AST lies in its ability to expedite treatment decisions and tailoring of therapy, support AMS and infection control, and enhance healthcare efficiency. Current literature and preliminary intervention studies investigating the implementation of rapid AST systems in real-world scenarios have underscored the importance of rapid AST in improving patient outcomes and its contribution to the cost-effectiveness of healthcare economics. ASTar is primed as a key player in this field, providing a competitive time to result when compared to other rapid AST systems and offering strengths unique to ASTar that can potentially grant substantial health and economic benefits. Within the rapid AST landscape, ASTar is a comprehensive solution that can be seamlessly integrated into a diagnostic pipeline and encompasses the core tenets of healthcare policies, regulations, and overarching goals.

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D79509 V2 2024-05