

## A COMPREHENSIVE GUIDE

# PRIORITIZING SEPSIS MANAGEMENT

Essential Strategies for  
Optimizing Antimicrobial Therapy



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# 1.7 MILLION

Cases of sepsis among US adults each year<sup>1</sup>

# 270,000

Annual deaths that are caused by sepsis<sup>1</sup>

# 1 IN 3

Estimated number of patients that die in a hospital with sepsis<sup>1</sup>

## What is driving the sepsis crisis?

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Sepsis is the third leading cause of death in US hospitals,<sup>2</sup> and the cost to individual patients, the public, and the healthcare system is beyond measure. Sepsis is complex, difficult to diagnose, and even harder to treat.<sup>3</sup> Added to this is the impact sepsis care has on antimicrobial resistance, resulting in a true crisis.

With the rising incidence of sepsis, there is an urgent need to improve recognition and prevention efforts within our healthcare system.<sup>1,2,4</sup> Intensivists in both the emergency department (ED) and intensive care unit (ICU) are often on the front lines of the sepsis crisis, but it takes a multidisciplinary team, integrated management structure, consistent use of evidence-based strategies, and ongoing quality improvement to change the course of this urgent crisis. It also requires an integrated approach to sepsis management and antimicrobial stewardship. In other words, it takes a total sepsis solution—one that is comprehensive, integrated, and fully ingrained within the sepsis management process.

**This guide examines the challenges posed by sepsis, presents evidence-based strategies to address the crisis, describes a nationally accepted infrastructure for establishing sepsis management as a priority within healthcare systems, and promotes a complementary approach to antimicrobial stewardship. By taking a holistic perspective on sepsis, healthcare professionals can potentially drive improvements in patient outcomes, reduce mortality rates, and foster a more informed and cohesive approach to tackling this healthcare challenge.**

## The clinical and economic burden of sepsis

Costs attributed to sepsis are unsustainable. Beyond high mortality rates, the human cost of sepsis includes post-sepsis syndrome, and long-term physical and psychological effects, which impact an estimated 50% of sepsis survivors.<sup>5</sup> Sepsis also:

- Is the number one expense of US hospitalizations, costing an estimated \$62 billion annually.<sup>6</sup>
- Often leads to hospital readmissions—within 30 days of hospital discharge, about 20% of sepsis patients are readmitted to the hospital.<sup>7</sup>
- Can result in an economic burden for hospitals. One study showed an average annual marginal loss for hospitals with 200 beds or less of \$9.9 million and for hospitals with 500 beds or more of 34 million.<sup>8</sup>

With the shift to value-based care, these costs can place a high burden on an institution's reimbursement rates. Furthermore, poor sepsis outcomes for patients can damage a health system's reputation.



## Reversing the trend in sepsis care

With the shift to value-based care, these costs can place a high burden on an institution's reimbursement rates. Furthermore, poor sepsis outcomes for patients can damage a health system's reputation.

Sepsis symptoms mirror other conditions, making the condition difficult to diagnose and increasing the risk of mis- or under-diagnosis. For every hour of delayed treatment, the risk of death increases by 9%.<sup>9</sup> It is estimated that rapid and appropriate antimicrobial treatment can lead to an 80% survival rate following the onset of septic shock hypotension.<sup>10</sup> In fact, giving antimicrobials to suspected sepsis patients within the first hour reduces mortality by 33%.<sup>11</sup>

In research conducted by bioMérieux in 2022, 67% of clinicians reported their institutions experienced some delays in the diagnosis of sepsis and 56% acknowledged some cases of sepsis go undiagnosed in the hospital where they work.<sup>12</sup> Additionally, one study suggested 18% of patients whose symptoms mimicked culture-positive sepsis and therefore received antimicrobials in the ED were later confirmed to have had a non-infectious disease.<sup>13</sup> Sepsis trends cannot be reversed if they continue to be undiagnosed or misdiagnosed.





## REVERSING THE TREND IN SEPSIS CARE

Finding the right balance between speed to sepsis treatment and appropriate use of antimicrobials is another challenge clinicians face. To respond quickly and prevent mortality, many clinicians treat suspected cases of sepsis with broad-spectrum antimicrobials. However, without pathogen identification and antimicrobial susceptibility information, the empiric use of broad-spectrum antimicrobials may be inappropriate and could contribute to antimicrobial resistance (AMR).<sup>14</sup> The consequences can be dire. One study suggested broad-spectrum antimicrobials were inappropriate in approximately 20% of patients with septic shock and associated with a fivefold reduction in survival.<sup>15</sup> Another study found both inadequate and unnecessarily broad empiric antimicrobials were associated with higher mortality after detailed risk adjustment.<sup>16</sup>

Operationalizing sepsis management is another crucial element for effective sepsis care. Effective sepsis management demands a widespread, integrated, comprehensive approach to sepsis care—in effect, a total solution.

### Key facts

- About 80% of sepsis cases originate outside of the hospital.<sup>17</sup>
- From 2016 to 2019, the number of all sepsis-related inpatient stays in the US increased by 20.1 % from 1.8 to 2.1 million stays.<sup>18</sup>
- Aggregate hospital costs for sepsis stays increased by 66.8 % from 2016 to 2021 to \$52.1 billion.<sup>18</sup>
- The average length of stay for patients with sepsis is 75% longer than for patients hospitalized for other conditions.<sup>19</sup>

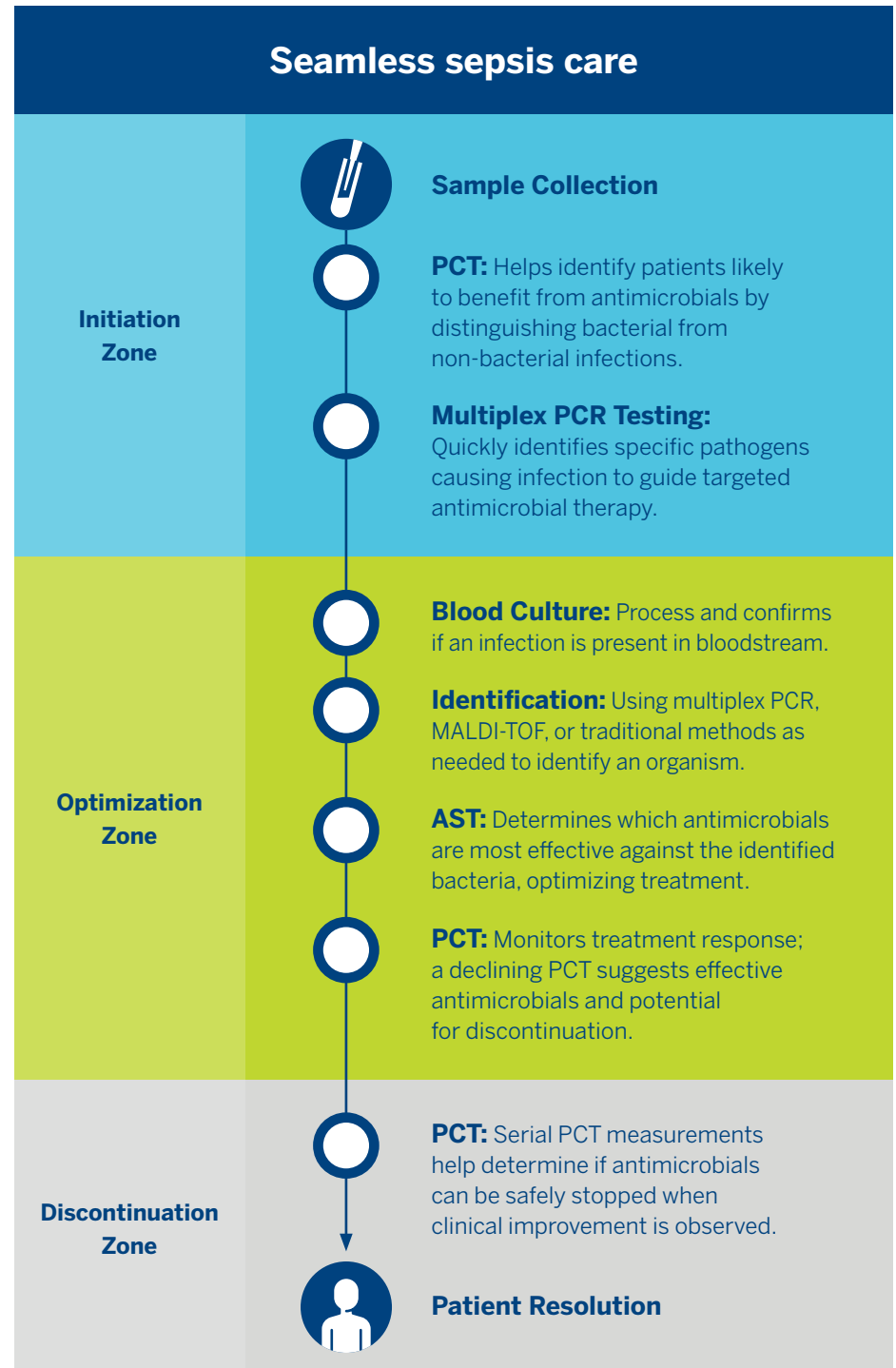
# Enhancing the patient journey with a total sepsis solution

In 2002, the Society of Critical Care Medicine established a comprehensive initiative to develop guidelines for sepsis management through its Surviving Sepsis Campaign (SSC).<sup>20</sup> Today, the updated Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock remains the standard of care for sepsis.<sup>20</sup> But guidelines alone are not enough. Successful treatment depends on a comprehensive sepsis diagnostic solution for sepsis that provides rapid, actionable decision-making information to optimize therapy and patient care for individuals with sepsis.

To start, we examine the SSC guidelines which recommend the implementation of a time-based, one-hour bundle for adults to speed diagnostic identification and time to antimicrobial treatment.<sup>21</sup> Within the first hour of suspecting or recognizing sepsis or septic shock, these five steps should be taken:

- **Measure lactate level** and repeat step if levels are  $>2\text{mmol/L}$ .
- **Obtain blood cultures** prior to administration of antimicrobials.
- **Administer broad-spectrum antimicrobials** until pathogen identification and susceptibilities have been established and the right regimen has been determined.
- **Begin rapid administration of 30 mL/kg crystalloid** for hypotension or lactate  $\geq 4\text{ mmol/L}$ .
- **Apply vasopressors** if patient is hypotensive during or after fluid resuscitation to maintain a mean arterial pressure (MAP) of  $\geq 65\text{ mmHg}$ .

The one-hour bundle provides early indicators that support a quick response to suspected sepsis.



## ENHANCING THE PATIENT JOURNEY WITH A TOTAL SEPSIS SOLUTION

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Now we examine a total diagnostic solution for sepsis management:

### Phase 1: Suspected or Recognized Sepsis or Septic Shock

A patient presents in the ED and after examination is suspected of having sepsis or septic shock. A history is taken to ascertain if the exposure was nosocomial or community-based. The clinician determines the likely source and type of culture needed. The one-hour bundle is executed. Diagnostic testing should include blood cultures, procalcitonin (PCT) biomarker testing, comprehensive and rapid assay testing to identify pathogens and antimicrobial-resistant genes, and imaging. If acute kidney injury (AKI) is suspected, testing to assess the risk level could be considered.

### Phase 2: Antimicrobial Decision

During the next phase, diagnostic testing is completed to trend PCT levels, provide source determination, and guide clinical decision-making regarding appropriate antimicrobial treatment. This includes microbial identification and susceptibility testing that establishes minimum inhibitory concentration (MICs) levels for potential targeted antimicrobial treatment options. Based on these outcomes, antimicrobial therapy should be re-evaluated either to continue with broad-spectrum antimicrobials or to replace the empiric treatment with narrow-spectrum, targeted antimicrobials.

### Phase 3: Targeted Therapy

At this stage, one of two things happen: either the patient's condition improves or worsens. If the condition improves, re-testing of PCT levels and blood cultures provides insight into treatment duration and, with pathogen identification and susceptibility testing results, de-escalation of antimicrobials can occur. Antimicrobial discontinuation is recommended when the PCT value declines to  $\leq 0.5$  pg/L or decrease by  $\geq 80\%$  from the peak.<sup>22</sup> If the patient's condition deteriorates, additional diagnostic testing is advised to determine the potential of a hospital-acquired infection (HAI), missing source control, multidrug-resistant organisms (MDROs), central line bloodstream infection (CLABSI), or AKI.

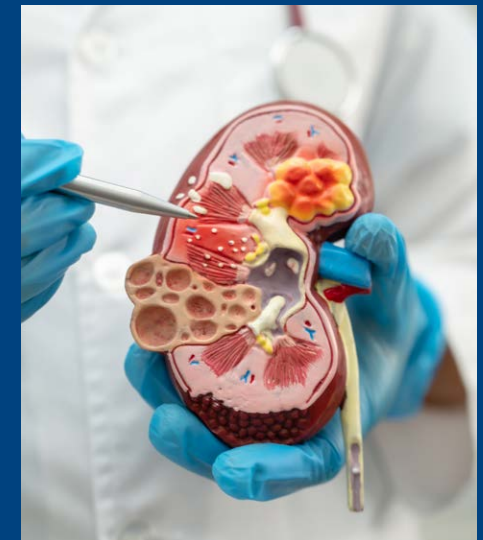
### Phase 4: Optimized Therapy

With the diagnostic insights obtained in the previous phase, clinicians can revisit and enhance the antimicrobial treatment, target antimicrobial duration, prognosticate outcomes and resolution, deescalate antimicrobials at the appropriate time, and determine when to discontinue antimicrobial treatment. Again, discontinuation is recommended when the PCT value declines to  $\leq 0.5$  pg/L or decreases by  $\geq 80\%$  from peak.<sup>22</sup> In the event the patient's condition continues to worsen, a separate treatment pathway for MDROs may be needed.

With rapid and accurate diagnostics informing timely clinical decision-making, healthcare professionals can be proactive, systematic, and responsive to each patient's sepsis journey.

## Sepsis-associated acute kidney injury (S-AKI)

Abrupt deterioration of renal function in the presence of sepsis, or S-AKI, is a common yet life-threatening complication in sepsis cases. One study showed sepsis was a contributing factor to AKI in 47.5% of sepsis cases.<sup>23</sup> S-AKI is associated with higher hospital mortality and longer lengths of stay.<sup>23,24</sup> Additionally, up to 20% of individuals with S-AKI may need renal replacement therapy.<sup>25</sup> Given the high incidence of S-AKI, it is reasonable to conduct diagnostic testing for its presence when sepsis is confirmed.



# Maximizing the hospital sepsis management program

In 2023, the Centers for Disease Control and Prevention published its Hospital Sepsis Program Core Elements, a coordinated approach for hospitals to monitor and optimize their sepsis management systems and operations.<sup>26</sup>

**The core elements are designed to address five factors that are critical for improving the delivery of effective sepsis practices:**<sup>26</sup>

1. Healthcare staff knowing what to do and why
2. Healthcare staff understanding the risks and benefits of treatment
3. Healthcare staff having strong team collaboration
4. Healthcare staff feeling empowered and supported
5. Hospitals having adequate staffing

**The seven core elements of an effective hospital sepsis management program include:**

## 1 Hospital leadership commitment

Hospital leadership must be vocal supporters of the sepsis program and make sepsis performance improvement a priority for all staff. This can be achieved by allocating adequate staffing, time, financial, and information technology resources to the program.

## 2 Accountability

Hospital sepsis programs need one leader or two co-leaders who are accountable for program management and outcomes. Programs led by a physician-nurse team are highly recommended. Sepsis program leaders should possess strong leadership and communications skills as well as sepsis expertise.

## 3 Multi-professional expertise

A multidisciplinary team is advised for the sepsis management program encompassing both clinicians and other healthcare professionals. This includes establishing dedicated sepsis coordinators who are responsible for sepsis case review. These coordinators should provide feedback to staff on reviewed cases; identify areas of focus for sepsis quality improvement initiatives; monitor adherence to sepsis protocols; and track and communicate sepsis performance. The multidisciplinary sepsis program team should also include representation from:

- Antimicrobial stewardship
- Case management
- Clinicians and leaders from the ED, intensive care units (ICUs), and inpatient wards across all locations
- Critical care and emergency medicine
- Epidemiology
- Hospital medicine
- Infectious diseases
- Information technology
- Laboratory medicine
- Microbiology
- Nursing
- Oncology
- Obstetrics
- Pediatrics
- Pharmacy
- Public health
- Social work
- Surgery

It may also be useful to include patients, family members, caregivers, and community members as part of the sepsis management team.

## 4 Action

Hospital sepsis programs should develop structures and processes to facilitate evidence-based sepsis systems, including quality improvement processes. The sepsis management team should choose, monitor, and refine interventions to optimize sepsis treatment and outcomes.



## MAXIMIZING THE HOSPITAL SEPSIS MANAGEMENT PROGRAM

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### 5 Tracking

Tracking sepsis activities and outcomes enables sepsis management teams to identify gaps, trends, and improvement opportunities and to understand the impact of sepsis interventions on the institution's sepsis goals. The sepsis management team will need to prioritize which metrics to monitor so the focus shifts to the processes and outcomes that drive the best results for patients.

### 6 Reporting

To keep staff engaged and motivated, regular reporting on sepsis management interventions and outcomes is needed. Clear, transparent reporting can help staff at different levels understand sepsis protocols and their performance/contributions to improving sepsis outcomes for the health system. Reporting also provides leadership with critical feedback on sepsis priorities, achievements, and performance.

### 7 Education

Hospital staff must have knowledge about sepsis and their team-based roles in sepsis management. Different education formats are recommended, including simulation or case-based training, in-person or on-demand video lectures, and emails and newsletters. Patient education is also an important element in effective hospital management of sepsis. Diverse patient education resources should also be a part of the hospital's sepsis management program.

While sepsis patients must receive antimicrobial treatment as quickly as possible, there is an inherent dilemma—short-term broad-spectrum antimicrobials used empirically before susceptibility testing is completed may lead to greater antimicrobial resistance.<sup>24</sup> That means clinicians must strike the right balance in treatment between short-term, patient-focused efforts to improve outcomes with longer-term, community-wide efforts to prevent AMR. This frequently translates into using broad-spectrum empiric antimicrobial treatment and narrow-spectrum antimicrobials once susceptibility testing is available. Given the scope and complexity of sepsis, antimicrobial stewardship has become a diagnostic imperative.



## Rory's Regulations

One successful strategy for sepsis management is to adopt sepsis protocols and standard guidelines for healthcare providers to identify and treat sepsis early.<sup>27</sup> Protocols help healthcare staff understand sepsis guidelines and the specific actions needed to impact patient outcomes.

In New York state, a set of regulations to improve the rapid diagnosis and treatment of sepsis were approved, called Rory's Regulations. The protocols provide for:<sup>27</sup>

- Screening and early recognition of patients with sepsis and septic shock.
- Guidelines on early delivery of antimicrobials.
- Training, resources, and equipment for healthcare clinicians to enhance early identification and treatment.
- Reporting requirements for all sepsis-related data to be used in statewide monitoring, compliance, and updating best practices.

In the first 30 months of implementation, Rory's Regulations reduced the mortality for adult sepsis patients by 4.3% and reduced ICU admissions by 17.2%.<sup>28</sup> In 2022, the New York State Department of Health reported these mandatory sepsis protocols saved 16,000 lives between 2015-2019.<sup>29</sup>

# Pairing sepsis management with antimicrobial stewardship

Timely antimicrobial treatment is one key imperative for solving the sepsis crisis. But there is another, similarly dire global threat impacted by the use of antimicrobials for sepsis—antimicrobial resistance (AMR). These two priorities can be at odds when clinicians must balance a speedy response to sepsis with preventing AMR.

In the US, more than 2.8 million drug-resistant infections occur each year, and more than 35,000 people die as a result.<sup>30</sup> In 2019, the number of ED visits with infectious and parasitic diseases as the primary diagnosis was 3.8 million.<sup>31</sup> The direct cost to the US healthcare system from HAIs alone is estimated between \$28.4 billion–\$45 billion each year.<sup>32</sup> They also increase lengths of stay; one study showed a 23.8% increase in lengths of stay for HAIs caused by gram-negative pathogens.<sup>33</sup>

The primary cause of AMR in humans is the inappropriate use of antimicrobials.<sup>34</sup> Research shows as many as 30% to 50% of all antimicrobials prescribed in US acute-care hospitals are either unnecessary or inappropriate.<sup>35</sup> Add to this that roughly 20% of hospitalized patients on antimicrobials experience side effects<sup>36</sup> and complications from antimicrobials, resulting in an estimated 145,000 emergency department visits annually.<sup>37</sup>

A leading strategy to combat AMR is antimicrobial stewardship (AMS), a systemic approach to ensure antimicrobials are used responsibly and effectively in healthcare settings.<sup>38</sup> AMS offers coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal regimen, dose, duration of therapy, and route of administration. The goals of AMS are to achieve the best clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, reduce healthcare costs for infections, and limit the selection of drug-resistant strains. It also delivers improvements in susceptibility/resistance, shorter patient lengths of stay, and maintained or reduced mortality rates.<sup>38</sup>

Sepsis management and AMS must work in unison. Effective sepsis management should consider the potential risk of prescribing potentially unnecessary antimicrobials. But clinicians walk a fine line. On the one hand, they must respond quickly to suspected sepsis cases with empiric antimicrobial treatment to reduce mortality and lengthy hospital stays. On the other hand, they do not want to contribute to the misuse or overuse of antimicrobials, which could fuel AMR.

## An AMS approach to sepsis management enables:

- **Optimal timing of antimicrobials in patients with sepsis:** Currently, this means using the standard for initial treatment within three hours from the time of presentation.
- **Antimicrobial de-escalation (ADE) in patients with sepsis:** Including ADE in the post-prescription review process, an evidence-based antimicrobial stewardship program (ASP) intervention, has been shown to be effective in reducing antimicrobial use.<sup>39</sup>
- **Duration of antimicrobial therapy in patients with sepsis:** International and national guidelines for both sepsis management and AMS support clinical decision-making related to duration of antimicrobial therapy.<sup>40</sup>
- **Rapid diagnosis of MDROs:** Rapid microbiology testing is crucial, in part, because 40% of patients with sepsis have culture-negative results.<sup>41</sup>
- **Implementation of an ASP for patients with sepsis:** Hospital antimicrobial stewardship programs are administered by multidisciplinary committees similar to those included on the sepsis management team. By dovetailing the expertise of these two teams, healthcare systems can prioritize the most meaningful interventions and drive improvements for both sepsis care and antimicrobial use.

## Case Example

In 2019, Barb H., a middle-aged microbiologist, wife, and mother of three, returned to the hospital two weeks after having surgery to remove two large blockages in her small intestine. Because she had a high fever and extremely low blood pressure—two important indicators of sepsis—her medical team began a course of intravenous antimicrobials.

A computed tomography (CT) scan revealed Barb's surgical site had perforated and was leaking bowel content into her abdomen, resulting in a systemic infection and sepsis. Doctors performed emergency surgery to repair the perforation and other damage caused by the leakage and infection.

It turned out that the bacteria causing the infection was *Klebsiella pneumoniae*, a common underlying cause of sepsis. In Barb's case, the bacteria was susceptible to a few different antimicrobials. Her infectious disease doctor chose piperacillin-tazobactam, which was the agent Barb's doctors gave her when she was initially admitted for sepsis. The infectious disease doctor tried to switch Barb to different agents (ceftriaxone and metronidazole), but she had an adverse reaction to those drugs.

Because Barb's original surgery failed and she developed septicemia and abscesses, an ostomy was performed to give her bowels and internal organs time to heal. She ended up having short bowel syndrome, severe malnutrition, and a series of complications, including unstable potassium levels, low iron levels requiring iron infusions, and severe weight loss. Her kidneys started to have issues, so a nephrologist started her on total parenteral nutrition (TPN). After about a month, Barb went home with infusions of saline, piperacillin/tazobactam, and the TPN and began a long, arduous process to regain her strength and increase her weight. Four months later, she had a third surgery to reverse the ostomy.

This is just one example of how complicated and entrenched sepsis can be. It exemplifies the need for quick antimicrobial treatment at the start, followed by ongoing assessment, re-evaluation, and adjustment based on pathogen identification, susceptibility testing, and each patient's unique experiences with antimicrobial treatment.



## Adopting a proactive approach to sepsis management

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Intensivists in the ED and ICU, as well as other front-line clinicians encounter the sepsis crisis every day. With the number of incidents trending up, high mortality rates, longer lengths of stay, high hospital readmission rates, and high rates of long-term sepsis syndrome, the costs to our society and our healthcare system are simply too high. Urgent, disciplined, and effective sepsis management must become a greater priority throughout our healthcare system. Leadership must dedicate staffing, time, technology, and financial resources to enable incorporation of evidence-based interventions and continuous improvement in sepsis care. By adopting a total sepsis solution that includes integration with AMS, healthcare providers can change the course of sepsis within their institutions, improve patient outcomes, and significantly reduce the associated healthcare costs.



# bioMérieux: your partner for sepsis management

bioMérieux is committed to helping healthcare providers improve sepsis management on an individual patient basis as well as an organizational management basis. In addition to our diagnostic solutions, we offer a comprehensive support system that includes software, lab consultancy, technical support, medical education, and on-site training related to sepsis management.



## Resources

We also offer a variety of educational resources related to sepsis.

### Our online sepsis resources page

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[www.biomerieux.com/us/en/our-offer/point-of-care/sepsis-solutions.html](http://www.biomerieux.com/us/en/our-offer/point-of-care/sepsis-solutions.html)

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Our diagnostic solutions bring high medical value testing to healthcare professionals, providing them with the most relevant and reliable information, as quickly as possible, to support treatment decisions and better patient care.

bioMérieux's mission entails a commitment to support medical education, by promoting access to diagnostic knowledge for as many people as possible. Focusing on the medical value of diagnostics, our collection of educational booklets aims to raise awareness of the essential role that diagnostics test results play in healthcare decisions.

Other educational booklets are available.  
Consult your local bioMérieux representative or visit [biomerieux.com/en/education/educational-booklets](https://biomerieux.com/en/education/educational-booklets)



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