



42nd Critical Care Congress Review

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CE/CME Enduring Material
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Learning Objectives

At the conclusion of this activity participants should be able to:

- Discuss approaches to screen for delirium and consider both pharmacologic and nonpharmacologic approaches to prevention and management
- Minimize the development of malnutrition through goal-directed therapy combining the use of enteral and parenteral nutrition
- Recognize new therapies for sepsis in the intensive care unit and the limitations of current research for better translation of evidence to the bedside

Type of Activity

This activity was designed as an evidenced based forum to review expert opinions of various topics in critical care. This activity will focus on increasing knowledge and its application to practice.

Competencies

SCCM supports recommendations that will promote life-long learning through continuing education. SCCM promotes activities that encourage the highest quality in education that will enhance knowledge, competence or performance in critical care practice. This activity will meet the following:

- Patient- and Family-Centered Care
- Practice Applications
- Quality Improvement
- Multiprofessionalism

Target Audience

This continuing medical education offering is intended to meet the needs of all physicians, nurses, pharmacists, respiratory therapists and other providers who care for critically ill patients.

Physicians

Accreditation Statement

The Society of Critical Care Medicine (SCCM) is accredited by the Accreditation Council for Continuing Medical Education (ACCMME) to provide continuing medical education for physicians.

Designation Statement

SCCM designates this home study educational activity for a maximum of 1 AMA PRA Category 1 credits™. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Nurses

SCCM is approved by the California Board of Registered Nursing, Provider No. 8181 and approves this panel for 1 contact hour.

Pharmacists



The Society is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education. This monograph will provide 1 continuing education hour. (0236-0000-13-469-H01-P) SCCM reports to a continuing pharmacy education (CPE) tracking service, CPE Monitor that will authenticate and store data for completed CPE units received by pharmacists and pharmacy technicians. The tracking system will make CPE data for each participant available to the state boards of pharmacy where the participant is licensed or registered. After CPE units are processed by ACPE and NABP, pharmacists and pharmacy technicians will be able to login to a comprehensive electronic profile to access information about their completed CPE.

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Upon completion of this free purchase and the complete review of the material, please login to www.mysccm.org with your SCCM Customer ID and password. In the My Learning section of MySCCM.org, links will appear for this activity's post-test and evaluation under Congress Review. After earning a passing score of 70% or higher on the posttest, you will be able to claim credit for this activity.

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Surviving Sepsis Campaign: 2012 Guidelines

In 2002, the Surviving Sepsis Campaign (SSC) was launched as an international collaboration to reduce mortality from sepsis. With the recent publication of the SSC's 2012 guidelines and two revised bundles, and with a 25% relative reduction in mortality from sepsis noted over the time period of the Campaign, the Campaign now moves into a new phase and challenges all hospitals to join this remarkable global effort

The SSC Guidelines: Using a Limited Evidence Base to Guide Clinical Practice



Presented by R. Phillip Dellinger, MD, MSc, MCCM, Professor of Medicine at Cooper Medical School of Rowan University, and Professor of Medicine at University of Medicine and Dentistry of New Jersey, Camden, New Jersey, USA. He is also Director of Critical Care Medicine at Cooper University Hospital.

The release of the 2012 Surviving Sepsis Campaign guidelines (Dellinger RP, et al. *Crit Care Med.* 2013;41:580-637) brings to fruition an important achievement for critical care worldwide. "Our new guidelines are truly international, setting a foundation for establishing an international performance improvement program to save lives," said R. Phillip Dellinger, MD, MSc, MCCM. In discussing the guidelines, Dellinger pointed out that the evidence reviewed in making recommendations was limited and often complicated.

The guidelines committee utilized the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system to evaluate the evidence upon which the guidelines are based. "In past guidelines, we used only letters to grade the quality of the evidence, with A the highest level, as in randomized control trials, and D the lowest level, consisting of case series or expert opinion," explained Dellinger. "With the 2012 guidelines, we had the added ability to signify an ungraded recommendation, reflecting the opinion of the committee."

The GRADE system also allowed the committee to assign a number to predict the strength of the recommendation (1 = strong recommendation; 2 = weak [suggested] recommendation). The determinants of strength were the quality of the evidence, relative importance of outcomes, risks and costs, and absolute magnitude and precision of effect.

Dellinger summarized the 2012 recommendations, beginning with antibiotic therapy. "We continue to recommend that intravenous antibiotics be given as early as possible and within the first hour of recognition of septic shock and severe sepsis without septic shock," he said. These are graded as strong recommendations, although the evidence regarding severe sepsis without shock is less robust than that for septic shock.

"In the 2012 guidelines, we added the remark that although the weight of evidence supports the prompt administration of antibiotics following recognition of severe sepsis and septic shock, the feasibility with which clinicians may achieve the ideal state has not been scientifically validated," explained Dellinger. "We want physicians to strive each day to begin antibiotic therapy earlier, recognizing that current standard of care falls short of this goal."

Regarding fluid therapy, the 2012 guidelines reflect changes that now recommend using crystalloids as the initial fluid of choice in every patient with severe sepsis and septic shock. Furthermore, the guidelines suggest adding albumin to fluid resuscitation when patients require substantial amounts of crystalloids.

"We recommend against the use of hydroxyethyl hetastarches for fluid resuscitation of severe sepsis and septic shock," said Dellinger. "This recommendation is an example of a complicated area. We based it on the results of the Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP) trial, the Effects of Voluven on

Hemodynamics and Tolerability of Enteral Nutrition in Patients with Severe Sepsis (CRYSTMAS) trial, the Scandinavian Starch for Severe Sepsis/Septic Shock (6S) trial, and the Crystalloid Versus Hydroxyethyl Starch Trials (CHEST). However, the results of the recently completed Efficacy and Safety of Colloids Versus Crystalloids for Fluid Resuscitation in Critically Ill Patients (CRISTAL) trial were not considered, and we will need to do so when making future recommendations."

Regarding the use of vasopressors, the 2004 guidelines had recommended norepinephrine and dopamine equally, but a large trial comparing these agents has since shown a strong trend favoring norepinephrine across all subgroups of shock (De Backer D, et al. *N Engl J Med.* 2010;362:779-789), and a meta-analysis of comparative studies supports norepinephrine over dopamine, as shown in Figure 1 (De Backer D, et al. *Crit Care Med.* 2012;40:725-730). There is also concern about the association of dopamine with serious tachyarrhythmias. "Based on these findings, we recommend norepinephrine as the first-choice vasopressor," said Dellinger, "and we suggest that dopamine be reserved only for highly selected patients who are at very low risk of tachyarrhythmias and with relative or absolute bradycardia."

The new second-choice vasopressor is epinephrine, either added to or potentially substituting for norepinephrine when norepinephrine alone does not achieve adequate blood pressure. "We also have an ungraded recommendation for adding vasopressin, 0.3 units per minute, to norepinephrine with the intent of raising the mean arterial pressure to target or decreasing norepinephrine dosage."

Phenylephrine is not recommended in the treatment of septic shock except in three circumstances: 1) if norepinephrine is associated with serious tachyarrhythmias; 2) if cardiac output is known to be high and blood pressure is persistently low with alternative vasopressors; or 3) as salvage therapy when no other vasopressor achieves target.

Meta-analysis: Norepinephrine Versus Dopamine in Sepsis Treatment

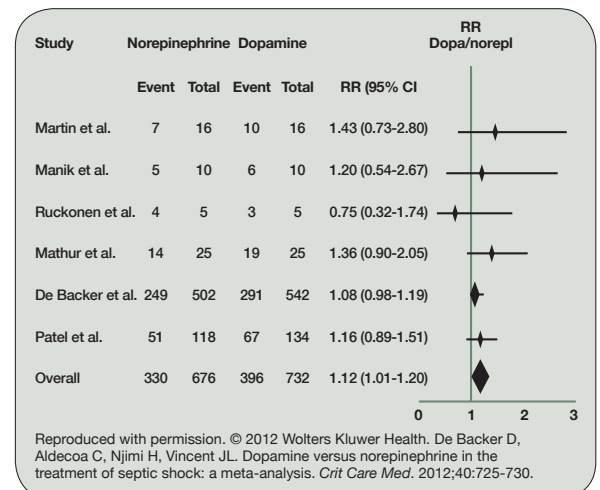


Figure 1.

In patients with sepsis-induced tissue hypoperfusion, the new guidelines recommend that the protocol target a mean arterial pressure of 65 mm Hg and a urine output of 0.5 mL/kg/h.

“The guidelines raise the initial fluid challenge in sepsis-induced tissue hypoperfusion to a minimum of 30 mL/kg of crystalloids, a portion of which can be albumin equivalent,” said Dellinger. “We continue to recommend the early goal-directed therapy targets of a central venous pressure of 8 mm Hg to 12 mm Hg and achieving a superior vena cava O₂ saturation of 70% or less.”

Recognizing the limitation of using pressure measurement to predict fluid responsiveness, the 2012 guidelines recommend that clinicians also

assess such dynamic measures of fluid responsiveness as change in pulse pressure, stroke volume variation, arterial pressure, heart rate variables, and other hemodynamic variables. “The effect on stroke volume of fluid resuscitation using pulse contour is also an alternative, as well as directly measuring stroke volume with either a pulmonary artery catheter or with Doppler,” said Dellinger.

New to the 2012 guidelines is the lactate clearance recommendation. This suggests that in patients with elevated lactate levels as a marker of hypoperfusion, resuscitation should be targeted to normalize lactate as rapidly as possible.

The SSC Improvement Initiative: 2012 Revised Sepsis Bundles

Two revised bundles reflecting the 2012 SSC guidelines are now available to provide hospitals and clinicians with invaluable road maps to evidence-based sepsis care (see Figure 2). “These bundles distill the information contained in the 95-plus pages of the guidelines,” said Mitchell M. Levy, MD, FCCM, noting that the bundles represent just one component of the multifaceted, collaborative Campaign.

Levy prefaced his talk with a discussion on early data regarding compliance with the SSC bundles (Levy MM, et al. *Crit Care Med.* 2010;38;367-374). “We found that over a two-year period we had a 20% to 30% increase in compliance with the bundles, and that was associated with about a 7.5% absolute risk reduction in mortality over the same period,” said Levy. These data encompassed SSC’s first analysis, which looked at the treatment of 15,000 patients with severe sepsis and septic shock worldwide from January 2005 through December 2006.

A more recent SSC analysis spans four years – January 2005 through December 2008 – and examines outcomes and other data for more than 28,000 patients with severe sepsis and septic shock. “The demographics of this database indicate that the Campaign has remained a multinational effort,” reported Levy. “Two-thirds of the patients are from North America, about 25% are from Europe and about 10% are from Latin America.”

An important finding of the four-year analysis was the decrease in the adjusted mortality rate, dropping from 36.8% to 28.2%. “The data demonstrated that in nearly 30,000 patients, a 25% relative risk reduction in mortality was associated with a statistically significant increase in compliance with the SSC,” said Levy.

“For every quarter that a site participated in the Campaign, there has been a 1% reduction in hospital mortality in sepsis per quarter,” Levy continued. “The longer that hospitals stayed in the campaign and worked on our quality-improvement intervention, the more patients survived sepsis in those institutions.” Higher compliance was associated with a significant improvement in hospital survival regardless of the patient’s point of origination. “These results build a case that not only do more patients survive if we identify sepsis and apply the sepsis bundles, but also hospital survival is better in the institutions where there is better compliance,” stated Levy.

Among other data that served as a basis for revising the sepsis bundles was the finding that linked hospital mortality to delays in antibiotic therapy for patients with severe sepsis or septic shock. “We saw an increase in the odds ratio of about 5% to 7% for every hour’s delay in receiving antibiotics,” said Levy. “This was what informed our recommendation to get antibiotics on board within the first hour.”

The two revised 2012 bundles consist of an initial resuscitation bundle (to be initiated immediately upon identifying patients with

severe sepsis and septic shock) and a septic shock bundle (to be initiated immediately and completed within six hours for patients with septic shock). The previous management bundle has been dropped in response to information that became available since publication of the 2008 guidelines.

The initial resuscitation bundle is intended to be completed within three hours of presentation. Time of presentation is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review. The bundle calls for measuring the patient’s lactate level, obtaining blood cultures prior to giving antibiotics, administering broad-spectrum antibiotics, and providing 30 mL/kg of crystalloid for hypotension or a lactate level of 4 mmol/L or higher.

Vasopressors should be administered for hypotension unresponsive to initial fluid resuscitation to maintain a mean arterial pressure of 65 mm Hg or higher. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or an initial lactate level of 4 mmol or higher, central venous pressure (CVP) and central venous oxygen saturation (ScvO₂) should be measured. The targets for quantitative resuscitation included in the 2012 SSC guidelines are a CVP of 8 mm Hg or higher, oxygen saturation of 70% or higher, and lactate normalization.

The Surviving Sepsis Campaign Care Bundles.

TO BE COMPLETED WITHIN 3 HOURS:

- 1) Measure lactate level
- 2) Obtain blood cultures prior to administration of antibiotics
- 3) Administer broad spectrum antibiotics
- 4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L

TO BE COMPLETED WITHIN 6 HOURS:

- 5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
- 6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmol/L (36 mg/dL):
 - Measure central venous pressure (CVP)*
 - Measure central venous oxygen saturation (ScvO₂)*
- 7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥ 8 mm Hg, ScvO₂ of $\geq 70\%$, and normalization of lactate.

Figure 2.

Presented by Mitchell M. Levy, MD, FCCM, Medical Director of the Medical Intensive Care Unit at Rhode Island Hospital and Professor of Medicine and Division Chief of Pulmonary and Critical Care Medicine at The Warren Alpert Medical School of Brown University in Providence, Rhode Island, USA.



Sepsis Performance Metrics: What Is on the Horizon for Regulatory Agencies?



Presented by Sean R. Townsend, MD, Vice President of Quality and Safety at California Pacific Medical Center, and Clinical Assistant Professor at the University of California, San Francisco.

Sean R. Townsend, MD, began his talk by discussing the death of Rory Staunton, a sixth-grade student who sustained abrasions playing basketball and subsequently died of undiagnosed, untreated sepsis. This fatal medical error met with national outcry and resulted in new regulations in the State of New York requiring hospitals to adopt aggressive procedures for identifying sepsis and beginning treatment within one hour.

“This boy did not fall into the typical age group of patients who develop severe sepsis and septic shock,” said Townsend. “Rather, this is a disease of the elderly, and considering that the population is aging, regulatory agencies have become increasingly interested in severe sepsis.” He noted that according to the National Hospital Discharge Database, hospitalization rates for sepsis have more than doubled from 2000 through 2008 (Hall MJ, et al. *NCHS Data Brief*. 2011;62:1-8). “Clearly, if you are a Medicare administrator, you’re going to start to pay greater attention to this disease,” Townsend said.

Townsend discussed procedures set forth by the National Quality Forum (NQF), a nongovernmental organization that reviews, endorses and recommends use of standardized performance measures to ensure high quality care for patients in the United States. The NQF consists of various stakeholders, including The Joint Commission, the Centers for Medicare & Medicaid Services (CMS), and the Agency for Healthcare Research and Quality. Every three years, NQF-endorsed measures are reviewed and reevaluated alongside any new proposals and measures.

The bundles of the Surviving Sepsis Campaign have moved successfully through this process of review and evaluation and recently earned NQF endorsement. NQF evaluates measures based on five criteria: 1) evidence, performance gap, and priority; 2) reliability and validity (scientific acceptance of measure properties); 3) feasibility; 4) usability and use; and 5) comparison to related or competing measures.

If a measure meets these criteria, it begins moving through the several-tiered NQF consensus development process.

The first four steps of this consensus process entail a call for nominations, a call for candidate standards, a review of the candidate consensus standard, and a period for public comment. The committee then votes to determine whether the measure should move forward, and the measure undergoes another period for comments from NQF member organizations. Board ratification of the measure signifies that it has achieved NQF endorsement, but this can be appealed at any time if adequate reasons are presented.

The SSC bundles attained NQF endorsement in February 2013. One area of controversy involves the initial resuscitation bundle, which requires completion within three hours of presentation and defines time differently for emergency departments versus other venues of care. “We have, in a sense, two standards for when the clock begins to tick,” said Townsend. “This was always the case with the Surviving Sepsis Campaign, but this may create some concern for providers when it becomes an accountability measure that will ultimately be tied to pay for performance.”

Townsend also discussed the potential controversy relating to value-based purchasing, noting that SSC data reveal a low degree of bundle compliance overall – compliance moved from 10% to 30% after eight quarters of participation in the campaign. “Providers might argue that they don’t want to be held accountable if 30% compliance is the best rate that can be achieved,” said Townsend. However, the counterargument to this concern asserts that quality measures currently used in value-based purchasing are converted to percentiles; therefore, if optimal compliance is 30%, that becomes the top decile of performance and the basis for reimbursement under value-based purchasing.

“The bundles may be difficult to do, but driving compliance higher will be important, and this will truly identify those who can best perform across the country under this particular measure set,” stated Townsend. Now that the SSC bundles have achieved NQF endorsement, they are available for providers, insurers, regulatory bodies, and ultimately CMS to pick up for use across the country as the accepted measures of quality performance in sepsis care.

The Global SSC: Regional and National Variation in Performance

A recent report on SSC outcomes for ICU sepsis patients in the United States and Europe reveals striking differences between these regions and raises some interesting questions (Levy MM, et al. *Lancet Infect Dis.* 2012;12:919-924). “One of the first differences we see relates to SSC participation, which was 74% in the U.S. and 26% in Europe,” said Richard J. Beale, MD, FRCA, FFICM, who practices in the United Kingdom.

Hospital mortality also differed dramatically, showing a higher rate in Europe (41%) than in the U.S. (28%). “The question is, why?” asked Beale “Does the way sepsis is treated in the United States account for a far better mortality outcome?”

Beale theorized that another significant regional difference – the original point of care for patients – may underpin the mortality differential. Most ICU patients in the United States originated from the emergency department (65%), whereas most ICU patients in Europe came from the wards (51.5%) and only 33% came from the emergency department. “In my own experience, patients who came to the ICU from the wards always did much worse,” said Beale. “Does this mean there is a group of patients who have not been identified quickly enough and have gone to the ward without appropriate intervention?”

Other outcome data showed that organ failure was higher among patients treated in European hospitals, although cardiovascular organ failure was the same in the United States and Europe. Nosocomial infection occurred in significantly more patients in Europe than in the U.S. “The incidence of pneumonia – the biggest driver of sepsis – was similar in both regions, but urinary tract infections were more common in the U.S. and abdominal infections occurred more in Europe,” noted Beale. “This might suggest that the U.S. patients were a little less sick and would therefore do better,” he said.

“The infection data also raise an alternative explanation that where there are more resources, more people may be admitted who don’t need to go to the ICU, and that is why their outcomes are better,” Beale continued. “It’s possible that if those same patients were admitted to a European hospital, many would do well on the ward and never move to the ICU.”

Although overall bundle compliance is higher in the United States than in Europe, this is not true for all of components of the bundle. “For example, there is higher performance in Europe for reaching the recommended CVP of 8 mm Hg or higher within six hours of presentation,” said Beale. Another finding was the significantly greater use of drotrecogin alfa in Europe within 24 hours of presentation in the ICU. [Note: drotrecogin alfa has been withdrawn from the market.]

Presented by Richard J. Beale, MBBS, FRCA, FFICM, a Consultant Intensivist, and Head of Perioperative, Critical Care and Pain Services at Guy’s and St Thomas’ NHS Foundation Trust in London, United Kingdom.



An unadjusted odds ratio analysis showed that hospital mortality was worse in Europe than the United States. “However, when the data are adjusted looking at various confounding factors, the odds ratio differences largely, but not completely, disappeared,” stated Beale. “This suggests that sick patients in the ICU are treated in much the same way, with much the same results.”

Survivors generally had shorter hospital and ICU lengths of stay in the United States compared with Europe. Shorter stays were also noted for hospitalized patients who died in the U.S. versus Europe. “This is interesting, because in Europe we don’t associate that there is a culture of early withdrawal or denial of care in the United States. We’re aware that strenuous efforts are undertaken in the United States and there is much more shared involvement with families in decision making,” Beale said. “This is a generalization, of course, but it may suggest that some fundamental difference exists in the way we handle our patients.”

In summarizing the many conclusions that can be drawn from this data, Beale emphasized that healthcare systems in the United States and Europe are different and neither region is homogeneous, although the differences are more marked in Europe. More patients come to the ICU from the emergency department in the United States, whereas more patients come to the ICU from the ward in Europe. Delay on the ward appears to be associated with a worse outcome. Some differences are seen in patients in United States versus European hospitals, such as urosepsis versus abdominal sepsis, as well as some differences in practice.

Based on these conclusions, two fundamental questions remain: Are patients being denied early ICU access in Europe compared with the United States and, hence, doing worse? Or are patients being unnecessarily overtreated in the United States, thus increasing cost and burden?

“The answer probably lies somewhere in the middle, although my personal prejudice is that it’s not in the middle,” said Beale “Rather, I suspect that what is being done in the United States is closer to what we need to be doing in Europe. There are enough tantalizing signals in these data, even if they raise hypotheses rather than provide firm questions, to reinforce the whole point of the Surviving Sepsis Campaign – that early recognition and prompt treatment, in an appropriate environment and by the right staff, are crucial.”

SSC Phase IV: What's Next?



Presented by Andrew Rhodes, MBBS a Consultant in Intensive Care Medicine at St. George's Hospital in London, United Kingdom.

Rhodes outlined SSC's accomplishments over the past 10 years. The original goal was to reduce mortality from severe sepsis and septic shock by 25%. "That was a challenging target, and we've achieved it," he said. Activities toward this goal included evidence-based guidelines for appropriate care, published in 2004, 2008 and 2012. In addition, SSC has developed tools and initiatives to improve the diagnosis of sepsis, educate healthcare professionals, build better awareness of sepsis, and increase the use of appropriate treatment. "The Campaign will also develop new software to help clinicians use the revised bundles based on the 2012 guidelines," stated Rhodes.

"To me, the Surviving Sepsis Campaign isn't just about the guidelines," said Rhodes. "It's also about utilizing the database and having clinicians share their experiences, so we can look at all the different aspects of care and learn from each other." He noted that a series of papers from the database are now beginning to be published.

Rhodes detailed the Campaign's achievements to date, including improved awareness of the incidence and prevalence of sepsis in hospitals and increased knowledge of the evidence-based treatments for sepsis. "Furthermore, this is a global effort, with 30 international specialist societies on board, supporting and developing the guidelines for 2012," he said. "It's clear that this set of guidelines is now the gold standard for sepsis care."

Public interest in sepsis also helps to advance the goals of the Campaign, as seen in the increased political activity and recognition of this problem within the American system. "Politicians are pointing

out that sepsis is a huge problem and is the number one cause of death in U.S. hospitals," reported Rhodes. "Policymakers and politicians are coming to us and saying that experts agree: the solution is basically a standardized protocol to facilitate quick and accurate diagnosis and fast, effective treatment."

With the 2012 guidelines now published, the Society of Critical Care Medicine and European Society of Intensive Care Medicine have released their 2013 declaration for what lies ahead for the Campaign over the next five to ten years. "We believe that what we've achieved is great, but there is still much work to do," said Rhodes. "We invite clinicians from around the world to join us in renewing our commitment to the goals set in 2002: to further reduce mortality from sepsis worldwide, and to provide the imperative for healthcare providers to improve the care and outcomes of patients with sepsis."

The SSC is also issuing three challenges: 1) to increase the number of hospitals contributing data to the Campaign to 10,000 worldwide, 2) to apply the guidelines to 100% of patients suspected of a sepsis diagnosis, and 3) to develop a strategy to improve the care of patients with sepsis in areas where resources are limited.

"Assuming that the reduction in mortality seen to date can be sustained and 10,000 hospitals comply with SSC recommendations, we could save 400,000 lives if we treat only half of the eligible patients with the SSC bundles," emphasized Rhodes. "In addition, extension of the SSC to under-resourced populations may have an even greater impact."

In summing up, Rhodes said he viewed the campaign as a global effort at knowledge translation. "It's a model for translating what's in the literature into guidelines we can utilize in a simplified fashion to standardize care. It's not about removing variation, but about understanding variation and why it's there – and making us ask the right questions so we can learn and improve what we're doing."

Continuing Education Self-Assessment

Surviving Sepsis Campaign (SSC): 2012 Guidelines

1. Which of the following is included in the 2012 Surviving Sepsis Campaign guidelines?
 - a. Use of hydroxyethyl hetastarches is recommended for fluid resuscitation in selected patients with septic shock.
 - b. The recommended first- and second-choice vasopressors are dopamine and epinephrine, respectively.
 - c. Dopamine and norepinephrine are recommended equally as the first-line vasopressor for all subgroups of septic shock.
 - d. The recommended initial fluid challenge in sepsis-induced tissue hypoperfusion is a minimum of 30 mL/kg of crystalloids.
2. Surviving Sepsis Campaign data comparing hospitals in the United States and Europe reveal which of the following results?
 - a. The percentage of participating hospitals was similar in the U.S. compared with Europe.
 - b. In the U.S., about two-thirds of ICU patients originated from the emergency department.
 - c. The incidence of urinary tract infection was higher among patients treated in Europe versus the U.S.
 - d. U.S. hospitals performed better than European hospitals in reaching the recommended central venous pressure of 8 mm Hg within six hours of presentation.