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Sepsis without borders

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Sepsis is among the most common conditions encountered in critical care, with extraordinarily high prevalence in many developed countries [1, 2]. Septic shock is widely considered the leading cause of death in many western ICUs, contributing significantly more in health-care utilization due to the higher complexity of illness and intensity of life-saving interventions. Severe sepsis and septic shock are more consistent in incidence, at least in developed countries [3], but it is less well understood how much variation there is in sepsis between developed and developing countries [4]. Infection prevalence varies tremendously between hospitals and countries, and directly influences the risk of patient mortality [5]. The prevalence of infection and sepsis in critically ill patients is among the highest in Brazil [6, 7], where variations in critical

care beds, health-care delivery programs, and constraints on health-care resources are common, comparable at least to those found within Europe [8]. Fortunately for patients, although constituting a tremendous challenge for health-care services worldwide, this increase in prevalence has been accompanied by a decrease in mortality since the late 1970s or early 1980s. This change has been well documented in the USA [2] and Europe [9], but also in other good epidemiological studies aggregating clinical trials demonstrating a reduction in case-fatality rate. Is this a global and universal phenomenon? Has this turning point in mortality been attained in countries with fewer resources and/or with more heterogeneous health-care systems such as Brazil [10]? Can we explain it by looking at the countries with greater variability?

Our greater understanding of sepsis epidemiology and pathophysiology led to the Barcelona Declaration in 2002 and to the launch of the Surviving Sepsis Campaign (SSC), for which the foundation of implementation rests on delivering optimal care using a “bundle” approach, first proposed by the Institute for Healthcare Improvement (IHI). The bundled approach to sepsis care has been shown to be effective in many settings, with more consistent and timely application of evidence-based care, reductions in practice variability, and improvements in both institutional and patient-centered outcomes [11–13]. However, these findings are almost exclusively reported from the developed world [12, 14], and given the human and material resources needed for effective sepsis bundles, we must wonder if sepsis bundles are appropriate, feasible, and cost-effective, especially in the developing world [15].

In a study published in this issue of *Intensive Care Medicine*, Noritomi and colleagues [16] undertook to establish the feasibility, efficacy, and cost of implementing a comprehensive sepsis bundle in Brazil. In collaboration with the Latin American Sepsis Institute, they implemented a multifaceted sepsis quality

improvement program over 21 months in 10 vertically integrated managed care non-teaching hospitals in São Paulo, representing 1,650 hospital beds and 191 ICU beds. The program intended to extend the classical recommendations of the SSC by including more extensive educational, screening, and treatment components, particularly by ensuring that all aspects of the program were continuously monitored and improved. During the program period, they identified 2,120 patients with severe sepsis and septic shock and increased the compliance with the entire sepsis bundle by fourfold (from 13 to 62 %). These changes resulted in patients being identified progressively earlier and at a lower illness severity, and were associated with a decrease in hospital mortality, a decrease in hospital costs, and an increase in health-related quality of life.

Can we explain these very important findings with what we understand today? Possibly, yes. First, the authors went beyond the classical SSC 2008 approach and implemented revised bundles that were accompanied by more emphasis on continuous support of education and process improvement. While this was a similar approach to that by Ferrer in Cataluña in 2008, it was more effective in changing behavior and care processes, and resulted in even more impactful results [10]. Second, the notion that sepsis is a time-dependent disease was strongly stressed in this Brazilian study. At least on the basis of the regression analyses, we can also explain a significant portion of the results through early administration of antibiotics, and to a lesser degree by earlier and more aggressive fluid challenge in hypotensive patients. Perhaps most importantly, this project was successful because of the planning and societal support necessary for success in a large-scale quality improvement program. We should always remember the data from the SOAP study in 2002 [1] and from the EPIC II study in 2008 [5] in which the prevalence of sepsis in an ICU was strongly correlated to all-cause mortality in that ICU, suggesting that greater attention to this group of patients will produce

a broader effect for all critically ill patients admitted to that ICU.

Overall, we must congratulate the authors for four important reasons:

1. They proved beyond any doubt that it is possible to conduct very high quality research in a country with limited resources and very heterogeneous patients and health-care systems [8].
2. They demonstrated that a dedicated quality improvement program will improve sepsis outcomes despite differences in organisms, different typologies of patients, and different health-care systems [5].
3. They impressively demonstrated that SSC 2008 (and we hope SSC 2012) can be improved and effectively incorporated into an inclusive package of education, awareness, and clinical support.
4. The current results suggest that countries like Brazil are closing the gap to more developed countries at a greater pace than expected by passage of time alone.

With these results, the challenge is now set for more countries to prove that we can do the same or better. And to determine and demonstrate what aspects of the SSC guidelines and sepsis bundles are most effective and necessary in each health-care setting, in order to customize care delivery on both a regional or institutional basis and on an individual patient basis. Obviously, many questions remain. Is Brazil representative of the rapidly evolving BRIC (Brazil, Russia, India, China) countries, or is Brazil a unique phenomenon among them? Are developing countries more similar to western nations than we realize, perhaps only being time-shifted backwards? Do the results translate to countries with even more difficulties than Brazil, including the most severely underdeveloped countries, even if the bundles and the associated measures must be changed? These questions are only a few that prove why we must continue learning from international collaborations, as much improvement yet lies ahead.

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