We thank Dr. Ventura for interest in the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children recently published in *Pediatric Critical Care Medicine* (1). As noted, these guidelines did not intend to review or revise prevailing pediatric sepsis definitions. Instead, the guidelines used the current definition of septic shock in children, which is severe infection leading to cardiovascular dysfunction, and sepsis-associated organ dysfunction defined as cardiovascular and/or non-cardiovascular organ dysfunctions (often referred to as "severe sepsis" in the literature). We applied this approach because the majority of studies used to establish evidence for these guidelines referred to criteria established by the 2005 International Pediatric Sepsis Consensus Conference (sometimes with modifications) (2).

Dr. Ventura questions whether the fluid resuscitation recommendations should be the same for children with septic shock and children with sepsis-associated organ dysfunction. In particular, she makes the important point that not every organ dysfunction attributable to severe infection requires fluid as a treatment given variable mechanisms of injury beyond hypovolemia such as mitochondrial alterations, endothelial activation/dysfunction, glycocalyx degradation, direct cellular injury, inflammation, anemia, and microthrombi. We, therefore, interpret her key question as whether it is necessary to treat sepsis-associated *non-cardiovascular* dysfunction with fluid bolus therapy?

Cardiovascular dysfunction, defined as impaired perfusion, hypotension, and/or treatment with vasoactive medications, is the most common organ compromise in children with sepsis (3, 4). Similarly, most children with non-cardiovascular organ dysfunctions attributable to infection also have some degree of cardiovascular dysfunction at the time of initial presentation (3, 4). As a result, the overwhelming majority of children included in studies of septic shock or sepsis-

associated organ dysfunction had cardiovascular compromise in isolation or in concert with other organ systems as part of multiple organ dysfunction syndrome. This makes it difficult to tease out evidence-based recommendations for the majority of children who have sepsis with cardiovascular dysfunction from the minority with preserved cardiovascular function in the presence of other organ compromise. One exception may be those children with acute respiratory distress syndrome (ARDS) caused by a pulmonary infection, who may well exhibit respiratory dysfunction without shock (5). However, our literature search did not include studies focused solely on pediatric ARDS as direct evidence. Faced with the ubiquity of cardiovascular dysfunction in children with septic shock or other sepsis-associated organ dysfunction, the panel issued recommendations intended to guide fluid therapy for all children with sepsis.

However, we do agree with Dr. Ventura that not all children with sepsis-associated organ dysfunction require fluid resuscitation. Indeed, fluid resuscitation is most likely to be effective to correct hypovolemia caused by capillary leak, vasodilation, and fluid losses and should always be titrated to clinical markers of cardiac output. Thus, in healthcare systems with availability of intensive care (either at the local facility or via inter-facility transport), we suggest fluid bolus therapy of up to 40-60 mL/kg over the first hour titrated to "clinical markers of cardiac output and discontinued if signs of fluid overload develop". In healthcare systems with no availability of intensive care, we suggest fluid bolus therapy up to 40 mL/kg only in those children *with hypotension* (i.e., clear cardiovascular dysfunction), again titrated to "clinical markers of cardiac output and discontinued if signs of fluid overload develop". We appreciate the opportunity to clarify that our recommendation for fluid to be "titrated to clinical markers of cardiac output" reflected our intent that fluid be used to treat shock/cardiovascular dysfunction, irrespective of the diagnosis of septic shock or sepsis-associated organ dysfunction. This is emphasized in the

accompanying algorithm, where the recommendation to "administer fluid bolus(es)" is conditioned on whether "shock is present", defined as abnormal perfusion in health care systems with intensive care and hypotension in health care systems without intensive care (6).

In summary, we recommend fluids for children with septic shock and other sepsis-associated organ dysfunction only when shock is present and the intent is to improve cardiac output.

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