

Re: Re-submission of invited manuscript # 3991 titled: **Controversies in Fluid Therapy: Type, Dose and Toxicity**

Thank you for the opportunity to revise and resubmit our manuscript. We have reviewed the comments in your letter dated July 20, 2013 and revised the manuscript in response to the Reviewer comments as outlined below. We appreciate the thoughtful comments by the Reviewer's and recognize the manuscript has now been strengthened.

Response to Reviewer 1 Comments:

This review deals with the efficacy and safety of the type and dose of fluid therapy for acutely ill hospitalized patients. Useful information is provided. The manuscript was also well prepared.

1. Abbreviations must be defined once they appear for the first time and used thereafter.

This has been corrected.

2. Table 2 and 3 are the same.

This has been corrected.

3. The description of hydroxyethyl starch (HES) is suggested to be moved from the section of "dose of fluid therapy" to "type of fluid therapy".

Upon review, we believe there is currently very little reference to HES in the section titled "Dose of Fluid Therapy" and we are uncertain of whether there is any significant content to move.

4. Most of the examples were provided randomly. It is easier to follow if the authors add a section (or table) to describe why certain examples were selected in this study.

This data have been selected to represent the most recent and relevant published data on the type and dose of fluid administered for acute resuscitation and in critically ill patients. This article is not intended as a systematic review but rather a state-of-the art narrative review of the most compelling controversies emerging on this issue. If the Editors would prefer a "Methods" section to this article be added - we would be happy to add this.

5. Reasoning for the efficacy and safety of the type and dose of fluids shall be discussed in more detail.

We appreciate the Reviewer's comment. We have revised and added additional context throughout the manuscript.

Response to Reviewer 2 Comments:

Comments to the authors: It is a well written extensive review of fluid therapies in terms of fluid type, dose and toxicity. However, the manuscript is limited to a simple review of the most recent randomized trials regarding the above subject.

See response to Reviewer 1 Comment 4 above.

Further analysis of the findings derived from the trials is needed, including algorithms with proposed criteria to be used for the appropriate dose and the type of fluid therapy in any circumstance of patients with fluid deficits.

We appreciate the Reviewer's comment. We believe the article adequately dissects the mostly recently available literature, draws attention to current knowledge gaps and controversies, and provide further context for a paradigm shift to the clinician's view about the nature of fluid therapy across a range in acute ill patients and phases of illness. We believe our article will not benefit from the inclusion of detailed algorithms for how, when and in who to administer fluid. This is beyond the scope of this article – which current stands at 4000 words. We believe that such as article will also have to focus on additional aspects of resuscitation (i.e., vasopressors/inotropes; blood transfusions; adjuvant measures; advanced monitoring; ideal target endpoints). Moreover, many of these aspects of resuscitation are also quite controversial and currently debated in the literature (i.e. ScvO2 vs. lactate as acute resuscitation targets). We believe this would be better addressed in a dedicated article.

Table 3 is not included in the manuscript as is a copy of Table 2.

This has been corrected.

If you require any additional information, please contact us as necessary. We appreciate your consideration of our manuscript for possible publication in WJCCM and look forward to your review.

Sincerely,

Sean M Bagshaw