



**BAISHIDENG PUBLISHING GROUP INC**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242 Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com <http://www.wjgnet.com>

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**Name of Journal:** *World Journal of Critical Care Medicine*

**ESPS Manuscript NO:** 22925

**Manuscript Type:** Review

### **Response to reviewers**

#### **Reviewer: 1**

##### *Comments to the Author*

*With the data managed and discussed by the authors it would have been very appropriate to make a final algorithm summing up the most powerful indications for ulcer prevention at the ICU setting. We missed this final algorithm about the truly indication of stress related ulcer bleeding, and the authors should include it*

Response: We would like to thank the reviewer for the constructive comment. We created an additional figure to our manuscript to sum up indications for stress ulcer prophylaxis. In order to integrate the comments by reviewer #4, we have also added the level of evidence for the different indications in the figure (new figure 2 in the revised manuscript). We hope that this proposed algorithm will greatly facilitate to implement the concept in clinical practice.

#### **Reviewer: 2**

##### *Comments to the Author*

*The paper titled 'Prevention of stress-related ulcer bleeding at the Intensive Care Unit: risks and benefits of stress ulcer prophylaxis' from Buendgens L. and coworkers is an interesting and updated review in the field. The sentence in the Risk factors for stress ulcer-related bleeding paragraph 'A large, prospective multicenter trial of 2,252 ICU patients was able to identify two main risk factors:' should be modified as follow: 'A large, prospective multicenter trial of 2,252 ICU patients was able to identify at multiple regression analysis two main risk factors:'. Moreover, OR, RR and HR are not followed by 95% Confidence Interval or P when available. For example, in the Risk factors for stress ulcer-related bleeding paragraph: OR 15.6 (P<0.001), OR 4.3 (P<0.001), OR (95% CI) 8.9 (2.7-28.8), OR (95% CI) 7.6 (3.3-17.6), OR (95% CI) 6.9 (2.7-17.5), OR (95% CI) 5.2 (2.3-11.8), OR (95% CI) 4.2 (1.7-10.2), OR (95% CI) 1.4 (1.2-1.5). The same is for Adverse Events paragraph: OR (95% CI) 3.11 (1.11-8.74), ..... HR (95% CI) 2.33 (1.264-4.296).*

Response: We sincerely thank the reviewer for his/her fair and positive evaluation of our work and his/her helpful commentary. We added confidence intervals and/or P

values for every OR and HR in our manuscript. Also, we modified the sentence, as suggested by the referee.

### **Reviewer: 3**

#### *Comments to the Author*

*The topic is interesting, but there is a reservation, which needs revision: The title does not accurately reflect the major contents of the article. Most contents of the manuscript describe the epidemiology, pathophysiology and strategy in management of stress ulcer bleeding, but not “risks and benefits of stress ulcer prophylaxis” as noted in the title. In addition, the manuscript focuses on acid-suppressive medication, but not all approaches to “stress ulcer prophylaxis”.*

Response: We appreciate the reviewer’s comment and agree that our review article covers a larger topic than reflected by the title. However, we implemented several changes during the revision process that intended to focus the review more clearly on the clinical management of stress ulcer prophylaxis at the ICU. We still believe that it is necessary to review the pathophysiology and epidemiology. However, the main part of the review deals with benefits (table 1) and risks (table 2-3) of SUP as well as with practical recommendations weighing measures to prevent stress-related bleedings (e.g., new figure 2). We are certain that the title now fits well to the revised manuscript.

### **Reviewer: 4**

#### *Comments to the Author*

*The reviewer feels that this is an important topic that deserves publication consideration. I have taken steps to improve the grammar throughout the manuscript. Please review this. The manuscript would be substantially improved if the authors had a Table 4 with overall recommendations to include the level of evidence for these recommendations. It might look something like: Prevention of SRMD and Hemorrhage in the ICU Column 1: Underlying Condition: Head trauma Previous GI bleed Sepsis with broad spectrum antibiotic treatment Dialysis Liver/kidney transplant ... Column two: Prevention Recommended (Y/N); or PPI/H2 blocker or sucralfate or tube feeding) Column three: Level of evidence*

Response: We thank the reviewer for his/her productive and useful remarks. We reviewed the grammar as proposed throughout the manuscript. Also, we appreciate the idea of the suggested table. In order to comply with the suggestions by reviewer #1, we have now generated a new figure (figure 2) with an evidence-based algorithm for SUP in the ICU. All the requested information is now included in the new figure 2 of the revised manuscript.