Reviewer’s report

Title: Epidemiological trends of sepsis in the 21st century (2000-2013): an analysis of incidence, mortality, and associated costs in Spain

Version: 0 Date: 08 Aug 2017

Reviewer: Kristina Rudd

Reviewer's report:

This is an interesting, well-written, and methodologically sound paper. It adds important information to the field of sepsis epidemiology. The dataset used is very impressive, with excellent coverage of public hospital admissions. I have the following comments:

- I found at least one paper on a very similar topic using the same dataset (Bouza et al, "Epidemiology and recent trends of severe sepsis in Spain," BMC Infectious Diseases 2014), but this analysis covers a larger time period and uses perhaps a superior method of identifying sepsis cases. Despite the fact that the two papers cover the same time period with the same dataset, research objectives, and outcomes of interest, the conclusions are quite different. It would be helpful for the authors to compare their findings to those of others with similar work in the Discussion section, highlighting possible reasons for these different findings.

- In Background, on line 10, the authors state that sepsis "is the main cause of death among hospitalized patients." I reviewed the cited studies, and found no evidence to support this claim. Please clarify.

- In Background, on line 12, the authors state that "around 3% of patients admitted to hospital have sepsis, and half of these patients are treated in the intensive care unit." This should be clarified to reflect that these data are from a single US study which is quite old. The reason this is important is that the proportion of patients with sepsis who are treated in the intensive care unit vs acute care wards varies dramatically depending upon resource availability.

- In Background, on line 29, "Information" should be changed to "information," and "…impact of the economic crisis on critical care unit." should be changed to "…impact of the economic crisis on critical care utilization."

- In Materials and Methods section "study design and data source," on line 5, the "." Should be removed after the word "study"

- In Materials and Methods section "study variables," on line 45, the authors should clarify that they adapted the Angus criteria, also using methods from Shen and Bateman as described in Appendix 1.
- In the first page of the Discussion section, on line 7, the word "cases" should be added after "the percentage of sepsis…".

- The authors spend considerable time mentioning the possible biases and limitations of their paper due to issues of ICD-9 coding for sepsis. However, as I understand their methods, they did not actually use ICD-9 code 995.9x for sepsis or severe sepsis, nor 785.52 for septic shock. I think this is actually one of the strengths of their paper, as these codes are highly problematic. Lines 25-34 and 46-52 seem to suggest that this paper used sepsis-specific ICD-9 codes to identify patients. If this is the case, the methods section needs to be edited to reflect this. If it is not the case, the discussion section should be clarified.

- In the second page of the Discussion section, on line 10, the statement "the reduction of LOHS leads to a faster return to normal life…" is not supported by the data. Patients may be discharged with high degrees of disability and perhaps not even going home but to a nursing facility. This statement should be removed.

- In the second page of the Discussion section, the sentences on lines 26-34 are poorly written and need to be revised.

- In the third page of the Discussion section, line 6, the authors should clarify that they modified the Angus criteria.

- In Table 1, the sub-categories for "acute organ dysfunction" and "site of infection" should be reordered alphabetically or in order of highest to lowest frequency.

- In Figure 1, the title is clear but the left and right Y-axes need to be re-labelled to clarify that these are proportions of those patients admitted to the hospital. Additionally, the word "severe" should be completely removed from this figure, as it is confusing and not mentioned elsewhere in the paper.

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