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:** 11 Dec 2016

**Reviewer:** Antonio Artigas

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This is a retrospective study to analyze incidence, mortality rate and costs of sepsis during 21st century in Spain. The authors used a MBDS of the National Surveillance System for public hospitals data in Spain. The major concerns are:

1. MBDS used is a large bank of data with the risk of missing and non-precise information. Is there a quality control of data introduced in the system?

2. Algorithm of Angus was used to define sepsis in previous reports but did not coincide with the current definition of sepsis-3. Diagnosis of sepsis is crucial. The authors presumed that Angus methodology, i.e. combination of infection and organ dysfunction based on primary and secondary diagnosis, would not identify patients with sepsis consistent with the new sepsis-3 definition. However this hypothesis should be validated. The new sepsis-3 definition defines SOFA score-based organ dysfunction differently from sepsis-1 and 2. For example, a platelet count of 100 to 150,000 indicates a SOFA score of 1 for coagulation system, which by no means be identified as organ dysfunction by previous sepsis definitions.

3. The increase incidence seems to be related to the inclusion of less severely ill patients, thus resulting also in a reduction of length of stay and reduction of mortality. The adjusted analysis did not include severity of illness scores. This need to be better addressed in the discussion.

4. It is unexpected the high incidence of urinary infection (19%-23.4%). This seems to be a bias of the data base as it is probably more reliable to report urinary infection than the other sources. This need to be mentioned as a limitation of the study. As we know, urinary sepsis has a lower mortality rates and can have contributed to the rate reported by this study.

5. It is also unexpected the low incidence of cardiovascular dysfunction (10.2%) and this suggests that the data collection was not appropriate. Registering renal and respiratory dysfunctions seems to be more accurate.
6. Mortality adjustment was based only in age and the authors did not include other important non-modifiable factors as co-morbidities, severity of illness, gender. What was the mortality in patients without co-morbidities?

7. Cost were calculated using DRG extracted from MBDS and adjusted by the inflation. DRG is not a precise method to determine the costs of ICU patients.

8. Referral population: The population in Spain may vary according to the number of foreign habitants that can develop a sepsis and treated in a public hospital. Private hospitals may attend a large proportion of septic patients. How this was considered by the authors?

9. Finally it could be interesting to include some information on the regional differences of sepsis patients in Spain.

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An article of importance in its field

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Acceptable

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