Author's response to reviews

Title: Hospital staff education on severe sepsis/septic shock and hospital mortality: An original hypothesis

Authors:

Maurizia Capuzzo (cpm@unife.it)
Marco Rambaldi (m.rambaldi@ausl.mo.it)
Giovanni Pinelli (g.pinelli@ausl.mo.it)
Manuela Campesato (emanuela.campesato@virgilio.it)
Antonia Pigna (a.pigna@aosp.bo.it)
Marco Zanello (Marco.Zanello@ausl.bologna.it)
Maria Barbagallo (mbarbagallo@ao.pr.it)
Massimo Girardis (massimo.girardis@unimore.it)
Elena Toschi (elena.toschi@tiscali.it)

Version: 2 Date: 10 July 2012

Author's response to reviews:

Dear Sir,

We have reviewed our manuscript according to the suggestions of the reviewers and we hope that you find it improved enough to be suitable for publication.
The authors thank editor and reviewers for their work and suggestions

ANSWERS TO REVIEWERS

Rev 1

WE THANK THIS REVIEWER FOR HIS COMMENTS.

Please explain abbreviations in the abstract.

RESPONSE: Done

Introduction and purpose - it is suggested to be a little more specific in the description of the purpose of the study.

R: The last paragraph of the introduction has been changed as follows:
"Since signs of clinical deterioration in ward patients overlap with signs of severe sepsis and septic shock (SS/SS), we hypothesised that any education dedicated to early recognition and treatment of signs of SS/SS may affect the outcome of all hospital patients. Therefore, we designed a study to assess the trend of the mortality rate of adults admitted to hospital for at least one night in relationship with a hospital staff educational program on severe sepsis/septic shock."
Method section – it is suggested to explain the statistic methods more. Not all might be familiar with the tests used.

R: This has been done. The second paragraph of the statistical analysis has been changed as follows:

"We performed a time series analysis, which is a sequence of data points (dependent variable) measured at successive time instants, spaced at uniform time intervals. Admission data were available from October 2003 to October 2009. We used months as time intervals and the dependent variable was the monthly hospital mortality rate calculated for each of the 69 months from December 2003 to August 2009. We excluded data regarding the two months before and after this period in order to include all the patients with known outcomes present in hospital every month, and for each month we computed the mortality for the patients present in the hospital in that month. The SDO records are collected on an individual patient basis; so, collapsing the data into a time series of monthly average values or proportions enabled us to model the mortality rate trend over time (months). A Poisson regression model which is suitable for any situation that involves counting events was developed. We expected that changes in patient characteristics and treatments had occurred over more than six years. Therefore the analysis was adjusted for a linear time trend (which takes into account each month and sums up all those modifications that may have occurred over the previous time), seasonality (11 monthly indicator variables) and monthly average values of four variables which had a potentially confounding effect (age, Charlson score, hospital length of stay and urgent/non-urgent admission)."

Results section - it would be nice to know the percentage of nurses, doctors etc. who participated in the educational program. The number of nurses trained are higher than the number of doctors (see discussion) - should be mentioned in result section. Also to know the percentage of staff from each hospital - related to mortality.

R: Detailed information about educated staff are presented in Table 1. We were not able to identify single hospitals in the file abstracted from the SDO database, so we cannot give mortality by hospitals.

Discussion:

Overall, the number of staff trained is small. The major drawback of the study is mentioned by the research group in the discussion. The research group did not investigate whether the educated ward staff may have identified or better treated clinical deterioration, or both according to the education received. Further the authors mention the incidence of sepsis and based on this it does not appear reasonable to hypothesize that the strong effect found in this study was due to the education as the number of patients with sepsis was low. It is suggested to weaken the conclusion accordingly.

R: We have weakened the conclusion, which is now as follows:
This study suggests that an educational program specifically devoted to severe sepsis/septic shock according to the Surviving Sepsis Campaign, was associated with a decrease in the hospital mortality of the patients admitted to the hospital wards/units responsible for most of the cumulative hospital mortality. If this finding is confirmed, the information would be useful for hospital administrations and health policy makers.

It is suggested to compare the results of this study with the data from reference number 14. In this study multi-professional education of 50% of doctors and 70% of nurses did not affect the rate of mortality or staff awareness of patients at risk. You training programme might have been better, but less were trained. Thereto, your data could be compared with other studies.

R: We do not believe that the results of Fuhrmann L et al. are related to the educational program.

In 2008 (Resuscitation 2008, 77:325-330), Fuhrmann L et al. collected data on 877 patients during 2 months. 155 of them had abnormal vital signs and ward nurses were not aware of all patient’s abnormalities in 67 (43%) cases.). The lack of awareness of patients with abnormal vital signs among ward nurses was related to the lack of systematic monitoring on the general wards. In the discussion (page 329) the authors write: "During the last 20 years, Danish healthcare has drifted away from the routine assessment of vital signs for all ward-patients. Routine assessments have now been replaced by specific monitoring regimes for specific categories of patients, leading to a culture in which assessment of vital signs in patients without a clear-cut diagnosis is not done on a routine basis, but depends on the judgment of staff............. The lack of routine assessment of vital signs represents a potential risk for suboptimal care, which is confirmed by studies demonstrating lacking patient monitoring as a cause of insufficient use of MET and worse outcome after cardiac arrest."

Subsequently the same group demonstrated the feasibility of a multi-professional full-scale simulation course dedicated to recognition and management of deteriorating hospital patients. They trained 50% of doctors and 70% of nursing staff on four wards (approximately 220 members) during a 5-month period (Resuscitation 2009, 80:669-673).

The results of the study on the effectiveness of the previously described training were reported by the same group (Resuscitation 2009, 80:1357–1360). No significant differences were observed in the staff awareness of patients at risk between the pre and post-intervention periods. In the discussion (page 1359), the authors admit that "The needs assessment and the educational intervention do not, however, target issues of the organisation and this may contribute to the lack of effect. For example, routines for taking vital sign measurements in patients without clear-cut diagnoses may not be changed by the educational intervention and this barrier has been reported to cause insufficient use of the Medical Emergency Team and worse outcome after cardiac arrest. Organisational issues that are also not addressed by the intervention may be local values, action strategies, planning and prioritisation of tasks, assumptions, allocation of
resources and rewarding/punishing behaviour, which all influence how patients on the general wards are assessed and monitored.

In conclusion, the last article may be an elegant demonstration of the effect of the lack of well defined rules for patient assessment at regular intervals. It seems quite logical: if you perform regular assessments of your patients, you can identify early signs of clinical deterioration, and use your knowledge (improved by education) to treat and/or to call for advice.

In our region (and country) the nursing staff check all patients at least three times a day (usually at 8.00, 16.00 and 24.00). We have added the information about routine assessment of ward nurses, and the previous concept about patient routine assessment in the discussion (page 11, last line).

"....., the training of 50% of the doctors and 70% of the nurses of four wards by medical simulation in a single hospital [25] did not increase the staff awareness of the patients at risk despite a similar incidence of patients with abnormal vital signs in the pre and post-intervention periods [26]. The reason for this result may relay on the lack of routine assessment of vital signs for all ward patients in the study hospital, as reported by the authors in a previous study [14], and not changed in the meanwhile [26].

Rev 2
WE THANK ALSO THIS REVIEWER FOR THE COMMENTS.

Major compulsory revisions
1. The major issue in my opinion is derived from the hypothesis of the study. Is the assessment of all-causes hospital mortality in a general population without sepsis a reasonable outcome for a before-after study which intervention was sepsis education?

R: this is not a traditional before-after study, as performed by others (i.e. Ferrer), but a time series analysis (as described in the statistical analysis section). In our view this is the only way we have to test our hypothesis in a big sample of patients.

It is tempting to believe in this hypothesis as sepsis protocols are very wide in their nature, meaning that its implementation would generate a quality improvement in many aspects not only related to sepsis care. However, I am not sure we can attribute only to the intervention the reduction in hospital mortality found here using this design. We would need a better definition of before and after periods (see comments bellow) and a better description of the population in these periods to assure severity of disease and diagnosis categories did not vary during study period. The authors had access to hospitals register to generate mortality rates. Was this the only variable assessed?

There are many known mortality risks factors that were not measured or at least not mentioned. Without knowing that population were similar, how can the mortality reduction be attributed to education? Even the four variables used to
adjust mortality analysis are not shown. So, I would suggest the authors to get as much as information as possible to better characterize their population across the years.

R: The following variables were assessed: gender, age, type of admission (urgent), Charlson score, length of stay in hospital (Data are now reported in table 2).

Really, the population changes over time: people live longer and the increased exposure time allows them to develop also comorbidities (with some comorbidities strongly related to age). This is why we developed a model taking into account these factors to adjust mortality. The following sentence was added in the statistical analysis section (page 9, paragraph 2, sentence before the last):

" We expected that changes in patient characteristics and treatments had occurred over more than six years. Therefore the analysis was adjusted for a linear time trend (which takes into account each month and sums up all those modifications that may have occurred over the previous time), seasonality (11 monthly indicator variables) and monthly average values of four variables which had a potentially confounding effect (age, Charlson score, hospital length of stay and urgent/non-urgent admission)."

2. Although for the purpose of the study sepsis incidence is not an absolute required data, it would be nice to have it along the years, as well. Moreover, we need some type of performance measurement to indicate training really results in change in sepsis bundles or in any other quality indicators.

R: We answer this point in the discussion (page 13, first line):

" We did not distinguish the populations with and without SS/SS due to the following reasons: i) our data were collected for administrative reasons (reimbursement) and diagnosis codes may not be properly recorded by the individual physician [28]; ii) it has not been definitely clarified which international classification of diseases codes correspond to the definition of severe sepsis accepted by the ACCP/SCCM; iii) the coexistence of diagnostic codes for infection and organ failure does not necessarily mean that a causal or temporal relation exists [29]. Finally, we can speculate that international classification of diseases coding habits may be influenced by culture, and training courses aiming at improving attention to a clinical phenomenon can sensitize health professionals in the detection of that clinical phenomenon and increase their reporting."

Really, we wonder whether the increasing number of severe sepsis combined with declining mortality rates frequently reported in recent years (Kumar, etc) may be related to the emphasis on sepsis in the literature and media overall in the word which stimulates recording of sepsis not really severe and frequently omitted in the past.

As far as performance measurement is concerned, we respectfully disagree with the Reviewer. In the study of Ferrer R et al (JAMA 2008,299:2294-2303) the increases in guideline adherence were modest, with some process measures
increasing by only a few percentage points. Even after the intervention, performance on many measures was far below what would be considered ideal. Nor were all improvements sustained in a subset of hospitals that measured process and outcome for a year after the intervention; many measures returned to baseline rates (Kahn JM & Bates DW. JAMA. 2008;299:2322-2323).

3. Another major issue is the absence of data in hospital mortality, as well as sepsis mortality, across the study period. Hospital mortality and sepsis mortality are decreasing over the years. The mortality rates in each year needs to be shown to assure the reduction was present only after intervention and not progressively during the precedent years.
R: we added the Figure 2 showing the trend of adjusted monthly hospital mortality and the percentage of staff educated.

4. The intervention is not well characterized.
R: We added some points in the educational program (page 6, paragraph 2).
"The Regional Health Agency arranged an educational package consisting of information about epidemiology, morbidity and mortality of SS/SS, scientific literature, electronic presentations for lectures, format of clinical cases for practice training, and booklets reporting clinic and laboratory signs of SS/SS [15]. In the first three quarters of 2007 (Figure 1), the Regional Health Agency acted as coordinating centre and organized meetings with the Multidisciplinary Sepsis Teams. The Multidisciplinary Sepsis Teams included doctors and nurses of infectious disease wards, intensive care, and the emergency department, a microbiologist and a pharmacist, selected by each hospital management among the senior staff. They participated in a course where they were taught about principles of adult learning [16], problem based learning [17] and Surviving Sepsis guidelines. As teamwork activity, they developed an algorithm to remind clinical signs of sepsis and to recommend timely assessment of patients with these signs as well as to improve and standardize decisions. The Multidisciplinary Sepsis Teams were provided with educational material (scientific literature, electronic presentations for lectures, scenarios of clinical cases for practice training and booklets) and started delivering courses and seminars each to their own hospital staff in the last quarter of 2007 (Figure 1). The methodology adopted for the educational courses in each hospital included delivery of short lectures, discussions as well as problem based learning on SS/SS scenarios. A typical course session held in the study hospital lasted four hours (14:30 to 18:30), included the presentation of the objectives of the course, definition, general and local epidemiology, early recognition, early goal-directed therapy, microbiological diagnosis, and early antibiotic treatment of SS/SS. At the end of the session the attendees answered a multiple item questionnaire to assess learning. The algorithm developed by the Multidisciplinary Sepsis Teams was reproduced and given to participants to be displayed as poster in the working areas.
The target of the present educational program consisted of attending physicians and nurses involved in direct patient care, excluding staff involved in only administrative duties. Residents were free to attend the educational sessions but they were not included either in the clinical staff or in the educated staff."

Why authors state that reaching only 30% of training in two years is adequate? It seems to me a low rate of training in a quite long period of time. If training was initiated in October 2007 and only 25% of people was trained up to December 2008, what is the possible explanation for the reduction in mortality already found in this first year? Do you think that training only one quarter of your goal would really result in such a impact? And training a 10% more would increase it further? These results would be really impressive, thus it urges to better describe what you really have done.

R: We agree with the reviewer that this is a key point. In the discussion (page 12, paragraph 2, sentence 2) we stress these points:

"Firstly, the education started involving the staff of emergency departments, ICUs and larger wards, which were also those included in the study and with higher mortality. The lower percentages of educated staff found in larger hospitals should be due to the lack of education of the staffing for specialised wards with very low mortality (for example allergology, endocrinology, rheumatology), because they were present in these larger hospitals but were not involved in this phase of the educational project. As a consequence, the percentage of the educated hospital staff is certainly underestimated for the wards/units included in the present analysis. Secondly, some spread of the Surviving Sepsis Campaign guidelines happened before starting the present project. We don't have any measure of this phenomenon but our time series analysis started before. Thirdly, the Multidisciplinary Sepsis Teams consisted of senior staff who acted as tutors for the problem based learning used in the education of our target staff, and this may have facilitated the learning of our well experienced (we excluded residents and medical students) hospital staff [27]."

Minor essential revisions

Title
1. It seems inadequate as authors were not only talking about ward patients. Emergency rooms and ICU were among the nine settings included in the study.

R: You are right. The new title is: "Hospital staff education on severe sepsis/septic shock and hospital mortality: An original hypothesis"

Abstract
The abstract is quite confusing.

R: The abstract has been changed with the help of a mother tongue English expert.
2. The method section should state clearly what was the study period, how pre-intervention data was collected. First and second education period (as described in methods) means the same as first and second year after education (as described in results)? The expression "end of the study period" is used in the abstracts results. What does it mean?

R: Right. We mean first and second period (not year) of education.

Figure 1 should clarify that education of Multidisciplinary Sepsis Team was performed in the first three quarters of 2007, while education of ward staff started in the last quarter of 2007.

3. Some sentences looks out of the scope like "For most of the cumulative hospital mortality, irrespective of the presence of severe sepsis/septic shock" because we only get the aim of the study (the impact in mortality regardless the presence of sepsis) latter on in the discussion section.

R: Moved, as suggested.

4. I would not agree that with the conclusion where two years of training is considered as a "short period". I think for training it is quite long.

R: The sentence has been modified as follows:

"An educational program devoted to severe sepsis/septic shock would seem to be associated with a decrease in the hospital mortality of the patients admitted to the hospital wards/units responsible for most of the cumulative hospital mortality."

5. The authors can't conclude that effect is obtained in a short period if education is focused in the wards, as they do have trained ER and ICU teams.

R: We have modified all the sentences mentioning "ward" staff education.

Methods

6. The participating hospitals could have a better description, with the exact number of beds, staff and ICU beds. Who is in charge during the night in the wards? Only the daily staff is described.

R: The following sentences have been added:

"A senior attending physician is present at night and during weekends. The nurses check and record vital signs of the patients at least three times a day (usually at 8.00, 16.00 and 24.00)."

We have added also information about ICU staff.

"The Intensive Care Units of these hospitals are closed with at least one physician specialist in intensive medicine present 24/24 and 7/7, and a nurse to
patient ratio of 1:2. The study hospitals do not have a formally dedicated Rapid Response Team and calls from wards or Emergency Department are managed by the ICU medical staff."

Table 1 shows the information about the hospitals participating in the study.

7. As already mentioned, the timetable for the study is rather confusing. How the time for collection was defined? If intervention started on the last quarter of 2007, why should you collect data since 2003? For the mortality assessment, why the first period is a 11 months and the second on only 8? And why they were compared with a four year period pre-intervention and not just one or two years before? It is well know that mortality is decreasing over time in this last decade in many places around the world. If you take into account such a long period of time, this would compromise your ability to associate the reduction in mortality with your intervention. In the data source of general hospital mortality section times are October 2003 to October 2009, in the statistics section it is written December 2003 to August 2009. Please, be consistent.

R: Hospital data concern admissions to the study hospitals which are collected in a discharge database and stored by the Regional Health Agencies. We selected from this discharge SDO database the admissions from October 2003, before the publication of the first version of the Surviving Sepsis Campaign (March 2004), to October 2009. We excluded data regarding the two months before and after this period in order to include all the patients with known outcomes present in hospital every month, so the monthly hospital mortality rate was calculated for each of the 69 months from December 2003 to August 2009 (see statistical analysis section).

Your comment demonstrates that this part was not understandable, so we have clarified this point in the statistical analysis section.

R: For the mortality assessment, the first period lasted 13 months (November 2007 to December 2008) and the second one 8 (January to August 2009).

For the first period, the start (November 2007) corresponds to the start of education in the study hospitals and the end was chosen considering that Christmas holidays could be considered a cut-off point. The end of the second period corresponds to the end of the period analysed for hospital mortality (we had data to October 2009 but we excluded data regarding the last two months to include all the patients with known outcomes present in hospital every month).

R: In the time series trend analysis, the question is, will it bend? Will it alter its course?

Any extrapolation procedure is based on the assumption that there is valid information in past data and knowledge, and thus that the future is conditioned by the same (or similar) factors to those that have operated previously. The amount of information available in the historic record also depends on the length of that record and the accuracy of the data collected. Our discharge database is active since 2000, so it reasonable to think that data recording run regularly at the end of 2003. Moreover, the first version of the Surviving Sepsis Campaign was published in March 2004, so we expected some effect of the natural spread of
the Campaign. As a consequence, only a long pre-education time could allow us to assess the real trend of mortality.

To use only more recent data can have dangers, especially if there are large, random, short-term variations in the data, which mean that any apparent short-term trend is relatively uninformative. Moreover non-linear (seasonal) variations are often detectable only with relatively long runs of data.

8. The statistics needs more clarity.

R: we have changed that part as follows:

"We performed a time series analysis, which is a sequence of data points (dependent variable) measured at successive time instants, spaced at uniform time intervals. Admission data were available from October 2003 to October 2009. We used months as time intervals and the dependent variable was the monthly hospital mortality rate calculated for each of the 69 months from December 2003 to August 2009. We excluded data regarding the two months before and after this period in order to include all the patients with known outcomes present in hospital every month, and for each month we computed the mortality for the patients present in the hospital in that month. The SDO records are collected on an individual patient basis; so, collapsing the data into a time series of monthly average values or proportions enabled us to model the mortality rate trend over time (months). A Poisson regression model which is suitable for any situation that involves counting events was developed. We expected that changes in patient characteristics and treatments had occurred over more than six years. Therefore the analysis was adjusted for a linear time trend (which takes into account each month and sums up all those modifications that may have occurred over the previous time), seasonality (11 monthly indicator variables) and monthly average values of four variables which had a potentially confounding effect (age, Charlson score, hospital length of stay and urgent/non-urgent admission). The effect of the education on hospital mortality was measured as the coefficients of two dummy variables identifying a first (November 2007 to December 2008) and a second education period (January to August 2009). The analysis was adjusted for a linear time trend, seasonality (11 monthly indicator variables) and monthly average values of four variables which had a potentially confounding effect (age, Charlson score, hospital length of stay and urgent/non-urgent admission). Durbin-Watson statistics and visual inspection of the residuals versus time were used to check for possible autocorrelation."

Results

9. As already state, data is not available. Authors should state clearly how many patients were analyzed in each period, type of admission, diagnosis, age, gender, LOS, Charlson score, mortality rates and any other information they have to characterize the two (or three) population: pre intervention, post intervention first period, post intervention second period.

R: The data about study population in the periods considered are reported in Table 2.
10. How did the authors measure the percentage of hospital training? It is not clear in the methods section.

R: percentage of hospital training was computed as follows:
Numerator: number of hospital clinical staff members participating in the educational project;
Denominator: number of hospital clinical staff, that is involved in direct patient care, including physicians and nurses and excluding staff involved in only administrative duties. Residents were free to attend the educational sessions but we did not include them either in the clinical staff or in the educated staff, because they received anyway education as part of their training all over the period for hospital mortality analysis (starting in 2003).

11. I did not get the meaning of "training was homogeneous in all the study hospitals". What did you mean? The percentage of trained healthcare workers was similar? The training was completed in the same time?

R: "training was homogeneous in all the study hospitals" means that the same information about regional epidemiology, the scientific literature, the electronic presentations for lectures, and the format of clinical cases for practice training, as well as the poster with the rules for monitoring patients were given in all the study hospitals.

Discussion

12. I don't think authors can state that the mortality significantly reduced when the percentage of educated staff increased from 25 to 30%. This sounds quite arbitrary, as 30% is not a recognized goal to be reached. In the second paragraph they also state that this percentage is "quite good". I would suggest authors to be more technical in their statement. What is considered in the literature a goal to be reached? I miss references here.

R: We have softened the sentences you mentioned, critically analysed other pertinent papers, and emphasized that our original hypothesis needs to be tested in other settings (Page 11, second paragraph).

"The positive effect of SS/SS education on care and outcome of ICU patients with SS/SS has been already demonstrated [20-21]. In these as in our study, efforts to improve the care of SS/SS patients targeted nearly all physicians specialties, because a wide variety of medical specialties care for severe sepsis patients [22]. Nevertheless, clear information about the number of staff educated is generally lacking in the literature. Ferrer et al [20] standardized the educational program and used multidisciplinary teams to deliver education to the staff of emergency department, medical and surgical wards, and ICUs. Their before-after study demonstrated a significant reduction in hospital mortality, but they studied only the patients with SS/SS admitted to 59 ICUs and reported a mean time dedicated to lectures of 10.6 hours at each center, without mentioning the number of the trained staff members. In a study performed in 165 hospitals, Levy
et al [23] found that a multi-faced intervention to facilitate compliance with the guidelines of the Surviving Sepsis Campaign in ICU, emergency department and wards was associated with a decrease of hospital mortality of the severe sepsis patients enrolled in an ad hoc database. No information was given about the number of the trained staff or the time dedicated to education [23]. At hospital level, a multi-format educational approach on sepsis for all workers involved in patient care in a single institution without rapid response team was effective in reducing the mortality of the patients with sepsis [24]. On the other hand, the training of 50% of the doctors and 70% of the nurses of four wards by medical simulation in a single hospital [25] did not increase the staff awareness of the patients at risk despite a similar incidence of patients with abnormal vital signs in the pre and post-intervention periods [26]. The reason for this result may relay on the lack of routine assessment of vital signs for all ward patients in the study hospital, as reported by the authors in a previous study [14], and not changed in the meanwhile [26]."

13. 2nd paragraph - The statement that the percentage of treatment is underestimated for the wards included in this analysis needs better supporting data. To calculate the total percentage certainly the authors have the exactly percentage of treatment in each hospital, setting and also the total numbers of healthcare providers. Thus, it would be easy to measure the real percentage of treatment in the selected settings.

R: As reported in point 10, we have the total number of healthcare providers, as well as the number of those who attended the educational activities, but we did not collect the ward where they worked at the time of education. Consider that the nursing staff may change ward, and sometimes hospital (also if to change hospital is not frequent in our country).

14. 3rd paragraph - The influenza epidemic is not the only potential cause of case mix in this study. As already mentioned, the authors should state clearly which were the main causes of hospital admission during the study period.

R: We could not abstract the main diagnoses from the regional database.

15. Limitation should be better described, containing many of the aspects mentioned above.

R: Done. See the paragraph before the last in the discussion.

" This study has strengths and weaknesses. Our study is limited by its observational design, which cannot exclude the possibility of our results being confounded by case-mix heterogeneity, but appropriately designed observational studies can provide valuable information on intervention effect [31]. We assessed the percentages of staff educated in the study hospitals, but not those of the staff working in the wards or units assessed for mortality or those previously performed by the staff. We were able to identify only the starting time of the educational program, because the Regional Health Agency opted to continue education. Finally, we did not address specifically the patients with SS/SS. "
Conclusion
16. The second paragraph is inadequate and should be removed
R: the paragraph has been moved.

Discretionary Revisions
1. CAPS are used inadequately. Examples: abstract Regional, Relative Risk
2. This text would benefit from a native English-spoken reviewer.
R: Both have been done

Rev 3
This paper is very interesting and important.
WE THANK A LOT THIS HIGHLY ESTEEMED REVIEWER FOR VALUING THE MEANING OF OUR STUDY AND FOR HIS COMMENTS.

Major Compulsory Revisions
There should be a flow diagram to describe and detail the methodology. This should include the implementation and time period.
R: we have replaced the previous diagram with a timeline graphic reporting the milestones of the study as well as the periods of education (new figure 1).

The authors should provide baseline demographics and data used to compare groups so that the reader can examine and compare to other studies. The actual mortality at baseline and after the education process should be provided.
R: The characteristics of the patients included in the mortality analysis before hospital staff education, in the first and in the second period after starting hospital staff education are reported in table 2.

The discussion is prolonged and would be more interesting if more data was provided in the results and discussed.
Other articles have examined similar concepts and should be reviewed to improve the discussion.1-6


R: Thank. The abstract supports the involvement of various specialties in education on sepsis, as we did in our project. We present it in the discussion
The positive effect of SS/SS education on care and outcome of ICU patients with SS/SS has been already demonstrated [20-21]. In these as in our study, efforts to improve the care of SS/SS patients targeted nearly all physicians specialties, because a wide variety of medical specialties care for severe sepsis patients [22].


R: In our project residents were free to attend the educational sessions but we did not include them either in the clinical staff or in the educated staff, because they received anyway education as part of their training all over the period for hospital mortality analysis (starting in 2003).

As reported in the first part of Methods, second paragraph, a senior attending physician is always present in wards/units, according to the rules of our Health Service. Therefore, we did not mention this letter and the reply in our paper, because they refer to a setting different from that of the present study.


R: We did not involve medical student in our educational project, and medical simulation by mannequin was adopted in only one centre. Unfortunately we don't have patient data by single centres.


R: In the new version, we have discussed the methods of this study (page 11, paragraph 2): "Ferrer et al [20] standardized the educational program and used multidisciplinary teams to deliver education to the staff of emergency department, medical and surgical wards, and ICUs. Their before-after study demonstrated a significant reduction in hospital mortality, but they studied only the patients with SS/SS admitted to 59 ICUs and reported a mean time dedicated to lectures of 10.6 hours at each center, without mentioning the number of the trained staff members."

R: This is the same reference as 4. The other paper of Ferrer in the blue Journal is not pertinent.


R: The reference has been used to support the effect of education in septic patients (page 11, last sentence).

"At hospital level, a multi-format educational approach on sepsis for all workers involved in patient care in a single institution without rapid response team was effective in reducing the mortality of the patients with sepsis [24]."

Rev 4

WE THANK THIS WELL-KNOWN REVIEWER FOR THE WORK SPENT IN REVIEWING OUR MANUSCRIPT HIS COMMENTS ALLOWED US TO UNDERSTAND THAT THE MANUSCRIPT WAS NOT CLEAR. WE HOPE THAT THE NEW VERSION CLARIFIES OUR HYPOTHESIS.

WE THANK HIM ALSO FOR HONESTLY SAYING THAT HE WAS DISAPPOINTED BY OUR MANUSCRIPT. THE BEST PEOPLE CAN CHANGE HIS MIND...... SO WE CAN HOPE.

Although this is an important area to pursue research in, this paper falls short of providing a good scientific approach to the problem of better identification and treatment of patients with severe sepsis on the floors of hospitals.

R: This was not the aim of our study. We explain better our study hypothesis.

The clinical signs of severe sepsis and septic shock (SS/SS) are quite unspecific and require the observation of basic vital signs. Indeed, signs of severe sepsis and septic shock (SS/SS) overlap with signs of clinical deterioration due to other reasons in ward patients. Therefore, hospital staff who has been educated to early recognize the clinical signs of SS/SS and early resuscitate the patients with these signs should early identify ward patients with clinical deterioration due to ANY reasons. Things could go as follows: an educated nurse realizes that a patient has high respiratory rate and lower arterial pressure than at the previous assessment. The nurse, made aware of the risk of SS/SS by education, will pay attention to these and other clinical signs, and will call for the ward physician. The ward physician may suspect pneumonia, but he will take into account other diagnoses (cardiac failure, pulmonary embolism, etc). In any case, the ward patient will be early examined by the doctor, who will early resuscitate and/or require investigations for diagnosis and/or call for help. In any case, the suitable treatment will be shortly prescribed and started. Early diagnosis and early treatment improve outcome (Chen J, et al. Crit Care Med 2009,37:148-153).

In other words, our hypothesis is that education on early recognition and
treatment (including resuscitation) of SS/SS will positively affect hospital patient mortality facilitating diagnosis and treatment of those showing clinical deterioration. So our study does not take into account the patients with SS/SS.

The last paragraph of the introduction has been changed as follows:
"Since signs of clinical deterioration in ward patients overlap with signs of severe sepsis and septic shock (SS/SS), we hypothesised that any education dedicated to early recognition and treatment of signs of SS/SS may affect the outcome of all hospital patients. Therefore, we designed a study to assess the trend of the mortality rate of adults admitted to hospital for at least one night in relationship with a hospital staff educational program on severe sepsis/septic shock."

(1) It is not clear to me as to what the flow of patients admitted to the ICU with severe sepsis is in these hospitals. Surely some are directly admitted to the ICU and some first to the floors(wards) and then to the ICU. It is the latter group that should represent the study population.

R: We did not assess patients with SS/SS.

In the discussion (page 12, last paragraph), we explain the reason for the choice.
"As far as hospital mortality is concerned, we did not distinguish the populations with and without SS/SS due to the following reasons: i) our data were collected for administrative reasons (reimbursement) and diagnosis codes may not be properly recorded by the individual physician [28]; ii) it has not been definitely clarified which international classification of diseases codes correspond to the definition of severe sepsis accepted by the ACCP/SCCM; iii) the coexistence of diagnostic codes for infection and organ failure does not necessarily mean that a causal or temporal relation exists [29]. Finally, we can speculate that international classification of diseases coding habits may be influenced by culture, and training courses aiming at improving attention to a clinical phenomenon can sensitize health professionals in the detection of that clinical phenomenon and increase their reporting."

(2) How as severe sepsis defined for the education program and for inclusion as a patient in the study analysis?

R: Education was based on the Surviving Sepsis Campaign, so the definitions of severe sepsis and septic shock were the same as in the original papers (the version 2008 was used from February 2008). We did not assess patients with SS/SS.

(3) What was the education plan, content and methods?

R: The educational program has been widely described in the methods as follows:
"The Regional Health Agency arranged an educational package consisting of information about epidemiology, morbidity and mortality of SS/SS, scientific literature, electronic presentations for lectures, format of clinical cases for
practice training, and booklets reporting clinic and laboratory signs of SS/SS [15]. In the first three quarters of 2007 (Figure 1), the Regional Health Agency acted as coordinating centre and organized meetings with the Multidisciplinary Sepsis Teams. The Multidisciplinary Sepsis Teams included doctors and nurses of infectious disease wards, intensive care, and the emergency department, a microbiologist and a pharmacist, selected by each hospital management among the senior staff. They participated in a course where they were taught about principles of adult learning [16], problem based learning [17] and Surviving Sepsis guidelines. As teamwork activity, they developed an algorithm to remind clinical signs of sepsis and to recommend timely assessment of patients with these signs as well as to improve and standardize decisions. The Multidisciplinary Sepsis Teams were provided with educational material (scientific literature, electronic presentations for lectures, scenarios of clinical cases for practice training and booklets) and started delivering courses and seminars each to their own hospital staff in the last quarter of 2007 (Figure 1). The methodology adopted for the educational courses in each hospital included delivery of short lectures, discussions as well as problem based learning on SS/SS scenarios. A typical course session held in the study hospital lasted four hours (14:30 to 18:30), included the presentation of the objectives of the course, definition, general and local epidemiology, early recognition, early goal-directed therapy, microbiological diagnosis, and early antibiotic treatment of SS/SS. At the end of the session the attendees answered a multiple item questionnaire to assess learning. The algorithm developed by the Multidisciplinary Sepsis Teams was reproduced and given to participants to be displayed as poster in the working areas.

The target of the present educational program consisted of attending physicians and nurses involved in direct patient care, excluding staff involved in only administrative duties. Residents were free to attend the educational sessions but they were not included either in the clinical staff or in the educated staff."

(4) Were the number of patients admitted to the ICU from the wards decreased with the initiation of the educational program? How about ICU and hospital stay?

R: This was out of the aim of our study. However, we have data showing that the monthly unplanned ICU admissions/1000 hospital admissions did not change according to the linear regression analysis from Oct 2008 to Sept 2009. In the same period, the monthly number of patients ICU admitted without infection showed a significant increase, suggesting that more patients with infection were possibly treated in wards.

(5) What was the mortality during the two time periods in pts. with severe sepsis?

R: See the answer to the first point.

(6) Why was the % of education achieved so low?

R: There are different ways to educate staff: you can organize a two-hour lesson for 200 persons who will physically attend it, you can adopt a web program which
will measure how long people will be connected, or you can involve small numbers of persons. Nearly 20 persons attended the courses organized by Multidisciplinary Sepsis Teams and a range of 12 to 30 courses per hospital was performed in 2008.

(7) The single table included does not show the study plan and results with great illustration capabilities.

R: We hope that the timeline graphic reporting the milestones of the study (new Figure 1) be clear.