Author’s response to reviews

Title: Surveillance of Device Associated Infections and mortality in a major Intensive Care Unit in the Republic of Cyprus

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Author’s response to reviews:

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To: Editor

BMC Infectious Diseases

Dear Editor,

We are pleased to submit our revised manuscript entitled “Surveillance of Device Associated Infections and mortality in a major Intensive Care Unit in the Republic of Cyprus” for your consideration.

Thank you very much for your valuable comments. We have made every effort to revise our manuscript based on the reviewer’s comments and recommendations. Below we provide a detailed response based on the reviewer’s comments.

Should you have any questions or require additional information, please feel free to contact me via e-mail. I would like to thank you very much in advance for your consideration.

Sincerely,

Dr Vasilios Raftopoulos

Associate Prof
Cyprus University of Technology

Response to Reviewer’s comments

Reviewer: Yingxi Chen

We deeply appreciate your constructive comments on the article.

The revisions based on your comments are recorded in track changes on the manuscript.

Abstract:

Line 30: While additional length of stay (ALOS) is defined in abstract, this term does not appear in the main body of manuscript. Please clarify.

ALOS was changed to LOS. Now it appears in the main body of the manuscript.

Abstract:

Line 35: "This was the most frequent DA-HAI with 11.4 cases per 1000 CVC says." Is this an incidence? If so, please specify.

Should spell out CVC upon first mention in the text.

This has been changed to: This was the most frequent DA-HAI with an 11.4 incidence rate per 1000 CVC days

Changed to: Central Venus Catheter (CVC)

Main text:

Page 4, line 13: Spell out CLABSIs, VAPs and CAUTIs upon first mention in the main text

Changed to: (range: 3.9-14.3/1000 device days) with the lowest rates to be reported in Luxemburg (3.2 [2.7-3.9]/1000 device days) and the highest in France (12.8 [8.4-18.3]/1000 device days) [7]. The median rate of CLABSIs among ten EU countries was 1.5 per 1000 central vein catheter (CVC) days (0.93-3.27/1000 CVC days) [8] and for CAUTI’s among 23 EU countries was 1.3 per 1000 urine catheter days (1.2-1.5/1000 CVC days)

Page 4, line 20: Should include unit of every rate.
Units added

Page 4, line 27: Please spell out "UC" for the first mention.

UC changed to Urine Catheter (UC)

Page 7, line 7: The authors used reported cost per HAI in the US hospitals to estimate cost of patients hospitalized in ICU in Cyprus. My major concern is the validation of those estimates, as healthcare cost is subject to local healthcare system as well as other national and institutional factors. Is it scientifically robust to do so?

Cost estimation removed according to the suggestion made by the other reviewer

Page 7, line 49: How were the relative risks estimated? Did the authors use regressions? If so, please specify. In addition, as evidence suggests that age is associated with length of stay as well as mortality, all analyses should at least adjust for age.

The RRs were estimated using a GLM with a binomial distribution and a log link function. This regression provides RRs instead of ORs. The model also adjusted for Age. Both unadjusted and adjusted RRs are now reported.

The methodology is now reported in the Statistical Analysis section

Page 8, Line 22: "One hundred and fifty of the 198 patients were admitted without an HAI...(Table 1)". However, according to table 1, there were 173 patients without infection, among which 151 patients without infection on admission. Please clarify the discrepancy.

Discrepancy corrected: One hundred and fifty-one of the 173 patients were admitted without an HAI and did not acquire a DA-HAI during their stay (Table 1).

We also made some modifications to the RRs in table 3.

Page 8, line 39: Provide unit for incidence.

Unit for incidence provided
Page 9, line 24: "...and patients with CAUTI is twice higher than that of ..." The result is not statistically significant and it is not clear how the RRs were calculated. Therefore, I'd be cautious when providing such statement.

The reference to the non-significant confidence intervals of CLABSI and CAUTI RR has been removed. The RRs were estimated using a GLM with a binomial distribution and a log link function. This regression provides RRs instead of ORs/. The model also adjusted for Age. Both unadjusted and adjusted RRs are now reported. This calculation method is now reported in the Statistical Analysis section.

Discussion:

The impact of reverse causality on length of stay, mortality and cost should be discussed and be included in the study limitations.

Cost estimation removed as suggested by the other reviewer – no need to be discussed

Cost estimation mentioned in the study limitations

Reviewer: Cristiano Alicino

Please check your computations for all the DA-HAIs or explain in more details the methods followed for the cost estimation.

Cost estimation was removed from paper as suggested

In addition, the authors estimated the costs related to DA-HAIs on the basis of the current hospital bed cost per ICU day. However, it is not clear whether this cost accounts also for the diagnostic exams, the antibiotic therapy and other procedures for the diagnosis and the treatment of DA-HAIs. Please, clarify this issue.

Cost estimation was removed from paper as suggested

The results and the limits of the cost estimation were not discussed in the "discussion" section. I suggest or to improve all the cost estimation analysis or to remove it from the paper

Cost estimation was removed from paper as suggested
Please report in more details the objectives of the study at the end of the introduction.

The objectives are reported in more details at the end of the introduction section.

In the methods section, please describe in more details the setting of the study reporting the name of the hospital, its characteristics (is it a primary, a secondary or a tertiary hospital? Is an adult hospital or also pediatric patients can be admitted? the number of yearly admission, etc.)

Hospital, patient’s characteristics, and numbers of yearly admissions were reported.

In the methods section, please describe in more details the inclusion and the exclusion criteria adopted for the enrolment of patients.

Done

Should the patients or their legal tutors sign an informed consent before the enrolment in the surveillance?

Added in the paper: the Cyprus Democracy Personal Data Commissioner approved the study protocol. There is no need for patients’ or their legal tutors’ consent before the enrolment in the surveillance, since the data were anonymously collected.

Discussion section, page 11, line 41-43. Authors stated that "LOS was correlated with the time of the occurrence of the first DA-HAI" but the correlation between LOS and time of occurrence of first DA-HAI has not been assessed with proper statistical methods. You can only state that patient with DA-HAI had a median LOS longer than patients without DAI-HAI.

Discussion section, page 11, line 41-43. Authors stated that "LOS was correlated with the time of the occurrence of the first DA-HAI" replaced as advised by reviewer.

In table 1, all percentages are miscalculated. Please, check carefully your computations. Moreover the percentages of the variables "infection on admission" were reported for row instead of for column (as done for the other variables). Finally, I suggest to add a column with the results of the overall population.

Percentages miscalculations recomputed and corrected

Results for the overall sample are now included.
The percentages of infection on admission are removed and only reported in the main body. This was to avoid confusion since row percentages are more appropriate than column percentages in this case.

Please at the first use of any acronym, please report for which this stand (in the abstract and in the text)

Done

Introduction, page 4, line 12, please specify that CLAB, VAP and CAUTI are the three most common DA-HAIs in intensive care units as reported in the reference 6

Done

Methods section, page 6 lines 7-9, please report which types of samples from lower respiratory tract were used for the diagnosis of VAP (BAL, BAS, other)

Reported: Lower respiratory tract secretions were collected using tracheal aspiration or bronchoalveolar lavage (BAL)

Methods section, page 4, line 52-53, you reported that the nurse to patient ratio is one to two (corresponding to 0.5), but in the following sentence you stated that during the day time shift the nurse per bed ratio is 0.75 whereas during the afternoon and night shift the nurse per bed ratio is 0.5. Please, clarify.

Recalculated and changed accordingly

- results section, page 8, line 10-12, please report also the percentage of the males and substitute & with and.

Percentage of the males reported as advised

Results section, page 8, line 39-41, please clarify what you mean for device utilization. Maybe you intended that the proportion of patients that were exposed to mechanical ventilation was 70%, those exposed to central catheters were 58% and so on.

Device utilization clarified as advised
Results section, page 8-9, the figure 1 is not informative so I suggest to remove it and the related comment in the section. I suggest the authors to report only the median time before the identification of DA-HAIs and the median time after the identification of the first DAI until discharge without any inference (remove the p-value).

- Figure 1 removed
- p value removed
- Median time before and after the DA-HAI identification reported as advised (only median time)

Please consider to add a multivariable analysis to study the factors associated with HA-DAIs mortality in addition to the computation of crude mortality rate. Some variables could potentially influence the excess of mortality.

A multivariate model (Binomial regression with a log link function) is also reported.

Results section, page 10, chapter "resistance", please remove all the acronyms for bacteria and antibiotics.

Acronyms removed

Conclusions: the study reported the DA-HAIs incidence and not DA-HAIs prevalence, please modify accordingly.

Modified accordingly