Author's response to reviews

Title: Epidemiology and impact of a multifaceted approach in controlling Central Venous Catheter Associated Blood Stream Infections outside the intensive care unit.

Authors:

José F. García-Rodríguez (jose.francisco.garcia.rodriguez@sergas.es)
Hortensia Álvarez-Díaz (hortensia.alvarez.diaz@sergas.es)
Laura Vilariño-Maneiro (laura.vilarino.maneiro@sergas.es)
María V. Lorenzo-García (maria.virginia.lorenzo.garcia@sergas.es)
Ana Cantón-Blanco (ana.canton.blanco@sergas.es)
Patricia Ordoñez-Barrosa (patricia.ordonez.barrosa@sergas.es)
Ana I. Mariño-Callejo (ana.isabel.marino.callejo@sergas.es)
Pascual Sesma-Sánchez (pascual.sesma.sanchez@sergas.es)

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Philippa Harris, PhD.
Executive Editor
BMC-series Journals
BMC Central
e-mail: editorial@biomedcentral.com

We submit our revised manuscript MS: : 1715919755833707 “Epidemiology and impact of a multifaceted approach in controlling Central Venous Catheter Associated Blood Stream Infections outside the intensive care unit” following your instructions and addressing reviewer comments.

Revisions made:
In Methods we specify that "The study was conducted in a 350-bed teaching hospital from 1991 to 2011 with the approval of hospital ethics Committee."
We include an authors' contributions section, page 15.

Comments to reviewer Francois L´Hériteau

Major compulsory revisions.
Prevalence studies.
1. We have performed correction of the mistake in the number of patients included in the prevalence studies and we have changed “followed” by “surveyed” (page 8, last paragraph in the results section).
2. The number of catheter-days retrieved from the prevalence studies are displayed in page 9, 1st paragraph "The estimated number of catheter-days retrieved from the prevalence studies varied significantly over time, ranged from 1,487 catheter-days in 2001 to 2,587 in 2008, p < 0.05";
in page 11, 2nd paragraph "From 2008 to 2009-2011, the estimated number of catheter-days per year decreased significantly" an in Table 1.

Bacteraemia surveillance
1. We have clarified the number of CVC-ABSI that were recorded in 260 patients, page 9, 2nd paragraph.
2. We have clarified the 3 “other Gram-negative micro-organisms” and ESBL-producing strains among Enterobacteriaceae isolates, page 9, last paragraph.
3. We have clarified in Methods section that Odds Ratios in the result section is referred to "... variables associated with CVC-ABSI versus peripheral intravascular catheter-ABSIs, were expressed as unadjusted odds ratios (ORs) and 95% confidence interval (CIs)", page 8 2nd paragraph.
4. We present the results with their 95%CI, page 11, 1st paragraph. We do not make an adjusted analysis (Poisson regression analysis) because we do not know the incidence and duration of all inserted catheter; second limitation of our study, page 14, 2nd paragraph.
5. We describe in Method section how we have calculated device utilisation ratios, page 8, 1st paragraph.

To not increase the length of the article we have not introduced separate data from outside-ICU wards other than internal Medicine and Surgery because of the small number of cases as well as until Oncology and Haemodialysis wards were opened, some patients with conditions requiring this specialized care were treated in Internal Medicine Wards.

We have described the limitations of our study,
OK, in page 11, 2nd paragraph we say “From 2008 to 2009-2011, the estimated number of catheter-days per year decreased significantly, the rate of inpatient blood cultures performed and the rate of alcohol-based handrub consumption increased slightly, and there was no significant difference between the years in rate of central line use and in other variables analysed”. We don’t describe data to support this because “there was no significant difference between the years” and to avoid increasing the length of manuscripts.

In table 1, the rate of inpatients blood cultures performed and the rate of alcohol-based handrub consumption increase is not statistically significant, but is statistically significant the No. of CVC-ABSI/No. of blood cultures performed and the No. of CVC-ABSI/1,000 catheter-days in Internal Medicine ward appear as statistically significant.

Page 13, 1st paragraph: “The incidence increased possibly due to an increasing
use of these catheters in a progressively ageing population, with greater comorbidity and more invasive treatments, as well as due to better detection of blood stream infections”. OK, our data possibly don’t support a better detection of BSI, but in prevalence studies results, page 8, last paragraph we say “Over time the mean age of patients and severity of the underlying rapidly fatal illness increased”, and data from 2008 to 2011 show that the rate of performed inpatients blood cultures increased slightly.

Page 13, 2nd paragraph: we say “CVC-ABSIs were associated with parenteral nutrition use and CVC-ABSIs rate was higher in surgical rather than medical wards. CVC and parenteral nutrition use was similar over time, but was greater in surgical wards and this could explain the difference in rate between admission wards20. In the same paragraph: “Another issue that could have contributed to different results is the difference in staff training and their motivation to participate in the prevention and control programme.” We don’t say that the difference in CVC-ABS1 rates between Surgical and Internal Medicine wards is only related to the difference in alcohol-based handrub consumption between these wards. We say that “the difference in staff training and their motivation to participate in the prevention and control programme seems to be reflected in the different alcohol-based hand-rub consumption”.

The data about the number of CVC-ABSIs increased in summer are in Results section, page 10, 1st paragraph. OK, in page 9 2nd paragraph we say “In the summer of 1993, prevalence of CVC use and parenteral nutrition utilisation were similar to the rest of that year (in summer, prevalence use of CVC 3.1% vs 2.3%; parenteral nutrition use: 2.3% vs 1.5%, no significant difference ). We didn’t perform more studies in summer, and we say in page 13, last lines “This increase of CVC-ABSIs numbers in summer…… makes us to formulate the hypothesis that this could be explained by the temporal recruitment of nurses with less experience in the handling of the catheters to work for the hospital.

Minor essential revisions
In table 1, we describe the meaning of "#": #Differences in prevalence use of CVC and PN between Surgery and Internal Medicine wards are significant when comparing the total sum of the years, p<0.05.

In table 1, it is now displayed "Estimated number of catheter-days".

We have clarified typing mistakes:
Page 12, 3rd paragraph, 7th line: “burn patients”
Page 19, table 1 title: “Epidemiology”.

Discretionary revisions
The “bacteraemia zero” program was implemented only in ICU, page 7th, 3rd paragraph.
Yes, the location of CVC insertion (inside vs outside ICU) was recorded and BSI that occurred outside ICU in a patient with a CVC inserted earlier in ICU were included in the surveillance. ICU physicians inserted 19.1% of all
CVC-ABSI, page 10, 3rd paragraph.

Page 13, last paragraph "the majority (65%) of patients with CVC inserted by ICU physicians was followed in Internal Medicine wards"

Page 6, 3rd paragraph "aqueous povidone-iodine solution was used as a skin antiseptic for CVCs inserted by physicians outside ICU and for all catheters after care performed by ward nurses."

The manuscript have been revised by a native English speaker.

We submit our revised manuscript. All authors have read and approved the submission of the manuscript.

The manuscript has not been published elsewhere and it is not currently under consideration for publication by another journal.

Thank you very much in advance.

Dr. José Francisco García-Rodríguez
Infectious Diseases Unit.
Internal Medicine Ward.
Health Area of Ferrol.
Sergas. La Coruña. Spain
E-mail: jose francisco garcia rodriguez@sergas.es