Author's response to reviews

Title: Healthcare-associated infections in Pediatric Cancer Patients: Results of a Prospective Surveillance Study from University Hospitals in Germany and Switzerland

Authors:

Arne Simon (asimon@ukb.uni-bonn.de)
Roland A Ammann (roland.ammann@insel.ch)
Udo Bode (udo.bode@ukb.uni-bonn.de)
Gudrun Fleischhack (gudrun.fleischhack@ukb.uni-bonn.de)
Hans-Martin Wenchel (hans-martin.wenchel@uk-koeln.de)
Dorothee Schwamborn (dorothee.schwamborn@uk-koeln.de)
Chara Gravou (Chara.Gravou@kinder.imed.uni-erlangen.de)
Paul Gerhardt Schlegel (schlegel_p@kinderklinik.uni-wuerzburg.de)
Stefan Rutkowski (rutkowski_s@kinderklinik.uni-wuerzburg.de)
Claudia Dannenberg (paediatrie@medizin.uni-halle.de)
Dieter Koerholz (paediatrie@medizin.uni-halle.de)
Hans Juergen Laws (laws@med.uni-duesseldorf.de)
Michael H Kramer (OXM3@aol.com)

Version: 3 Date: 24 April 2008

Author's response to reviews: see over
Dear colleagues,

today we submit the revised (R2) version of our original article

Healthcare-associated infections in Pediatric Cancer Patients: Results of a Prospective Surveillance Study from University Hospitals in Germany and Switzerland

duly considering the comments of the reviewers.

Please find attached the point by point list, as requested.

Many thanks for the decision to publish our work in BMC Infectious Diseases.

Best regards on behalf of all authors

Arne Simon

Arne Simon MD
Children's Hospital Medical Center, University of Bonn
Pediatric Hematology and Oncology
Adenauer Allee 119
53113 Bonn
Tel 0049 22828733254
Fax 0049 22828733301

Email asimon@ukb.uni-bonn.de
Point by Point List

(1) We went through the manuscript formatting checklist one more time and ensure that your revised manuscript conforms to all of the points.

(2) The email addresses of the contributors were added.

(3) A Competing interest declaration was added as requested.

Reviewer 1

Version: 2 Date: 17 March 2008

Reviewer: Victor Rosenthal

Reviewers report:
(1) This study was originally designed in order to analyze outcome related with neutropenia in cancer patients, and was not designed and planed to determinate health care associated infections (HAI) and FUO in cancer patients.

Comment by the authors: This is not the case. The study was designed to describe the epidemiology of HAI in paediatric cancer patients during intensive treatment. As described in detail in the methods section, the study included all inpatients with a confirmed HAI or nFUO event, irrespective of their neutrophil counts. We only used the item ‘neutropenia at the time of the event’ to describe
- The proportion of patients with neutropenia at the time of the diagnosis of the HAI and nFUOs,
- The proportion of neutropenia in the documented specific events.
- Any significant correlation between ‘neutropenia at the time of the diagnosis and fatal outcome (mortality).

Since neutrophil counts are not investigated daily in paediatric cancer patients, the data sets in this study do not allow conclusions considering the effect of duration of neutropenia on outcome variables. We discussed this issue in the Discussion section as one limitation of our study.

Please refer to the result subsection
Presence of Severe Neutropenia at Diagnosis of the HAI

One important conclusion of our study was that ‘surveillance should not be limited to the period of neutropenia, and for the calculation of IDs days of neutropenia should not be used as the (sole) denominator’ (see Discussion).

(2) It is not useful for the readers providing data of patients with HAI plus patients with FUO.

Comment of the authors:
At about 60% of all febrile events in paediatric cancer patients are FUOs (actually 64% in our study). Other groups have included nFUO events in their studies, too [1-3]. Thus, we included a separated analysis of these nFUO events in our study protocol. Our results confirm, that only age, but ‘neither malignancy diagnosis nor treatment modality preceding the event differed significantly between HAI and nFUOs.’ nFUOs are treated empirically with antimicrobial chemotherapy and thus contribute significantly to inpatient treatment days, selection pressure on resistant isolates and cost in paediatric oncology units.
Since the description of nFUO events in paediatric cancer patients is no complete, we added the following statement to the Discussion:

‘In the light of the profoundly restricted time budget of infection control personnel, the inclusion of pneumonias without a confirmed pathogen, blood-culture negative BSIs, urinary tract infections, and nFUOs should be reconsidered critically in surveillance efforts in this population.’

(3) This study was not designed to analyze impact of infection control activities on health care associated infections rates.

Comment by the authors:
This is correct. The study was designed to describe the epidemiology of HAI in pediatric cancer patients during intensive treatment. Only one short paragraph and figure 3 address this issue. We were able to demonstrate a significant reduction of the incidence density of HAs in one study centre and mentioned this in the Discussion

‘While we did not control for confounding variables such as demographic characteristics of the patients, duration of neutropenia or illness severity, further studies are needed to confirm that participation in such a surveillance study results in a significant decrease in HAI rates. This was not an interventional study and each participating center decided on its own responsibility about any practical consequence related to the reported HAI rates.’

(4) The authors are not providing number of patients, are not providing demographic characteristics of the patients, both are critical in order to analyze rates of infections and potential confounders.

Comment by the authors:
As described in the method section, ‘the surveillance module did not ask for admissions or numbers of individual patients in the participating institution during the surveillance period.’ Thus, we were not able to calculate overall infection rates. On the other hand, the incidence density of HAI per 1000 inpatient days is internationally accepted and gives a more robust estimation of the basic epidemiology of HAs than infection rates in % of all patients [4]. Nonetheless, detailed data considering the number of patients, basic demographic characteristics, underlying disease, disease status and preceeding treatments for all patients with at least one HAI or nFUO are provided in Table 2. Our study aimed at the description of these patients, not of the overall population of cancer patients treated in these units. This was a well known limitation in our study design (see Comment 3). We did not aim at the description of significant correlations between the underlying disease or other confounders and specific HAs or outcome data.

(5) Quality of written English: Needs some language corrections before being Published

Comment by the authors:
The manuscript was checked by a native speaker in front of the first submission.
Reviewer 2

Title: Healthcare-associated infections in Pediatric Cancer Patients: Results of a Prospective Surveillance Study from University Hospitals in Germany and Switzerland

Version: 2 Date: 18 February 2008

Reviewer: elio castagnola

Reviewer's report:
Acceptable.

At page 8 is still present a NI instead of HAI
Changed as requested

What next?: Accept without revision

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests

References