Reply to Weber, von Cube, Sommer, Wolkewitz: Necessity of a Competing Risk Approach in Risk Factor Analysis of Central-Line–Associated Bloodstream Infection

To the Editor—We thank Ms. Weber and colleagues[1] for their comments regarding the use of the Cox proportional hazards model to analyze risk factors for central-line–associated bloodstream infections (CLABSIs) in children, in which we used a Cox proportional hazards model to determine risk factors for this outcome. In our analysis,[2] removal of the central venous cathether was treated as censoring. Weber et al suggest that removal of the line constitutes a competing risk for CLABSI because children without a line can no longer be assumed to be at the same risk for CLABSI than those with a line (the fundamental assumption of censoring).

We sincerely appreciate these comments, which highlight the need for increased awareness of the assumptions of the Cox proportional hazard method in this setting. We agree that removal of the central venous catheter indeed constitutes a competing risk.

In our cohort study, there were only 2 possible outcomes with regard to the life of the central venous catheter: infection and catheter removal. Because all lines are followed by the infection control team until removal, there was no censoring due to loss to follow-up.

We have re-analyzed the data and have graphed the cumulative incidence function of CLABSI as suggested by Weber et al. The curve reaches the empirical cumulative incidence of CLABSI of 6.8% on the day of the last event (Figure 1).

We have further rerun the Cox proportional hazards model using (1) the subdistribution hazard (SHR) approach[3] and (2) the cause-specific hazard approach (modeling the time to line infection or catheter removal separately, each time treating the other as the censoring event).

After reviewing the literature and in discussion with statistician colleagues, we feel that the first approach (SHR) is not suitable to answer our research question. The SHR approach describes the CLABSI risk in patients who already had their line removed (the competing event), ie, in a non-existing, theoretical population.[3] This approach has been advocated in the literature for prediction modeling rather than etiologic research (like our study).[4] By contrast, the hazard ratios from the cause-specific models can be interpreted as the risk of CLABSI in patients who have not (yet) had CLABSI and have not had their catheter removed (the competing event).[4] Within this interpretation of the hazard ratios, the estimates presented in our paper are correct.

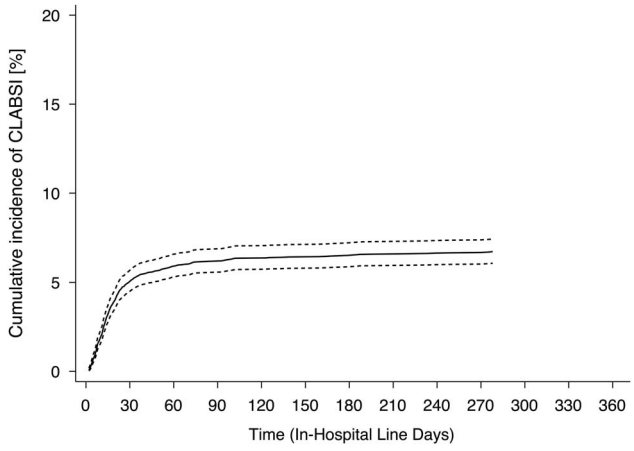

FIGURE 1. Cumulative incidence of central line-associated bloodstream infection in 5,648 children with central venous catheters. Dashed lines indicate the 95% confidence interval boundaries of the estimate.

Potential conflicts of interest: All authors report no conflicts of interest relevant to this article.

Stefan Kuhle, MD, PhD;[1]
Jillian H. Carter, MSc;[2]
Susan Kirkland, PhD;[3]
Joanne M. Langley, MD, MSc;[4]
Bryan Maguire, MSc;[1]
Bruce Smith, PhD[5]

Affiliations: 1. Departments of Pediatrics and Obstetrics & Gynaecology, Dalhousie University, Halifax, NS, Canada; 2. Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada; 3. Department of Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada; 4. Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada; 5. Departments of Mathematics and Statistics, Dalhousie University, Halifax, Nova Scotia, Canada.

Address correspondence to Joanne M. Langley MD, MSc, FSHEA, IWK Health Centre, Goldbloom RCC Pavilion, 4th floor, 5850/5980 University Avenue, Halifax, NS, Canada B3K 6R8 (joanne.langley@dal.ca).

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