Published in final edited form as:

Crit Care Med. 2018 July ; 46(7): e730–e731. doi:10.1097/CCM.0000000000003178.

The authors reply

Patrick Donnelly Tyler, MD,

Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA

Barret Rush, MD, MPH, and

Division of Critical Care Medicine, St. Paul's Hospital, University of British Columbia, Vancouver, BC, Canada

Leo A Celi, MD, MPH, MS

Division of Pulmonary, Critical Care, and Sleep Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA

Keywords

sepsis; interhospital transfer

We appreciate the thoughtful commentary of Wilcox et al (1) in response to our recent manuscript (2). On their most important point, we agree: “transfer of critically ill patients warrants further study.”

We recognize that the results of our study must be interpreted in the context of its design. In our discussion section, we describe the limitations noted by Wilcox et al (absence of patient-level data, the reason for transfer), and many others: potential for selection and misclassification bias, small sample size, absence of information about severity of illness, limitations in propensity score matching, and so on. We encourage readers to interpret the study results in light of those findings. To quote the original manuscript: “The intention of this analysis was not to definitively answer the question regarding the outcomes of patients in the ICU who undergo IHT, but rather to form a basis for hypothesis generation and to encourage future more rigorous research from the community” (2).

The second point made by Wilcox et al is somewhat misleading. We do not state that we are studying the patients who were sickest; rather, we used mechanical ventilation *a priori* as a proxy to identify the sickest patients within an administrative database. A practicing intensivist would agree that, among a cohort of patients with sepsis, those who are mechanically ventilated would be overall sicker than those who are not. Because we specified our analysis plan prior to analyzing the data, we had no way of knowing in advance what the mortality would be. Severity-of-illness scores were on our list of confounding variables but, regrettably, were not part of the database. We agree that the mortality in the population we studied was lower than expected. We hypothesized that errors in coding,

Correspondence to pdtyler@bidmc.harvard.edu.

Copyright form disclosure: Drs. Tyler and Celi received support for article research from the National Institutes of Health. Dr. Rush has disclosed that he does not have any potential conflicts of interest.

selection bias, and perhaps some patients being “too sick to transfer” may have driven this result, and agree that it is of interest and should be explored further.

Wilcox and colleagues disagree that there are few outcomes studies among transferred patients and cite the CESAR trial as evidence of ample literature on the subject matter (3). We maintain that there are relatively few high-quality studies on outcomes in transferred patients and that the CESAR trial does not evaluate the benefit of ICU transfers. The CESAR trial was designed to compare conventional ARDS management to ECMO, and because of the specialized nature of this therapy, a fraction of patients randomized to ECMO had to be transferred to a larger medical center to receive it. It is also important to note that the study suffers from multiple weaknesses, including a lack of structured protocol for “conventional treatment,” as well as a fragility index of only 1 (calculated from the data in Table 3)(3).

We had modified a model that was developed and validated by Ford and colleagues to predict in-hospital mortality using administrative data to represent severity of illness (4). In the model development, Ford and colleagues excluded patients who were transferred between hospitals. The reason for this is clear from a machine learning perspective: transferred patients may differ significantly from those who presented to the Emergency Department because of treatments received prior to transfer, and these differences may not be reflected by hospital administrative data. However, it doesn’t necessarily follow that a model that was developed on a cohort that excluded patients who were transferred will not perform well in predicting hospital mortality among transferred patients. Indeed, among patients in our study cohort who were transferred, the severity of illness score that we employed has an area under the receiver operating characteristic curve of 0.83 when plotted against hospital mortality.

Regarding the writers’ point about transport modality, we had not thought of it; that it occurred to Wilcox et al heartens us, because we hoped that sharing our ideas and findings would tap the collective potential of the critical care research community on this topic. However, as they have point out, very few patients have access to specialized critical care air transport teams, so the population affected is likely too small to influence the effect size.

Overall, our team agrees with Wilcox et al (1) regarding the limitations and generalizability of our work. A major impediment to studying this topic is the lack of structured data from both sending and receiving hospitals, as we stated in our paper. We enlist other investigators to brainstorm on novel means of studying inter-hospital transfers, to devise ways to collect comprehensive data about these patients, and to replicate, refute or build upon our findings. We hope that future studies will clarify how to better incorporate inter-hospital transfer into the care of critically ill patients.

Acknowledgments

We thank Wilcox et al (1) for reviewing our work.

References

1. Wilcox SR, Frakes MA, Marcolini EG, et al. Limitations in Conclusions Regarding Critical Care Transport. *Crit Care Med*. 2018 in press.
2. Rush B, Tyler PD, Stone DJ, Geisler BP, Walley KR, Celi LA. Outcomes of Ventilated Patients With Sepsis Who Undergo Interhospital Transfer. *Crit Care Med*. 2018; 46(1)
3. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*. 2009; 374(9698):1351–63. [PubMed: 19762075]
4. Ford DW, Goodwin AJ, Simpson AN, Johnson E, Nadig N, Simpson KN. A Severe Sepsis Mortality Prediction Model and Score for Use With Administrative Data. *Crit Care Med*. 2016; 44(2):319–27. [PubMed: 26496452]