Published in final edited form as:

Crit Care Med. 2017 April ; 45(4): e464–e465. doi:10.1097/CCM.0000000000002276.

The Author's Response: In Response to “Nutritional Assessment must be prioritized for critically ill children in the PICU” by L.J. Bouchard and N.M. Mehta

Shan L Ward, MD¹ and Heidi Flori, MD²

¹Department of Pediatrics, Division of Critical Care, UCSF Benioff Children's Hospital San Francisco, San Francisco, CA

²Division of Pediatric Critical Care Medicine, C.S. Mott Children's Hospital, Ann Arbor, MI

Dear Editor

We appreciate the interest in our study and the opportunity to promote a dialogue about the impact of the obesity epidemic on the care of critically ill children (1). We agree that obesity is associated with numerous comorbidities and with poor health outcomes and it is not our intent to promote the benefit of obesity but rather to determine whether the pathobiologic responses to ARDS are different in the underweight, normal weight and obese. In the adult critically ill population, being overweight or obese is associated with reduced in-hospital mortality risk in patients with ARDS as well as in those with sepsis, despite the fact that this same group of patients require longer periods of mechanical ventilation (2, 3). Our findings are similar except that the reduced mortality risk was primarily accounted for by those with an indirect cause of lung injury (4). No other pediatric or adult study has evaluated such a stratified analysis.

While Bouchard and colleagues report concern that our finding was only found in this indirect lung injury sub-group, we offer a counter point to this concern: The presence of the obesity paradox in those with indirect lung injury only (for example sepsis or systemic inflammatory response syndrome from polytrauma or systemic vasculitis) may point to a pathobiologic, mechanistic link between increased adiposity, ARDS and the systemic inflammatory response. In fact, Stapleton et al. evaluated biomarkers of systemic inflammatory response in 1,409 adult ARDS subjects and found lower levels of pro-inflammatory markers (IL-8, TNF α) as BMI increased, with lower levels of such markers correlating to reduced mortality (5). Further investigation is clearly needed to parse out this attenuated inflammatory response to critical illness. Such exploration is a future direction of

Corresponding Author: Shan L Ward, MD, UCSF Benioff Children's Hospital, San Francisco, 550 16th St, 5th Floor, Box 0106, San Francisco, CA 94143, Phone: (415) 476-3708, shan.ward@ucsf.edu.

Shan L. Ward, MD, UCSF Benioff Children's Hospital, San Francisco

Heidi R. Flori, MD, University of Michigan, C.S. Mott Children's Hospital.

Conflicts of Interest: Drs. Ward and Flori have no conflicts of interest to report.

Copyright form disclosure: Dr. Ward received support for article research from the National Institutes of Health (NIH). Dr. Flori received support for article research from the NIH; she received funding from Vannucci Law Firm (expert testimony), Genentech (expert opinion on next study design), and San Joaquin General Hospital (lecture honorarium).

this research team because we believe that understanding these differences in pathobiology by weight category and mechanism of injury may be useful in adjusting our protocol driven therapeutic strategies to better meet each patient's specific premorbid and illness-focused characteristics.

Regarding our method of defining obesity utilizing CDC-defined BMI z-score cutoffs and excluding those less than 2 years old, we agree that our methodology is not perfect. Unfortunately such issues plague all pediatric obesity research. This age-based exclusion criteria reduces the generalizability of our findings to our infant patients, but we chose to exclude those less than two years old for two reasons: 1) BMI is not a validated method in children less than 2 years old, and 2) the inclusion of children < 2 years old would introduce several confounders including impact of prematurity and intrauterine growth retardation, as well as the variation in dietary habits. This challenge of limiting confounders versus maximizing generalizability is an important one in our field and we hope such discussions will drive the pediatric critical care community to work together and form a consensus of definitions regarding obesity and nutrition that would benefit all nutrition based research.

Bouchard and colleagues discuss the impact of premorbid conditions on outcomes studies in pediatric critical care and we completely agree that such factors, including past medical history and pre-illness nutritional status are important. Unfortunately, we did not have an objective way to assess pre-morbid nutritional status in this cohort. Once again, the lack of objective pre-illness health status plagues all of pediatric critical care (and adult critical care, for that matter) and limits, not only studies of mortality and duration of hospitalization, but also longer term outcomes such as post-ICU function and neurocognitive status. Both our and Bouchard's findings point to the need for the critical care, and the pediatric community as a whole, to frequently and objectively assess for risk factors of critical illness including nutritional status. Additionally we need to form consensus on how to address such important limitations in our research endeavors when study designs such as randomized control studies that reduce the impact of such characteristics, are limited due to the low frequency of critical illness within the pediatric population.

In closing, the purpose of our study was to determine if the obesity paradox may exist in pediatric ARDS similar to what has been seen in adults. We hope that our findings promote further investigation so that our understanding of such differences may inform the field on how to adjust therapeutic strategies by degree of adiposity and potentially improve future treatment options and patient outcomes for all weight groups.

References

1. Bechard LJ, Mehta NM. Nutritional assessment must be prioritized for critically ill children in the PICU. *Crit Care Med*. 2017 in press.
2. O'Brien JM, et al. Body mass index is independently associated with hospital mortality in mechanically ventilated adults with acute lung injury. *Crit Care Med*. 2006; 34:738–744. [PubMed: 16521268]
3. Pepper DJ, et al. Increased body mass index and adjusted mortality in ICU patients with sepsis or septic shock: a systematic review and meta-analysis. *Crit Care*. 2016; 20:181. [PubMed: 27306751]
4. Ward SL, et al. Impact of Weight Extremes on Clinical Outcomes in Pediatric Acute Respiratory Distress Syndrome. *Crit Care Med*. 2016 June Publi.

5. Stapleton RD, Dixon AE, Parsons PE, Ware LB, Suratt BT. The association between BMI and plasma cytokine levels in patients with acute lung injury. *Chest*. 2010; 138:568–77. [PubMed: 20435656]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript