

We read with interest Numa et al's recent article in the Journal investigating possible harm from hyperoxia and the associated editorial. (1, 2)

We were disappointed however that the authors stated "*no studies in mixed PICU patients have been reported.*" Neither they, nor the editorial writers, have captured some of the most relevant literature. Our 10-year cohort study (n= 7410) in Pediatric Critical Care Medicine in 2016 is a mixed PICU patient study. We demonstrated a 'U'-shaped relationship between admission arterial partial pressure of oxygen (PaO₂) and unadjusted mortality. In addition, similar to Numa et al, we investigated the Standardised Mortality Ratio vs. PaO₂ relationship by modifying the PaO₂ component of the Paediatric Index of Mortality 2 score. (3) We have subsequently published high-resolution data on >1 million SpO₂ observations and confirmed that current clinical practice is for very liberal oxygenation. (4) Most recently we have completed a pilot multiple-centre randomised control trial comparing restrictive SpO₂ targets of 88-92% with standard care of >94%. This confirmed the feasibility of a definitive Oxy-PICU study, which is currently being planned.

This is an area of a great deal of research activity globally. Large scale trials are in progress in children with respiratory distress in Africa (5) and critically ill adults in Europe, Australia and New Zealand. Being able to reproduce results across settings and contexts is powerful: it points to a strong physiological effect, detectable despite variations in populations and healthcare systems. It is unfortunate that this was overlooked by the authors, reviewers and editorial team.

References

1. Numa A, Aneja H, Awad J, et al.: Admission Hyperoxia Is a Risk Factor for Mortality in Pediatric Intensive Care. *Pediatr Crit Care Med* 2018; 19:699–704
2. Smith LS, Khemani RG: The Therapeutic Index* [Internet]. *Pediatr Crit Care Med* 2018; 19:775–776 Available from: <http://insights.ovid.com/crossref?an=00130478-201808000-00012>
3. Raman S, Prince NJ, Hoskote A, et al.: Admission PaO₂ and Mortality in Critically Ill Children [Internet]. *Pediatr Crit Care Med* 2016; 17:e444–e450 Available from: <http://insights.ovid.com/crossref?an=00130478-201610000-00031>
4. Ray S, Rogers L, Raman S, et al.: Liberal oxygenation in paediatric intensive care: retrospective analysis of high-resolution SpO₂ data. *Intensive Care Med* 2017; 43:146–147
5. Maitland K, Kiguli S, Opoka RO, et al.: Children's Oxygen Administration Strategies Trial (COAST): A randomised controlled trial of high flow versus oxygen versus control in African children with severe pneumonia. *Wellcome Open Res* 2017; 2:100