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Liberal oxygenation in paediatric intensive care: retrospective analysis of high resolution SpO_2 data

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Conflicts of Interest: Sainath Raman is a co-investigator and Mark Peters is the Chief Investigator on Oxy-PICU: A randomised feasibility multiple centre trial of conservative versus liberal oxygenation targets in critically ill children, funded by Great Ormond Street Hospital Children's Charity. The other investigators are: Dr P Ramnarayan, Prof M Grocott, Dr D Harrision, Prof Kathy Rowan, P Mouncey, Dr S Eaton, Dr D Inwald, Dr J Pappachan, N and S Heinoch

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Ethical approval: The study was registered with the institutional audit department (ref 2013). Individual patient consent was not sought as this is a retrospective observational study and no patient identifiable data is reported.

Severe hypoxia is detrimental during critical illness, but hyperoxia has also been associated with adverse outcomes [1-3]. Harm from hyperoxia may be a biological consequence of oxidative damage or reflect iatrogenic injury resulting from more aggressive care. ARDSnet protocols include conservative oxygenation targets (SpO_2 88-95%) [4] recognizing that the harms of high inspired oxygen fractions (FiO_2) and ventilation volumes and pressures may outweigh any advantage of an additional buffer against hypoxia.

Where does this balance of harm and benefit of oxygenation lie on the paediatric intensive care unit (PICU)? As part of preliminary work towards our Oxy-PICU trial for conservative versus liberal oxygenation targets, we investigated current practice at a large general PICU over 12 months. Children were selected on the basis of measurement of a PaO2:FiO2 ratio (PF) <300 mmHg (8217 values in 326 children). This excluded children likely to have high SpO_2 values without supplemental oxygen or ventilator support. We analysed SpO_2 data at 5-second intervals in the hour before and after 5096 PF values <300 mmHg from 227 children with available data: a total of 7,352,388 SpO_2 values collected using the Etiometry T3 system (Etiometry Inc, MA). Concurrent hourly FiO_2 and mean airway pressure (MAP) data were collected from the electronic health record. SpO_2 data were analysed in 4 groups based on FiO_2>= or <0.6, and MAP>= or <16 cm H_20 in the hour of measurement. The SpO2 distributions were compared using the Kolmogorov-Smirnov test. A multi-level linear regression model was used to test whether the SpO2 (dependent variable), FiO2 and MAP (as categorical fixed effect variables) relationship was skewed by individual patients (random effects variable). Any crude mortality effect of oxygenation was sought by comparing the mean SpO2 value over the first 48 hours of admission according to survival status at discharge. All data were processed using Microsoft Excel (Microsoft Corp., WA) and R (www.r-cran.org).

The distribution of SpO2 values are shown (figure). In all 4 combinations of FiO2 and MAP, 99-100% was the modal SpO2; 26.4% of all SpO2 values were 99 or 100%, and 70.8% were above 95%. Each of the 4 distributions were significantly different to each other (Kolmogorov-Smirnov $p<0.001$), with the greatest difference between high and low FiO_2 groups. The multi-level regression model confirmed high FiO2 was associated with lower SpO2 regardless of individual patients. There were no significant differences between the 48 hour mean SpO2 values in those who died or survived (see Supplementary Materials).

These data demonstrate: (1) current practice is for very liberal oxygenation above recommended targets even in children with low PF ratios. (2) Children receiving higher treatment levels (FiO_2>=0.6, MAP>16) have a slightly lower SpO_2 distribution, an effect more pronounced with high FiO_2 than with high MAP.

These high resolution data demonstrate that PICU practice does not follow what clinicians report [5], recent evidence [3] or existing guidelines [4]. A pragmatic clinical trial of oxygenation targets in critically ill children is necessary, and can reasonably include a control group of >94% SpO_2 to reflect current practice.

Figure: SpO_2 distributions according to FiO_2 and MAP. The top left panel shows the SpO_2 distribution when FiO_2>=0.6 and MAP<16 cm H_20; the top right panel with FiO_2>=0.6 and MAP>=16; the bottom left panel FiO_2<0.6 and MAP<16; bottom right panel FiO_2<0.6 and MAP>=16. All 4 distributions differ significantly according to the Kolmogorov-Smirnov test, with the greatest difference between FiO_2 <0.6 and >=0.6 i.e. top and bottom panels (high vs low FiO_2 D-statistic 0.12, $p<2.2 \times 10^{-16}$; high vs low MAP D-statistic 0.05, $p<2.2 \times 10^{-16}$)

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Figure

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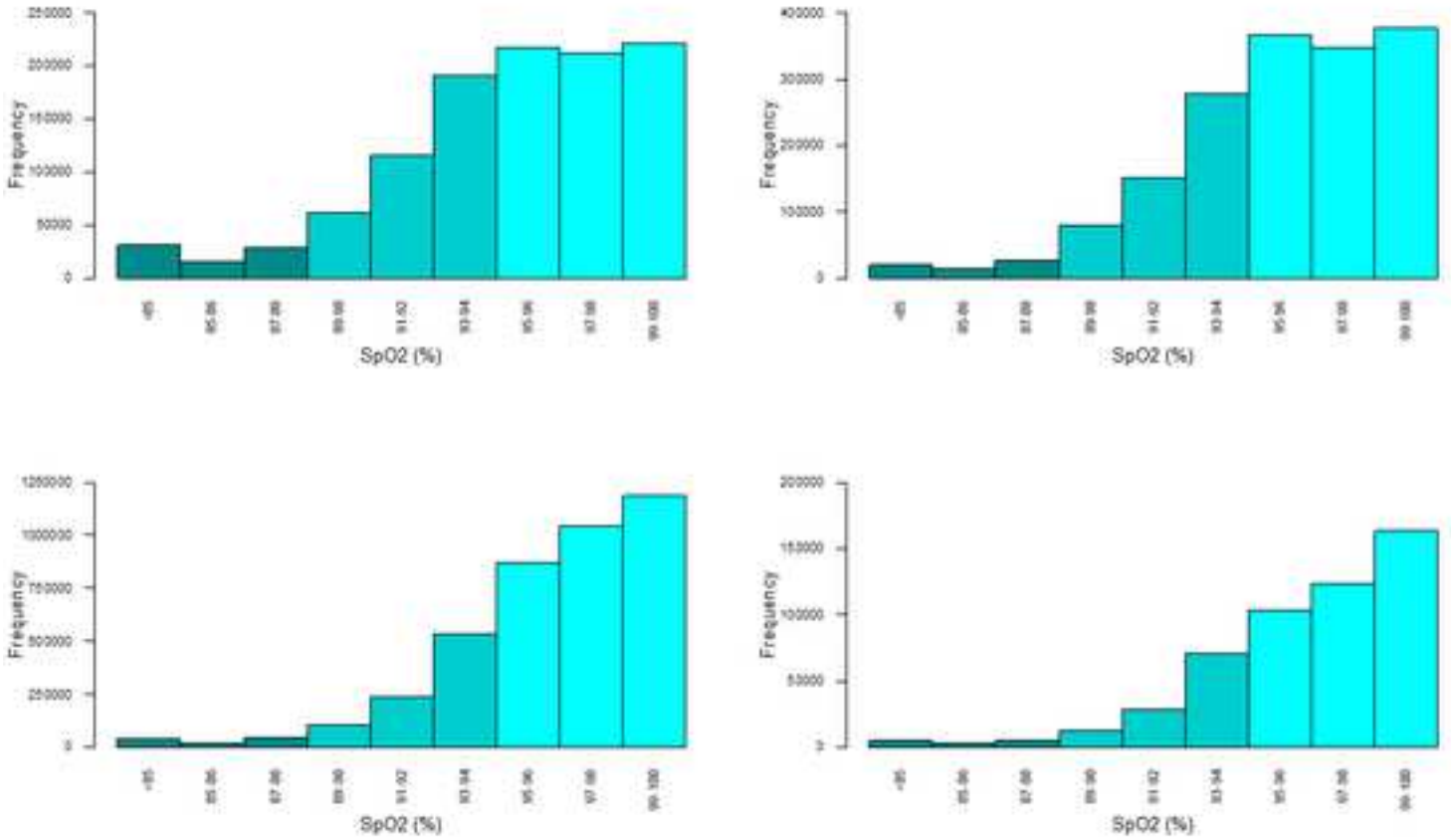

Figure: SpO_2 distributions according to FiO_2 and MAP. The top left panel shows the SpO_2 distribution when FiO_2>=0.6 and MAP<16 cm H_2O; the top right panel with FiO_2>=0.6 and MAP>=16; the bottom left panel FiO_2<0.6 and MAP<16; bottom right panel FiO_2<0.6 and MAP>=16. All 4 distributions differ significantly according to the Kolmogorov-Smirnov test, with the greatest difference between FiO_2 <0.6 and >=0.6 i.e. top and bottom panels (high vs low FiO_2 D-statistic 0.12, $p<2.2 \times 10^{-16}$; high vs low MAP D-statistic 0.05, $p<2.2 \times 10^{-16}$)