

Paediatric Intensive Care admission blood pressure and risk of death in 30,334 children

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Systolic blood pressure (SBP) is associated with mortality in critically ill children. It is used in mortality prediction models such as the Paediatric Index of Mortality (PIM) and the Pediatric Risk of Mortality score (PRISM). Shann et al described a U-shaped relationship between SBP on admission to the paediatric intensive care unit (PICU) and mortality in 5695 children in the course of developing the PIM score in 1997 (1). The lowest risk of death was at 120 mmHg, regardless of age; 120mmHg is above the 99th centile for children less than 2 years. Given that most of the PICU population are <2 years of age, the nadir of 120 mmHg may reflect low mortality in older children or low mortality with supra-normal BP. We sought to test this association in children according to age. We hypothesized that there would be a U-shaped association between blood pressure and mortality but that the nadir would be lower than previously described.

In this retrospective cohort study, we determined the relationship between SBP on admission to PICU and risk-adjusted mortality in four PICUs in London, United Kingdom (two general and two cardiac). Infants with a corrected gestational age of <37 weeks at admission were excluded. Data were available for 30,334 children between 2004-2018. We described the relationship between mortality and SBP on admission using a 4-knot restricted cubic spline, with knots at 51, 74, 91 and 122 mmHg (5th, 35th, 65th and 95th centiles) for the under 2 year-old cohort and knots at 70, 95, 112 and 143 mmHg (5th, 35th, 65th and 95th centiles) for the 2 years and over cohort. The PIM-2 probability of death with the blood pressure component removed was used to risk adjust the relationship. The risk-adjusted odds ratio of death according to admission SBP is shown in Figure 1. The lowest risk of mortality was at 70 mmHg in the <2 year-olds, and 95 mmHg in the ≥2 year-olds (Figure 1).

The association between admission SBP and mortality was more complex than previously described. Expectedly, the risk of death associated with low SBP on admission was greater than with high SBP, especially in children ≥2 years. Children <2 and ≥2 years show a nadir of risk around the 35th centile SBP for the population. Both nadirs are considerably lower than the 120mmHg used in PIM. Although there is a risk of our model over-fitting the data, given the size of our cohort with data from 4 PICUs, this association is likely to be generalizable. Our data do not consider interventions and are limited to a single measurement at admission. However, most children in our cohort had an admission SBP higher than that associated with the lowest risk. Age-associated SBP should be considered in future iterations of PIM. Furthermore, there is need for a large interventional trial, similar to SEPSISPAM in adults, to understand the risk associated with different SBP targets in the ongoing care of critically ill children (2).

References:

- (1) Shann F, Pearson G, Slater A, Wilkinson K (1997). Paediatric index of mortality (PIM): a mortality prediction model for children in intensive care. *Intensive Care Medicine* 23:201-207.
- (2) Asfar P, Meziani F, Hamel JF et al (2014). High versus low blood-pressure target in patients with septic shock. *N Engl J Med* 370:1583–1593.

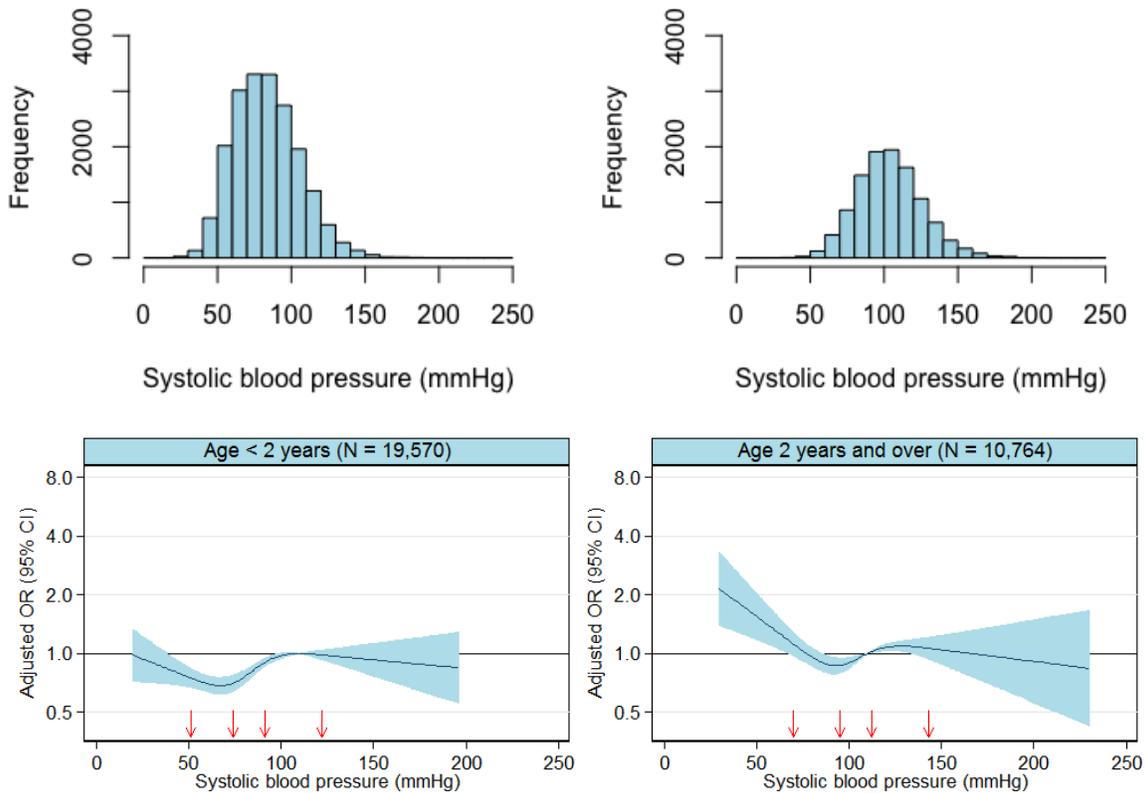


Figure: Systolic blood pressure at admission to ICU in children (a) less than 2 years of age (n=19570), left, and (b) 2 years and over (n=10764), right. The top panel shows the frequency histogram of systolic blood pressure for children on admission to ICU. The bottom panel shows the association between admission systolic blood pressure and mortality, adjusted for the Paediatric Index of Mortality with the blood pressure component removed. The adjusted odds ratios on the y-axis are derived from logistic regression following restricted cubic spline transformation of the systolic blood pressure variable. The spline transformation was carried out using 4 knots at the 5th, 35th, 65th and 95th centiles for each cohort: these are at 51, 74, 91 and 122 mmHg for children < 2 years and at 70, 95, 112 and 143 mmHg for children 2 years and over (shown by red arrows on the x-axis).