# Age associated blood pressure distributions in pediatric intensive care units differ from healthy children.

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Normal blood pressure (BP) centiles for age and height in children have been derived from healthy children by the US NIH Task Force (1,2). Restoration of BP towards healthy normal values in the resuscitation phase of childhood critical illness has been associated with an outcome benefit (3). However, paediatric intensive care unit (PICU) admission systolic BP has a U-shaped association with mortality (4). Current studies in critically-ill adults are exploring a more permissive approach to BP (5). Description of the distribution of BP in critically-ill children is an essential step towards similar work.

We aimed to describe the systolic and mean BP distribution according to sex and age in children admitted to two PICUs in London, UK. Electronic health records were interrogated to yield all non-invasive oscillometric blood pressure measurements (Intellivue, Philips, Netherlands) in children admitted to the general (non-cardiac) PICUs at Great Ormond Street Hospital (between 2012-2016) and St Mary's Hospital (between 2009-2015). Only non-invasive measurements were considered because (a) all children underwent non-invasive measurement, and (b) the NIH normal values were derived from non-invasive measurements. Systolic measurements <30 mmHg and >250 mmHg, and mean measurements <16 mmHg and >216 mmHg were excluded as likely spurious.

To account for multiple measurements in each patient, multi-level quantile regression analysis was used, with blood pressure as the dependent variable, age in years as the fixed effect variable and the unique patient identifier as the random effects variable. The 50$^{th}$ centile for each year of age were compared with the 50$^{th}$ centile from the ~~US Task Force~~NIH data: as height data were not routinely available for children in our cohort, the 50th height centile values were used for comparison. The values were considered significantly different ($p<0.05$) if the 50$^{th}$ centile value from the ~~Task Force~~NIH data lay outwith the 95% confidence interval for the 50$^{th}$ centile value from our cohort. Data were analysed using r (www.cran.r-project.org).

Systolic BP centiles were generated from 309520 measurements from 2415 boys and 251877 measurements from 1946 girls; mean BP centiles from 313492 measurements from 2413 boys and 256662 measurements from 1944 girls ~~(Figure)~~. Following multi-level quantile regression for the 50$^{th}$ centile, the PICU 50$^{th}$ centile values for systolic BP were significantly higher for boys between 1 and 9 years, and girls between 2 and 8 years compared to the ~~Task Force~~NIH 50$^{th}$ centile (Figure)~~e~~. The PICU 50$^{th}$ centile values for mean BP were significantly higher for boys between 1 and 3 years, and girls aged 2 years and 4 years (Electronic Supplementary Material 1, 2).

Compared to population-based normal values, younger children in our cohort had higher observed BP measurements. ~~It is not clear if this is due to therapeutic intervention, varying levels of sedation or individual disease pathophysiology. However, the therapeutic benefit of such supra-normal values has not been demonstrated~~This may not be therapeutically driven, but a consequence of levels of sedation, or disease pathophysiology (Electronic Supplementary Material 3). The frequency of measurements is likely to be biased by haemodynamic status. ~~Our data suggest~~Regardless, we demonstrate uncertainty regarding optimal BP targets in ~~PICUs~~critically-ill children. Prospective trials examining the effect of different BP targets on outcome in children in intensive care, similar to the adult SEPSISPAM trial (5), are needed to guide practice.

**Ethical approval and consent to participate:** Ethical approval was not sought as we used routinely collected clinical data retrospectively. Consent to participate was not sought as this is a retrospective observational study and no patient identifiable data are presented.

**Consent to publish:** Consent was not sought as no patient identifiable data are reported.

**Availability of data and materials:** The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

**Competing interest:** The authors declare that they have no conflict of interest.

**Author's contributions:** SA, SR, MJP, and DPI conceived and designed the study; SA, LR, SR and DPN collected and verified the data; SR and LR analysed the data. SA and SR drafted the manuscript, all authors contributed to and approved the final version of the manuscript.

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**Figure:** Systolic non-invasive blood pressure distributions of children in 2 PICUs. The blue line in the top left panel shows the 50$^{th}$ centile of 309520 systolic blood pressure measurements from 2415 boys according to age. The blue shaded area represents the area between the 5$^{th}$ and 95$^{th}$ centiles. The red lines show the population 5$^{th}$, 50$^{th}$ and 95$^{th}$ centile values for boys according to age, for the 50$^{th}$ centile for height (as described by the NIH Task Force, and Haque and Zaritsky). The green line in the top right panel shows the 50$^{th}$ centile of 251877 systolic blood pressure measurements from 1946 girls according to age. The green shaded area represents the area between the 5$^{th}$ and 95$^{th}$ centiles. The red lines show the population 5$^{th}$, 50$^{th}$ and 95$^{th}$ centile values for girls according to age, for the 50$^{th}$ centile for height (as described by the NIH Task Force, and Haque and Zaritsky).

The bottom panels show the 50$^{th}$ centile systolic blood pressure values for each age group following multi-level quantile regression, with 95% confidence intervals for boys (blue) and girls (green). Systolic blood pressure in our cohort is significantly higher than NIH Task Force 50th centiles in boys between 1 and 9 years and girls 2 and 8 years of age.

~~**Figure:** Systolic and mean non-invasive blood pressure distributions of children in 2 PICUs. The blue line in the top left panel shows the 50$^{th}$ centile of 309520 systolic blood pressure measurements from 2415 boys according to age. The blue shaded area represents the area between the 5$^{th}$ and 95$^{th}$ centiles. The red lines show the population 5$^{th}$, 50$^{th}$ and 95$^{th}$ centile values for boys according to age, for the 50$^{th}$ centile for height (as described by the NIH Task Force, and Haque and Zaritsky). The green line in the top right panel shows the 50$^{th}$ centile of 251877 systolic blood pressure measurements from 1946 girls according to age. The green shaded area represents the area between the 5$^{th}$ and 95$^{th}$ centiles. The red lines show the population 5$^{th}$, 50$^{th}$ and 95$^{th}$ centile values for girls according to age, for the 50$^{th}$ centile for height (as described by the NIH Task Force, and Haque and Zaritsky).~~

~~The bottom panels show the corresponding mean blood pressure distributions, based on 313492 measurements from 2413 boys (left), and 256662 measurements from 1944 girls (right). The red~~

~~lines show the population 5$^{th}$, 50$^{th}$ and 95$^{th}$ centile values according to age for 50$^{th}$ centile for height (as described by Haque and Zaritsky).~~