**Association of early childhood abdominal circumference and weight gain with blood pressure at 36 months of age: secondary analysis of data from a prospective cohort study**

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**Key words:** paediatrics, growth and development, blood pressure, body weight, abdominal circumference

**Abbreviations:** BMI: body mass index; CI: confidence interval; m: months, SWS: Southampton Women’s Survey

**Wordcoun**t: 3,044.

# ABSTRACT

**Objectives:** To assess if changes in measures of fat distribution and body size during early life are associated with blood pressure at 36 months of age.

**Design:** Analysis of data collected from a prospective cohort study.

**Setting:** Community-based investigation in Southampton, UK.

**Participants:** 761 children with valid blood pressure measurements, born to women participating in the Southampton Women's Survey.

**Primary and secondary outcome measures:** Anthropometric measurements were collected at 0, 6, 12, 24 and 36 months (mo) and conditional changes between the time-points calculated. Blood pressure was measured at 36 mo. Factors possibly influencing the blood pressure were assessed using linear regression. All independent variables of interest and confounding variables were included in stepwise multiple regression to identify the model that best predicted blood pressure at 36mo.

**Results:** Greater conditional gains in abdominal circumference (AC) between 0–6 and 24–36mo were associated with higher systolic and diastolic blood pressures at 36mo (P<0.001). Subscapular skinfold and height gains were weakly associated with higher blood pressures, while greater weight gains between 0–6, 12–24 and 24–36mo were more strongly associated, but the dominant influences were abdominal circumference gains, particularly from 0-6mo and 24-36mo. Thus one standard deviation score (SDS) increases in AC between 0-6mo and between 24–36mo were associated with 1.59 mmHg (95% CI: 0.97, 2.21) and 1.84 mmHg (1.24, 2.46) higher systolic blood pressures, respectively, and 1.04 mmHg (0.57, 1.51) and 1.02 mmHg (0.56, 1.48) higher diastolic pressures, respectively.

**Conclusions:** Conditional gains in abdominal circumference, particularly within six months of birth and in the year preceding measurement, were more positively associated with blood pressure at 36mo than gains in other anthropometric measures. Above-average abdominal circumference gains in early childhood may contribute to adult hypertension and increased cardiovascular disease risk.

**Strengths and Limitations of this Study**

* This is one of few studies that have investigated detailed anthropometric changes in relation to blood pressure in early age and examined conditional changes between different age-points.
* Key confounding risk factors were adjusted for in the models, including maternal education attainment and smoking during pregnancy.
* A large number of children from a cross-section of socioeconomic backgrounds were included in the study.
* We were not able to include all the children born in the course of the cohort study as blood pressure measurements were not available for all children, but the study sample was found to be similar to the larger group at 36 months of age.
* Abdominal girth at this young age may only represent a gross measure of central fat deposition and differences between individuals may represent genetically/prenatally-determined differences in physique.

# INTRODUCTION

Low birth weight and rapid postnatal weight gain have been linked to increased risk of cardiovascular disease,[1](#_ENREF_1) obesity, and the metabolic syndrome - including hypertension[2](#_ENREF_2) and insulin resistance[3](#_ENREF_3) - later in life. Accelerated weight gain, characterised by above-average velocities of skeletal and non-skeletal postnatal growth, has been associated with higher blood pressure in childhood.[4](#_ENREF_4) Low birth weight predicts blood pressure in later life,[5](#_ENREF_5) but it is not clear how much this association can be attributed to low birth weight independently of accelerated postnatal weight gain, as infants who are born small for gestational age tend to gain weight more rapidly during the early postnatal period.[6](#_ENREF_6)

It is thought that there may be critical periods at specific time-points early in life when accelerated growth predisposes to hypertension later in life.[7-10](#_ENREF_7) Furthermore, rapid increase in weight-for-length in the first 6 months has been associated with higher systolic blood pressure in 3-year-olds.[11](#_ENREF_11) Few studies have assessed indicators of body fat distribution in infants and young children. Body fat distribution has been associated with risk factor scores for cardiovascular risk in young children[12](#_ENREF_12) and postnatal rapid weight gain has been linked to deposition of fat centrally in children at 5 years.[6](#_ENREF_6)

Therefore, insight into whether postnatal alterations in body composition influence blood pressure in early childhood is relevant to the development of preventative strategies to reduce the risk of cardiovascular disease in later life. Our aim was to assess how gains in adiposity, fat distribution and body size between birth, 6, 12, 24 and 36 months relate to the blood pressure of children at 36 months.**METHODS**

## **Study sample: the Southampton Women’s Survey (SWS)**

 The SWS is a large prospective cohort study which commenced in 1998.[13](#_ENREF_13) A total of 12,583 non-pregnant women aged 20 to 34 years were recruited to the study. Detailed information on diet and socio-demographic factors was collected and children born to SWS women were assessed at birth and then followed up at home by trained research nurses. The SWS was approved by the Southampton and South West Hampshire Local Research Ethics Committee, and participants gave written informed consent. The research conformed to the principles embodied in the Declaration of Helsinki.

 There were 1,981 singleton live births to women in the SWS by the end of 2003. After exclusion of infants with major congenital abnormalities (n=2) and neonatal deaths (n=6), 1,973 SWS infants remained for postnatal follow-up.

## **Maternal and child data**

 When each child was 24 months old, the occupations of its mother and her partner were recorded and the highest-ranking of these used to define the child’s social class. The social class scale was: Professional (I), Management and technical (II), Skilled non-manual (IIIN), Skilled manual (IIIM), Partly skilled (IV), and Unskilled (V). For 10 children whose parental occupations were missing at this time, employment status recorded during early pregnancy was used. Educational attainment of the mother recorded before pregnancy was defined in six groups, from ‘none’ to ‘degree or above’.

## **Body composition and blood pressure assessment**

Anthropometric measurements were taken by trained researchers at birth, 6mo, 12mo, 24mo and 36mo. Apart from those at birth, all measurements were taken in the children’s homes. Infant crown-heel length was measured with a neonatometer (CMS Ltd, London, United Kingdom). Child height was measured with a portable stadiometer (Leicester height measurer; CMS Ltd). Skinfold thicknesses were measured using Holtain skinfold callipers (Holtain Ltd) at specified sites, and abdominal circumference measured at the end of expiration using a blank tape measured against a fixed scale. Strict monitoring of the nurses’ measurement techniques was performed by the senior research nurse and regular inter-observer variation studies were conducted.

Blood pressure was measured using a Critikon DINAMAP 1846 SX automated blood pressure device [14](#_ENREF_14) with the child seated. Three measurements were recorded and the average of the last two used in the analysis. Due to limited equipment availability, blood pressure measurements were only available for approximately 47% of the SWS children.

## **Statistical analysis**

 Regression coefficients (β), with associated 95 % confidence intervals (CI), were used to assess the strength of association between body size indicators (body weight, length/height, abdominal circumference and subscapular skinfold thickness). Z-scores were calculated for body weight and length/height using the 1990 British growth references for time points 6mo, 12mo, 24mo and 36mo.[15](#_ENREF_15) Z-scores for abdominal circumference and subscapular skinfolds were calculated internally using the SWS sample and were adjusted for gender, current age and gestational age. Conditional growth was derived from the residuals resulting from regression of the z-score for the measurement at a specific time point on the z-scores for measurements at all preceding ages. For example, the dependent variable ‘conditional gain in body weight from 12mo to 24mo’ was derived as the residual of the regression of body weight z-score at 24mo on the z-scores for body weight at 12mo, 6mo and birth.

 Factors reported to be associated with blood pressure were assessed using linear regression, including: age, social class, maternal education attainment, smoking in late pregnancy (an indicator of smoking throughout pregnancy) and crying of the child during blood pressure measurement. Factors that were univariately associated with blood pressure at age 36mo were retained for inclusion in regression models, namely crying, smoking and education.

 Multiple regression analysis was performed by entering all independent variables of interest into the model, in addition to the confounding variables. A stepwise multiple regression analysis was used to identify the growth variables that were most strongly associated with blood pressure at 36mo. Statistical analyses were performed using SPSS PASW Statistics Release 18 (IBM SPSS, IBM Corp, New York), and Stata 12.0 (StataCorp, Texas, USA).

# RESULTS

At 36mo of age, 1,640 children (83% of the 1,973 available for follow-up) were followed-up. Birth weights and 36mo blood pressure measurements were available for 773 infants. Seven children with missing height and weight data at age 36mo and five with systolic pressures more than 3 standard deviations from the mean were excluded, leaving 761 in the analysis. Children in this study were similar to the larger population sample of SWS children seen at 36mo (Table 1). Owing to a relative unavailability of blood pressure machines during later fieldwork, children included in the analyses were more likely to have been visited earlier in the study, and their mothers were slightly younger. Additionally, compared with those not included, those children in the study were marginally older (by approximately 1 week), and lighter and shorter at birth, and their mothers were of lower social class, had lower educational qualifications and were more likely to have been smoking in late pregnancy. The full ranges of social classes and educational levels were represented in the analysis sample, although the ‘Professional/Management & technical’ social class accounted for around 40% of the population, and just over half the mothers had completed higher school/post-school qualifications.

**Table 1.** Maternal and infant characteristics of the Southampton Women’s Survey study group

|  |  |  |
| --- | --- | --- |
|  | **With BP measurement (n=761)** | **Without BP measurement (n=879)** |
| **Mothers** | Mean | SD | Mean | SD |
| Maternal age at birth of the child\*\*\* | 29.7 | 3.7 | 30.6 | 3.8 |
| Pre-pregnancy weight (kg) | 67.3 | 13.9 | 68.3 | 13.9 |
| Height (cm)  | 163.0 | 6.5 | 163.4 | 6.3 |
| Maternal BMI (pre-pregnancy) (kg/m2) | 25.3 | 4.8 | 25.5 | 4.8 |
|  | Percent | Percent  |
| Smoking in pregnancy\*  | 16.2 |  | 12.2 |  |
| Social class  |  |  |  |  |
|  Professional/Management & technical (I/II) | 39.2 |  | 43.0 |  |
|  Skilled manual/non-manual (III) | 48.4 |  | 46.5 |  |
|  Partly skilled/unskilled (IV/V) | 12.4 |  | 10.6 |  |
| Educational attainment\*  |  |  |  |  |
|  Compulsory education to age 16 years | 44.9  |  | 39.0 |  |
|  Post compulsory education | 55.1 |  | 61.0 |  |
| **Infants** |  |  |  |  |
| Gender - male, n (%) | 397(52.2) | 473 (53.8) |
|  | Mean | SD | Mean | SD |
| Age in years at 36mo visit\*\*\* | 3.09 | 0.10 | 3.07 | 0.09 |
| Weight (kg) at 36mo visit | 15.0 | 1.9 | 15.1 | 1.8 |
| Height (cm) at 36mo visit | 95.7 | 3.7 | 96.0 | 3.6 |
| Abdominal circumference (cm) at 36mo visit | 51.2 | 3.2 | 51.3 | 3.1 |
| Subscapular skinfold (mm) at 36mo visit | 6.63 | 1.85 | 6.49 | 1.76 |
| Systolic blood pressure (mmHg) at 36mo visit | 93.8 | 8.3 |  |  |
| Diastolic blood pressure (mmHg) at 36mo visit | 58.1 | 6.3 |  |  |
| Birth weight (kg)\*\* | 3.42 | 0.57 | 3.50 | 0.52 |
| Birth length (cm)\* | 49.8 | 2.1 | 50.0 | 2.0 |

*BP: blood pressure, SD: standard deviation,BMI: body mass index*

\*P<0.05, \*\*P<0.01, \*\*\*P<0.001

The greatest relative and absolute increases in body weight, height/length, abdominal circumference and subscapular skinfold thickness occurred between birth and 6mo (Table 2), with the other age intervals (6-12mo, 12-24mo and 24-36mo) indicating smaller positive increments for body weight and height. Mean values of height and weight were comparable to the 50th percentile.[15](#_ENREF_15) For subscapular skinfold, average changes between later ages from 6m were negative, as was the average change in abdominal circumference between 24 and 36mo. During this final age period, abdominal circumference increased in 39% of children but decreased in 60%.

## **Confounding variables**

 Age, gender and social class were not associated with blood pressure, but the 45 infants who cried during measurement had higher systolic (P=0.004) and diastolic pressures (P=0.001). Smoking in late pregnancy was associated with higher systolic (P=0.067) and diastolic pressures (p=0.005). Lower educational attainment (P=0.024) was associated with higher diastolic pressure.

**Table 2.** Body composition at 0, 6, 12, 24, and 36 months and incremental changes

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Absolute change** | **% change1** |
|  | Mean | SD |  | Mean | SD | Mean | SD |
| N=712 |  |  |  |  |  |  |  |
| Birth weight (kg) | 3.4 | 0.6 | *Δ wt (kg): 0 - 36mo* | *11.6* | *1.8* | *349.7* | *92.7* |
| Weight (kg) 6mo | 7.9 | 1.0 | Δ wt (kg): 0 - 6mo | 4.4 | 0.9 | 134.4 | 43.6 |
| Weight (kg) 12mo | 10.0 | 1.2 | Δ wt (kg): 6 - 12mo | 2.1 | 0.6 | 27.2 | 8.2 |
| Weight (kg) 24mo | 12.5 | 1.5 | Δ wt (kg):12 - 24mo | 2.6 | 0.9 | 26.0 | 8.5 |
| Weight (kg) 36mo | 15.0 | 1.9 | Δ wt (kg): 24 - 36mo | 2.5 | 0.9 | 20.1 | 7.0 |
| N=666 |  |  |  |  |  |  |  |
| Birth length (cm) | 49.8 | 2.1 | *Δ ht (cm): 0 - 36mo* | *46* | *3.2* | *92.7* | *8.3* |
| Height (cm) 6mo | 67.2 | 2.5 | Δ ht (cm): 0 - 6mo | 17.4 | 2.1 | 35.1 | 5.0 |
| Height (cm) 12mo | 75.6 | 2.7 | Δ ht (cm): 6 - 12mo | 8.4 | 1.8 | 12.6 | 2.8 |
| Height (cm) 24mo | 86.3 | 3.1 | Δ ht (cm): 12 - 24mo | 10.8 | 1.9 | 14.3 | 2.5 |
| Height (cm) 36mo | 95.8 | 3.6 | Δ ht (cm): 24 - 36mo | 9.5 | 1.6 | 11.0 | 1.9 |
| N=682 |  |  |  |  |  |  |  |
| Abdominal circum.2(cm) 0mo | 31.5 | 2.2 | *Δ circum. (cm): 0 - 36mo* | *19.8* | *3.1* | *63.3* | *12.3* |
| Abdominal circum. (cm) 6mo | 47.4 | 3.2 | Δ circum. (cm): 0 - 6mo | 15.9 | 3.3 | 50.9 | 12.3 |
| Abdominal circum.(cm) 12mo | 49.6 | 3.2 | Δ circum. (cm): 6 -12mo | 2.2 | 2.6 | 4.7 | 5.7 |
| Abdominal circum. (cm) 24mo | 51.9 | 3.4 | Δ circum. (cm): 12 - 24mo | 2.3 | 2.9 | 4.8 | 6.0 |
| Abdominal circum.(cm) 36mo | 51.3 | 3.1 | Δ circum. (cm): 24 - 36mo | -0.6 | 2.5 | -1.0 | 4.7 |
| N=645 |  |  |  |  |  |  |  |
| Subscapular skinfold (mm) 0mo | 5.0 | 1.0 | *Δ subscap3.(mm): 0 - 36mo* | *1.7* | *1.9* | *37.2* | *42.4* |
| Subscapular skinfold (mm) 6mo | 7.4 | 1.6 | Δ subscap. (mm): 0 - 6mo | 2.4 | 1.7 | 52.7 | 41.7 |
| Subscapular skinfold (mm) 12mo | 7.2 | 1.6 | Δ subscap. (mm): 6- 12mo | -0.2 | 1.5 | -1.8 | 19.3 |
| Subscapular skinfold (mm) 24mo | 6.6 | 1.6 | Δ subscap. (mm): 12 -24mo | -0.6 | 1.4 | -7.3 | 19.3 |
| Subscapular skinfold (mm) 36mo | 6.7 | 1.9 | Δ subscap. (mm): 24 -36mo | 0.1 | 1.4 | 3.6 | 20.1 |

*SD: standard deviation*

1 calculated from previous time interval 2abdominal circumference 3subscapular skinfold thickness

## **Associations with blood pressure at 36 months**

 Initially, the four anthropometric measurements were considered separately (Table 3). Each model contained the measurement at birth and the conditional changes in the measure over the four age periods (0-6mo, 6-12mo, 12-24mo, and 24-36mo), along with the confounding factors that contributed significantly to the regression analysis; the slope represents the change in blood pressure (mmHg) per SD change in growth measurement. In all four models, the measurements at birth were not associated with blood pressure, independently of measurements of postnatal growth. The model for abdominal circumference explained more of the variance in blood pressure (8.8% and 7.7%, respectively, for systolic and diastolic blood pressure) (Figure 1) than the models for the other three measures, with the model for weight coming a close second (6.7% and 5.5% of the variance explained for systolic and diastolic blood pressure). The change in abdominal circumference closest to the blood pressure measurement, 24-36mo, was related most strongly to blood pressure (both systolic and diastolic), but change during the first six months of life was also significantly associated with both systolic and diastolic blood pressure. Weight change between birth and 6mo was related to blood pressure at 36mo, but weight change between 12 and 24mo also appeared to influence both systolic and diastolic blood pressure. Neither height nor subscapular skinfold thickness changes were related to blood pressure as strongly as abdominal circumference or weight changes, although for diastolic blood pressure there was a robust association with height change between 12 and 24mo. The effect sizes for the significant associations of body fat distribution and body weight were such that a 1 SDS increase in the measurement between the two ages under consideration was associated with an increase of around 1-2 mmHg in systolic blood pressure and approximately 1 mmHg in diastolic pressure

**Table 3.** Multiple regression models: associations between conditional gain (z-scores) in body composition measures and blood pressure1,2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Systolic Pressure** |  | **Diastolic Pressure** |  |
|  | Adj.R2 |  β 95% CI  | P- value | Adj.R2 |  β 95% CI | P-value |
| **Model 1 – Weight3 (N=684)** | 0.067 |   |   |   |   | .055 |   |   |   |   |
| Birth weight z-score |  | 0.22 | -0.45 | 0.89 | 0.5 |  | 0.12 | -0.38 | 0.62 | 0.6 |
| Weight: 0-6mo4 |  | 1.40 | 0.76 | 2.02 | <0.001 |  | 0.81 | 0.34 | 1.27 | 0.001 |
| Weight: 6-12mo4 |  | 0.51 | -0.09 | 1.12 | 0.1 |  | 0.36 | -0.09 | 0.82 | 0.1 |
| Weight: 12-24mo4 |  | 1.20 | 0.59 | 1.81 | <0.001 |  | 0.76 | 0.30 | 1.22 | 0.001 |
| Weight: 24-36mo4 |  | 1.07 | 0.46 | 1.67 | 0.001 |  | 0.44 | -0.01 | 0.89 | 0.06 |
| **Model 2 – Length/height3 (N=649)** | 0.027 |  |  |  |  | .038 |  |  |  |  |
| Birth length z-score |  | 0.41 | -0.36 | 1.18 | 0.3 |  | 0.08 | -0.49 | 0.65 | 0.8 |
| Height: 0-6mo4 |  | 0.91 | 0.27 | 1.54 | 0.005 |  | 0.42 | -0.05 | 0.89 | 0.08 |
| Height: 6-12mo4 |  | 0.66 | 0.02 | 1.30 | 0.04 |  | 0.27 | -0.20 | 0.74 | 0.3 |
| Height: 12-24mo4 |  | 0.74 | 0.09 | 1.38 | 0.03 |  | 0.72 | 0.25 | 1.20 | 0.003 |
| Height: 24-36mo4 |  | 0.32 | -0.33 | 0.96 | 0.3 |  | 0.15 | -0.32 | 0.63 | 0.5 |
|  |  |  |  |  |  |  |  |  |  |  |
| **Model 3 – Abdominal circumference5 (N=664)** | .088 |  |  |  |  | .077 |  |  |  |  |
| Birth abdominal circumference z-score |  | 0.22 | -0.40 | 0.84 | 0.5 |  | -0.29 | -0.76 | 0.18 | 0.2 |
| Abdominal circumference4: 0-6mo |  | 1.59 | 0.97 | 2.21 | <0.001 |  | 1.04 | 0.57 | 1.51 | <0.001 |
| Abdominal circumference4: 6-12mo |  | -0.03 | -0.64 | 0.59 | 0.9 |  | -0.23 | -0.70 | 0.23 | 0.3 |
| Abdominal circumference4: 12-24mo |  | 0.58 | -0.03 | 1.19 | 0.06 |  | 0.46 | -0.005 | 0.92 | 0.053 |
| Abdominal circumference4: 24-36mo |  | 1.84 | 1.24 | 2.46 | <0.001 |  | 1.02 | 0.56 | 1.48 | <0.001 |
| **Model 4 – Subscapular skinfold thickness5 (N=630)** | 0.018 |  |  |  |  | .035 |  |  |  |  |
| Birth subscapular skinfold |  | -0.17 | -0.85 | 0.52 | 0.6 |  | -0.25 | -0.76 | 0.26 | 0.3 |
| Subscapular skinfold4: 0-6mo |  | 0.35 | -0.33 | 1.02 | 0.3 |  | 0.09 | -0.41 | 0.59 | 0.7 |
| Subscapular skinfold4: 6 - 12mo |  | 0.99 | 0.32 | 1.65 | 0.004 |  | 0.79 | 0.30 | 1.28 | 0.002 |
| Subscapular skinfold4: 12 - 24mo |  | 0.52 | -0.14 | 1.17 | 0.1 |  | 0.02 | -0.46 | 0.50 | 0.9 |
| Subscapular skinfold4: 24 - 36mo |   | 0.54 | -0.12 | 1.19 | 0.1 |   | 0.25 | -0.24 | 0.73 | 0.3 |

*CI: confidence interval*

1residuals derived from regression model with the specified z-score as the independent variable, 2all analyses adjusted for crying, maternal education and maternal smoking in late pregnancy, 3z-scores derived from percentile curve growth charts UK [15](#_ENREF_15), 4adjusted for measurements at all preceding time points, 5z-scores derived internally from Southampton Women’s Survey data.

The results of the final regression models are presented in Table 4. In the combined model, both abdominal circumference (0-6mo and 24-36 mo) and weight change (12-24mo) remained significantly associated with systolic blood pressure. The growth variables contributing to the final models were not highly correlated, with all correlations being less than 0.15. There was considerable variability in the gains of abdominal mass between 24 to 36mo, where 39% of children experienced an increase in abdominal circumference. Abdominal circumference change in the age period leading up to the blood pressure measurement was the key influence on blood pressure, with a 1 SDS change in the circumference being associated with a 1.66mmHg increase in systolic blood pressure. The final model for diastolic blood pressure was similar, with key associations being abdominal circumference change in the earliest and latest age periods (0-6mo and 24-36mo) with a 1 SD increase in abdominal circumference change associated with approximately 1 mmHg higher diastolic blood pressure. After the abdominal circumference changes were included in the model, changes in weight no longer appeared to influence blood pressure, but height change between 12 and 24mo was retained in the model. The addition of the variables ‘ever breast-fed’ or ‘duration of breast feeding’ to the final models did not affect the relationships between blood pressure and body composition measures.

**Table 4.** Multivariate regression model of best fit: conditional gain (z-scores) in body size and fat distribution associations with blood pressure at 36 months2

|  |  |  |
| --- | --- | --- |
|  **Systolic Pressure** |   |  |
|  N=650 | Adj.R2 |  β 95% CI  | P-value |
|  | .094 |  |  |  |  |
| Abdominal circumference3,4: 0-6mo |  | 1.52 | 0.07 | 1.71 | 0.04 |
| Abdominal circumference3,4: 24-36mo |  | 1.66 | 0.94 | 2.27 | <0.0001 |
| Weight: 12-24mo3,5 |  | 0.79 | 0.16 | 1.39 | 0.01 |
|  |  |  |  |  |  |
|  **Diastolic Pressure** |  |  |  |
|  N=625 | Adj.R2 |  β 95% CI | P-value |
|  | .076 |  |  |  |  |
| Abdominal circumference3,4: 0-6mo |  | 0.95 | 0.48 | 1.42 | <0.001 |
| Abdominal circumference3,4: 24-36mo |  | 0.94 | 0.46 | 1.43 | <0.001 |
| Height: 12-24mo3,5 |  | 0.60 | 0.12 | 1.08 | .015 |

*CI: confidence interval*

1residuals derived from regression model with the specified z-score as the independent variable, 2all analyses adjusted for crying, maternal education and maternal smoking in late pregnancy, 3adjusted for all the preceding time intervals (0-6mo, 6-12mo, 12-24mo, 24-36mo), 4Z-scores based on sample population data from Southampton Women’s Survey, 5z-scores derived from percentile curve growth charts UK [15](#_ENREF_15)

DISCUSSION

## **Main findings**

Our data indicate that conditional gains in abdominal circumference between birth and 6 months, as well as in the 12 months prior to blood pressure measurement, were associated with both systolic and diastolic blood pressure at 36 months of age. Changes in weight were also associated with blood pressure, particularly systolic pressure, but to a lesser extent. In the multivariate regression model, a one-SD gain in abdominal circumference z-score between 24 and 36mo was associated with a 1.66 mmHg increase in systolic blood and a one-SD increase between birth and 6mo with 1.56mmHg.

There was considerable variability in the gains of abdominal mass at the time interval most predictive of blood pressure (24 to 36mo), with 39% of children experiencing an increase, suggesting the impact of environmental factors. It is possible that dietary intake and/or physical activity levels during this early period could alter abdominal circumference gain early in life, or it may be related to differences in growth trajectories,[16](#_ENREF_16) which predict later obesity. Given that abdominal circumference in the majority of children decreases between the ages of 24 and 36mo, increases seen in this time period might be an early marker for problems in later life, particularly if the effect of abdominal circumference change on blood pressure amplifies with age.

It is of note that subscapular skinfold thickness change, an indicator of subcutaneous fat deposition, had much weaker associations with blood pressure than abdominal circumference, which is an indicator of abdominal or visceral fat deposition. The finding that abdominal circumference gain between 0-6mo was more strongly associated with blood pressure at age 36mo than gains during 6-12mo and 12-24mo could reflect the proposed critical period for childhood adiposity in the first two months of life,[17](#_ENREF_17) or could reflect gains in adiposity associated with an adverse intrauterine environment in late gestation.

## **Strengths and weaknesses**

 As summarised earlier, a strength of this study is the large sample size drawn from the general population. A post-hoc power calculation (n=650, with SD of 8mmHg for systolic pressure) indicated there was 80% power to detect a regression coefficient of 0.88mmHg per 1SD of an independent variable at 5% level of significance. Our study was thus sufficiently large to detect effect sizes of clinical relevance. In addition, we have assessed conditional growth, accounting for measurements at previous ages (thus ensuring independence of growth summaries between age periods), and have adjusted for relevant confounding factors.

Few studies have collected such detailed anthropometric measurements with the methodological rigor to provide indicators of fat distribution in the early postnatal period, encompassing the transition from milk-only to a mixed diet at the age of 36 months.

It is clear from the data that the strongest association with blood pressure from all the anthropometric measurements is the gain in abdominal circumference; however, we acknowledge that when building a multivariate regression model of best fit, there is an element of chance as to which variables are included, even when they are not highly correlated.

A limitation of the study is the inability to measure blood pressure in all children in the cohort, although there do not appear to be noteworthy differences between those who were measured and the remainder.

## **Comparison with other studies**

Central adiposity and a large waist circumference have been associated with higher blood pressure in adults, but there are few reports for children. In one study, children with accelerated weight gain in the first two years of life were fatter and had more central fat distribution at five years of age than other children.[6](#_ENREF_6) However, the relationship of central fat deposition specifically to blood pressure, which is only one component of the metabolic syndrome, is not clear in children. Rapid weight gain during infancy (0–6mo) but not during early childhood (3–6 years) was associated with a higher metabolic risk score at age 17 years, but the association between waist circumference and blood pressure was not statistically significant in that study.[18](#_ENREF_18) Waist-for-height ratio in school children has not been found to confer additional discriminative power to BMI in some studies,[19](#_ENREF_19), [20](#_ENREF_20) but recently weight and weight-for-height changes through infancy and childhood have been associated with blood pressure at age 10 years[21](#_ENREF_21) and at age 9.1 and 15.5 years.[22](#_ENREF_22) These studies did not consider the periods 0-6mo and 6-12mo separately, nor examine change in abdominal circumference. However, similar to both reports, we found that weight changes at ages closest to those at which the blood pressure measurement was made were most strongly associated.

There is considerable debate as to whether there are specific age-periods early in life during which weight gain and/or fat deposition are more influential in predicting cardiovascular risk. Our findings are similar to a report that weight gain between 24 and 36mo was positively associated with systolic blood pressure.[23](#_ENREF_23) The mean blood pressure values in our study of 94/58 mmHg are similar to those reported (92/58 mmHg),[23](#_ENREF_23) as are the correlations between systolic blood pressure and current weight and height at 36mo. Similarly, we also did not find an inverse association between birth weight and blood pressure. However, in contrast we found that conditional gains in body weight between all age periods were positively associated with systolic blood pressure and a similar trend for diastolic pressure, except for the period between 6 to 12mo. The differences in results may be related to our adjustment for all previous time intervals when we determined conditional growth.

Our data support a developmental contribution to the origin of elevated blood pressure in childhood, and therefore potentially in later adulthood. Indeed, we have previously demonstrated that higher fetal liver blood flow is strongly correlated with greater fat mass at birth and at 4 years, indicating that influences on body composition operate very early in life.[24](#_ENREF_24) Our data show that changes in abdominal circumference during the first six months and in the third year of life are associated with systolic and diastolic blood pressure. This suggests that the tracking of blood pressure, evident by later childhood, might be a consequence of under-supply of conditionally essential nutrients associated with elevated fetal liver blood flow and prioritisation of fat deposition in the infant.

It is not clear whether postnatal interventions would be effective in limiting growth in abdominal circumference, and any interventions to limit abdominal circumference gains would likely also reduce the rate of growth. However, there is accumulating evidence that accelerated early growth has long-term adverse physiological effects in later life, increasing cardiovascular risk factors, including high blood pressure.[25](#_ENREF_25) Promotion of lifestyle practices, such as exclusive breast feeding up to 6 months, later introduction of solid foods and maximising opportunities for safe physical activity, could contribute to a reduction in accelerated growth early in life and be one pathway that results in a reduction in cardiovascular disease later in life.

# Conclusion

We have demonstrated that although conditional gains in body weight and height during specific age periods are associated with systolic and diastolic blood pressure, as previously recognised, conditional gains in abdominal circumference (associated with central fat deposition) have the strongest association with blood pressure at 36 months of age. This is especially true for the first 6 months of life and between 24 and 36 months (i.e., the year prior to blood pressure measurement). Therefore, central deposition of fat in early childhood, indicated by abdominal circumference, may contribute to an increased risk of developing hypertension later in life. Follow-up blood pressure measurements for the study group may enable confirmation of this at a later date.

**Figure 1**

Association between change in abdominal circumference (residuals derived from regressing the z-score at each specific age on the z-score at all preceding ages, adjusted for crying and maternal educational attainment and smoking during pregnancy) as the independent variable and blood pressure at 36 months (mmHg). Z-scores are based on data from the Southampton Women’s Survey, adjusted for gender, current age and gestational age.

# Acknowledgements

The Southampton Women’s Survey Study Group includes Patsy Coakley, Vanessa Cox, Julia Hammond, Tina Horsfall and the Research Nurses who collected and processed the data for the Survey. The authors are very grateful to the families who participated in the research.

# Competing Interests

None

**Funding**

This work was supported by grants from the Medical Research Council, British Heart Foundation, Arthritis Research UK, National Institute for Health Research (NIHR) Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, and NIHR Musculoskeletal Biomedical Research Unit, University of Oxford. The work was also financially supported in part by the Commission of the European Community, specifically the RTD Programme "Quality of Life and Management of Living Resources", within the 7th Framework Programme, research grant no. FP7/2007-13 (Early Nutrition Project). This manuscript does not necessarily reflect the views of the funders and in no way anticipates the future policy in this area. KMG is supported by the National Institute for Health Research through the NIHR Southampton Biomedical Research Centre.

**Author contributions**

Caryl Nowson conceptualised the study, performed the analysis, contributed to the interpretation and drafted the initial manuscript. Sarah Crozier assisted with the analysis and contributed to the interpretation. **Siân Robinson contributed to interpretation. Keith Godfrey**, **Wendy Lawrence, Catherine Law and Cyrus Cooper reviewed and revised the manuscript. Hazel Inskip conceptualised the study and designed the analysis plan, performed analysis, contributed to the interpretation and revised the manuscript. All authors approved the final manuscript as submitted.**

**Data sharing**

**No additional data available.**

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