

Perinatal factors and respiratory health in children

B. K. Brew, G. B. Marks and for the CAPS (Childhood Asthma Prevention Study) Investigators

Woolcock Institute of Medical Research, The University of Sydney, Sydney, NSW, Australia

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Summary

Background There is conflicting evidence regarding the associations between anthropometric birth measures and asthma and lung function in children, particularly for apparently healthy infants born at term.

Objective Our objective was to elucidate these relationships paying particular attention to features of study design and analysis that may threaten the validity of previous studies in this field.

Methods We analysed data from a cohort of children with a family history of asthma who were recruited antenatally. Anthropometric birth measures and potential confounders were recorded at birth and within the first year of life. Lung function and asthma outcomes were measured at 8 years of age. Airway hyperresponsiveness (AHR) was measured by methacholine challenge. The potential for a reversal paradox, due to inclusion of covariates on the causal pathway, was investigated.

Results Four hundred and fifty (73% of the initial cohort) children were tested at age 8 years. Birth weight in the lowest tertile was associated with current asthma (OR 1.95, 95% CI 1.08, 3.54) and recent wheeze (OR 1.87, 95% CI 1.08, 3.24), but not with AHR (OR 1.37, 95% CI 0.68, 2.78). Birth weight was positively associated with lung function. Current height modified the relationship between birth length and lung function suggesting that post-natal growth has an effect on this relationship.

Conclusions Low birth weight is associated with a greater risk of current asthma and lower lung function at 8 years in children with a family history of asthma. Current height should be treated as an effect modifier when investigating the fetal origins hypothesis.

Keywords airway hyperresponsiveness, asthma, birth length, birth weight, lung function

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Correspondence:

Bronwyn K. Brew, Woolcock Institute of Medical Research, PO Box M77, Missenden Road PO, Sydney, NSW 2050, Australia. E-mail: bronwynbrew@woolcock.org.au

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Introduction

According to the 'fetal origins' hypothesis, programming during fetal development has long term effects on health outcomes including risk of diabetes, coronary heart disease and impaired lung function. One way to measure the quality of the fetal environment is to

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examine anthropometric birth measures, such as birth weight, length, head circumference and ponderal index (an infant measure related to BMI) [1]. Barker was the first to propose the fetal origins hypothesis to explain his observation that for every one pound increase in birth weight, lung function in adult men increased by 60 mL [2]. Several other studies, including a meta-analysis [3], have also found evidence of link between birth weight and adult lung function [4–7]. Prematurity and birth weight < 2.5 kg are both associated with impaired lung function during childhood [8,9], but evidence for a positive association between birth weight and lung function within the normal birth weight range is limited to two cross-sectional studies [10,11].

However, there are some serious limitations to the existing evidence in on the relation between

anthropometric measures at birth and later lung function. Both studies examining the effect of anthropometric measures at birth on subsequent lung function during childhood adjusted for confounding due to current height. There has been methodological criticism of this adjustment when testing the fetal origins hypothesis [12,13]. This is because current height (and weight) may be on the causal pathway between fetal origins, that is birth weight and length and the health outcomes in question. Including these terms as confounders, when they are in fact on the causal pathway, may lead to a bias known as 'reversal paradox' [12,13]. Hence, previous studies in this area may have been influenced by the reversal paradox. There is a need for further study to explore the impact of the reversal paradox on the apparent association between anthropometric measures at birth and subsequent lung function.

The fetal origins hypothesis has also been proposed as an explanation of associations between anthropometric measures at birth and subsequent asthma symptoms. Although there has been much research in this area, the results have been conflicting. Although some studies have found low birth weight to be a risk factor for asthma [14–16], others have found high birth weight to be a risk factor for asthma [17–20], and still others have found no association [10, 21–24]. Other anthropometric measures, such as birth length, head circumference and ponderal index, have also been shown to be risk factors for asthma in some studies [19, 23, 25], whereas other studies have found no association [21, 22, 24]. These conflicting findings may be due to heterogeneity in study design and implementation, including differences in outcome definitions, age at outcome assessment, study sizes and confounder assessment [26], or could indicate the presence of complex, non-linear associations that are not captured using simple linear statistical analyses. There is a lack of 'gold standard' criterion for asthma for use in epidemiological studies. Marks describes asthma 'as a syndrome comprised of common features that arises via a number of alternative pathways' [27]. A range of criteria have been used to identify asthma in epidemiological studies including; parental questionnaires recalling wheeze in the last 12 months, doctor's diagnoses, hospitalizations due to asthma and physiological measures such as airway hyperresponsiveness (AHR). Furthermore, it has been shown that varying the diagnostic criteria for asthma can change the association with the risk factor in question [28].

Most studies in this field are cross-sectional or historical cohorts. Although these studies have access to birth records for the main risk factor of interest, anthropometric measures at birth, the risk of bias arises in the measurement of birth-related potentially confounding factors, e.g. breast feeding and smoking

during pregnancy, at the time of outcome measurement there by introducing a substantial risk for recall bias.

The aim of this study is to investigate the association of anthropometric measures at birth with childhood lung function and asthma. In addressing this aim using data from a birth cohort study, we sought to overcome some of the methodological limitations of previous study in this field and to explore the impact of the reversal paradox and of various diagnostic criteria for asthma.

Methods

Study design

The Childhood Asthma Prevention Study (CAPS) is a randomized controlled trial designed to test the effectiveness of house dust mite avoidance and dietary fatty acid modification during the first 5 years of life as strategies for preventing asthma and allergy in high-risk children. The study design and outcomes have been previously reported [29–31]. In brief, 616 pregnant mothers and their unborn babies were recruited between September 1997 and November 1999 from two Sydney hospitals. The main eligibility criteria were that either parent or an older sibling had a history of asthma or recurrent wheeze, and that the child was born at > 36 weeks gestation. Six children who had been randomized were withdrawn for medical reasons immediately after birth. These reasons included the following: birth weight of < 2.5 kg; babies requiring major surgery or hospitalization for > 1 week; and babies with congenital malformations or other significant neonatal disease.

Data on the child's birth weight, birth length, head circumference, sex, and gestational age at birth and on the mother's parity and age were obtained from hospital records soon after delivery. Ponderal index was calculated as birth weight (g) multiplied by 100 and divided by length (cm) cubed. Ponderal index is a measure of body mass index used for infants. Information on parental education (both parents) and maternal smoking during pregnancy was obtained by interview during the antenatal period and information about infant feeding was recorded at age 1 month, 3 months and then at three monthly intervals during the first year of life.

At 5 and 8 years, the children attended appointments to test lung function, parents filled in symptom and environment questionnaires. Height and weight were measured using a stadiometer and bathroom scales, respectively.

Lung function

Spirometric function was measured before, and 10 min after, the administration of salbutamol 200 µg via a

large volume spacer using a Spirocard (QRS Diagnostic, LLC, Plymouth, MN, USA) device linked to a laptop computer. Pre- and post-bronchodilator spirometry and methacholine challenge tests were performed on separate days.

The procedure was performed with child standing, wearing a nose clip and in accordance with American Thoracic Society/European Respiratory Society recommendations[32] except that a 6 s expiratory time criterion was not applied. The child repeated the procedure until at least three acceptable flow volume loops had been recorded. If the best two acceptable values of FEV₁ (forced expiratory volume in 1 s) or the best two values of FVC (forced vital capacity) were more than 5% and more than 200 mL different then we asked the child to repeat the procedure up to two more times (until the best two were within this margin). Spirometry was reviewed *post-hoc* and curves that did not meet acceptability criteria were excluded. The highest values for FEV₁ and FVC from any of the acceptable curves were selected for analysis.

Airway hyperresponsiveness

AHR was measured at the 8-year clinical assessment. A methacholine inhalation challenge test was performed according to the rapid method [33]. Subjects with cumulative provoking dose for 20% fall in FEV₁ (PD₂₀FEV₁) < 7.98 µmol were classified as having AHR. Also, subjects who experienced > 10% fall in FEV₁ with normal saline alone were regarded as having deep inspiration-induced bronchoconstriction and were classified as having AHR. Finally, subjects who did not undertake a methacholine challenge, but who had a > 15% increase in FEV₁ after administration of bronchodilator were also classified as having AHR for this analysis.

Asthma

Asthma was defined based on data from the 8-year symptoms questionnaires given to parents. Recent wheeze was defined as any wheeze in the last 12 months. Current asthma was defined as wheeze in the last 12 months and a doctor's diagnosis of asthma. Poorly controlled asthma was defined as one or more of the following in the preceding 12 months: more than 12 attacks of wheezing, disturbed sleep caused by wheezing at least once per week, wheezing limiting the child's speech to only one or two words at a time between breaths, use of a bronchodilator for night-time waking or early morning chest tightness more than three times per week, or hospital emergency department visits or admissions for asthma.

Statistical analysis

The anthropometric measures at birth were classified into tertiles. Univariate associations with asthma outcomes were estimated using logistic regression with the middle tertile as the reference category. Univariate associations with asthma were also estimated using the anthropometric measures at birth as continuous predictor variables in the logistic regression model. Multivariate analyses were undertaken adjusting for the following potential confounders: gestational age, sex, maternal age, maternal asthma, any breastfeeding for at least 6 months, number of older siblings, parent's education level and maternal smoking during pregnancy.

Linear regression was used to determine the relationship of birth weight and birth length to pre- and post-bronchodilator spirometric function. Initially, a univariate relationship was assessed, then all confounders as listed above were included in the model. Non-linearity was tested for by including quadratic birth weight and birth length terms into each respective model, when these were found to be non-significant they were removed from the model. Following the suggested analysis method of Lucas et al. regarding reversal paradox, current height at 8 years was added separately to the model to determine the effect of current height on the relationship between anthropometric measures and lung function. In addition, we examined the interaction of current height with birth weight and birth length [12].

The study was approved by the Human Research Ethics Committees of the University of Sydney, the Children's Hospital at Westmead, and Western and South Western Sydney Area Health Services.

Results

Of the 616 participants recruited at birth, 64 withdrew from the study by 18 months, a further 58 withdrew by 8 years and a further 45 were not available for clinical assessment at 8 years. The final analyses at 8 years contained 449 (75%) of the original participants (Fig. 1).

Table 1 displays the birth characteristics of the study population and the prevalence of respiratory symptoms at age 8 years. Birth weight, birth length, head circumference and ponderal index were approximately normally distributed. The characteristics of the study population for this analysis do not differ to those of the original cohort except that the parents of those remaining in the study at 8 years had a higher education level.

The unadjusted associations of anthropometric measures at birth with asthma symptoms at 8 years are

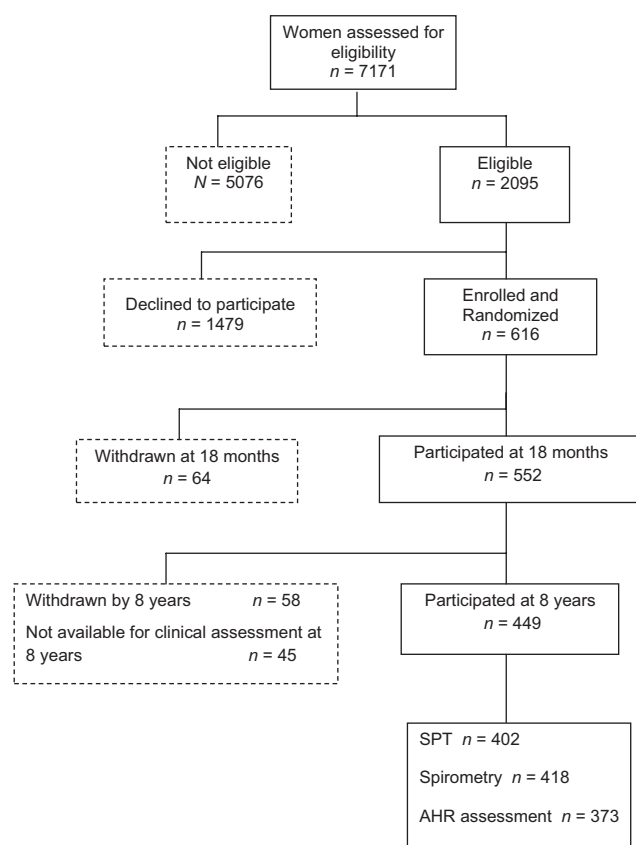


Fig. 1. Flow chart displaying the participation in CAPS from birth to 8 years.

shown in Table 2. Lower birth weight (≤ 3.27 kg) was associated with recent wheeze, current asthma and poorly controlled asthma, but not with AHR at 8 years. Adjustment for confounders (Table 3) made little difference to the estimates, but the association with poorly controlled asthma was no longer significant. For every 1 kg increase in birth weight, the adjusted odds of current asthma at 8 years decreased by 46% (Table 3).

There was a U-shaped relationship between birth length and AHR. Small (≤ 50 cm) and large (≥ 52.5 cm) birth length were both associated with a greater odds of having AHR at 8 years (Table 3).

Babies with large ponderal index were less likely to have current asthma at 8 years (Table 2), although the association was of borderline significance after adjusting for confounders. For every 100 g/cm³ increase in ponderal index, the odds of current asthma at 8 years decreased by 55% (Table 3).

There was a significant linear relation between birth weight and lung function. For every 1 kg increase in birth weight, the unadjusted pre- and post-bronchodilator FEV₁ and FVC at 8 years increased between 165 and 205 mL (Table 4). For every 1 cm increase in birth length, the pre- and post-bronchodilator FEV₁ and FVC

Table 1. General characteristics of the study population at 8 years ($n = 449$) compared with the original cohort at birth ($n = 616$)

Birth Characteristics	Mean $\pm$ SD or n (%) Study population	Mean $\pm$ SD or n (%) Original cohort
Birth weight, kg	3.5 $\pm$ 0.49	3.49 $\pm$ 0.49
Birth length, cm	51.03 $\pm$ 2.48	51.04 $\pm$ 2.45
Head circumference, cm	34.72 $\pm$ 1.5	34.71 $\pm$ 1.48
Ponderal index, g/cm ³	2.63 $\pm$ 0.31	2.63 $\pm$ 0.31
Gestational age, weeks	39.56 $\pm$ 1.27	39.57 $\pm$ 1.26
Age of mother, years	29.45 $\pm$ 5.04	28.97 $\pm$ 5.28
Sex, male	224 (49.9)	312 (50.7)
Mother has asthma	240 (53.5)	347 (56.3)
Parental Education		
Mother's education $\leq$ year 10	151 (33.6)	230 (37.3)
Father's education $\leq$ year 10	154 (34.7)	223 (36.7)
Mother smoked during pregnancy	108 (24.1)	150 (24.4)
Number of siblings		
0	151 (33.6)	199 (32.6)
1	156 (34.7)	214 (35)
2	89 (19.8)	129 (21.1)
≥ 3	53 (11.8)	69 (11.3)
Breastfeeding		
any ≥ 6 months	183 (40.8)	227 (39.1)
Status at 8 years		
Height at 8 years, cm	128.43 $\pm$ 5.7	
Recent wheeze	124 (27.6)	
Current asthma	98 (21.8)	
Poor asthma control	44 (9.8)	
Airway hyper-responsiveness	66/357* (18.5)	

*Where a denominator is shown this is the number of subjects for whom that outcome was measured.

at 8 years increased between 24 and 31 mL. When all potential confounders, other than current height, were added to the model these relationships did not substantially change. However, when current height at 8 years was added to the model it had a marked attenuating effect on these relationships. The relationships between birth weight, FVC and FEV₁ remained positive, although much smaller in magnitude. The relationships between birth length, FVC and FEV₁ were also attenuated and no longer significant. This implies that the relationship between birth length and lung function at 8 years is mediated by the relationship between birth length and current height.

Table 5 shows that the relationship between birth length, but not birth weight, and lung function at 8 years was modified by current height (Table 5). For each 1 cm increase in current height, the effect of birth length on pre-bronchodilator FVC increased by 1.9 mL/cm (95% CI 0.3, 3.4).

Table 2. Association between birth factors and respiratory outcomes at 8 years. crude odds ratios (OR) and 95% confidence intervals

Birth factor tertiles	<i>n</i>	Recent wheeze	Current asthma	Poorly controlled asthma	AHR
Birth weight (kg)					
(2.10–3.27)	150	1.76 (1.07, 2.91)**	1.92 (1.12, 3.31)**	2.44 (1.11, 5.35)**	1.42 (0.74, 2.75)
(3.28–3.70)	152	1	1	1	1
(3.71–5.00)	148	1.0 (0.59, 1.70)	1.03 (0.57, 1.86)	1.25 (0.52, 3.0)	1.12 (0.58, 2.18)
Birth weight (per 1 kg increase)		0.65 (0.42, 0.99)*	0.58 (0.36, 0.93)*	0.54 (0.28, 1.04)	0.75 (0.43, 1.32)
Birth length (cm)					
(44.5–50.0)	172	0.88 (0.54, 1.41)	0.87 (0.52, 1.45)	1.28 (0.62, 2.63)	1.95 (0.98, 3.91)
(50.2–52.0)	150	1	1	1	1
(52.5–59.0)	125	0.71 (0.42, 1.22)	0.69 (0.38, 1.24)	0.85 (0.36, 1.97)	1.94 (0.94, 4.0)
Birth length (per 1 cm increase)		0.96 (0.88, 1.05)	0.97 (0.88, 1.06)	0.93 (0.82, 1.06)	0.99 (0.89, 1.09)
Head circumference (cm)					
(29.5–34.1)	171	1.40 (0.86, 2.27)	1.66 (0.97, 2.84)	1.95 (0.91, 4.16)	1.02 (0.55, 1.90)
(34.2–35.6)	156	1	1	1	1
(35.7–39.0)	120	1.18 (0.69, 2.03)	1.39 (0.76, 2.52)	1.33 (0.56, 3.18)	0.93 (0.46, 1.85)
Head circumference (per 1 cm increase)		0.97 (0.84, 1.11)	0.94 (0.81, 1.09)	0.90 (0.74, 1.11)	0.94 (0.78, 1.13)
Ponderal index (100 g/cm ³)					
(1.68–2.53)	159	1.08 (0.66, 1.77)	1.00 (0.59, 1.68)	1.02 (0.49, 2.13)	1.02 (0.55, 1.90)
(2.54–2.76)	143	1	1	1	1
(2.77–3.68)	145	0.79 (0.47, 1.34)	0.53 (0.30, 0.96)*	0.77 (0.35, 1.71)	0.67 (0.34, 1.33)
Ponderal index (per 100 g/cm ³ increase)		0.63 (0.32, 1.23)	0.47 (0.23, 0.98)*	0.64 (0.24, 1.74)	0.66 (0.28, 1.56)

P* < 0.05, *P* < 0.01.Table 3. Association between birth weight, ponderal index and respiratory outcomes, eczema and atopy at 8 years. Adjusted[†] odds ratios (OR) and 95% confidence intervals

	<i>n</i>	Recent wheeze	Current asthma	Poorly controlled asthma	AHR
Birth weight (kg)					
(2.10–3.27)	150	1.87 (1.08, 3.24)**	1.95 (1.08, 3.54)*	2.23 (0.92, 5.43)	1.37 (0.68, 2.78)
(3.28–3.70)	152	1	1	1	1
(3.71–5.00)	148	0.96 (0.53, 1.72)	0.91 (0.48, 1.75)	1.15 (0.42, 3.18)	1.24 (0.59, 2.58)
Birth weight (per 1 kg increase)		0.63 (0.38, 1.05)	0.54 (0.31, 0.94)*	0.60 (0.27, 1.34)	0.83 (0.44, 1.57)
Birth length (cm)					
(44.5–50.0)	172	0.90 (0.54, 1.51)	0.90 (0.52, 1.58)	1.72 (0.73, 4.07)	2.04 (0.99, 4.21)
(50.2–52.0)	150	1	1	1	1
(52.5–59.0)	125	0.71 (0.4, 1.28)	0.73 (0.39, 1.38)	1.59 (0.59, 4.28)	2.49 (1.15, 5.40)**
Birth length (per 1 cm increase)		0.96 (0.88, 1.06)	0.98 (0.88, 1.08)	0.98 (0.84, 1.15)	1.01 (0.90, 1.13)
Head circumference (cm)					
(29.5–34.1)	171	1.38 (0.81, 2.33)	1.60 (0.90, 2.87)	1.62 (0.69, 3.84)	1.02 (0.52, 1.99)
(34.2–35.6)	156	1	1	1	1
(35.7–39.0)	120	1.02 (0.56, 1.84)	1.15 (0.60, 2.18)	1.28 (0.47, 3.46)	1.05 (0.50, 2.24)
Head circumference (per 1 cm increase)		0.95 (0.81, 1.11)	0.91 (0.77, 1.08)	0.93 (0.73, 1.20)	0.96 (0.78, 1.18)
Ponderal index (100 g/cm ³)					
(1.68–2.53)	159	1.12 (0.65, 1.91)	1.05 (0.59, 1.85)	1.13 (0.48, 2.65)	0.97 (0.50, 1.90)
(2.54–2.76)	143	1	1	1	1
(2.77–3.68)	145	0.85 (0.48, 1.51)	0.53 (0.28, 1.02)*	0.84 (0.32, 2.19)	0.68 (0.32, 1.41)
Ponderal index (per 100 g/cm ³ increase)		0.68 (0.33, 1.41)	0.45 (0.20, 1.01)*	0.53 (0.16, 1.71)	0.64 (0.26, 1.60)

[†]Adjusted for maternal asthma, sex, maternal age, breastfeeding for ≥ 6 months, mother's education, father's education, gestational age, parity and mother smoked in pregnancy.**P* < 0.05, ***P* < 0.01.

Table 4. Birth factors and lung function (forced vital capacity and forced expiratory volume in 1 s)

	Pre-bronchodilator FVC (mL)	Post-bronchodilator FVC (mL)	Pre-bronchodilator FEV1 (mL)	Post-bronchodilator FEV1 (mL)
Birth weight (per 1 kg increase)				
Unadjusted	205 (149,261)	195 (140,250)	174 (130, 218)	165 (119, 212)
Adjusted for all confounders [†]	221 (162, 281)	213 (155,271)	192 (143, 240)	183 (134, 233)
Adjusted for all [†] + current height	72 (25, 119)	52 (9,94)	71 (30, 111)	44 (6, 81)
Birth length (per 1 cm increase)				
Unadjusted	31 (20,42)	31 (20,42)	26 (17, 35)	24 (15, 34)
Adjusted for all confounders [†]	30 (19,42)	31 (20,42)	25 (16, 35)	25 (16, 34)
Adjusted for all [†] + current height	4 (-5,13)	4 (-3,12)	4 (-3, 12)	2 (-5,9)

[†]All confounders = maternal asthma, sex, maternal age, breastfeeding for ≥ 6 months, mother's education, father's education, gestational age, parity and mother smoked in pregnancy.

Table 5. Testing for effect modification by height at 8 years on the relationships between birth weight, birth length and lung function

	Effect estimates in mL (lung function)/cm (current height) (95% CI)			
	Pre FVC	Post FVC	Pre FEV1	Post FEV1
Birth weight (per 1 kg increase)	5.3 (-2.0, 12.6)	5.8 (-0.9, 12.6)	2.7 (-3.4, 8.8)	4.2 (-1.6, 10.1)
Birth length (per 1 cm increase)	1.9 (0.3, 3.4)*	2.2 (0.8, 3.6)**	1.0 (-0.3, 2.2)	1.4 (0.2, 2.6)*

* $P < 0.05$, ** $P < 0.01$.

Discussion

This study has shown, in a cohort of predominantly healthy infants born at term, those in the lower tertile of birth weights are at increased risk of subsequent asthma symptoms and diagnosis, but not of AHR, compared to others. Further, both birth length and birth weight are positively related to spirometric lung volumes at age 8 years, but this association is apparently mediated through the association with height at that age.

This study was conducted in a setting with a high prevalence of asthma, which increases the power the study, despite the relatively small sample size. However, the context of subjects with a family history of asthma needs to be considered in generalizing findings from this study. The birth cohort study design represents a further strength of this study. This enabled recording of information about potential confounders during the perinatal period, reducing the risk of recall bias and other measurement error. This is a definite advantage of this study design compared with cross-sectional and some historical cohort studies. The use of multiple measures of asthma status, including objective measures, such as AHR, is a further strength of the study design.

This study examined the association between birth weight and subsequent asthma using a variety of diagnostic or other criteria for asthma. We found significant associations of low birth weight with parent-reported wheeze, diagnosed current asthma and poorly controlled asthma (unadjusted). In addition, there were

negative linear associations between birth weight, ponderal index and current asthma. These findings are supported by a recent large historical cohort study in the UK [14] and two twin studies from Scandinavia [15, 34]. Furthermore, a study measuring fetal growth during the first and second trimesters found that persistent low fetal growth increased the risk of asthma at age 10 years [35]. However, other studies that have measured this relationship have found/not found any associations between birth weight and a range of markers for asthma including a history of hospitalization for asthma [36,37], self-report of recently diagnosed current asthma [20–22], ever diagnosed for asthma [20, 38] and AHR [38]. Hence, presence or absence of an association with 'asthma' may depend on how asthma is measured.

The current study also demonstrated the absence of an association between birth weight and AHR. AHR is physiological abnormality that is characteristic of established and persisting asthma [39–41]. We have previously shown that in a cohort of 8–10 year olds, the presence of AHR a better predictor of asthma in early adulthood than the presence of symptoms of asthma [41]. Therefore, it is possible that the association between low birth weight and parent-reported wheeze and current asthma at age 8 years that we have observed in this cohort, is a relatively transient phenomenon and that, at older ages, this association will disappear. In the PIAMA birth cohort in which low birth weight was associated with increased respiratory symptoms from ages 2–6 years, the association with

symptoms had already disappeared by age 7 years [42]. The authors proposed that the respiratory symptoms could be a transitory phenomenon associated with airways that are small, relative to lung size, because of slower fetal growth and that this dysanapsis reduces with age and increased lung growth [43]. Furthermore, studies conducted among adults have failed to find an association between birth weight and asthma [7, 44]. Therefore, our study together with studies in children and adults are all consistent with a conclusion that anthropometric measures at birth predict early life wheezing illness rather than persistent asthma, although extent of persistence into mid-childhood differs between this study and the PIAMA study.

We have carefully assessed the role of current height in explaining the relation between anthropometric measures at birth and current lung function. To avoid the possibility of reversal paradox, we did not include height at 8 years as an initial confounder in measuring the relationships between birth weight, birth length and lung function. Current height cannot be considered to be a confounder of these relationships as it is associated with both birth length and lung function and is on the causative pathway between them. This is demonstrated clearly when height is added into the model analysing birth length and lung function, the relationship disappears, because birth length correlates with current height which in turn correlates with current lung function. This phenomenon also affects the relationship between birth weight and lung function at 8 years because birth weight and length are related. However, we did find that when height was added to the model between birth weight and lung function, the effect was reduced, but not completely, which suggests that there is some additional factor that determines the relationship between birth weight and lung function at 8 years.

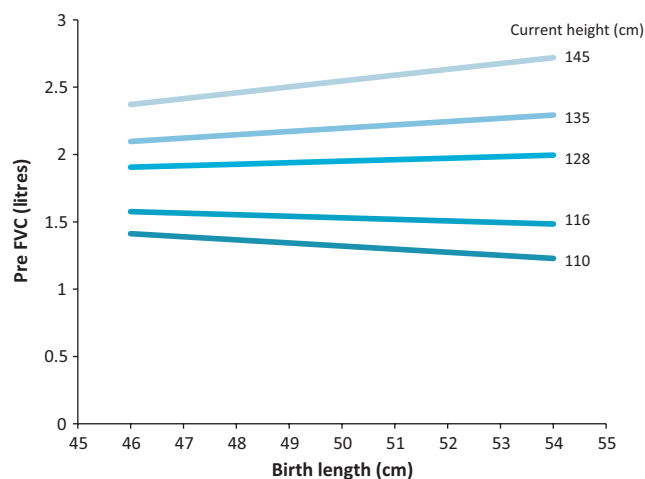


Fig. 2. Variation in the relationship between birth length and pre-bronchodilator FVC as a function of height at 8 years.

A positive association between birth weight and lung function has been found in other studies on children [10,11] and adults [4–6], although this is the first study to treat height as a separate entity in the model.

However, there is evidence that the relation among birth length, current height and current lung function is complex due to interaction between birth length and current height. Figures 2, 3 show a model of this effect modification from different perspectives. Figure 2 displays the association between birth length and FVC for different current heights. This demonstrates that effect of current height on lung function is greater in those with long birth length than those with short birth length. Figure 3 shows the association between current height and FVC for different birth lengths. This figure

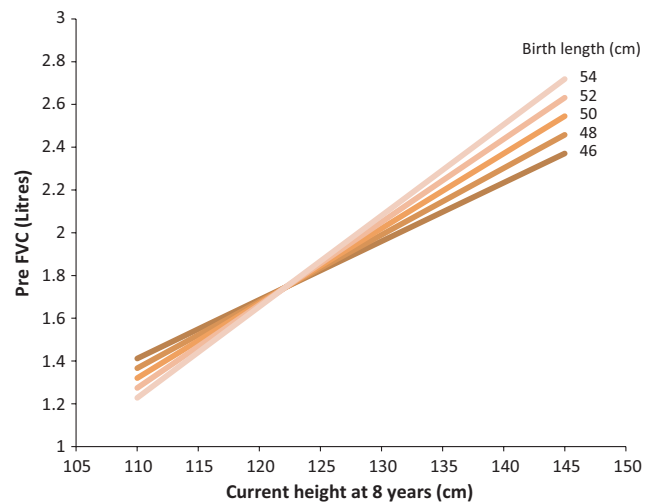


Fig. 3. Variation in the relationship between height at 8 years and pre-bronchodilator FVC as function of birth length.

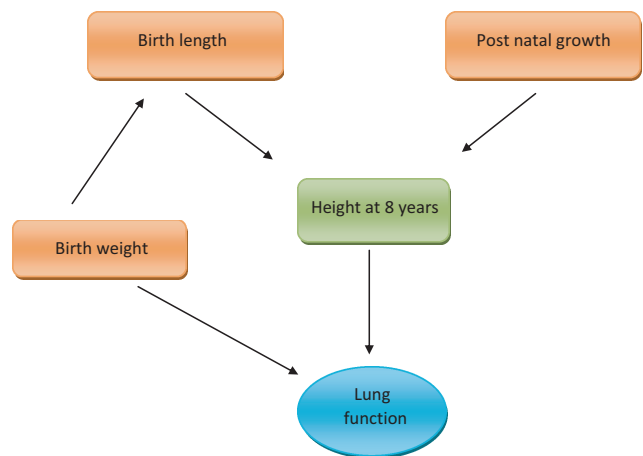


Fig. 4. A model demonstrating the effect of perinatal and post-natal growth on lung function at 8 years.

demonstrates that for those with a long birth length, there is a steep relation between current height and lung function, whereas for those with a short birth length, the relationship is less steep. A baby who is born long, but is short at age 8 years has the worse lung function than a child who is born short but is tall at age 8 years. This implies that slow post-natal growth has had an adverse effect on lung development. The baby born long who grows to be tall has the best possible lung function, consistent with favourable pre- and post-natal growth. Figure 4 outlines a model for the relation among birth weight, birth length, current height, post-natal growth and lung function at 8 years.

Conclusions

In conclusion, our research has found that birth weight, birth length, post-natal growth and current height all

contribute in determining lung function in childhood. Although low birth weight is associated with parent-reported current asthma and wheeze in children with a family history of asthma, the lack of association with AHR suggests that the birth weight may be a less important predictor in the longer term.

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