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Geographical variation in relationships between parental body size and offspring phenotype at birth

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Abstract

Background—Size and body proportions at birth are partly determined by maternal body composition, but most studies of mother-baby relationships have only considered the effects of maternal height and weight on offspring birthweight, and few have examined the size of effects. Paternal size and body composition also play a role, primarily through the fetal genome, although few studies have investigated relationships with neonatal phenotype.

Methods—Data from the UK, Finland, India, Sri Lanka, China, DR Congo, Nigeria and Jamaica were used to investigate the effects of maternal measures including estimates of muscle and fat (derived at 30-weeks gestation, N=16 418), and also paternal size (N=3 733) on neonatal phenotype, for singleton, liveborn, term births.

Results—After accounting for variation in maternal size and shape across populations, differences in neonatal phenotype were markedly reduced. Mother-baby relationships were similar across populations, although some were stronger in developing countries. Maternal height was generally the strongest predictor of neonatal length, maternal head circumference of neonatal head circumference, and maternal skinfold thickness of neonatal skinfolds. Relationships with maternal arm muscle area were generally weak. Data from fathers were limited to height and body mass

index, but when compared with maternal height and body mass index, paternal effects were weaker in most studies.

Conclusions—Differences in maternal body composition account for a large part of the geographical variation in neonatal phenotype. The size of the effects of all maternal measures on neonatal phenotype suggests that nutrition at every stage of the mother's life cycle may influence fetal growth. Further research is needed into father-baby relationships and the genetic mechanisms which influence fetal growth.

Keywords

Size at birth; maternal body composition; maternal birthweight; paternal size; worldwide variation

Introduction

Small body size and disproportion at birth is associated with increased morbidity in infancy and childhood, and susceptibility to coronary heart disease and associated disorders in later life (1). There are variations in neonatal phenotype around the world (see accompanying paper), and it is important to understand their determinants in order to develop strategies to optimise fetal growth. Maternal size and body composition influence neonatal phenotype (2), but most studies have only considered maternal height and weight, and their effects on offspring birthweight.

Mother-baby relationships may be a result of environmental factors, epigenetic influences and inherited genes, and from interactions between these. In contrast, father-baby relationships that are independent of maternal phenotype are likely to have a genetic basis. Some studies have assessed effects of paternal height and weight on offspring birthweight (3), but few have examined other birth measurements, or compared maternal and paternal influences.

Data from 18 studies around the world have been used (a) to assess the extent to which maternal size accounts for geographical differences in neonatal phenotype, in order to test the hypothesis that variations in maternal size account for a large proportion of these differences (b) to compare the effects of different components of maternal body composition on neonatal phenotype across and within populations, to test the hypothesis that specific components of maternal body composition relate consistently to specific components of neonatal body composition, and (c) to compare maternal and paternal effects on neonatal phenotype, to test the hypothesis that there are significant genetic effects on size at birth.

Materials and Methods

Studies

As many of the studies as possible from the accompanying paper were used for this analysis. These included the UK (Southampton (4-7), Farnborough (8), Isle of Man (9), Aberdeen (10)), Finland (Helsinki (11)), India (Mysore (12, 13), Pune (14, 15)), Sri Lanka (Kandy (16)), China (Beijing (17)), DR Congo (Kasaji (18)), Nigeria (Imesi (19)), and Jamaica (Kingston (20, 21)). Two studies (Preston and Sheffield) were excluded because only maternal pelvic dimensions were recorded.

The setting, years of birth and numbers used for this analysis for each of the studies are shown in Table I. Shaded rows refer to prospective studies (mothers recruited at or before delivery and babies measured as part of research studies of fetal growth) and non-shaded rows refer to retrospective studies (data abstracted from existing routine obstetric records) in

this and subsequent tables. Restriction was made to singleton, full-term, live-born babies, who were measured within seven days of birth. Further details of the original studies can be found in the accompanying paper.

Measurements

Neonatal anthropometry—Birthweight, placental weight, crown-heel (CH), crown-rump (CR) and leg length, head, chest and abdomen circumference, mid-upper-arm circumference (MUAC), arm muscle area (AMA), triceps and subscapular skinfolds were measured or derived in the neonates (see accompanying paper).

Maternal anthropometry—Height was generally measured without shoes using a stadiometer, but was self-reported in Southampton 4. Weight was measured using digital scales or beam balances. There may have been inconsistencies across studies with regard to clothes worn during measurement. Head, MUAC and skinfolds were measured using the same techniques as for neonates, with metal, steel or fibreglass tapes used for the circumferences. These measurements were made before pregnancy, and/or at various times during gestation. We selected 30-weeks gestation as the timepoint for which data were most complete. Measures at this time were derived using linear regression (for prospective studies with data collected at specific timepoints) or interpolation (for retrospective studies based on antenatal records); Table I shows when the measurements were taken in each study. Body mass index (BMI) was calculated as weight divided by height squared, and AMA was based on the standard formula (22), corrected for bone area (23). Maternal birthweight was available for six studies, although was self-reported in the four UK studies. It was not known whether the mothers were singleton or multiple births, and their gestational age was not available.

Paternal anthropometry—Where available, height was self-reported in the UK studies, and measured in India and Africa. Weight was only recorded outside the UK.

Gestation, parity and maternal age—Gestation was derived from the mother's reported last menstrual period, ultrasound scans or clinical examinations of the newborn; or clinical observation (Imesi only). Parity was recorded in all studies; in the Isle of Man and Aberdeen all mothers studied were primiparous. Maternal age was calculated from maternal and neonatal dates of birth, or taken as the age recorded closest to the delivery.

Statistical analysis

BMI (maternal and paternal), AMA and triceps had skewed distributions, so medians and inter-quartile ranges (IQRs) were used to describe all parental measurements. Spearman correlation coefficients were used to assess associations between maternal and paternal variables within each study.

The effects of sex, gestation, parity and maternal age on neonatal size were examined, and the linearity of the mother- and father-baby relationships checked using regression (comparing quadratic with linear, then if appropriate, linear with no relationships). Individual relationships between each maternal or paternal measurement and neonatal outcome were compared across studies, by testing whether a common regression slope for all studies could be used to summarise each relationship, or whether separate slopes were required for each study (F tests for inclusion of interactions between parental measures and study). Within each study, the effects of IQR increases in each maternal or paternal measurement on each neonatal measure were compared using regression models. This enabled comparison between parental measurements recorded in different units (e.g. maternal height and maternal skinfolds). Six combinations of measurements were used in

regression models as not all were recorded in every study; (a) maternal height and BMI (available in most studies), (b) maternal height, head circumference, AMA and triceps (separating the main components of BMI; skeleton, muscle and fat), (c) maternal height, AMA and triceps (both Kasaji and Kingston 2 included measures of muscle and fat but not head circumference), (d) maternal birthweight, height, head circumference, AMA and triceps (all the maternal components), (e) maternal and paternal height and BMI (the only paternal measures available), and (f) maternal and paternal height (paternal BMI was not available in the UK studies).

Within each study, regression models were used to calculate the percentage of variation in neonatal measures accounted for by parental variables. The extent to which geographical differences in neonatal phenotype were accounted for by differences in their parent's phenotype was examined using mean birth measurements in each study. These were compared, first without adjustment for the parental variables, and then using constrained linear regression to estimate what the values would have been if the parents were the same size in all studies.

All regression models were adjusted for sex and gestation where possible, and mother-baby analyses were repeated adjusting also for parity and maternal age. Studies may have included siblings, so not all parent-baby pairs were independent. In some studies it was not possible to identify siblings, but where it was possible, there were generally very few, and these tended to be part of the larger studies. The highest proportion of siblings (21%) was in Beijing; data from this study were analysed with and without accounting for the dependence between sibling pairs, and findings were almost identical. Where possible, effect sizes rather than p-values (reliant on sample sizes which varied widely across the studies) were used to interpret results. All analyses were undertaken in Stata version 7.0.

Results

Maternal and paternal size

Table II summarises maternal and paternal anthropometry within each study, and shows the IQR ranges across the studies. European and Jamaican mothers were the largest in most measures, while those from India and Sri Lanka were the smallest. Maternal birthweight was between 50 and 340g lower than that of the female offspring, depending on the study (data not shown). Fathers from the UK were the tallest; BMI was not available in these populations. Within India and Africa, those from Mysore and Imesi were taller and heavier than those from Pune and Kasaji. Correlations between maternal and paternal height ranged from 0.02 (Nigeria) to 0.28, and were highest in India (0.18 to 0.28). In the UK the correlations were between 0.03 and 0.12. BMI correlations ranged from 0.10 to 0.24 (not available in the UK). Maternal age, gestation, parity, and neonatal anthropometry within each study are shown in the accompanying paper.

Mother to baby relationships

All analyses are presented after adjusting for sex and gestation. Findings were similar if additional adjustment was made for parity and maternal age.

Comparison of mother-baby relationships across studies—The effects of each maternal measurement on each neonatal outcome were compared across studies (data not shown). The maternal variables had mainly positive effects on the neonatal measures, and these were often similar across the studies. The effects on neonatal outcomes were generally similar for maternal head circumference and skinfold thickness across the studies. However, there were stronger relationships with some of the neonatal measures for maternal height,

BMI (Figure 1) and birthweight in the developing countries, and for maternal AMA in Kasaji.

Comparison of components of maternal body composition effects on neonatal phenotype—IQR increases in all the maternal variables, particularly maternal birthweight in Mysore, had important effects on the neonatal measures. They were generally little changed by simultaneous adjustment for other maternal variables (Tables IIIa and IIIb for five of the neonatal outcomes). Within each study, the effects of an IQR increase in maternal height was similar to that of an IQR increase in BMI. Maternal height generally had the strongest effect on neonatal length, and maternal head on neonatal head circumference in all the studies. Maternal skinfold thickness was the strongest predictor of neonatal skinfolds in Mysore and Kasaji, but not Pune. Maternal arm muscle area effects were relatively weak, except in Kasaji. When maternal birthweight was also included in the model, it was among the strongest predictors of all neonatal measurements (Mysore 2 and Southampton 2 only).

Comparison of neonatal phenotype after adjusting for variations in maternal size—Each maternal variable accounted for between 2 and 15% of the variation in neonatal birthweight within studies (data not shown). Eight to 25% of the variation was explained by the combinations of the adult maternal variables, and if maternal birthweight was included, 12 and 45% of the variation was explained in Southampton 2 and Mysore 2 respectively. As described in the accompanying paper, UK neonates were largest for all measures, those in India, Sri Lanka and Africa smallest, and those in China and Jamaica similar to the overall means based on all studies for each neonatal measure (Table IV for five neonatal outcomes based on a selection of the studies). However, after adjustment for maternal height and BMI, these differences were substantially reduced. For example, birthweight differences from the overall mean were reduced by up to 200g in each study (Figure 2). Adjustment for the other sets of maternal measures did not further reduce these differences (data not shown).

Father to baby relationships

Paternal height and BMI were mainly positively related to the neonatal measures (data not shown). In contrast to mother-baby relationships, common slopes could adequately represent all relationships with paternal height, and most with paternal BMI. However, separate slopes were required for relationships between paternal BMI and neonatal birthweight, CH length, head and chest circumference, due to contrasting effects in the two African studies (stronger positive effects in Kasaji, negative but weaker effects in Imesi).

Comparison of parental effects

Table IIIc shows the simultaneous effects of maternal and paternal heights and BMIs (India and Africa), and maternal and paternal heights (UK, India and Africa), on five of the neonatal outcomes. Paternal effects were mainly weaker than maternal effects, although the differences were least for paternal height and neonatal skeletal measures.

Maternal and paternal height together accounted for between 3 and 12% of the variation in the neonatal birthweight within each study. If the BMIs of both parents were also included, explanation of variation increased to 10 - 22%. Adjusting for parental height substantially reduced differences in neonatal size between studies (Table IV, for five neonatal outcomes in a selection of studies). Additional adjustment for parental BMI also reduced differences in neonates, although these reductions appeared smaller than adjustment for maternal height and BMI alone as the UK studies could not be included in the analyses. If the same studies were included in each analysis, birthweight differences from the overall mean were reduced

by up to 60g after adjustment for maternal variables, 30g for paternal variables, and 70g for both.

Discussion

This study has demonstrated important relationships between anthropometric measures of parental size and newborn size, in a wide variety of populations. Strengths of the study are the synthesis of data from different geographical locations around the world, the use of methods that enabled comparison of effect sizes between different components of parental and neonatal body composition and between mother-baby and father-baby relationships, and the ability to take parity and gestational age at birth into account.

Differences in neonatal size between populations were considerably reduced after adjustment for maternal body composition. Other factors such as maternal diet, physical activity, smoking, alcohol consumption, illness and social class would vary across populations, and these along with genetic and epigenetic mechanisms are likely to be important sources of variation between populations. The absence of data on these factors in many of our studies, or the wide variety of methods used to collect such data, precluded adjustment for these. The variation in birthweight explained by social class was 0.1% in Pune, India, 1.7% in Southampton, UK, 4.9% in Kandy, Sri Lanka, and 11.3% in Kasaji, Congo. Knowledge of individual components of maternal body composition such as muscle and fat did not explain geographical differences any better than height and BMI alone. Crude measurements of soft tissue at only one site such as the arm, at one timepoint in late pregnancy, may not distinguish between populations as well as a measure of total mass such as BMI. Effects of adjusting for maternal body composition may be greater if more sophisticated measurements of muscle and fat were used, and if measurements before pregnancy or in early pregnancy, and *changes* in measurements during pregnancy, were available. Adjustment for paternal as well as maternal height and BMI reduced geographical differences in neonatal phenotype further, but the data did not allow adjustment for more detailed measurements of paternal body composition.

Within each study, all measures of maternal size and body composition were related to neonatal phenotype. Maternal birthweight was one of the strongest predictors of neonatal size in Mysore, India and, as previously described, in Southampton, UK (24), and showed independent associations with offspring birth length, head circumference and MUAC as well as with birthweight. Few other studies have examined the relationship of maternal birthweight to offspring neonatal measurements other than birthweight, but a study from Guatemala also showed significant associations between maternal birthweight and offspring birth length (25). In most of the populations in our study, the effects of maternal height were similar in magnitude to those of maternal BMI. Previous analyses have generally compared effects of maternal height and weight. In a meta-analysis based on 25 studies in both developed and developing countries, maternal weight, which is a summary measure of all aspects of maternal body composition, was found to be a stronger predictor of offspring birthweight than maternal height (2). Our data suggest that the mother's skeletal size and soft tissue mass have independent effects on birthweight.

As previously reported from the study in Pune, India, included in this analysis (15), the mother's adult measurements predicted 'like' measurements in the newborns. Thus maternal height was generally the strongest predictor of neonatal length, maternal head circumference of neonatal head circumference, and maternal skinfold thickness of neonatal skinfolds. Neggers et al. reported a similar phenomenon in US mothers and babies for height/length and skinfolds (26) and, although they did not compare effect sizes with other maternal measurements, others have described significant associations between maternal height and

newborn length (25), and maternal and neonatal skinfolds (27-31). Maternal head circumference has been measured in few studies, and relationships with neonatal head size have not been described previously. Except in one population (Kasaji, DR Congo), 'like with like' relationships were not seen for measures of maternal and neonatal muscle (MUAC and arm muscle area). This may be because MUAC is a difficult measurement in newborns, and the formula used to derive AMA in neonates does not correct for bone size. However, two previous studies, one from the USA and another from Peru, showed significant positive associations between maternal and neonatal MUAC or AMA (26, 29). The importance of maternal muscularity as a predictor of newborn size requires more research.

For some of the maternal measures, notably BMI, stronger effects on neonatal phenotype were seen in the developing countries. In a review of the literature, Ramakrishnan et al. (25) found maternal birthweight to have a stronger effect on neonatal birthweight in Guatemala than in any UK studies. They speculated that intergenerational effects may be greater in developing countries because women inherit inadequate environments across generations. Another possible environmental factor may be that the effects of the mother's own intra-uterine experience have permanent effects on her adult size, the development of her reproductive organs, or her hormonal and metabolic systems. It may also be that women in some developing countries inherit genes that are more similar across generations than in developed countries due to a higher frequency of consanguineous marriage.

Since the mother's birthweight reflects her own intra-uterine growth, and her height and head circumference reflect her infant and childhood growth, one interpretation of our findings is that the nutrition of a female throughout her life cycle, as well as during pregnancy, may influence the growth of her fetus. If so, our analysis indicates the effect on neonatal size in future generations that might be expected from changes in women's birthweight, height and BMI due to nutritional improvement. Increases of one IQR in maternal measurements were associated with increases of 10 to 250g in offspring birthweight. It could be argued that an IQR change is large and hence unlikely; however increases in height of up to 5 cm between generations have been recorded (32) (IQRs for height ranged from 7 to 10 cm in the populations included in this study) and could result in increases in birth size. Parental heights, and BMIs where available, were correlated in most of the populations studied, and most strongly in India. This is likely to reflect 'assortative mating' (non-random mating); height is one of the matching criteria often used in arranged marriages. Consistent with a number of other studies (mainly from developed countries and mostly limited to birthweight as the outcome) (33-36) the mother's adult measures generally had stronger effects on neonatal size than paternal measures. There were markedly fewer data from fathers, which limited the comparisons that could be made. Furthermore our analysis may have underestimated paternal effects as paternity was not confirmed in any of the studies. Maternal and paternal BMI measures were not strictly comparable as the maternal values were derived at 30-weeks gestation so included the weight of the fetus. In some studies maternal height was measured, while paternal height was reported. Stronger maternal effects would be expected, as the father's contribution to neonatal size is mainly genetic, while the mother contributes both genetic and environmental influences. Previous studies, based on correlations between the birthweights of siblings and half-siblings related through either the mother or the father (37), and on studies of pregnancies resulting from ovum donation (38) have suggested that the latter are predominant. However, a number of genetic mutations or polymorphisms have recently been described, which are associated with alterations in dimensions at birth (39-41).

As previously reported from one of the Southampton studies included in our analysis (24), differences between maternal and paternal effects were least for measurements of newborn skeletal size. While the associations of maternal BMI with birthweight were generally

stronger than those of paternal BMI, associations between paternal height and neonatal length and head circumference were comparable with and sometimes stronger than those of maternal height. In Southampton, because of a strong positive effect of paternal height on birth length but only a weak effect on birthweight, babies of taller fathers had a lower mean ponderal index at birth (24). The same study also showed that while maternal birthweight had a strong positive effect on neonatal ponderal index, paternal birthweight had a strong effect on newborn length. In another recent study from Mysore, not included in this analysis, paternal birthweight had an effect on birthweight similar to that of maternal birthweight, and paternal birth length was more strongly related than maternal birth length to offspring birth length (36). Taken together, these findings suggest strong genetic effects on size at birth, with stronger effects on skeletal measures at birth than on soft tissue components of neonatal body composition. However, the paucity of paternal data, and the small number of studies with detailed neonatal anthropometry limited the comparisons that could be made between maternal and paternal effects on neonatal measures of muscle and adipose tissue.

This study has shown that geographical differences in newborn phenotype can be accounted for by differences in maternal size and body composition to a large extent. Based on available data, maternal effects on neonatal size appear to be stronger than paternal effects. Future studies using better measurements of maternal body composition, such as DXA (dual x-ray absorptiometry) before pregnancy, and bioimpedance or isotope dilution both before and during pregnancy, would be informative. More importantly, a better understanding is required of the environmental and genetic mechanisms linking the mother's body composition to neonatal phenotype and both short and long term functional outcomes. Information on paternal and genetic influences on neonatal body composition is a glaring deficiency in the literature. Understanding these relationships is important for developing appropriate interventions to achieve the millennium development goal of improving maternal health by 2015 (42). In addition, caution is required when using fetal growth curves from another population in assessing ultrasound data; provision of local population data is therefore of great importance.

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Abbreviations

AMA	Arm muscle area
BMI	Body mass index
CH length	Crown-heel length
CR length	Crown-rump length

IQR	Inter-quartile range
MUAC	Mid-upper-arm circumference
DXA	Dual x-ray absorptiometry

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Figure 1.
Maternal 30-week BMI effect on neonatal birthweight, by study

Figure 2.
Study effects on neonatal birthweight, before and after adjusting for maternal height and 30-week BMI

Description of the 18 studies

Table 1

Study	Setting	Year of birth	Time of maternal measurement (weeks)	Number for mother-baby analyses	Number for father-baby analyses
Southampton 1	Princess Anne Maternity Hospital, Southampton, UK	1992-93	15-42 ^a	557	543
Southampton 2	Princess Anne Maternity Hospital, Southampton, UK	1994-96	28 ^a	521	511
Southampton 3	Princess Anne Maternity Hospital, Southampton, UK	1987	28-34 ^a	376	
Southampton 4	Princess Anne Maternity Hospital, Southampton, UK	1985	6-20 ^a	102	98
Farnborough	Farnborough Hospital, Farnborough, Kent, UK	1975-77	1-41 ^b	1677	
Isle of Man	Nobles Isle of Man Hospital, Isle of Man, UK	1991-92	1-36 ^a	388	385
Aberdeen	Aberdeen Maternity Hospital, Aberdeen, Scotland,	1948-54	17-36 ^b	233	
Helsinki	Helsinki University Central Hospital, Helsinki, Finland	1924-33	N/A	5979	
Mysore 1	Holdsworth Memorial Hospital, Mysore, South India	1938-95	9-41 ^b	1071	690
Mysore 2	Holdsworth Memorial Hospital, Mysore, South India	1997-98	28-32 ^a	597	496
Pune 1	6 rural villages, 50km from Pune, India	1994-96	28 ^a	633	599
Pune 2	King Edward Memorial Hospital, Pune, India	1998	N/A	258	
Kandy	Kandy Hospital, Kandy, Sri Lanka	1985	27-42 ^a	446	
Beijing	Peking Union Medical College Hospital, Beijing, China	1948-54	6-42 ^b	2421	
Kasaji	Kasaji Hospital, DR Congo, rural Central Africa	1995-98	17-37 ^b	338	217
Imesi	Imesi village, rural West Nigeria	1957-58	21-40 ^b	266	194
Kingston 1	University Hospital of the West Indies, Kingston, Jamaica	1993-96	21-33 ^a	489	
Kingston 2	University Hospital of the West Indies, Kingston, Jamaica	1979-81	29-31 ^a	66	
Total				16418	3733

^a30-week values derived using linear regression^b30-week values derived using interpolation

Table II
Median (IQR) maternal and paternal anthropometric measurements in each of the 18 studies

Study	Maternal			Paternal		
	Height cm	BMI ^b kg/m ²	Head cm	AMA ^b cm ²	Triceps ^b mm	Birthweight g
Southampton 1, UK	163(159,167)	26.5(24.2,29.5)	54.8(53.9,55.8)			3288(2948,3657) ^a
Southampton 2, UK	163(160,168)	26.8(24.5,30.2)	55.3(54.3,56.3)	32.1(27.9,37.2)	19.6(15.6,24.9)	3260(2910,3629) ^a
Southampton 3, UK	163(158,168)	26.8(24.4,30.1)				
Southampton 4, UK	165(160,168) ^a	24.5(22.1,27.5)				3303(2927,3629) ^a
Farnborough, UK	163(159,168)	24.7(23.0,26.6)				
Isle of Man, UK	163(159,167)	22.8(21.0,25.2)				3289(2948,3629) ^a
Aberdeen, UK	158(154,161)	24.8(23.0,26.5)				
Helsinki, Finland	158(154,162)					
Mysore 1, India	152(148,156)	21.4(19.7,23.3)				2720(2440,3008)
Mysore 2, India	155(151,158)	23.3(21.0,25.9)	53.5(52.4,54.5)	21.4(18.5,24.4)	16.8(12.3,24.4)	2807(2523,3033)
Pune 1, rural India	152(149,156)	20.3(19.2,21.5)	52.2(51.3,53.2)	24.2(21.0,26.7)	9.0(7.1,11.3)	165(161,169)
Pune 2, India	153(149,157)		53.6(51.9,55.0)			19.0(17.6,20.8)
Kandy, Sri Lanka	151(147,155)	20.0(18.7,22.2)				
Beijing, China	155(152,159)	23.6(22.0,25.2)				
Kasaji, rural DR Congo	154(151,159)	21.7(20.3,23.4)		24.8(21.9,28.5)	11.0(8.8,13.6)	164(160,169)
Imesi, rural Nigeria	160(155,163)	21.6(20.4,22.7)				170(165,173)
Kingston 1, Jamaica	164(159,167)	26.9(24.0,30.2)			17.4(13.0,22.8)	
Kingston 2, Jamaica	163(157,165)	24.1(22.6,27.0)		34.6(31.1,42.0)	10.2(8.6,14.2)	
Range of IQRs	7 to 10cm	2 to 6kg/m ²	2 to 3cm	6 to 11 cm ²	4 to 12mm	500 to 750g
						8 to 10cm
						2 to 5kg/m ²

^a Self-reported values

^b Derived at 30-weeks gestation

Table IIIa

Simultaneous effects of IQR increases in maternal height and BMI on five neonatal measurements Values are changes in neonatal measure per IQR increase in maternal variable in bold (95% confidence intervals)

	Maternal measures	Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
Southampton 1, UK	Height	127.2 (83.2, 171.2)	0.56 (0.40, 0.72)	0.24 (0.16, 0.40)	0.16 (0.08, 0.24)	
	BMI ^a	101.2 (56.7, 145.8)	0.32 (0.16, 0.48)	0.32 (0.16, 0.42)	0.21 (0.16, 0.32)	
Southampton 2, UK	Height	99.8 (56.3, 143.3)	0.60 (0.45, 0.83)	0.15 (0.08, 0.30)	0.08 (0.00, 0.15)	
	BMI ^a	112.3 (65.6, 159.6)	0.17 (-0.02, 0.34)	0.29 (0.17, 0.45)	0.23 (0.11, 0.34)	
Southampton 3, UK	Height	200.0 (132.0, 267.0)	1.00 (0.80, 1.30)	0.40 (0.20, 0.60)	0.20 (0.10, 0.40)	0.10 (-0.04, 0.30)
	BMI ^a	157.9 (99.1, 217.3)	0.39 (0.11, 0.62)	0.39 (0.22, 0.56)	0.22 (0.11, 0.39)	0.28 (0.11, 0.45)
Southampton 4, UK	Height	105.6 (0.8, 210.4)	0.40 (-0.16, 0.88)	0.16 (-0.08, 0.48)	0.08 (-0.16, 0.32)	
	BMI ^a	162.0 (44.8, 279.2)	0.11 (-0.43, 0.70)	0.49 (0.16, 0.76)	0.38 (0.16, 0.65)	
Farnborough, UK	Height	149.5 (120.2, 178.9)	0.71 (0.53, 0.89)	0.36 (0.27, 0.45)		
	BMI ^a	131.0 (108.0, 154.4)	0.50 (0.36, 0.65)	0.32 (0.25, 0.40)		
Isle of Man, UK	Height	154.7 (98.0, 212.2)	0.57 (0.41, 0.89)	0.24 (0.08, 0.41)		
	BMI ^a	63.0 (10.5, 115.9)	0.08 (-0.13, 0.29)	0.17 (0.02, 0.29)		
Aberdeen, UK	Height	104.1 (34.2, 173.3)				
	BMI ^a	121.0 (54.7, 187.0)				
Mysore 1, India	Height	225.6 (52.8, 398.4)	0.88 (-0.16, 2.00)	-0.56 (-1.68, 0.56)		
	BMI ^a	267.5 (104.8, 430.2)	1.91 (0.83, 3.02)	-0.32 (-1.55, 0.90)		
Mysore 2, India	Height	63.7 (25.2, 102.9)	0.42 (0.21, 0.56)	0.14 (0.03, 0.28)	0.07 (-0.02, 0.14)	0.07 (-0.07, 0.14)
	BMI ^a	209.2 (167.1, 251.4)	0.59 (0.34, 0.78)	0.49 (0.34, 0.64)	0.34 (0.25, 0.44)	0.34 (0.25, 0.44)
Pune 1, rural India	Height	71.4 (37.1, 106.4)	0.63 (0.42, 0.77)	0.14 (-0.01, 0.21)	0.14 (0.03, 0.21)	0.01 (-0.07, 0.07)
	BMI ^a	92.7 (61.0, 124.2)	0.23 (0.05, 0.39)	0.25 (0.16, 0.37)	0.14 (0.07, 0.23)	0.09 (0.01, 0.18)

	Maternal measures	Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
Kandy, Sri Lanka	Height	155.2 (101.6, 208.8)	1.28 (0.80, 1.76)	0.40 (0.08, 0.72)		
	BMI ^a	139.7 (82.1, 196.9)	0.72 (0.29, 1.19)	0.32 (0.01, 0.72)		
Beijing, China	Height	132.6 (108.8, 157.1)	0.61 (0.48, 0.75)	0.34 (0.20, 0.41)		
	BMI ^a	138.2 (113.9, 162.9)	0.48 (0.35, 0.61)	0.32 (0.22, 0.42)		
Kasaji, rural DR Congo	Height	145.1 (96.7, 193.4)	0.62 (0.39, 0.86)	0.16 (0.02, 0.31)	0.23 (0.08, 0.31)	0.08 (−0.04, 0.23)
	BMI ^a	152.8 (100.4, 205.2)	0.56 (0.31, 0.84)	0.40 (0.25, 0.56)	0.25 (0.12, 0.34)	0.19 (0.06, 0.31)
Imesi, rural Nigeria	Height	130.7 (69.9, 192.3)	0.61 (0.23, 0.99)	0.30 (0.03, 0.53)		
	BMI ^a	119.6 (61.0, 178.3)	0.28 (−0.07, 0.64)	0.30 (0.07, 0.55)		
Kingston 1, Jamaica	Height	88.8 (33.2, 143.6)	0.58 (0.25, 0.83)	0.17 (−0.02, 0.33)	0.08 (−0.08, 0.17)	
	BMI ^a	147.6 (92.7, 201.9)	0.61 (0.31, 0.98)	0.37 (0.18, 0.55)	0.31 (0.18, 0.43)	
Kingston 2, Jamaica	Height	189.6 (29.6, 349.6)	1.60 (0.24, 2.96)	0.64 (−0.16, 1.36)		
	BMI ^a	135.0 (−28.8, 299.3)	0.50 (−0.90, 1.89)	−0.09 (−0.86, 0.68)		

^aDerived at 30-weeks gestation

Table IIIb

Simultaneous effects of IQR increases in maternal height, head, AMA, triceps and birthweight on five neonatal measurements Values are changes in neonatal measure per IQR increase in maternal variable in bold (95% confidence intervals)

Maternal measures	Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
Southampton 2, UK	Height	0.59 (0.41, 0.75)	0.08 (-0.08, 0.23)	0.08 (-0.08, 0.15)	
	Head	0.10 (-0.12, 0.32)	0.24 (0.08, 0.38)	0.04 (-0.06, 0.16)	
	AMA ^a	-0.28 (-0.46, -0.09)	0.01 (-0.12, 0.14)	0.00 (-0.09, 0.09)	
	Triceps ^a	0.37 (0.19, 0.56)	0.19 (0.09, 0.37)	0.19 (0.09, 0.28)	
Mysore 2, India	Height	0.28 (0.05, 0.50)	0.01 (-0.14, 0.14)	0.00 (-0.07, 0.07)	0.02 (-0.07, 0.14)
	Head	0.13 (-0.15, 0.38)	0.27 (0.13, 0.44)	0.08 (-0.02, 0.19)	-0.04 (-0.15, 0.08)
	AMA ^a	0.12 (-0.12, 0.35)	0.18 (0.06, 0.30)	0.12 (0.01, 0.18)	0.12 (0.01, 0.18)
	Triceps ^a	0.37 (0.12, 0.61)	0.24 (0.12, 0.37)	0.24 (0.12, 0.37)	0.37 (0.24, 0.49)
Pune 1, India	Height	0.54 (0.34, 0.74)	0.03 (-0.07, 0.14)	0.07 (-0.03, 0.14)	-0.07 (-0.14, 0.07)
	Head	0.38 (0.19, 0.55)	0.30 (0.19, 0.38)	0.13 (0.06, 0.23)	0.10 (0.00, 0.17)
	AMA ^a	-0.17 (-0.34, 0.06)	-0.06 (-0.17, 0.06)	0.00 (-0.11, 0.11)	0.06 (-0.06, 0.17)
	Triceps ^a	-0.04 (-0.21, 0.13)	0.04 (-0.04, 0.17)	0.02 (-0.08, 0.08)	0.01 (-0.08, 0.08)
Southampton 2, UK	Height	0.60 (0.45, 0.83)	0.15 (0.02, 0.23)	0.08 (-0.03, 0.15)	
	AMA ^a	-0.28 (-0.46, -0.09)	0.04 (-0.09, 0.18)	0.01 (-0.09, 0.09)	
	Triceps ^a	0.37 (0.19, 0.56)	0.28 (0.09, 0.37)	0.19 (0.09, 0.28)	
Mysore 2, India	Height	0.35 (0.14, 0.56)	0.07 (-0.07, 0.21)	0.01 (-0.07, 0.14)	0.00 (-0.09, 0.10)
	AMA ^a	0.12 (-0.12, 0.30)	0.18 (0.06, 0.30)	0.12 (0.03, 0.18)	0.11 (0.02, 0.20)
	Triceps	0.37 (0.12, 0.61)	0.37 (0.12, 0.49)	0.24 (0.12, 0.37)	0.29 (0.18, 0.40)
Pune 1, rural India	Height	0.63 (0.42, 0.77)	0.07 (-0.07, 0.21)	0.07 (0.01, 0.21)	-0.02 (-0.11, 0.08)
	AMA ^a	-0.06 (-0.29, 0.11)	0.01 (-0.11, 0.11)	0.03 (-0.06, 0.11)	0.07 (-0.02, 0.16)
	Triceps ^a	-0.01 (-0.17, 0.17)	0.08 (-0.04, 0.21)	0.03 (-0.04, 0.13)	0.02 (-0.06, 0.10)
Kasaji, rural DR Congo	Height	0.70 (0.31, 1.01)	0.08 (-0.16, 0.31)	0.16 (-0.02, 0.23)	0.02 (-0.14, 0.17)

Maternal measures	Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
AMA ^a	106.9 (33.0, 180.2)	0.46 (0.13, 0.86)	0.33 (0.13, 0.59)	0.20 (0.03, 0.33)	0.03 (-0.14, 0.19)
Triceps ^a	69.6 (-0.5, 144.1)	0.20 (-0.20, 0.54)	0.05 (-0.20, 0.29)	0.05 (-0.10, 0.20)	0.06 (-0.11, 0.23)
Kingston 2, Jamaica					
Height	173.6 (2.4, 344.8)	1.44 (-0.08, 2.88)	0.56 (-0.24, 1.36)		
AMA ^a	42.5 (-135.2, 221.3)	0.33 (-1.31, 1.96)	-0.04 (-0.98, 0.87)		
Triceps ^a	127.1 (-63.3, 317.5)	0.28 (-1.46, 1.96)	0.01 (-0.95, 1.01)		
Southampton 2, UK					
Height	48.8 (-0.40, 97.5)	0.45 (0.30, 0.68)	-0.02 (-0.15, 0.15)	-0.02 (-0.08, 0.08)	
Head	23.0 (-32.8, 78.8)	0.04 (-0.20, 0.26)	0.22 (0.08, 0.38)	0.02 (-0.10, 0.14)	
AMA ^a	-11.0 (-59.8, 38.6)	-0.18 (-0.37, -0.01)	0.04 (-0.09, 0.18)	0.02 (-0.09, 0.09)	
Triceps ^a	103.2 (51.2, 155.3)	0.28 (0.09, 0.56)	0.19 (0.09, 0.37)	0.19 (0.09, 0.28)]	
Birthweight	96.7 (49.6, 143.9)	0.34 (0.14, 0.53)	0.14 (0.01, 0.26)	0.20 (0.11, 0.29)	
Mysore 2, India					
Height	-160.3 (-266.7, -53.2)	-0.14 (-0.77, 0.49)	0.01 (-0.28, 0.35)	-0.28 (-0.56, 0.02)	-0.42 (-0.84, 0.11)
Head	112.1 (7.1, 217.1)	0.32 (-0.29, 0.90)	0.40 (0.11, 0.71)	0.17 (-0.11, 0.44)	-0.10 (-0.45, 0.25)
AMA ^a	113.9 (-7.1, 235.4)	0.12 (-0.53, 0.83)	0.24 (-0.12, 0.65)	0.18 (-0.12, 0.53)	0.44 (-0.22, 1.10)
Triceps ^a	148.8 (25.6, 272.1)	0.37 (-0.24, 1.10)	0.37 (0.01, 0.73)	0.37 (0.01, 0.61)	2.20 (-0.06, 0.55)
Birthweight	253.8 (155.4, 352.2)	0.88 (0.32, 1.44)	0.54 (0.25, 0.83)	0.68 (0.43, 0.94)	0.43 (0.04, 0.84)

^aDerived at 30-weeks gestation

Table IIIc

Simultaneous effects of IQR increases in maternal and paternal height and BMI on five neonatal measurements Values are changes in neonatal measure per IQR increase in parental variable in bold (95% confidence intervals)

		Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
Mysore 2, India	Maternal height	41.7 (-3.0, 86.5)	0.29 (0.06, 0.52)	0.07 (-0.07, 0.22)	0.07 (-0.04, 0.17)	0.06 (-0.05, 0.17)
	Maternal BMI ^a	182.2 (136.0, 228.3)	0.50 (0.26, 0.75)	0.42 (0.27, 0.56)	0.34 (0.23, 0.44)	0.34 (0.23, 0.46)
	Paternal height	42.3 (-2.8, 87.3)	0.36 (0.13, 0.60)	0.09 (-0.05, 0.23)	0.04 (-0.07, 0.15)	0.01 (-0.10, 0.11)
	Paternal BMI	46.2 (-5.5, 97.8)	0.04 (-0.23, 0.31)	0.21 (0.04, 0.37)	0.12 (0.00, 0.24)	0.04 (-0.08, 0.16)
Pune 1, rural India	Maternal height	67.8 (31.5, 104.0)	0.53 (0.34, 0.73)	0.09 (-0.03, 0.22)	0.10 (0.01, 0.20)	0.01 (-0.09, 0.10)
	Maternal BMI ^a	84.7 (49.8, 119.6)	0.15 (-0.03, 0.34)	0.22 (0.10, 0.34)	0.12 (0.03, 0.21)	0.08 (-0.01, 0.17)
	Paternal height	19.1 (-13.8, 52.1)	0.31 (0.13, 0.49)	0.14 (0.03, 0.25)	0.09 (0.01, 0.18)	-0.03 (-0.11, 0.06)
	Paternal BMI	33.3 (1.2, 65.4)	0.11 (-0.07, 0.28)	0.04 (-0.06, 0.15)	0.07 (-0.01, 0.16)	0.04 (-0.05, 0.12)
Kasaji, rural DR Congo	Maternal height	114.0 (52.1, 175.9)	0.51 (0.22, 0.81)	0.12 (-0.07, 0.32)	0.14 (0.01, 0.27)	0.06 (-0.09, 0.22)
	Maternal BMI ^a	118.9 (54.7, 183.2)	0.56 (0.26, 0.86)	0.35 (0.15, 0.54)	0.17 (0.03, 0.31)	0.05 (-0.11, 0.22)
	Paternal height	45.4 (-23.4, 114.4)	0.14 (-0.19, 0.46)	0.11 (-0.09, 0.32)	0.11 (-0.04, 0.26)	0.04 (-0.13, 0.22)
	Paternal BMI	89.6 (33.6, 145.7)	0.36 (0.10, 0.63)	0.18 (0.01, 0.35)	0.26 (0.00, 0.24)	0.12 (-0.03, 0.26)
Imesi, rural Nigeria	Maternal height	83.9 (35.7, 132.0)	0.52 (0.28, 0.76)	0.22 (0.03, 0.41)		
	Maternal BMI ^a	112.8 (47.6, 178.0)	0.37 (0.05, 0.69)	0.43 (0.18, 0.68)		
	Paternal height	-13.5 (-80.8, 53.7)	0.17 (-0.17, 0.51)	0.04 (-0.23, 0.30)		
	Paternal BMI	5.8 (-67.3, 79.0)	-0.20 (-0.57, 0.16)	0.14 (-0.15, 0.43)		
Southampton 1, UK	Maternal height	119.9 (74.8, 165.0)	0.50 (0.31, 0.67)	0.24 (0.12, 0.35)	0.16 (0.06, 0.26)	
	Paternal height	40.0 (-10.5, 90.4)	0.38 (0.18, 0.59)	0.13 (0.00, 0.26)	-0.01 (-0.11, 0.10)	
Southampton 2, UK	Maternal height	56.9 (15.5, 98.2)	0.46 (0.29, 0.62)	0.11 (0.00, 0.22)	0.03 (-0.06, 0.11)	
	Paternal height	51.2 (1.9, 100.5)	0.40 (0.19, 0.60)	0.04 (-0.10, 0.17)	0.05 (-0.05, 0.15)	
Southampton 4, UK	Maternal height	111.9 (6.7, 217.1)	0.34 (-0.14, 0.82)	0.10 (-0.16, 0.38)	0.11 (-0.10, 0.33)	
	Paternal height	28.9 (-67.9, 125.7)	0.52 (0.08, 0.96)	0.02 (-0.22, 0.28)	0.01 (-0.19, 0.21)	
Isle of Man, UK	Maternal height	142.5 (81.6, 203.5)	0.58 (0.34, 0.83)	0.20 (0.04, 0.36)		

	Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
Paternal height	21.0 (-43.7, 85.5)	0.18 (-0.08, 0.44)	0.05 (-0.12, 0.21)		
Mysore 1, India					
Maternal height	73.0 (37.6, 108.4)	0.27 (0.01, 0.53)	0.10 (-0.04, 0.24)		
Paternal height	73.2 (32.2, 114.1)	0.20 (-0.10, 0.50)	0.14 (-0.03, 0.30)		
Mysore 2, India					
Maternal height	26.5 (-20.4, 73.4)	0.24 (0.01, 0.47)	0.05 (-0.10, 0.20)	0.04 (-0.06, 0.15)	0.02 (-0.08, 0.13)
Paternal height	46.1 (-2.0, 94.3)	0.37 (0.14, 0.62)	0.09 (-0.06, 0.24)	0.05 (-0.06, 0.15)	0.02 (-0.10, 0.13)
Pune 1, rural India					
Maternal height	65.2 (28.4, 101.9)	0.53 (0.34, 0.92)	0.08 (-0.04, 0.20)	0.11 (0.01, 0.20)	0.01 (-0.09, 0.10)
Paternal height	23.9 (-10.1, 58.0)	0.32 (0.14, 0.50)	0.16 (0.05, 0.27)	0.11 (0.02, 0.21)	-0.02 (-0.10, 0.06)
Kasaji, rural DR Congo					
Maternal height	135.0 (71.2, 198.7)	0.62 (0.32, 0.92)	0.17 (-0.02, 0.36)	0.17 (0.04, 0.30)	0.08 (-0.07, 0.24)
Paternal height	71.1 (-0.4, 142.5)	0.26 (-0.08, 0.59)	0.17 (-0.04, 0.38)	0.14 (0.00, 0.29)	0.07 (-0.10, 0.24)
Imesi, rural Nigeria					
Maternal height	136.5 (67.7, 205.3)	0.69 (0.34, 1.04)	0.20 (-0.08, 0.46)		
Paternal height	-13.6 (-74.1, 46.8)	0.24 (-0.08, 0.56)	0.05 (-0.20, 0.29)		

^aDerived at 30-weeks gestation

Table IV

Study differences from the overall mean for five neonatal measures, before and after adjusting for maternal and paternal height and BMI Values are regression coefficients for each study, unadjusted then adjusted for maternal and paternal height and BMI^a (adjusted in bold) Constants in models are constrained to equal mean neonatal values

	Overall means	Neonatal birthweight (g) 3140g	CH length (cm) 49.5cm	Neonatal head (cm) 33.8cm	Neonatal MUAC (cm) 10.7cm	Neonatal subscapular (mm) 4.4cm
Southampton 1, UK	Unadjusted	269.7	0.62	1.26	0.91	
	Adjusted ^b	141.1	0.12	0.97	0.72	
Mysore 2, India	Unadjusted	-180.9	-0.31	0.26	-0.29	0.17
	Adjusted ^b	-104.2	0.05	0.42	-0.22	0.21
Kandy, Sri Lanka	Unadjusted	-373.9	-1.23	-0.19		
	Adjusted ^b	-173.2	-0.34	0.29		
Beijing, China	Unadjusted	43.8	0.16	-1.76		
	Adjusted ^b	101.0	0.43	-1.64		
Kasaji, rural DR Congo	Unadjusted	-299.9	-1.64	0.27	-1.16	-0.55
	Adjusted ^b	-171.1	-1.12	0.56	-0.97	-0.41
Imesi, rural Nigeria	Unadjusted	-250.0	-1.69	0.19		
	Adjusted ^b	-179.9	-1.51	0.37		
Kingston 1, Jamaica	Unadjusted	94.5	0.45	0.81	-0.27	
	Adjusted ^b	-40.1	-0.08	0.50	-0.46	
Overall means		2843g	48.4cm	33.8cm	10.0cm	4.3cm
Mysore 2, India	Unadjusted	107.0	0.74	0.28	0.41	0.25
	Adjusted ^c	43.5	0.52	0.11	0.29	0.15
Kasaji, rural DR Congo	Unadjusted	21.9	-0.50	0.36	-0.42	-0.45
	Adjusted ^c	31.1	-0.41	0.39	-0.39	-0.43

Overall means		Neonatal birthweight (g)	CH length (cm)	Neonatal head (cm)	Neonatal MUAC (cm)	Neonatal subscapular (mm)
Imesi, rural Nigeria	Unadjusted	40.6	-0.88	0.19	10.7cm	4.4cm
	Adjusted ^c	-23.9	-1.23	0.06		
Overall means		3092g	49.1cm	34.4cm	10.7cm	4.3cm
Southampton 1, UK	Unadjusted	316.8	0.98	0.69	0.89	
	Adjusted ^d	229.7	0.45	0.55	0.78	
Mysore 2, India	Unadjusted	-141.4	0.03	-0.32	-0.31	0.25
	Adjusted ^d	-97.8	0.32	-0.26	-0.26	0.24
Kasaji, rural DR Congo	Unadjusted	-226.2	-1.20	-0.25	-1.13	-0.45
	Adjusted ^d	-172.0	-0.87	-0.15	-1.05	-0.45
Imesi, rural Nigeria	Unadjusted	-169.7	-1.40	-0.35		
	Adjusted ^d	-183.4	-1.45	-0.38		

^aMaternal BMI derived at 30-weeks gestation

^bAdjusted for maternal height and BMI

^cAdjusted for maternal and paternal height and BMI

^dAdjusted for maternal and paternal height