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ORIGINAL ARTICLE

Geographical variation in neonatal phenotype

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Abstract

Background. Recent studies have shown associations between size and body proportions at birth and health outcomes throughout the life cycle, but there are few data on how neonatal phenotype varies in different populations around the world. *Methods.* Data from the UK, Finland, India, Sri Lanka, China, DR Congo, Nigeria, and Jamaica ($n = 22{,}067$) were used to characterize geographical differences in phenotype in singleton, live-born newborns. Measurements included birth weight, placental weight, length, head, chest, abdominal and arm circumferences, and skinfolds. *Results.* Neonates in Europe were the largest, followed by Jamaica, East Asia (China), then Africa and South Asia. Birth weight varied widely (mean values 2,730–3,570 g), but in contrast, head circumference was similar in all except China (markedly smaller). The main difference in body proportions between populations was the head to length ratio, with small heads relative to length in China and large heads relative to length in South Asia and Africa. *Conclusions.* These marked geographical differences in neonatal phenotype need to be considered when investigating determinants of fetal growth, and optimal phenotype for short-term and long-term outcomes.

Key words: *Size at birth, body proportions, neonatal anthropometry, worldwide variation, fetal origins of adult disease*

Abbreviations: *AMA: arm muscle area, CH length: crown–heel length, CR length: crown–rump length, CV: coefficient of variation, IQR: interquartile range, LMP: last menstrual period, MUAC: mid–upper-arm circumference, PC: principal component, PCA: principal components analysis, SD: standard deviation*

There are associations between size at birth and both short- and long-term health outcomes. Small size at birth has been associated with increased morbidity in infancy and childhood, and susceptibility to coronary heart disease and associated disorders in later life (1). Body proportions at birth predict adult coronary heart disease, high blood pressure, glucose intolerance, and insulin resistance (1). These relationships vary across populations, for example in the UK and Finland a low ponderal index (birth weight/birth length^3) predicted an increased risk of developing adult type 2 diabetes (2,3), while the opposite was

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found in India (4). In order to interpret these differences, geographical variation in neonatal phenotype and the factors that determine it need to be understood.

Most published studies presenting data on birth size only include weight, which is a crude summary measure of size at birth. Anthropometric measurements can be used to assess some of the individual components of birth weight: skeletal size, muscle and adipose tissue mass, and the size of internal organs. Some studies provide data on length and head size at birth (UK (5), Canada (6), India (7), China (8), Japan (9) Ethiopia (10), and Zambia (11)), although they do not all present sex- and gestation-specific values. In older studies, the values given may be outdated, due to secular trends (12). To our knowledge, there is only one published study, based in Holland (13), that has presented comprehensive data, including standard deviation (SD) and percentile values for measures of neonatal muscle and fat in addition to weight, length, and head size. Published data on neonatal body proportions are even more sparse; Denham et al. (14) and Hindmarsh et al. (15) have characterized shape based on birth weight and measures of skeleton, muscle, and fat within the USA and UK respectively, but, up to now, no analyses of this type have compared shape across populations.

Thus 20 studies from a wide geographical range of populations with data on 22,067 births have been used to characterize differences in neonatal phenotype. They have been made as comparable as possible by restriction to singleton, live-born term births and adjusting for gestational age where recorded. Many of the studies include high-quality detailed measurements. Our primary hypothesis was that differences in neonatal phenotype across geographical populations exist, and our secondary hypothesis was that, within populations, phenotypes would be similar.

Materials and methods

Studies

Studies carried out by, or in collaboration with, the Medical Research Council Environmental Epidemiology Unit in Southampton were considered for inclusion. All studies based on normal populations that provided maternal (reported in accompanying paper) and neonatal anthropometric measurements were used. The studies selected included the UK (Southampton (16–19), Preston (20), Sheffield (21), Farnborough (22), Isle of Man (23), Aberdeen (24)), Finland (Helsinki (25)), India (Mysore (26,27), Pune (28,29)), Sri Lanka (Kandy (30)), China (Beijing (31)), DR Congo (Kasaji (32)), Nigeria (Imesi (33,34)), and Jamaica (Kingston (35,36)). Most of these had previously been used to investigate associations between size at birth and later disease; others studied size at birth as the outcome.

The setting and main characteristics of each of the studies are detailed in Table I. All were urban-based except Pune 1, Kasaji, and Imesi. Study designs were prospective (mothers recruited at or before delivery and babies measured as part of research studies of fetal growth, shaded rows in tables) or retrospective (data abstracted from existing routine obstetric records). Neonatal year of birth ranged from 1907 to 1998. All the prospective studies took place in the latter half of the 20th century, and covered relatively short periods, while retrospective studies were based on earlier years of birth, and covered longer periods.

The current analysis was restricted to singleton, full-term (at least 37 weeks) live-borns measured within seven days of birth. Neonates with gestational age greater than 44 weeks were excluded, as there were likely to have been errors in last menstrual period (LMP) dates. Large differences between numbers in the original study and the current analysis (Table I) are generally due to missing values for gestational age.

Measurements

Anthropometry. In prospective studies, anthropometric measurements were generally made by specially trained fieldworkers. Repeated measurements were often taken, and the mean value calculated to increase accuracy. For retrospective studies, measurements were made by midwives who had not received any specific training, and details of equipment and techniques were often unknown. Birth weight and placental weight were measured using digital scales or beam balances. In some studies, placentas were trimmed before weighing, removing the membranes and umbilical cord. In others, usually those based on obstetric records, placentas were weighed untrimmed, so 19% was subtracted from the weight of the placenta for comparability (37).

Crown–heel (CH) and crown–rump (CR) lengths were measured using a neonatal stadiometer, neonatometer, or rollameter in prospective studies. In those based on obstetric records, length was likely to have been measured by holding up the neonate and using a tape measure, which may lead to overestimation of values. Leg length was derived by subtracting CR length from CH length.

Table I. Description of the 20 studies

Study	Setting	Design	Year of birth	Number in original study	Number in current study[a]
Southampton 1	Princess Anne Maternity Hospital, Southampton, UK	Prospective	1992–93	596	557
Southampton 2	Princess Anne Maternity Hospital, Southampton, UK	Prospective	1994–96	562	521
Southampton 3	Princess Anne Maternity Hospital, Southampton, UK	Prospective	1987	390	377
Southampton 4	Princess Anne Maternity Hospital, Southampton, UK	Prospective	1985	102	102
Preston	Sharoe Green Hospital, Preston, UK	Retrospective	1935–43	1,298	1,014
Sheffield	Jessop Hospital for Women, Sheffield, UK	Retrospective	1907–30	8,577	4,418
Farnborough	Farnborough Hospital, Farnborough, Kent, UK	Prospective	1975–77	1,677	1,677
Isle of Man	Nobles Isle of Man Hospital, Isle of Man, UK	Prospective	1991–92	452	388
Aberdeen	Aberdeen Maternity Hospital, Aberdeen, Scotland	Retrospective	1948–54	260	233
Helsinki	Helsinki University Central Hospital, Helsinki, Finland	Retrospective	1924–33	7,088	5,989
Mysore 1	Holdsworth Memorial Hospital, Mysore, South India	Retrospective	1938–95	2,676	1,237
Mysore 2	Holdsworth Memorial Hospital, Mysore, South India	Prospective	1997–98	676	597
Pune 1	6 rural villages, 50km from Pune, India	Prospective	1994–96	773	633
Pune 2	King Edward Memorial Hospital, Pune, India	Prospective	1998	362	269
Kandy	Kandy Hospital, Kandy, Sri Lanka	Prospective	1985	506	455
Beijing	Peking Union Medical College Hospital, Beijing, China	Retrospective	1948–54	2,943	2,433
Kasaji	Kasaji Hospital, DR Congo, rural Central Africa	Prospective	1995–98	347	338
Imesi	Imesi village, rural West Nigeria	Prospective	1957–58	301	269
Kingston 1	University Hospital of the West Indies, Kingston, Jamaica	Prospective	1993–96	561	490
Kingston 2	University Hospital of the West Indies, Kingston, Jamaica	Prospective	1979–81	78	70
Total					22,067

[a]Live-born, singleton, term births, with anthropometry measured within seven days of birth.

Head circumference was taken as the maximum occipital–frontal circumference. Chest circumference was measured at the level of the nipple, while abdominal circumference was measured at the level of the xiphisternum. In Pune, because abdominal measurements were taken at the level of the umbilicus, they were adjusted to the xiphisternum using regression, based on a study of 50 neonates with measurements at both levels (29). Mid–upper-arm circumference (MUAC) was measured mid-way between the acromion and olecranon. For all circumferences, plastic, paper, or fiberglass tapes were used.

Triceps and subscapular skinfolds were measured using Harpenden or Holtain calipers. There is no universal measurement technique for skinfolds, and there were variations in the side of body used (this also applied to MUAC), the location of measurement point, picking up the skinfold, positioning the calipers, and timing of the reading. Arm muscle area (AMA) was calculated from MUAC and tricep measurements (38).

Sex, gestation, parity, and maternal age. The effect of the baby's sex, gestational age, mother's parity, and age at delivery on size and shape were also examined. Gestational age at delivery was calculated from the mother's LMP in most cases, although ultrasound scans were used if LMP was not recorded. In two studies, clinical examinations were used to determine gestation; in the Isle of Man Dubowitz scoring (39) was used if there was no other information, and in Kandy, where menstrual histories were unreliable, Narayanan scoring (40) was used. Gestation was not determined in Imesi, although midwives identified pre-terms based on physical appearance, and these were excluded. 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

All neonatal anthropometric variables were approximately normally distributed. For all analyses, the values were adjusted to 40 weeks' gestation (males and females separately) where possible, using linear regression. Gestation and maternal age had skewed distributions in some studies. Means and SDs are presented for the normally distributed variables, and medians and interquartile ranges (IQRs) for skewed variables. Coefficients of variation (CVs) were calculated to quantify the variation in neonatal anthropometric measurements across studies (SD of the study means/overall mean based on all studies).

Neonatal phenotype was characterized using principal components analysis (PCA) to generate new uncorrelated linear combinations (the principal components, PCs). The PCA was based on the

correlation matrix, using mean birth weight, CH length, and head circumference values from each study. In Aberdeen, length and head were not recorded, so this study was excluded from the PCA. All analyses were undertaken with Stata version 7.0.

Results

There were similar male:female ratios in all studies (Table II). In India and Africa, gestational duration was shorter, the proportion of first borns lower, and mothers were younger than the other populations, while the opposite was true in most of the UK studies (Table II).

Size of neonates

European neonates were generally the largest in all dimensions, followed by Jamaican, Chinese then African and South Asian neonates (Table III). The lowest birth weights (Figure 1a), placental weights, and abdominal circumferences were seen in Pune 1, the rural Indian population. African neonates were the shortest, and those in Kasaji had the smallest chest, muscle (MUAC and AMA), and fat (skinfold) measurements. There was wide variation in many of the measurements across the studies, as demonstrated by the CVs (Table III). The skeletal measurements varied least, head circumference in particular (Figure 1b), with the exception of China, where this measurement was markedly lower. Other characteristics seen in specific populations included relative adiposity in the Indian neonates; they were smaller in all dimensions than European neonates, but their subscapular skinfolds were similar. Also, the Chinese neonates had short legs but long bodies, while those from Mysore 2 had short bodies but long legs.

Shape of neonates

From the PCA (Table IV), the coefficients of the first PC were all positive and of a similar size, reflecting the overall size of the neonate. In the second PC, the coefficients for length and head circumference were of a similar size but the former had a negative sign, while the coefficient for birth weight was relatively small. This suggested that the main difference between populations was the contrast between length and head size. Relative to length, neonates had larger heads in India, Sri Lanka, and Africa, and to a lesser extent, Europe. Neonates in China had small heads in relation to length.

Placental weight was available in all studies except Kandy, and when this measure was added to the analysis with birth weight, CH length, and head, the first PC was a weighted average of all the variables, and the second was still a contrast between head and length, as the coefficient for placental weight was relatively small (Table IV). Therefore, knowledge of the placental weight did not aid distinction between

Table II. Sex, gestation, parity, and maternal age distributions in the 20 studies

	Sex	Gestation	Parity	Maternal age
Study	*n* (%) male	Median (IQR) days	*n* (%) first born	Median (IQR) years
Southampton 1, UK	296 (53.1)	282 (275, 288)	293 (52.6)	26 (23, 30)
Southampton 2, UK	263 (50.5)	282 (275, 287)	249 (47.8)	28 (24, 31)
Southampton 3, UK	190 (50.4)	281 (275, 286)	180 (47.8)	27 (23, 30)
Southampton 4, UK	46 (45.1)	279 (273, 287)	56 (54.9)	28 (24, 32)
Preston, UK	503 (49.6)	282 (275, 288)	824 (82.3)	25 (22, 29)
Sheffield, UK	2,284 (51.7)	281 (275, 288)	1,701 (39.1)	27 (23, 32)
Farnborough, UK	879 (52.4)	284 (277, 284)	778 (46.7)	28 (25, 30)
Isle of Man, UK	192 (49.5)	284 (278, 290)	338 (100.0)	26 (22, 29)
Aberdeen, UK	113 (48.5)	281 (274, 287)	233 (100.0)	23 (21, 25)
Helsinki, Finland	3,051 (50.9)	279 (273, 286)	2,567 (42.9)	27 (23, 31)
Mysore 1, India	651 (52.6)	279 (272, 283)	472 (38.2)	23 (20, 26)
Mysore 2, India	291 (48.7)	276 (270, 281)	300 (50.3)	24 (20, 26)
Pune 1, rural India	340 (53.7)	275 (270, 282)	195 (30.8)	21 (19, 23)
Pune 2, India	136 (50.6)	276 (270, 283)	48 (18.1)	25 (22, 28)
Kandy, Sri Lanka	232 (51.0)	284 (284, 286)	218 (47.9)	27 (23, 31)
Beijing, China	1,180 (48.5)	281 (274, 287)	1,165 (47.9)	27 (24, 32)
Kasaji, rural DR Congo	177 (52.4)	277 (271, 283)	95 (28.1)	23 (19, 29)
Imesi rural Nigeria	120 (44.6)		9 (3.8)	25 (20, 30)
Kingston 1, Jamaica	218 (44.5)	278 (271, 284)	239 (48.9)	26 (23, 30)
Kingston 2, Jamaica	36 (51.4)	279 (271, 284)	39 (55.7)	26 (20, 31)

Table III. Mean (SD) neonatal anthropometric measurements in each of the 20 studies

Study	Birth weight (g)	Placental weight (g)	CH length (cm)	CR length (cm)	Leg length (cm)	Head (cm)	Chest (cm)	Abdomen (cm)	MUAC (cm)	AMA (cm^2)	Triceps (mm)	Subscapular (mm)
Southampton 1, UK	3,413 (444)	532 (120)	50.1 (1.8)	33.3 (1.4)	16.8 (0.9)	35.1 (1.2)		33.6 (1.6)	11.6 (0.9)			
Southampton 2, UK	3,423 (420)	563 (127)	49.8 (1.8)	33.2 (1.3)	16.6 (0.8)	34.9 (1.2)		33.4 (1.5)	11.6 (0.8)			
Southampton 3, UK	3,472 (452)	518 (108)	49.7 (1.8)			35.2 (1.2)		33.5 (1.7)	11.5 (0.9)			4.8 (1.1)
Southampton 4, UK	3,568 (434)	529 (107)	50.5 (2.0)	34.0 (1.4)	16.5 (1.5)	35.3 (1.2)		34.4 (1.7)	11.5 (0.9)			
Preston, UK	3,179 (434)	486 (109)	51.6 (2.4)			34.7 (1.7)						
Sheffield, UK	3,294 (465)	502 (108)	51.2 (2.7)			34.7 (1.7)	33.0 (1.9)					
Farnborough, UK	3,322 (430)	506 (104)	50.7 (2.6)			34.6 (1.4)						
Isle of Man, UK	3,372 (447)	493 (101)	50.1 (1.8)			34.7 (1.2)		32.5 (1.6)				
Aberdeen, UK	3,224 (416)	529 (101)										
Helsinki, Finland	3,436 (458)	515 (100)	50.2 (1.7)			34.7 (1.3)						
Mysore 1, India	2,877 (426)	359 (68)	48.5 (3.0)			34.1 (1.7)						
Mysore 2, India	2,958 (413)	419 (86)	49.1 (2.1)	32.2 (1.7)	16.9 (1.4)	34.1 (1.3)		32.2 (1.7)	10.4 (0.9)	22.7 (1.9)	4.3 (0.9)	4.5 (0.9)
Pune 1, rural India	2,731 (334)	364 (76)	48.2 (1.8)			33.3 (1.1)	31.5 (1.6)	29.8 (1.8)	9.8 (0.8)	21.2 (1.9)	4.3 (0.8)	4.2 (0.8)
Pune 2, India	2,840 (392)	419 (96)	47.8 (2.1)			33.3 (1.3)	31.8 (1.9)	29.8 (2.4)	9.8 (0.8)	21.2 (1.8)	4.3 (0.8)	4.2 (0.7)
Kandy, Sri Lanka	2,761 (459)		48.2 (2.3)			33.6 (1.2)						
Beijing, China	3,156 (394)	431 (76)	49.5 (1.9)	33.6 (1.6)	15.9 (1.4)	32.0 (1.5)						
Kasaji, rural DR Congo	2,842 (394)	382 (77)	47.8 (1.9)			34.1 (1.2)	29.7 (1.8)		9.6 (0.8)	21.0 (1.6)	3.8 (0.8)	3.8 (0.9)
Imesi rural Nigeria	2,904 (397)	468 (98)	47.8 (2.3)			34.0 (1.5)	33.1 (1.9)					
Kingston 1, Jamaica	3,221 (438)	475 (102)	49.9 (2.6)	33.2 (2.0)	16.6 (1.6)	34.6 (1.4)	32.7 (1.8)	32.7 (1.7)	10.5 (0.9)			
Kingston 2, Jamaica	3,159 (526)	470 (96)	49.7 (3.9)	33.0 (3.0)	16.7 (2.8)	34.4 (2.0)						
Coefficient of variation	8.1%	12.6%	2.3%	1.7%	2.1%	2.3% 1.7%[a]	4.2%	4.7%	7.9%	3.8%	6.0%	8.7%

[a]Excluding China.

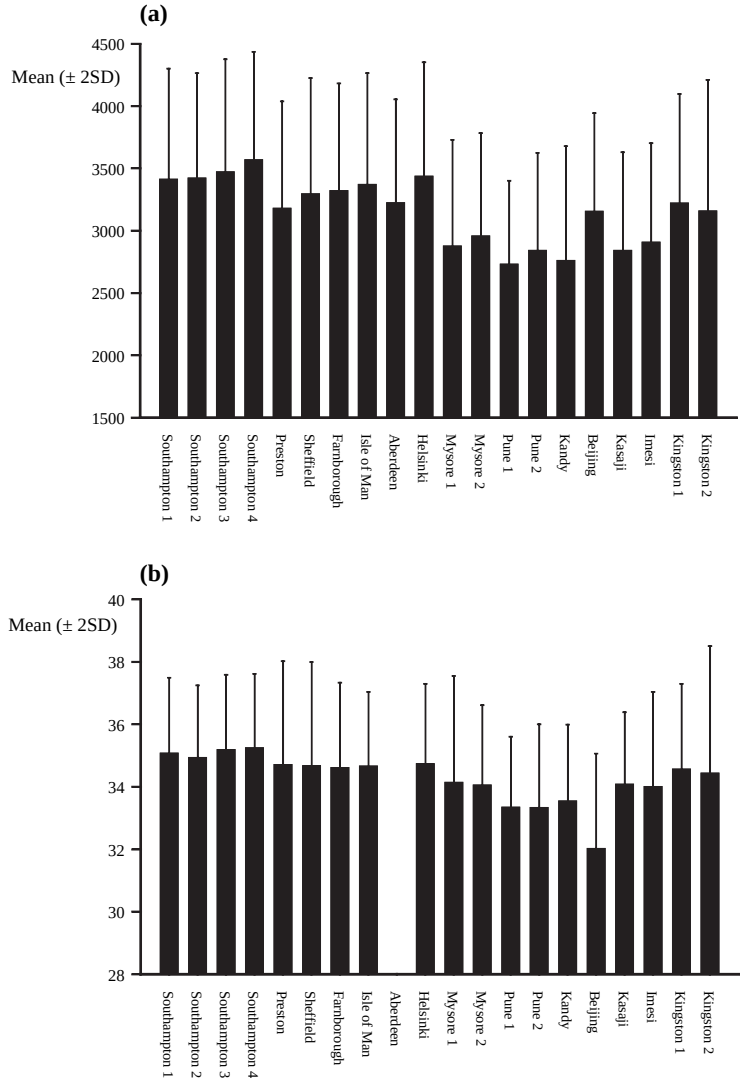

Figure 1. (a) Mean (±2SD) birth weight (g) by study. (b) Mean (±2SD) head circumference (cm) by study.

neonatal size and shape in different populations to a great extent. When MUAC and subscapular skinfold were added to birth weight, CH length, and head, this PCA yielded a second component that was a contrast between skeleton and fat (Table IV). However, these results must be interpreted with caution as they were based only on one Southampton, three Indian, and one African study.

In all studies, females were smaller than males, firstborns were smaller than subsequent births, and neonatal size increased as mothers became older. Despite these differences in overall size across the sex, parity, and maternal age subgroups, within each study neonates were a similar shape in each subgroup; e.g. females were smaller than males in China, but both had small heads in relation to length (data not shown).

Discussion

Apart from birth weight, geographical variation in neonatal size and body proportions has not been well documented. This analysis compared the size and shape of neonates across a number of geographical populations, and to our knowledge, no similar work has been presented before. The main differences between populations were overall size, head size (reduced in China compared to other populations), body fat (increased relative to other body measurements in India compared to other populations), components of length (short legs and long bodies in Beijing, China compared to long legs and short bodies in Mysore, India), and head to length ratio. As expected, within geographical regions, neonatal phenotypes were similar.

Table IV. Three principal components analyses based on mean values from each study

Measurement	PCA1[a]		PCA2[b]		PCA3[c]	
	PC1	PC2	PC1	PC2	PC1	PC2
Birth weight	0.61	−0.17	0.54	−0.17	0.51	−0.05
CH length	0.58	−0.57	0.48	−0.56	0.42	−0.43
Head	0.54	0.80	0.45	0.81	0.44	−0.39
Placenta			0.52	−0.02		
Subscapular					0.38	0.80
MUAC					0.48	0.15
Proportion of variance (%)	79	15	78	12	69	13

All neonatal measurements were standardized before PCA was performed.
Figures in bold show largest coefficients.
[a]All studies except Aberdeen.
[b]All studies except Aberdeen and Kandy.
[c]Southampton 3, Mysore 2, Pune 1, Pune 2, Kasaji.

Although there was generally the least variation in the skeletal measurements between populations, the neonates in Beijing had markedly reduced head size. This might have been due to measurement error as data were taken from obstetric records. However, in a WHO study based on seven populations, all of which used the same protocol, head size in China was smaller than in the other populations, which included India and Africa (data not shown) (41). In addition, Meredith (42) has shown neonatal head size in China to be among the smallest when compared to a number of other populations.

In the Indian neonates, who were among the smallest overall, fat was less reduced than other body measurements. This finding was based on three high-quality studies from Mysore and Pune, so seems to be a consistent phenomenon. Yajnik (43) proposed that this reflects a 'thrifty phenotype', whereby *in utero* Indian neonates have preserved fat at the expense of muscle. The subscapular skinfold, i.e. central fat was preserved more than the triceps skinfold, and this may be a feature of fetal growth restriction. Hediger et al. (44) and Yajnik et al. (29) also demonstrated relative fat preservation in small-for-gestational-age neonates in the USA and UK respectively.

There was a strong contrast between the length components of trunk and leg in Beijing and Mysore 2. The Chinese neonates had short legs and long bodies, while the Indian neonates had long legs and short bodies. There may have been measurement error in the Beijing data, as these were based on obstetric records, but the Mysore data were based on measurements made by trained observers. However, as no other studies from China or India have included measurement of the length components, it is not yet possible to confirm that these patterns are characteristic of these populations.

The main difference in neonatal shape between populations when considering only birth weight, length, and head circumference was in the head to length ratio. Neonates in India, Sri Lanka, and Africa had large heads compared to their length while those in China had relatively small heads. It might be argued that subjects may not have been representative of the population from which they were sampled. However, Pune 1 and Imesi, Nigeria were based on population samples. The other studies were of women giving birth in hospitals, and in countries where there are many hospitals available such as India, the choice of hospital may reflect a particular socioeconomic group. In some areas, hospital maternity attenders may represent a 'high-risk' subgroup, but in other areas such as Sri Lanka, hospital delivery is the norm for 80% of births. Also, in Kasaji, DR Congo for example, there was active community recruitment of everyone antenatally, and then personal encouragement to attend for delivery to help complete the study. In some of the Southampton and Jamaican studies, women were only included if they had booked early and/or known their menstrual dates. They may have been more motivated than the general population, or had a history of previous pregnancy or delivery complications. Not all studies used the same method of recording gestational duration, and although most used LMP, there are likely to have been differences in the women's abilities to report accurate dates across the studies. The year of birth ranged from 1907 to 1998 across the studies, and secular trends in height, and to a lesser extent weight, have been demonstrated over the last century (12). Although these are stronger in adults, they have also been observed at birth, which may affect the validity of comparisons made between studies undertaken many years apart. However, within studies, even those spanning wide

time periods, the effect of year of birth was minimal (−0.1 g (Aberdeen) to 10 g (Preston) per year for birth weight, considering studies spanning at least five years). In addition, this possible difficulty is countered by the geographic regions showing some striking similarities between studies undertaken years apart, and at the same time marked differences from other geographical regions. These also counter the known difficulties with comparing anthropometric measurements across studies due to use of different equipment and techniques, and in the degree of accuracy in recording. Further confidence in the findings can be drawn from the similar patterns seen across the sex, parity, and maternal age groups.

The reasons for geographical variation in neonatal phenotype are likely to be multiple, including effects of both inherited genes (i.e. genes selected for by environmental conditions in the past) and the current environment (the mother) on fetal gene expression. Genes likely to influence neonatal size and shape are those controlling fetal growth hormones (insulin and the insulin-like growth factors IGF-I and IGF-II). Environmental factors associated with fetal growth include any that influence the supply of nutrients to the fetus. The maternofetal supply line is complex, including the mother's dietary intake, metabolism, endocrine status, body composition, hemodynamic and vascular function, and the microstructure and function of the placenta (45). The mother's age and aspects of her lifestyle (smoking, alcohol intake, and psychosocial stress) can influence the supply line. Nutrient concentrations in the fetal circulation determine the secretion of insulin, IGFs, and other growth factors. In experimental animals, different nutrients have varying effects on the individual fetal growth factors (46,47), and these in turn promote the growth of different body tissues (48). Thus geographical differences in the maternal diet could theoretically translate into differences in body composition, although currently there are few data from humans, and these processes remain poorly understood. An additional environmental phenomenon influencing fetal growth is 'maternal constraint', whereby a small mother limits the size of her fetus (49). The mechanisms by which this occurs are unknown. Maternal size is a reflection of both her genotype and nutritional status during childhood and adolescence. Data on maternal size and body composition are available for many of the populations included in this analysis, and their effects on neonatal phenotype is the subject of the accompanying paper.

Different body proportions at birth in small babies may reflect the timing of environmental effects on fetal growth during gestation when growth became restricted. Different body tissues have their maximum growth rates at different gestational ages: head (and brain) growth is most rapid in early gestation, length growth in mid-gestation, and soft tissues (fat, muscle, abdominal viscera) in the last trimester. Chinese babies may grow slowly from early gestation (reflected in small head size) while Indian babies may grow rapidly in early gestation but be unable to sustain rapid growth in late gestation (reflected in larger head size but small abdominal circumference).

The relative fat preservation in Indian neonates may be an adaptation with some survival advantage (resistance to cold, substrate for brain growth and immunological responses (50), increasing the baby's 'visual appeal' encouraging adults to invest in its survival (51)). Alternatively, this phenotype may reflect inadequate nutrient supply, leading to deposition of fat rather than lean tissue (52).

In addition to our lack of knowledge about the causes of variability in neonatal size and shape, the 'optimal' neonatal phenotype for both short- and long-term outcomes, and how this varies between populations is not yet known. For example, it is likely that the optimal birth weight in terms of infant mortality in European countries is higher than in developing countries (53). Therefore, further studies investigating these issues are required to enable recommendations to be made to improve fetal growth in different populations. This is particularly important for developing appropriate interventions to achieve by 2015 the millennium development goal of reducing child mortality (of which neonates are a significant component) (54).

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