Babies of South Asian and European ancestry show similar associations with genetic risk score for birth weight despite the smaller size of South Asian newborns

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ABSTRACT

Size at birth is known to be influenced by various fetal and maternal factors including genetic effects. South Asians have a high burden of low birthweight and cardiometabolic diseases, yet studies of common genetic variations underpinning these phenotypes are lacking. We generated independent, weighted fetal genetic score (fGS) and maternal genetic score (mGS) from 196 birthweight-associated variants identified in Europeans and conducted association analysis with various fetal birth parameters and anthropometric and cardiometabolic traits measured at different follow-up stages (5-6 years' intervals) from seven Indian and Bangladeshi cohorts of South Asian ancestry. The results from above cohorts were compared with South Asians in UK BioBank and The Exeter Family Study of Childhood Health, a European ancestry cohort. Birthweight increased by 50.7g and 33.6g per standard deviation of fGS ($p = 9.1x10^{-11}$) and mGS ($p = 0.003$) respectively in South Asians. A relatively weaker maternal genetic score effect compared to Europeans indicates possible different intrauterine exposures between Europeans and South Asians. Birthweight was strongly associated with body size in both childhood and adolescence ($p = 3x10^{-5}$ - $1.9x10^{-51}$), however, fetal genetic score was associated with body size in childhood only ($p < 0.01$) and with head circumference, fasting glucose and triglycerides in adults ($p < 0.01$). The substantially smaller newborn size in South Asians with comparable fetal genetic effect to Europeans on birthweight suggests a significant role of factors related to fetal growth that were not captured by the present genetic scores. These factors may include different environmental exposures, maternal body size, health and nutritional status etc. Persistent influence of genetic loci on size at birth and adult metabolic syndrome in our study supports a common genetic mechanism partly explaining associations between early development and later cardiometabolic health in various populations, despite marked differences in phenotypic and environmental factors in South Asians.

Keywords

Birthweight, anthropometric traits, association, cardiometabolic risk, DOHaD, fetal genetic score, maternal genetic score, South Asian populations

Abbreviations

DOHaD	**D**evelopmental **O**rigins of **H**ealth **a**nd **D**isease
EAF	Effect allele frequency
EFSOCH	The **E**xeter **F**amily **S**tudy **o**f **C**hildhood **H**ealth
EGG	Early Growth Genetics
fGS	Fetal genetic score
GDM	Gestational diabetes mellitus
GIFTS	**G**enomic and l**I**festyle predictors of **F**etal ou**T**come**S**
GWASs	Genome-wide association studies
MBRC	Mysore Birth Records Cohort
mGS	Maternal genetic score
MMNP	Mumbai Maternal Nutritional Project
PMNS	Pune Maternal Nutrition Study
PS	Parthenon Study
SEM	Structural equation modelling
UK-Bang	London UK Bangladeshi cohort
UKBB	UK Biobank
UKBB-SAS	UK Bio Bank South Asian Subjects
WP2	GIFTS Work Package 2
WP3	GIFTS Work Package 3

INTRODUCTION

Size at birth is a summary measure for intrauterine nutrition, growth and development (1; 2). It is influenced by genetic and environmental factors, and in clinical practice helps predict neonatal wellbeing (3; 4). Several longitudinal population-based studies both in higher and lower-middle-income countries including India have demonstrated a correlation between birth size (both small and large) and future risk of cardiometabolic diseases (1; 2; 5-8). This led to the 'Fetal Programming' or Developmental Origins of Health and Disease (DOHaD) hypothesis which proposes that the intrauterine environment (meaning maternal diet, smoking, etc) drives fetal growth and also affects the development of metabolic organs, setting up later risk of disease (1; 2). Up to one third of South Asians living in the Indian sub-continent are born low birthweight (9). They also have a high prevalence of type 2 diabetes and cardiovascular diseases and develop these conditions at a younger age and a lower BMI than Europeans (10). Understanding the genetic determinants of neonatal size and their association with later phenotypes may provide important insights into mechanisms of how fetal growth and development relate to later risk of cardiometabolic diseases in various ancestral groups with different environmental exposures.

Large-scale genome-wide association studies (GWASs), mostly in individuals of European ancestry, including participants from the Early Growth Genetics (EGG) consortium and the UK Biobank (UKBB) have identified several genetic variants associated with birthweight (11-15). These genetic associations include (i) direct effects, where the fetus's own genotype influences its birthweight, (ii) indirect effects of the maternal genotype which influence birthweight via the intrauterine environment, and (iii) those which have a combination of direct fetal and indirect maternal effects (11; 15). A recent study in Europeans reported 209 conditionally independent GWAS significant genetic variants at 190 independent loci that were associated with birthweight and explained 7% of birthweight variance (fetal genotype 6%, maternal genotype 2%, and covariance -0.5%) further confirming the relatively weaker effect of maternal genetics than fetal genetics (15). It further partitioned the genetic effects on birthweight into fetal and maternal effects using structure equation model (SEM) and also demonstrated their association with various cardiometabolic traits. Genetic risk score is one of the approaches to summarise the genetic effects of multiple risk genes on a given trait such as birthweight. Based on the observations that fetal genetic score (fGS) for birthweight is negatively associated with adult BP, lipids, glucose and insulin levels, and insulin resistance, Warrington et al. concluded that common genetic variants contribute to the observed associations between lower birthweight and later cardiometabolic disease. This is something akin to the 'Fetal Insulin Hypothesis' first set out by Hatterseley et al. (16), which purports that the same genotype at a variant can influence birthweight and later cardiometabolic risk.

The dual burden of low birthweight and cardiometabolic diseases in South Asians and the fact that South Asians, especially those living in lower and middle income countries are not well represented in the majority of GWAS studies demands investigating genetic variants associated with fetal development, and how they relate to later cardiometabolic traits (17-19). Here, we studied associations of the weighted genetic scores with birth size in ~1900 mother-offspring pairs from South Asian birth cohorts in India, Bangladesh and UK. Association analysis was also conducted with body size and cardiometabolic traits among children, adolescents and adults using available follow-up data from Indian cohorts. Overall, the study has tried to answer two questions: (1) are fetal and maternal genetic scores related to newborn size in South Asians in the same way as in Europeans and (2) do the genetic scores related to birthweight influence cardiometabolic risk in a direction that would support a genetic contribution to the birthweight-cardiometabolic diseases link in the South Asian population?

RESEARCH DESIGN AND METHODS

Study participants

The participants in this study were mother-child pairs from different prospective birth cohort studies from India, Bangladesh and UK. The Indian cohorts comprise the Pune Maternal Nutrition Study (PMNS), Parthenon Study (PS), Mumbai Maternal Nutritional Project (MMNP) and Mysore Birth Records Cohort (MBRC). The individuals from PMNS and MMNP are Indo-Europeans, and those from the PS and MBRC are Dravidians, the two major ethnic populations in the Indian sub-continent (20; 21). Informed consent was obtained from all participants following the guidelines of Indian Council of Medical Research, Govt. of India, New Delhi. The Bangladeshi cohorts were from a sub-study of a prospective multi-center European Union FP7 project GIFTS (**G**enomic and l**I**festyle predictors of **F**etal ou**T**come relevant to diabetes and obesity and their relevance to prevention strategies in **S**outh Asian people) consisting of work package (WP2), work package (WP3) and London UK Bangladeshi cohort (UK-Bang) that was conducted following appropriate Institutional Review Board approval.

Pune Maternal Nutrition Study (PMNS)

The PMNS cohort, based in six rural villages near Pune in Western India, was established in 1993 to examine the relationship of maternal health and nutrition during pregnancy to fetal growth and development, and future cardiometabolic risk (22). Women were recruited pre-conceptionally. A 75gm oral glucose tolerance test was carried out at 28 weeks' gestation in pregnancy and GDM was diagnosed based on then prevalent WHO guidelines. Gestational age was based on last menstrual period dates (recorded every month during the pre-conception period) unless it differed from early (<20 weeks' gestation) ultrasound scan dating by 2 weeks or more, in which case the latter was used. Detailed new born anthropometry was carried out by trained research staff within 72 hours of birth. Multiple follow-up studies have been conducted starting from pre-pregnancy, during pregnancy, at birth, early childhood, adolescence and young adulthood and detailed anthropometric and biochemical data have been collected. At 6 years of age, we measured anthropometry, resting systolic and diastolic blood pressure, plasma glucose and insulin (fasting and after an oral glucose load) and fasting lipids (triglycerides and LDL- and HDL-cholesterol). At 12 years, detailed anthropometry, and measurements of blood pressure, fasting glucose, insulin and lipids were repeated. At both time points, the same measurements were carried out in both parents. We have used these data in the current study. The DNA samples isolated from the 6 years follow up stage were used for genotyping.

Parthenon Study (PS)

The Parthenon study (PS) was established in 1997-98 in Mysore, South India, to examine the long-term effects of maternal glucose tolerance and nutritional status during pregnancy on cardiovascular risk factors and cognition in the offspring (23). Women (<32 weeks' gestation) were recruited in the antenatal clinic of the Holdsworth Memorial Hospital, Mysore. Gestational age was assessed using last menstrual period dates collected at recruitment. A 100gm oral glucose tolerance test was carried out at 28-32 weeks' gestation and GDM was diagnosed based on Carpenter and Coustan criteria (24). Detailed newborn anthropometry was carried out by trained research staff within 72 hours of birth. At 5 and 13.5 years of age, we measured anthropometry, resting systolic and diastolic blood pressure, plasma fasting glucose and insulin) and fasting lipids (triglycerides and LDL- and HDL-cholesterol). At 5 years, the same measurements were carried out in their mothers and only fasting glucose and insulin in the fathers. These data were used in this study. Genotyping was performed on the DNA samples isolated from the 5 years follow up stage blood samples.

Mumbai Maternal Nutritional Project (MMNP)

The Mumbai Maternal Nutrition Project was a randomised controlled trial, set up in 2006 among women living in slums in the city of Mumbai, Western India with the objective to test whether improving women's dietary micronutrient quality before and during conception improves birthweight and other related outcomes (25). Women were recruited before conception. As in the PMNS, gestational age was assessed using a combination of last menstrual period dates (which were collected monthly during the pre-conceptional period) and ultrasound scans conducted before 20 weeks' gestation. A 75g oral glucose tolerance test was carried out at 28-32 weeks' gestation and GDM was diagnosed based on revised WHO 1999 guidelines. Trained research staff carried out newborn anthropometry within 10 days of birth. In the current study, we have used the child phenotype data at birth (anthropometry) and in early childhood (5-7-year follow-up), when detailed anthropometry, systolic and diastolic blood pressure, fasting and post-load glucose and insulin, and fasting LDL- and HDL-cholesterol and triglycerides were measured (26). Maternal anthropometry, blood pressure and fasting plasma glucose and insulin concentrations were also measured at this follow-up. Genomic DNA isolated from blood samples at the same stage were used for genotyping.

Mysore Birth Records Cohort (MBRC)

The MBRC is a retrospective birth cohort of urban men and women born at the CSI Holdsworth Memorial Hospital during 1934-55 (27). They were recruited for the first time as adults (mean age 47 years) in 1993-95 and cardiometabolic risk factors were measured (7). Birthweight, length and head circumference were obtained from their mothers' obstetric records. We have included the anthropometric data at birth and cardiometabolic parameters measured between 40 and 70 years during 2013-2017. Gestational age was missing in the majority of subjects and gestational diabetes status was not available. Since maternal DNA samples were not available, the analyses were restricted to the association of fetal genetic score and their birth measures and later life outcomes.

GIFTS Dhaka Bangladeshi cohorts (WP2 and WP3)

WP2 samples were collected between 2011 and 2012 in Dhaka, Bangladesh from women attending the Maternal and Child Health Training Institute, a tertiary Government hospital for antenatal care and registration in Dhaka. Primigravid pregnant women who were in the first trimester of their pregnancy (≤14 week gestation), with a singleton pregnancy conceived naturally and who were willing to participate in the study were included in an observational study during pregnancy and immediately post-partum after written consent (28). GDM was diagnosed based on revised WHO 1999 guidelines. Women with a prior history of type 2 diabetes, or gestational diabetes or pregnancy induced hypertension were excluded. The aim of WP2 was to establish the methods and feasibility of recruitment and follow-up for an interventional study (WP3). WP3 samples were collected between 2014 and 2015 in Dhaka, Bangladesh from pregnant women attending MCHTI who consented to an open-label micro-nutrient supplement trial of vitamin D and vitamin B12 supplementation (29). All consenting women eligible under the WP2 criteria were included in the study and samples were collected from mother and baby under the same sampling frame as WP2. Women who were diagnosed later in pregnancy with GDM remained in the study.

London UK Bangladeshi cohort (UK-Bang)

The cohort was set up between 2012-2015 as an exploratory observational study of gestational diabetes and its consequences on offspring. Pregnant women of Bangladeshi origin were recruited from the Royal London Hospital antenatal clinics at 28 weeks gestation at the time of 75 gm OGTT. GDM was diagnosed based on Revised WHO, 1999 guidelines. Women were recruited during routine antenatal care and enriched for the presence of GDM. Women with multiple pregnancies, pre-existing or overt type 1 or type 2 diabetes were excluded. Gestational age was based on ultrasound scan dating. Detailed new born anthropometry was carried out by trained research staff within 72 hours of birth.

The Exeter Family Study of Childhood Health (EFSOCH)

EFSOCH is a prospective study of children born between 2000 and 2004, and their parents, from a geographically defined region of Exeter, UK. All women gave informed consent and ethical approval was obtained from the local review committee. Details of study protocol, including measurement of birthweight, are described in Knight et al (30). Maternal and paternal DNA samples were extracted from parental blood samples obtained at the study visit (when the women were 28 weeks pregnant), and offspring DNA was obtained from cord blood at birth. Genotyping and imputation of EFSOCH samples has been described previously (31).

UK Bio Bank South Asian participants (UKBB-SAS)

The UK Biobank phenotype preparation has been described in detail elsewhere (15). Briefly, a total of 280,315 participants reported their own birthweight in kilograms and 216,839 women reported the birthweight of their first child on at least one assessment centre visit. Multiple birth were excluded where reported. In the absence of gestational data, participants with birthweight values <2.5kg or >4.5kg were considered pre-term births and excluded. In addition to the genotype quality control metrics performed centrally by the UK Biobank, we defined a subset of "South Asian" ancestry samples (32). To do this, we generated ancestry informative principal components (PCs) in the 1000 genomes samples. The UK Biobank samples were then projected into this PC space using the SNP loadings obtained from the principal components analysis using the 1000 genomes samples. The UK Biobank participants' ancestry was classified using K-means clustering centred on the three main 1000 genomes populations (European, African, and South Asian). Those clustering with the South Asian cluster were classified as having South Asian ancestry.

Inclusion and exclusion criteria, and phenotype measurements

In all the cohorts, the association analysis was restricted to individuals with both genotype and phenotype data available. The anthropometric measurements at birth were conducted within 72 hours after birth, and babies with congenital defects were excluded from the analysis. Twins and babies born lesser than 37 weeks of gestational age (9-14%) were excluded from the association analysis at birth. For anthropometric and cardiometabolic analysis at follow up stages during childhood and adolescence, we included all the individuals with phenotype-genotype data available irrespective of their gestational age at birth. For adults, phenotypes data were taken from the follow up stages as PMNS mother at 6 years, PMNS fathers at 12 years, PS mother and father at 5 years, MMNP mother at 7 years, and MBRC at the latest follow up during 2013-2017. Anthropometric measurements at birth and follow up stages were conducted using standard methods. Body fat percentage was measured by whole-body dual energy X-ray absorptiometry (DEXA) scans. Biochemical measurements were conducted from fasting plasma samples using standard methods. Plasma glucose was measured by the glucose oxidase peroxidase method, plasma insulin was measured using Delfia technique. Insulin resistance was calculated using the homeostatic model assessment of insulin resistance (HOMA-IR). Plasma lipid levels including total cholesterol, triglycerides, high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterols were measured by standard enzymatic methods. Individuals with missing phenotype were excluded from the analysis of the particular trait.

Genotyping and imputation QCs

For Indian cohorts, genome-wide genotyping were performed using Affymetrix Genome-Wide Human SNP Array 6.0 for fathers of PMNS cohort; Illumina Infinium Human CoreExome-24 array for children and mothers of PMNS and PS cohorts; and Illumina Infinium Global Screening Array for children and mothers of MMNP, fathers of PS and individuals of MBRC cohorts. Individuals with genotyping call rate $\leq$ 95% and SNPs with call rate $\leq$ 95% and Hardy Weinberg equilibrium $P \leq 10^{-6}$ were removed. Genome-wide imputation was performed by using IMPUTEv2 software (https://mathgen.stats.ox.ac.uk/impute/impute_v2.html) and 1000 Genome Phase 3 as reference panel and SNPs with imputation info score $\leq$ 0.4 were removed. The genome-wide genotyping for the children and mothers of all the Bangladeshi cohorts were performed using Illumina Infinium Global Screening Array and genome-wide imputation using HRC imputation panel.

Selection of genetic variants and calculation of weighted genetic scores

The scheme for selecting SNPs for the calculation of birthweight genetic score is shown in Figure 1. Of the 205 autosomal SNPs reported as associated with birthweight in Warrington et al., 9 SNPs were excluded due to either being missing or having an imputation info score less than 0.4 in at least one of the cohorts (15). Finally, 196 autosomal SNPs were used for generating weighted fetal genetic score (fGS) and maternal genetic score (mGS). Details of the 196 SNPs were provided in Supplementary Table 1. The SNP weights for generating the fGS and mGS were taken from the SEM adjusted effect estimates of the fetal and maternal effects respectively from the recent GWAS of birthweight from the EGG/UKBB consortium (Supplementary Table 1) (15). The SEM estimates associations of both maternal and fetal scores with birthweight while accounting for the relationship between fetal and maternal genotypes, thereby producing independent estimates of the fetal and maternal genetic effects on birthweight. The weighted genetic score was calculated using the following formula:

$$Weighted\ genetic\ score = \frac{[\beta 1 \times SNP1 + \dots + \beta n \times SNPn]}{\Sigma \beta n} \times nSNPs$$

Where β_n is the weight of SNP_n taken from the EGG/UKBB birthweight GWAS, nSNPs is the number of SNP available (n=196), and $\Sigma\beta_n$ is the sum total weight of all 196 SNPs.

We identified independent genetic variants from the 196 SNPs used above by looking at pairwise linkage disequilibrium ($r^2<0.01$) in a window of 1000kb in the 1000 Genome Phase 3 reference panel and freshly conducted association analysis with birthweight.

Statistical analysis and power calculation

Birthweight and other birth measures were transformed to standardized Z-scores (Z-score = (value – mean)/standard deviation). Association analysis was performed by linear regression, using Z-scores as the dependent variables and weighted genetic score as the independent variable, adjusted for the child's sex and gestational age. The models were as follows:

For the fetal analysis:

Birthweight Z-score ~ fGS + Sex + Gestational Age

Birthweight Z-score ~ fGS + Sex + Gestational Age + mGS

For the maternal analysis:

Birthweight Z-score ~ mGS + Sex + Gestational Age

Birthweight Z-score ~ mGS + Sex + Gestational Age + fGS

Power calculations were conducted to estimate the probable association observable in our analysis with a sample size of 2693 individuals of South Asian ancestry. If the birthweight SNPs explain equal variance in South Asians to that explained in Europeans (6% and 2% for fGS and mGS respectively) (Warrington et al, 2019), we would have > 99% power to see an association with the fGS and 98% power with the mGS at $\alpha = 0.05$. However, it is likely that due to differing linkage disequilibrium between marker SNPs and underlying causal genetic variants, genetic variants identified in GWAS samples that were largely of European ancestry may explain less variation in non-European samples. Therefore, assuming that the genetic scores explain only 75% of the European ancestry variation in South Asian ancestry individuals, we would still have 99% and 83% power for fGS and mGS respectively to detect an association with birthweight.

Association analysis of the anthropometric and cardiometabolic phenotype data acquired during follow-up at childhood and adolescence was performed by linear regression, using log10 transformed standardized Z-scores as the dependent variables and weighted genetic score as an independent variable, adjusted for sex and age. Imputed genotype data from parents of children in the PMNS and PS, mothers of children in MMNP, and men and women in MBRC were utilized for investigating the effect of the genetic risk scores on adult anthropometric and cardiometabolic phenotypes. BMI was included as an additional covariate for the cardiometabolic traits. The models were as follows:

For the anthropometric traits

Log10 transformed Z-score ~ fGS + Sex + Age

For the cardiometabolic traits

Log10 transformed Z-score ~ fGS + Sex + Age + BMI

The association analyses for birthweight and other birth measures and for anthropometric and cardiometabolic traits were conducted independently for each cohort and fixed effect inverse variance weighted meta-analysis (using the metan command in STATA) was performed to combine the final results. A total of 57 tests in the three stages (childhood, adolescence and adulthood) were conducted and the significance level was set at $p < 0.001$ ($\alpha < 0.05/57$ tests) to allow for multiple testing.

RESULTS

Clinical and demographic characteristics of study participants

Newborn measurements, maternal details and phenotypes at different follow-up stages are shown in Table 1 and Supplementary Tables 2, 3, 4 and 5. The mean birthweight of term babies in different cohorts ranged between 2.64 and 3.12 kg. Within the cohorts of South Asian ancestry, babies born in India and Bangladesh were comparatively smaller, whereas Bangladeshi babies born in UK from the UK-Bang and the UKBB-SAS were relatively larger (Supplementary Table 2 and 3). Birthweight was much higher in the European babies as observed in the EFSOCH (Table 1). Boys were bigger than girls across all the cohorts. In contrast, sum of skin-fold thickness, a measure of adiposity, was greater in girls. Amongst all the cohorts, PMNS mothers living in rural India were the thinnest (mean BMI = 18.0 kg/m^2) whereas Bangladeshi mothers living in the UK (UK-Bang) were the heaviest (mean BMI = 26.2 kg/m^2). Mean BMI in the mothers from the other cohorts were in the normal range, between 20.3 to 23.6 kg/m^2. The percentage of mothers with gestational diabetes mellitus (GDM) was higher in the Bangladeshi cohorts (UK-Bang = 50%, WP2 = 24.5% and WP3 = 25.8%), whereas, in the Indian cohorts, it was 0.6%, 6.1% and 6.9% in

PMNS, PS and MMNP respectively. The UK-Bang cohort was positively selected to have higher rates of GDM than the underlying population, but the high rates of GDM in the Bangladeshi Dhaka WP2 and WP3 cohorts represent the high rates of GDM in the community. The mothers of MBRC individuals were not tested for diabetes. Principal Components Analysis did not reveal any evidence of population stratification within the cohorts (The data can be made available on request).

Association of genetic scores with birthweight and other birth measures

The effect allele frequencies (EAFs) of 196 SNPs were similar in all seven South Asian cohorts, except two outliers, one each in the MBRC (rs2306547) and GIFTS (rs9851257) cohorts (Supplementary Figure 1A and Supplementary Table 1). Although, the EAFs at several SNPs varied considerably between South Asians and the EGG/UKBB subjects (Supplementary Figure 1B and Supplementary Table 1), mean values for both fGS and mGS in South Asian cohorts were similar to those in the European cohort, EFSOCH (Table 1).

We noted that the fGS calculated from 196 SNPs was strongly associated with birthweight in South Asians (Table 2). The meta-analysis of the South Asian cohorts showed a 0.013 SD higher birthweight per 1 unit higher fGS, adjusted for the child's sex and gestational age ($p = 9.1x10^{-11}$) (Figure 2A and Table 2). This is equivalent to 50.7 g of birthweight per SD unit of fGS (Figure 2E). The strength of association was only partially attenuated after additional adjustment for the mGS (Effect = 0.015 SD, $p = 1.1x10^{-10}$) (Figure 2B and Table 2). The mGS was also directly associated with offspring birthweight although compared to the fGS, the effect size was smaller (effect = 0.006 SD, p = 0.003). This is equivalent to 33.6 g of birthweight per SD unit of mGS and adjustment for fGS made little difference (effect = 0.006 SD; p = 0.004) (Figures 2C, 2D and 2F, Table 2). Analyses of only Indians and only Bangladeshis showed consistent and overlapping effect sizes in the fGS association analysis, but the mGS association with birthweight was largely driven by the Bangladeshi cohorts (Supplementary Tables 8 and 9). Since GDM is associated with excess fetal growth, we repeated association analysis after the exclusion of offspring of GDM women and observed similar associations (effect = 0.010; p = 5.1×10^{-8} for the fGS and effect = 0.005; p = 0.011 for the mGS) (Supplementary Tables 6 and 7). A plot of fGS versus birthweight showed that for each fGS, birthweight was substantially smaller in the South Asians (Figures 3A and 3B). Similar observations were noted for the association of mGS with birthweight (Figures 3C and 3D). The effect sizes of the fGS on birthweight in the South Asian cohorts was comparable to the same in EFSOCH (n = 674) and also with South Asians in the UK Biobank study (UKBB-SAS; n = 2732) (p = 0.17; p = 0.23 respectively) (Figure 2E). Similarly, the association between mGS and offspring birthweight in our study was similar to that observed in UKBB-SAS (p = 0.93). However, we noted a statistically significant smaller effect size of mGS among all the South Asian cohorts combined than in EFSOCH (p = 0.048) (Figure 2F). The fGS was also positively associated with other birth measures; no associations were seen with the mGS (Table 3). Respective adjustments for mGS and fGS did not substantially change the strength of these associations (Supplementary Table 10). Further, sensitivity analysis using 167 LD-pruned SNPs (after exclusion of 29 SNPs with an r2>0.01 with other variants from the list of 196 SNPs) did not make any significant changes in the strength of association (Supplementary Tables 11-13).

Associations of birthweight and fetal genetic score with anthropometric and cardiometabolic traits in follow-up stages

The associations of birthweight and the fGS with later anthropometric and cardiometabolic traits in early childhood and early adolescence were investigated in the Indian cohorts only, since they had longitudinal follow-up data. Birthweight was strongly positively associated with all anthropometric traits in childhood (5-7 years; p = 3×10^{-5} - 1.9×10^{-51}) and adolescence (11-14 years; p = 5.7×10^{-6} – 8.1×10^{-27}) (Figure 4A; Supplementary Table 14). It also showed strong evidence of a negative association with triglycerides levels in childhood (p = 9.8×10^{-4}) and a weak association in adolescence ($p = 0.002$). We observed a negative association with SBP and DBP and a positive association with fat percentage both in childhood and adolescence but these did not pass the Bonferroni-corrected threshold of $p < 0.001$ (Figure 4A; Supplementary Table 14). Similar to birthweight, a higher fGS was associated with larger body size in childhood (Table 3). We observed a strong positive association of the fGS with waist circumference (effect = 0.01 SD per standard unit, $p = 5.7x10^{-5}$) but the associations with other anthropometric parameters including weight, height, BMI, head circumference and mid-upper arm circumference were weaker ($p = 0.017 – 0.001$) and did not pass the multiple testing threshold of $p < 0.001$ (Table 4; Figure 4B)]. No evidence of associations between fGS and anthropometric traits were detected in adolescents. The fGS was not associated with any of the cardiometabolic parameters in children or in adolescents (Table 4) and mGS had no association with any anthropometric and cardiometabolic parameters in children or in adolescents (Supplementary Table 15).

Using data on parents of children in the PMNS and PS, men and women in the MBRC and mothers in the MMNP cohort, we investigated the influence of fGS on anthropometric and cardiometabolic traits in adults (Figure 4B, Table 4). The fGS showed a strong positive association with head circumference (effect = 0.006; $p = 5.5x10^{-4}$) and a statistically insignificant positive association with adult height (effect = 0.002; $p = 0.037$) (Table 4; Figure 4B). It was also negatively associated with fasting glucose (effect = -0.006; $p = 9.3x10^{-4}$) and showed a weak negative association with HOMA-IR and triglycerides ($p = 0.022$ and $2.0x10^{-3}$ respectively). The direction of associations was the same as the genome-wide correlations reported in Europeans (p range, 0.002 - $5.5x10^{-4}$) (Figure 4B; Table 4) [14]. No evidence of association was noted between fGS and other anthropometric and cardiometabolic traits in adults ($p > 0.05$) (Table 4).

DISCUSSION

In this study which included four Indian and three Bangladeshi cohorts from both the Indian subcontinent and the UK, we investigated whether the genetic variants identified in a GWAS of birthweight in Europeans also influence birth size in South Asians (Warrington et al, 2019) (15). We further investigated whether the same genetic variants (either fetal variants that directly influence birthweight, or those in the mother that act indirectly via the intrauterine environment) were associated with anthropometric and cardiometabolic parameters measured during childhood, adolescence and adulthood. We observed strong positive associations of fetal genetic score with birthweight and other birth measurements in these populations of South Asian ancestry despite a large variation in maternal BMI and fetal birthweight. While birthweight positively predicted body size in both children and adolescents, fGS did so only in children but not in adolescents. We also noted a strong association of birthweight with plasma triglycerides levels both in children and adolescents, but fGS was not related to any of the child/adolescent cardiometabolic outcomes. However, fGS was inversely associated with plasma glucose and triglycerides in adults. Maternal genetic score was weakly positively linked to birthweight and was unrelated to body size and cardiometabolic traits in both children and adolescents. Our study thus reports a strong association of fGS and relatively weak association of mGS with birthweight and other birth measures in a non-European population. Further, the genetic constitution of the fetus at specific variants influences body size and the data from the adults suggest that it contributes to future cardiometabolic risk in Indians. Overall, it provides support to the observational association between low birth size and non-communicable diseases like type 2 diabetes and cardiovascular diseases in South Asians. Follow up studies on a larger sample size will be required to answer our second research question (is the birthweight–cardiometabolic risk association explained by shared genetic variants) with confidence.

Most genetic studies associating early life parameters with future risk of cardiometabolic disorders have been conducted in Europeans. As far as we are aware, this is first such analysis in South

Asians. We found similar associations of fGS generated using weights from European studies with birth size in a consortium of seven birth cohorts of South Asian ancestry comprising Indian and Bangladeshi mother-child pairs. This was despite a wide variability in birthweight and maternal BMI within the South Asian cohorts and significant differences in the EAFs of many of the birthweight associated variants between the EGG/UKBB and the South Asian subjects. Despite similar fGS association with birthweight as in Europeans, the newborn size of South Asian babies was substantially smaller indicating a significant role of factors not captured by the genetic score on fetal growth. These factors may include different environmental exposures, maternal body size, health and nutritional status etc. We noted an increase of 50.7g of birthweight per SD of fGS which is consistent with the observation in the UKBB-SAS and is marginally smaller than in EFSOCH, examples of South Asian and European ancestry cohorts respectively. The significant association of fGS with body size at birth persisted even after adjustment for mGS, indicating that the genetic effect is not significantly influenced by aspects of the intrauterine environment predicted by the genetic variants used in this study. This is further supported by a similar strength of association after exclusion of children born to GDM mothers which suggests that the fetal genetic effects are independent of maternal diabetes status during pregnancy. The similar association for fGS with birthweight observed between South Asian and European ancestry individuals in this study suggests that although it is difficult to conclude at individual variant level, there are likely common genetic pathways for fetal growth and development in both ancestry groups. Although mGS was relatively weakly associated with fetal birthweight, the association was unaffected by the fetus's own genotype suggesting that the maternal genetic effect on birthweight was mediated through intrauterine environment. The weaker association of mGS is not unexpected given the lower proportion of variance explained in birthweight by the mGS (~2%) compared to fGS (~6%). Thus, birthweight (body size) is an outcome of the baby's genetic constitution and an influence of the intrauterine environment, partly determined by the mother's genotype. However, with the exception of a small number of variants that are known to influence fasting glucose levels, it is largely unclear which intrauterine exposures are influenced by which genetic variants used in the study, making it difficult to dissect their individual role. It was interesting to note that the influence of the maternal genetic score on birthweight varied considerably amongst the cohorts investigated in this study (heterogeneity p = 0.018). This heterogeneity in effect estimates could be driven by ethnicity, maternal BMI, height and nutritional status, socio-economic status, and GDM status; this needs further investigation.

Genome-wide studies have established a robust association between fetal genetic score and later cardiometabolic risk including glycaemic and lipid parameters in Europeans (13; 15). An important feature of our study is that we have been able to independently compare associations of birthweight and birthweight-associated genetic variants with later anthropometric and cardiometabolic traits. Birthweight showed a strong positive association with body composition, and an inverse association with blood triglycerides concentrations in both childhood and adolescence. Fetal genetic score explains only about 6% of the variance in birthweight in European individuals (15) and considering equal effect of fetal genetic score on birthweight in South Asians as in Europeans, it is worth noting that a positive association with body size in childhood and height and head circumference in adults was observed. Effect estimates of fGS with other anthropometric traits was directionally consistent with the direct effect of birthweight; a lack of strong association may be due to a relatively smaller sample size and the smaller effect size compared to the birthweight itself. Absence of association between fGS and any of the traits during adolescence is consistent with findings from even larger studies that have found little evidence of influence of fetal birthweight variants on BMI beyond early childhood (33). Similar to our study, previous studies have demonstrated a pattern of positive genetic correlations with birthweight, and with childhood and adulthood height (13; 15). The fact that the fetus's genotype at birthweight-associated genetic variants also influenced plasma glucose and triglycerides in adulthood is consistent with the fetal insulin hypothesis, which proposes that birthweight and later cardiometabolic risk are two effects of the same genotype (34). Our findings need to be replicated in larger independent studies of South Asian subjects. Further understanding of the link between birthweight and future cardiometabolic risk will be possible as we understand the exact role of each genetic variant, whether it operates directly or indirectly through its effects on intrauterine environment.

Our study has several strengths and a few limitations. This is the first study exploring the influence of fetal and/or maternal genotype on birth size and their role in future cardiometabolic risk in South Asians. We combined diverse cohorts from India (including both Indo-European and Dravidian ethnicity) and from Bangladesh (local and migrants to the UK), hence the observations can be considered representative of South Asians. The greatest strength of the study is availability of mother-child pairs and anthropometric and cardiometabolic traits in early childhood and adolescence and hence the conclusions drawn from these prospective cohorts are robust. The limitations of the study include a relatively small sample size although assuming equal variance explained by these SNPs in Europeans, our study in South Asians had > 99% and 98% power to detect association of fGS and mGS with birthweight respectively. Lack of adult phenotype data in children of these cohorts is another limitation, but we have partly circumvented this issue by using the genotype and phenotype data from parents of the children in the Indian cohorts. However, lack of birth size and maternal genotype data for these parents did not allow us to study the maternal influence in this group. The availability of a genetic score specific to individuals of South Asian ancestry would also allow us to further investigate the difference in association of mGS with birthweight compared to European ancestry individuals observed here, helping to disentangle environmental effects from those expected from a GS which may not capture the same underlying genetic associations in different ancestry groups.

The observations made in this study are important because the sub-continent is facing the twin burden of poor fetal health and an emerging epidemic of type 2 diabetes and cardiovascular diseases (9; 35; 36). This has been linked to unique phenotypic features, environmental exposures, and a different genetic makeup of South Asians compared to Europeans (17-21). However, this study suggests that the genetic contribution to birth size is largely similar to that in the Europeans, and that other factors may be responsible for the thin-fat phenotype of South Asians which predisposes them to a higher risk of diabetes and related disorders compared to Caucasians. The validation of genetic associations with birthweight in populations of two ancestries, Europeans and South Asians provides a hint that there may be common pathways affecting fetal development which can be influenced by different environmental exposures.

To conclude, we report the associations of genetic scores identified in Europeans with size at birth in participants of South Asian ancestry. However, fetal genetic score is known to explain only about 6% variability in birthweight in Europeans. Interestingly, despite similar association of fetal genetic scores with birthweight as in Europeans, South Asians have a considerably lower birthweight. This indicates a significant role of other factors on fetal growth such as different environmental exposures which are not captured by the genetic variants included in the present study. These genetic loci also influenced early childhood body size and were associated with fasting glucose and triglycerides levels in adults, suggesting that common genetic variants explain part of the association between birth size and adult metabolic syndrome. This supports the "fetal insulin hypothesis" but also highlights an important interaction with environment (16; 34). Lack of association between fetal genetic scores and cardiometabolic traits in the children and adolescents deserves more exploration. Further, birthweight-fetal genotype associations were consistent across all cohorts, association of fetal birthweight with maternal genotype showed heterogeneity between cohorts. This may be related to differences in maternal size, glycemia and socio-economic status and needs further research.

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Data and Resource Availability

The datasets and generated during and/or analyzed during the current study are available upon reasonable request. Researchers interested in accessing the data are expected to send a reasonable request by sending an email to the contact authors as detailed below.

Indian cohorts (PMNS, PS, MMNP and MBRC): Giriraj R Chandak at chandakgrc@ccmb.res.in

EFSOCH: The Exeter Clinical Research Facility at crf@exeter.ac.uk

GIFTS (WP2 & WP3) and UK Bang cohorts: Graham A Hitman at g.a.hitman@qmul.ac.uk

UK-biobank data - https://www.ukbiobank.ac.uk/using-the-resource/ [ukbiobank.ac.uk]

No applicable resources were generated or analyzed during the current study.

Authors' contributions

G.R.C., C.S.Y., G.A.H., C.H.D.F., S.F. and R.M.F. conceptualised and contributed to the study design; collated and interpreted overall results from various cohorts in the study. G.V.K., K.K., S.A.S., R.D.P., M.K., C.D.G., C.S.Y. and C.H.D.F. are coordinators for various Indian cohorts and played important role in the follow-up and acquisition of phenotype data at different stages. G.R.C. supervised the overall Indian cohort studies. S.F., G.A.H. are the lead supervisor of UK cohort while A.H. and A.K.A.K. managed the Bangladeshi cohort studies. B.W.B. oversaw data collection and phenotyping of subjects in Bangladeshi cohorts. B.A.K. carried out sample collection and phenotyping in the EFSOCH cohort. I.D.M. provided technical support in DNA isolation and quality control analysis in Indian cohorts. S.S.N. and A.D. performed high throughput genotyping of Indian cohorts while B.O., Z.H. T.M.F. and R.M.F. were responsible for preparing samples and genotyping in the Bangladeshi and EFSOCH cohorts. S.S.N., A.D., A.S. cleaned Indian cohorts' genotype data and generated imputed genotypes whereas R.N.B. performed quality control and imputation of the Bangladeshi and EFSOCH cohort genotype data. A.R.W. defined the South Asian samples of the UK Biobank dataset using ancestry principal components. S.S.N. and R.N.B. performed the central analysis and wrote the first draft of the manuscript. All authors have contributed to manuscript writing, provided critical inputs and approved the final version of the manuscript.

Competing Interests

The authors have no competing interests to declare.

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TABLES

Table 1. Maternal and newborn details in the study cohorts, and fetal and maternal genetic scores for the South Asian and European cohorts

Traits	PMNS (N=515)	PS (N=511)	MMNP (N=466)	MBRC (N=684)	Dhaka-WP2 (N=53)	Dhaka-WP3 (N=314)	UK-Bang (N=150)	UKBB-SAS* (N=2732)	EFSOCH* (N=674)
Birthweight (kg)	2.68 (0.34)	2.91 (0.41)	2.64 (0.37)	2.76 (0.42)	2.90 (0.38)	2.84 (0.42)	3.12 (0.45)	3.10 (0.68)	3.52 (0.47)
Birth length (cm)	47.8 (1.97)	48.8 (2.11)	48.2 (2.26)	48.0 (2.95)	46.2 (2.56)	49.6 (2.60)	46.6 (2.03)	NA	50.3 (2.12)
Ponderal index (kg/m^3)	24.5 (2.44)	25.0 (2.75)	23.6 (2.60)	25.3 (4.85)	29.5 (4.42)	23.3 (3.50)	28.9 (4.27)	NA	27.7 (2.58)
Head circumference (cm)	33.1 (1.24)	33.9 (1.28)	33.2 (1.20)	35.6 (1.58)	33.4 (1.39)	33.0 (2.40)	33.6 (1.31)	NA	35.2 (1.26)
Chest circumference (cm)	31.2 (1.59)	32.0 (1.64)	30.9 (1.75)	NA	NA	NA	33.4 (1.97)	NA	34.2 (1.86)
Abdomen circumference (cm)	28.7 (1.91)	30.0 (1.92)	28.4 (2.08)	NA	NA	NA	31.4 (2.56)	NA	NA
Mid-upper arm circumference (cm)	9.7 (0.88)	10.4 (0.92)	9.7 (0.82)	NA	9.9 (0.71)	10.2 (2.09)	10.9 (2.13)	NA	11.1 (0.90)
Triceps skinfold (mm)	4.3 (0.87)	4.3 (0.90)	4.2 (1.05)	NA	NA	NA	5.0 (1.93)	NA	4.86 (1.08)
Subscapular skinfold (mm)	4.2 (0.89)	4.5 (0.91)	4.2 (0.99)	NA	NA	NA	5.3 (1.87)	NA	4.87 (1.08)
Gestational age (weeks)	39.0 (1.06)	39.5 (1.14)	39.3 (1.17)	NA	40.3 (1.17)	39.2 (1.53)	40.0 (3.44)	NA	40.1 (1.22)
Maternal Age (years)	21.4 (3.56)	23.8 (4.24)	24.8 (3.83)	NA	19.9 (2.45)	22.7 (4.29)	29.7 (5.40)	NA	30.5 (5.19)
Maternal Height (cm)	152.1(4.9)	154.5(5.4)	151.3(5.4)	NA	151.1 (5.8)	150.9 (5.7)	156.0 (5.8)	NA	165.0 (6.3)
Maternal BMI (kg/m^2)	18.0 (1.9)	23.6 (3.55)	20.3 (3.67)	NA	20.6 (3.40)	22.7 (4.03)	26.2 (4.34)	NA	24.0 (4.34)
Maternal GDM status [n (%)]	3 (0.6)	31 (6.1)	32 (6.9)	NA	13 (24.5)	81 (25.8)	75 (50.0)	NA	NA
Year of birth	1994-95	1998-99	2006-12	1934-66	2011-12	2015-16	2011-15	1934-70	2000-04
Fetal Genetic Score	191.0 (9.0)	191.0 (9.6)	189.0 (9.4)	189.0 (9.6)	191.0 (8.1)	188.0 (9.4)	188.0 (9.3)	192.0 (9.9)	192.0 (9.8)
Maternal Genetic Score	215.0 (10.3)	215.0 (10.4)	215.0 (10.5)	NA	218.0 (10.2)	217.0 (10.2)	216.0 (9.3)	214.8 (11.0)	214.0 (10.8)

All values are mean (SD); N, subjects included in this study; SD, standard deviation; GDM, Gestational diabetes mellitus; PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort; UKBB-SAS, UK Biobank South Asian component; EFSOCH, The Exeter Family Study of Childhood Health study; *, Not used for meta-analysis. Fetal and maternal genetic scores were calculated from 196 birthweight-associated variants in children and mothers respectively.

Table 2: Associations of fetal genetic score with own birthweight and maternal genetic score with its offspring birthweight in South Asian cohorts

Cohort	fGS adjusted for sex and GA*					fGS adjusted for sex, GA and mGS†				
	N	**Effect**	**L95**	**U95**	**P**	**N**	**Effec**	**L95**	**U95**	**P**
PMNS	515	0.009	0.000	0.018	0.042	443	0.010	0.001	0.020	0.040
PS	511	0.021	0.012	0.029	3.8×10^{-6}	458	0.021	0.012	0.030	1.0×10^{-5}
MMNP‡	466	0.013	0.003	0.022	0.007	460	0.013	0.004	0.022	0.006
MBRC§	684	0.006	-0.002	0.013	0.154	NA	NA	NA	NA	NA
Dhaka-WP2	53	0.020	-0.015	0.055	0.277	53	0.019	-0.014	0.052	0.269
Dhaka-WP3	314	0.013	0.003	0.024	0.015	314	0.013	0.002	0.023	0.022
UK-Bang	150	0.024	0.008	0.040	0.004	150	0.021	0.004	0.037	0.015
Meta-analysis	**2693**	**0.013**	**0.009**	**0.017**	**9.1×10^{-11}**	**1878**	**0.015**	**0.01**	**0.020**	**1.1×10^{-10}**

	mGS adjusted for sex and GA‖					mGS adjusted for sex, GA and fGS¶				
	N	**Effect**	**L95**	**U95**	**P**	**N**	**Effec**	**L95**	**U95**	**P**
PMNS	461	0.000	-0.008	0.008	0.976	443	0.001	-0.008	0.009	0.876
PS	475	0.011	0.003	0.020	0.013	458	0.011	0.003	0.019	0.011
MMNP‡	467	-0.001	-0.009	0.007	0.804	460	0.000	-0.009	0.008	0.957
Dhaka-WP2	53	0.034	0.009	0.059	0.011	53	0.034	0.009	0.059	0.011
Dhaka-WP3	314	0.010	0.001	0.020	0.040	314	0.009	0.000	0.019	0.060
UK-Bang	150	0.016	0.001	0.032	0.041	150	0.012	-0.004	0.028	0.150
Meta-analysis	**1920**	**0.006**	**0.002**	**0.010**	**0.003**	**1878**	**0.006**	**0.002**	**0.010**	**0.004**

Association analysis was performed using linear regression with standardized birthweight adjusted for sex and gestational age as the dependent variable for each cohort separately and finally the summary results were meta-analyzed. †, In MMNP, allocation group was additionally adjusted for, and §, in MBRC only sex was adjusted for, since gestational age data was not available for the majority of the sample. The effect size is in standard deviation units of birthweight per unit change in genetic score. The standard deviation of birthweight in kg in all these cohorts ranged from 0.34 to 0.45 kg. N, number of term babies; GA, gestational age; I^2, heterogeneity; Het-P, P value for heterozygosity; P, P value; fGS, fetal genetic score; mGS, maternal genetic score; GA, gestational age. PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort.

For fGS, *, I^2 = 32.8 and Het-P = 0.177; **†**, I^2= 0 and Het-P = 0.643

For mGS, ||, I^2= 63.5 and Het-P = 0.018; ¶, I^2=53.7 and Het-P = 0.056.

Table 3: Associations of fetal and maternal genetic scores with other birth measures in South Asian populations

Trait	fGS adjusted for sex and gestational age*							mGS adjusted for sex and gestational age*						
	N	Effect	L95	U95	P	I^2	Het-P	N	Effect	L95	U95	P	I^2	Het-P
Birth length (Z)	2544	0.004	0.000	0.009	0.048	44.1	0.097	1820	0.003	-0.002	0.008	0.153	42.5	0.122
Ponderal Index (Z)	2517	0.009	0.004	0.013	$2.1x10^{-4}$	28.3	0.213	1796	0.000	-0.004	0.006	0.906	14.3	0.323
Head circumference (Z)	2564	0.005	0.000	0.009	0.030	48.0	0.073	1844	0.002	-0.002	0.007	0.425	0	0.741
Chest circumference (Z)	1586	0.012	0.007	0.017	$8.2x10^{-6}$	23.1	0.273	1477	0.002	-0.002	0.007	0.383	3.7	0.374
Abdominal circumference (Z)	1586	0.014	0.008	0.019	$3.4x10^{-7}$	68.5	0.023	1477	0.002	-0.003	0.007	0.554	62.0	0.048
Mid-upper arm circumference (Z)	1953	0.014	0.009	0.019	$1.3x10^{-7}$	0	0.485	1844	0.005	0.000	0.010	0.045	0	0.982
Triceps skinfold (Z)	1564	0.013	0.007	0.018	$3.6x10^{-6}$	44.6	0.144	1455	0.003	-0.001	0.009	0.181	61.7	0.050
Subscapular skinfold (Z)	1563	0.012	0.006	0.017	$2.4x10^{-5}$	42.3	0.158	1454	0.003	-0.002	0.008	0.260	25.7	0.258

Association analysis was performed using linear regression with standardized birth measures adjusted for sex and gestational age as the dependent variables for each cohort independently and finally the summary results were meta-analyzed. The effect size is in standard deviation units of the birth measure per unit change in genetic score. The South Asian populations include PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project from India; MBRC, Mysore Birth Records Cohort; Dhaka-WP2 of GIFTS; Dhaka-WP3 of GIFTS; UK-Bang, London UK Bangladeshi cohort. *, In MMNP, allocation group was additionally adjusted for, and in MBRC only sex was adjusted for since gestational age data was not available for the majority of the sample. N, number of term babies; L95, U95, 95% confidence interval; I^2, heterogeneity; Het-P, P value for heterozygosity; P, P value; fGS, fetal genetic score; mGS, maternal genetic score. The N was different for each trait due to missingness of some phenotype data in MBRC, Dhaka-WP2 and Dhaka-WP3.

Table 4: Meta-analysis of associations of fetal genetic score with anthropometric and cardiometabolic traits in early childhood, adolescence and adults in Indians

Traits	Children					Adolescents					Adults				
	N	Effect	P	I^2	Het-P	N	Effect	P	I^2	Het-P	N	Effect	P	I^2	Het-P
Weight (Z)	1866	0.008	0.001	0	0.830	1120	0.002	0.592	0	0.641	3311	0.002	0.341	0	0.698
Height (Z)	1865	0.006	0.017	0	0.846	1120	0.002	0.437	0	0.889	3307	0.003	0.037	0	0.574
Body mass index (Z)	1865	0.007	0.007	0	0.666	1120	0.001	0.844	0	0.581	3306	0.000	0.977	0	0.438
Head circumference (Z)	1866	0.007	0.003	0	0.999	1115	0.004	0.223	0	0.633	3256	0.006	$5.5x10^{-4}$	32.2	0.194
Waist circumference (Z)	1864	0.010	$5.5x10^{-5}$	0	0.463	1096	0.004	0.254	0	0.918	3251	0.001	0.528	13.8	0.326
Hip circumference (Z)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	3256	0.001	0.456	0	0.680
Waist to hip ratio (Z)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	3247	0.001	0.603	9.8	0.353
Mid upper arm circumference (Z)	1865	0.005	0.032	0	0.705	1112	0.000	0.976	0	0.595	3258	0.000	0.852	0	0.645
Triceps skinfold (Z)	1865	0.002	0.511	0	0.760	1114	0.002	0.487	0	0.790	3259	0.001	0.748	0	0.725
Subscapular skinfold (Z)	1865	0.003	0.280	52.2	0.123	1113	0.002	0.603	0	0.825	3238	-0.001	0.673	0	0.926
Fat percentage (Z)	1860	0.003	0.254	50.3	0.133	1085	0.002	0.475	45.8	0.174	NA	NA	NA	NA	NA
Systolic blood pressure (Z)*	1847	-0.002	0.411	0	0.410	1102	-0.005	0.112	88.6	0.003	3081	0.000	0.801	0	0.454
Diastolic blood pressure (Z)*	1848	0.000	0.989	0	0.765	1102	0.000	0.904	92.4	0.000	3082	0.000	0.922	0	0.467
Fasting glucose (Z)*	1840	-0.002	0.483	0	0.497	1110	0.000	0.908	92.8	0.000	2601	-0.006	$9.3x10^{-4}$	30.5	0.218
120 minutes glucose (Z)*	1809	0.002	0.321	0	0.434	NA	NA	NA	NA	NA	1320	0.000	0.905	0	0.707
Fasting insulin (Z)*	1831	0.002	0.369	18.9	0.291	1111	0.002	0.463	47.7	0.167	2596	-0.002	0.359	0	0.823
HOMA-IR (Z)*	1756	0.002	0.401	0	0.997	1110	0.002	0.407	74.4	0.048	2432	-0.005	0.022	0	0.802
Total cholesterol (Z)*	1838	-0.005	0.050	50.7	0.131	1111	0.004	0.224	0	0.488	2601	-0.003	0.118	0	0.968
LDL-cholesterol (Z)*	1847	-0.003	0.280	52.9	0.119	1111	0.006	0.070	0	0.676	2600	-0.001	0.594	0	0.957
HDL cholesterol (Z)*	1849	-0.005	0.059	0	0.513	1111	0.002	0.632	0	0.631	2584	0.000	0.867	0	0.809
Triglycerides (Z)*	1838	-0.001	0.666	0	0.668	1111	-0.002	0.440	37.8	0.205	2601	-0.006	0.002	0	0.673

Association analysis was performed using linear regression with standardized log10 transformed traits as the dependent variable for each cohort independently and finally the summary results were meta-analyzed. Age and sex were included as covariates in the regression model for all traits; BMI was additionally included as a covariate for analysis of traits marked with an asterisk (*). Allocation group was additionally adjusted for in MMNP. Meta-analysis for children included those from Pune Maternal Nutrition Study at 6 yrs, Parthenon Study at 5 yrs, and Mumbai Maternal Nutrition Project at 7 yrs of age; for adolescents from Pune Maternal Nutrition Study at 12 yrs and Parthenon Study at 13.5 yrs; and for adults from parents from Pune Maternal Nutrition Study and Parthenon Study, mothers from Mumbai Maternal Nutrition Project, and individuals from Mysore Birth Records Cohort; P, P value; I^2, heterogeneity; Het-P, P value for heterozygosity; SNP, single nucleotide polymorphism; HOMA-IR, homeostasis model assessment of insulin resistance, LDL, low density lipoprotein; HDL, high density lipoprotein, NA, not available. Those passing the Bonferroni corrected $P \leq 0.001$ were considered as statistically significant.

Figure titles and legends

Figure 1: Flow chart showing the overall study design including SNP selection, generation of weighted fetal and maternal genetic scores, association analysis and final meta-analyses at different stages of follow-up. SNP, single nucleotide polymorphism; SEM, structure equation model; EGG, Early Growth Genetics Consortium; UKBB, UK Biobank; PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort.

*, Warrington NM, et al. 2019 (15)

Figure 2: Meta-analysis of associations of fetal genetic score with birthweight in South Asian populations and comparison with European cohorts. Panel A-D: Fetal genetic score with birthweight. (A) Fetal genetic score adjusted for sex and gestational age; (B) Fetal genetic score adjusted for sex, gestational age and maternal genetic score; (C) Maternal genetic score adjusted for sex and gestational age and (D) Maternal genetic score adjusted for sex, gestational age and fetal genetic score. The X-axis indicates the effect size for standardized birthweight per unit of weighted genetic score. In MMNP, allocation group was additionally adjusted for and in MBRC, only sex was adjusted for, since gestational data was not available for the majority of the samples. **Panel E-F: Comparison between South Asians and European cohorts.** (E) Weighted fetal genetic score and (F) Weighted maternal genetic score. The X-axis indicates the effect size for birthweight in gram (g) per standardized weighted genetic score. PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MBRC, Mysore Birth Records Cohort; MMNP, Mumbai Maternal Nutrition Project; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort; UK Biobank

South Asian component (UKBB-SAS); EFSOCH, The Exeter Family Study of Childhood Health; fGS, fetal genetic score; mGS, weighted maternal genetic score; ES, effect size; CI, confidence interval; I^2, heterogeneity; p, p- value. Heterogeneity p value for fGS is 0.1777 and for mGS is 0.0046.

Figure 3: Scatter plot comparing the correlation between birthweight and fetal genetic score and maternal genetic score in South Asian and European cohorts. Panel A-B: **birthweight and fetal genetic score (fGS).** A, indicates absolute birthweight and fGS; B, shows the same between cohort-specific birthweight Z-scores and fGS; **Panel C-D**: **birthweight and maternal genetic score (mGS).** C, indicates absolute birthweight and mGS and D, shows the same between cohort-specific birthweight Z-scores and mGS.

South Asian cohorts include PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort) while EFSOCH (The Exeter Family Study of Childhood Health) is the European Cohort.

Figure 4: Birthweight and fetal genetic score associations with various anthropometric and cardiometabolic traits at different follow-up stages in the Indian cohorts. (A) Birthweight (B) fetal genetic score. The X-axis shows anthropometric and cardiometabolic traits at different stages of follow-up including birth, early childhood, early adolescence and adults. The Y-axis indicates the effect size in standard deviation units. HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; LDL, low density lipoprotein; HDL, high density lipoprotein. 'Early childhood 5-7 years' included children from Pune Maternal Nutrition Study at 6 yrs, Parthenon Study at 5 yrs, and Mumbai Maternal Nutrition Project at 7 yrs of age whereas adolescents from

Pune Maternal Nutrition Study at 12 yrs and Parthenon Study at 13.5 yrs formed the group 'Early adolescence 12-14 years'. 'Adults' consisted of parents from Pune Maternal Nutrition Study and Parthenon Study, mothers from Mumbai Maternal Nutrition Project, and individuals from Mysore Birth Records Cohort. @, P-value ≤ 0.001; #, P-value ≤ 0.01; *, P-value ≤ 0.05.

Figure 1

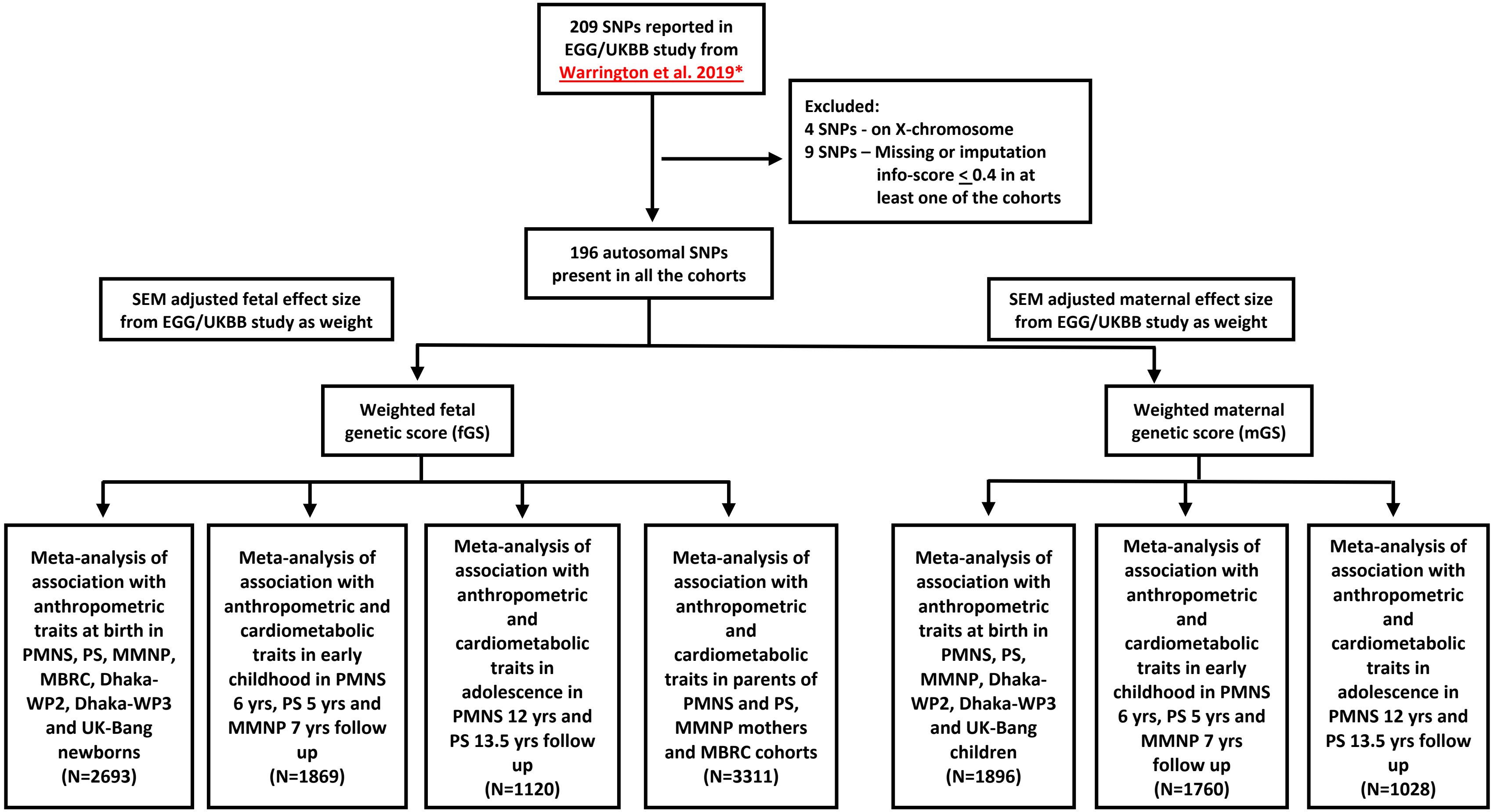

209 SNPs reported in EGG/UKBB study from Warrington et al. 2019*
Excluded:
4 SNPs - on X-chromosome
9 SNPs – Missing or imputation info-score < 0.4 in at least one of the cohorts
196 autosomal SNPs present in all the cohorts
SEM adjusted fetal effect size from EGG/UKBB study as weight
SEM adjusted maternal effect size from EGG/UKBB study as weight
Weighted fetal genetic score (fGS)
Weighted maternal genetic score (mGS)
Meta-analysis of association with anthropometric traits at birth in PMNS, PS, MMNP, MBRC, Dhaka-WP2, Dhaka-WP3 and UK-Bang newborns (N=2693)
Meta-analysis of association with anthropometric and cardiometabolic traits in early childhood in PMNS 6 yrs, PS 5 yrs and MMNP 7 yrs follow up (N=1869)
Meta-analysis of association with anthropometric and cardiometabolic traits in adolescence in PMNS 12 yrs and PS 13.5 yrs follow up (N=1120)
Meta-analysis of association with anthropometric and cardiometabolic traits in parents of PMNS and PS, MMNP mothers and MBRC cohorts (N=3311)
Meta-analysis of association with anthropometric traits at birth in PMNS, PS, MMNP, Dhaka-WP2, Dhaka-WP3 and UK-Bang children (N=1896)
Meta-analysis of association with anthropometric and cardiometabolic traits in early childhood in PMNS 6 yrs, PS 5 yrs and MMNP 7 yrs follow up (N=1760)
Meta-analysis of association with anthropometric and cardiometabolic traits in adolescence in PMNS 12 yrs and PS 13.5 yrs follow up (N=1028)

Figure 2

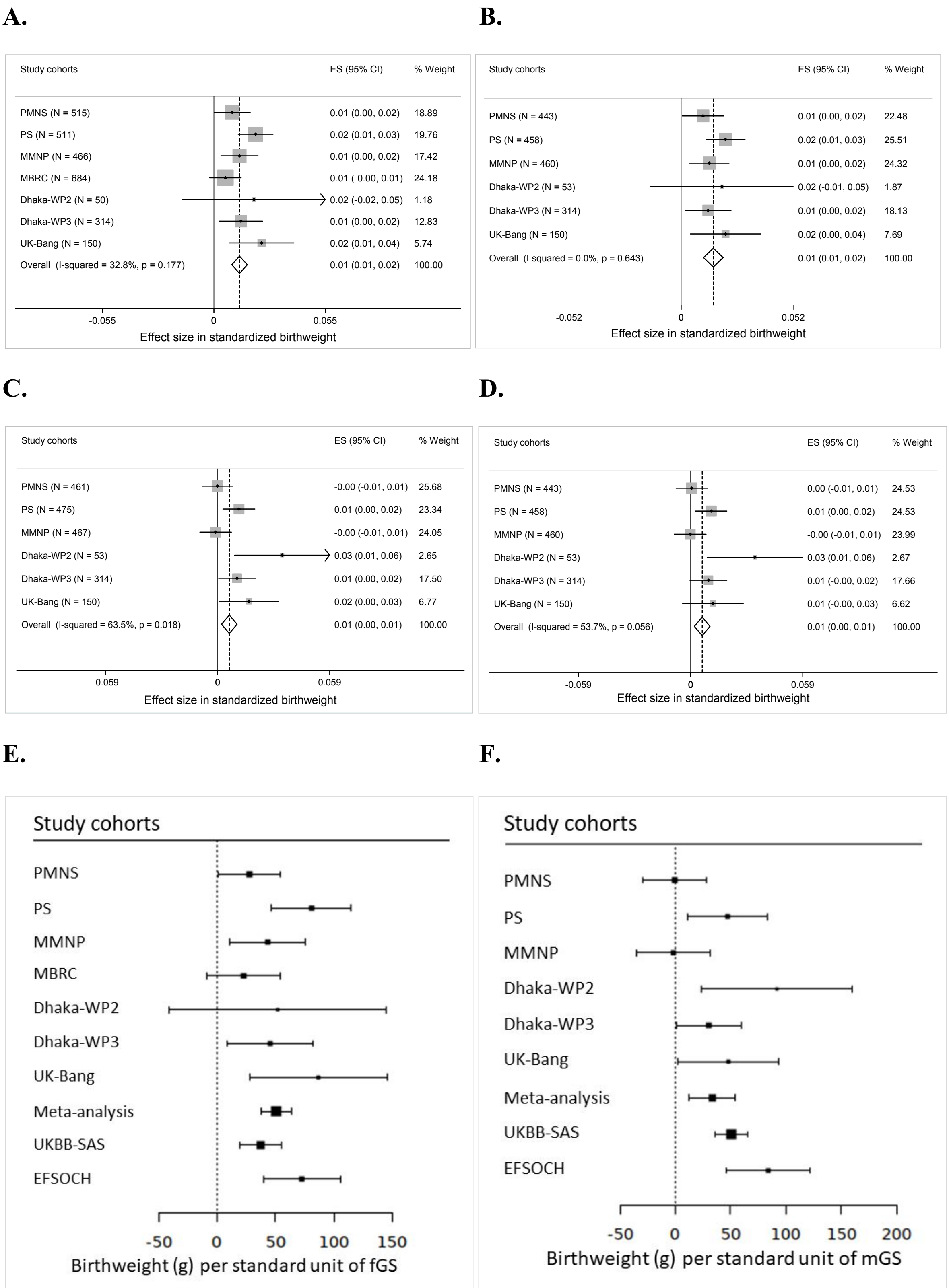

A.
Study cohorts
ES (95% CI)
% Weight
PMNS (N = 515) 0.01 (0.00, 0.02) 18.89
PS (N = 511) 0.02 (0.01, 0.03) 19.76
MMNP (N = 466) 0.01 (0.00, 0.02) 17.42
MBRC (N = 684) 0.01 (-0.00, 0.01) 24.18
Dhaka-WP2 (N = 50) 0.02 (-0.02, 0.05) 1.18
Dhaka-WP3 (N = 314) 0.01 (0.00, 0.02) 12.83
UK-Bang (N = 150) 0.02 (0.01, 0.04) 5.74
Overall (I-squared = 32.8%, p = 0.177) 0.01 (0.01, 0.02) 100.00
-0.055
0
0.055
Effect size in standardized birthweight
B.
Study cohorts
ES (95% CI)
% Weight
PMNS (N = 443) 0.01 (0.00, 0.02) 22.48
PS (N = 458) 0.02 (0.01, 0.03) 25.51
MMNP (N = 460) 0.01 (0.00, 0.02) 24.32
Dhaka-WP2 (N = 53) 0.02 (-0.01, 0.05) 1.87
Dhaka-WP3 (N = 314) 0.01 (0.00, 0.02) 18.13
UK-Bang (N = 150) 0.02 (0.00, 0.04) 7.69
Overall (I-squared = 0.0%, p = 0.643) 0.01 (0.01, 0.02) 100.00
-0.052
0
0.052
Effect size in standardized birthweight
C.
Study cohorts
ES (95% CI)
% Weight
PMNS (N = 461) -0.00 (-0.01, 0.01) 25.68
PS (N = 475) 0.01 (0.00, 0.02) 23.34
MMNP (N = 467) -0.00 (-0.01, 0.01) 24.05
Dhaka-WP2 (N = 53) 0.03 (0.01, 0.06) 2.65
Dhaka-WP3 (N = 314) 0.01 (0.00, 0.02) 17.50
UK-Bang (N = 150) 0.02 (0.00, 0.03) 6.77
Overall (I-squared = 63.5%, p = 0.018) 0.01 (0.00, 0.01) 100.00
-0.059
0
0.059
Effect size in standardized birthweight
D.
Study cohorts
ES (95% CI)
% Weight
PMNS (N = 443) 0.00 (-0.01, 0.01) 24.53
PS (N = 458) 0.01 (0.00, 0.02) 24.53
MMNP (N = 460) -0.00 (-0.01, 0.01) 23.99
Dhaka-WP2 (N = 53) 0.03 (0.01, 0.06) 2.67
Dhaka-WP3 (N = 314) 0.01 (-0.00, 0.02) 17.66
UK-Bang (N = 150) 0.01 (-0.00, 0.03) 6.62
Overall (I-squared = 53.7%, p = 0.056) 0.01 (0.00, 0.01) 100.00
-0.059
0
0.059
Effect size in standardized birthweight
E.
Study cohorts
PMNS
PS
MMNP
MBRC
Dhaka-WP2
Dhaka-WP3
UK-Bang
Meta-analysis
UKBB-SAS
EFSOCH
-50 0 50 100 150
Birthweight (g) per standard unit of fGS
F.
Study cohorts
PMNS
PS
MMNP
Dhaka-WP2
Dhaka-WP3
UK-Bang
Meta-analysis
UKBB-SAS
EFSOCH
-50 0 50 100 150 200
Birthweight (g) per standard unit of mGS

Figure 3

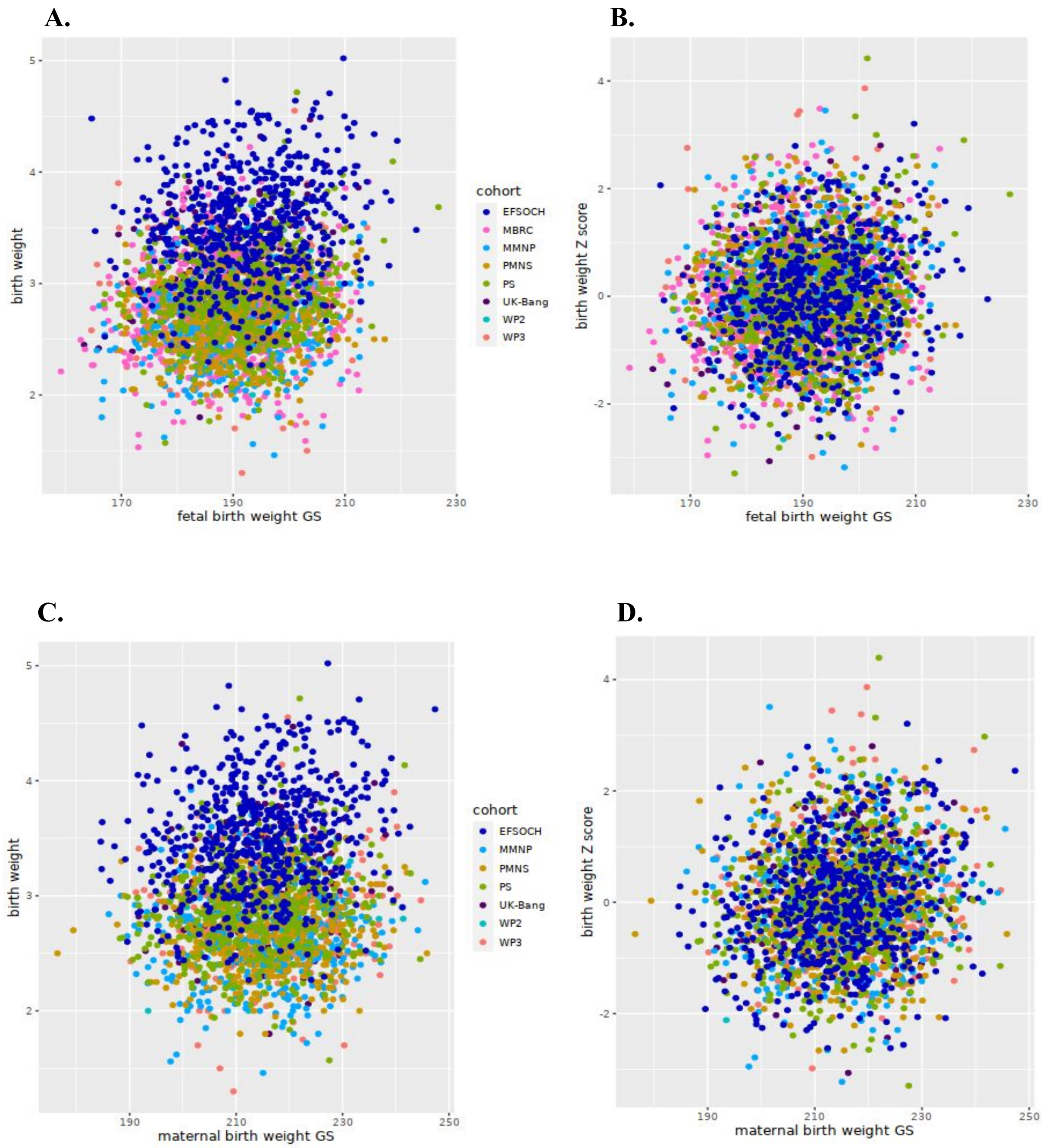
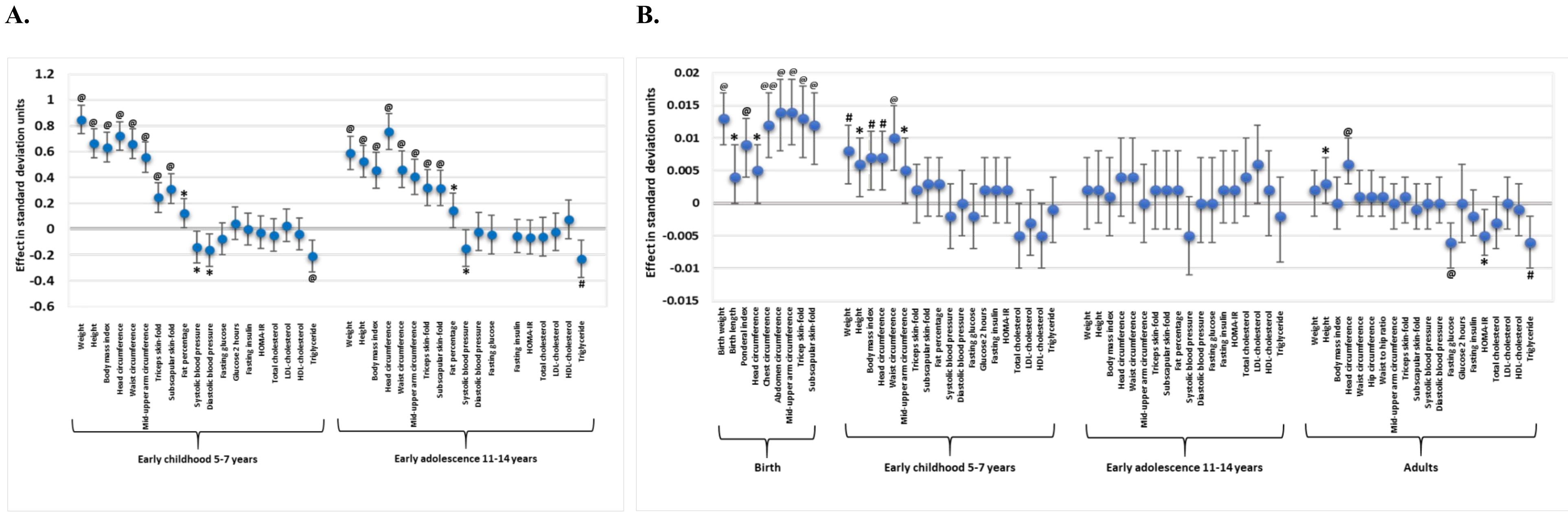
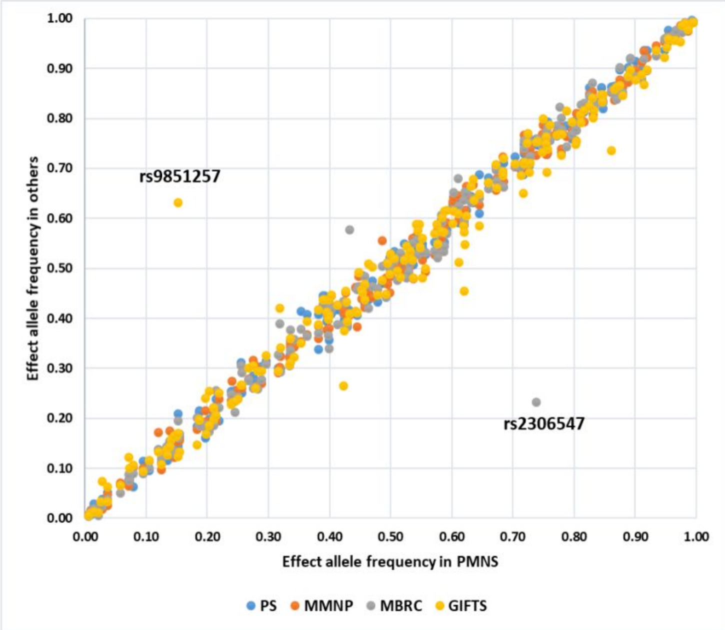

A.
B.
C.
D.
birth weight
fetal birth weight GS
birth weight Z score
maternal birth weight GS
cohort
EFSOCH
MBRC
MMNP
PMNS
PS
UK-Bang
WP2
WP3
170
190
210
230
250

Figure 4

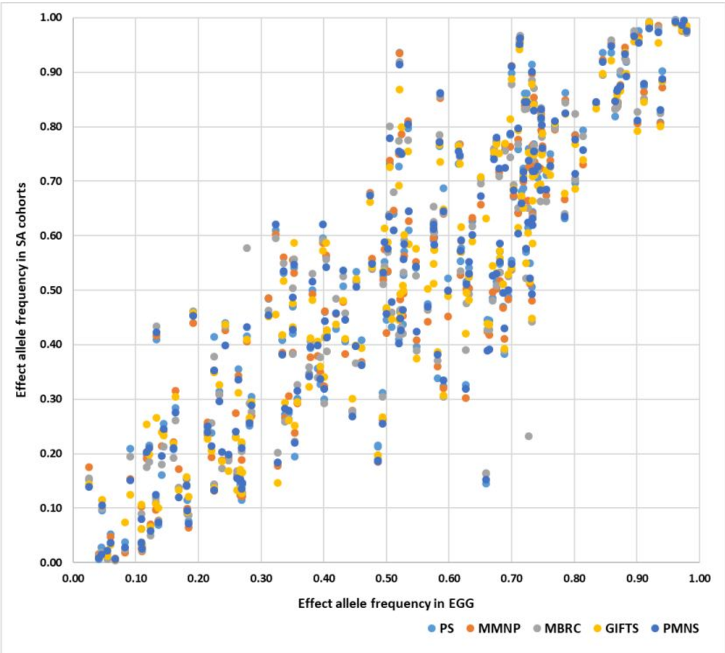

A.
B.
Effect in standard deviation units
Early childhood 5-7 years
Early adolescence 11-14 years
Birth
Adults

Supplementary Figures

A.



B.



Supplementary Figure 1: Comparison of the effect allele frequency of 196 birthweight-associated single nucleotide polymorphisms between EGG/UKBB and cohorts from South Asia (PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; GIFTS, Bangladeshi Cohorts which included Dhaka-WP2, Dhaka-WP3 and UK-Bang). (A) Between South Asian cohorts. PMNS is on the X-axis and the other South Asian cohorts are on the Y-axis, each marked with specific colours. The variants rs9851257 and rs2306547 are outliers in GIFTS and MBRC cohorts respectively. (B) Between EGG/UKBB and South Asians. EGG/UKBB is on the X-axis and the South Asian cohorts are on the Y-axis, each indicated by specific colours. EGG, Early Growth Genetics Consortium; UKBB, UK Biobank.

Supplementary Tables

Supplementary Table 2: Newborn and maternal anthropometry in the Indian cohorts

Traits	PMNS			PS			MMNP			MBRC		
	Boys (N=271)	Girls (N=244)	All (N=515)	Boys (N=245)	Girls (N=266)	All (N=511)	Boys (N=271)	Girls (N=210)	All (N=481)	Boys (N=385)	Girls (N=299)	All (N=684)
Birthweight (kg)	2.74 (0.33)	2.62 (0.34)	2.68 (0.34)	2.96 (0.43)	2.87 (0.38)	2.91 (0.41)	2.67 (0.37)	2.59 (0.37)	2.64 (0.37)	2.81 (0.43)	2.71 (0.39)	2.76 (0.42)
Birth length (cm)	48.2 (1.94)	47.4 (1.92)	47.8 (1.97)	49.1 (2.13)	48.6 (2.05)	48.8 (2.11)	48.5 (2.29)	47.7 (2.14)	48.2 (2.26)	48.26 (3.00)	47.7 (2.85)	48.0 (2.95)
Ponderal index (kg/m^3)	24.4 (2.17)	24.6 (2.71)	24.5 (2.44)	24.9 (2.68)	25.1 (2.82)	25.0 (2.75)	23.4 (2.35)	23.9 (2.83)	23.6 (2.58)	25.3 (4.6)	25.4 (5.16)	25.3 (4.85)
Head circumference (cm)	33.4 (1.18)	32.7 (1.20)	33.1 (1.24)	34.2 (1.31)	33.6 (1.19)	33.9 (1.28)	33.5 (1.20)	32.9 (1.13)	33.2 (1.21)	33.7 (1.63)	33.3 (1.50)	33.6 (1.58)
Chest circumference (cm)	31.4 (1.56)	31.0 (1.59)	31.2 (1.59)	32.1 (1.68)	32.0 (1.6)	32.0 (1.64)	31.0 (1.83)	30.7 (1.69)	30.9 (1.77)	NA	NA	NA
Abdominal circumference (cm)	28.8 (1.93)	28.7 (1.89)	28.7 (1.91)	30.0 (2.01)	30.0 (1.83)	30.0 (1.92)	28.5 (2.07)	28.4 (2.08)	28.4 (2.07)	NA	NA	NA

Mid-upper arm circumference (cm)	9.7 (0.87)	9.6 (0.89)	9.7 (0.88)	10.4 (0.94)	10.3 (0.89)	10.4 (0.92)	9.7 (0.80)	9.7 (0.86)	9.7 (0.82)	NA	NA	NA
Triceps skinfold (mm)	4.2 (0.87)	4.3 (0.87)	4.3 (0.87)	4.2 (0.91)	4.3 (0.89)	4.2 (0.90)	4.1 (0.98)	4.3 (1.11)	4.2 (1.04)	NA	NA	NA
Subscapular skinfold (mm)	4.2 (0.88)	4.3 (0.91)	4.2 (0.89)	4.4 (0.89)	4.6 (0.93)	4.5 (0.91)	4.0 (0.93)	4.3 (1.03)	4.2 (0.98)	NA	NA	NA
Gestational age (weeks)	39.1 (1.05)	39.0 (1.06)	39.1 (1.06)	39.4 (1.20)	39.6 (1.07)	39.5 (1.14)	39.3 (1.18)	39.3 (1.15)	39.3 (1.17)	NA	NA	NA
Maternal age (years)	21.4 (3.48)	21.4 (3.65)	21.4 (3.56)	23.8 (4.16)	23.8 (4.31)	23.8 (4.24)	24.7 (3.94)	24.77 (3.77)	24.73 (3.86)	NA	NA	NA
Maternal BMI (kg/m^2)	18.2 (1.93)	17.9 (1.87)	18.1 (1.90)	23.4 (3.51)	23.8 (3.58)	23.6 (3.55)	20.2 (3.54)	20.4 (3.86)	20.3 (3.68)	NA	NA	NA

The values are mean (SD). N, number of term babies with both genotype and phenotype data available; BMI, body mass index; SD, standard deviation; NA, not available.

PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort.

Supplementary Table 3: Newborn and maternal anthropometry in the Bangladeshi cohorts

Traits	Dhaka-WP2			Dhaka-WP3			UK-Bang		
	Boys (N=29)	Girls (N=24)	All (N=53)	Boys (N=162)	Girls (N=152)	All (N=314)	Boys (N=71)	Girls (N=72)	All (N=151)
Birthweight (kg)	2.99 (0.36)	2.80 (0.39)	2.90 (0.38)	2.90 (0.39)	2.77 (0.43)	2.84 (0.42)	3.18 (0.48)	3.06 (0.41)	3.12 (0.45)
Birth length (cm)	46.5 (2.81)	45.9 (2.23)	46.2 (2.56)	49.8 (2.58)	49.4 (2.61)	49.6 (2.60)	47.1 (1.84)	46.2 (2.08)	46.7 (2.03)
Ponderal index (kg/m^3)	29.9 (4.84)	28.9 (3.89)	29.5 (4.42)	23.6 (3.50)	23.0 (3.49)	23.3 (3.50)	28.7 (4.48)	29.1 (4.21)	28.9 (4.27)
Head circumference (cm)	33.7 (1.49)	33.0 (1.18)	33.4 (1.39)	33.1 (3.01)	32.7 (1.49)	32.9 (2.40)	34.0 (1.08)	33.1 (1.39)	33.6 (1.31)
Chest circumference (cm)	NA	NA	NA	NA	NA	NA	33.55 (2.37)	33.25 (1.46)	33.4 (1.97)

Abdominal circumference (cm)	NA	NA	NA	NA	NA	NA	31.86 (2.60)	30.95 (2.47)	31.41 (2.56)
Mid-upper arm circumference (cm)	10.0 (0.68)	9.7 (0.74)	9.9 (0.71)	10.5 (2.76)	10.0 (0.94)	10.2 (2.09)	11.4 (2.16)	10.3 (1.96)	10.9 (2.13)
Triceps skinfold (mm)	NA	NA	NA	NA	NA	NA	4.8 (2.08)	5.2 (1.80)	5.0 (1.93)
Subscapular skinfold (mm)	NA	NA	NA	NA	NA	NA	5.2 (2.02)	5.3 (1.75)	5.3 (1.87)
Gestational age (week)	40.2 (0.86)	40.4 (1.47)	40.3 (1.17)	39.2 (1.42)	39.2 (1.63)	39.2 (1.53)	38.7 (4.61)	39.2 (1.23)	39.0 (3.44)
Maternal Age (years)	20.07 (2.36)	19.83 (2.66)	19.91 (2.45)	22.74 (4.00)	22.66 (4.60)	22.68 (4.29)	29.22 (5.47)	30.19 (5.31)	29.68 (5.40)
Maternal BMI (kg/m^2)	20.10 (3.36)	21.36 (3.40)	20.58 (3.40)	22.39 (4.12)	22.91 (3.92)	22.65 (4.03)	25.75 (4.02)	26.79 (4.65)	26.24 (4.34)

The values are mean (SD). N, number of term babies with both genotype and phenotype data available; BMI, body mass index; SD, standard deviation; NA, not available; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort.

Supplementary Table 4: Body size and composition, and cardiometabolic measures during childhood and early adolescence in the Indian cohorts

Traits	Childhood			Early adolescence	
	PMNS (N=608)	PS (N=562)	MMNP (N=696)	PMNS (N=604)	PS (N=516)
Age (years)	6.17 (0.21)	5.0 (0.04)	5.85 (0.32)	11.6 (0.93)	13.53 (0.14)
Weight (kg)	16.2 (1.9)	15.2 (1.9)	16.2 (2.5)	29.3 (6.8)	41.9 (8.6)
Height (cm)	109.9 (4.7)	105.6 (4.2)	109.6 (4.9)	139.6 (8.4)	153.7 (6.9)
Body mass index (kg/m^2)	13.4 (0.9)	13.6 (1.1)	13.4 (1.4)	14.9 (2.1)	17.7 (3.1)
Head circumference (cm)	48.6 (1.5)	48.5 (1.4)	48.7 (1.5)	51.3 (1.8)	51.4 (1.4)
Waist circumference (cm)	50.3 (2.6)	45.9 (3.0)	49.1 (3.6)	57.4 (5.8)	66.3 (7.9)
Mid-upper arm circumference (cm)	15.2 (1.1)	15.3 (1.2)	15.4 (1.4)	18.8 (3.1)	22.1 (2.8)
Triceps skinfold (mm)	6.3 (1.4)	8.0 (2.1)	7.4 (2.0)	7.8 (3.3)	13.3 (5.7)
Subscapular skinfold (mm)	5.1 (1.1)	6.2 (1.9)	5.9 (1.7)	6.9 (3.9)	13.9 (7.1)
Fat percent (%)	19.6 (5.5)	25.5 (5.5)	15.3 (5.2)	16.7 (6.6)	21.7 (7.5)
Systolic blood pressure (mm Hg)	90.4 (12.2)	96.6 (8.3)	92.1 (8.5)	106.3 (10.0)	109.4 (8.1)
Diastolic blood pressure (mm Hg)	53.6 (10.2)	58.1 (6.8)	56.1 (7.6)	62.6 (6.8)	61.2 (7.0)
Fasting glucose (mmol/L)	4.9 (0.5)	4.8 (0.5)	4.8 (0.7)	4.8 (0.4)	5.0 (0.5)
120 minutes glucose(mmol/L)	5.5 (1.1)	5.9 (1.0)	4.7 (0.9)	NA	NA
Fasting insulin (pmol/L)	25.70 (17.22)	28.89 (21.95)	28.96 (35.98)	40.91 (22.64)	45.07 (29.03)
HOMA-IR	0.82 (0.6)	0.89 (0.7)	0.63 (0.6)	1.27 (0.8)	1.69 (1.2)
Total cholesterol (mmol/L)	3.3 (0.6)	3.5 (0.7)	3.8 (0.9)	3.4 (0.6)	3.5 (0.7)
LDL-cholesterol (mmol/L)	1.9 (0.5)	1.1 (0.3)	2.3 (0.7)	2.0 (0.5)	2.1 (0.5)
HDL-cholesterol (mmol/L)	1.1 (0.3)	2.1 (1.0)	1.0 (0.2)	1.1 (0.2)	1.1 (0.3)
Triglycerides (mmol/L)	0.7 (0.3)	0.6 (0.3)	0.9 (0.4)	0.7 (0.2)	0.8 (0.4)

Values are mean (SD). N, Number of individuals where both genotype and phenotype data are available (variable with different traits). PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; HOMA-IR, homeostasis model assessment of insulin resistance, LDL, low density lipoprotein; HDL, high density lipoprotein; NA, not available.

Supplementary Table 5: Body size and composition, and cardiometabolic measures in the Indian adult cohorts

Traits	PMNS Mother (N=543)	PMNS Father (N=402)	PS Mother (N=525)	PS Father (N=499)	MMNP Mother (N=691)	MBRC (N=684)
Age (years)	27.9 (3.5)	39.4 (4.11)	28.9 (4.3)	36.4 (4.71)	32.9 (4.48)	62.2 (5.42)
Weight (kg)	44.4 (6.8)	59.9 (11.0)	56.4 (11.1)	67.1 (11.1)	55.0 (11.4)	66.56 (13.82)
Height (cm)	153.0 (5.1)	165.5 (6.1)	154.5 (5.3)	167.6 (6.3)	152.3 (5.5)	158.4 (9.7)
Body mass index (kg/m^2)	18.9 (2.7)	21.8 (3.6)	23.6 (4.5)	23.9 (3.6)	23.7 (4.7)	26.6 (5.3)
Head circumference (cm)	53.0 (1.5)	54.6 (1.6)	52.4 (1.5)	54.7 (1.6)	52.4 (1.4)	53.2 (1.7)
Waist circumference (cm)	65.8 (7.2)	80.1 (9.6)	82.2 (11.8)	86.2 (10.3)	77.7 (11.4)	93.0 (12.3)
Hip circumference (cm)	85.5 (7.2)	88.5 (6.9)	92.4 (8.7)	92.8 (7.3)	87.8 (7.8)	95.7 (11.2)
Waist to hip ratio	0.77 (0.07)	0.90 (0.07)	0.89 (0.07)	0.93 (0.06)	69.7 (9.52)	0.98 (0.11)
Mid upper arm circumference (cm)	23.5 (2.4)	26.4 (2.6)	26.6 (3.6)	28.6 (2.8)	26.5 (3.9)	29.5 (3.9)
Triceps skinfold (mm)	9.7 (4.6)	8.8 (4.3)	23.0 (9.7)	13.3 (5.6)	18.5 (7.2)	19.3 (7.7)
Subscapular skinfold (mm)	12.8 (6.5)	12.4 (6.0)	31.0 (12.6)	26.1 (11.3)	27.8 (11.5)	31.3 (9.8)

Systolic blood pressure (mmHg)*	107.3 (9.6)	110.6 (9.2)	108.7 (11.2)	116.9 (14.7)	107.6 (12.2)	127.0 (15.5)
Diastolic blood pressure (mmHg)*	63.7 (6.9)	63.7 (8.1)	65.7 (9.1)	73.6 (11.1)	67.2 (9.6)	75.2 (10.7)
Fasting glucose (mmol/L)*	5.2 (1.0)	5.2 (1.0)	5.6 (1.2)	6.0 (2.0)	NA	7.2 (3.0)
120 minutes glucose(mmol/L)*	5.5 (1.6)	5.2 (2.2)	6.4 (2.8)	NA	NA	NA
Fasting insulin (pmol/L)*	34.73 (25.77)	47.02 (33.20)	60.56 (39.31)	60.77 (39.24)	NA	90.49 (91.54)
HOMA-IR*	1.19 (0.93)	1.63 (1.5)	2.18 (1.6)	2.45 (2.2)	NA	4.03 (3.8)
Total cholesterol (mmol/L)*	3.6 (0.7)	4.0 (0.8)	4.1 (0.8)	4.6 (1.0)	NA	4.7 (1.1)
LDL-cholesterol (mmol/L)*	2.1 (0.6)	2.5 (0.7)	2.5 (0.6)	2.7 (0.8)	NA	2.8 (0.9)
HDL-cholesterol (mmol/L)*	1.2 (0.3)	1.1 (0.3)	1.1 (0.2)	1.0 (0.2)	NA	1.2 (0.3)
Triglycerides (mmol/L)*	0.7 (0.4)	1.1 (0.6)	1.2 (0.7)	2.0 (1.4)	NA	1.7 (0.9)

Values are mean (SD). N, Number of individuals with genotype phenotype data available and this can be variable with different traits. BMI was additionally included as a covariate for analysis of traits marked with an asterisk (*). SD, standard deviation; PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; HOMA-IR, homeostatic model assessment insulin resistance; LDL, low density lipoprotein; HDL, high density lipoprotein; NA, not available.

Supplementary Table 6: Associations of fetal genetic score with birthweight in South Asian populations (excluding GDM mothers)

Cohort	fGS adjusted for sex and GA[@]				fGS adjusted for sex, GA, and mGS[#]			
	N	Effect	SE	P	N	Effect	SE	P
PMNS	512	0.009	0.004	0.048	441	0.010	0.005	0.047
PS	480	0.023	0.005	$3.0x10^{-7}$	428	0.023	0.005	$1.3x10^{-6}$
MMNP*	434	0.012	0.005	0.012	428	0.013	0.005	0.009
Dhaka-WP2	40	0.010	0.009	0.286	40	0.009	0.008	0.266
Dhaka-WP3	233	0.004	0.003	0.200	233	0.004	0.003	0.218
UK-Bang	75	0.012	0.006	0.058	75	0.011	0.007	0.094
Meta-analysis	1774	0.010	0.002	$5.1x10^{-8}$	1645	0.010	0.002	$1.8x10^{-7}$

@, I^2= 64.90%, Het-P=0.014 and #, I^2=62.50%, Het-P=0.02

Supplementary Table 7: Associations of maternal genetic score with birthweight in South Asian populations (excluding GDM mothers)

Cohort	mGS adjusted for sex and GA[@]				mGS adjusted for sex, GA, and fGS[#]			
	N	Effect	SE	P	N	Effect	SE	P
PMNS	459	0.000	0.004	0.975	441	0.001	0.004	0.881
PS	444	0.010	0.004	0.031	428	0.010	0.004	0.020
MMNP*	428	0.000	0.004	0.946	428	0.001	0.004	0.874
Dhaka-WP2	40	0.020	0.008	0.019	40	0.020	0.008	0.019
Dhaka-WP3	233	0.004	0.003	0.256	233	0.003	0.003	0.280
UK-Bang	75	0.009	0.007	0.217	75	0.006	0.007	0.386
Meta-analysis	1679	0.005	0.002	0.014	1645	0.005	0.002	0.011

@, I^2=34.30%, Het-P=0.179 and #, I^2=30%, Het-P=0.210

Association analysis was performed using linear regression, with standardized birthweight adjusted for sex and gestational age as the dependent variable for each cohort separately, and finally the summary results were meta-analyzed. *In MMNP, the allocation group was additionally adjusted for. The effect size is in standard deviation units. The standard deviation of birthweight in kg in all the cohorts ranged between 0.34 to 0.45 kg. N, number of term babies; GA, gestational age; SE, standard error; I^2, heterogeneity; Het-P, P value for heterozygosity; P, P value; mGS, maternal genetic score; fGS, fetal genetic score; GDM; gestational diabetes mellitus; PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort.

Supplementary Table 8: Country-wise meta-analysis of association of fetal genetic score with own birthweight

Cohort	fGS adjusted for sex and GA				fGS adjusted for sex, GA and mGS			
	N	Effect	SE	P	N	Effect	SE	P
Indians	2176	0.012	0.002	8.9×10^{-8}	1361	0.015	0.003	6.4×10^{-8}
Bangladeshis	517	0.017	0.004	1.4×10^{-4}	517	0.015	0.004	5.5×10^{-4}

Supplementary Table 9: Country-wise meta-analysis of association of maternal genetic score with offspring birthweight

Cohort	mGS adjusted for sex and GA				mGS adjusted for sex, GA and fGS			
	N	Effect	SE	P	N	Effect	SE	P
Indians	1386	0.003	0.003	0.197	1361	0.004	0.0026	0.128
Bangladeshis	517	0.014	0.004	4.0×10^{-4}	517	0.012	0.004	0.002

Association analysis was performed using linear regression with standardized birthweight adjusted for sex and gestational age as the dependent variable for each cohort independently and finally the summary results were meta-analyzed. In MMNP, the allocation group was additionally adjusted for. The effect size is in standard deviation units of birthweight per unit change in genetic score. The standard deviation of birthweight ranged from 0.34 to 0.45 kg. N, number of term babies having both genotype and phenotype date; SNP, single nucleotide polymorphism; GA, gestational age; SE, standard error; P, P value; fGS, fetal genetic score; mGS, maternal genetic score. Indians include Pune Maternal Nutrition Study (PMNS), Parthenon Study (PS), Mumbai Maternal Nutrition Project (MMNP) and Mysore Birth Records Cohort (MBRC). Bangladeshis include Work Package 2 of GIFTS (Dhaka-WP2), Work Package 3 of GIFTS (Dhaka-WP3), and UK-Bang, London UK Bangladeshi cohort.

Supplementary Table 10: Associations of fetal and maternal genetic scores with other birth measurements in South Asian populations

Trait	fGS adjusted for sex, GA and mGS							mGS adjusted for sex, GA and fGS						
	N	Effect	L95	U95	P	I^2	Het-P	N	Effect	L95	U95	P	I^2	Het-P
Birth length	1795	0.007	0.002	0.012	0.011	0	0.558	1795	0.003	-0.002	0.008	0.222	37.5	0.156
Ponderal Index	1771	0.011	0.005	0.016	$3.3x10^{-4}$	39.7	0.141	1771	0.001	-0.004	0.006	0.713	0	0.441
Head circumference	1819	0.010	0.005	0.015	$2.3x10^{-4}$	0	0.722	1819	0.002	-0.002	0.007	0.320	0	0.970
Chest circumference	1452	0.013	0.007	0.018	$2.8x10^{-6}$	12.0	0.333	1452	0.002	-0.002	0.007	0.321	0	0.467
Abdominal circumference	1452	0.015	0.010	0.021	$6.9x10^{-8}$	52.1	0.099	1452	0.002	-0.003	0.007	0.463	52.2	0.099
Mid-upper arm circumference	1819	0.014	0.009	0.020	$2.5x10^{-7}$	0	0.575	1819	0.005	0.000	0.010	0.034	0	0.992
Triceps skinfold	1430	0.013	0.007	0.018	$1.6x10^{-5}$	11.8	0.334	1430	0.004	-0.001	0.009	0.161	55.4	0.081
Subscapular skinfold	1429	0.012	0.007	0.018	$2.4x10^{-5}$	0	0.518	1429	0.003	-0.002	0.008	0.225	14.8	0.318

Association analysis was performed using linear regression with standardized birth measures adjusted for sex and gestational age as dependent variables, for each cohort independently and finally the summary results were meta-analyzed. In MMNP, the allocation group was additionally adjusted for, and in MBRC only sex was adjusted for, since gestational data was not available for the majority of the sample. The effect size is in standard deviation units. The South Asian populations include (from India) the PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; and MBRC, Mysore Birth Records Cohort; (from Bangladesh) WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; and (from the UK) the UK-Bang, London UK Bangladeshi cohort. N, number of term babies having both genotype and phenotype date; SNP, single nucleotide polymorphism; GA, gestational age; L95 and U95, 95% confidence interval; I^2, heterogeneity; Het-P, P value for heterogeneity; P, P value; fGS, fetal genetic score; mGS, maternal genetic score.

Supplementary Table 11: Details of LD SNP pairs with r2≥0.01 in 1000Genome Phase 3 South Asians

CHR	SNP1	BP (hg19)_SNP1	Nearest gene_SNP1	SNP2	BP (hg19)_SNP2	Nearest gene_SNP2	r2
1	rs905938	154991389	DCST2/KCNN3	rs670523	155878732	RIT1/LMNA	0.015
2	rs10495563	9662210	ADAM17	rs11893688	9695282	ADAM17	0.975
2	rs17034876	46484310	EPAS1	rs4953353	46567276	EPAS1	0.012
3	rs11708067	123065778	ADCY5	rs9851257	123125711	ADCY5	0.11
4	rs4144829	17903654	LCORL/DCAF16	rs2174633	17917781	LCORL/DCAF16	0.94
4	rs2189234	106075498	TET2	rs6533183	106133184	TET2	0.14
4	rs6845999	145565826	LOC646576/HHIP	rs2131354	145599908	LOC646576/HHIP	0.928
5	rs6871635	133830395	PHF15	rs1981627	133838180	PHF15	0.324
6	rs9366778	31269173	HLA-C	rs6911024	31368451	MICA/HLA-C	0.01
6	rs75104038	34190104	HMGA1	rs75034466	34199815	HMGA1	0.211
6	rs6911621	35529025	FKBP5/MAPK13/TEAD3	rs9348981	35687249	FKBP5/MAPK13/TEAD3	0.039
6	rs6569647	130337266	L3MBTL3	rs1415701	130345835	L3MBTL3	0.586
6	rs10872678	152039964	ESR1	rs7772579	152042502	ESR1	1.000
7	rs1724889	2741021	AMZ1/GNA12	rs4719648	2756832	AMZ1/GNA12	0.083
7	rs59084784	22739562	IL6	rs7808457	22798265	IL6	0.128

7	rs2908279	44174857	MYL7/GCK	rs2971669	44231778	GCK	0.042
7	rs13231367	127509070	SND1	rs6467157	127660763	SND1	0.857
8	rs732563	23345526	ENTPD4/NKX3-1	rs11778247	23403378	SLC25A37	0.081
8	rs13257363	142252580	SLC45A4	rs9657468	142362391	GPR20	0.014
9	rs1411424	113892963	LPAR1	rs2418135	113901309	LPAR1	0.811
10	rs5030938	70975916	HKDC1/HK1	rs9645500	70986723	HKDC1/HK1	0.851
10	rs10509669	95969913	PLCE1	rs2274224	96039597	PLCE1	0.22
10	rs3740360	96025491	PLCE1	rs2274224	96039597	PLCE1	0.063
10	rs7076938	115789375	ADRB1	rs1801253	115805056	ADRB1	0.804
11	rs12574749	32405355	WT1	rs5030317	32410337	WT1	0.674
11	rs10437653	46297631	CREB3L1	rs10734564	48160429	PTPRJ	0.029
12	rs8756	66359752	HMGA2	rs7968682	66371880	HMGA2	0.994
12	rs8756	66359752	HMGA2	rs1480470	66412130	HMGA2	0.022
12	rs7968682	66371880	HMGA2	rs1480470	66412130	HMGA2	0.022
15	rs7183988	91428589	FES/FURIN	rs4932373	91429287	FES/FURIN	0.453
17	rs222857	7164563	CLDN7/SLC2A4	rs2428362	7180274	CLDN7/SLC2A4	0.751
17	rs73354194	79905947	MYADML2	rs9912553	79959703	ASPSCR1	0.083

CHR, chromosome; BP, base pair; SNP, single nucleotide polymorphism; LD, linkage disequilibrium; r2, squared coefficient of correlation.

Supplementary Table 12: Details of 167 LD-pruned independent SNPs included for sensitivity analysis of fetal genetic and maternal genetic scores

SNP*	CHR	BP (hg19)	Nearest gene	Fetal_LD_pruned SNPs#	Maternal_LD_pruned SNPs#
rs17367504	1	11862778	*MTHFR*	YES	YES
rs12401656	1	43456767	*FLJ32224/SLC2A1*	YES	YES
rs80278614	1	119412317	*TBX15*	YES	YES
rs905938	1	154991389	*DCST2/KCNN3*	NO	NO
rs670523	1	155878732	*RIT1/LMNA*	YES	YES
rs72480273	1	161644871	*FCGR2B/FCGR2C/HSPA6*	YES	YES
rs10913200	1	176521655	*PAPPA2*	YES	YES
rs61830764	1	212289976	*DTL*	YES	YES
rs3806315	1	214724668	*PTPN14*	YES	YES
rs708122	1	228216997	*WNT3A*	YES	YES
rs10495563	2	9662210	*ADAM17*	YES	NO
rs11893688	2	9695282	*ADAM17*	NO	YES
rs2551347	2	23912401	*KLHL29*	YES	YES

rs1179494	2	36809496	*FEZ2*	YES	YES
rs754868	2	43185532	*HAAO*	YES	YES
rs4952673	2	43423870	*ZFP36L2*	YES	YES
rs17034876	2	46484310	*EPAS1*	NO	NO
rs4953353	2	46567276	*EPAS1*	YES	YES
rs560887	2	169763148	*G6PC2*	YES	YES
rs2280235	2	191843830	*STAT1*	YES	YES
rs10181515	2	227019461	*LOC646736/COL4A4/IRS1*	YES	YES
rs9855896	3	14287150	*LSM3*	YES	YES
rs2168443	3	46947087	*PTH1R*	YES	YES
rs11708067	3	123065778	*ADCY5*	NO	NO
rs9851257	3	123125711	*ADCY5*	YES	YES
rs6440006	3	141142691	*ZBTB38*	YES	YES
rs2306700	3	142123841	*XRN1*	YES	YES
rs10935733	3	148622968	*CPA3/AGTR1*	YES	YES
rs4679760	3	155855418	*KCNAB1*	YES	YES
rs1482852	3	156798294	*LOC339894/CCNL1*	YES	YES
rs11711420	3	183349010	*KLHL24*	YES	YES
rs4144829	4	17903654	*LCORL/DCAF16*	YES	NO

rs2174633	4	17917781	*LCORL/DCAF16*	NO	YES
rs2189234	4	106075498	*TET2*	NO	YES
rs6533183	4	106133184	*TET2*	YES	NO
rs6845999	4	145565826	*LOC646576/HHIP*	YES	NO
rs2131354	4	145599908	*LOC646576/HHIP*	NO	YES
rs4579095	4	174726635	*NBLA00301*	YES	YES
rs1818782	5	39424628	*DAB2*	YES	YES
rs351930	5	52003397	*PELO*	YES	YES
rs854037	5	57091783	*ACTBL2*	YES	YES
rs28365970	5	67585723	*PIK3R1*	YES	YES
rs6871635	5	133830395	*PHF15*	NO	YES
rs1981627	5	133838180	*PHF15*	YES	NO
rs2946179	5	157886627	*EBF1*	YES	YES
rs34471628	5	172196752	*DUSP1*	YES	YES
rs9379084	6	7231843	*RREB1*	YES	YES
rs35261542	6	20675792	*CDKAL1*	YES	YES
rs9379832	6	26186200	*HIST1H2BE/HIST1H2BH*	YES	YES
rs9366778	6	31269173	*HLA-C*	YES	YES
rs6911024	6	31368451	*MICA/HLA-C*	YES	YES

rs9267812	6	32128394	*PPT2*	YES	YES
rs1547669	6	33775641	*MLN*	YES	YES
rs75104038	6	34190104	*HMGA1*	YES	NO
rs75034466	6	34199815	*HMGA1*	NO	YES
rs6911621	6	35529025	*FKBP5/MAPK13/TEAD3*	NO	YES
rs9348981	6	35687249	*FKBP5/MAPK13/TEAD3*	YES	NO
rs7744700	6	53349401	*GCLC*	YES	YES
rs76094073	6	109288036	*ARMC2/SESN1*	YES	NO
rs6568554	6	109290319	*ARMC2/SESN1*	NO	YES
rs6925689	6	126865884	*CENPW*	YES	YES
rs6569647	6	130337266	*L3MBTL3*	YES	NO
rs1415701	6	130345835	*L3MBTL3*	NO	YES
rs6930558	6	141878920	*NMBR*	YES	YES
rs962554	6	142734204	*GPR126*	YES	YES
rs10872678	6	152039964	*ESR1*	YES	NO
rs7772579	6	152042502	*ESR1*	NO	YES
rs2934844	6	166142456	*PDE10A*	YES	YES
rs1724889	7	2741021	*AMZ1/GNA12*	NO	YES
rs4719648	7	2756832	*AMZ1/GNA12*	YES	NO

rs59084784	7	22739562	*IL6*	NO	NO
rs7808457	7	22798265	*IL6*	YES	YES
rs34776209	7	23513093	*IGF2BP3*	YES	YES
rs2908279	7	44174857	*MYL7/GCK*	NO	NO
rs2971669	7	44231778	*GCK*	YES	YES
rs10265133	7	45895604	*IGFBP1/IGFBP3*	YES	YES
rs11983722	7	46298647	*IGFBP3*	YES	YES
rs10265057	7	47275737	*TNS3*	YES	YES
rs2237467	7	50733316	*GRB10*	YES	YES
rs112139215	7	73034559	*MLXIPL*	YES	YES
rs2282978	7	92264410	*CDK6*	YES	YES
rs45446698	7	99332948	*CYP3A7-CYP3AP1*	YES	YES
rs13231367	7	127509070	*SND1*	NO	YES
rs6467157	7	127660763	*SND1*	YES	NO
rs3918226	7	150690176	*NOS3*	YES	YES
rs62496903	8	6446938	*MCPH1*	YES	YES
rs732563	8	23345526	*ENTPD4/NKX3-1*	YES	NO
rs11778247	8	23403378	*SLC25A37*	NO	YES
rs34036147	8	38366249	*C8orf86/FGFR1*	YES	YES

rs13266210	8	41533514	*ANK1*	YES	YES
rs72656010	8	57122215	*PLAG1*	YES	YES
rs6995390	8	77611012	*ZFHX4*	YES	YES
rs7819593	8	106115172	*ZFPM2*	YES	YES
rs13271368	8	126506140	*TRIB1*	YES	YES
rs13257363	8	142252580	*SLC45A4*	NO	NO
rs9657468	8	142362391	*GPR20*	YES	YES
rs7854962	9	96900505	*PTPDC1*	YES	YES
rs28457693	9	98217348	*PTCH1/FANCC*	YES	YES
rs1411424	9	113892963	*LPAR1*	NO	YES
rs2418135	9	113901309	*LPAR1*	YES	NO
rs72760655	9	116916214	*COL27A1*	YES	YES
rs1323438	9	119115531	*PAPPA*	YES	YES
rs3933326	9	123633948	*PHF19*	YES	YES
rs10985827	9	125701608	*RABGAP1/GPR21*	YES	YES
rs28505901	9	139241030	*GPSM1*	YES	YES
rs4350272	10	25056118	*ARHGAP21*	YES	YES
rs5030938	10	70975916	*HKDC1/HK1*	NO	YES
rs9645500	10	70986723	*HKDC1/HK1*	YES	NO

rs1112718	10	94479107	*HHEX/IDE*	YES	YES
rs10509669	10	95969913	*PLCE1*	YES	YES
rs3740360	10	96025491	*PLCE1*	YES	YES
rs2274224	10	96039597	*PLCE1*	NO	NO
rs10883846	10	104958244	*NT5C2/CYP17A1*	YES	YES
rs7903146	10	114758349	*TCF7L2*	YES	YES
rs7076938	10	115789375	*ADRB1*	YES	NO
rs1801253	10	115805056	*ADRB1*	NO	YES
rs71486610	10	124134803	*PLEKHA1*	YES	YES
rs11042596	11	2118860	*INS-IGF2*	YES	YES
rs234864	11	2857297	*KCNQ1*	YES	YES
rs2168101	11	8255408	*LMO1*	YES	YES
rs4444073	11	10331664	*ADM*	YES	YES
rs12574749	11	32405355	*WT1*	NO	YES
rs5030317	11	32410337	*WT1*	YES	NO
rs10437653	11	46297631	*CREB3L1*	YES	YES
rs10734564	11	48160429	*PTPRJ*	YES	YES
rs667515	11	69449076	*CCND1*	YES	YES
rs61885091	11	69791952	*ANO1/FGF4*	YES	YES

rs10830963	11	92708710	*MTNR1B*	YES	YES
rs10895278	11	102095335	*YAP1*	YES	YES
rs11055030	12	12878349	*APOLD1*	YES	YES
rs2306547	12	26877885	*ITPR2*	YES	YES
rs11051061	12	30914668	*CAPRIN2*	YES	YES
rs6582623	12	46613394	*SLC38A1*	YES	YES
rs180438	12	47187260	*SLC38A4*	YES	YES
rs8756	12	66359752	*HMGA2*	NO	YES
rs7968682	12	66371880	*HMGA2*	YES	NO
rs1480470	12	66412130	*HMGA2*	NO	NO
rs1533688	12	102772745	*IGF1*	YES	YES
rs2647873	12	103081192	*LINC00485/IGF1*	YES	YES
rs17033114	12	103123339	*LINC00485/IGF1*	YES	YES
rs3184504	12	111884608	*SH2B3*	YES	YES
rs9549046	13	40647206	*LINC00332*	YES	YES
rs34217484	13	48854550	*LINC00441/RB1*	YES	YES
rs9318511	13	78601413	*LINC00446*	YES	YES
rs6575803	14	101257755	*MIR2392/DLK1*	YES	YES
rs75844534	15	38667117	*SPRED1*	YES	YES

rs2928148	15	41401550	*INO80*	YES	YES
rs339969	15	60883281	*RORA*	YES	YES
rs3784789	15	75082552	*CSK*	YES	YES
rs12909648	15	86224570	*KLHL25/AKAP13*	YES	YES
rs12443252	15	91064690	*CRTC3*	YES	YES
rs7183988	15	91428589	*FES/FURIN*	NO	YES
rs4932373	15	91429287	*FES/FURIN*	YES	NO
rs55958435	15	96852638	*NR2F2*	YES	YES
rs7402983	15	99193276	*IGF1R*	YES	YES
rs11630479	15	99240481	*IGF1R*	YES	YES
rs2045457	16	20046115	*GPR139/GPRC5B*	YES	YES
rs40434	16	55699525	*SLC6A2*	YES	YES
rs28544888	16	55741204	*SLC6A2*	YES	YES
rs11641308	16	75312023	*BCAR1*	YES	YES
rs222857	17	7164563	*CLDN7/SLC2A4*	YES	NO
rs2428362	17	7180274	*CLDN7/SLC2A4*	NO	YES
rs4511593	17	7455536	*TNFSF12-TNFSF13*	YES	YES
rs9909342	17	25652275	*WSB1*	YES	YES
rs7223535	17	29211667	*ATAD5*	YES	YES

rs11867479	17	68090207	*KCNJ16*	YES	YES
rs10221267	17	68464662	*KCNJ2*	YES	YES
rs73354194	17	79905947	*MYADML2*	NO	NO
rs9912553	17	79959703	*ASPSCR1*	YES	YES
rs11082304	18	20720973	*CABLES1*	YES	YES
rs2779165	19	4915447	*UHRF1*	YES	YES
rs8106042	19	7161849	*INSR*	YES	YES
rs2967676	19	8789666	*ACTL9*	YES	YES
rs41355649	19	33790556	*CEBPA*	YES	YES
rs1129156	19	40719076	*MAP3K10/AKT2*	YES	YES
rs147957154	19	43431040	*PSG7*	YES	YES
rs516246	19	49206172	*FUT2*	YES	YES
rs255773	19	54723546	*LILRB3/RPS9*	YES	YES
rs147110934	19	55993436	*ZNF628*	YES	YES
rs12461110	19	56320663	*NLRP11*	YES	YES
rs304001	19	56423668	*NLRP13*	YES	YES
rs6040076	20	10658882	*JAG1*	YES	YES
rs6033062	20	11207419	*LOC339593*	YES	YES
rs1203876	20	22540915	*LINC00261/FOXA2*	YES	YES

rs11698914	20	31327144	*COMMD7*	YES	YES
rs181451002	20	32466219	*CHMP4B*	YES	YES
rs2889874	20	33715777	*EDEM2/MYH7B*	YES	YES
rs1012167	20	39159119	*MAFB*	YES	YES
rs753381	20	39797465	*PLCG1*	YES	YES
rs6026449	20	57272617	*STX16-NPEPL1/GNAS*	YES	YES
rs73143584	20	62445702	*ZBTB46*	YES	YES
rs2229742	21	16339172	*NRIP1*	YES	YES
rs220193	21	43581308	*UMODL1*	YES	YES
rs134594	22	29468456	*KREMEN1*	YES	YES
rs41311445	22	42070374	*NHP2L1/SREBF2*	YES	YES
rs7285579	22	46441980	*LOC100271722*	YES	YES

*, Warrington et al, 2019; SNP - Single nucleotide polymorphism; CHR - chromosome; BP - base position

#, Among the LD pair SNPs, most significant SNPs were selected for sensitivity analysis of 167 LD-pruned SNPs

Supplementary Table 13: Associations results of 167 LD-pruned SNPs with own birthweight and maternal genetic score with its offspring birthweight in South Asian cohorts

Cohort	fGS adjusted for sex and GA[*]					fGS adjusted for sex, GA and mGS[†]				
	N	**Effect**	**L95**	**U95**	**P**	**N**	**Effect**	**L95**	**U95**	**P**
PMNS	515	0.011	0.000	0.022	0.049	443	0.011	-0.001	0.023	0.065
PS	511	0.023	0.012	0.035	9.3×10^{-5}	458	0.024	0.012	0.036	1.1×10^{-4}
MMNP[‡]	466	0.013	0.002	0.024	0.024	460	0.014	0.003	0.026	0.016
MBRC[§]	684	0.006	-0.003	0.015	0.217	NA	NA	NA	NA	NA
Dhaka-WP2	53	0.016	-0.030	0.061	0.496	53	0.015	-0.029	0.059	0.500
Dhaka-WP3	314	0.019	0.005	0.032	0.007	314	0.019	0.006	0.032	0.005
UK-Bang	150	0.021	0.002	0.039	0.032	150	0.017	-0.002	0.036	0.079
Meta-analysis	**2693**	**0.014**	**0.009**	**0.018**	**1.5×10^{-8}**	**1878**	**0.017**	**0.011**	**0.023**	**6.3×10^{-9}**
	mGS adjusted for sex and GA[||]					**mGS adjusted for sex, GA and fGS[¶]**				
	N	**Effect**	**L95**	**U95**	**P**	**N**	**Effect**	**L95**	**U95**	**P**
PMNS	461	0.000	-0.009	0.009	0.983	443	0.001	-0.008	0.011	0.762
PS	475	0.014	0.004	0.024	0.008	458	0.015	0.005	0.025	0.003
MMNP[‡]	467	0.000	-0.009	0.009	0.997	460	0.002	-0.008	0.011	0.742
Dhaka-WP2	53	0.031	0.003	0.058	0.035	53	0.030	0.003	0.058	0.037
Dhaka-WP3	314	0.014	0.003	0.025	0.016	314	0.014	0.003	0.026	0.011
UK-Bang	150	0.022	0.005	0.040	0.015	150	0.019	0.002	0.037	0.035
Meta-analysis	**1920**	**0.008**	**0.003**	**0.012**	**0.001**	**1878**	**0.009**	**0.004**	**0.014**	**1.6×10^{-4}**

Association analysis was conducted for LD-pruned 167 independent SNPs (please refer supplementary table 12 for details) using linear regression with standardized birthweight adjusted for sex and gestational age as the dependent variable for each cohort separately and finally the summary results were meta-analyzed. †, In MMNP, allocation group was additionally adjusted for, and §, in MBRC only sex was adjusted for, since gestational age data was not available for the majority of the sample. The effect size is in standard deviation units of birthweight per unit change in genetic score. The standard deviation of birthweight in kg in all these cohorts ranged from 0.34 to 0.45 kg. N, number of term babies; GA, gestational age; I^2, heterogeneity; Het-P, P value for heterozygosity; P, P value; fGS, fetal genetic score; mGS, maternal genetic score; GA, gestational age. PMNS, Pune Maternal Nutrition Study; PS, Parthenon Study; MMNP, Mumbai Maternal Nutrition Project; MBRC, Mysore Birth Records Cohort; Dhaka-WP2, Work Package 2 of GIFTS; Dhaka-WP3, Work Package 3 of GIFTS; UK-Bang, London UK Bangladeshi cohort.

For fGS, *, I^2 = 8.8 and Het-P = 0.361; **†**, I^2= 0 and Het-P = 0.775

For mGS, ‖, I^2= 62.0 and Het-P = 0.02; ¶, I^2=54.0 and Het-P = 0.054

Supplementary Table 14: Associations of birthweight with anthropometric and cardiometabolic traits in Indian children[$] and adolescents[#]

Trait	Children					Adolescents				
	N	Effect	P	I^2	Het-P	N	Effect	P	I^2	Het-P
Weight	1674	0.849	1.9×10^{-51}	50.3	0.134	1081	0.590	9.2×10^{-20}	0	0.977
Height	1673	0.665	1.3×10^{-31}	46.8	0.153	1081	0.523	8.6×10^{-17}	0	0.901
Body Mass Index	1673	0.634	2.5×10^{-27}	0	0.681	1081	0.456	8.7×10^{-11}	0	0.828
Head circumference	1674	0.721	3.2×10^{-39}	44.7	0.164	1076	0.755	8.1×10^{-27}	0	0.348
Waist circumference	1672	0.661	8.6×10^{-29}	45.4	0.160	1059	0.462	1.7×10^{-10}	0	0.986
Mid-upper arm circumference	1674	0.558	7.1×10^{-21}	0	0.943	1075	0.406	5.9×10^{-9}	0	0.925
Triceps skin-fold	1673	0.245	3.0×10^{-5}	0	0.856	1075	0.321	5.7×10^{-6}	0	0.830
Sub-scapular skin-fold	1673	0.311	1.3×10^{-7}	0	0.800	1074	0.318	5.7×10^{-6}	0	0.657
Fat percent	1659	0.123	0.030	28.3	0.248	1048	0.145	0.031	0	0.516
Systolic blood pressure*	1657	-0.140	0.024	4.7	0.350	1064	-0.148	0.041	0	0.714
Diastolic blood pressure*	1658	-0.162	0.010	52.2	0.123	1055	-0.020	0.794	51.8	0.150
Fasting glucose*	1653	-0.075	0.237	0	0.664	1071	-0.042	0.580	0	0.959

120 minutes glucose*	1624	0.045	0.478	35.7	0.211	NA	NA	NA	NA	NA
Fasting insulin*	1644	0.001	0.991	0	0.824	1072	-0.055	0.405	0	0.627
HOMA-IR*	1570	-0.025	0.691	0	0.838	1071	-0.061	0.365	0	0.655
Total cholesterol*	1652	-0.045	0.481	0	0.675	1072	-0.059	0.441	68.9	0.073
LDL-cholesterol*	1652	0.030	0.638	0	0.742	1072	-0.020	0.787	67.3	0.080
HDL-cholesterol*	1662	-0.036	0.573	13.5	0.315	1072	0.075	0.318	0	0.414
Triglycerides*	1652	-0.209	9.8×10^{-4}	41.3	0.182	1072	-0.228	0.002	0	0.344

Association analysis was performed using linear regression with standardized log10 transformed traits as dependent variables for each cohort independently and finally the summary results were meta-analyzed. Age and sex were included as covariates in the regression model for all traits; BMI was additionally included as a covariate for analysis of traits marked with an asterisk (*). In MMNP, the allocation group was additionally adjusted for. $, The meta-analysis for children included those from the Pune Maternal Nutrition Study at 6 yrs, the Parthenon Study at 5 yrs and the Mumbai Maternal Nutrition Project at 7 yrs of age. #, Meta-analysis included adolescents from Pune Maternal Nutrition Study at 12 yrs and from Parthenon Study at 13.5 yrs; P, P value; I^2, heterogeneity; Het-P, P value for heterozygosity; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low density lipoprotein; HDL, high density lipoprotein; NA, not available. Those passing the Bonferroni corrected $P \leq 0.001$ were considered as statistically significant.

Supplementary Table 15: Meta-analysis of associations of maternal genetic score with anthropometric and cardiometabolic traits in Indian children$ & adolescents#

Traits	Children					Adolescents				
	N	effect	P	I^2	Het-P	N	effect	P	I^2	Het-P
Weight	1760	0.003	0.152	0	0.911	1028	0.002	0.523	0	0.611
Height	1759	0.002	0.409	0	0.505	1028	0.002	0.478	0	0.480
Body mass index	1759	0.003	0.255	0	0.654	1028	0.001	0.723	20.9	0.261
Head circumference	1760	0.001	0.808	0	0.977	1023	0.002	0.510	0	0.645
Waist circumference	1758	0.003	0.263	0	0.915	1005	0.001	0.758	0	0.398
Mid-upper arm circumference	1759	0.004	0.122	0	0.916	1023	0.003	0.353	0	0.407
Triceps skinfold	1759	0.003	0.263	0	0.550	1022	-0.001	0.789	0	0.352
Subscapular skinfold	1759	0.003	0.227	0	0.628	1021	0.000	0.861	42.7	0.186
Fat percent	1753	-0.001	0.661	3.5	0.355	993	0.000	0.909	0	0.449
Systolic blood pressure*	1740	-0.002	0.348	0	0.967	1005	-0.001	0.784	0	0.629
Diastolic blood pressure*	1741	0.000	0.891	0	0.954	1005	-0.002	0.440	0	0.884

Fasting glucose*	1733	-0.002	0.449	11.1	0.325	1018	0.000	0.994	0	0.826
120 minutes glucose*	1710	-0.002	0.413	0	0.767	NA	NA	NA	NA	NA
Fasting insulin*	1727	0.000	0.963	26.9	0.255	1019	0.001	0.696	0	0.746
HOMA-IR*	1662	0.000	0.838	52.6	0.121	1018	0.001	0.738	0	0.776
Total cholesterol*	1732	0.004	0.056	5.7	0.346	1019	0.002	0.422	0	0.752
LDL-cholesterol*	1733	0.003	0.209	46.8	0.153	1019	0.000	0.911	0	0.674
HDL-cholesterol*	1742	0.003	0.219	59.4	0.085	1019	0.005	0.094	0	0.385
Triglycerides*	1731	0.000	0.840	57	0.098	1019	0.001	0.761	18.0	0.269

Association analysis was performed using linear regression with standardized log10 transformed traits as the dependent variable for each cohort independently and finally the summary results were meta-analyzed. Age and sex were included as covariates in the regression model for all traits; BMI was additionally included as a covariate for analysis of traits marked with an asterisk (*). $, Meta-analysis for children included those from Pune Maternal Nutrition Study at 6 yrs, Parthenon Study at 5 yrs; Mumbai Maternal Nutrition Project at 7 yrs of age; #, Meta-analysis included adolescents from Pune Maternal Nutrition Study at 12 yrs and from Parthenon Study at 13.5 yrs; P, P value; I^2, heterogeneity; Het-P, P value for heterozygosity; SNP, single nucleotide polymorphism; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low density lipoprotein; HDL, high density lipoprotein; NA, not available. Those passing the Bonferroni corrected $P \leq 0.001$ were considered as statistically significant.

Supplementary Table 1: Details of SNPs included in the study for calculating the fetal genetic and maternal genetic scores*

						GWAS of own birth weight						GWAS of offspring birth weight						
																		SEM-adj
SNP	CHR	BP (hg19)	Nearest gene	EA	OA	EAF	Beta	SE	P-value	Sample size	Het P	EAF	Beta	SE	P-value	Sample size	Het P	Beta
rs17367504	1	11862778	*MTHFR*	G	A	0.161	0.012	0.003	8.3E-04	298129	0.723	0.167	0.030	0.004	3.2E-13	210264	0.581	-0.005
rs12401656	1	43456767	*FLJ32224/SLC2A1*	G	A	0.865	0.025	0.004	3.4E-11	292712	0.255	0.862	0.009	0.005	0.058	197947	0.768	0.029
rs80278614	1	119412317	*TBX15*	A	G	0.054	0.040	0.006	6.5E-12	292074	0.676	0.051	0.015	0.007	0.044	197948	0.004	0.052
rs905938	1	154991389	*DCST2/KCNN3*	C	T	0.262	0.026	0.003	2.8E-19	298135	0.149	0.268	0.018	0.003	1.5E-07	210262	0.347	0.023
rs670523	1	155878732	*RIT1/LMNA*	G	A	0.669	0.019	0.003	7.6E-12	291451	0.075	0.669	0.008	0.003	0.012	210262	0.477	0.016
rs72480273	1	161644871	*FCGR2B/FCGR2C/HSPA6*	C	A	0.182	0.023	0.003	4.0E-11	291667	0.319	0.189	0.016	0.004	6.0E-05	197947	0.368	0.022
rs10913200	1	176521655	*PAPPA2*	G	A	0.972	0.051	0.008	2.0E-10	287089	0.200	0.971	0.048	0.009	4.0E-07	197948	0.904	0.038
rs61830764	1	212289976	*DTL*	A	G	0.377	0.017	0.003	1.1E-09	291445	0.004	0.375	0.004	0.003	0.188	197948	0.012	0.018
rs3806315	1	214724668	*PTPN14*	A	G	0.591	0.018	0.003	2.8E-11	289070	0.439	0.596	0.012	0.003	1.1E-04	197948	0.426	0.016
rs708122	1	228216997	*WNT3A*	C	A	0.681	0.017	0.003	2.5E-09	292718	0.543	0.680	0.013	0.003	4.2E-05	210264	0.144	0.015
rs10495563	2	9662210	*ADAM17*	A	G	0.664	0.022	0.003	2.1E-16	298133	0.253	0.668	0.019	0.003	1.8E-09	210265	0.823	0.016
rs11893688	2	9695282	*ADAM17*	T	C	0.661	0.022	0.003	1.3E-15	292716	0.452	0.666	0.020	0.003	1.1E-09	210263	0.826	0.015
rs2551347	2	23912401	*KLHL29*	T	C	0.749	0.024	0.003	1.9E-16	292714	0.621	0.746	0.008	0.004	0.032	197947	0.208	0.029
rs1179494	2	36809496	*FEZ2*	G	C	0.676	0.010	0.003	1.5E-04	292716	0.291	0.672	0.020	0.003	9.1E-10	210204	0.298	0.002
rs754868	2	43185532	*HAAO*	G	A	0.419	0.016	0.003	6.7E-10	298139	0.998	0.420	0.005	0.003	0.110	210264	0.460	0.019
rs4952673	2	43423870	*ZFP36L2*	A	G	0.474	0.007	0.003	3.8E-03	292715	0.778	0.474	0.020	0.003	2.0E-11	210111	0.658	-0.004
rs17034876	2	46484310	*EPAS1*	T	C	0.700	0.042	0.003	3.1E-47	287749	0.044	0.696	0.030	0.003	1.4E-18	210261	0.784	0.039
rs4953353	2	46567276	*EPAS1*	G	T	0.632	0.018	0.003	3.5E-11	292721	0.330	0.629	0.005	0.003	0.086	210262	0.998	0.019
rs560887	2	169763148	*G6PC2*	C	T	0.700	-0.008	0.003	5.8E-03	298139	0.392	0.701	0.026	0.003	1.2E-14	210264	0.374	-0.025
rs2280235	2	191843830	*STAT1*	G	A	0.259	0.018	0.003	6.9E-10	292718	0.979	0.265	0.013	0.003	3.0E-04	210215	0.213	0.014
rs10181515	2	227019461	*LOC646736/COL4A4/IRS1*	T	C	0.225	0.021	0.003	2.1E-12	298138	0.742	0.226	0.006	0.004	0.099	210265	0.821	0.021
rs9855896	3	14287150	*LSM3*	G	A	0.214	0.004	0.003	0.186	286866	0.395	0.222	0.023	0.004	2.4E-10	210257	0.546	-0.014
rs2168443	3	46947087	*PTH1R*	T	A	0.379	0.017	0.003	3.9E-10	292713	0.617	0.380	0.016	0.003	9.1E-07	197947	0.765	0.010
rs11708067	3	123065778	*ADCY5*	G	A	0.238	0.041	0.003	1.6E-42	298128	0.029	0.246	0.001	0.004	0.674	210168	0.253	0.056
rs9851257	3	123125711	*ADCY5*	T	A	0.733	0.020	0.003	2.4E-12	298130	0.249	0.744	0.030	0.004	7.2E-17	197947	0.324	0.005
rs6440006	3	141142691	*ZBTB38*	A	G	0.446	0.010	0.003	7.3E-05	292713	0.170	0.448	0.021	0.003	4.3E-12	210249	0.670	-0.001
rs2306700	3	142123841	*XRN1*	T	C	0.136	0.023	0.004	1.8E-09	290416	0.644	0.141	0.015	0.004	5.8E-04	210265	0.394	0.022

rs10935733	3	148622968	*CPA3/AGTR1*	T	C	0.399	0.019	0.003	2.3E-13	292713	0.848	0.391	0.012	0.003	2.1E-04	197948	0.196	0.021
rs4679760	3	155855418	*KCNAB1*	G	C	0.581	0.009	0.003	3.2E-04	292718	0.259	0.586	0.033	0.003	1.8E-25	197948	0.918	-0.009
rs1482852	3	156798294	*LOC339894/CCNL1*	A	G	0.599	0.050	0.003	1.6E-82	298130	0.007	0.599	0.023	0.003	2.3E-13	210264	0.078	0.054
rs11711420	3	183349010	*KLHL24*	T	G	0.747	0.019	0.003	3.2E-10	292710	0.983	0.745	0.006	0.004	0.095	197947	0.254	0.022
rs4144829	4	17903654	*LCORL/DCAF16*	C	T	0.267	0.036	0.003	4.3E-34	292713	0.407	0.262	0.023	0.004	6.7E-11	197947	0.473	0.032
rs2174633	4	17917781	*LCORL/DCAF16*	A	C	0.270	0.035	0.003	7.1E-33	292712	0.324	0.268	0.024	0.003	3.8E-12	210263	0.429	0.031
rs2189234	4	106075498	*TET2*	G	T	0.618	0.015	0.003	1.2E-08	292719	0.387	0.616	0.026	0.003	2.9E-16	210262	0.218	0.001
rs6533183	4	106133184	*TET2*	C	T	0.352	0.022	0.003	6.8E-16	292715	0.947	0.341	0.027	0.003	7.2E-16	197948	0.653	0.008
rs6845999	4	145565826	*LOC646576/HHIP*	T	C	0.431	0.026	0.003	1.5E-24	298140	0.168	0.429	0.023	0.003	4.1E-14	210264	0.607	0.017
rs2131354	4	145599908	*LOC646576/HHIP*	A	G	0.527	0.026	0.003	3.5E-24	292719	0.438	0.527	0.026	0.003	2.8E-16	197948	0.686	0.016
rs4579095	4	174726635	*NBLA00301*	G	A	0.402	0.003	0.003	0.319	288031	0.198	0.407	0.019	0.003	8.5E-10	210243	0.217	-0.007
rs1818782	5	39424628	*DAB2*	C	A	0.637	0.016	0.003	4.2E-09	313072	0.714	0.649	0.006	0.003	0.054	217750	0.547	0.015
rs351930	5	52003397	*PELO*	T	A	0.801	0.019	0.003	2.9E-09	292714	0.674	0.800	0.007	0.004	0.056	210254	0.086	0.020
rs854037	5	57091783	*ACTBL2*	A	G	0.814	0.027	0.003	9.4E-16	292718	0.032	0.809	0.019	0.004	1.6E-06	210228	0.174	0.020
rs28365970	5	67585723	*PIK3R1*	C	A	0.741	0.020	0.003	1.7E-11	292712	0.682	0.740	0.016	0.004	5.7E-06	197947	0.789	0.015
rs6871635	5	133830395	*PHF15*	G	A	0.566	0.016	0.003	3.0E-09	292716	0.554	0.563	0.026	0.003	3.3E-17	210234	0.569	0.005
rs1981627	5	133838180	*PHF15*	G	A	0.585	0.017	0.003	8.4E-11	292716	0.599	0.581	0.025	0.003	2.6E-16	210238	0.376	0.007
rs2946179	5	157886627	*EBF1*	C	T	0.734	0.020	0.003	1.1E-11	298129	0.901	0.735	0.046	0.004	1.8E-37	197948	0.638	-0.004
rs34471628	5	172196752	*DUSP1*	A	G	0.962	0.018	0.007	9.4E-03	288465	0.436	0.962	0.059	0.008	3.7E-13	197948	0.578	-0.014
rs9379084	6	7231843	*RREB1*	G	A	0.883	0.022	0.004	1.2E-07	298128	0.420	0.883	0.041	0.005	1.3E-16	208332	0.519	0.004
rs35261542	6	20675792	*CDKAL1*	C	A	0.733	0.041	0.003	2.8E-45	298124	0.074	0.738	0.005	0.004	0.137	197948	0.116	0.049
rs9379832	6	26186200	*HIST1H2BE/HIST1H2BH*	A	G	0.730	0.022	0.003	1.1E-13	291448	0.156	0.746	0.015	0.004	5.7E-05	197948	0.311	0.019
rs9366778	6	31269173	*HLA-C*	G	A	0.627	0.018	0.003	2.9E-11	282578	0.744	0.635	0.011	0.003	4.9E-04	210260	0.641	0.014
rs6911024	6	31368451	*MICA/HLA-C*	T	C	0.901	0.017	0.004	1.3E-04	277158	0.461	0.902	0.038	0.005	1.9E-13	210233	0.173	-0.002
rs9267812	6	32128394	*PPT2*	T	C	0.133	0.023	0.004	3.1E-09	280156	0.130	0.135	0.022	0.005	1.8E-06	197947	0.485	0.015
rs1547669	6	33775641	*MLN*	G	A	0.497	0.018	0.003	6.2E-12	289000	0.908	0.499	0.007	0.003	0.023	208983	0.648	0.018
rs75104038	6	34190104	*HMGA1*	A	G	0.060	0.045	0.006	4.3E-16	289515	0.228	0.061	0.054	0.007	2.1E-16	197947	0.193	0.024
rs75034466	6	34199815	*HMGA1*	T	C	0.046	0.046	0.006	1.8E-13	289010	0.532	0.048	0.062	0.007	1.6E-17	197947	0.097	0.020
rs6911621	6	35529025	*FKBP5/MAPK13/TEAD3*	T	C	0.344	0.018	0.003	1.6E-11	292722	0.749	0.349	0.026	0.003	2.2E-16	210264	0.522	0.006
rs9348981	6	35687249	*FKBP5/MAPK13/TEAD3*	T	G	0.710	0.021	0.003	2.2E-13	292710	0.905	0.708	0.018	0.003	3.0E-07	197948	0.198	0.015
rs7744700	6	53349401	*GCLC*	T	A	0.711	0.020	0.003	1.6E-11	291448	0.128	0.704	0.012	0.003	4.0E-04	209445	0.062	0.018
rs76094073	6	109288036	*ARMC2/SESN1*	G	C	0.121	0.027	0.004	1.6E-11	292719	0.235	0.121	0.027	0.005	1.2E-08	197947	0.132	0.011

rs6568554	6	109290319	*ARMC2/SESN1*	A	C	0.145	0.021	0.004	1.1E-08	292717	0.971	0.144	0.027	0.004	1.7E-09	197948	0.216	0.006
rs6925689	6	126865884	*CENPW*	T	C	0.494	0.015	0.003	6.4E-09	292716	0.322	0.494	0.001	0.003	0.852	197948	0.928	0.018
rs6569647	6	130337266	*L3MBTL3*	T	C	0.802	0.020	0.003	6.3E-10	292720	0.715	0.797	0.014	0.004	1.8E-04	210265	0.426	0.014
rs1415701	6	130345835	*L3MBTL3*	G	A	0.736	0.018	0.003	1.4E-09	298129	0.138	0.729	0.022	0.003	6.4E-10	208908	0.307	0.007
rs6930558	6	141878920	*NMBR*	T	G	0.747	0.022	0.003	3.4E-13	292714	0.744	0.743	0.012	0.004	5.8E-04	210263	0.812	0.022
rs962554	6	142734204	*GPR126*	T	C	0.715	0.017	0.003	3.8E-09	292717	0.679	0.712	0.012	0.003	5.1E-04	210263	0.379	0.015
rs10872678	6	152039964	*ESR1*	T	C	0.724	0.032	0.003	9.8E-29	298136	0.022	0.722	0.020	0.003	4.3E-09	210262	0.366	0.028
rs7772579	6	152042502	*ESR1*	A	C	0.721	0.031	0.003	6.4E-28	292718	0.049	0.718	0.021	0.003	5.6E-10	210263	0.310	0.027
rs2934844	6	166142456	*PDE10A*	T	A	0.672	0.021	0.003	1.8E-13	292253	0.363	0.671	0.010	0.003	2.8E-03	197947	0.871	0.018
rs1724889	7	2741021	*AMZ1/GNA12*	G	A	0.735	0.016	0.003	1.5E-07	291447	0.207	0.740	0.023	0.004	2.9E-10	197947	0.397	0.006
rs4719648	7	2756832	*AMZ1/GNA12*	C	T	0.577	0.019	0.003	2.6E-13	292711	0.750	0.578	0.017	0.003	1.1E-07	197948	0.317	0.014
rs59084784	7	22739562	*IL6*	A	C	0.323	0.017	0.003	2.4E-09	292716	0.878	0.323	0.017	0.003	6.3E-07	197947	0.408	0.011
rs7808457	7	22798265	*IL6*	A	T	0.586	0.010	0.003	7.1E-05	292719	0.168	0.586	0.019	0.003	1.5E-09	210254	0.160	0.002
rs34776209	7	23513093	*IGF2BP3*	C	T	0.755	0.023	0.003	8.5E-15	292718	0.419	0.752	0.021	0.004	7.9E-09	197948	0.856	0.015
rs2908279	7	44174857	*MYL7/GCK*	T	G	0.495	0.011	0.003	2.2E-05	292716	0.068	0.495	0.016	0.003	3.6E-07	197948	0.208	0.007
rs2971669	7	44231778	*GCK*	T	C	0.214	0.011	0.003	4.2E-04	298134	0.842	0.219	0.028	0.004	8.2E-14	210172	0.269	-0.003
rs10265133	7	45895604	*IGFBP1/IGFBP3*	G	T	0.859	0.001	0.004	0.859	288682	0.414	0.858	0.027	0.005	2.3E-09	197947	0.843	-0.020
rs11983722	7	46298647	*IGFBP3*	A	T	0.938	0.032	0.005	3.1E-09	290622	0.653	0.931	0.019	0.006	2.5E-03	210253	0.347	0.029
rs10265057	7	47275737	*TNS3*	G	A	0.092	0.027	0.004	1.3E-09	292446	0.143	0.098	0.005	0.005	0.304	210265	0.760	0.036
rs2237467	7	50733316	*GRB10*	A	G	0.221	0.018	0.003	5.3E-09	292710	0.762	0.221	0.015	0.004	6.0E-05	207377	0.236	0.011
rs112139215	7	73034559	*MLXIPL*	A	C	0.068	0.047	0.005	2.8E-20	295398	0.144	0.069	0.017	0.006	6.5E-03	197947	0.635	0.056
rs2282978	7	92264410	*CDK6*	C	T	0.326	0.018	0.003	1.7E-11	298140	0.498	0.326	0.007	0.003	0.033	210264	0.377	0.021
rs45446698	7	99332948	*CYP3A7-CYP3AP1*	G	T	0.041	0.025	0.007	1.7E-04	284207	0.481	0.042	0.067	0.008	1.7E-17	197948	0.088	-0.017
rs13231367	7	127509070	*SND1*	G	A	0.714	0.017	0.003	4.4E-09	292714	0.339	0.705	0.020	0.003	2.0E-09	210264	0.577	0.009
rs6467157	7	127660763	*SND1*	T	C	0.713	0.020	0.003	1.5E-11	292717	0.426	0.703	0.019	0.003	2.3E-08	210264	0.899	0.014
rs3918226	7	150690176	*NOS3*	C	T	0.919	0.015	0.005	1.9E-03	296402	0.041	0.919	0.040	0.006	9.0E-12	197948	0.059	-0.005
rs62496903	8	6446938	*MCPH1*	T	C	0.083	0.033	0.005	6.7E-12	290687	0.861	0.084	0.025	0.006	1.2E-05	197948	0.750	0.028
rs732563	8	23345526	*ENTPD4/NKX3-1*	C	T	0.504	0.017	0.003	1.3E-11	292723	0.288	0.506	0.007	0.003	0.021	210265	0.564	0.019
rs11778247	8	23403378	*SLC25A37*	G	A	0.835	0.014	0.003	8.2E-05	291448	0.813	0.834	0.025	0.004	3.7E-09	197948	0.062	0.000
rs34036147	8	38366249	*C8orf86/FGFR1*	T	C	0.688	0.018	0.003	8.4E-11	292711	0.239	0.692	0.008	0.003	0.016	197948	0.888	0.019
rs13266210	8	41533514	*ANK1*	A	G	0.786	0.027	0.003	1.5E-17	292718	0.617	0.784	0.011	0.004	3.2E-03	210263	0.439	0.030
rs72656010	8	57122215	*PLAG1*	T	C	0.868	0.028	0.004	1.4E-13	292713	0.006	0.869	0.014	0.005	2.1E-03	197948	0.002	0.026

rs6995390	8	77611012	*ZFHX4*	T	A	0.163	0.006	0.003	0.079	292714	0.207	0.165	0.030	0.004	8.4E-13	210050	0.797	-0.014
rs7819593	8	106115172	*ZFPM2*	C	T	0.243	0.022	0.003	6.2E-13	292718	0.427	0.238	0.012	0.004	1.3E-03	210150	0.037	0.023
rs13271368	8	126506140	*TRIB1*	C	T	0.761	0.020	0.003	2.3E-11	296867	0.256	0.761	0.011	0.004	4.7E-03	197948	0.659	0.021
rs13257363	8	142252580	*SLC45A4*	G	A	0.591	0.018	0.003	2.0E-11	292711	0.278	0.590	0.012	0.003	2.6E-04	197948	0.672	0.017
rs9657468	8	142362391	*GPR20*	G	T	0.334	0.015	0.003	7.9E-08	286868	0.722	0.334	0.003	0.003	0.335	197947	0.522	0.018
rs7854962	9	96900505	*PTPDC1*	C	G	0.785	0.022	0.003	1.0E-11	292711	0.808	0.785	0.015	0.004	8.8E-05	197948	0.280	0.016
rs28457693	9	98217348	*PTCH1/FANCC*	G	A	0.109	0.044	0.004	9.9E-26	288037	0.431	0.106	0.030	0.005	3.7E-09	197948	0.851	0.040
rs1411424	9	113892963	*LPAR1*	A	G	0.523	0.020	0.003	1.5E-14	292717	0.213	0.523	0.023	0.003	2.9E-14	210255	0.836	0.012
rs2418135	9	113901309	*LPAR1*	A	G	0.522	0.020	0.003	1.5E-14	292715	0.229	0.519	0.023	0.003	6.8E-14	210248	0.775	0.012
rs72760655	9	116916214	*COL27A1*	C	A	0.681	0.007	0.003	0.010	292710	0.478	0.678	0.026	0.003	4.1E-15	197947	0.397	-0.009
rs1323438	9	119115531	*PAPPA*	C	T	0.718	0.019	0.003	5.6E-11	292712	0.567	0.717	0.007	0.003	0.038	209854	0.751	0.020
rs3933326	9	123633948	*PHF19*	G	A	0.676	0.021	0.003	2.3E-14	292715	0.416	0.676	0.010	0.003	2.3E-03	210259	0.952	0.023
rs10985827	9	125701608	*RABGAP1/GPR21*	G	T	0.141	0.030	0.004	6.1E-16	292715	0.739	0.139	0.017	0.005	1.5E-04	197948	0.577	0.027
rs28505901	9	139241030	*GPSM1*	A	G	0.249	0.024	0.003	2.5E-15	286903	0.967	0.245	0.017	0.004	4.4E-06	197947	0.346	0.024
rs4350272	10	25056118	*ARHGAP21*	A	G	0.269	0.017	0.003	3.6E-09	298133	0.021	0.272	0.011	0.003	9.9E-04	210119	0.564	0.017
rs5030938	10	70975916	*HKDC1/HK1*	T	C	0.686	0.024	0.003	1.2E-17	292718	0.918	0.687	0.020	0.003	4.6E-10	210264	0.320	0.019
rs9645500	10	70986723	*HKDC1/HK1*	G	T	0.694	0.024	0.003	1.8E-18	298136	0.943	0.694	0.020	0.003	1.3E-09	210263	0.237	0.019
rs1112718	10	94479107	*HHEX/IDE*	G	A	0.404	0.026	0.003	3.8E-23	298134	0.400	0.406	0.001	0.003	0.824	197948	0.686	0.036
rs10509669	10	95969913	*PLCE1*	A	T	0.746	-0.001	0.003	0.685	292711	0.989	0.745	0.026	0.004	3.9E-13	210110	0.844	-0.020
rs3740360	10	96025491	*PLCE1*	C	A	0.109	0.026	0.004	4.0E-10	292719	0.902	0.114	0.046	0.005	5.5E-21	210265	0.124	0.003
rs2274224	10	96039597	*PLCE1*	C	G	0.434	0.021	0.003	9.8E-17	298132	0.376	0.433	0.018	0.003	1.0E-08	210042	0.634	0.019
rs10883846	10	104958244	*NT5C2/CYP17A1*	C	T	0.615	0.017	0.003	1.3E-10	298138	0.184	0.606	0.012	0.003	1.1E-04	197948	0.521	0.016
rs7903146	10	114758349	*TCF7L2*	T	C	0.285	0.011	0.003	5.3E-05	298140	0.004	0.291	0.022	0.003	9.1E-11	210264	0.361	0.003
rs7076938	10	115789375	*ADRB1*	T	C	0.735	0.032	0.003	2.1E-28	298136	0.005	0.732	0.020	0.003	7.3E-09	210265	0.618	0.029
rs1801253	10	115805056	*ADRB1*	C	G	0.727	0.031	0.003	1.4E-25	297700	0.117	0.734	0.021	0.003	5.3E-10	210262	0.935	0.026
rs71486610	10	124134803	*PLEKHA1*	C	G	0.477	0.020	0.003	3.2E-15	292714	0.517	0.471	0.017	0.003	4.3E-08	197948	0.566	0.016
rs11042596	11	2118860	*INS-IGF2*	T	G	0.336	0.027	0.003	4.3E-22	292715	0.944	0.335	0.006	0.003	0.085	197948	0.113	0.027
rs234864	11	2857297	*KCNQ1*	A	G	0.547	0.016	0.003	1.7E-09	296865	0.837	0.556	0.004	0.003	0.160	197947	0.604	0.017
rs2168101	11	8255408	*LMO1*	C	A	0.689	0.007	0.003	0.011	292716	0.112	0.691	0.033	0.003	2.9E-21	206024	0.595	-0.015
rs4444073	11	10331664	*ADM*	A	C	0.520	0.020	0.003	2.7E-15	298137	0.708	0.515	0.008	0.003	8.5E-03	210253	0.016	0.023
rs12574749	11	32405355	*WT1*	C	A	0.723	0.015	0.003	1.1E-07	292714	0.190	0.720	0.021	0.003	1.3E-09	209490	0.810	0.004
rs5030317	11	32410337	*WT1*	C	G	0.733	0.017	0.003	2.7E-09	292715	0.339	0.731	0.021	0.003	1.7E-09	210230	0.922	0.007

rs10437653	11	46297631	*CREB3L1*	A	C	0.503	0.010	0.003	1.5E-04	315261	0.053	0.500	0.017	0.003	3.5E-09	230068	0.216	0.002
rs10734564	11	48160429	*PTPRJ*	A	G	0.181	0.005	0.003	0.106	292717	0.409	0.179	0.027	0.004	4.0E-11	197948	0.090	-0.009
rs667515	11	69449076	*CCND1*	G	C	0.618	0.018	0.003	9.3E-12	292266	0.287	0.613	0.016	0.003	6.7E-07	209612	0.215	0.013
rs61885091	11	69791952	*ANO1/FGF4*	A	G	0.169	0.023	0.004	4.8E-10	277677	0.718	0.171	0.018	0.004	1.9E-05	197948	0.062	0.024
rs10830963*	11	92708710	*MTNR1B*	G	C	0.277	0.019	0.003	2.8E-11	298126	0.045	0.279	0.045	0.003	9.1E-39	209954	0.147	-0.002
rs10895278	11	102095335	*YAP1*	C	T	0.338	0.011	0.003	6.6E-05	292716	0.856	0.340	0.023	0.003	6.7E-13	210263	0.944	-0.001
rs11055030	12	12878349	*APOLD1*	G	C	0.718	0.020	0.003	3.9E-12	292715	0.113	0.713	0.006	0.003	0.062	197948	0.580	0.022
rs2306547	12	26877885	*ITPR2*	C	T	0.534	0.019	0.003	4.4E-13	292721	0.874	0.531	0.016	0.003	1.5E-07	210190	0.762	0.016
rs11051061	12	30914668	*CAPRIN2*	A	G	0.266	0.011	0.003	1.1E-04	292716	0.198	0.268	0.026	0.003	2.6E-14	207299	0.627	0.001
rs6582623	12	46613394	*SLC38A1*	C	T	0.869	0.024	0.004	1.1E-09	292715	0.750	0.862	0.021	0.004	4.5E-06	209612	0.530	0.020
rs180438	12	47187260	*SLC38A4*	G	A	0.192	0.011	0.003	7.5E-04	292716	0.117	0.195	0.036	0.004	8.9E-21	210265	0.947	-0.007
rs8756	12	66359752	*HMGA2*	C	A	0.487	0.041	0.003	2.4E-59	298139	0.077	0.486	0.028	0.003	1.1E-19	210262	0.897	0.037
rs7968682	12	66371880	*HMGA2*	G	T	0.486	0.042	0.003	4.2E-60	298092	0.083	0.486	0.028	0.003	1.4E-19	210265	0.963	0.037
rs1480470	12	66412130	*HMGA2*	G	A	0.631	0.024	0.003	1.4E-19	292712	0.712	0.630	0.007	0.003	0.022	197948	0.934	0.028
rs1533688	12	102772745	*IGF1*	C	T	0.769	0.005	0.003	0.090	298133	0.385	0.774	0.022	0.004	3.4E-09	197948	0.325	-0.004
rs2647873	12	103081192	*LINC00485/IGF1*	A	G	0.520	0.018	0.003	2.9E-12	292715	0.228	0.519	0.022	0.003	1.2E-12	209613	0.753	0.009
rs17033114	12	103123339	*LINC00485/IGF1*	T	C	0.940	0.016	0.006	7.7E-03	289671	0.967	0.934	0.054	0.007	1.1E-15	210248	0.110	-0.008
rs3184504	12	111884608	*SH2B3*	C	T	0.521	0.023	0.003	2.6E-19	296867	0.011	0.518	0.037	0.003	1.4E-33	210260	0.784	0.005
rs9549046	13	40647206	*LINC00332*	A	G	0.118	0.029	0.004	8.0E-13	291448	0.584	0.111	0.013	0.005	7.7E-03	197947	0.523	0.027
rs34217484	13	48854550	*LINC00441/RB1*	A	T	0.264	0.019	0.003	6.8E-11	287438	0.477	0.264	0.018	0.004	2.3E-07	197948	0.734	0.012
rs9318511	13	78601413	*LINC00446*	C	A	0.873	0.027	0.004	6.0E-12	292266	0.058	0.876	0.015	0.005	2.1E-03	197947	0.642	0.024
rs6575803	14	101257755	*MIR2392/DLK1*	C	T	0.895	0.032	0.004	1.3E-12	284076	0.317	0.889	0.006	0.005	0.222	208906	3.9E-04	0.034
rs75844534	15	38667117	*SPRED1*	A	C	0.124	0.026	0.004	4.9E-11	292715	0.649	0.124	-0.004	0.005	0.387	197947	0.102	0.036
rs2928148	15	41401550	*INO80*	A	G	0.526	0.006	0.003	0.018	292719	0.645	0.523	0.018	0.003	2.6E-09	210263	0.089	-0.004
rs339969	15	60883281	*RORA*	A	C	0.619	0.017	0.003	2.2E-10	292719	0.689	0.614	0.015	0.003	2.4E-06	210264	0.684	0.011
rs3784789	15	75082552	*CSK*	G	C	0.659	-0.004	0.003	0.152	298136	0.638	0.674	0.022	0.003	2.2E-11	210261	0.532	-0.018
rs12909648	15	86224570	*KLHL25/AKAP13*	G	A	0.524	0.012	0.003	1.7E-06	292716	0.926	0.523	0.026	0.003	2.6E-18	210254	0.607	-0.003
rs12443252	15	91064690	*CRTC3*	T	C	0.548	0.006	0.003	0.017	292423	0.469	0.550	0.018	0.003	4.8E-09	197948	0.350	-0.007
rs7183988	15	91428589	*FES/FURIN*	G	T	0.529	0.018	0.003	1.7E-12	294939	0.676	0.526	0.029	0.003	1.4E-20	197947	0.594	0.007
rs4932373	15	91429287	*FES/FURIN*	A	C	0.680	0.020	0.003	3.0E-13	295749	0.851	0.675	0.028	0.003	1.7E-17	197948	0.847	0.010
rs55958435	15	96852638	*NR2F2*	A	G	0.748	0.025	0.003	1.6E-16	292710	0.693	0.750	0.013	0.004	5.4E-04	197948	0.378	0.022
rs7402983	15	99193276	*IGF1R*	A	C	0.405	0.024	0.003	2.6E-19	292717	0.986	0.398	0.015	0.003	2.0E-06	197948	0.048	0.027

rs11630479	15	99240481	*IGF1R*	G	A	0.703	0.014	0.003	8.9E-07	292721	0.234	0.698	0.017	0.003	3.5E-07	210262	0.098	0.007
rs2045457	16	20046115	*GPR139/GPRC5B*	G	A	0.311	0.016	0.003	6.3E-09	292716	0.051	0.307	0.013	0.003	9.6E-05	210264	0.859	0.012
rs40434	16	55699525	*SLC6A2*	G	A	0.391	0.017	0.003	3.0E-10	292714	0.798	0.390	0.003	0.003	0.386	197948	0.725	0.017
rs28544888	16	55741204	*SLC6A2*	C	T	0.911	0.026	0.005	1.6E-08	292236	0.064	0.913	0.015	0.006	6.7E-03	197947	0.675	0.027
rs11641308	16	75312023	*BCAR1*	T	C	0.350	0.007	0.003	0.013	292710	0.553	0.346	0.020	0.003	1.1E-09	197948	0.051	-0.005
rs222857	17	7164563	*CLDN7/SLC2A4*	T	C	0.575	0.026	0.003	1.1E-24	298132	0.131	0.568	0.018	0.003	2.2E-09	209557	0.905	0.026
rs2428362[†]	17	7180274	*CLDN7/SLC2A4*	T	C	0.576	0.025	0.003	1.80E-22	292709	0.152	0.571	0.021	0.003	5.1E-11	197093	0.566	0.023
rs4511593	17	7455536	*TNFSF12-TNFSF13*	T	C	0.650	0.017	0.003	1.1E-10	292717	0.847	0.649	0.006	0.003	0.054	210267	0.262	0.019
rs9909342	17	25652275	*WSB1*	A	G	0.381	0.018	0.003	2.2E-11	292713	0.334	0.384	0.009	0.003	2.9E-03	209613	0.664	0.019
rs7223535	17	29211667	*ATAD5*	G	A	0.732	0.021	0.003	2.1E-13	292715	0.984	0.728	0.016	0.004	9.6E-06	197948	0.433	0.020
rs11867479	17	68090207	*KCNJ16*	T	C	0.353	0.017	0.003	1.1E-10	298138	0.200	0.360	0.008	0.003	0.012	210262	0.890	0.018
rs10221267	17	68464662	*KCNJ2*	T	C	0.512	0.017	0.003	6.5E-11	296641	0.314	0.514	0.007	0.003	0.035	197948	0.589	0.018
rs73354194	17	79905947	*MYADML2*	C	T	0.025	0.061	0.009	1.0E-11	268519	0.321	0.023	0.016	0.011	0.120	197948	0.538	0.060
rs9912553	17	79959703	*ASPSCR1*	G	C	0.726	0.014	0.003	1.7E-06	288184	0.155	0.725	0.021	0.004	1.8E-09	197947	0.718	0.006
rs11082304	18	20720973	*CABLES1*	T	G	0.508	0.016	0.003	4.2E-10	296792	0.035	0.512	0.010	0.003	1.4E-03	209553	0.188	0.013
rs2779165	19	4915447	*UHRF1*	G	C	0.184	0.022	0.003	7.6E-11	291447	0.340	0.189	0.017	0.004	2.5E-05	208905	0.283	0.018
rs8106042	19	7161849	*INSR*	G	C	0.281	0.020	0.003	2.2E-12	291451	0.691	0.280	0.007	0.003	0.043	197947	0.291	0.023
rs2967676	19	8789666	*ACTL9*	A	C	0.845	0.021	0.004	1.1E-08	284486	0.197	0.842	0.044	0.004	2.2E-25	210262	0.748	-0.003
rs41355649	19	33790556	*CEBPA*	G	A	0.934	0.034	0.005	1.2E-10	291155	0.911	0.932	0.018	0.006	3.8E-03	197948	0.490	0.042
rs1129156	19	40719076	*MAP3K10/AKT2*	T	C	0.268	0.017	0.003	2.5E-09	292719	0.188	0.268	0.007	0.003	0.040	210262	0.770	0.022
rs147957154	19	43431040	*PSG7*	T	C	0.132	0.023	0.004	2.7E-09	269001	0.722	0.137	0.000	0.004	0.947	197947	0.645	0.026
rs516246	19	49206172	*FUT2*	C	T	0.506	0.018	0.003	9.3E-12	295749	0.285	0.495	0.008	0.003	6.0E-03	210213	0.107	0.017
rs255773	19	54723546	*LILRB3/RPS9*	C	T	0.536	0.018	0.003	1.3E-11	288702	0.945	0.534	0.012	0.003	2.8E-04	197948	0.440	0.018
rs147110934	19	55993436	*ZNF628*	G	T	0.975	0.052	0.009	1.6E-09	276061	0.299	0.976	0.028	0.010	5.7E-03	197947	0.884	0.055
rs12461110	19	56320663	*NLRP11*	A	G	0.358	0.006	0.003	0.028	286534	0.799	0.364	0.021	0.003	5.3E-11	209560	0.385	-0.005
rs304001	19	56423668	*NLRP13*	G	A	0.395	0.009	0.003	8.5E-04	287103	0.105	0.394	0.022	0.003	2.6E-12	210264	0.837	-0.003
rs6040076	20	10658882	*JAG1*	C	G	0.500	0.019	0.003	4.4E-13	292711	0.407	0.504	0.015	0.003	2.0E-06	197948	0.905	0.015
rs6033062	20	11207419	*LOC339593*	A	T	0.460	0.016	0.003	5.2E-10	292717	0.859	0.460	0.011	0.003	2.7E-04	210264	0.724	0.014
rs1203876	20	22540915	*LINC00261/FOXA2*	C	A	0.046	0.038	0.006	9.4E-10	291539	0.843	0.050	-0.005	0.007	0.475	210257	0.124	0.055
rs11698914	20	31327144	*COMMD7*	C	G	0.233	0.032	0.003	1.2E-24	292713	0.910	0.229	0.015	0.004	4.9E-05	197948	0.742	0.029
rs181451002	20	32466219	*CHMP4B*	G	A	0.979	0.020	0.009	0.026	300702	0.875	0.979	0.063	0.011	3.0E-09	217750	0.905	-0.006
rs2889874	20	33715777	*EDEM2/MYH7B*	G	T	0.452	0.016	0.003	9.4E-10	292712	0.731	0.454	0.013	0.003	2.4E-05	197948	0.499	0.014

rs1012167	20	39159119	*MAFB*	C	T	0.401	0.024	0.003	1.2E-19	292373	0.541	0.408	0.011	0.003	2.9E-04	210260	0.101	0.024
rs753381	20	39797465	*PLCG1*	T	C	0.451	0.015	0.003	3.4E-09	297797	0.031	0.451	0.004	0.003	0.241	210262	0.222	0.018
rs6026449	20	57272617	*STX16-NPEPL1/GNAS*	C	T	0.627	0.017	0.003	2.5E-10	292375	0.387	0.632	0.005	0.003	0.129	197948	0.483	0.018
rs73143584	20	62445702	*ZBTB46*	A	G	0.110	0.029	0.004	1.8E-11	286584	0.719	0.113	0.011	0.005	0.025	197948	0.711	0.031
rs2229742	21	16339172	*NRIP1*	G	C	0.881	0.027	0.004	7.4E-11	297794	0.095	0.892	0.016	0.005	1.6E-03	210164	0.596	0.028
rs220193	21	43581308	*UMODL1*	A	G	0.225	0.021	0.003	4.1E-11	292712	0.940	0.213	0.007	0.004	0.076	197947	0.965	0.018
rs134594	22	29468456	*KREMEN1*	C	T	0.351	0.017	0.003	5.8E-10	290627	0.227	0.352	-0.002	0.003	0.573	208643	0.097	0.022
rs41311445	22	42070374	*NHP2L1/SREBF2*	A	C	0.903	0.033	0.004	3.3E-13	289016	0.024	0.904	0.017	0.005	1.2E-03	197947	0.517	0.034
rs7285579	22	46441980	*LOC100271722*	C	T	0.698	0.017	0.003	2.7E-09	290177	0.230	0.703	0.010	0.003	3.8E-03	197947	0.917	0.018

SNP-Single nucleotide polymorphism; CHR - chromosome; BP - base position; EA - effect allele; OA - other allele; EAF - effect allele frequency; Beta - effect size; SE - standard error; HetP - heterogeneity

PMNS - Pune Maternal Nutrition Study, PS - Parthenon Study, MMNP - Mumbai Maternal Nutrition Project, MBRC - Mysore Birth Record Cohort, GIFTS includes Dhaka-WP2, Dhaka-WP3 and UK-Bang cc

*, Warrington et al, 2019

Structural equation model (SEM)					EAF in South Asian cohorts				
justed Fetal Effects		SEM-adjusted Maternal Effects							
SE	P-value	Beta	SE	P-value	PMNS	PS	MMNP	MBRC	GIFTS
0.006	4.0E-01	0.032	0.006	2.5E-07	0.211	0.208	0.221	0.193	0.219
0.006	1.6E-06	-0.006	0.007	4.2E-01	0.847	0.819	0.833	0.832	0.848
0.009	4.0E-08	-0.014	0.011	2.1E-01	0.022	0.013	0.014	0.006	0.012
0.005	7.9E-07	0.005	0.005	3.4E-01	0.155	0.162	0.157	0.168	0.133
0.004	3.7E-04	0.005	0.005	3.4E-01	0.526	0.486	0.497	0.480	0.545
0.005	4.7E-05	0.005	0.006	4.6E-01	0.096	0.115	0.100	0.090	0.093
0.013	2.6E-03	0.029	0.014	4.1E-02	0.987	0.984	0.975	0.983	0.978
0.004	3.0E-05	-0.003	0.005	5.3E-01	0.342	0.347	0.343	0.359	0.322
0.004	1.1E-04	0.006	0.005	2.6E-01	0.334	0.324	0.320	0.305	0.307
0.004	6.9E-04	0.004	0.005	4.5E-01	0.586	0.571	0.533	0.533	0.572
0.004	2.8E-04	0.013	0.005	7.7E-03	0.391	0.445	0.418	0.427	0.438
0.004	4.5E-04	0.013	0.005	6.3E-03	0.389	0.446	0.424	0.428	0.438
0.005	2.2E-09	-0.006	0.005	2.4E-01	0.761	0.757	0.765	0.755	0.787
0.004	6.8E-01	0.017	0.005	5.2E-04	0.531	0.515	0.502	0.509	0.531
0.004	4.7E-06	-0.004	0.005	4.2E-01	0.457	0.429	0.457	0.484	0.437
0.004	3.3E-01	0.025	0.005	1.2E-07	0.674	0.675	0.679	0.675	0.662
0.005	5.5E-17	0.011	0.005	3.0E-02	0.548	0.554	0.538	0.539	0.541
0.004	6.5E-06	-0.004	0.005	4.3E-01	0.530	0.503	0.503	0.493	0.524
0.004	2.8E-08	0.038	0.005	5.4E-14	0.911	0.898	0.912	0.878	0.888
0.005	2.2E-03	0.005	0.005	3.2E-01	0.240	0.231	0.274	0.230	0.230
0.005	1.3E-05	-0.005	0.006	4.0E-01	0.133	0.143	0.132	0.144	0.137
0.005	6.1E-03	0.033	0.006	2.6E-09	0.251	0.241	0.257	0.243	0.239
0.004	1.5E-02	0.011	0.005	1.9E-02	0.396	0.393	0.377	0.405	0.412
0.005	6.3E-32	-0.029	0.005	3.8E-08	0.203	0.188	0.188	0.173	0.186
0.005	2.6E-01	0.027	0.005	1.1E-06	0.619	0.643	0.639	0.636	0.585
0.004	8.1E-01	0.020	0.005	1.3E-05	0.268	0.276	0.279	0.278	0.301
0.006	3.4E-04	0.006	0.007	4.0E-01	0.073	0.069	0.077	0.076	0.100

0.004	5.0E-07	-0.001	0.005	7.6E-01	0.620	0.595	0.587	0.592	0.573
0.004	3.3E-02	0.038	0.005	6.5E-15	0.381	0.339	0.360	0.371	0.387
0.004	7.6E-39	-0.003	0.005	4.7E-01	0.499	0.522	0.451	0.500	0.489
0.005	2.7E-06	-0.006	0.005	2.6E-01	0.832	0.829	0.824	0.834	0.817
0.005	1.1E-11	0.010	0.005	7.6E-02	0.150	0.148	0.123	0.133	0.164
0.005	3.6E-11	0.011	0.005	3.9E-02	0.146	0.144	0.122	0.128	0.166
0.004	9.1E-01	0.026	0.005	7.3E-08	0.572	0.553	0.527	0.535	0.570
0.004	6.2E-02	0.024	0.005	1.0E-06	0.547	0.541	0.531	0.556	0.587
0.004	2.8E-05	0.017	0.005	3.7E-04	0.537	0.507	0.479	0.526	0.481
0.004	1.9E-04	0.019	0.005	7.5E-05	0.557	0.528	0.494	0.532	0.499
0.004	9.2E-02	0.023	0.005	1.5E-06	0.443	0.460	0.462	0.414	0.414
0.004	4.1E-04	-0.001	0.005	9.1E-01	0.601	0.627	0.633	0.617	0.590
0.005	8.1E-05	-0.005	0.006	3.9E-01	0.714	0.697	0.704	0.703	0.686
0.005	1.4E-04	0.011	0.006	7.3E-02	0.757	0.793	0.730	0.783	0.739
0.005	1.7E-03	0.010	0.005	7.8E-02	0.727	0.707	0.721	0.719	0.691
0.004	2.3E-01	0.022	0.005	3.1E-06	0.470	0.475	0.442	0.464	0.502
0.004	7.3E-02	0.020	0.005	1.7E-05	0.772	0.765	0.773	0.785	0.767
0.005	4.5E-01	0.045	0.005	3.7E-17	0.632	0.643	0.640	0.632	0.664
0.011	1.8E-01	0.067	0.012	5.2E-08	0.992	0.996	0.994	0.995	0.990
0.006	5.7E-01	0.040	0.007	4.7E-08	0.892	0.919	0.894	0.921	0.897
0.005	3.2E-26	-0.019	0.005	6.1E-04	0.718	0.748	0.766	0.740	0.710
0.005	6.4E-05	0.004	0.006	4.3E-01	0.522	0.549	0.513	0.521	0.516
0.004	8.0E-04	0.005	0.005	3.4E-01	0.318	0.326	0.303	0.390	0.420
0.007	7.2E-01	0.040	0.008	2.2E-07	0.812	0.806	0.806	0.827	0.792
0.006	1.2E-02	0.014	0.007	4.8E-02	0.423	0.410	0.416	0.434	0.265
0.004	9.3E-06	-0.002	0.005	6.4E-01	0.588	0.552	0.575	0.544	0.614
0.009	6.0E-03	0.041	0.010	3.6E-05	0.036	0.053	0.047	0.036	0.033
0.010	4.0E-02	0.051	0.011	5.6E-06	0.015	0.028	0.016	0.019	0.013
0.004	1.4E-01	0.022	0.005	4.9E-06	0.279	0.274	0.306	0.264	0.261
0.005	7.5E-04	0.009	0.005	1.0E-01	0.797	0.759	0.776	0.769	0.793
0.005	1.1E-04	0.001	0.005	8.4E-01	0.603	0.643	0.641	0.651	0.615
0.006	8.0E-02	0.023	0.007	1.4E-03	0.211	0.216	0.210	0.185	0.198

0.006	3.0E-01	0.025	0.007	1.7E-04	0.246	0.255	0.242	0.212	0.234
0.004	2.1E-05	-0.008	0.005	1.1E-01	0.255	0.312	0.262	0.304	0.267
0.005	5.4E-03	0.006	0.006	2.9E-01	0.777	0.785	0.783	0.823	0.768
0.005	1.4E-01	0.019	0.005	4.2E-04	0.719	0.729	0.735	0.756	0.712
0.005	3.3E-06	0.000	0.005	9.8E-01	0.817	0.813	0.794	0.830	0.817
0.005	6.8E-04	0.004	0.005	3.9E-01	0.660	0.681	0.671	0.659	0.673
0.005	8.2E-10	0.004	0.005	3.9E-01	0.845	0.861	0.838	0.833	0.848
0.005	5.8E-09	0.006	0.005	2.2E-01	0.845	0.861	0.838	0.832	0.848
0.004	4.3E-05	0.000	0.005	9.7E-01	0.741	0.746	0.757	0.760	0.754
0.005	1.8E-01	0.017	0.006	2.0E-03	0.830	0.843	0.854	0.871	0.841
0.004	1.1E-03	0.009	0.005	5.3E-02	0.583	0.597	0.574	0.606	0.574
0.004	1.1E-02	0.009	0.005	7.3E-02	0.621	0.610	0.602	0.595	0.455
0.004	7.0E-01	0.017	0.005	3.0E-04	0.861	0.863	0.852	0.856	0.735
0.005	1.3E-03	0.014	0.006	9.6E-03	0.685	0.711	0.673	0.663	0.720
0.004	1.1E-01	0.010	0.005	4.0E-02	0.532	0.527	0.519	0.511	0.535
0.005	5.9E-01	0.028	0.006	4.9E-07	0.239	0.254	0.235	0.248	0.227
0.006	9.7E-04	0.034	0.007	8.9E-07	0.948	0.936	0.953	0.959	0.922
0.009	7.0E-04	0.000	0.009	9.9E-01	0.831	0.808	0.806	0.825	0.801
0.007	4.6E-07	-0.014	0.008	8.4E-02	0.152	0.209	0.154	0.195	0.124
0.005	2.2E-02	0.012	0.006	2.9E-02	0.214	0.238	0.194	0.256	0.205
0.008	1.2E-11	-0.010	0.009	2.7E-01	0.006	0.008	0.008	0.003	0.005
0.004	1.6E-06	-0.003	0.005	5.5E-01	0.183	0.184	0.178	0.202	0.146
0.010	1.1E-01	0.077	0.012	1.1E-10	0.009	0.007	0.016	0.013	0.010
0.005	4.7E-02	0.018	0.005	4.8E-04	0.963	0.964	0.966	0.967	0.956
0.005	3.0E-03	0.014	0.005	4.9E-03	0.951	0.948	0.958	0.962	0.942
0.008	5.2E-01	0.040	0.009	7.4E-06	0.981	0.987	0.991	0.992	0.991
0.008	2.0E-04	0.003	0.009	7.5E-01	0.028	0.037	0.018	0.024	0.074
0.004	6.1E-06	-0.002	0.005	6.9E-01	0.636	0.639	0.637	0.638	0.636
0.006	9.5E-01	0.026	0.006	6.2E-05	0.846	0.842	0.845	0.843	0.834
0.004	1.6E-05	-0.002	0.005	6.7E-01	0.430	0.382	0.410	0.389	0.393
0.005	3.1E-09	-0.005	0.006	3.6E-01	0.825	0.862	0.849	0.844	0.824
0.006	1.6E-05	-0.001	0.007	8.7E-01	0.866	0.864	0.836	0.847	0.859

0.006	1.0E-02	0.039	0.006	3.9E-10	0.276	0.284	0.315	0.261	0.305
0.005	2.1E-06	-0.002	0.005	7.4E-01	0.399	0.440	0.427	0.434	0.437
0.005	2.5E-05	0.002	0.006	7.3E-01	0.729	0.750	0.738	0.725	0.711
0.004	5.8E-05	0.002	0.005	6.3E-01	0.645	0.688	0.640	0.641	0.649
0.004	3.6E-05	-0.005	0.005	3.0E-01	0.382	0.408	0.385	0.417	0.418
0.005	1.7E-03	0.010	0.006	8.8E-02	0.635	0.632	0.667	0.640	0.678
0.007	1.7E-09	0.009	0.008	2.2E-01	0.079	0.062	0.102	0.090	0.107
0.004	3.9E-03	0.016	0.005	6.1E-04	0.426	0.431	0.451	0.431	0.454
0.004	2.9E-03	0.015	0.005	9.1E-04	0.448	0.460	0.483	0.463	0.492
0.004	4.4E-02	0.031	0.005	7.6E-10	0.552	0.549	0.517	0.533	0.559
0.005	1.3E-05	-0.001	0.005	7.9E-01	0.704	0.723	0.703	0.704	0.710
0.004	2.2E-07	-0.001	0.005	8.6E-01	0.780	0.774	0.771	0.777	0.768
0.006	4.1E-06	0.004	0.007	6.1E-01	0.196	0.161	0.214	0.180	0.240
0.005	4.2E-07	0.001	0.006	8.4E-01	0.198	0.192	0.193	0.188	0.168
0.005	1.8E-04	0.001	0.005	8.9E-01	0.135	0.115	0.137	0.139	0.127
0.004	1.6E-05	0.010	0.005	4.5E-02	0.495	0.470	0.468	0.512	0.510
0.004	1.0E-05	0.010	0.005	4.2E-02	0.500	0.488	0.484	0.525	0.529
0.004	1.5E-17	-0.018	0.005	1.7E-04	0.542	0.561	0.564	0.556	0.587
0.005	2.6E-05	0.039	0.005	3.6E-13	0.684	0.693	0.723	0.663	0.694
0.007	7.0E-01	0.044	0.007	1.6E-09	0.037	0.033	0.026	0.037	0.062
0.004	6.5E-06	0.008	0.005	1.0E-01	0.446	0.406	0.383	0.458	0.411
0.004	1.4E-04	0.003	0.005	5.2E-01	0.755	0.731	0.765	0.767	0.764
0.005	5.5E-01	0.020	0.005	1.2E-04	0.289	0.304	0.269	0.277	0.295
0.005	2.9E-10	0.007	0.005	1.9E-01	0.754	0.768	0.727	0.765	0.749
0.005	2.2E-08	0.010	0.005	5.1E-02	0.738	0.759	0.726	0.233	0.752
0.004	1.7E-04	0.011	0.005	2.4E-02	0.548	0.551	0.558	0.539	0.543
0.004	1.6E-09	-0.007	0.005	1.9E-01	0.536	0.532	0.560	0.550	0.517
0.004	4.9E-05	-0.002	0.005	6.3E-01	0.544	0.542	0.553	0.527	0.576
0.005	1.0E-03	0.039	0.005	5.9E-14	0.725	0.759	0.766	0.756	0.770
0.004	2.2E-08	-0.005	0.005	2.5E-01	0.755	0.727	0.750	0.775	0.692
0.005	3.7E-01	0.022	0.005	2.4E-05	0.577	0.570	0.576	0.522	0.549
0.005	1.4E-01	0.020	0.005	1.1E-04	0.493	0.507	0.481	0.442	0.449

0.004	6.9E-01	0.018	0.005	9.5E-05	0.576	0.534	0.535	0.570	0.589
0.005	8.7E-02	0.033	0.006	1.2E-07	0.141	0.154	0.143	0.140	0.157
0.004	1.5E-03	0.011	0.005	2.6E-02	0.748	0.746	0.768	0.745	0.732
0.006	2.5E-05	0.004	0.006	5.5E-01	0.120	0.137	0.172	0.138	0.133
0.005	6.7E-01	0.046	0.005	4.6E-19	0.433	0.416	0.406	0.578	0.409
0.004	7.3E-01	0.025	0.005	3.3E-07	0.282	0.272	0.266	0.259	0.294
0.005	1.0E-06	-0.005	0.005	3.8E-01	0.717	0.687	0.699	0.712	0.651
0.004	1.5E-04	0.007	0.005	1.5E-01	0.804	0.797	0.811	0.775	0.754
0.005	9.1E-01	0.026	0.005	1.1E-06	0.152	0.144	0.152	0.160	0.170
0.006	8.9E-04	0.011	0.007	1.0E-01	0.870	0.843	0.846	0.838	0.863
0.005	1.6E-01	0.039	0.006	4.1E-11	0.452	0.455	0.439	0.462	0.457
0.004	1.7E-19	0.009	0.005	5.0E-02	0.187	0.215	0.187	0.186	0.198
0.004	4.9E-20	0.009	0.005	5.5E-02	0.186	0.213	0.185	0.190	0.196
0.004	1.1E-10	-0.007	0.005	1.5E-01	0.552	0.541	0.526	0.532	0.481
0.005	4.4E-01	0.025	0.006	1.6E-05	0.810	0.802	0.795	0.797	0.807
0.004	3.3E-02	0.017	0.005	3.3E-04	0.403	0.409	0.446	0.419	0.446
0.009	3.7E-01	0.053	0.010	6.2E-08	0.888	0.902	0.872	0.883	0.884
0.004	2.2E-01	0.034	0.005	1.8E-13	0.915	0.936	0.935	0.919	0.868
0.006	2.2E-05	0.001	0.008	8.7E-01	0.204	0.198	0.191	0.176	0.254
0.005	1.1E-02	0.013	0.005	1.3E-02	0.336	0.356	0.343	0.336	0.312
0.006	1.5E-04	0.007	0.007	3.6E-01	0.875	0.897	0.877	0.902	0.866
0.007	9.9E-07	-0.005	0.008	5.3E-01	0.966	0.969	0.969	0.976	0.956
0.006	1.5E-08	-0.021	0.007	2.9E-03	0.058	0.065	0.070	0.050	0.066
0.004	3.2E-01	0.020	0.005	1.6E-05	0.463	0.438	0.453	0.420	0.509
0.004	1.2E-02	0.010	0.005	3.6E-02	0.592	0.577	0.591	0.570	0.617
0.004	2.4E-05	0.030	0.005	1.2E-09	0.152	0.145	0.163	0.165	0.631
0.004	5.1E-01	0.027	0.005	3.4E-09	0.750	0.752	0.786	0.750	0.799
0.004	7.3E-02	0.023	0.005	1.7E-06	0.424	0.396	0.409	0.389	0.375
0.004	9.1E-02	0.024	0.005	6.1E-07	0.585	0.572	0.562	0.592	0.601
0.004	2.1E-02	0.019	0.005	1.7E-04	0.723	0.719	0.716	0.710	0.751
0.005	5.7E-06	0.004	0.006	5.0E-01	0.803	0.789	0.756	0.781	0.748
0.004	4.6E-10	0.000	0.005	9.5E-01	0.413	0.417	0.427	0.387	0.427

0.004	1.4E-01	0.013	0.005	8.9E-03	0.684	0.671	0.674	0.694	0.687
0.004	5.7E-03	0.008	0.005	9.8E-02	0.454	0.485	0.485	0.463	0.452
0.004	4.8E-05	-0.006	0.005	2.5E-01	0.399	0.356	0.379	0.339	0.406
0.007	2.5E-04	0.002	0.008	8.2E-01	0.879	0.874	0.863	0.852	0.846
0.004	2.2E-01	0.023	0.005	7.9E-06	0.487	0.469	0.556	0.504	0.476
0.004	5.8E-10	0.004	0.005	3.8E-01	0.621	0.607	0.617	0.653	0.548
0.004	7.2E-08	0.008	0.005	1.1E-01	0.612	0.591	0.597	0.625	0.512
0.004	7.4E-06	-0.004	0.005	3.8E-01	0.673	0.705	0.657	0.696	0.708
0.004	6.7E-06	0.001	0.005	8.3E-01	0.516	0.500	0.493	0.530	0.482
0.005	2.4E-05	0.007	0.005	2.2E-01	0.901	0.914	0.897	0.885	0.878
0.004	2.2E-05	-0.002	0.005	7.5E-01	0.219	0.195	0.238	0.222	0.251
0.004	1.9E-05	-0.002	0.005	6.9E-01	0.610	0.640	0.646	0.679	0.610
0.014	1.7E-05	-0.011	0.016	5.0E-01	0.139	0.152	0.175	0.155	0.144
0.005	2.0E-01	0.017	0.005	1.9E-03	0.624	0.615	0.664	0.652	0.605
0.004	1.0E-03	0.003	0.005	4.9E-01	0.479	0.432	0.459	0.459	0.447
0.005	1.0E-03	0.007	0.006	2.4E-01	0.072	0.077	0.065	0.088	0.121
0.005	6.6E-07	-0.006	0.005	2.9E-01	0.257	0.251	0.260	0.292	0.266
0.006	5.8E-01	0.048	0.006	4.4E-14	0.919	0.935	0.923	0.895	0.897
0.008	4.5E-07	-0.010	0.009	2.7E-01	0.974	0.975	0.985	0.982	0.954
0.005	1.9E-06	-0.007	0.005	1.7E-01	0.211	0.219	0.189	0.204	0.221
0.006	2.4E-05	-0.012	0.007	7.3E-02	0.124	0.111	0.097	0.118	0.107
0.004	3.4E-05	0.000	0.005	9.2E-01	0.779	0.732	0.738	0.800	0.726
0.004	2.5E-05	0.004	0.005	4.4E-01	0.645	0.610	0.627	0.645	0.585
0.014	6.5E-05	0.001	0.015	9.7E-01	0.995	0.994	0.991	0.993	0.992
0.004	2.6E-01	0.022	0.005	3.4E-06	0.316	0.301	0.292	0.327	0.295
0.004	5.4E-01	0.023	0.005	1.9E-06	0.337	0.328	0.349	0.377	0.360
0.004	2.6E-04	0.009	0.005	7.0E-02	0.457	0.445	0.422	0.465	0.468
0.004	7.1E-04	0.003	0.005	5.3E-01	0.363	0.408	0.368	0.365	0.394
0.010	1.3E-08	-0.040	0.011	1.6E-04	0.105	0.096	0.115	0.100	0.115
0.005	2.7E-09	0.003	0.006	5.7E-01	0.296	0.315	0.309	0.309	0.326
0.014	6.5E-01	0.059	0.016	3.1E-04	0.976	0.978	0.984	0.972	0.985
0.004	9.0E-04	0.007	0.005	1.6E-01	0.506	0.534	0.517	0.515	0.520

0.004	1.9E-08	-0.003	0.005	5.5E-01	0.319	0.300	0.324	0.293	0.340
0.004	9.1E-06	-0.007	0.005	1.6E-01	0.398	0.397	0.398	0.366	0.399
0.004	3.2E-05	-0.006	0.005	2.5E-01	0.511	0.515	0.503	0.476	0.495
0.007	3.3E-06	-0.007	0.008	3.6E-01	0.025	0.028	0.021	0.024	0.033
0.006	1.3E-05	0.002	0.007	8.1E-01	0.934	0.938	0.945	0.926	0.935
0.005	2.9E-04	-0.001	0.006	8.8E-01	0.353	0.414	0.353	0.379	0.350
0.004	6.0E-07	-0.009	0.005	5.3E-02	0.428	0.421	0.386	0.383	0.433
0.007	1.3E-06	-0.002	0.008	7.8E-01	0.954	0.976	0.964	0.957	0.959
0.005	1.1E-04	-0.002	0.005	7.0E-01	0.788	0.786	0.763	0.744	0.814

' p-value

ɔhorts