SUPPLEMENTARY MATERIAL

Genetic evidence for causal relationships between maternal obesity-related traits and birth weight

Overview of Supplementary Material

eMethods

Maximising specificity of genetic variants: excluding single nucleotide polymorphisms (SNPs) with effects on multiple traits ("pleiotropic" SNPs)

It was important to ensure that each genetic score would enable us, as far as possible, to capture specifically the respective maternal trait. To identify SNPs with pleiotropic effects, we queried each of our initial 193 selected SNPs and all SNPs in linkage disequilibrium with these (r^2>0.2) using the National Human Genome Research Institute (NHGRI) catalog of published genome-wide association studies (GWAS)[1] and listed SNPs associated with other traits at $P < 5x10^{-8}$. Starting with this list, we excluded SNPs whose location near a candidate gene and/or the strength of association with another trait suggested that the association with the maternal exposure of interest is almost certainly secondary to the other trait (e.g. exclusion of index SNPs at *FTO* and *MC4R* from the type 2 diabetes genetic score, since these are primarily associated with BMI and secondarily with type 2 diabetes via their effect on BMI). We additionally excluded SNPs from the list with strong evidence of effects on two or more traits that are potentially relevant to the maternal environment and birth weight. Details of SNPs in the final selected list are shown in **eTable 3**.

We performed an updated search of the NHGRI catalog, while writing the research paper, to check for further pleiotropic associations identified for SNPs used in our analyses, which were published after our initial search. We performed sensitivity analyses excluding these additional SNPs to check that they did not alter our findings (results available from the authors on request).

Maximising specificity of genetic variants: separating genetic scores for closely-related maternal traits

Fasting glucose and type 2 diabetes share several genetic susceptibility variants, reflecting the overlap between these two phenotypes (**eTable 3**). We excluded from the type 2 diabetes genetic score the index SNPs at the two fasting glucose loci that explain the most variance in fasting glucose, but have relatively moderate effects on type 2 diabetes risk (*MTNR1B* and *GCK*). Likewise, we excluded the index SNP at the *TCF7L2* locus from the fasting glucose genetic score as it has a proportionately much larger effect on type 2 diabetes risk. In this way, our fasting glucose genetic score would predominantly capture variation in maternal fasting glucose in the normal physiological range, while our type 2 diabetes genetic score would be more likely to capture pathologically-raised fasting and non-fasting maternal glucose levels.

Maternal triglycerides and HDL-cholesterol also share associations with several genetic variants. We therefore attempted to make our genetic scores for these exposures as specific as possible. For HDL- cholesterol, we included only SNPs near genes associated with known Mendelian lipid disorders (see **eTable 3**)[2]. For triglyceride levels, SNPs were included in the genetic score if they were solely associated with triglyceride levels, or if their effect on triglyceride levels was at least three times greater than that of HDL-, LDL- or total cholesterol, based on effect sizes reported in [2]. To facilitate these comparisons, the raw effect sizes in mg/dL were first converted to percentages of the mean of the corresponding lipid concentration.

SNPs missing from studies

When index SNPs were missing from individual studies, we used the SNP Annotation and Proxy Search tool, SNAP[3] to identify suitable proxy SNPs ($r^2 > 0.8$). If a study had fewer than 80% of the index or proxy SNPs required to generate a specific genetic score, it was excluded from the analysis. The one exception to this was the HAPO (non-GWAS) Study, for which only 6 of 17 triglyceride SNPs had been genotyped. We included this study, despite the missing SNPs, because the 6 genotyped SNPs included those with the largest effects on triglyceride levels, covering the majority of variation captured by the 17-SNP score.

Imputation quality

For each study with GWAS data, we examined the imputation quality (r^2 [4] or proper_info[5]) of SNPs selected for each score. We excluded four studies (B58C-WTCCC, NFBC1966, QIMR and TwinsUK) from analyses of the adiponectin genetic score due to imputation quality scores <0.8 for either 1 or 2 of the 3 SNPs in that score. In each of the remaining 7 genetic scores, a small number of included SNPs had imputation quality scores <0.8, but this only affected a median of 0 to 1 SNP per study, equivalent to a maximum of 6% of the SNPs comprising the score, so we did not exclude them. Finally, we identified that 3 individual SNPs were poorly imputed (r2<0.8) in multiple studies: rs10830963 (fasting glucose genetic score, 4 of 15 studies), rs11063069 (type 2 diabetes genetic score; 11 of 13 studies) and rs13238203 (triglycerides genetic score; 11 of 16 studies). To verify that these individual SNPs did not materially alter our results, we performed sensitivity analyses: (i) we repeated the meta-analyses of the fasting glucose genetic score excluding the 4 studies in which SNP rs10830963 was poorly imputed; (ii) we performed weighted meta-analyses of existing summary GWAS data[6], as described previously[7] both including and excluding the rs11063069 and rs13238203 SNPs. Results of these analyses are available from the authors on request.

Calculation of maternal genetic scores

We calculated a weighted genetic score for each maternal exposure to account for the fact that some SNPs have relatively larger effects than others. Formula 1 below describes the calculation, where w is the weight and SNP is the number of trait-raising or lowering alleles at that locus. The decision to model according to the trait-raising or lowering allele was informed by the known association between each maternal trait and BMI (**Box 1**). The weights used for each SNP were obtained from published GWAS of non-pregnant individuals, which either did not include any of the studies used in this paper or had at most 17% of participants overlapping. These weights and their sources, are summarised in **eTable 3**.

$$\text{Weighted score} = w_1 \times SNP_1 + w_2 \times SNP_2 + \cdots w_n \times SNP_n \quad (1)$$

We rescaled each weighted genetic score (GS) to reflect the number of available SNPs using formula 2 as described in Lin *et al* [8]

$$GS = \frac{\text{Weighted Score x Number of SNPs available}}{\text{Sum of weights of available SNPs}} \qquad (2)$$

Meta-analyses

We meta-analysed data from all available studies to give an overall result from each side of the triangle (**Figure 1**): the genetic score-maternal exposure association; the genetic score-birth weight association; and the observational maternal exposure-birth weight association. We combined the regression coefficients and standard errors from individual study analyses by performing inverse variance meta-analyses with fixed effects as there was little evidence of between-study heterogeneity of effect size. All meta-analyses were performed using the user-written Stata command, metan.[9] We estimated the percentage of total variation among study estimates due to between-study heterogeneity using Cochran's *Q* test and the I^2 statistic.[10] To convert the overall results from birth weight and ponderal index *Z*-scores into grams and kgm^{-3} respectively, we multiplied the effect size and their upper and lower 95% confidence limits by a representative value of the standard deviation of birth weight (484g)[11] or ponderal index (2.78 kgm^{-3}; ALSPAC study).

Mendelian randomization analysis

We performed instrumental variable (IV) estimation using the ratio estimator [12]. We estimated the effect of each maternal exposure on either birth weight or ponderal index by dividing the overall genetic score -birth weight or genetic score -ponderal index association by the overall genetic score -maternal exposure association. The standard error of these estimates was calculated using a Taylor series approximation [13]: we used a 2nd order Taylor series expansion to obtain the variance of the IV estimate. We then made a normal distribution assumption by calculating the 95% confidence interval as follows: IV estimate -/+ 1.96*sqrt(variance of IV estimate from Taylor series expansion).

We used a *Z*-test to test for a difference between the instrumental variable (genetic) and observational associations. The *Z*-score was calculated by estimating the covariance between the observational and instrumental variable (genetic) estimates using a bootstrapping procedure. We used the following formula for our Z-test:

Z = (difference between IV and observational estimate)/sqrt(variance of difference between the estimates)

where the variance of the difference between the estimates is given by:
var(IV estimate) + var(observational estimate) - 2*cov(IV estimate, obs estimate)

The covariance between the IV and observational estimates was estimated by nonparametric bootstrapping the IV and observational estimates using 20 replications (we chose a relatively small number of replications because we included meta-analyses with up to 18 studies). We then compared the Z-statistic with a standard normal distribution.

Guarding against weak instrument bias

Mendelian randomization studies may be susceptible to weak instrument bias. Bias is the difference between the estimated value of a parameter and its true value. Weak instrument bias occurs in the direction of the confounded observational association if the instrument (i.e. the genetic score) is only weakly associated with the phenotype (i.e. the maternal trait).[14] The strength of each instrument used in our study is a function of (i) the proportion of variance in the maternal trait explained by the genetic score and (ii) the sample size. Since the variance in each maternal trait explained by the genetic score was modest, we maximized the sample size (**Table 2**). The possible causal associations identified in our study are therefore unlikely to be due to weak instrument bias.

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Control for population stratification

The presence of subpopulations, which differ in mean birth weight and have genetic variants present at different frequencies, can cause artificial associations between genotypes and birth weight. To ensure that the genetic associations we tested were not confounded in this way, we took the following steps: (i) we included only women of European ancestry; (ii) where necessary, analyses in the individual studies were adjusted for ancestry principal components; (iii) in those studies that had performed a genome-wide association study of birth weight, we checked the genomic control lambda values (ratio of median of the empirically observed distribution of the test statistic to the expected median), which suggested only minimal inflation: median lambda = 1.006 [inter-quartile range: 1.004-1.012]; (iv) we combined summary statistics from individual studies by inverse variance meta-analysis, thereby controlling for any population stratification between studies in the overall sample.

Sensitivity analyses

The ascertainment of offspring birth weight or gestational age data varied among the individual studies, from measurement by trained study personnel, to ascertainment from medical records or birth registries, to self-report. To verify that our results were unaffected by the varying quality or availability of phenotypic data, we performed sensitivity meta-analyses of the associations between the 8 genetic scores and birth weight in up to 12 studies with best quality data (i.e. measured or medical record birth weight and gestational age available). Results of these analyses are available from the authors on request.

To verify that the SBP genetic score-birth weight associations were unaffected by using weights from the original GWAS[15] which were adjusted for BMI, we performed a blood pressure GWAS in 127,698 individuals of British descent using the UK Biobank data. The UK Biobank recruited over 500,000 individuals aged 37-73 years (99.5% were between 40 and 69 years) in 2006-2010 from across the country[16]. Two blood pressure readings were taken approximately 5 minutes apart using an automated Omron blood pressure monitor. Two valid measurements were available for most participants, and the average was taken. Individuals were excluded if the two readings differed by more than 4.56SD, and blood pressure measurements more than 4.56SD away from the mean were excluded. We accounted for blood pressure medication use by adding 15 to the systolic blood pressure measure. Valid blood pressure measurements were available for 120,008 individuals. Blood pressure was adjusted for age, sex and centre location and then inverse normalized.The weights from the blood pressure GWAS in the UK Biobank were utilised to create a genetic risk score in the ALSPAC study (n=7,304). We investigated the correlation of the two blood pressure risk scores (r^2=0.77) and performed Mendelian randomization. The results are available from the authors on request.

Estimating how much of the possible causal effect of BMI on birth weight is mediated by fasting glucose

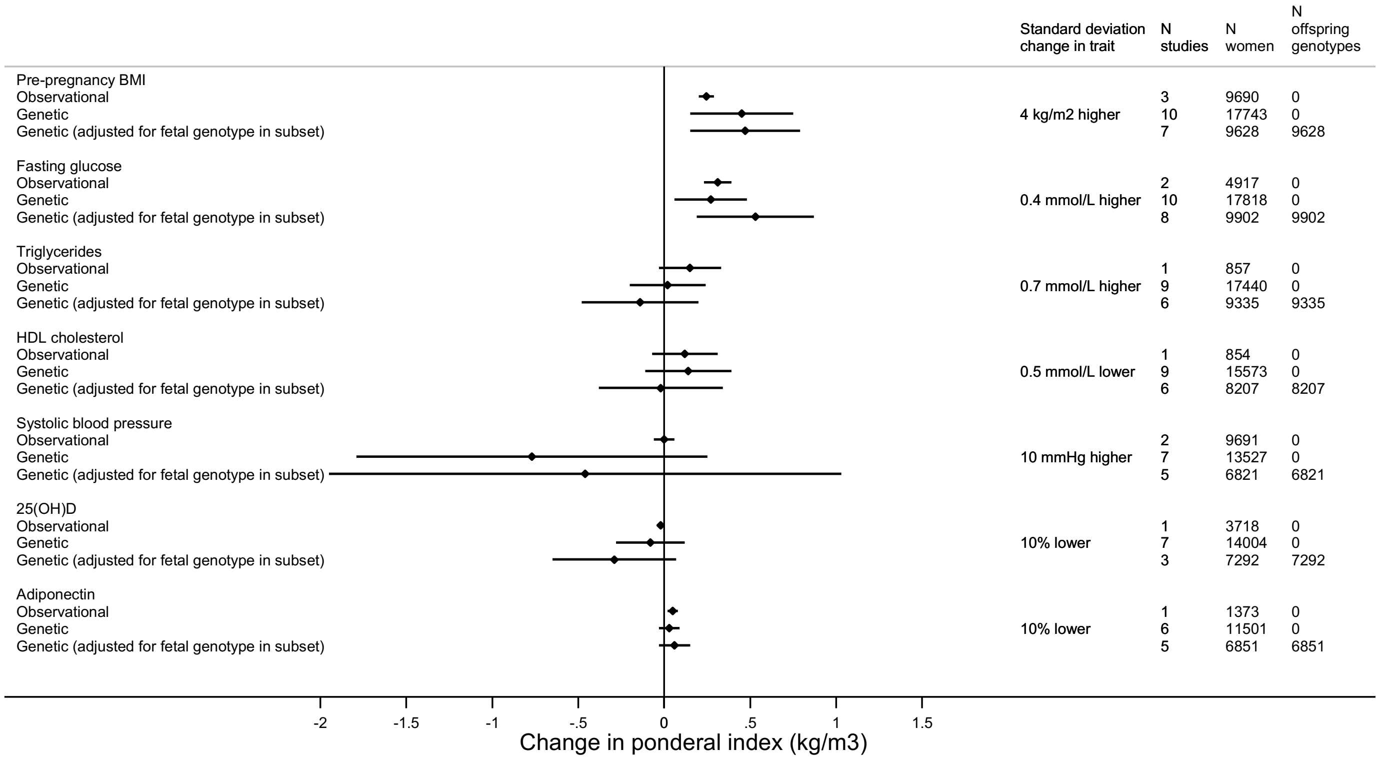
To begin to understand what proportion of the estimated causal effect of BMI on birth weight might be mediated by fasting glucose, we first estimated the causal effect of BMI on maternal fasting glucose. Using available studies (see **eTable 6a**), each additional allele of the BMI genetic score was associated with a 0.145 kg/m^2 (95%CI: 0.126, 0.164) higher BMI and a 0.005 mmol/L (95%CI: 0.001, 0.009) higher fasting glucose. This is equivalent to 0.34 SD higher fasting glucose level per 1 SD higher genetically instrumented BMI. (To convert to SD units, we used BMI SD = 4 kg/m^2 and fasting glucose SD = 0.4 mmol/l.) We then multiplied the genetic estimate and 95%CI for the effect of fasting glucose on birth weight (114g [95%CI: 80, 147g]) by 0.34 to represent the possible causal effect of fasting glucose on birth weight for every 1 SD higher maternal BMI.

Since we found genetic evidence that systolic blood pressure (SBP) was causally associated with birth weight in the opposite direction *and* positively associated with BMI, we additionally estimated the causal effect of BMI on SBP. Each additional allele of the BMI genetic score was associated with a 0.07 mmHg (95%CI: 0.02, 0.11) higher SBP. This is equivalent to 0.19 SD higher SBP per 1 SD higher genetically instrumented BMI. (To convert to SD units, we used SBP SD = 10 mmHg.) We then multiplied the IV estimate and 95%CI for the effect of SBP on birth weight (-208g [95% CI: -394, -21]) by 0.19 to represent the causal effect of SBP on birth weight for every 1 SD higher maternal BMI.

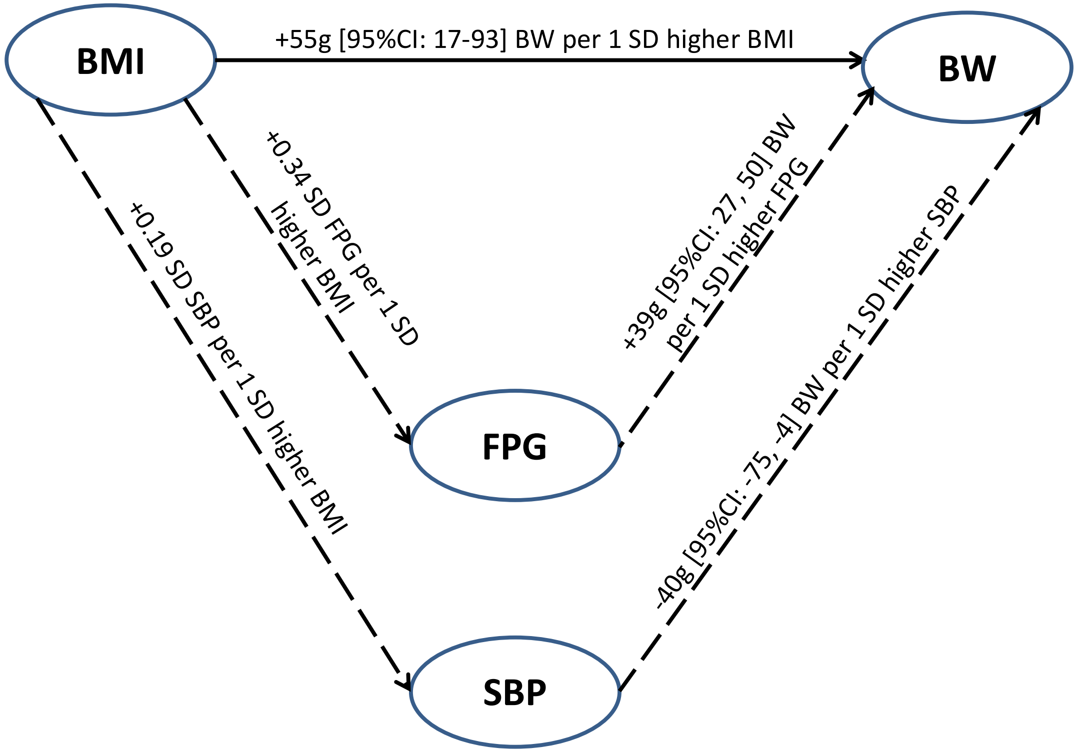
Power calculations

Using data available from the ALSPAC study, we estimated the variance explained in birth weight (BW) by each maternal genetic score as the difference in adjusted-R^2 values between linear regression models (i) and (ii) as follows:
(i) BW = sex + gestational_age
(ii) BW = sex + gest_age + genetic_score
We then used these values to estimate (a) the power available in our included sample to detect evidence of association between maternal genetic score and birth weight at $P<0.05$, and (b) the minimum sample size needed to detect association between maternal genetic score and birth weight at $P<0.05$ with 80% power. Power calculations were performed using Quanto v.1.2 (http://biostats.usc.edu/software).

eFigure 1. Comparison of the observational with the genetic change in ponderal index (in kg/m^3) for a 1 standard deviation (SD) change in each maternal trait. For 25[OH]D and adiponectin, we present the change in ponderal index for a 10% change in maternal trait level because these variables were logged for analysis. The genetic change was estimated from Mendelian randomization analysis, in which a genetic score was used to estimate the possible causal effect of the maternal trait on ponderal index. The genetic estimate is presented twice: in the second case it was adjusted for fetal genotype using a subset of the available studies. The error bars represent the 95% confidence intervals around the effect size estimates.



eFigure 2. Estimating how much of the estimated possible causal effect of maternal BMI on birth weight is mediated by maternal fasting glucose. The solid, horizontal arrow indicates our genetic estimate [95%CI] of the causal effect of BMI on birth weight. The dashed arrows on the left side show genetic causal estimates of a 1 SD (≈ 4kg/m^2) higher maternal pre-pregnancy BMI on maternal fasting glucose (+0.34SD ≈ 0.14 mmol/L) and maternal systolic blood pressure in pregnancy (+0.19 SD ≈ 2 mmHg). The dashed arrows on the right show the scaled genetic causal estimates of these changes in fasting glucose and systolic blood pressure on birth weight. The effect of maternal BMI on birth weight via fasting glucose (+ 39g) is broadly similar to the total effect of maternal BMI on birth weight (+55g), but that effect is opposed by the birth weight lowering effect of SBP (-40g). Overall, this suggests that while maternal fasting glucose mediates part of the positive association between maternal BMI and birth weight, other BMI-related factors are likely to be involved. Abbreviations: BMI, body mass index; BW, birth weight; FPG, fasting plasma glucose; SBP, systolic blood pressure.



eTable 1(a) Basic characteristics of study participants and their offspring (studies 1-5)

	STUDY	ALSPAC Mothers	Berlin Birth Cohort (BBC) Mothers	1958 British Birth Cohort or NCDS (B58C-WTCCC)	1958 British Birth Cohort or NCDS (B58C-T1DGC)	CHOP Mothers
STUDY INFORMATION	Ethnicity	British/European descent	European descent	British/European descent	British/European descent	European American
	Country (Sample source)	UK	Germany	UK	UK	United States of America
	Collection type (e.g. population-based)	Population-Based	Community-based	Population-based	Population-based	Population-based
	N women with birth weight of 1 child and genotypes for at least one genetic score	7,304	1,357	855	836	312
	Year(s) of birth of offspring	April 1991 - Dec 1992	2000-2004	1972-2000	1972-2000	1987-present
	Fetal genotype data available? (Y/N)	Y	Y	N	N	Y
BIRTH WEIGHT	Method by which offspring birth weight (and length, if available) were collected	Obstetric records / measured by trained study personnel	Measured by trained personnel immediately after birth	Maternal self-report (information from questionnaires at age 33 and 42 years)	Maternal self-report (information from questionnaires at age 33 and 42 years)	Questionnaire and EPIC medical records (9.5% of questionnaire values were checked against medical records: r=0.83).
GESTATIONAL AGE	Method by which gestational age was collected	By date of last menstrual period (LMP), paediatric assessment, obstetric assessment, ultrasound assessment.	Calculated from LMP and corrected by ultrasound, if the difference was > 2 weeks	From maternal self-report at ages 33 and 42 years: a question inquiring if the child was born at term, or alternatively how many weeks in advance or late.	From maternal self-report at ages 33 and 42 years: a question inquiring if the child was born at term, or alternatively how many weeks in advance or late.	NA

		ALSPAC Mothers	Berlin Birth Cohort (BBC) Mothers	1958 British Birth Cohort or NCDS (B58C-WTCCC)	1958 British Birth Cohort or NCDS (B58C-T1DGC)	CHOP Mothers
SUMMARY MATERNAL CHARACTERISTICS, where available in the INCLUDED sample, DURING PREGNANCY (median (IQR) given where the trait distribution deviates strongly from the normal distribution	Maternal age at delivery, unless otherwise stated [Mean (sd)], years	28.5 (4.8)	30.1 (5.4)	26.2 (5.2)	26.1 (5.4)	NA
	Maternal pre-pregnancy BMI [Mean (sd)], kg/m2	22.93 (3.73)	22.78 (3.93)	NA	NA	NA
	Maternal pregnancy BMI [Mean (sd)], kg/m2	26.63 (4.03)	28.39 (4.25)	NA	NA	NA
	Fasting glucose [Mean (sd)], mmol/L	NA	NA	NA	NA	NA
	Triglycerides [Mean (sd)], mmol/L	NA	NA	NA	NA	NA
	HDL-cholesterol [Mean (sd)], mmol/L	NA	NA	NA	NA	NA
	Blood pressure [Mean (sd)], mmHg	112.9 (7.5)/65.5 (4.8)	117.28 (10.85)/70.73 (7.56) This was measured at the 3rd trimester.	NA	NA	NA
	25-hydroxyvitamin D [Median (IQR)], nmol/L	62.1 (43.6, 85.4)	NA	NA	NA	NA
	Adiponectin [Mean (sd)], ug/mL	NA	NA	NA	NA	NA
	% of mothers who smoked in pregnancy	17.5%	15.6%	38.0%	34.1%	NA
	Mean gestational week of collection of maternal characteristics	28	28	Retrospective	Retrospective	NA
	Parity (% primiparous births)	34%	53.6%	100	100	NA

		ALSPAC Mothers	Berlin Birth Cohort (BBC) Mothers	1958 British Birth Cohort or NCDS (B58C-WTCCC)	1958 British Birth Cohort or NCDS (B58C-T1DGC)	CHOP Mothers
SUMMARY OFFSPRING CHARACTERISTICS (offspring of the INCLUDED sample of mothers)	**Birth weight [Mean (sd)], grams**	3481 (475)	3472 (511)	3325 (483)	3379 (469)	3440 (562)
	Gestational age at delivery [Median (IQR)], weeks	40 (39, 41)	40 (38, 40)	40 (40, 41)	40 (40, 41)	NA
	Birth length [Mean (sd)], cm	51 (2)	51.31 (2.50)	NA	NA	NA
	Ponderal index [Mean (sd)], kg/m3	26 (3)	25.68 (3.40)	NA	NA	NA
REFERENCES	**Reference - cohort**	MOTHERS: Fraser, A. et al. (2013) Cohort Profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. Int J Epidemiol. 42(1):97-110.[17] CHILDREN: Boyd A et al. (2013). Cohort Profile: the 'children of the 90s'--the index offspring of the Avon Longitudinal Study of Parents and Children. Int J Epidemiol. 42(1):111-27.[18]	a) Schlemm et al., J Hypertens. 2010 Apr;28(4):732-9[19] b) Hocher et al., Pharmacogenet Genomics. 2009 Sep;19(9):710-8.,[20] c) Pfab et al., Circulation. 2006 Oct 17;114(16):1687-92[21]	Power C, Elliott J. Cohort profile: 1958 British birth cohort (National Child Development Study). Int J Epidemiol 2006; 35(1):34-41[22]	Power C, Elliott J. Cohort profile: 1958 British birth cohort (National Child Development Study). Int J Epidemiol 2006; 35(1):34-41[22]	NA
	Study URL	http://www.bristol.ac.uk/alspac/ [a]	NA	www.cls.ioe.ac.uk and www.wtccc.org.uk	www.cls.ioe.ac.uk	NA

[a]Please note that the study website contains searchable details of all data, available through: http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/

NA, not available

Informed consent was obtained from all participants, and study protocols were approved by the local regional or institutional ethics committees (ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees)

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eTable 1(b) Basic characteristics of study participants and their offspring (studies 6-10)

	STUDY	COPSAC-2000 Mothers	DNBC-GOYA Random Set	DNBC-PTB-CONTROL Mothers	EFSOCH Mothers	GEN-3G Mothers
STUDY INFORMATION	Ethnicity	Danish/European descent	Danish/European descent	Danish/European descent	British/European descent	Canadian/European descent
	Country (Sample source)	Denmark	Denmark	Denmark	UK	Canada
	Collection type (e.g. population-based)	High-risk asthma birth cohort	Population based[a]	Population-based	Community-based	Population-based
	N women with birth weight of 1 child and genotypes for at least one genetic score	282	1,805	1,649	746	676
	Year(s) of birth of offspring	1998 - 2001	1996-2002	1987-2009	2000-2004	2010-2013
	Fetal genotype data available? (Y/N)	Y	N	Y	Y	N
BIRTH WEIGHT	Method by which offspring birth weight (and length, if available) were collected	Medical Records	Obstetric data from medical birth register	Obstetric data from medical birth register	At birth using standard neonatal anthropometry measures	Hospital electronic medical records
GESTATIONAL AGE	Method by which gestational age was collected	Medical Records	The National Birth Register, where gestational age is reported by doctors and midwives at birth	Consensus algorithm for gestational age was developed based on information from medical birth register, hospital discharge register, LMP, LMP corrected for menstrual cycle length, Expected date of delivery (often based on ultrasound), and mother's selfreport of gestational age.	Hospital records and study midwives	Hospital electronic medical records

		COPSAC-2000 Mothers	DNBC-GOYA Random Set	DNBC-PTB-CONTROL Mothers	EFSOCH Mothers	GEN-3G Mothers
SUMMARY MATERNAL CHARACTERISTICS, where available in the INCLUDED sample, DURING PREGNANCY (median (IQR) given where the trait distribution deviates strongly from the normal distribution	**Maternal age at delivery, unless otherwise stated [Mean (sd)], years**	30.4 (4.3)	29.2 (4.2)	29.9 (4.2)	30.5 (5.3)	28.4 (4.4)
	Maternal pre-pregnancy BMI [Mean (sd)], kg/m2	NA	23.57 (4.27)	23.57 (4.27)	24.07 (4.42)	24.83 (5.63)
	Maternal pregnancy BMI [Mean (sd)], kg/m2	NA	NA	NA	28.01 (4.55)	27.98 (5.38)
	Fasting glucose [Mean (sd)], mmol/L	NA	NA	NA	4.35 (0.38)	4.20 (0.41)
	Triglycerides [Mean (sd)], mmol/L	NA	NA	NA	2.13 (0.73)	1.93 (0.64)
	HDL-cholesterol [Mean (sd)], mmol/L	NA	NA	NA	2.08 (0.46)	1.91 (0.43)
	Blood pressure [Mean (sd)], mmHg	NA	NA	NA	NA	107.5 (9.2) / 67.6 (6.8)
	25-hydroxyvitamin D [Median (IQR)], nmol/L	NA	NA	NA	NA	61.7 [50.1 ; 75.5] (at ~9 weeks)
	Adiponectin [Mean (sd)], ug/mL	NA	NA	NA	NA	12.57 (4.72)
	% of mothers who smoked in pregnancy	12.8%	25.8%	17.8%	13.0%	8.88%
	Mean gestational week of collection of maternal characteristics	NA	NA	NA	28	~26
	Parity (% primiparous births)	63.2%	50.0%	30.9%	49.8%	47.5%

		COPSAC-2000 Mothers	DNBC-GOYA Random Set	DNBC-PTB-CONTROL Mothers	EFSOCH Mothers	GEN-3G Mothers
SUMMARY OFFSPRING CHARACTERISTICS (offspring of the INCLUDED sample of mothers)	Birth weight [Mean (sd)], grams	3560 (505)	3643 (495)	3595 (497)	3512 (480)	3448 (433)
	Gestational age at delivery [Median (IQR)], weeks	40 (39, 41)	40.3 (39.4 , 41.1)	40 (39, 40)	40 (37, 43)	39.7 [38.9, 40.4]
	Birth length [Mean (sd)], cm	52.5 (2.2)	52.5 (2.2)	52 (2)	50 (2)	51.1 (2.1)
	Ponderal index [Mean (sd)], kg/m3	24.6 (2.4)	25.0 (2.3)	25 (2)	28 (3)	25.9 (2.5)
REFERENCES	Reference - cohort	Bisgaard H. The Copenhagen Prospective Study on Asthma in Childhood (COPSAC): design, rationale, and baseline data from a longitudinal birth cohort study. Ann Allergy Asthma Immunol 2004;93:381–389.[23]	Nohr et al. (2009) PLoS One. 4(12):e8444[24]	Olsen, J., Melbye, M., Olsen, S. F. *et al* (2001). The Danish National Birth Cohort-its background, structure and aim. *Scandinavian journal of public health*, *29*(4), 300-307.[25]	Knight, B., Shields, B. M., Hattersley, A. T. (2006). The Exeter Family Study of Childhood Health (EFSOCH): study protocol and methodology[26]	Lacroix M et al. Diabetes Care 2013[27]
	Study URL	www.copsac.com	www.dnbc.dk	www.dnbc.dk	www.diabetesgenes.org	NA

[a]Pregnant women recruited 1996-2002 as part of the Danish National Birth Cohort. A random (according to BMI) selection with genotype data are included in the current study.
NA, not available
Informed consent was obtained from all participants, and study protocols were approved by the local regional or institutional ethics committees

eTable 1(c) Basic characteristics of study participants and their offspring (studies 11-14)

	STUDY	Generation R Mothers	HAPO Mothers (GWAS)	HAPO Mothers (nonGWAS)	MoBa (Mothers)
STUDY INFORMATION	Ethnicity	Dutch/European descent	Northern European	European descent	Norwegian/European descent
	Country (Sample source)	The Netherlands	UK, Canada, Australia	USA, UK, Canada, Australia	Norway
	Collection type (e.g. population-based)	Population-based	Population-based	Population-based	Population based
	N women with birth weight of 1 child and genotypes for at least one genetic score	3,810	1,380	3,590	650
	Year(s) of birth of offspring	2002-2006	2000-2006	2000-2006	1999-2008
	Fetal genotype data available? (Y/N)	Y	Y	Y	Y
BIRTH WEIGHT	Method by which offspring birth weight (and length, if available) were collected	Hospital records and community midwives	Medical record abstraction	Medical record abstraction	From The Medical Birth Registry of Norway
GESTATIONAL AGE	Method by which gestational age was collected	Hospital records and community midwives	Estimated according to last menstrual period or ultrasound gestational age and estimated date of delivery or confinement	Estimated according to last menstrual period or ultrasound gestational age and estimated date of delivery or confinement	Gestational age was obtained from ultrasound at gestational week 17-19 of pregnancy.

		Generation R Mothers	HAPO Mothers (GWAS)	HAPO Mothers (nonGWAS)	MoBa (Mothers)
SUMMARY MATERNAL CHARACTERISTICS, where available in the INCLUDED sample, DURING PREGNANCY (median (IQR) given where the trait distribution deviates strongly from the normal distribution	**Maternal age at delivery, unless otherwise stated [Mean (sd)], years**	31.2 (4.5) [=Maternal age at intake, when average gestational age = 14.4 weeks]	31.5(5.3) [=Maternal age at OGTT, when average gestaional age = 28 weeks]	30.4 (5.4) [=Maternal age at OGTT, when average gestaional age = 28 weeks]	28.5 (3.3)
	Maternal pre-pregnancy BMI [Mean (sd)], kg/m2	23.12 (3.92)	24.5 (5.0)	24.63 (5.33)	23.93 (3.94)
	Maternal pregnancy BMI [Mean (sd)], kg/m2	26.98 (4.04)	28.46 (4.82)	28.58 (5.25)	24.78 (3.80)
	Fasting glucose [Mean (sd)], mmol/L	NA	4.56 (0.37)	4.54 (0.37)	NA
	Triglycerides [Mean (sd)], mmol/L	NA	-	-	NA
	HDL-cholesterol [Mean (sd)], mmol/L	NA	-	-	NA
	Blood pressure [Mean (sd)], mmHg	120.0 (11.4) / 69.3 (9.2)	108.6 (9.9) / 71.4 (8.0)	108.3 (9.6) / 70.7 (8.1)	113.5 (11.8) / 68.5 (8.4)
	25-hydroxyvitamin D [Median (IQR)], nmol/L	NA	-	-	NA
	Adiponectin [Mean (sd)], ug/mL	NA	20.37(12.83)	-	NA
	% of mothers who smoked in pregnancy	27.1%	13.5%	15.0%	8.1%
	Mean gestational week of collection of maternal characteristics	30	28.5	28.3	18
	Parity (% primiparous births)	58.7%	56.9%	50.0%	45.8%

		Generation R Mothers	HAPO Mothers (GWAS)	HAPO Mothers (nonGWAS)	MoBa (Mothers)
SUMMARY OFFSPRING CHARACTERISTICS (offspring of the INCLUDED sample of mothers)	Birth weight [Mean (sd)], grams	3528 (494)	3557 (517)	3526 (463)	3679 (430)
	Gestational age at delivery [Median (IQR)], weeks	40 (39, 41)	40 (39, 41)	40 (39, 41)	40.1 (39.3, 41.0)
	Birth length [Mean (sd)], cm	51 (2)	50.6 (2.3)	50.8 (2.3)	50.6 (1.8)
	Ponderal index [Mean (sd)], kg/m3	27 (3)	27.48 (3.19)	26.87 (2.86)	28.31 (2.53)
REFERENCES	Reference - cohort	Jaddoe, van Duijn, Franco et al. 2012 Eur J Epidemiol. 27(9):739-56.[28]	Metzger et al., Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008; 358:1991–2002[29]	Metzger et al., Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008; 358:1991–2002 [29]	Cohort profile: The Norwegian Mother and Child Cohort Study (MoBa) Per Magnus, Lorentz M Irgens, Kjell Haug, Wenche Nystad, Rolv Skjærven, Camilla Stoltenberg and The Moba Study Group. Int. J. Epidemiol. (October 2006) 35 (5): 1146-1150.[30] Rønningen KS, Paltiel L, Meltzer HM et al. The biobank of the Norwegian Mother and Child Cohort Study—A Resource for the next 100 years.Eur J Epidemiol. 2006;21(8):619-25.[31]
	Study URL	www.generationr.nl	http://www.hapo.northwestern.edu/index.html	http://www.hapo.northwestern.edu/index.html	http://www.fhi.no/morogbarn

NA, not available

Informed consent was obtained from all participants, and study protocols were approved by the local regional or institutional ethics committees

eTable 1(d) Basic characteristics of study participants and their offspring (studies 15-18)

	STUDY	NFBC1966	NTR	QIMR	TWINSUK
STUDY INFORMATION	Ethnicity	Finnish/European descent	Dutch/European descent	European descent	European descent
	Country (Sample source)	Northern Finland, Provinces of Oulu and Lapland	The Netherlands	Australia	UK
	Collection type (e.g. population-based)	Prospective general population-based	Population-based controls	Population-based recruitment of adult twins	population based
	N women with birth weight of 1 child and genotypes for at least one genetic score	2,035	706	892	1,602
	Year(s) of birth of offspring	1987-2001	1946 - 2003	1929-1990	NA
	Fetal genotype data available? (Y/N)	N	N	N	N
BIRTH WEIGHT	Method by which offspring birth weight (and length, if available) were collected	Birth Register Data	From longitudinal surveys by self-report/parental report. Birth weight determined as average of all valid data points.	Self-report through questionnaire	Questionnaire
GESTATIONAL AGE	Method by which gestational age was collected	Last menstrual period and Scans. Based on hospital records	From longitudinal surveys by self-report/parental report. Gestational age determined as average of all valid data points.	NA	Questionnaire

		NFBC1966	NTR	QIMR	TWINSUK
SUMMARY MATERNAL CHARACTERISTICS, where available in the INCLUDED sample, DURING PREGNANCY (median (IQR) given where the trait distribution deviates strongly from the normal distribution	**Maternal age at delivery, unless otherwise stated [Mean (sd)], years**	26.5 (3.7) available for 2010 participants	27.1 (3.7)	24.5 (4.0)	NA
	Maternal pre-pregnancy BMI [Mean (sd)], kg/m2	NA	NA	22.79 (5.13)	NA
	Maternal pregnancy BMI [Mean (sd)], kg/m2	NA	NA	NA	NA
	Fasting glucose [Mean (sd)], mmol/L	NA	NA	NA	NA
	Triglycerides [Mean (sd)], mmol/L	NA	NA	NA	NA
	HDL-cholesterol [Mean (sd)], mmol/L	NA	NA	NA	NA
	Blood pressure [Mean (sd)], mmHg	NA	NA	NA	NA
	25-hydroxyvitamin D [Median (IQR)], nmol/L	NA	NA	NA	NA
	Adiponectin [Mean (sd)], ug/mL	NA	NA	NA	NA
	% of mothers who smoked in pregnancy	NA	NA	NA	NA
	Mean gestational week of collection of maternal characteristics	NA	NA	NA	NA
	Parity (% primiparous births)	NA	84.0%	NA	NA

		NFBC1966	NTR	QIMR	TWINSUK
SUMMARY OFFSPRING CHARACTERISTICS (offspring of the INCLUDED sample of mothers)	Birth weight [Mean (sd)], grams	3525 (461)	3469 (529)	3344 (532)	3365 (581)
	Gestational age at delivery [Median (IQR)], weeks	40 (39, 41)	40 (38, 42)	NA	NA
	Birth length [Mean (sd)], cm	50.3 (2.0)	NA	NA	NA
	Ponderal index [Mean (sd)], kg/m3	27.61 (2.44)	NA	NA	NA
REFERENCES	Reference - cohort	Rantakallio P. Groups at risk in low birth weight infants and perinatal mortality. Acta Paediatr Scand 1969;193(suppl 193):1–71;[32] Järvelin M-R., Sovio U., King V., Laurén L., Xu B., McCarthy M., Hartikainen A-L., Laitinen J., Zitting P., Rantakallio P., Elliott P.: Early Life Factors and Blood Pressure at Age 31 Years in the 1966 Northern Finland Birth Cohort. Hypertension 44:838-846, 2004.[33]	[1] Boomsma DI et al. Netherlands Twin Register: from twins to twin families. Twin Research and Human Genetics. 2006, 9, 849-57[34]; [2] Willemsen et al. The Adult Netherlands Twin Register: twenty-five years of survey and biological data collection. Twin Research and Human Genetics, 2013, 16, 271-81[35].	Medland SE et al. (2009) Common variants in the trichohyalin gene are associated with straight hair in Europeans. American Journal of Human Genetics 85:750-755.[36]	[1] Moayyeri A, Hammond CJ, Hart DJ, et al., 2013, The UK Adult Twin Registry (TwinsUK Resource)., Twin Research and Human Genetics, Vol:16, ISSN:1832-4274, Pages:144-149 [37] [2] Moayyeri A, Hammond CJ, Valdes AM, et al., 2013, Cohort Profile: TwinsUK and healthy ageing twin study., Int J Epidemiol, Vol:42, 0300-5771, Pages:76-85 [38]
	Study URL	http://www.oulu.fi/nfbc/	www.tweelingenregister.org	http//www.genepi.qimr.edu.au/general/researchtopics.cgi	www.twinsuk.co.uk

NA, not available

Informed consent was obtained from all participants, and study protocols were approved by the local regional or institutional ethics committees

Deleted: NA

eTable 2(a) Genotyping information (studies 1-5)

	STUDY	ALSPAC Mothers	Berlin Birth Cohort (BBC) Mothers	1958 British Birth Cohort or NCDS (B58C-WTCCC)	1958 British Birth Cohort or NCDS (B58C-T1DGC)	CHOP Mothers
MATERNAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	Illumina Human660W-Quad BeadChip	Human Exomechip ver1.1	Affymetrix Genome-wide Human SNP Array 6.0	Illumina 550K Infinium	Illunina550, Illumina610 Infinium
	Genotyping centre	Centre National de Génotypage (CNG), Evry, France	Oxfor Centre for Diabete, Endocrinology and Metabolism, University of Oxford, UK	Wellcome Trust Sanger Institute, Cambridge, UK	JDRF/WT DIL Lab in Cambridge, UK	The Center for Applied Genomics, Children's Hospital of Philadelphia, USA
	N SNPs in QC'd dataset	526,688	NA	721,428	520,413	513,518
	Imputation software / reference panel	MACH v.1.0.16 / HapMap Phase II	NA	Impute /HapMap Phase II	Impute /HapMap Phase II	Impute /HapMap Phase II
	N QC'd SNPs available for GWAS analysis	2,450,866	NA	2,543,926	2,451,644	2,546,219
	Genomic control lambda from GWAS analysis of offspring birth weight	1.039	NA	0.984	1.007	NA
FETAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	Illumina HumanHap550 quad array	Human Exomechip ver1.1	NA	NA	Illunina550, Illumina610 Infinium
	Genotyping centre	Sample Logistics and Genotyping Facilities at the Wellcome Trust Sanger Institute and LabCorp (Laboratory Corportation of America) using support from 23andMe	Oxford Centre for Diabete, Endocrinology and Metabolism, University of Oxford, UK	NA	NA	The Center for Applied Genomics
	N SNPs in QC'd dataset	500,541	NA	NA	NA	513,518
	Imputation software / reference panel	MACH v.1.0.16 / HapMap Phase II	NA	NA	NA	Impute /HapMap Phase II
DATA ANALYSIS	Analysis software	Stata v.13	PLINK and R	Stata, version 12	Stata, version 12	SNPtest and R

		ALSPAC Mothers	Berlin Birth Cohort (BBC) Mothers	1958 British Birth Cohort or NCDS (B58C-WTCCC)	1958 British Birth Cohort or NCDS (B58C-T1DGC)	CHOP Mothers
REFERENCES	**Reference - MATERNAL genotyping**	Evans DM et al. (2013) Genome-wide association study identifies loci affecting blood copper, selenium and zinc. Hum Mol Genet. 22(19):3998-4006.[39]	NA	Sawcer S, Hellenthal G, Pirinen M, Spencer CC, Patsopoulos NA, et al. (2011) Genetic risk and a primary role for cell-mediated immune mechanisms in multiple sclerosis. Nature 476: 214–219[40]	Barrett JC, Clayton DG, Concannon P et al. Genome-wide assocition study and meta-analysis find that over 40 loci affect risk of type 1 diabetes. Nat. Genet 2009[41]	NA
REFERENCES	**Reference -FETAL genotyping**	Paternoster L. et al. (2012) Genome-wide association study of three-dimensional facial morphology identifies a variant in PAX3 associated with nasion position. Am J Hum Genet. 90(3):478-85.[42]	NA	NA	NA	NA

eTable 2(b) Genotyping information (studies 6-10)

	STUDY	COPSAC-2000 Mothers	DNBC-GOYA Random Set	DNBC-PTB-CONTROL Mothers	EFSOCH Mothers	GEN-3G Mothers
MATERNAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	Illumina 550K	Illumina Human610-Quad v1.0	Illumina Human 660W-quad Bead Array	Illumina Human Exome Beadchip v1	NA
	Genotyping centre	Children's Hospital of Philadelphia, Center for Applied Genomics	Centre National de Génotypage (CNG), Evry, France	Center for Inherited Disease Research, Johns Hopkins University, Baltimore, Maryland, USA	Centre National de Génotypage, France	NA
	N SNPs in QC'd dataset	486,373	545,349	518,097	234,763	NA
	Imputation software / reference panel	MacH-minimac/Hapmap Phase II	Mach 1.0	MaCH/HapMap Phase II	NA	NA
	N QC'd SNPs available for GWAS analysis	NA	2,449,993	2,543,887	57 QC'd SNPs available for analysis of genetic scores selected for the current project	NA
	Genomic control lambda from GWAS analysis of offspring birth weight	NA	1.006	1.006	NA	NA
MATERNAL CUSTOM GENOTYPING	Genotyping centre and method	NA	NA	NA	LGC Genomics (formerly Kbiosciences); KASPar	Genome Quebec Innovation Centre
	Call rate [Median (range)]; N SNPs genotyped	NA	NA	NA	0.953 [0.932, 0.999] (N=16 SNPs)	0.99 [0.98 ; 1] (N=4 snps)
	Did any SNPs deviate from HWE (Bonferroni corrected P<0.05)? Y/N	NA	NA	NA	N	N
	Duplicate concordance (%)	NA	NA	NA	>99% (approx. 10%)	100%

		COPSAC-2000 Mothers	DNBC-GOYA Random Set	DNBC-PTB-CONTROL Mothers	EFSOCH Mothers	GEN-3G Mothers
FETAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	Illumina 550K	NA	Illumina Human 660W-quad Bead Array	NA	NA
	Genotyping centre	Children's Hospital of Philadelphia, Center for Applied Genomics	NA	Center for Inherited Disease Research, Johns Hopkins University, Baltimore, Maryland, USA	NA	NA
	N SNPs in QC'd dataset	486,373	NA	514,382	NA	NA
	Imputation software / reference panel	MacH-minimac/Hapmap Phase II	NA	MaCH/HapMap Phase II	NA	NA
FETAL CUSTOM GENOTYPING	Genotyping centre and method	NA	NA	NA	LGC Genomics (formerly Kbiosciences); KASPar	NA
	Call rate [Median (range)]; N SNPs genotyped	NA	NA	NA	0.926 [0.907, 0.934] (N=13 SNPs)	NA
	Did any SNPs deviate from HWE (Bonferroni corrected P<0.05)? Y/N	NA	NA	NA	N	NA
	Duplicate concordance (% duplicated genotypes)	NA	NA	NA	>99% (approx. 10%)	NA
DATA ANALYSIS	Analysis software	R-project	Stata	R	Stata v.13	R

		COPSAC-2000 Mothers	DNBC-GOYA Random Set	DNBC-PTB-CONTROL Mothers	EFSOCH Mothers	GEN-3G Mothers
REFERENCES	**Reference - MATERNAL genotyping**	HakonarsonH,GrantSF,BradfieldJP,MarchandL,KimCE,GlessnerJT, Grabs R, Casalunovo T, Taback SP, Frackelton EC, et al. A genome- wide association study identifies KIAA0350 as a type 1 diabetes gene. Nature 2007;448:591–594.[43]	Paternoster et al. (2011) PLoS One. 6(9):e24303	Ryckman, K. K., Feenstra, B., Shaffer, J. R., *et al* (2012). Replication of a genome-wide association study of birth weight in preterm neonates. *The Journal of pediatrics*, *160*(1), 19-24.[44]	NA	NA
REFERENCES	**Reference -FETAL genotyping**	HakonarsonH,GrantSF,BradfieldJP,MarchandL,KimCE,GlessnerJT, Grabs R, Casalunovo T, Taback SP, Frackelton EC, et al. A genome- wide association study identifies KIAA0350 as a type 1 diabetes gene. Nature 2007;448:591–594.[43]	NA	Ryckman, K. K., Feenstra, B., Shaffer, J. R., *et al* (2012). Replication of a genome-wide association study of birth weight in preterm neonates. *The Journal of pediatrics*, *160*(1), 19-24.[44]	NA	NA

eTable 2(c) Genotyping information (studies 11-14)

	STUDY	Generation R Mothers	HAPO Mothers (GWAS)	HAPO Mothers (nonGWAS)	MoBa (Mothers)
MATERNAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	NA	Illumina Human 610 Quad v1 B SNP array	NA	Illumina 660Wquad
	Genotyping centre	NA	Broad Institute Center for Genotyping and Analysis (CGA), USA	NA	The Norwegian Cancer Hospital, Oslo
	N SNPs in QC'd dataset	NA	559,739	NA	432,270
	Imputation software / reference panel	NA	Beagle / HapMap3 CEU & TSI	NA	PLINK /HapMap Phase II
	N QC'd SNPs available for GWAS analysis	NA	1,968,447	NA	NA
	Genomic control lambda from GWAS analysis of offspring birth weight	NA	1.016	NA	None
MATERNAL CUSTOM GENOTYPING	Genotyping centre and method	LGC Genomics (formerly Kbiosciences); KASPar	NA	LGC Genomics (formerly Kbiosciences); KASPar	NA
	Call rate [Median (range)]; N SNPs genotyped	99.3% (N=34 snps)	NA	0.983 [0.977, 0.988] (N=23 SNPs)	NA
	Did any SNPs deviate from HWE (Bonferroni corrected P<0.05)? Y/N	Y: rs4836133 (P = 3x10-15; excluded)	NA	N	NA
	Duplicate concordance (% duplicated genotypes)	99.80%	NA	>=99% (min 4%)	NA

		Generation R Mothers	HAPO Mothers (GWAS)	HAPO Mothers (nonGWAS)	MoBa (Mothers)
FETAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	Ilumina 610 Quad and 660W	Illumina Human 610 Quad v1 B SNP array	NA	Illumina 660Wquad
	Genotyping centre	Human Genotyping Facility (HuGeF), Dept Internal Medicine, Erasmus MC, The Netherlands	Broad Institute Center for Genotyping and Analysis (CGA)	NA	The Norwegian Cancer Hospital, Oslo
	N SNPs in QC'd dataset	489,879	559,739	NA	432270
	Imputation software / reference panel	Minimac and MACH	Beagle / HapMap3 CEU & TSI	NA	PLINK /HapMap Phase II
FETAL CUSTOM GENOTYPING	Genotyping centre and method	NA	NA	LGC Genomics (formerly Kbiosciences); KASPar	NA
	Call rate [Median (range)]; N SNPs genotyped	NA	NA	0.983 [0.977, 0.988] (N=23 SNPs)	NA
	Did any SNPs deviate from HWE (Bonferroni corrected P<0.05)? Y/N	NA	NA	N	NA
	Duplicate concordance (%)	NA	NA	>=99% (min 4%)	NA
DATA ANALYSIS	Analysis software	Stata version 12	R 3.0.2	Stata v.13	IBM SPSS Statistics 20
REFERENCES	Reference - MATERNAL genotyping	NA	Hayes et al., Identification of HKDC1 and BACE2 as genes influencing glycemic traits during pregnancy through genome-wide association studies. Diabetes. 2013 Sep;62(9):3282-91[45]	NA	NA
REFERENCES	Reference -FETAL genotyping	Jaddoe, van Duijn, Franco et al. 2012 Eur J Epidemiol. 27(9):739-56.[28]	Urbanek et al., The chromosome 3q25 genomic region is associated with measures of adiposity in newborns in a multi-ethnic genome-wide association study.Hum Mol Genet. 2013 Sep 1;22(17):3583-96.[46]	NA	NA

eTable 2(d) Genotyping information (studies 16-18)

	STUDY	NFBC1966	NTR	QIMR	TWINSUK
MATERNAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	Illumina HumanCNV-370DUO Analysis BeadChip	Perlegen-Affymetrix, Affymetrix 6.0, Illumina 370K, 600K, 1M Omni	HumanCNV370-Quadv3	HumanHap3001,2, HumanHap610Q, 1M-Duo and 1.2MDuo 1M
	Genotyping centre	Broad Institute	Perlegen Sciences Mountain View CF USA, Finnish Genome Center Helsinki Finland, SNP technology Platform Uppsala Sweden, Molecular Epidemiology Leiden The Netherlands, Translational Genomics Research Institute Phoenix AZ USA, Institute of Human Genetics LIFE & BRAIN Center Bonn Germany.	CIDR	Sanger
	N SNPs in QC'd dataset	324,896	312,214-814,708	323,093, reduced to a common set of 274,604 SNPs (across the QIMR sample)	up to 874,733 SNPs
	Imputation software / reference panel	Impute version 2 / HapMap2	Impute 1.0 / Build 36r24 Hapmap 2	MACH/HapMap Phase II	IMPUTE software package (v2) 5 using two referencepanels, P0 (HapMap2, rel 22, combined CEU+YRI+ASN panels) and P1 (610k+, including combinedHumanHap610k and 1M reduced to 610k SNP content).
	N QC'd SNPs available for GWAS analysis	2,487,934	2385474	2,454,244	2,401,373
	Genomic control lambda from GWAS analysis of offspring birth weight	1.020	1.002	1.012	1

		NFBC1966	NTR	QIMR	TWINSUK
FETAL GENOME- OR EXOME-WIDE GENOTYPING	Genotyping platform and SNP panel	NA	Perlegen-Affymetrix, Affymetrix 6.0, Illumina 370K, 600K, 1M Omni	NA	NA
	Genotyping centre	NA	Perlegen Sciences Mountain View CF USA, Finnish Genome Center Helsinki Finland, SNP technology Platform Uppsala Sweden, Molecular Epidemiology Leiden The Netherlands, Translational Genomics Research Institute Phoenix AZ USA, Institute of Human Genetics LIFE & BRAIN Center Bonn Germany.	NA	NA
	N SNPs in QC'd dataset	NA	312214-814708	NA	NA
	Imputation software / reference panel	NA	Impute 1.0 / Build 36r24 Hapmap 2	NA	NA
DATA ANALYSIS	Analysis software	R 2.14.2	Stata	R	SNPTEST , Stata
REFERENCES	Reference - MATERNAL genotyping	Sabatti et al. Genome-wide association analysis of metabolic traits in a birth cohort from a founder population. Nat Genet. 2009;41:35-46 and Prokopenko et al. Variants in MTNA1B influence fasting glucose levels. Nat Genet 2009;41:77-81.[47]	[1] Willemsen et al. The Netherlands Twin Register biobank: a resource for genetic epidemiological studies. Twin Research and Human Genetics. 2010, 13, 231-45.[35]	Medland SE et al. (2009) Common variants in the trichohyalin gene are associated with straight hair in Europeans. American Journal of Human Genetics 85:750-755.[36]	Moayyeri A, Hammond CJ, Hart DJ, et al., 2013, The UK Adult Twin Registry (TwinsUK Resource)., Twin Research and Human Genetics, Vol:16, ISSN:1832-4274, Pages:144-149[37]

eTable 3. Details of single nucleotide polymorphisms (SNPs) used to construct the genetic scores

Trait	SNP	Nearest/nearby gene	Trait-raising allele[a]	Trait-lowering allele[a]	Beta for weighting genetic score	Units of beta and source (including any extra details)
Adiponectin	rs17300539	*ADIPOQ*	A	G	0.330	Units: age- and sex-adjusted z-scores. Source: Yaghootkar et al (2013) Diabetes 62(10):3589-98[48]
Adiponectin	rs3774261	*ADIPOQ*	A	G	0.354	
Adiponectin	rs3821799	*ADIPOQ*	C	T	0.352	
BMI	rs10150332	*NRXN3*	C	T	0.13	Units: kg/m2 increase Source: Speliotes et al., Nature Genetics (2010)[49]
BMI	rs10767664	*BDNF*	A	T	0.19	
BMI	rs10938397	*GNPDA2*	G	A	0.18	
BMI	rs10968576	*LRRN6C*	G	A	0.11	
BMI	rs11847697	*PRKD1*	T	C	0.17	
BMI	rs12444979	*GPRC5B*	C	T	0.17	
BMI	rs13078807	*CADM2*	G	A	0.1	
BMI	rs1514175	*TNNI3K*	A	G	0.07	
BMI	rs1555543	*PTBP2*	C	A	0.06	
BMI	rs1558902	*FTO*	A	T	0.39	
BMI	rs206936	*NUDT3*	G	A	0.06	
BMI	rs2112347	*FLJ35779*	T	G	0.1	
BMI	rs2241423	*MAP2K5*	G	A	0.13	
BMI	rs2287019	*QPCTL*	C	T	0.15	
BMI	rs2815752	*NEGR1*	A	G	0.13	
BMI	rs2867125	*TMEM18*	C	T	0.31	
BMI	rs2890652	*LRP1B*	C	T	0.09	
BMI	rs29941	*KCTD15*	G	A	0.06	
BMI	rs3810291	*TMEM160*	A	G	0.09	
BMI	rs3817334	*MTCH2*	T	C	0.06	
BMI	rs4771122	*MTIF3*	G	A	0.09	
BMI	rs4836133	*ZNF608*	A	C	0.07	
BMI	rs4929949	*RPL27A*	C	T	0.06	
BMI	rs543874	*SEC16B*	G	A	0.22	
BMI	rs571312	*MC4R*	A	C	0.23	
BMI	rs713586	*RBJ*	C	T	0.14	
BMI	rs7138803	*FAIM2*	A	G	0.12	
BMI	rs887912	*FANCL*	T	C	0.1	
BMI	rs9816226	*ETV5*	T	A	0.14	
BMI	rs987237	*TFAP2B*	G	A	0.13	

Trait	SNP	Nearest/nearby gene	Trait-raising allele[a]	Trait-lowering allele[a]	Beta for weighting genetic score	Units of beta and source (including any extra details)
Blood pressure	rs2932538	*MOV10*	G	A	0.3884	Units: mmHg per BP-raising allele; Sources: Ehret et al 2010 Nature[15]; Johnson et al 2010 Hypertension[50]; Wain et al 2010 Nat Genet.[51]
Blood pressure	rs13082711	*SLC4A7*	C	T	0.3151	
Blood pressure	rs419076	*MECOM*	T	C	0.4088	
Blood pressure	rs13139571	*GUCY1A3-GUCY1B3*	C	A	0.3213	
Blood pressure	rs1173771	*NPR3-C5orf23*	G	A	0.5041	
Blood pressure	rs11953630	*EBF1*	C	T	0.4119	
Blood pressure	rs805303	*BAT2-BAT5*	G	A	0.3756	
Blood pressure	rs4373814	*CACNB2(5')*	C	G	0.3726	
Blood pressure	rs932764	*PLCE1*	G	A	0.4837	
Blood pressure	rs7129220	*ADM*	A	G	0.6186	
Blood pressure	rs633185	*FLJ32810-TMEM133*	C	G	0.5647	
Blood pressure	rs2521501	*FURIN-FES*	T	A	0.6498	
Blood pressure	rs17608766	*GOSR2*	C	T	0.5564	
Blood pressure	rs1327235	*JAG1*	G	A	0.3404	
Blood pressure	rs6015450	*GNAS-EDN3*	G	A	0.8964	
Blood pressure	rs17367504	*MTHFR-NPPB*	A	G	0.9031	
Blood pressure	rs3774372	*ULK4*	C	T	0.0666	
Blood pressure	rs1458038	*FGF5*	T	C	0.7057	
Blood pressure	rs1813353	*CACNB2(3')*	T	C	0.5686	
Blood pressure	rs4590817	*C10orf107*	G	C	0.6457	
Blood pressure	rs11191548	*CYP17A1-NT5C2*	T	C	1.0952	
Blood pressure	rs381815	*PLEKHA7*	T	C	0.5747	
Blood pressure	rs17249754	*ATP2B1*	G	A	0.9282	
Blood pressure	rs3184504	*SH2B3*	T	C	0.5976	
Blood pressure	rs10850411	*TBX5-TBX3*	T	C	0.3541	
Blood pressure	rs1378942	*CYP1A1-ULK3*	C	A	0.6125	
Blood pressure	rs12940887	*ZNF652*	T	C	0.3622	
Blood pressure	rs1801253	*ADRB1*	C	G	0.57	
Blood pressure	rs13002573	*FIGN*	A	G	0.416	
Blood pressure	rs17477177	*PIK3CG*	C	T	0.552	
Blood pressure	rs1446468	*FIGN*	C	T	0.499	
Blood pressure	rs319690	*MAP4 (intron)*	T	C	0.423	
Blood pressure	rs2782980	*ADRB1*	C	T	0.406	

Trait	SNP	Nearest/nearby gene	Trait-raising allele[a]	Trait-lowering allele[a]	Beta for weighting genetic score	Units of beta and source (including any extra details)
Fasting Glucose	rs560887	*G6PC2*	C	T	0.075	Units: mmol/L per fasting glucose raising allele Source: Dupuis et al., 2010 Nature Genetics[52]
Fasting Glucose	rs13266634	*SLC30A8*	C	T	0.027	
Fasting Glucose	rs11708067	*ADCY5*	A	G	0.027	
Fasting Glucose	rs10830963	*MTNR1B*	G	C	0.067	
Fasting Glucose	rs2191349	*DGKB/TMEM195*	T	G	0.03	
Fasting Glucose	rs7944584	*MADD*	A	T	0.021	
Fasting Glucose	rs10885122	*ADRA2A*	G	T	0.022	
Fasting Glucose	rs11605924	*CRY2*	A	C	0.015	
Fasting Glucose	rs340874	*PROX1*	C	T	0.013	
Fasting Glucose	rs11920090	*SLC2A2*	T	A	0.02	
Fasting Glucose	rs7034200	*GLIS3*	A	C	0.018	
Fasting Glucose	rs11071657	*C2CD4B*	A	G	0.008	
Fasting Glucose	rs4607517	*GCK*	A	G	0.062	
HDL-specific[b]	rs1532085	*LIPC*	A	G	1.45	Units: mg/dL per HDL raising allele Source: Teslovich et al., (2010) Nature Genetics[2]
HDL-specific	rs16942887	*LCAT*	A	G	1.27	
HDL-specific	rs1883025	*ABCA1*	C	T	0.94	
HDL-specific	rs3764261	*CETP*	A	C	3.39	

Trait	SNP	Nearest/nearby gene	Trait-raising allele[a]	Trait-lowering allele[a]	Beta for weighting genetic score	Units of beta and source (including any extra details)
Triglyceride main effect[c]	rs10761731	*JMJD1C*	A	T	2.38	Units: mg/dL per triglyceride raising allele Source: Teslovich et al., (2010) Nature Genetics[2]
Triglyceride main effect	rs10889353	*DOCK7*	A	C	4.94	
Triglyceride main effect	rs11613352	*LRP1*	C	T	2.7	
Triglyceride main effect	rs11649653	*CTF1*	C	G	2.13	
Triglyceride main effect	rs13238203	*TYW1B*	C	T	7.91	
Triglyceride main effect	rs1495741	*NAT2*	G	A	2.97	
Triglyceride main effect	rs2068888	*CYP26A1*	G	A	2.28	
Triglyceride main effect	rs2412710	*CAPN3*	A	G	7	
Triglyceride main effect	rs2929282	*FRMD5*	T	A	5.13	
Triglyceride main effect	rs2954029	*TRIB1*	A	T	5.64	
Triglyceride main effect	rs328	*LPL*	C	G	13.64	
Triglyceride main effect	rs442177	*KLHL8*	T	G	2.25	
Triglyceride main effect	rs5756931	*PLA2GS*	T	C	1.54	
Triglyceride main effect	rs645040	*MSL2L1*	T	G	2.22	
Triglyceride main effect	rs714052	*BAZ1B*	A	G	7.91	
Triglyceride main effect	rs964184	*APOA1*	G	C	16.95	
Triglyceride main effect	rs9686661	*MAP3K1*	T	C	2.57	

Trait	SNP	Nearest/nearby gene	Trait-raising allele[a]	Trait-lowering allele[a]	Beta for weighting genetic score	Units of beta and source (including any extra details)
Type 2 diabetes	rs10203174	*THADA*	C	T	0.131	Units: Natural logarithm of odds ratio for type 2 diabetes per type 2 diabetes increasing allele Source: Morris et al., (2012) Nature Genetics[53]
Type 2 diabetes	rs10758593	*GLIS3*	A	G	0.058	
Type 2 diabetes	rs10811661	*CDKN2A/B*	T	C	0.166	
Type 2 diabetes	rs10842994	*KLHDC5*	C	T	0.095	
Type 2 diabetes	rs10923931	*NOTCH2*	T	G	0.077	
Type 2 diabetes	rs11063069	*CCND2*	G	A	0.077	
Type 2 diabetes	rs1111875	*HHEX/IDE*	C	T	0.104	
Type 2 diabetes	rs11257655	*CDC123/CAMK1D*	T	C	0.068	
Type 2 diabetes	rs11634397	*ZFAND6*	G	A	0.049	
Type 2 diabetes	rs11717195	*ADCY5*	T	C	0.104	
Type 2 diabetes	rs12242953	*VPS26A*	G	A	0.068	
Type 2 diabetes	rs12427353	*HNF1A (TCF1)*	G	C	0.077	
Type 2 diabetes	rs12497268	*PSMD6*	G	C	0.030	
Type 2 diabetes	rs12571751	*ZMIZ1*	A	G	0.077	
Type 2 diabetes	rs12899811	*PRC1*	G	A	0.077	
Type 2 diabetes	rs1359790	*SPRY2*	G	A	0.077	
Type 2 diabetes	rs1496653	*UBE2E2*	A	G	0.086	
Type 2 diabetes	rs1552224	*ARAP1 (CENTD2)*	A	C	0.104	
Type 2 diabetes	rs163184	*KCNQ1*	G	T	0.086	
Type 2 diabetes	rs16927668	*PTPRD*	T	C	0.039	
Type 2 diabetes	rs17168486	*DGKB*	T	C	0.104	
Type 2 diabetes	rs17301514	*ST64GAL1*	A	G	0.049	
Type 2 diabetes	rs17791513	*TLE4*	A	G	0.113	
Type 2 diabetes	rs17867832	*GCC1*	T	G	0.086	
Type 2 diabetes	rs1801282	*PPARG*	C	G	0.122	
Type 2 diabetes	rs2007084	*AP3S2*	G	A	0.020	
Type 2 diabetes	rs2075423	*PROX1*	G	T	0.068	
Type 2 diabetes	rs2261181	*HMGA2*	T	C	0.122	
Type 2 diabetes	rs2334499	*DUSP8*	T	C	0.039	
Type 2 diabetes	rs243088	*BCL11A*	T	A	0.068	
Type 2 diabetes	rs2447090	*SRR*	A	G	0.039	
Type 2 diabetes	rs2796441	*TLE1*	G	A	0.068	
Type 2 diabetes	rs3734621	*KCNK16*	C	A	0.068	
Type 2 diabetes	rs3802177	*SLC30A8*	G	A	0.131	
Type 2 diabetes	rs4299828	*ZFAND3*	A	G	0.039	
Type 2 diabetes	rs4402960	*IGF2BP2*	T	G	0.122	
Type 2 diabetes	rs4430796	*HNF1B (TCF2)*	A	G	0.095	
Type 2 diabetes	rs4458523	*WFS1*	G	T	0.095	
Type 2 diabetes	rs4502156	*C2CD4A*	T	C	0.058	
Type 2 diabetes	rs459193	*ANKRD55*	G	A	0.077	
Type 2 diabetes	rs4812829	*HNF4A*	A	G	0.058	
Type 2 diabetes	rs516946	*ANK1*	C	T	0.086	
Type 2 diabetes	rs5215	*KCNJ11*	C	T	0.068	

Type 2 diabetes	rs6819243	*MAEA*	T	C	0.068	
Type 2 diabetes	rs6878122	*ZBED3*	G	A	0.095	
Type 2 diabetes	rs7177055	*HMG20A*	A	G	0.077	
Type 2 diabetes	rs7202877	*BCAR1*	T	G	0.113	
Type 2 diabetes	rs7569522	*RBMS1*	A	G	0.048	
Type 2 diabetes	rs7756992	*CDKAL1*	G	A	0.157	
Type 2 diabetes	rs7845219	*TP53INP1*	T	C	0.058	
Type 2 diabetes	rs7903146	*TCF7L2*	T	C	0.329	
Type 2 diabetes	rs7955901	*TSPAN8/LGR5*	C	T	0.068	
Type 2 diabetes	rs8108269	*GIPR*	G	T	0.068	
Type 2 diabetes	rs8182584	*PEPD*	T	G	0.039	
Type 2 diabetes	rs849135	*JAZF1*	G	A	0.104	
Trait	**SNP**	**Nearest/nearby gene**	**Trait-raising allele**[a]	**Trait-lowering allele**[a]	**Beta for weighting genetic score**	**Units of beta and source (including any extra details)**
Vitamin D - synthesis	rs10741657	*CYP2R1*	A	G	0.03	Units: nmol/L per vitamin D raising allele Source: Wang et al., (2010) Lancet[54]
Vitamin D - synthesis	rs12785878	*DHCR7/NADSYN1*	T	G	0.05	

[a] Based on the positive strand according to HapMap Phase 2

[b] HDL-specific SNPs were selected due to being near genes with known Mendelain lipid disorder

[c] Triglyceride main effect SNPs were included in the genetic score if they were solely associated with triglyceride levels, or if their effect on triglyceride levels was at least three times greater than that of HDL-, LDL- or total cholesterol (using Teslovich et al 2010, *Nat Genet* [2]).

eTable 4. Studies with maternal traits ascertained during pregnancy (or for BMI, pre-pregnancy) and available for association analysis with genetic scores

Trait	Total N women	N Studies	Study Name	Time of ascertainment	Brief description of maternal phenotype ascertainment and reference, if available
BMI	11,822	5	ALSPAC Mothers	Pre-pregnancy	Self-reported weight and height, weight validated with clinic measure (Lawlor et al., (2010) Diabetologia 53: 89-97)[55]
			DNBC-GOYA Random Set	Pre-pregnancy	Registry data (Olsen et al., (2001) Scandinavian Journal of Public Health 29:300-307)[25]
			DNBC-PTB-CONTROL Mothers	Pre-pregnancy	Registry data (Olsen et al., (2001) Scandinavian Journal of Public Health 29:300-307[25]
			EFSOCH Mothers	Pre-pregnancy	Measured height 3 times and averaged, pre-pregnancy weight self reported (Knight et al., (2006) Paediatric Perinal Epidemiology 20:172-179)[26]
			HAPO Mothers (GWAS)	Pre-pregnancy	Height measured, pre-pregnancy weight self reported (Metzger et al., (2008) NEJM 358:1991-2002)[29]
Fasting glucose	5,402	3	EFSOCH Mothers	Gestational week 28	Fasting blood samples (10 hours fasting minimum) (Knight et al., (2006) Paediatric Perinal Epidemiology 20:172-179)[26]
			HAPO Mothers (GWAS)	Gestational week 28	Fasting blood samples (Metzger et al., (2008) NEJM 358:1991-2002)[29]
			HAPO Mothers (non-GWAS)	Gestational week 28	
Gestational or existing diabetes	6,827	1	ALSPAC Mothers	Gestational week 28	Questionnaire at recruitment about existing diabetes and history of gestational diabetes. Data abstracted on gestational diabetes and glycosuria (Lawlor et al., (2010) Diabetologia 53: 89-97)[55]
Triglycerides	663	1	EFSOCH Mothers	Gestational week 28	Fasting blood samples (10 hours fasting minimum) (Knight et al., (2006) Paediatric Perinal Epidemiology 20:172-179)[26]
HDL	733	1	EFSOCH Mothers	Gestational week 28	Fasting blood samples (10 hours fasting minimum) (Knight et al., (2006) Paediatric Perinal Epidemiology 20:172-179)[26]
Blood pressure	9,100	3	ALSPAC Mothers	Gestational week 28	Data abstracted from obstetric medical charts at various time points in pregnancy. Data for 28 weeks gestation predicted using fractional polynomials and spline multilevel models. (Macdonald-Wallis et al., (2011) Journal of Hypertension 29: 1703-1711)[56]
			HAPO Mothers (GWAS)	Gestational week 28	Measured blood pressure (Metzger et al., (2008) NEJM 358:1991-2002)[29]
			MoBa Mothers[a]	Gestational week 18	Self-reported blood pressure from medical card http://www.fhi.no/dokumenter/1f32a49514.pdf
Vitamin D status (25(OH)D levels)	5,305	2	ALSPAC Mothers	Gestational week 28	Measured in non-fasting blood samples. Data for 28 weeks gestation predicted using fractional polynomials and spline multilevel models. (Lawlor et al., (2013) Lancet 6736: 62203)[57]
			GEN-3G[b]	Yes (9 weeks)	Measured in blood samples
Adiponectin	1,376	1	HAPO Mothers GWAS	Gestational week 28	Measured in fasting serum samples (Lowe et al., (2010) Journal Clinical Endocrinology and Metabolism 95: 5427-5434)[58]

[a]Blood pressure was measured in the MoBa study and showed strong evidence of association with the genetic score (P=0.001), but since it was measured at 18 weeks of gestation, we chose not to meta-analyse with ALSPAC and HAPO data (measured at 28 weeks). [b]Vitamin D status was measured in the GEN-3G study and showed strong evidence of association the genetic score (P<5x10-5), but since it was measured at 9 weeks of gestation, we chose not to meta-analyse with ALSPAC data above (measured at 28 weeks).

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eTable 5. Associations between maternal genetic scores and maternal traits during and post-pregnancy in the same individuals

Trait	Study	N women with both pregnancy and post-pregnancy data available	Mean (SD) of trait measured during pregnancy	Mean (SD) age of mother when pregnancy measurement taken	Change in maternal trait per trait-increasing allele (95% CI) during pregnancy	P value (during pregnancy)	Mean (SD) of trait measured post-pregnancy	Mean (SD) age of mother when post-pregnancy measurement taken	Change in maternal trait per trait-increasing allele (95% CI) post-pregnancy	P value (post-pregnancy)
BMI (kg/m^2)	ALSPAC	2,927	26.02 (3.55)	29.7 (4.4)	0.13 (0.09, 0.16)	$7x10^{-14}$	26.54 (5.21)	48.0 (4.4)	0.14 (0.09, 0.19)	$1x10^{-8}$
BMI (kg/m^2)	EFSOCH	456	27.55 (4.19)	31.5 (4.7)	0.21 (0.11, 0.32)	$9x10^{-5}$	25.03 (4.60)	36.8 (4.9)	0.16 (0.05, 0.28)	0.006
Fasting glucose (mmol/L)	EFSOCH	312	4.39 (0.38)	32.0 (4.4)	0.04 (0.02, 0.05)	$1x10^{-6}$	4.60 (0.48)	37.1 (4.7)	0.04 (0.02, 0.06)	$2x10^{-4}$
Triglycerides (mmol/L)	EFSOCH	360	2.13 (0.70)	31.6 (4.7)	0.05 (0.03, 0.08)	$2x10^{-4}$	0.91 (0.40)	36.9 (4.9)	0.03 (0.01, 0.05)	$4x10^{-4}$
HDL-cholesterol (mmol/L)	EFSOCH	408	2.10 (0.46)	31.5 (4.7)	0.02 (0.01, 0.03)	$1x10^{-4}$	1.71 (0.42)	36.8 (4.9)	0.03 (0.02, 0.04)	$7x10^{-9}$
SBP (mmHg)	ALSPAC	2,930	112.3 (7.2)	29.6 (4.5)	0.17 (0.10, 0.24)	$4x10^{-6}$	117.9 (12.2)	47.9 (4.4)	0.43 (0.31, 0.56)	$2x10^{-12}$

SBP, systolic blood pressure

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(a) BMI genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, EFSOCH, HAPO (GWAS), DNBC-GOYA-RANDOM, DNBC-PTB-CONTROLS [0.18]	11,822	0.145 (0.126, 0.164)	$< 2x10^{-16}$
Waist-Hip Ratio	-	EFSOCH	438	0.001 (-0.001, 0.003)	0.18
Fasting glucose	mmol/L	HAPO, EFSOCH [0.14]	2,104	0.005 (0.001, 0.009)	0.026
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	1.04 (0.97, 1.12)	0.28
Triglycerides	mmol/L	EFSOCH	735	0.009 (-0.006, 0.023)	0.25
HDL-cholesterol	mmol/L	EFSOCH	732	-0.008 (-0.017, 0.002)	0.11
LDL-cholesterol	mmol/L	EFSOCH	727	-0.004 (-0.026, 0.019)	0.76
Systolic blood pressure	mmHg	ALSPAC, HAPO [0.08]	8,450	0.07 (0.02, 0.11)	0.003
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	0.002 (-0.001, 0.006)	0.25
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,376	-0.001 (-0.006, 0.000)	0.08
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO, EFSOCH [0.08]	9,212	1.00 (1.00, 1.01)	0.19
Highest educational qualification attained[a]		ALSPAC	6,855	-0.00 (-0.01, 0.01)	0.63
Occupational position[b]		ALSPAC	5,766	1.00 (0.99, 1.02)	0.67
Occupational position[c]		EFSOCH	612	0.015 (-0.003, 0.033)	0.11
Townsend deprivation score[d]		EFSOCH	743	0.035 (-0.029, 0.100)	0.28

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

[c]National Statistics Socio Economic Class Occuptation Code (3). Subjects grouped as 1=managerial & professional; 2=intermediate; 3=routine & manual

[d]Townsend deprivation score, a continuous variable based on UK postal code: 0=average; >0=more deprived; <0=more affluent

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(b) Fasting glucose genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, EFSOCH, HAPO (GWAS) [0.89]	8,232	0.007 (-0.025, 0.039)	0.68
Waist-Hip Ratio	-	EFSOCH	320	0.000 (-0.002, 0.003)	0.74
Fasting glucose	mmol/L	HAPO, EFSOCH [0.70]	5,402	0.029 (0.025, 0.032)	$< 2x10^{-16}$
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	1.06 (0.95, 1.17)	0.29
Triglycerides	mmol/L	EFSOCH	537	-0.007 (-0.029, 0.016)	0.57
HDL-cholesterol	mmol/L	EFSOCH	535	-0.004 (-0.018, 0.010)	0.57
LDL-cholesterol	mmol/L	EFSOCH	531	-0.014 (-0.049, 0.022)	0.45
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.69]	8,450	0.038 (-0.026, 0.102)	0.25
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	0.003 (-0.003, 0.008)	0.34
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,376	-0.001 (-0.006, 0.004)	0.72
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS), EFSOCH [0.49]	9,012	0.97 (0.99, 1.00)	0.32
Highest educational qualification attained[a]		ALSPAC	6,855	-0.01 (-0.02, 0.01)	0.24
Occupational position[b]		ALSPAC	5,766	1.01 (0.98, 1.03)	0.68
Occupational position[c]		EFSOCH	447	-0.018 (-0.046, 0.011)	0.22
Townsend deprivation score[d]		EFSOCH	542	-0.050 (-0.151, 0.051)	0.33

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

[c]National Statistics Socio Economic Class Occuptation Code (3). Subjects grouped as 1=managerial & professional; 2=intermediate; 3=routine & manual

[d]Townsend deprivation score, a continuous variable based on UK postal code: 0=average; >0=more deprived; <0=more affluent

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(c) Type 2 diabetes genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, HAPO (GWAS) [0.09]	7,901	0.010 (-0.008, 0.028)	0.28
Waist-Hip Ratio	NA				
Fasting glucose	mmol/L	HAPO (GWAS)	1,376	0.002 (-0.002, 0.006)	0.25
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	1.08 (1.03, 1.14)	0.003
Triglycerides	NA	-	-	-	-
HDL-cholesterol	NA	-	-	-	-
LDL-cholesterol	NA	-	-	-	-
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.27]	8,450	0.037 (0.004, 0.071)	0.028
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	0.001 (-0.002, 0.004)	0.37
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,376	0.001 (-0.002, 0.003)	0.63
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS) [0.24]	8,471	1.00 (1.00, 1.00)	0.55
Highest educational qualification attained[a]		ALSPAC	6,855	-0.01 (-0.01, 0.00)	0.10
Occupational position[b]	Odds ratio	ALSPAC	5,766	1.00 (0.99, 1.01)	0.95

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(d) Triglycerides genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, EFSOCH, HAPO (GWAS) [0.06]	8,353	-0.007 (-0.041, 0.027)	0.70
Waist-Hip Ratio	-	EFSOCH	392	0.000 (-0.002, 0.003)	0.84
Fasting glucose	mmol/L	HAPO (GWAS), EFSOCH [0.07]	2,036	0.002 (-0.003, 0.008)	0.42
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	0.93 (0.83, 1.04)	0.19
Triglycerides	mmol/L	EFSOCH	663	0.055 (0.032, 0.078)	$3x10^{-6}$
HDL-cholesterol	mmol/L	EFSOCH	660	-0.003 (-0.018, 0.012)	0.71
LDL-cholesterol	mmol/L	EFSOCH	656	0.003 (-0.033, 0.039)	0.88
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.97]	8,450	0.002 (-0.065, 0.069)	0.96
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	0.003 (-0.003, 0.009)	0.27
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,376	0.000 (-0.004, 0.004)	0.93
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS), EFSOCH [0.23]	9,142	1.00 (0.99, 1.01)	0.87
Highest educational qualification attained[a]		ALSPAC	6,855	0.00 (-0.01, 0.01)	0.78
Occupational position[b]	Odds ratio	ALSPAC	5,766	1.01 (0.98, 1.04)	0.47
Occupational position[c]		EFSOCH	556	-0.004 (-0.034, 0.026)	0.81
Townsend deprivation score[d]		EFSOCH	671	0.009 (-0.097, 0.115)	0.87

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

[c]National Statistics Socio Economic Class Occuptation Code (3). Subjects grouped as 1=managerial & professional; 2=intermediate; 3=routine & manual

[d]Townsend deprivation score, a continuous variable based on UK postal code: 0=average; >0=more deprived; <0=more affluent

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(e) HDL-cholesterol genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, EFSOCH, HAPO (GWAS) [0.10]	8,420	-0.048 (-0.097, 0.002)	0.06
Waist-Hip Ratio	-	EFSOCH	438	0.002 (-0.002, 0.005)	0.40
Fasting glucose	mmol/L	HAPO (GWAS), EFSOCH [0.48]	2,107	-0.002 (-0.011, 0.007)	0.70
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	0.83 (0.70, 0.99)	0.04
Triglycerides	mmol/L	EFSOCH	736	0.001 (-0.035, 0.037)	0.96
HDL-cholesterol	mmol/L	EFSOCH	733	0.050 (0.027, 0.072)	$1x10^{-5}$
LDL-cholesterol	mmol/L	EFSOCH	728	-0.032 (-0.088, 0.024)	0.26
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.77]	8,450	-0.013 (-0.112, 0.085)	0.79
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	-0.000 (-0.009, 0.008)	0.95
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,376	-0.001 (-0.007, 0.005)	0.81
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS), EFSOCH [0.38]	9,215	1.00 (0.99, 1.00)	0.29
Highest educational qualification attained[a]		ALSPAC	6,855	0.01 (-0.01, 0.02)	0.55
Occupational position[b]		ALSPAC	5,766	1.00 (0.96, 1.04)	0.93
Occupational position[c]		EFSOCH	613	0.004 (-0.042, 0.049)	0.87
Townsend deprivation score[d]		EFSOCH	744	0.081 (-0.081, 0.243)	0.33

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

[c]National Statistics Socio Economic Class Occuptation Code (3). Subjects grouped as 1=managerial & professional; 2=intermediate; 3=routine & manual

[d]Townsend deprivation score, a continuous variable based on UK postal code: 0=average; >0=more deprived; <0=more affluent

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(f) Systolic blood pressure genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, HAPO (GWAS) [0.78]	7,741	-0.011 (-0.030, 0.008)	0.27
Waist-Hip Ratio	NA				
Fasting glucose	mmol/L	HAPO (GWAS)	1,376	0.002 (-0.003, 0.007)	0.45
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	0.98 (0.91, 1.05)	0.52
Triglycerides	NA	-	-	-	-
HDL-cholesterol	NA	-	-	-	-
LDL-cholesterol	NA	-	-	-	-
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.04]	8,450	0.186 (0.140, 0.231)	$< 2x10^{-16}$
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	-0.001 (-0.005, 0.002)	0.45
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,376	0.001 (-0.002, 0.004)	0.46
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS) [0.36]	8,471	1.00 (0.99, 1.00)	0.17
Highest educational qualification attained[a]		ALSPAC	6,855	0.00 (-0.00, 0.01)	0.32
Occupational position[b]		ALSPAC	5,766	0.99 (0.97, 1.01)	0.43

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(g) Vitamin D genetic score

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Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, EFSOCH, HAPO (GWAS) [0.86]	8,420	0.073 (-0.019, 0.164)	0.12
Waist-Hip Ratio	-	EFSOCH	438	-0.001 (-0.008, 0.005)	0.68
Fasting glucose	mmol/L	HAPO (GWAS), EFSOCH [0.96]	2,109	-0.001 (-0.019, 0.016)	0.96
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	1.19 (0.88, 1.62)	0.25
Triglycerides	mmol/L	EFSOCH	736	0.001 (-0.060, 0.061)	0.98
HDL-cholesterol	mmol/L	EFSOCH	733	-0.034 (-0.072, 0.005)	0.09
LDL-cholesterol	mmol/L	EFSOCH	728	0.048 (-0.046, 0.141)	0.32
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.98]	8,454	-0.030 (-0.211, 0.151)	0.98
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	0.024 (0.009, 0.039)	0.002
Adiponectin	log10(ug/ml)	HAPO (GWAS)	1,339	-0.029 (-0.772, 0.713)	0.94
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS), EFSOCH [0.83]	9,217	1.00 (0.95, 1.05)	0.98
Highest educational qualification attained[a]		ALSPAC	6,855	0.033 (0.001, 0.065)	0.05
Occupational position[b]	Odds ratio	ALSPAC	5,766	0.95 (0.88, 1.02)	0.17
Occupational position[c]		EFSOCH	613	0.057 (-0.017, 0.130)	0.13
Townsend deprivation score[d]		EFSOCH	744	-0.058 (-0.329, 0.213)	0.67

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

[c]National Statistics Socio Economic Class Occuptation Code (3). Subjects grouped as 1=managerial & professional; 2=intermediate; 3=routine & manual

[d]Townsend deprivation score, a continuous variable based on UK postal code: 0=average; >0=more deprived; <0=more affluent

eTable 6. Associations between each maternal genetic score and potentially confounding or mediating variables

(h) Adiponectin genetic score

Outcome variable tested for association (measured or ascertained during pregnancy, except BMI and WHR)	Units of outcome variable	Study(ies) [Phet from meta-analysis]	Total N women	Estimated change in outcome variable per trait-raising allele (95%CI)	P-value
Body Mass Index	kg/m^2	ALSPAC, HAPO (GWAS) [0.79]	7,741	-0.04 (-0.23, 0.14)	0.61
Waist-Hip Ratio	NA	-	-	-	-
Fasting glucose	mmol/L	HAPO	1,376	-0.01 (-0.06, 0.04)	0.69
Gestational/existing diabetes	Odds ratio	ALSPAC	6,827	1.57 (0.94, 2.64)	0.09
Triglycerides	NA	-	-	-	-
HDL-cholesterol	NA	-	-	-	-
LDL-cholesterol	NA	-	-	-	-
Systolic blood pressure	mmHg	ALSPAC, HAPO (GWAS) [0.66]	8,450	-0.047 (-0.389, 0.295)	0.79
Vitamin D, ln[25(OH)D]		ALSPAC	4,767	-0.015 (-0.043, 0.012)	0.28
Adiponectin	ln(ug/ml)	HAPO (GWAS)	1,376	0.17 (0.11, 0.23)	$1x10^{-8}$
Smoking (current smoker vs non-smoker)	Odds ratio	ALSPAC, HAPO (GWAS) [0.91]	8,471	0.97 (0.93, 1.02)	0.22
Highest educational qualification attained[a]	NA	ALSPAC	6,855	-0.04 (-0.10, 0.02)	0.16
Occupational position[b]	Odds ratio	ALSPAC	5,766	0.96 (0.84, 1.10)	0.57

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree

[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

eTable 7. Associations between maternal genetic scores and ponderal index of offspring at birth

Maternal exposure for which genetic score was constructed	N Studies	Total N women	Change in ponderal index z-score per additional maternal trait raising/lowering allele (95% CI)[a]	Equivalent change in PI (kgm^{-3}) per allele (95% CI)[b]	P value	Heterogeneity P Value (I^2 %) from meta-analysis	N Studies with fetal genotype	Total N offspring with genotype data	Change in PI z-score per additional maternal trait raising /lowering[a] allele (95% CI)[c]	Equivalent change in PI (kgm^{-3}) per allele (95% CI)[b]	P value	Heterogeneity P Value (I^2 %) from meta-analysis
Higher pre-pregnancy BMI	10	17,743	0.006 (0.002, 0.010)	0.02 (0.01, 0.03)	0.003	0.48 (0)	7	9,628	0.006 (0.000, 0.012)	0.02 (0.00, 0.03)	0.05	0.38 (6.5)
Higher fasting glucose	10	17,818	0.007 (0.001, 0.012)	0.02 (0.00, 0.03)	0.02	0.49 (0)	8	9,902	0.014 (0.005, 0.022)	0.04 (0.01, 0.06)	0.001	0.78 (0)
Higher odds of type 2 Diabetes	7	13,518	0.002 (-0.002, 0.005)	0.01 (-0.01, 0.01)	0.3	0.20 (29.6)	5	6,800	0.005 (0.000, 0.011)	0.01 (0.00, 0.03)	0.05	0.11 (47.5)
Higher odds of type 2 Diabetes (excluding pre-existing and gestational diabetes)	6	11,653	0.002 (-0.001, 0.006)	0.01 (0.00, 0.02)	0.18	0.32 (14.9)	4	5,330	0.008 (0.002, 0.014)	0.02 (0.01, 0.04)	0.01	0.38 (2.9)
Higher triglycerides	9	17,440	0.000 (-0.006, 0.007)	0.00 (-0.02, 0.02)	0.89	0.11 (39.0)	6	9,335	-0.004 (-0.014, 0.005)	-0.01 (-0.04, 0.01)	0.41	0.07 (51.3)
Lower HDL-cholesterol	9	15,573	0.005 (-0.004, 0.014)	0.01 (-0.01, 0.04)	0.27	0.45 (0)	6	8,207	-0.001 (-0.013, 0.012)	0.00 (-0.04, 0.03)	0.92	0.13 (41.4)
Higher systolic blood pressure	7	13,527	-0.005 (-0.010, -0.001)	-0.01 (-0.03. 0.00)	0.03	0.74 (0)	5	6,821	-0.003 (-0.011, 0.004)	-0.01 (-0.03, 0.01)	0.43	0.14 (42.3)
Higher systolic blood pressure (excluding pre-eclampsia and hypertension)	6	10,770	-0.005 (-0.010, 0.000)	-0.01 (-0.03, 0.00)	0.07	0.60 (0)	4	4,735	-0.005 (-0.014, 0.004)	-0.01 (-0.04, 0.01)	0.25	0.28 (22.2)
Lower vitamin D status	7	14,004	-0.007 (-0.025, 0.011)	-0.02 (-0.07, 0.03)	0.44	0.22 (27.9)	3	7,292	-0.026 (-0.054, 0.002)	-0.07 (-0.15, 0.01)	0.07	0.04 (68.7)
Lower adiponectin	6	11,501	0.017 (-0.020, 0.054)	0.05 (-0.06, 0.15)	0.37	0.83 (0)	5	6,851	0.039 (-0.016, 0.094)	0.11 (-0.04, 0.26)	0.17	0.89 (0)

[a]The decision to model the association in relation to the trait-raising or trait-lowering allele depended on the known direction of association of each trait with higher BMI (see **Box 1**). Column 1 specifies each of these directions of association. Results are per average weighted allele, adjusted for sex and gestational age. [b]Standard deviation of ponderal index from ALSPAC study was used for these estimates (=2.78 kg/m3). [c]Results are per average weighted allele, adjusted for sex, gestational age and fetal genotype

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eTable 8. A comparison of the observational with the genetic association between each maternal trait and offspring ponderal index at birth

Maternal trait (value of 1 SD with units)	**Study/ies[a] used for observational estimates [Total N women]**	**N women**	**Observational estimate of the change in ponderal index (kg/m^3) per 1 SD (or 10% [b]) change in maternal trait, adjusted for sex and gestational age (95%CI)**	**Genetic estimate of the change in ponderal index (kg/m^3), adjusted for sex and gestational age, per 1 SD (or 10% [b]) change in maternal trait, unadjusted for fetal genotype (95%CI)**	**P value [c] comparing observational with genetic ponderal index associations (unadjusted for fetal genotype)**	**Genetic estimate of the change in ponderal index (kg/m^3), adjusted for sex, gestational age and fetal genotype, per 1 SD (or 10% [b]) change in maternal trait (95%CI)**	**P value [c] comparing observational with genetic ponderal index associations (adjusted for fetal genotype)**
Higher pre-pregnancy BMI (4 kg/m2)	ALSPAC Mothers, EFSOCH Mothers, HAPO Mothers	9,690	0.24 (0.19, 0.29)	0.45 (0.14, 0.75)	0.20	0.47 (0.14, 0.79)	0.21
Higher fasting glucose (0.4 mmol/L)	EFSOCH Mothers, HAPO Mothers	4,917	0.31 (0.22, 0.39)	0.27 (0.05, 0.48)	0.72	0.53 (0.20, 0.87)	0.24
Higher triglycerides (0.7 mmol/L)	EFSOCH Mothers	857	0.15 (-0.03, 0.33)	0.02 (-0.21, 0.24)	0.35	-0.14 (-0.48, 0.20)	0.14
Lower HDL-cholesterol (0.5 mmol/L)	EFSOCH Mothers	854	0.12 (-0.08, 0.31)	0.14 (-0.11, 0.39)	0.91	-0.02 (-0.37, 0.34)	0.51
Higher Systolic blood pressure (10 mmHg)	ALSPAC Mothers, HAPO Mothers	9,691	0.00 (-0.08, 0.06)	-0.77 (-1.80, 0.25)	0.16	-0.46 (-1.95, 1.03)	0.56
Lower vitamin D status (10%)[b]	ALSPAC Mothers	3,718	-0.02 (-0.03, 0.00)	-0.08 (-0.28, 0.13)	0.56	-0.29 (-0.65, 0.07)	0.14
Lower adiponectin (10%)[b]	HAPO Mothers (GWAS only)	1,373	0.05 (0.02, 0.08)	0.03 (-0.03, 0.09)	0.49	0.06 (-0.03, 0.15)	0.82

[a]Heterogeneity statistics from the meta-analyses of observational associations were: Phet = 0.35 and I2 = 9.1% for BMI; Phet = 0.23 and I2 =32.7% for fasting glucose; Phet = 0.67 and I^2 = 0% for SBP.
[b]For 25[OH]D and adiponectin, we present the estimated change in ponderal index per 10% reduction in maternal trait level because these variables were logged for analysis.
[c]P-values <0.05 are considered to indicate evidence that the genetic effect size estimate is different from the observational estimate, suggesting that the observational estimate is subject to confounding or bias.

eTable 9

(a) Observational associations between offspring birth weight and maternal socio-economic status or maternal smoking in the ALSPAC study

Maternal trait	N women	Change in birth weight (g) per unit change in maternal trait (95% CI)	P
Highest educational qualification attained[a]	6,855	19 (10, 29)	0.00004
Occupational position[b]	5,588	-34 (-68, 0)	0.06
Smoking (current smoker vs non-smoker)	7,021	-208 (-237, -179)	$1x10^{-43}$

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree
[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

(b) Observational associations between maternal BMI and maternal socio-economic status or maternal smoking in the ALSPAC study

Maternal trait	N women	Change in BMI (kgm-2) per unit change in maternal trait (95%CI)	P
Highest educational qualification attained[a]	6,115	-0.35 (-0.42, -0.27)	$9x10^{-20}$
Occupational position[b]	5,128	0.38 (0.11, 0.65)	0.005
Smoking (current smoker vs non-smoker)	6,238	0.01 (-0.24, 0.26)	0.95

[a]Subjects grouped as: 1=CSE; 2=Vocational; 3=Ordinary Level; 4=Advanced level; 5=Degree
[b]Derived from Office of Population Censuses & Surveys Standard Occupational Classification (1). Subjects dichotomized as: 0=I, II & III (non-manual); 1=III (manual), IV & V.

eTable 10. Power calculations

Maternal trait	Total N women	Adjusted-R2 from BW~GA sex	Adjusted-R2 from BW~GA sex GS	Estimated proportion of variance in birth weight explained by maternal genetic score	Power available in our included sample to detect evidence of association between maternal genetic score and birth weight at P<0.05	Minimum sample size needed to detect association between maternal genetic score and birth weight at P<0.05 with 80% power
BMI	25265	0.1308	0.1312	0.0004	0.89	19618
Fasting glucose	23902	0.1308	0.1319	0.0011	1.00	7131
Type 2 diabetes	18670	0.1308	0.1312	0.0004	0.78	19618
Triglycerides	24985	0.1308	0.1307	-0.0001*	0.35	78485
HDL-cholesterol	22167	0.1308	0.1307	-0.0001*	0.32	78485
Systolic Blood Pressure	20062	0.1308	0.1324	0.0016	1.00	4902
25-hydroxy vitamin D	30340	0.1308	0.1309	0.0001	0.41	78485
Adiponectin	14920	0.1308	0.1307	-0.0001*	0.23	78485

*Where the estimated variance explained was negative, we assumed a value of 0.0001 for the calculations. BW, birth weight; GA, gestational age; GS, genetic score.

eTable 11. Association between father's phenotypes and offspring birth weight using data from the ALSPAC study

Father's phenotype	N men	Correlation coefficient (95% CI) of father's phenotype with offspring birth weight
BMI*	7491	0.04 (0.02, 0.06)
BMI	1721	0.03 (-0.02, 0.07)
Systolic BP	1732	-0.03 (-0.07, 0.01)
Glucose	1656	-0.01 (-0.06, 0.03)
Triglycerides	1656	-0.02 (-0.07, 0.02)
HDLc	1656	0.02 (-0.03, 0.06)

* Based on paternal report of weight and height at the time that their partner was in early pregnancy; all other phenotypes were assessed at a clinic visit ~18-19 years after the child's birth.
Correlation coefficients of paternal phenotypes with offspring birth weight were all weak and mostly null (Pearson correlation coefficients all ≤ 0.04).
The correlation between and offspring birth weight and father's BMI, assessed when the mothers were pregnant, was similar to that between offspring birth weight and father's BMI 18 years later, suggesting that the postnatal measures for other phenotypes are a reasonable approximation for them before/at the time of their partner's pregnancy.

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Funding/support of individual studies

ALSPAC: The work undertaken in this paper was funded by the the US National Institute of Diabetes and Digestive and Kidney Diseases (R01 DK10324) and the Wellcome Trust (WT088806), with the WT088806 grant also providing funds for completion of genome wide genotyping on the ALSPAC mothers (WT088806). ALSPAC offspring GWAS data was generated by Sample Logistics and Genotyping Facilities at the Wellcome Trust Sanger Institute and LabCorp (Laboratory Corportation of America) using support from 23andMe. Additional maternal data were funded by the British Heart Foundation (SP/07/008/24066) and WellcomeTrust (WT087997). The UK Medical Research Council and Wellcome Trust (Grant ref: 102215/2/13/2) and the University of Bristol provide core support for ALSPAC.

***BBC*:** The Berlin Birth Cohort study was funded by the Deutsche Forschungsgemeinschaft (DFG), Else Kröner-Fresenius Foundation, Jackstädt-Foundation and a research grant of the University of Potsdam, Germany. Details of the study are provided in: Pharmacogenet Genomics. 2009;19(9):710-8.; Circulation. 2006 Oct 17;114(16):1687-92 and Lancet. 2000 Apr 8;355(9211):1241-2. We deeply acknowledge the contribution of the participating families. Replication genotyping was supported by ENGAGE Framework VII HEALTH-F4-2007-201413 and Wellcome Trust 098381.

1958BC WTCCC: Statistical analyses were funded by the Academy of Finland (Project 24300796 and SALVE/PREVMEDSYN). DNA collection was funded by MRC grant G0000934 and cell-line creation by Wellcome Trust grant 068545/Z/02. This study makes use of data generated by the Wellcome Trust Case-Control Consortium. A full list of investigators who contributed to generation of the data is available from the Wellcome Trust Case-Control Consortium website. Funding for the project was provided by the Wellcome Trust under the award 076113. Great Ormond Street Hospital/University College London, Institute of Child Health receives a proportion of funding from the Department of Health's National Institute for Health Research (NIHR) ('Biomedical Research Centres' funding).

1958BC T1DGC: Statistical analyses were funded by the Academy of Finland (Project 24300796 and SALVE/PREVMEDSYN). DNA collection was funded by MRC grant G0000934 and cell-line creation by Wellcome Trust grant 068545/Z/02. This research used resources provided by the Type 1 Diabetes Genetics Consortium, a collaborative clinical study sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases, National Human Genome Research Institute, National Institute of Child Health and Human Development, and Juvenile Diabetes Research Foundation International (JDRF) and supported by U01 DK062418. Great Ormond Street Hospital/University College London, Institute of Child Health receives a proportion of funding from the Department of Health's National Institute for Health Research (NIHR) ('Biomedical Research Centres' funding).

CHOP: This research was financially supported by an Institute Development Award from the Children's Hospital of Philadelphia, a Research Development Award from the Cotswold Foundation and NIH grant R01 HD056465.

COPSAC- 2000: COPSAC is funded by private and public research funds listed on www.copsac.com. The Lundbeck Foundation; The Danish Strategic Research Council; the Pharmacy Foundation of 1991; the Danish Medical Research Council and The Danish Pediatric Asthma Centre provided the core support for COPSAC research center.

DNBC-GOYA: The genotyping for GOYA was funded by the Wellcome Trust (WT 084762). GOYA is a nested study within The Danish National Birth Cohort which was established with major funding from the Danish National Research Foundation. Additional support for this cohort has been obtained from the Pharmacy Foundation, the Egmont Foundation, The March of Dimes Birth Defects Foundation, the Augustinus Foundation, and the Health Foundation.

DNBC-PTB Controls: The Danish National Birth Cohort is a result of major grants from the Danish National Research Foundation, the Danish Pharmacists' Fund, the Egmont Foundation, the March of Dimes Birth Defects Foundation, the Augustinus Foundation, and the Health Fund of the Danish Health Insurance Societies. The generation of GWAS genotype data for the Danish National Birth Cohort samples was carried out within the Gene Environment Association Studies (GENEVA) consortium with funding provided through the National Institutes of Health's Genes, Environment, and Health Initiative (U01HG004423; U01HG004446; U01HG004438).

EFSOCH: The Exeter Family Study of Childhood Health (EFSOCH) was supported by South West NHS Research and Development, Exeter NHS Research and Development, the Darlington Trust and the Peninsula National Institute of Health Research (NIHR) Clinical Research Facility at the University of Exeter. The opinions given in this paper do not necessarily represent those of NIHR, the NHS or the Department of Health.

Gen3G: The Gen3G prospective cohort was supported by the Fonds de Recherche du Québec – Santé (FRQS – subvention Fonctionnement – Recherche Clinique - grant #20697) and by a Canadian Institute of Health Research (CIHR) Operating grant (Institute of Nutrition, Metabolism and Diabetes; MOP- 115071).

Generation R: The general design of Generation R Study is made possible by financial support from the Erasmus Medical Center, Rotterdam, the Erasmus University Rotterdam, the Netherlands Organization for Health Research and Development (ZonMw), the Netherlands Organisation for Scientific Research (NWO), the Ministry of Health, Welfare and Sport and the Ministry of Youth and Families. This research also received funding from the European Union's Seventh Framework Programme (FP7/2007–2013), project EarlyNutrition under grant agreement n°289346. VWJ received an additional grant from the Netherlands Organization for Health Research and Development (VIDI 016.136.361).

HAPO: This study was supported by National Institutes of Health (NIH) grants HD34242, HD34243, HG004415, DK097534 and DK099820

MoBa: This work was supported by grants from the Norwegian Research Council (FUGE 183220/S10, FRIMEDKLI-05 ES236011), Swedish Medical Society (SLS 2008- 21198), Jane and Dan Olsson Foundations and Swedish government grants to researchers in the public health service (ALFGBG-2863, ALFGBG-11522), and the European Community's Seventh Framework Programme (FP7/2007-2013). The Norwegian Mother and Child Cohort Study was also supported by the Norwegian Ministry of Health and the Ministry of Education and Research, NIH/NIEHS (contract no N01-ES-75558), NIH/NINDS (grant no.1 UO1 NS 047537-01 and grant no.2 UO1 NS 047537-06A1), and the Norwegian Research Council/FUGE (grant no. 151918/S10).

NFBC1966: Academy of Finland (Grant no. 1114194, Grant no. 12926901), University Hospital Oulu and Unit of Primary Care, Biocenter, University of Oulu, and the European Commission (EURO-BLCS, Framework 5 award QLG1-CT-2000-01643 and EU FP7- EurHEALTHAgeing - European Research on Developmental, Birth and Genetic Determinants of Ageing. Grant no. 24000522). Medical Research Council Medical Research Council, UK (G0500539, G0600705, PrevMetSyn/SALVE, PS0476)

NTR: Funding was obtained from the Netherlands Organization for Scientific Research (NWO: MagW/ZonMW grants 904-61-090, 985-10-002,904-61-193,480-04-004, 400-05-717, Addiction-31160008 Middelgroot-911-09-032, Spinozapremie 56-464-14192), Center for Medical Systems Biology (CMSB, NWO Genomics), NBIC/BioAssist/RK(2008.024), Biobanking and Biomolecular Resources Research Infrastructure (BBMRI – NL), the VU University's Institute for Health and Care Research (EMGO+) and Neuroscience Campus Amsterdam (NCA), the European Science Foundation (ESF, EU/QLRT-2001-01254), the European Community's Seventh Framework Program (FP7/2007-2013), ENGAGE (HEALTH-F4-2007-201413); the European Research Council (ERC Advanced, 230374), Rutgers University Cell and DNA Repository (NIMH U24 MH068457-06), and the National Institutes of Health (NIH, R01D0042157-01A). Part of the genotyping and analyses were funded by the Genetic Association Information Network (GAIN) of the Foundation for the US National Institutes of Health, and by grants from GAIN and the NIMH (MH081802).

QIMR: Supported by National Institutes of Health Grants AA07535, AA0758O, AA07728, AA10249, AA13320, AA13321, AA14041, AA11998, AA17688, DA012854, DA018267, DA018660, DA23668 and DA019951; by Grants from the Australian National Health and Medical Research Council (241944, 339462, 389927, 389875, 389891, 389892, 389938, 442915, 442981, 496739, 552485, 552498, and 628911); by Grants from the Australian Research Council (A7960034, A79906588, A79801419, DP0770096, DP0212016, and DP0343921); and by the 5th Framework Programme (FP-5) GenomEUtwin Project (QLG2-CT-2002-01254).

Twins UK: The study was funded by the Wellcome Trust; European Community's Seventh Framework Programme (FP7/2007-2013). The study also receives support from the National Institute for Health Research (NIHR)- funded BioResource, Clinical Research Facility and Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust in partnership with King's College London. SNP Genotyping was performed by The Wellcome Trust Sanger Institute and National Eye Institute via NIH/CIDR.

Individual study acknowledgements:

ALSPAC: We are extremely grateful to all of the families who took part in this study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, receptionists, managers and nurses.

CHOP: The authors thank the network of primary care clinicians and the patients and families for their contribution to this project and to clinical research facilitated by the Pediatric Research Consortium (PeRC) at The Children's Hospital of Philadelphia. R. Chiavacci, E. Dabaghyan, A. (Hope) Thomas, K. Harden, A. Hill, C. Johnson-Honesty, C. Drummond, S. Harrison, F. Salley, C. Gibbons, K. Lilliston, C. Kim, E. Frackelton, F. Mentch, G. Otieno, K. Thomas, C. Hou, K. Thomas and M.L. Garris provided expert assistance with genotyping and/or data collection and management. The authors would also like to thank S. Kristinsson, L.A. Hermannsson and A. Krisbjörnsson of Raförninn ehf for extensive software design and contributions.

COPSAC: We gratefully express our gratitude to the children and families of the COPSAC2000 cohort study for all their support and commitment. We acknowledge and appreciate the unique efforts of the COPSAC research team.

Gen3G: Gen3G investigators would like to acknowledge the participants, the research staff from the endocrinology group at the Centre de Recherche clinique of the Centre Hospitalier de l'Université de Sherbrooke (CR-CHUS), the clinical and research staff of the Clinique de Prélèvement en Grossesse du CHUS, and the clinical staff from the CHUS Obstetric Department. The CR-CHUS is a FRQ-Sante affiliated research centre; recruitment and follow-up of Gen3G participants was possible based on the on-going support from the CR-CHUS.

Generation R: The Generation R Study is conducted by the Erasmus Medical Center in close collaboration with the School of Law and Faculty of Social Sciences of the Erasmus University Rotterdam, the Municipal Health Service Rotterdam area, Rotterdam, the Rotterdam Homecare Foundation, Rotterdam and the Stichting Trombosedienst and Artsenlaboratorium Rijnmond (STAR), Rotterdam. We gratefully acknowledge the contribution of participating mothers, general practitioners, hospitals, midwives and pharmacies in Rotterdam. The generation and management of GWAS genotype data for the Generation R Study were done at the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, The Netherlands. We would like to thank Karol Estrada, Dr. Tobias A. Knoch, Anis Abuseiris, Luc V. de Zeeuw, and Rob de Graaf, for their help in creating GRIMP, BigGRID, MediGRID, and Services@MediGRID/D-Grid, (funded by the German Bundesministerium fuer Forschung und Technology; grants 01 AK 803 A-H, 01 IG 07015 G) for access to their grid computing resources. We thank Mila Jhamai, Manoushka Ganesh, Pascal Arp, Marijn Verkerk, Lizbeth Herrera and Marjolein Peters for their help in creating, managing and QC of the GWAS database. Also, we thank Karol Estrada for his support in creation and analysis of imputed data.

HAPO: HAPO would like to acknowledge the participants and research personnel at the participating HAPO field centres.

MoBa: We are grateful to all the participating families in Norway who take part in this ongoing cohort study. Researchers interested in using MoBa data must obtain approval from the Scientific Management Committee of MoBa and from the Regional Committee for Medical and Health Research Ethics for access to data and biological material. Researchers are required to follow the terms of an Assistance Agreement containing a number of clauses designed to ensure protection of privacy and compliance with relevant laws.

QIMR: We thank Richard Parker, Soad Hancock, Judith Moir, Sally Rodda, Pieta-Maree Shertock, Heather Park, Jill Wood, Pam Barton, Fran Husband, Adele Somerville, Ann Eldridge, Marlene Grace, Kerrie McAloney, Anjali Henders, Lisa Bowdler, Alexandre Todorov, Steven Crooks, David Smyth, Harry Beeby, and Daniel Park. Finally, we thank the twins and their families for their participation.