Fetal middle cerebral artery and umbilical artery pulsatility index: effects of maternal characteristics and medical history

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Key words: Fetal middle cerebral artery Doppler, Umbilical artery pulsatility index, Cerebroplacental ratio, Pyramid of pregnancy care, First trimester screening, Second trimester screening, Third trimester screening.

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ABSTRACT

Objective: To define the contribution of maternal variables which influence the measured fetal middle cerebral artery (MCA) and umbilical artery (UA) pulsatility index (PI) in the assessment of fetal wellbeing.

Methods: Maternal characteristics and medical history were recorded and fetal MCA PI (n=34,183) and UA PI (34,433) were measured in women with singleton pregnancies attending for a routine hospital visit at 30^{+0}-37^{+6} weeks' gestation. For pregnancies delivering phenotypically normal live births or stillbirths at ≥30 weeks' gestation, variables from maternal demographic characteristics and medical history important in the prediction of MCA PI and UA PI were determined from multiple linear regression analysis.

Results: Significant independent contributions to MCA PI were provided by gestational age at assessment and birth weight Z-score of the neonate of the previous pregnancy. Significant independent contributions to UA PI were provided by gestational age, Afro-Caribbean racial origin, cigarette smoking and birth weight Z-score of the neonate of the previous pregnancy. Multiple linear regression analysis was used to define the contribution of maternal variables that influence the measured MCA PI and UA PI and express the values as multiples of the median (MoMs). The cerebroplacental ratio (CPR) MoM was calculated by dividing MCA PI MoM with UA PI MoM. The model was shown to provide an adequate fit of MoM values for all covariates both in pregnancies that delivered small for gestational age neonates and in those without this pregnancy complication.

Conclusions: A model was fitted to express MCA PI, UA PI and CPR into MoMs after adjustment for variables from maternal characteristics and medical history that affect this measurement.

Introduction

Fetal hypoxemia is associated with increased impedance to flow in the umbilical artery (UA) and decreased impedance in the fetal middle cerebral artery (MCA) [1-4]. Consequently, Doppler measurement of UA and MCA pulsatility index (PI) plays a central role in the assessment and monitoring for fetal oxygenation in pregnancies with impaired placentation. Most studies have investigated the use of UA PI and MCA PI in pregnancies with small for gestational age (SGA) fetuses with the aims of firstly, distinguishing between those which are constitutionally small from those that are growth restricted and therefore at increased risk of perinatal death and long-term neurological morbidity and secondly, deciding the best time, place and mode of delivery [5-8]. Recent evidence suggests that high UA PI and low MCA PI, regardless of fetal size, is independently associated with intrapartum fetal compromise, low neonatal blood pH and neonatal unit admission [9-12]. Consequently, measurement of MCA PI, UA PI and their ratio (cerebroplacental ratio or CPR), are widely used as part of routine third-trimester assessment of fetal wellbeing and screening for fetal hypoxemia.

Our approach to risk assessment and screening for pregnancy complications is to apply Bayes theorem to combine the *a priori* risk from maternal characteristics and medical history with the results of various combinations of biophysical and biochemical measurements. However, in the application of Bayes theorem it is essential to standardize the measured values of biomarkers for any variables included in the prior model. The risk of delivering SGA neonates is affected by maternal weight, height, racial origin, cigarette smoking, medical history of chronic hypertension, diabetes mellitus, systemic lupus erythematosus (SLE) or anti-phospholipid syndrome (APS), assisted conception, delivery of SGA neonate in the previous pregnancy and inter-pregnancy interval [13,14]. Consequently, for the effective use of MCA PI, UA PI and CPR in risk assessment these variables need to be taken into account and this can be achieved by standardizing the measured levels into multiples of the normal median (MoM) values.

The objectives of this paper are to firstly, identify and quantify the effects of variables from maternal characteristics and medical history on fetal MCA PI and UA PI levels, secondly, present a model for standardizing MCA PI and UA PI measurements into MoM values and calculating CPR MoM and thirdly, summarize the distribution of MoM values in pregnancies with normal outcomes and those that deliver SGA neonates. The main focus of this paper is on the pregnancies with normal outcomes. Further details of the distribution of MoM values in pregnancies with complications are the subject of other publications.

Methods

Study population

The data for this study were derived from prospective screening for adverse obstetric outcomes in women attending for a routine third-trimester hospital visit at King's College Hospital, University College London Hospital and Medway Maritime Hospital, UK between January 2006 and March 2014. This visit, initially at 30^{+0}-34^{+6} weeks and subsequently at 35^{+0}-37^{+6} weeks, included recording of maternal characteristics and medical history and ultrasound examination for estimation of fetal size from transabdominal ultrasound measurement of fetal head circumference, abdominal circumference and femur length. Gestational age was determined by the measurement of fetal crown-rump length at 11-13 weeks or the fetal head circumference at 19-24 weeks [15,16]. Transabdominal color Doppler ultrasound was used to visualize the UA and MCA and pulsed-wave Doppler was then used to assess impedance to flow and when three similar consecutive waveforms were obtained the PI was measured [17,18].

Written informed consent was obtained from the women agreeing to participate in a study on adverse pregnancy outcome, which was approved by the Ethics Committee of each participating hospital. The inclusion criteria for this study were singleton pregnancies delivering a phenotypically normal live birth or stillbirth at or after 30 weeks' gestation. We excluded pregnancies with aneuploidies and major fetal abnormalities.

Patient characteristics

Patient characteristics including maternal age, racial origin (Caucasian, Afro-Caribbean, South Asian, East Asian and mixed), method of conception (spontaneous or assisted conception requiring the use of ovulation drugs or *in vitro* fertilization), cigarette smoking during pregnancy (yes or no), medical history of chronic hypertension (yes or no), diabetes mellitus (yes or no), SLE or APS, family history of PE in the mother of the patient (yes or no) and obstetric history including parity (parous or nulliparous if no previous pregnancies at or after 24 weeks), previous pregnancy with PE (yes or no), gestational age at delivery and birth weight of the neonate in the last pregnancy and interval in years between birth of the last child and estimated date of conception of the current pregnancy. Maternal height was measured in the first visit and weight in each visit.

The birth weight Z-score for the neonate in the current and the last pregnancy was derived from our reference range of birth weight for gestational age at delivery [19].

Statistical analysis

The effect on MCA PI and UA PI levels of the following variables from maternal characteristics and medical history were examined: age, weight, height, racial origin, history of chronic hypertension, diabetes mellitus type 1 or type 2, SLE or APS, parous or nulliparous, previous pregnancy with PE, gestational age at delivery and birth weight Z-score of the neonate in the last pregnancy and inter-pregnancy interval, method of conception, smoking during pregnancy and gestational age at assessment.

Multiple linear regression models were fitted to $\log_{10}$ values of MCA PI and UA PI for the full set of explanatory variables, as outlined above. Continuous variables were initially coded into groups and represented as factors to identify suitable parametric forms. Backward elimination was used to identify potentially important terms in the model by sequentially removing non-significant ($p>0.05$) variables. Effect sizes were assessed relative to the standard deviation (SD) and a criterion of 0.1 SD was used to identify terms that had little substantive impact in model predictions. Residual analyses were used to assess the adequacy of the model. Graphical displays of the relationship between gestational age and MCA PI and UA PI and the effects of variables from maternal characteristics and medical history on MoM values were produced for the final model. A full analysis of residuals including an investigation of interactions was used to check the model fit and on the basis of this model refinements were made. The CPR MoM was derived from dividing MCA PI MoM with UA PI MoM.

The statistical software package R was used for data analyses [20].

Results

Characteristics of the study population

The maternal characteristics and medical history in the pregnancies that delivered SGA neonates with birth weight below the 5th percentile and unaffected pregnancies are compared in Table 1.

Variables affecting fetal MCA PI and UA PI

Significant independent contributions to MCA PI were provided by gestational age and birth weight Z-score of the neonate of the previous pregnancy (Figure 1). Significant independent contributions to UA PI were provided by gestational age, Afro-Caribbean racial origin, cigarette smoking and birth weight Z-score of the neonate of the previous pregnancy (Figure 2). Linear mixed models, with random effects to represent between women random effects, were fitted to the subset of variables that contributed substantively to the linear regression models (Table 2).

Figure 3 shows MCA PI MoM diagnostics for racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that delivered SGA neonates and those unaffected by SGA. Figure 4 shows MCA PI MoM diagnostics for gestational age, maternal weight and birth weight Z-score of the neonate in the last pregnancy in pregnancies that delivered SGA neonates and those unaffected by SGA.

Figure 5 shows UA PI MoM diagnostics for racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that delivered SGA neonates and those unaffected by SGA. Figure 6 shows UA PI MoM diagnostics for gestational age, maternal weight and birth weight Z-score of the neonate in the last pregnancy in pregnancies that delivered SGA neonates and those unaffected by SGA.

Figure 7 shows CPR MoM diagnostics for racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that delivered SGA neonates and those unaffected by SGA.

Distributional properties of MCA PI MoM, UA PI MoM and CPR MoM

Figure 8 shows the Gaussian distribution of MCA PI MoM, UA PI MoM and CPR MoM. The median and 5^{th}, 10^{th}, 90^{th} and 95^{th} percentiles, with 95% confidence intervals for MCA PI MoM, were 1.0000 (0.99765, 1.00199) and 0.77188 (0.76878, 0.77349), 0.81426 (0.81356, 0.81500), 1.18602 (1.18318, 1.18822) and 1.23327 (1.22904, 1.23663), respectively. The estimated standard deviation with 95% confidence interval for $\log_{10}$ MCA PI was 0.062374 (0.06211, 0.06264).

The median and 5^{th}, 10^{th}, 90^{th} and 95^{th} percentiles, with 95% confidence intervals for UA PI MoM, were 1.00000 (0.99786, 1.00142) and 0.75045 (0.74600, 0.75641), 0.80753 (0.80650, 0.80836), 1.19740 (1.19474, 1.20159) and 1.23670 (1.23411, 1.23937), respectively. The estimated standard deviation with 95% confidence interval for $\log_{10}$ UA PI was 0.065949 (0.06567, 0.06623).

The median and 5^{th}, 10^{th}, 90^{th} and 95^{th} percentiles, with 95% confidence intervals for CPR MoM ratio, were 1.00000 (0.99868, 1.00220) and 0.72096 (0.71670, 0.72480), 0.77462 (0.77200, 0.77795), 1.28745 (1.28255, 1.29199) and 1.38096 (1.37526, 1.38619), respectively. The estimated standard deviation with 95% confidence interval for $\log_{10}$ CPR MoM was 0.08626 (0.08580, 0.08662).

Discussion

Main findings of the study

The findings of this study demonstrate that during the third-trimester of pregnancy MCA PI decreases with gestational age and it is higher in parous than nulliparous women and increases with birth weight Z-score of the neonate of the previous pregnancy. Similarly, UA PI decreases with gestational age, it is lower in women of Afro-Caribbean racial origin than in Caucasian women, higher in cigarette smokers than in non-smokers, and women with low birth weight z-score of the neonate of the previous pregnancy and lower in parous women with high birth weight z-score of the neonate of the previous pregnancy.

Multiple linear regression was used to define the contribution of maternal variables that influence the measured MCA PI and UA PI and express the values as MoMs. The model was shown to provide an adequate fit of MoM values for all covariates both in pregnancies that delivered SGA neonates and those unaffected by SGA.

Strengths and limitations of the study

The strengths of this study are firstly, prospective examination of a large population of pregnant women attending for routine care in the third-trimester of pregnancy for assessment of fetal anatomy, growth and wellbeing, secondly, measurement of MCA PI and UA PI by appropriately trained sonographers and thirdly, application of multivariable regression analysis to define the contribution and interrelations of variables that influence the measured values of MCA PI and UA PI.

The main limitation of the study is that the data were confined to the third-trimester of pregnancy.

Comparison with findings of previous studies

We found that UA PI and MCI PI decrease with gestational age and these findings are compatible with those of previous studies [17,21-23]. We found that in parous women MCA PI is higher and UA PI is lower than in nulliparous women; one previous study at 37-42 weeks, reported that MCA PI is higher in parous than in nulliparous women, but UA PI is not significantly different [24]. We found that UA PI, but not MCA PI, is higher than in cigarette smokers than in non-smokers and these findings are compatible with those of previous studies [25-27]. We found that UA PI, but not MCA PI, is lower in women of Afro-Caribbean racial origin than in Caucasian women; one previous study reported that impedance to flow in the UA at 30-36 weeks is decreased in women of African racial origin [28].

Implications for clinical practice

Measurement of MCA PI, UA PI and CPR is useful in screening for fetal hypoxemia. The effective use of these Doppler indices in risk assessment and screening necessitates that gestational age and variables from maternal characteristics and medical history which affect these measurements in normal pregnancies are taken into account.

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29. Figure legends

Figure 1. Relationship between median levels of fetal middle cerebral artery pulsatility index (MCA PI) and gestational age (left). Effect of birth weight Z-score of the neonate in the last pregnancy on MCA PI (with 95% confidence intervals) plotted on the multiple of the median (MoM) scale after correcting for gestational age. The fitted effects are represented by the red lines. The horizontal black lines correspond to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation.

Figure 2. Relationship between median levels of umbilical artery pulsatility index (UA PI) and gestational age (left). Effect of Afro-Caribbean racial origin, cigarette smoking and birth weight Z-score of the neonate in the last pregnancy on UA PI (with 95% confidence intervals) plotted on the multiple of the median (MoM) scale after correcting for other factors. The fitted effects are represented by the red lines. The horizontal black lines correspond to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation.

Figure 3. Median fetal middle cerebral artery pulsatility index multiple of the median (MoM) (with 95% confidence intervals) derived from the model according to racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that delivered small for gestational age (SGA) neonates (red lines and numbers) and in those unaffected by SGA (black lines and numbers). The vertical black line corresponds to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation. The vertical red line corresponds to a median MoM of 0.9725 for the SGA group.

Figure 4. Median fetal middle cerebral artery pulsatility index multiple of the median (MoM) (with 95% confidence intervals) derived from the model according to gestational age, maternal weight and birth weight Z-score of the neonate in the last pregnancy in pregnancies that delivered small for gestational age (SGA) neonates (red lines and numbers) and in those unaffected by SGA (black lines and numbers). The horizontal black line corresponds to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation.

Figure 5. Median umbilical artery pulsatility index multiple of the median (MoM) (with 95% confidence intervals) derived from the model according to racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that delivered small for gestational age (SGA) neonates (red lines and numbers) and in those unaffected by SGA (black lines and numbers). The vertical black line corresponds to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation. The vertical red line corresponds to a median MoM of 1.0647 for the SGA group.

Figure 6. Median umbilical artery pulsatility index multiple of the median (MoM) (with 95% confidence intervals) derived from the model according to gestational age, maternal weight and birth weight Z-score of the neonate in the last pregnancy in pregnancies that delivered small for gestational age (SGA) neonates (red lines and numbers) and in those unaffected by SGA (black lines and numbers). The horizontal black line corresponds to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation.

Figure 7. Median cerebroplacental ratio multiple of the median (MoM) (with 95% confidence intervals) according to racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that delivered small for gestational age (SGA) neonates (red lines and numbers) and in those unaffected by SGA (black lines and numbers). The vertical black line corresponds to a median MoM of 1.0 and the two interrupted lines with the grey band are + / - 0.1 standard deviation. The vertical red line corresponds to a median MoM of 0.9133 for the SGA group.

Figure 8. Gaussian distribution of fetal middle cerebral artery pulsatility index and umbilical artery pulsatility index multiple of the median values.

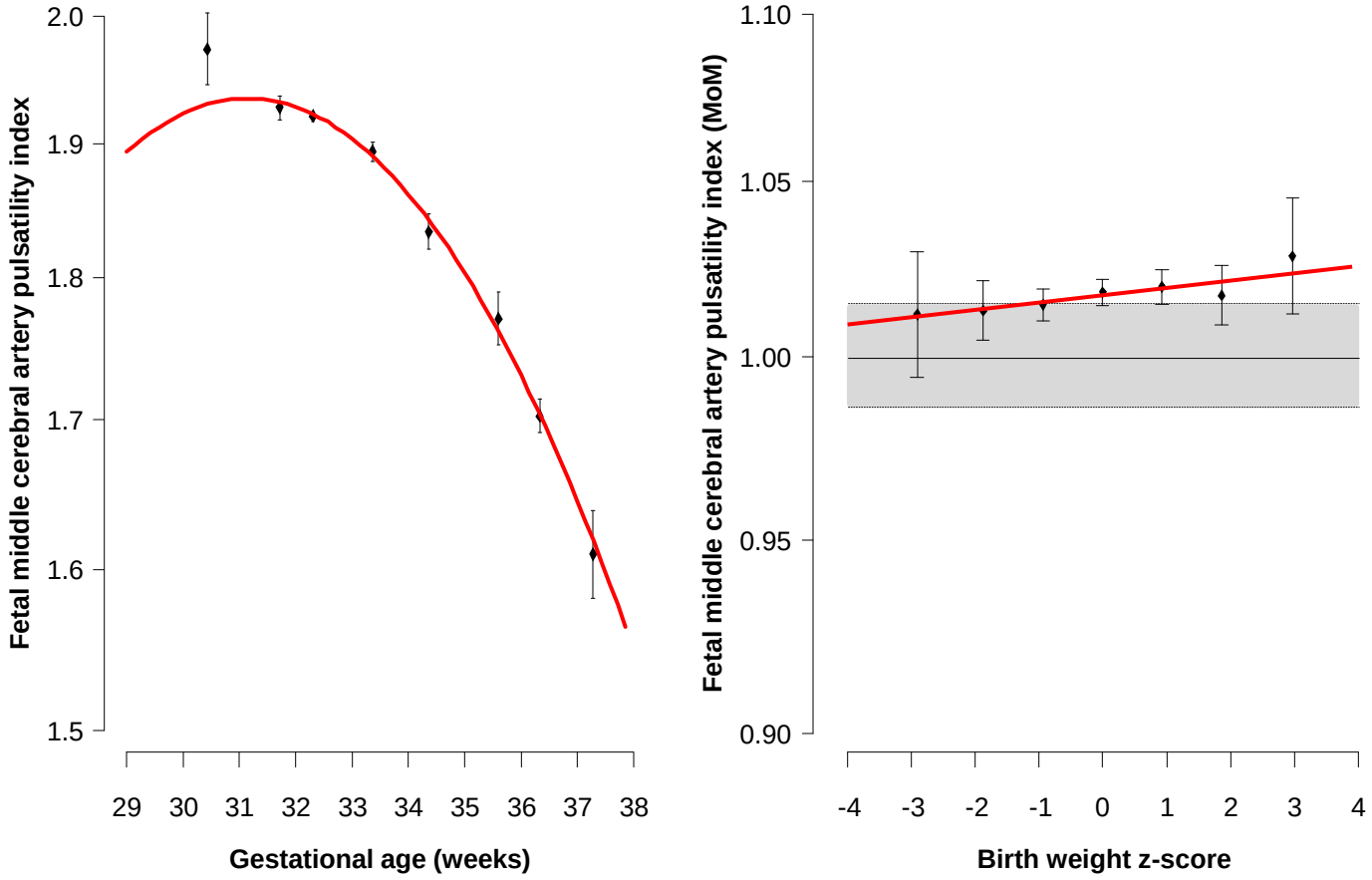
Fetal middle cerebral artery pulsatility index
2.0
1.9
1.8
1.7
1.6
1.5
29
30
31
32
33
34
35
36
37
38
Gestational age (weeks)
Fetal middle cerebral artery pulsatility index (MoM)
1.10
1.05
1.00
0.95
0.90
-4
-3
-2
-1
0
1
2
3
4
Birth weight z-score

Figure 1

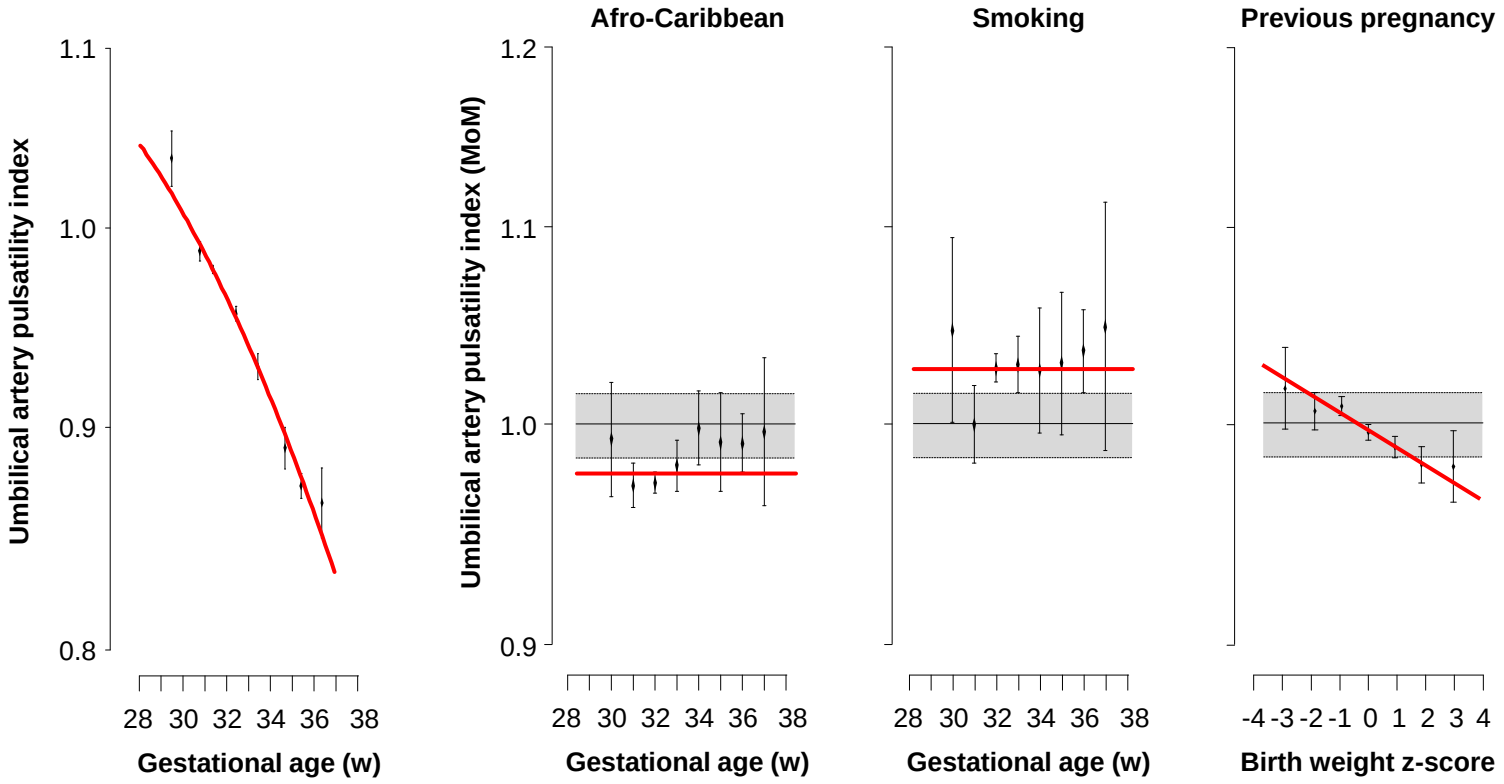
Umbilical artery pulsatility index
1.1
1.0
0.9
0.8
28 30 32 34 36 38
Gestational age (w)
Umbilical artery pulsatility index (MoM)
Afro-Caribbean
1.2
1.1
1.0
0.9
28 30 32 34 36 38
Gestational age (w)
Smoking
28 30 32 34 36 38
Gestational age (w)
Previous pregnancy
-4 -3 -2 -1 0 1 2 3 4
Birth weight z-score

Figure 2

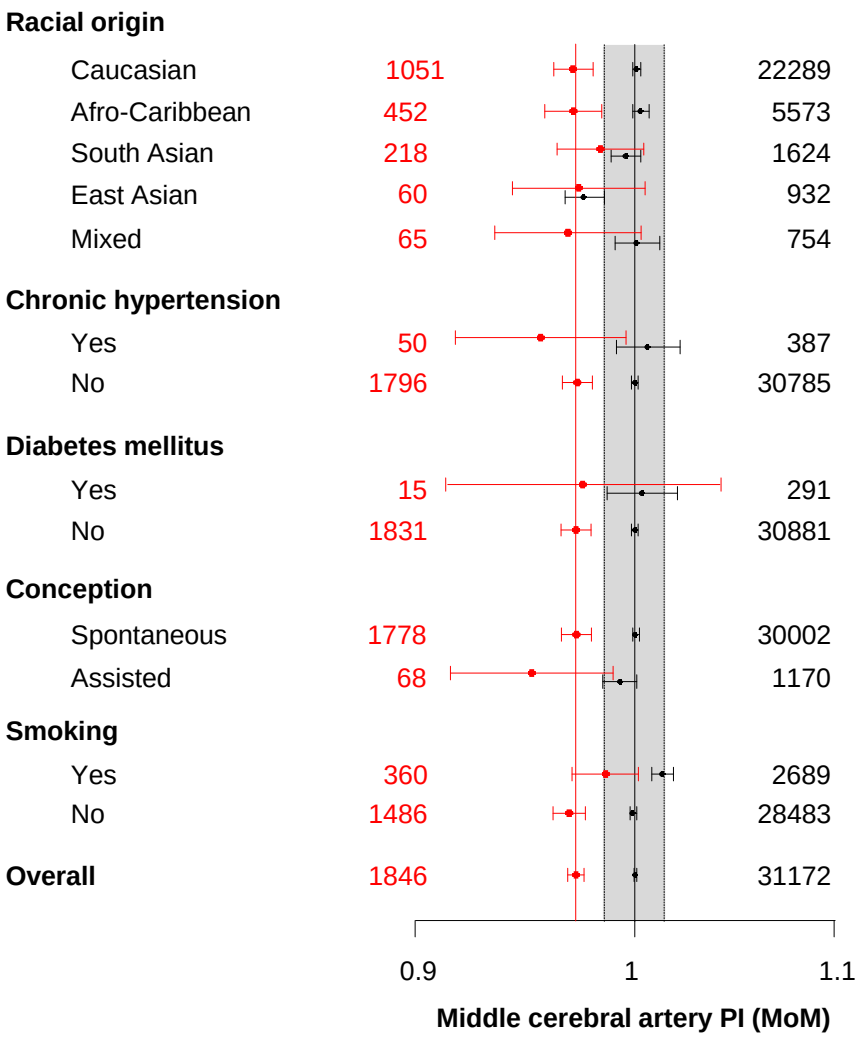
Racial origin
Caucasian 1051 22289
Afro-Caribbean 452 5573
South Asian 218 1624
East Asian 60 932
Mixed 65 754
Chronic hypertension
Yes 50 387
No 1796 30785
Diabetes mellitus
Yes 15 291
No 1831 30881
Conception
Spontaneous 1778 30002
Assisted 68 1170
Smoking
Yes 360 2689
No 1486 28483
Overall 1846 31172
0.9
1
1.1
Middle cerebral artery PI (MoM)

Figure 3

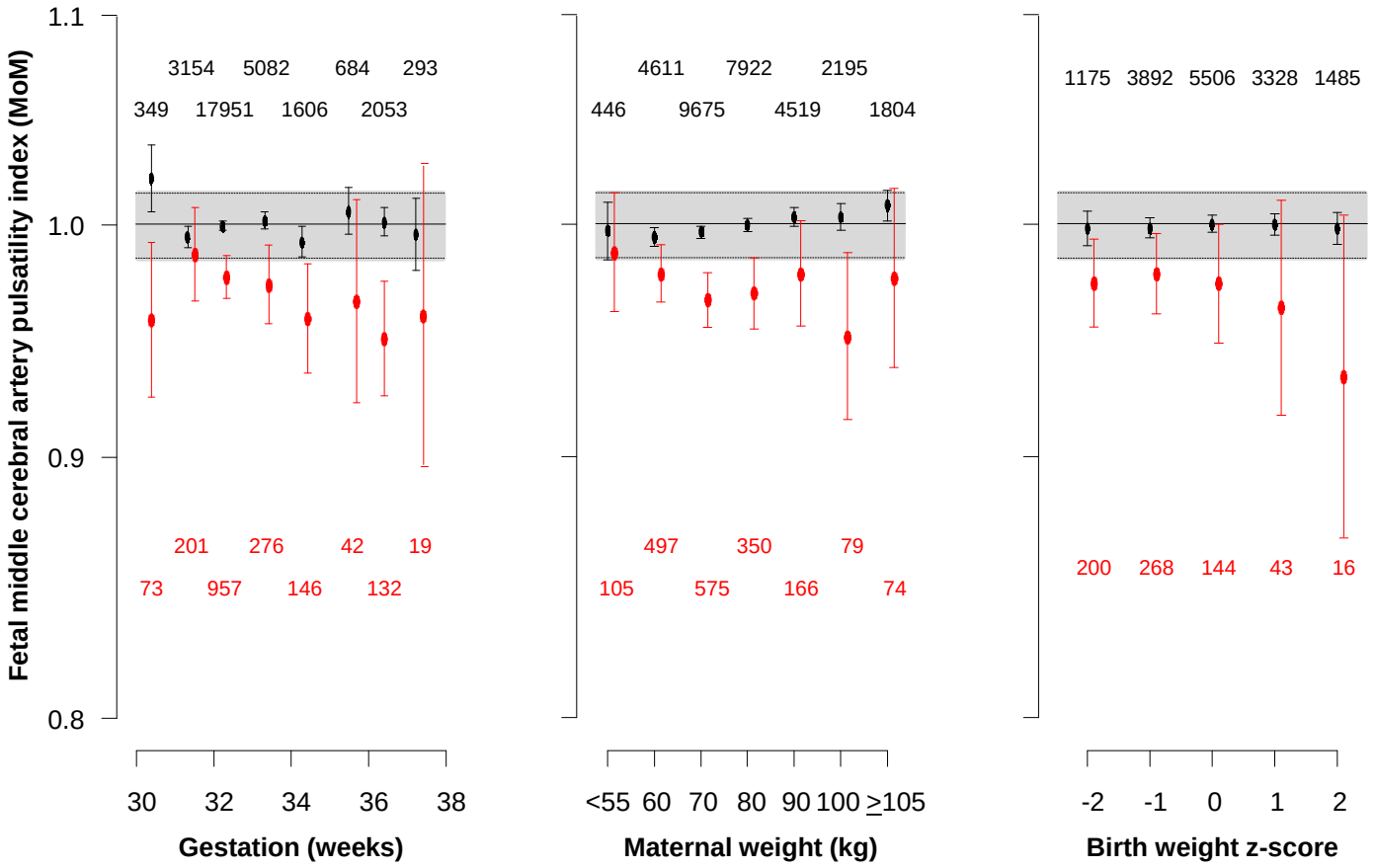
Fetal middle cerebral artery pulsatility index (MoM)
1.1
1.0
0.9
0.8
3154 5082 684 293
349 17951 1606 2053
201 276 42 19
73 957 146 132
30 32 34 36 38
Gestation (weeks)
4611 7922 2195
446 9675 4519 1804
497 350 79
105 575 166 74
<55 60 70 80 90 100 ≥105
Maternal weight (kg)
1175 3892 5506 3328 1485
200 268 144 43 16
-2 -1 0 1 2
Birth weight z-score

Figure 4

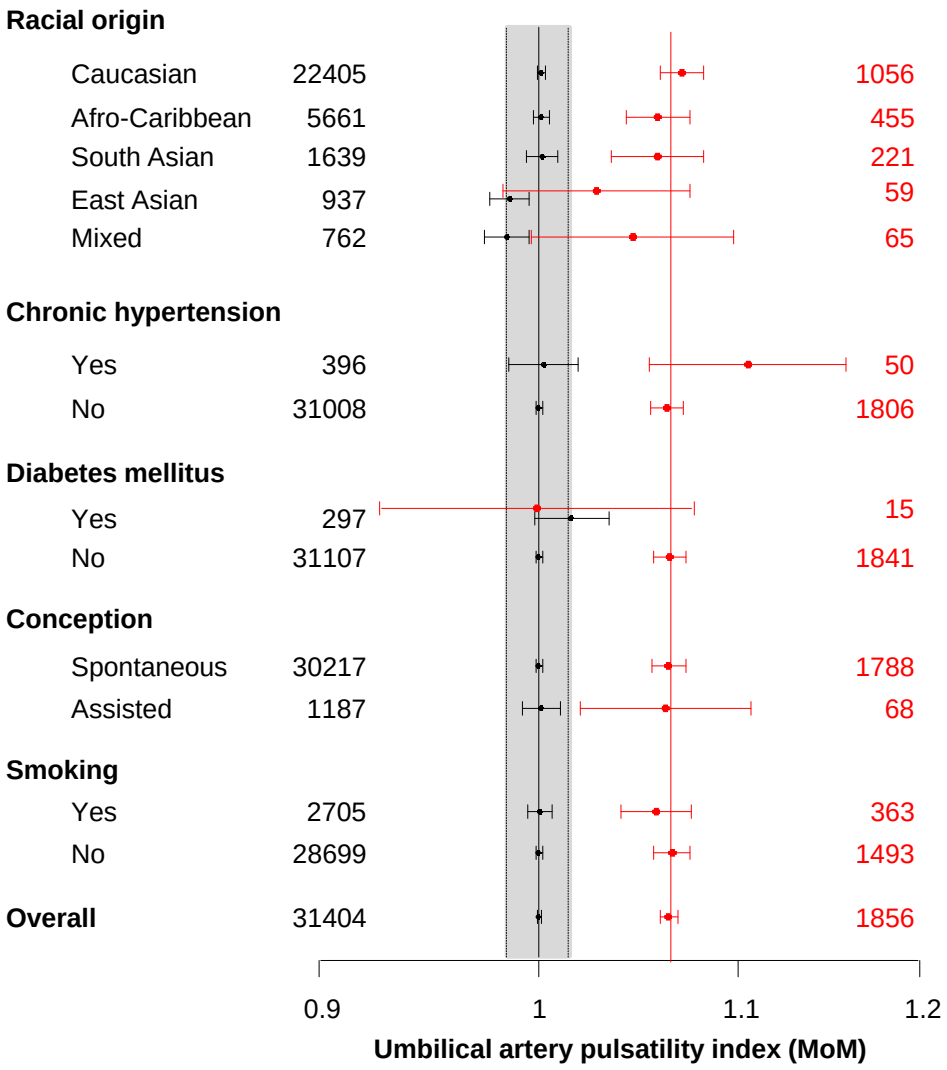
Racial origin
Caucasian 22405 1056
Afro-Caribbean 5661 455
South Asian 1639 221
East Asian 937 59
Mixed 762 65
Chronic hypertension
Yes 396 50
No 31008 1806
Diabetes mellitus
Yes 297 15
No 31107 1841
Conception
Spontaneous 30217 1788
Assisted 1187 68
Smoking
Yes 2705 363
No 28699 1493
Overall 31404 1856
0.9
1
1.1
1.2
Umbilical artery pulsatility index (MoM)

Figure 5

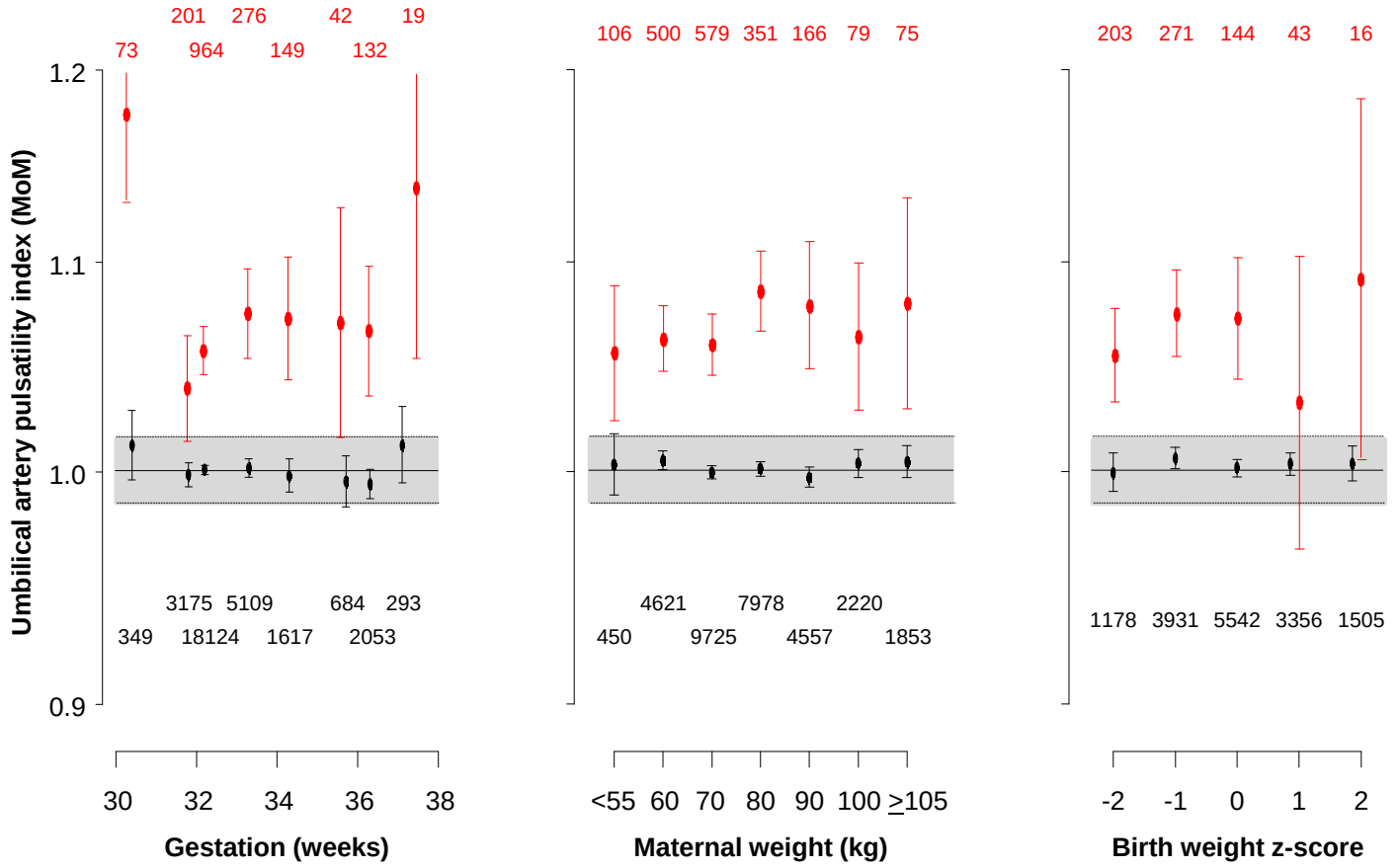
Umbilical artery pulsatility index (MoM)
1.2
1.1
1.0
0.9
73
201
964
276
149
42
132
19
349
3175
18124
5109
1617
684
2053
293
30
32
34
36
38
Gestation (weeks)
106
500
579
351
166
79
75
450
4621
9725
7978
4557
2220
1853
<55
60
70
80
90
100
≥105
Maternal weight (kg)
203
271
144
43
16
1178
3931
5542
3356
1505
-2
-1
0
1
2
Birth weight z-score

Figure 6

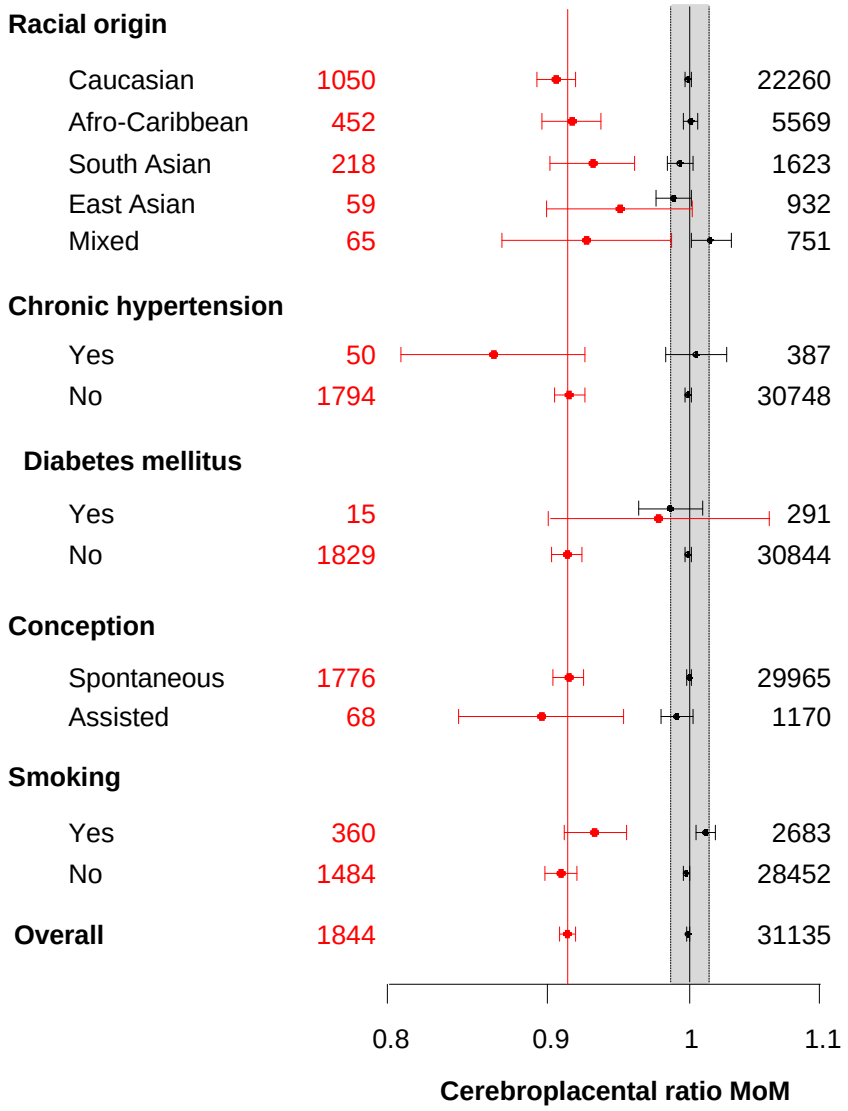
Racial origin
Caucasian 1050 22260
Afro-Caribbean 452 5569
South Asian 218 1623
East Asian 59 932
Mixed 65 751
Chronic hypertension
Yes 50 387
No 1794 30748
Diabetes mellitus
Yes 15 291
No 1829 30844
Conception
Spontaneous 1776 29965
Assisted 68 1170
Smoking
Yes 360 2683
No 1484 28452
Overall 1844 31135
0.8
0.9
1
1.1
Cerebroplacental ratio MoM

Figure 7

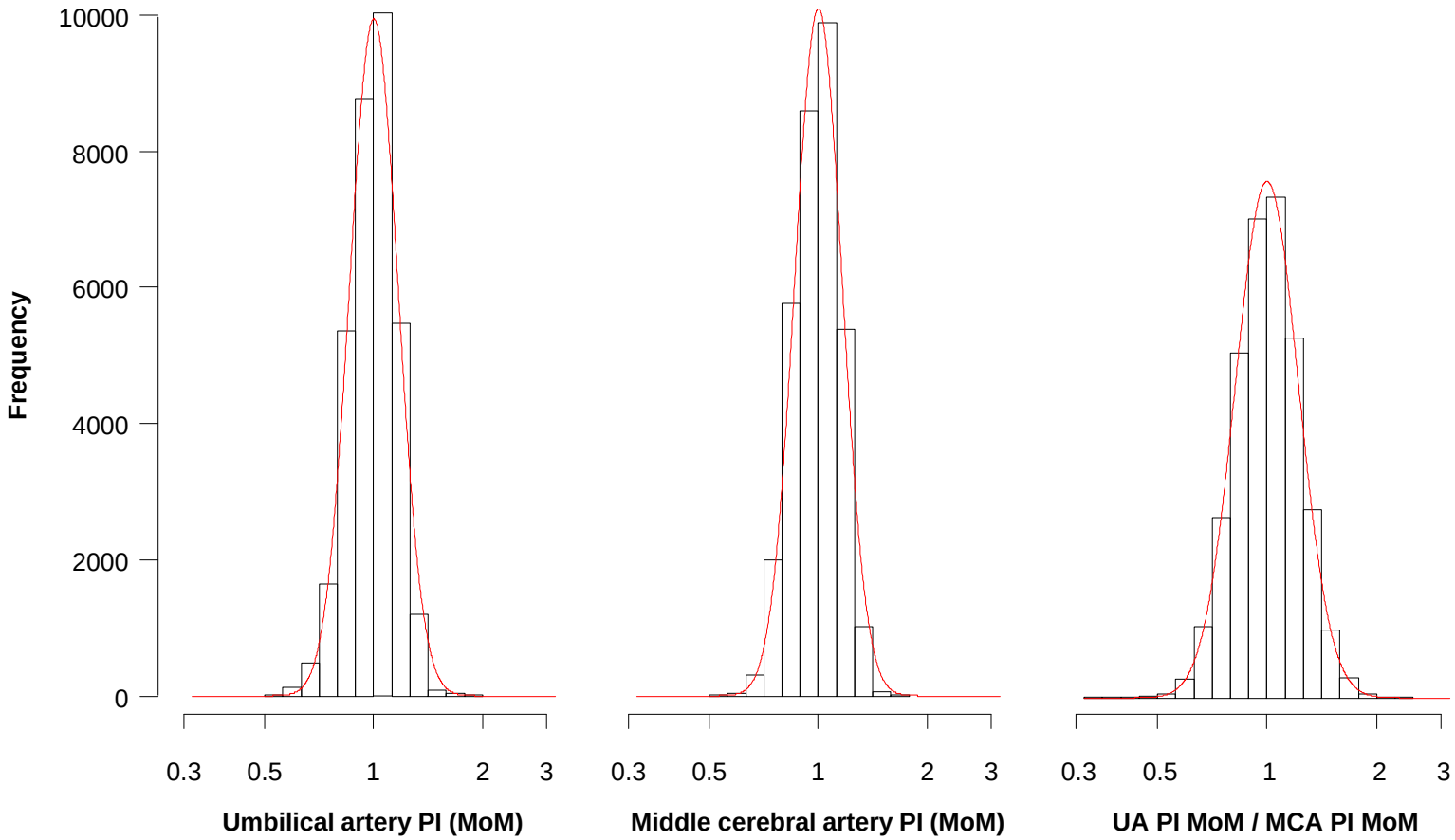
Frequency
10000
8000
6000
4000
2000
0
0.3
0.5
1
2
3
Umbilical artery PI (MoM)
Middle cerebral artery PI (MoM)
UA PI MoM / MCA PI MoM

Figure 8

Table 1. Maternal and pregnancy characteristics in the screening population.

Variables	Umbilical artery pulsatility index		Middle cerebral artery pulsatility index	
	Non SGA n=32,491	SGA n=1,942	Non SGA n=32,251	SGA n=1,932
Maternal age in years, median (IQR)	31.3 (26.8, 35.0)	30.1 (25.4, 34.6)	31.3 (26.8, 35.0)	30.1 (25.4, 34.6)
Maternal weight in kg, median (IQR)	76.0 (68.1, 86.5)	70.0 (62.7, 80.0)	76.0 (68.0, 86.4)	70.0 (62.7, 80.0)
Maternal height in cm, median (IQR)	165.0 (160.0, 169.0)	162.0 (157.4, 166.0)	165.0 (160.0, 169.0)	162.0 (157.4, 166.0)
Gestational age in weeks, median (IQR)	32.4 (32.1, 33.2)	32.4 (32.0, 33.3)	32.4 (32.1, 33.2)	32.4 (32.0, 33.3)
Racial origin				
Caucasian, n (%)	22,981 (70.7%)	1,089 (56.1%)	22,863 (70.9%)	1,084 (56.1%)
Afro-Caribbean, n (%)	6,032 (18.6%)	497 (25.6%)	5,938 (18.4%)	494 (25.6%)
South Asian, n (%)	1,710 (5.3%)	228 (11.7%)	1,695 (5.3%)	225 (11.6%)
East Asian, n (%)	984 (3.0%)	62 (3.2%)	979 (3.0%)	63 (3.3%)
Mixed, n (%)	784 (2.4%)	66 (3.4%)	776 (2.4%)	66 (3.4%)
Medical history				
Chronic hypertension	422 (1.3%)	56 (2.9%)	413 (1.3%)	56 (2.9%)
Diabetes mellitus	316 (1.0%)	16 (0.8%)	309 (1.0%)	16 (0.8%)
SLE/APS	56 (0.2%)	6 (0.3%)	56 (0.2%)	6 (0.3%)
Cigarette smokers, n (%)	2,772 (8.5%)	375 (19.3%)	2,755 (8.5%)	372 (19.3%)
Family history of preeclampsia, (n, %)	934 (2.9%)	71 (3.7%)	925 (2.9%)	71 (3.7%)
Parity				
Nulliparous, n (%)	15,892 (48.9%)	1,179 (60.7%)	15,786 (48.9%)	1,175 (60.8%)
Parous with no previous PE	15,622 (48.1%)	696 (35.8%)	15,499 (48.1%)	689 (35.7%)
Parous with previous PE, n (%)	977 (3.0%)	67 (3.5%)	966 (3.0%)	68 (3.5%)
Pregnancy interval in years, median (IQR)	3.0 (2.0, 4.9)	3.4 (2.1, 5.7)	3.0 (2.0, 4.9)	3.4 (2.1, 5.7)
Gestation of last birth in weeks, median (IQR)	40.0 (39.0, 40.0)	40.0 (38.0, 40.0)	40.0 (39.0, 40.0)	40.0 (38.0, 40.0)
Previous pregnancy birth weight in grams (IQR)	3377.0 (3036.0, 3700.0)	2894.0 (2525.0, 3206.0)	3377.0 (3036.0, 3700.0)	2894.0 (2538.0, 3208.0)
Conception				
Spontaneous, n (%)	31,276 (96.3%)	1,872 (96.4%)	31,053 (96.3%)	1,862 (96.4%)
Ovulation induction, n (%)	339 (1.0%)	25 (1.3%)	335 (1.0%)	25 (1.3%)
In-vitro fertilization, n (%)	876 (2.7%)	45 (2.3%)	863 (2.7%)	45 (2.3%)

SGA = small for gestational age ith birth weight below the 5th percentile; SLE/APS = systemic lupus erythematosus or antiphospholipid syndrome

Table 2. Regression models for $\log_{10}$ fetal middle cerebral artery pulsatility index and umbilical artery pulsatility index.

Term	Estimate	Standard error	95% Confidence interval	p-value
Middle cerebral artery pulsatility index				
Intercept	0.288106856	0.002151358	0.28389019, 0.29232352	<0.0001
Gestational age				
Gestational age in days - 210	0.00062096	0.00017769	0.00027269, 0.00096924	0.0005
(Gestational age in days - 210)^2	-0.00004074	0.00000317	-0.00004696, -0.00003452	<0.0001
Previous obstetric history				
Parous	0.00668499	0.00069162	0.00532942, 0.00804056	<0.0001
Parous: Birth weight z-score	0.00097980	0.00043579	0.00012565, 0.00183395	0.0246
Umbilical artery pulsatility index				
Intercept	0.01179300	0.00237500	0.00713810, 0.01644855	
Gestational age				
Gestational age in days - 210	-0.00112000	0.00019100	-0.00149195, -0.00074364	<0.0001
(Gestational age in days - 210)^2	-0.00000980	0.00000346	-0.00001658, -0.00000302	<0.0001
Afro-Caribbean racial origin	-0.00995000	0.00096600	-0.01184316, -0.00805495	<0.0001
Cigarette smoking	0.01182400	0.00127500	0.00932583, 0.01432241	
Previous obstetric history				
Parous	-0.00095000	0.00073900	-0.00239477, 0.00050118	0.1999
Parous: Birth weight z-score	-0.00368000	0.00046200	-0.00458541, -0.00277297	<0.0001