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Mean arterial pressure in the three trimesters of pregnancy: effects of maternal characteristics and medical history

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KEYWORDS: first-trimester screening; mean arterial pressure; pre-eclampsia; pyramid of pregnancy care; second-trimester screening; third-trimester screening

ABSTRACT

Objective *To define the contribution of maternal variables that influence the measured mean arterial pressure (MAP) in screening for pregnancy complications.*

Methods *Maternal characteristics and medical history were recorded, and MAP was measured, in women with a singleton pregnancy attending for three routine hospital visits at 11 + 0 to 13 + 6 weeks, 19 + 0 to 24 + 6 weeks and 30 + 0 to 34 + 6 weeks or 35 + 0 to 37 + 6 weeks' gestation. For pregnancies delivering phenotypically normal live births or stillbirths at ≥ 24 weeks' gestation, variables from maternal demographic characteristics and medical history that are important in the prediction of MAP were determined from linear mixed-effects multiple regression analysis.*

Results *MAP was measured in 75 841 cases in the first trimester, 30 447 in the second trimester and 31 673 in the third trimester. Significant independent contributions to MAP were provided by gestational age, maternal age, weight, height, Afro-Caribbean racial origin, cigarette smoking, family history of pre-eclampsia (PE), history of PE in the previous pregnancy, interpregnancy interval, chronic hypertension and diabetes mellitus. The effects of some variables were similar, and for others differed, in the three different trimesters. Random-effects multiple regression analysis was used to define the contribution of maternal variables that influence the measured MAP and express the values as multiples of the median (MoMs). The model was shown to provide an adequate fit of MoM values for all covariates, both in pregnancies that developed PE and in those without this complication.*

Conclusions *A model was fitted to express the measured MAP as MoMs after adjustment for variables from maternal characteristics and medical history that affect this measurement.*

INTRODUCTION

Pre-eclampsia (PE) is a major cause of maternal and perinatal morbidity and mortality, affecting 2–3% of all pregnancies[1–3]. Over the last decade, extensive research has been devoted to screening for PE with the aims of firstly, reducing the prevalence of the disease through pharmacological intervention in those at high risk[4,5] and secondly, minimizing adverse perinatal events for those who develop PE by determining the appropriate time and place for delivery[6]. Our approach to risk assessment and screening for PE 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 recorded at different times during pregnancy[7–9]. However, in the application of Bayes' theorem in combined screening for PE, it is essential to standardize the measured values of biomarkers for any variables included in the prior model.

A useful biophysical marker in screening for PE is mean arterial pressure (MAP)[8–10]. However, MAP is dependent on other characteristics, most importantly maternal weight and chronic hypertension, and for its effective use in risk assessment and screening, these covariates need to be taken into account. This can be achieved by standardizing MAP levels into multiples of the normal median (MoM) values.

The objectives of this study were first, to quantify the effects of maternal weight, chronic hypertension and other covariates from maternal characteristics and medical history on MAP levels; second, to present a model for standardizing MAP measurements into MoM values; and third, to summarize the distribution of MoM values in pregnancies with normal outcomes and in those that subsequently develop PE. The main focus of this paper is on pregnancies with normal outcome. Further details of the distribution of MoM values in pregnancies with PE and the use of MAP in risk assessment will be presented in a separate paper.

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METHODS

Study population

The data for this study were derived from prospective screening for adverse obstetric outcomes in women attending for three routine hospital visits at King's College Hospital, University College London Hospital, and Medway Maritime Hospital, UK, between January 2006 and March 2014. In the first visit, at 11 + 0 to 13 + 6 weeks' gestation, maternal characteristics and medical history were recorded and combined screening for aneuploidies was performed[11]. The second visit, at 19 + 0 to 24 + 6 weeks, and third visit, initially at 30 + 0 to 34 + 6 weeks and subsequently at 35 + 0 to 37 + 6 weeks, included an ultrasound examination of the fetal anatomy and estimation of fetal size from the measurement of fetal head circumference, abdominal circumference and femur length. Gestational age was determined by measurement of the fetal crown–rump length (CRL) at 11–13 weeks or the fetal head circumference at 19–24 weeks[12,13].

Written informed consent was obtained from the women agreeing to participate in this study on adverse pregnancy outcome, which was approved by the ethics committee of each participating hospital. The inclusion criteria were a singleton pregnancy delivering a phenotypically normal live birth or stillbirth at or after 24 weeks' gestation. We excluded pregnancies with aneuploidies or major fetal abnormalities and those ending in termination, miscarriage or fetal death before 24 weeks.

Patient characteristics

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

Mean arterial pressure

MAP was measured at each visit. Validated automated devices (3BTO-A2, Microlife, Taipei, Taiwan) were used, which were calibrated before, and at regular intervals during, the study. The recordings were made by doctors who had received appropriate training in the use of these machines. During the procedure the women were in the sitting position, with their arms supported at the level of their heart, and a small (22-cm), normal (22–32-cm) or large (33–42-cm) adult cuff was used depending on the mid-arm circumference. After resting for 5 min, two recordings of blood pressure were made in both arms simultaneously and the final MAP was calculated as the average of all four measurements[10].

Outcome measures

Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women. The obstetric records of all women with pre-existing or pregnancy-associated hypertension were examined to determine if the condition was chronic hypertension, PE or non-proteinuric gestational hypertension (GH).

The definitions of GH and PE were those of the International Society for the Study of Hypertension in Pregnancy[14]. GH was defined as systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg on at least two occasions, 4 h apart, developing after 20 weeks' gestation in a previously normotensive woman. PE was defined as GH with proteinuria of 300 mg or more in 24 h or two readings of at least ++ on dipstick analysis of midstream or catheter urine specimens if no 24-h collection was available. PE superimposed on chronic hypertension was defined as significant proteinuria (as defined above) developing after 20 weeks' gestation in women with known chronic hypertension (history of hypertension before conception or the presence of hypertension at the booking visit before 20 weeks' gestation in the absence of trophoblastic disease). The birth-weight *Z*-score for the neonate in the last pregnancy was derived from our reference range of birth weights for gestational age at delivery[15].

Statistical analysis

The effects of the following variables from maternal characteristics and medical history on MAP were examined: maternal age, weight, height and racial origin, history of chronic hypertension, diabetes mellitus Type 1 or 2, SLE or APS, parity, previous pregnancy with PE, gestational age at delivery and birth-weight *Z*-score of the neonate in the last pregnancy and the interpregnancy interval, method of conception, smoking during pregnancy and gestational age at the time of assessment[7].

As part of an exploratory analysis, multiple linear regression models were fitted to $\log_{10}$MAP within each trimester. 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 error SD and a criterion of 0.1 SD was used to identify terms that had

little substantive impact in model predictions. Residual analysis was used to assess the adequacy of the model.

Graphical displays of the relationship between gestational age and MAP levels and the effects of maternal age, weight, height and other characteristics on MAP MoM values were produced for the final model. Having identified potential models for each trimester, a parsimonious model was selected to cover the data for the three trimesters combined. This model was fitted using a linear mixed model with random effects to represent the between-women random effects. 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 statistical software package R (R Foundation for Statistical Computing, Vienna, Austria) was used for data analysis[16].

RESULTS

Characteristics of the study population

The maternal characteristics and medical history of the pregnancies that fulfilled the entry criteria are presented in Table 1. MAP was measured in 75 841 cases in the first trimester, 30 447 cases in the second trimester and 31 673 cases in the third trimester. In the first phase of the study, MAP was measured only at the first-trimester visit but this was subsequently extended to the second- and then the third-trimester visits. There were 19 253 MAP measurements in all three trimesters, 6269 measurements in the first and second trimesters, 6680 in the first and third trimesters, 2704 in the second and third trimesters, 43 639 in the first trimester only, 2221 in the second trimester only and 3036 in the third trimester only.

Variables affecting MAP

The variables with substantial effect on MAP were gestational age, maternal age, weight, height and racial origin, history of chronic hypertension, diabetes mellitus with a similar effect for Type 1 and Type 2 disease, a previous pregnancy with or without PE and smoking during pregnancy.

The effects of gestational age on median levels of MAP were different in the three trimesters (Figure 1). A smooth relationship across the three trimesters would have been more satisfactory from a theoretical perspective. However, the empirical data provided little support for

Table 1 Maternal and pregnancy characteristics of women with singleton pregnancy attending for routine visits between January 2006 and March 2014, according to trimester of pregnancy

Variable	*11 + 0 to 13 + 6 weeks* (n = *75 841*)	*19 + 0 to 24 + 6 weeks* (n = *30 447*)	*30 + 0 to 37 + 6 weeks* (n = *31 673*)
Maternal age (years)	31.4 (27.0–35.1)	31.0 (26.3–34.8)	31.2 (26.7–35.0)
Maternal weight (kg)	66.0 (58.9–76.0)	71.0 (63.2–82.0)	76.0 (68.0–86.2)
Maternal height (cm)	164 (160–169)	164.4 (160.0–168.9)	164.6 (160.0–169.0)
GA at examination (weeks)	12.7 (12.3–13.1)	22.1 (21.4–22.6)	32.4 (32.0–33.2)
Racial origin			
Caucasian	54 948 (72.5)	20 261 (66.5)	22 098 (69.8)
Afro-Caribbean	12 626 (16.6)	7327 (24.1)	6055 (19.1)
South Asian	4232 (5.6)	1348 (4.4)	1769 (5.6)
East Asian	2133 (2.8)	680 (2.2)	959 (3.0)
Mixed	1902 (2.5)	831 (2.7)	792 (2.5)
Medical history			
Chronic hypertension	994 (1.3)	477 (1.6)	396 (1.3)
Diabetes mellitus	622 (0.8)	289 (0.9)	305 (1.0)
SLE/APS	142 (0.2)	48 (0.2)	57 (0.2)
Cigarette smoker	6890 (9.1)	3027 (9.9)	2931 (9.3)
Family history of PE	2922 (3.9)	1090 (3.6)	925 (2.9)
Obstetric history			
Nulliparous	37 648 (49.6)	14 668 (48.2)	15 715 (49.6)
Parous with no previous PE	35 761 (47.2)	14 751 (48.4)	15 055 (47.5)
Parous with previous PE	2432 (3.2)	1028 (3.4)	903 (2.9)
Interpregnancy interval (years)	2.9 (1.9–4.8)	3.1 (2.0–5.1)	3.0 (2.0–4.9)
GA at delivery of previous pregnancy (weeks)	40 (39–40)	40 (39–40)	40 (39–40)
Birth weight of previous pregnancy (g)	3400 (3072–3726)	3384 (3055–3710)	3385 (3060–3710)
Mode of conception			
Spontaneous	72 984 (96.2)	29 476 (96.8)	30 522 (96.4)
Ovulation induction	977 (1.3)	343 (1.1)	327 (1.0)
In-vitro fertilization	1880 (2.5)	628 (2.1)	824 (2.6)
Pregnancy outcome			
PE	1805 (2.4)	853 (2.8)	669 (2.1)
No PE	74 036 (97.6)	29 594 (97.2)	31 004 (97.9)

Data are given as median (interquartile range) or *n* (%). APS, antiphospholipid syndrome; GA, gestational age; PE, pre-eclampsia; SLE, systemic lupus erythematosus.

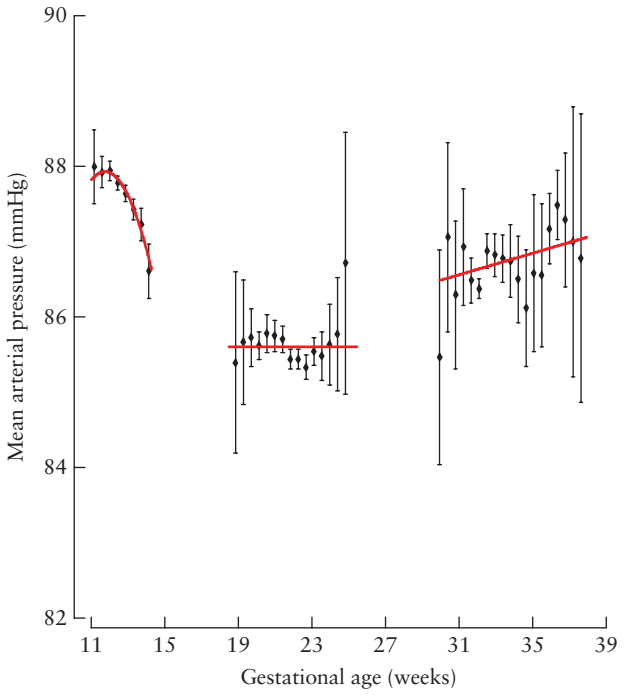

Figure 1 Relationship between median (95% CI) levels of mean arterial pressure and gestational age across three trimesters of pregnancy in a large cohort of pregnant women.

such a relationship and, consequently, trimester-specific effects were fitted for the final model.

The distribution of MAP values by maternal-weight quartile and history of chronic hypertension in pregnancies unaffected by PE or GH and those that developed PE is shown in Figure 2. Within any group defined by maternal weight and chronic hypertension, MAP was higher in women who developed PE. However, this increase was somewhat smaller than the increase due to chronic hypertension or to a change in weight from the first to the fourth quartile. This illustrates the need to adjust for weight and chronic hypertension when using MAP in risk assessment and screening.

Multiple regression analysis was performed to identify significant independent contributions to the prediction of $\log_{10}$MAP within each gestational age range of $11+0$ to $13+6$ weeks, $19+0$ to $24+6$ weeks and $30+0$ to $37+6$ weeks. Within each group there were significant contributions from most variables.

Family history of PE, PE in the previous pregnancy, history of chronic hypertension, diabetes mellitus and smoking were substantive contributors to MAP levels in all three trimesters, and their effect was similar across the three trimesters (Figure 3). Similarly, the relationships between maternal weight, height and interpregnancy interval and MAP showed no substantive differences across the three trimesters (Figure 4). For the sake of simplicity in the final model, we have assumed the effects of these variables to be independent of gestational age.

Afro-Caribbean racial origin showed a substantive effect on MAP that increased in magnitude with progression of the gestation, and this effect was modeled by a linear relationship on the log scale with gestation (Figure 3). There were no significant effects from South Asian and East Asian racial groups. Maternal age was a substantive contributor to MAP in the first but not in the second and third trimesters (Figure 4).

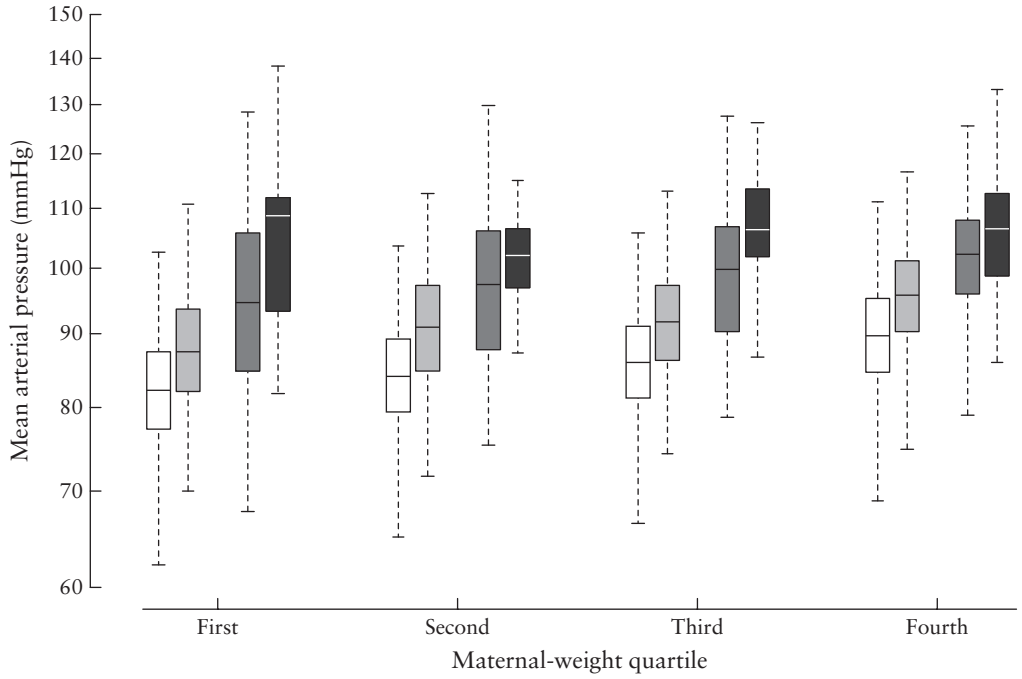

Figure 2 Distribution of mean arterial pressure according to maternal-weight quartile and history of chronic hypertension in pregnancies that developed pre-eclampsia (PE) and in those unaffected by PE: pregnancies without chronic hypertension that did not develop PE (□); pregnancies without chronic hypertension that did develop PE (▫); pregnancies with chronic hypertension that did not develop PE (■); pregnancies with chronic hypertension that did develop PE (■). Boxes and whiskers show median, interquartile range and range.

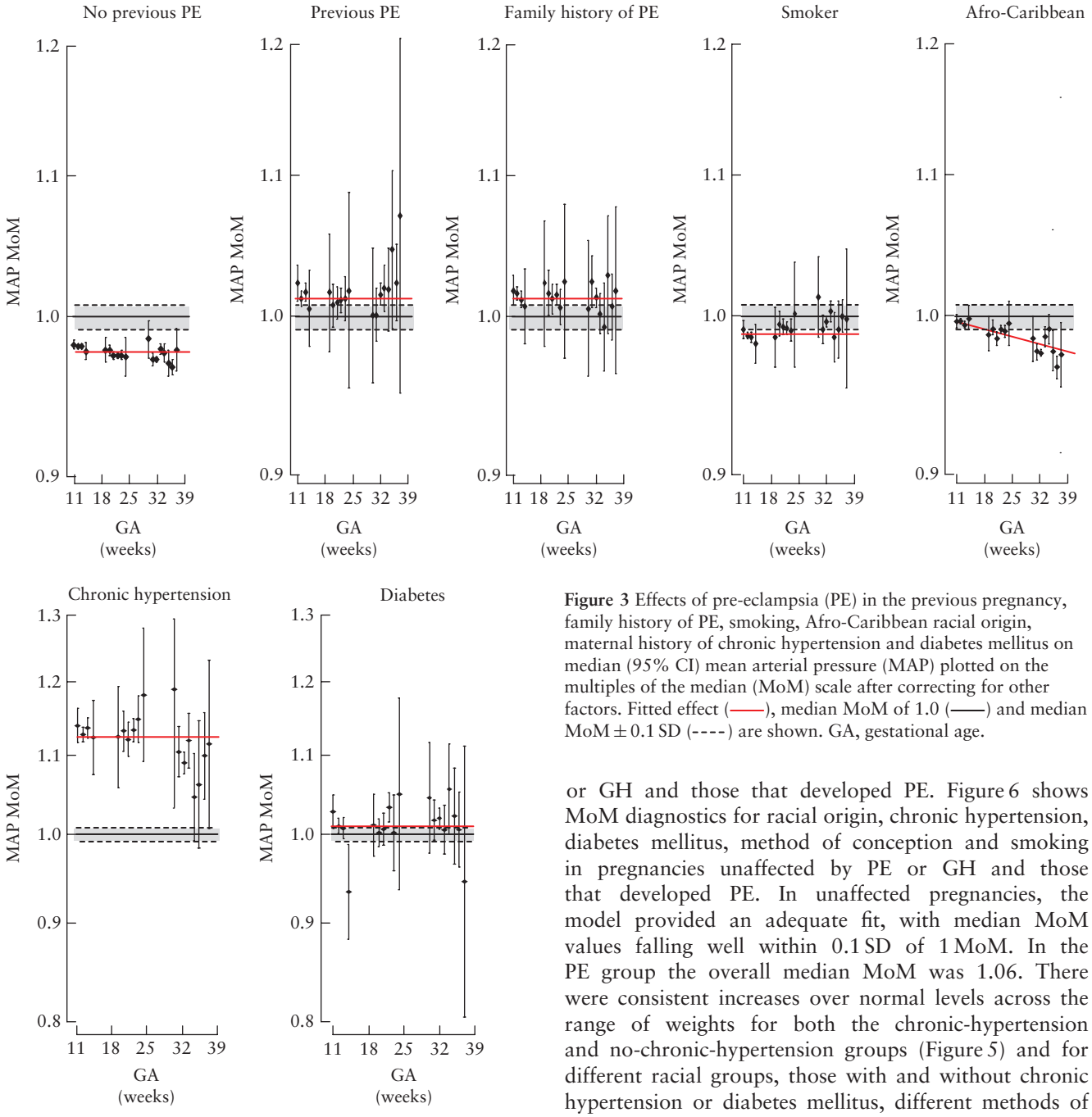

Figure 3 Effects of pre-eclampsia (PE) in the previous pregnancy, family history of PE, smoking, Afro-Caribbean racial origin, maternal history of chronic hypertension and diabetes mellitus on median (95% CI) mean arterial pressure (MAP) plotted on the multiples of the median (MoM) scale after correcting for other factors. Fitted effect (——), median MoM of 1.0 (——) and median MoM ± 0.1 SD (----) are shown. GA, gestational age.

Final model for calculation of MAP MoM

A linear mixed model, with random effects to represent between-women random effects, was fitted to the subset of variables that contributed substantively to the linear regression models (Table 2). Trimester effects were included, the first trimester being used as the reference. For relationships that were assumed to be constant, such as family history of PE and maternal weight, common effects were fitted. For relationships assumed not to be constant across the three trimesters, such as gestational age, trimester-specific effects were fitted.

Figure 5 shows MoM diagnostics for the two most important covariates, maternal weight and history of chronic hypertension, in pregnancies unaffected by PE or GH and those that developed PE. Figure 6 shows MoM diagnostics for racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies unaffected by PE or GH and those that developed PE. In unaffected pregnancies, the model provided an adequate fit, with median MoM values falling well within 0.1 SD of 1 MoM. In the PE group the overall median MoM was 1.06. There were consistent increases over normal levels across the range of weights for both the chronic-hypertension and no-chronic-hypertension groups (Figure 5) and for different racial groups, those with and without chronic hypertension or diabetes mellitus, different methods of conception and smoking or non-smoking (Figure 6).

Distributional properties of MAP MoM values

Figure 7 shows a Gaussian distribution of MAP-MoM values. The median and 5th, 10th, 90th and 95th percentiles were 1.00000 (95% CI, 0.99942–1.00054), 0.87635 (95% CI, 0.87557–0.87709), 0.90179 (95% CI, 0.90114–0.90246), 1.11182 (95% CI, 1.11093–1.11268) and 1.14691 (95% CI, 1.14572–1.14812), respectively. Estimated SDs and correlations, with 95% CIs, are given in Tables 3 and 4, respectively. The SDs were very similar but decreased slightly with trimester. The correlations between $\log_{10}$MAP MoM across trimesters were slightly stronger for the first and second trimesters, and second and third trimesters, than for the first and third trimesters.

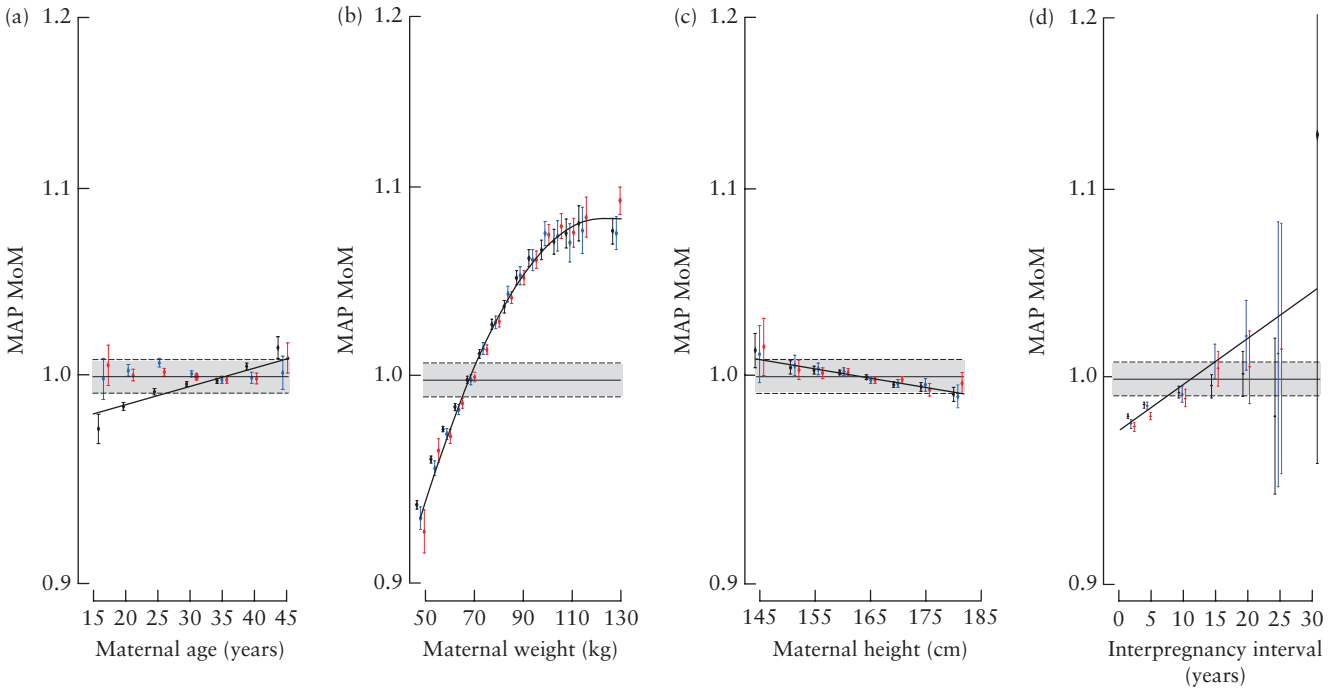

Figure 4 Effects of maternal age (a), weight (b) and height (c) and interpregnancy interval (d) in parous women without previous pre-eclampsia (with 95% CIs) on mean arterial pressure (MAP) at 11 + 0 to 13 + 6 weeks' gestation (black), 19 + 0 to 24 + 6 weeks (blue) and 30 + 0 to 37 + 6 weeks (red). These effects are shown on the multiples of the median (MoM) scale after correcting for other factors. Median MoM of 1.0 (——) and median MoM ± 0.1 SD (----) are shown.

DISCUSSION

Main findings of the study

The findings of this study demonstrate that, in pregnancy, significant independent contributions to the measured MAP are provided by maternal characteristics and variables from medical history. MAP increases with maternal weight, age and interpregnancy interval, and decreases with height; it is higher in women with a personal or family history of PE and in those with chronic hypertension or diabetes mellitus and is lower in parous women with no previous PE, in smokers and in women of Afro-Caribbean racial origin. The effects of maternal weight and height, family history of PE, PE in the previous pregnancy, history of chronic hypertension and diabetes mellitus are similar across the three trimesters. The effect of Afro-Caribbean racial origin increases with increasing gestational age. Maternal age is a substantive contributor to MAP in the first but not in the second and third trimesters.

Random-effects multiple regression analysis was used to define the contribution of maternal variables that influence the measured MAP 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 developed PE and in those without this complication.

Strengths and limitations of the study

The strengths of this study are first, prospective examination of a large population of pregnant women attending

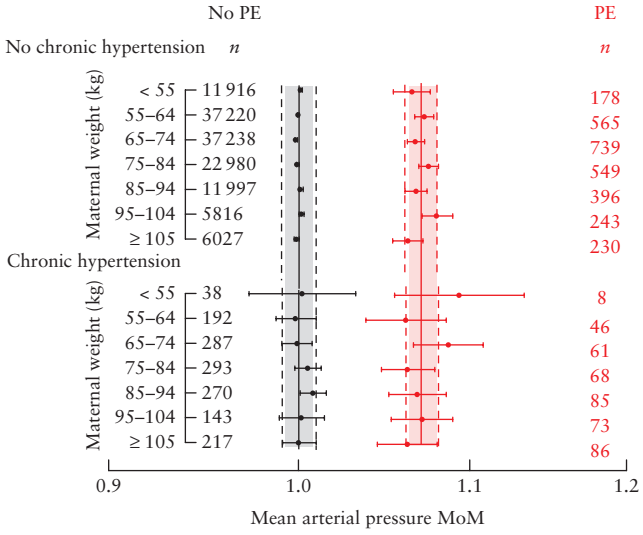

Figure 5 Median mean arterial pressure multiples of the median (MoM) with 95% CIs derived from the model, according to maternal weight in women with and those without chronic hypertension, in pregnancies that developed pre-eclampsia (PE) and in those unaffected by PE. Median MoM of 1.0 (——) and median MoM ± 0.1 SD (----) of women unaffected by PE and median MoM of 1.06 in women with PE (——) are indicated.

for routine care in three well-defined gestational-age ranges that are widely used for first-trimester screening for chromosomal defects and second- and third-trimester assessment of fetal anatomy, growth and wellbeing; second, use of a validated methodology and automated devices by trained doctors to measure MAP; and third, application of multiple regression analysis to define the

Table 2 Final model for calculating multiples of the median values for mean arterial pressure taken during first, second and third trimesters in women with a singleton pregnancy attending for routine hospital visits

Term	*Estimate*	*95% CI*	*SE*	P
Intercept	1.943223919	1.941470582 to 1.944977257	0.000894560	< 0.0001
Trimester-dependent effects				
First trimester				
Gestational age (−77)*	0.000209037	−0.000075512 to 0.000493585	0.000145178	0.0749
(Gestational age (−77))^{2*}	−0.000020452	−0.000031880 to −0.000009023	0.000005831	0.0002
Age (−35)†	0.000439271	0.000395501 to 0.000483040	0.000022331	< 0.0001
Second trimester				
Constant	−0.011200472	−0.012941379 to −0.009459566	0.000888218	< 0.0001
Third trimester				
Constant	−0.014046569	−0.020426847 to −0.007666291	0.003255244	< 0.0001
Gestational age (−77)*	0.000054294		0.000020516	0.0041
Trimester-independent effects				
Weight				
Weight (−69)‡	0.001193313	0.001172064 to 0.001214561	0.000010841	< 0.0001
(Weight (−69))^{2‡}	−0.000008823	−0.000009377 to −0.000008269	0.000000283	< 0.0001
Height				
Height (−164)§	−0.000206306	−0.000242022 to −0.000170589	0.000018223	< 0.0001
Smoker	−0.004523672	−0.005299863 to −0.003747480	0.000396016	< 0.0001
Racial origin				
Afro-Caribbean	−0.001191227	−0.001919370 to −0.000463084	0.000371501	0.0007
Afro-Caribbean: gestational age (−77)*	−0.000050679	−0.000058070 to −0.000043287	0.000003771	< 0.0001
Medical history				
Chronic hypertension	0.051007216	0.048537789 to 0.053476643	0.001259912	< 0.0001
Chronic hypertension: weight (−69)‡	−0.000421118	−0.000517235 to −0.000325000	0.000049040	< 0.0001
Diabetes mellitus	0.004445020	0.002036639 to 0.006853401	0.001228766	0.0001
Family history of PE	0.005976240	0.004792272 to 0.007160208	0.000604065	< 0.0001
Obstetric history				
Parous with no previous PE: intercept	−0.009402127	−0.010004956 to −0.008799299	0.000307566	< 0.0001
Parous with no previous PE: interpregnancy interval in years	0.000744526	0.000641731 to 0.000847321	0.000052446	< 0.0001
Parous with previous PE	0.006091903	0.004783203 to 0.007400604	0.000667704	< 0.0001

Continuous variables were centered by subtracting the mean from each measured value: *77 from gestational age in days; †35 from maternal age in years; ‡69 from maternal weight in kg; §164 from maternal height in cm. PE, pre-eclampsia; SE, standard error.

contributions and interrelationships of maternal variables that influence measured MAP across the three trimesters of pregnancy.

An alternative to the use of data from three gestational-age ranges would have been a cross-sectional study with inclusion of each gestational week from the beginning to the end of pregnancy. Such an approach could have overcome the observed discontinuity in the relationships of MAP with gestational age and maternal age across the three trimesters, which necessitated the fitting of trimester-specific effects in the model. A plausible explanation for the observed discontinuity is the effect of errors in the estimation of gestational age and range restriction close to the lower and upper ends of the allowed measurement ranges. In particular, in the first trimester, gestational age is derived from fetal CRL, and the lower and upper allowed measurements of 45 mm and 84 mm correspond to 11 + 0 and 13 + 6 weeks' gestation. In reality, any given true gestational age is likely to have a distribution of CRL measurements that are truncated at the prespecified cut-offs of 45 mm and 84 mm. The combination of errors in variables and range restriction will distort the underlying relationship[17].

Comparison with findings of previous studies

Extensive studies in screening for trisomies have established that the measured concentrations of serum metabolites should be expressed as MoMs after adjustment for the maternal characteristics that affect the measurements in euploid pregnancies[17,18]. The same rationale should apply to the use of biophysical markers in screening for pregnancy complications. In previous smaller studies examining the potential value of MAP in screening for PE in the first, second or third trimesters, we used multiple regression analysis to express the measured MAP as MoMs after adjustment for variables affecting this measurement in pregnancies unaffected by PE or GH[8,19,20]. In this expanded series of pregnancies in all three trimesters, we developed a model that incorporates variables with common effects across the trimesters and those with trimester-specific effects.

Implications for clinical practice

The effective use of MAP in risk assessment and screening necessitates that variables from maternal characteristics

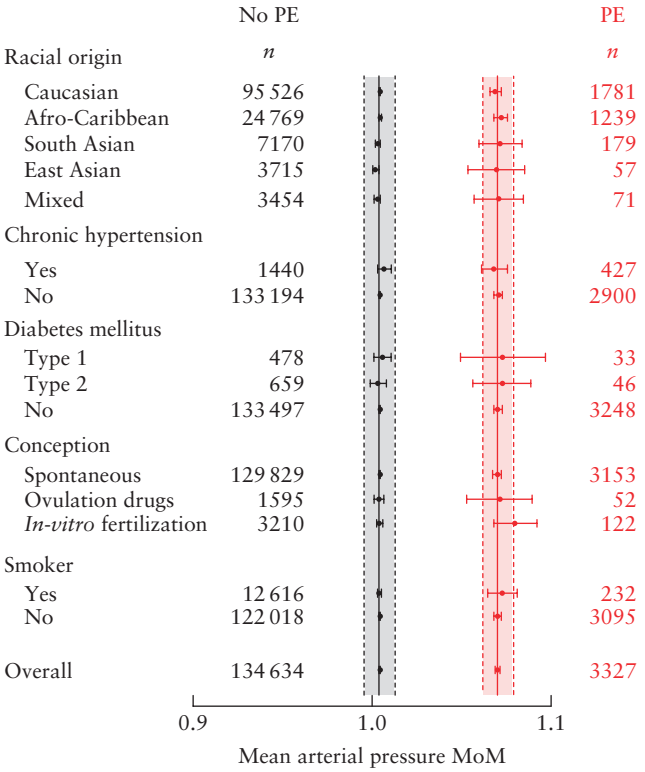

Figure 6 Median mean arterial pressure multiples of the median (MoM) with 95% CIs derived from the model, according to racial origin, chronic hypertension, diabetes mellitus, method of conception and smoking in pregnancies that developed pre-eclampsia (PE) and in those unaffected by PE. Median MoM of 1.0 (——) and median MoM ± 0.1 SD (----) of women unaffected by PE and median MoM of 1.06 in women with PE (——) are indicated.

Table 3 Standard deviations for $\log_{10}$mean arterial pressure multiples of the median values according to trimester of pregnancy

Trimester	*SD Estimate (95% CI)*
First	0.03720 (0.03705–0.03735)
Second	0.03647 (0.03633–0.03662)
Third	0.03493 (0.03480–0.03507)

and medical history that affect this measurement in normal pregnancy should be taken into account. To emphasize the need for standardizing into MoM values, consider a pregnancy at 12 weeks' gestation in a 35-year-old nulliparous Caucasian woman with a height of 164 cm without chronic hypertension. If the MAP is 100 mmHg and the maternal weight is 50 kg, the measurement is translated into a MoM value of 1.16, which is above the 95th percentile for normal pregnancies. For a woman with a weight of 120 kg, the same MAP corresponds to a MoM value of 1.00, which is on the 50th percentile for normal pregnancies. Consequently, for the same MAP, the risk for PE may be increased if the maternal weight is low or decreased if the weight is high.

In screening for PE by MAP in isolation, MAP would act as a proxy for other risk factors, including maternal weight and chronic hypertension, and in

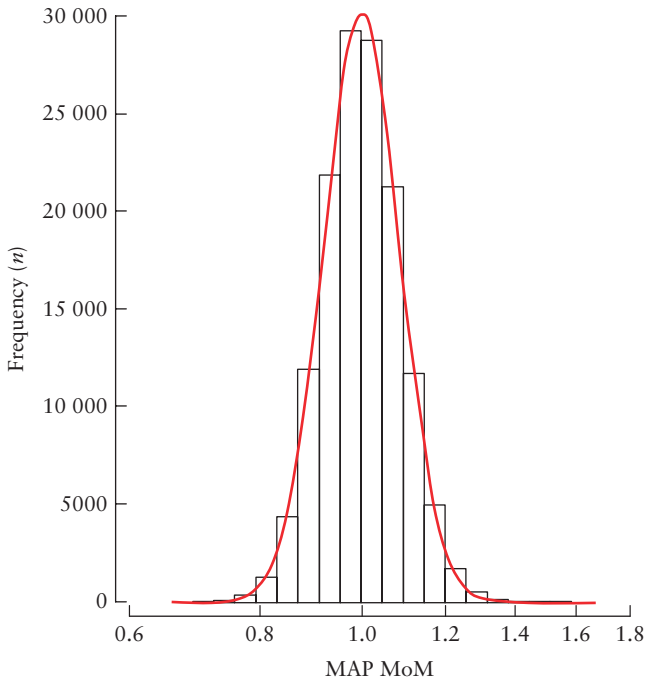

Figure 7 Gaussian distribution of mean arterial pressure (MAP) multiples of the median (MoM) values in a large cohort of pregnant women.

Table 4 Correlation of $\log_{10}$mean arterial pressure multiples of the median (MoM) values between the three trimesters of pregnancy

Trimester	*Second trimester*	*Third trimester*
First	0.42155 (0.40971–0.43324)	0.39143 (0.37925–0.40348)
Second	1	0.39227 (0.38009–0.40431)
Third	—	1

Values in parentheses are 95% CI.

such cases correction for these factors might well be counterproductive. However, our approach to risk assessment and screening is to use Bayes' theorem to combine information on maternal characteristics with that obtained from biomarkers. This involves a prior model incorporating the effect of maternal characteristics[7]. In this approach, the contribution of biomarkers such as MAP is the additional information they provide over that already captured in the prior model. To achieve this, the distribution of MAP should be specified conditionally on the variables included in the prior distribution, such as maternal weight and chronic hypertension, otherwise the contribution of these variables to risk assessment is overestimated.

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