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ORIGINAL RESEARCH

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Associations of Maternal and Paternal Blood Pressure Patterns and Hypertensive Disorders during Pregnancy with Childhood Blood Pressure

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***Background*—**Hypertensive disorders in pregnancy may affect the cardiovascular risk of offspring. We examined the associations of maternal blood pressure throughout pregnancy and hypertensive disorders in pregnancy with childhood blood pressure of offspring. Specific focus was on the comparison with paternal blood pressure effects, the identification of critical periods, and the role of birth outcomes and childhood body mass index in the observed associations.

***Methods and Results*—**This study was embedded in a population-based prospective cohort study among 5310 mothers and fathers and their children. We measured maternal blood pressure in each trimester of pregnancy and paternal blood pressure once. Information about hypertensive disorders in pregnancy was obtained from medical records. We measured childhood blood pressure at the median age of 6.0 years (95% range 5.7–8.0 years). Both maternal and paternal blood pressure were positively associated with childhood blood pressure (all $P<0.05$), with similar effect estimates. Conditional regression analyses showed that early, mid-, and late-pregnancy maternal blood pressure levels were all independent and positively associated with childhood blood pressure, with the strongest effect estimates for early pregnancy. Compared with children of mothers without hypertensive disorders in pregnancy, children of mothers with hypertensive disorders in pregnancy had higher diastolic blood pressure by a standard deviation score of 0.13 (95% CI 0.05–0.21). The observed associations were not materially affected by birth outcomes and childhood body mass index.

***Conclusions*—**Both maternal and paternal blood pressure affects childhood blood pressure, independent of fetal and childhood growth measures, with the strongest effect of maternal blood pressure in early pregnancy. **(*J Am Heart Assoc*. 2016;5:e003884 doi: 10.1161/JAHA.116.003884)**

Key Words: blood pressure • gestational hypertension • pediatrics • preeclampsia • pregnancy

Gestational hypertension and preeclampsia affect up to 8% of all pregnant women worldwide and are associated with both maternal and offspring cardiovascular health and disease.[1–4] It has been suggested that these associations are explained by maternal vasculotoxic factors in pregnancies with hypertensive disorders which affect vascular development.[5,6] Moreover, early placental and fetal microvasculature maladaptations may lead to higher blood pressure in both pregnant women and their offspring.[7] In addition to hypertensive disorders in pregnancy, higher blood pressure within the normal range during pregnancy may be associated with higher offspring blood pressure.[8–12] It is not known if the associations of maternal blood pressure with offspring blood pressure are explained by direct maternal or intrauterine mechanisms or rather reflect shared family-based lifestyle-related or genetic factors. Comparing maternal and paternal blood pressure effects may help disentangle the direct maternal or intrauterine mechanisms.[13] It is also unknown which period of pregnancy is most critical for the effects of maternal blood pressure on the offspring's blood pressure. Finally, the associations of hypertensive disorders in pregnancy with childhood blood pressure may be explained in part by lower offspring birth weight and higher body mass index (BMI).[8]

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Accompanying Data S1, Tables S1 through S4 and Figures S1, S2 are available at http://jaha.ahajournals.org/content/5/10/e003884/DC1/embed/inline-supplementary-material-1.pdf

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In a population-based prospective cohort study from early pregnancy onward among 5310 mothers, fathers, and children, we examined the associations of maternal blood pressure in different periods of pregnancy and hypertensive disorders in pregnancy with blood pressure in school-aged children. The specific focus was on the comparison with paternal blood pressure effects, the identification of critical periods, and the role of birth outcomes and childhood BMI in the observed associations.

Methods

Design and Study Population

This study was embedded in the Generation R Study, a population-based prospective cohort study from early pregnancy onward in Rotterdam, the Netherlands.[14,15] The study was approved by the local medical ethics committee. Written informed consent was obtained from the parents. All pregnant women were enrolled between 2001 and 2005. Of all eligible children in the study area, 61% participated at birth in the study. In total, 8713 initially normotensive mothers had available information about blood pressure measurements, and of those, 8475 gave birth to single live-born children. In total, 5810 (69%) of these children participated in detailed follow-up studies at the age of 6 years. We excluded children with missing blood pressure measurements (n=477) or with congenital cardiac abnormalities (n=23), leading to a population for analysis of 5310 mothers and their children (Figure S1).

Maternal and Paternal Blood Pressure

We measured maternal and paternal blood pressure using the Omron 907 automated digital oscillometric sphygmomanometer (OMRON Healthcare Europe).[16] As described previously, all participants were seated in an upright position with back support and were asked to relax for 5 minutes.[17] A cuff was placed around the nondominant upper arm, which was supported at the level of the heart, with the bladder midline over the brachial artery pulsation. For participants with an upper arm circumference >33 cm, a larger cuff (32–42 cm) was used. We used the mean value of 2 blood pressure readings over a 60-second interval. Blood pressure was measured in 4098 mothers in early pregnancy (median gestational age 13.4 weeks, 95% range 9.8–17.5 weeks), 5006 mothers in midpregnancy (median gestational age 20.5 weeks, 95% range 18.5–23.5 weeks), and 5104 mothers in late pregnancy (median gestational age 30.2 weeks, 95% range 28.5–32.9 weeks). Overall, 3842 mothers had 3 blood pressure measurements available, 1214 mothers had 2 available measurements, and 254 mothers had 1 available measurement. Of the population for analysis, blood pressure was measured during midpregnancy in 3805 fathers.

Hypertensive Disorders in Pregnancy

Information on hypertensive disorders in pregnancy, including gestational hypertension and preeclampsia, was obtained through medical records.[18] Mothers suspected of any hypertensive disorder in pregnancy based on the records were cross-checked with original charts by a trained medical record abstractor.[18] The following criteria were used to identify women with gestational hypertension: development of systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg after 20 weeks of gestation in previously normotensive women. These criteria and the presence of proteinuria (defined as ≥2 dipstick readings of ≥2, 1 catheter sample reading of ≥1, or 24-hour urine collection containing at least 300 mg of protein) were used to identify women with preeclampsia.[19]

Childhood Blood Pressure

Childhood blood pressure was measured at the right brachial artery 4 times with 1-minute intervals using the validated automatic Datascope Accutorr Plus sphygmomanometer (Paramus, NJ, USA).[20] A cuff was selected with a cuff width ≈40% of the arm circumference and long enough to cover 90% of the arm circumference.[20] We used the mean SBP and DBP values based on the last 3 blood pressure readings. Using normative values from the "Fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents" from the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents,[21,22] we calculated the standard deviation scores (SDSs) for individual SBP and DBP values. Subsequently, we used these individual SDSs to categorize children into blood pressure tertiles. Children whose average SBP and/or DBP based on 3 readings was ≥95th percentile for age, sex, and height were classified as hypertensive.

Covariates

We assessed maternal and paternal age at enrollment in the study. Information on maternal and paternal ethnicity and educational level, maternal parity, folic acid supplement use, smoking, and alcohol consumption was obtained by questionnaires.[14] At enrollment, we measured maternal and paternal height and weight without shoes and heavy clothing and calculated BMI. Information on infant sex, gestational age at birth, and birth weight was obtained from medical records. We measured child height and weight and calculated BMI at the age of 6 years.

Statistical Analysis

First, we performed a nonresponse analysis by comparing participant characteristics of children with and without follow-up blood pressure measurements by using *t* tests, chi-square tests, and Mann–Whitney tests. Second, we examined maternal longitudinal blood pressure patterns during pregnancy for mothers in tertiles of childhood blood pressure. For these analyses, we used mixed-effects regression models. These regression models enabled analyses of repeatedly measured outcomes, accounting for the correlation between repeated measurements within the same participant and allowing for incomplete outcome data.[23] Details of the mixed-effects regression models are given in Data S1. We also examined the associations of maternal blood pressure in different periods of pregnancy and paternal blood pressure with childhood blood pressure in 3 linear regression models: (1) a confounder model, which included covariates selected based on their associations with the outcome of interest based on previous studies or a change in effect estimate of >10%; (2) a birth model, which included gestational age and weight at birth in addition to the confounder model; and (3) a childhood model, which included the child's current BMI in addition to the confounder model. We used similar multiple regression models to examine the associations of hypertensive disorders in pregnancy with childhood blood pressure. Third, we used similar linear and logistic regression models to explore the combined effects of maternal blood pressure in early and late pregnancy and the combined effects of maternal blood pressure and paternal blood pressure on childhood blood pressure and risk of hypertension. For these analyses, we created tertiles of both maternal and paternal blood pressure. Fourth, we performed conditional regression analyses to identify the independent associations of maternal blood pressure measurements in early, mid-, and late pregnancy, taking into account their correlations with childhood blood pressure and risk of hypertension.[24] We constructed blood pressure values for each trimester that were statistically independent from blood pressure values for other trimesters by using standardized residuals obtained from regression of blood pressure values at a specific time point (dependent variable) on blood pressure values obtained at a previous time point.[24–26] This approach enabled identification of critical periods for maternal blood pressure during pregnancy that, independent of other periods during pregnancy, influenced childhood blood pressure. Details of these conditional regression models are given in Data S1. To reduce potential bias associated with missing data, missing values of covariates (maternal and paternal ethnicity, educational level, BMI, paternal age, maternal parity, folic acid supplement use, smoking and alcohol consumption, infant birth weight, and child BMI) were multiple imputed (n=5 imputations), according to the fully conditional specification method (predictive mean matching), assuming no monotone missing pattern. We reported the pooled effect estimates after the multiple imputation procedure.[27] Participant characteristics before and after imputation and the percentages of missing values are given in Table S1. The multiple imputation procedure and the statistical analyses were performed using SPSS version 21.0 (IBM Corp). The mixed effects regression analyses were performed with the SAS PROC MIXED module (version 9.3; SAS Institute Inc).

Results

Participant Characteristics

Table 1 shows the participant characteristics. In our cohort, 410 children (7.7%) were classified as hypertensive. Results from the nonresponse analysis showed that, compared with children with blood pressure follow-up measurements, those without these measurements had lower birth weight and gestational age. Mothers of children with blood pressure measurements were older and used less alcohol but smoked more frequently compared with mothers of children who were lost to follow-up. Moreover, maternal SBP throughout pregnancy was lower for the children without follow-up blood pressure measurements (Table S2).

Maternal and Paternal Blood Pressure and Childhood Blood Pressure

Figure 1 shows that children in the highest tertile of SBP had mothers with higher SBP throughout pregnancy than children in the lowest tertile of SBP. For each tertile of childhood blood pressure, maternal blood pressure increased with advanced gestational age. There was no significant difference in the slope of maternal SBP between tertiles of children's blood pressure. For all childhood DBP tertiles, maternal DBP had a midpregnancy dip with an increase thereafter. DBP was highest throughout pregnancy for mothers of children in the highest tertile. The exact corresponding regression coefficients for gestational age–independent (intercept) and gestational age–dependent differences (interaction of childhood blood pressure and gestational age) are given in Table S3. Additional analyses showed that higher maternal blood pressure in early, mid-, and late pregnancy and paternal blood pressure were all separately associated with higher childhood blood pressure (all $P<0.05$). The effect estimates for mother and father were similar and were not affected by birth outcomes or childhood BMI (Table S4).

Figure 2A shows the combined associations of maternal blood pressure during early and late pregnancy. Compared

Table 1. Participant Characteristics (n=5310)

Maternal characteristics	
Age, y	30.9 (19.7–39.3)
Height, cm	167.5 (7.5)
Weight, kg	69.3 (12.7)
BMI, kg/m^2	23.5 (3.8)
Parity, n (%)	
0	3008 (56.6)
≥1	2302 (43.4)
Educational level mother, n (%)	
Primary or secondary	2854 (53.7)
Higher	2456 (46.3)
Ethnicity, n (%)	
European	3167 (59.6)
Non-European	2143 (40.4)
Smoking during pregnancy, n (%)	
No	3792 (71.4)
Yes	1518 (28.6)
Alcohol using during pregnancy, n (%)	
No	2478 (46.7)
Yes	2832 (53.3)
Folic acid supplements during pregnancy, n (%)	
No	1695 (31.9)
Yes	3615 (68.1)
Blood pressure	
Early pregnancy	
Gestational age, weeks	13.4 (9.8–17.5)
SBP, mm Hg	115.5 (12.0)
DBP, mm Hg	68.1 (9.3)
Midpregnancy	
Gestational age, weeks	20.5 (18.5–23.5)
SBP, mm Hg	116.8 (11.9)
DBP, mm Hg	67.2 (9.3)
Late pregnancy	
Gestational age, weeks	30.2 (28.5–32.9)
SBP, mm Hg	118.4 (11.9)
DBP, mm Hg	69.1 (9.2)
Hypertensive disorders in pregnancy, n (%)	
Any	308 (5.8)
Gestational hypertension	215 (4.0)
Preeclampsia	93 (1.8)
Paternal characteristics	
Age, y	33.0 (21.7–45.2)
Height, cm	181.9 (7.7)
Weight, kg	83.7 (11.6)
BMI, kg/m^2	25.3 (3.2)
Ethnicity, n (%)	
European	3274 (61.7)
Non-European	2036 (38.3)
Educational level, n (%)	
Primary or secondary	2896 (54.5)
Higher	2414 (45.5)
SBP, mm Hg	130.2 (13.5)
DBP, mm Hg	73.4 (10.6)
Birth characteristics	
Female, n (%)	2656 (50.0)
Gestational age, weeks	40.1 (35.9–42.3)
Birth weight, g	3430 (548)
Childhood characteristics	
Age, y	6.0 (5.7–8.0)
Height, cm	119.5 (6.1)
Weight, kg	23.3 (4.3)
BMI, kg/m^2	16.2 (1.9)
SBP, mm Hg	102.7 (8.2)
DBP, mm Hg	60.7 (6.9)
Z score SBP*	0.53 (0.7)
Z score DBP*	0.34 (0.6)
Blood pressure ≥95th percentile, n (%)†	410 (7.7)

Values represent mean (SD), median (95% range), or number (%). BMI indicates body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

*Z scores of SBP and DBP were calculated using normative values from the "Fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents" from the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.[21,22]

†Blood pressure ≥95th percentile (SBP and/or DBP ≥95th percentile) for age, sex, and height on 3 measurements. Participant characteristics before and after imputation are shown in Table S1.

with children from mothers with blood pressure in the lowest tertiles during both early and late pregnancy, those with blood pressure in the highest tertiles during both early and late pregnancy had higher SBP and DBP by SDSs of 0.24 (95% CI 0.16–0.31) and 0.18 (95% CI 0.11–0.24), respectively. In addition, within each tertile of maternal early pregnancy blood pressure, maternal late pregnancy blood pressure was associated with higher childhood blood pressure, with the strongest effect estimates in early pregnancy. Figure 2B shows the combined associations of maternal early pregnancy and paternal blood pressure. Compared with children of mothers and fathers with blood pressure in the lowest tertiles, children of mothers and fathers with blood pressure in the highest tertiles had higher SBP and DBP by SDSs of 0.26 (95%

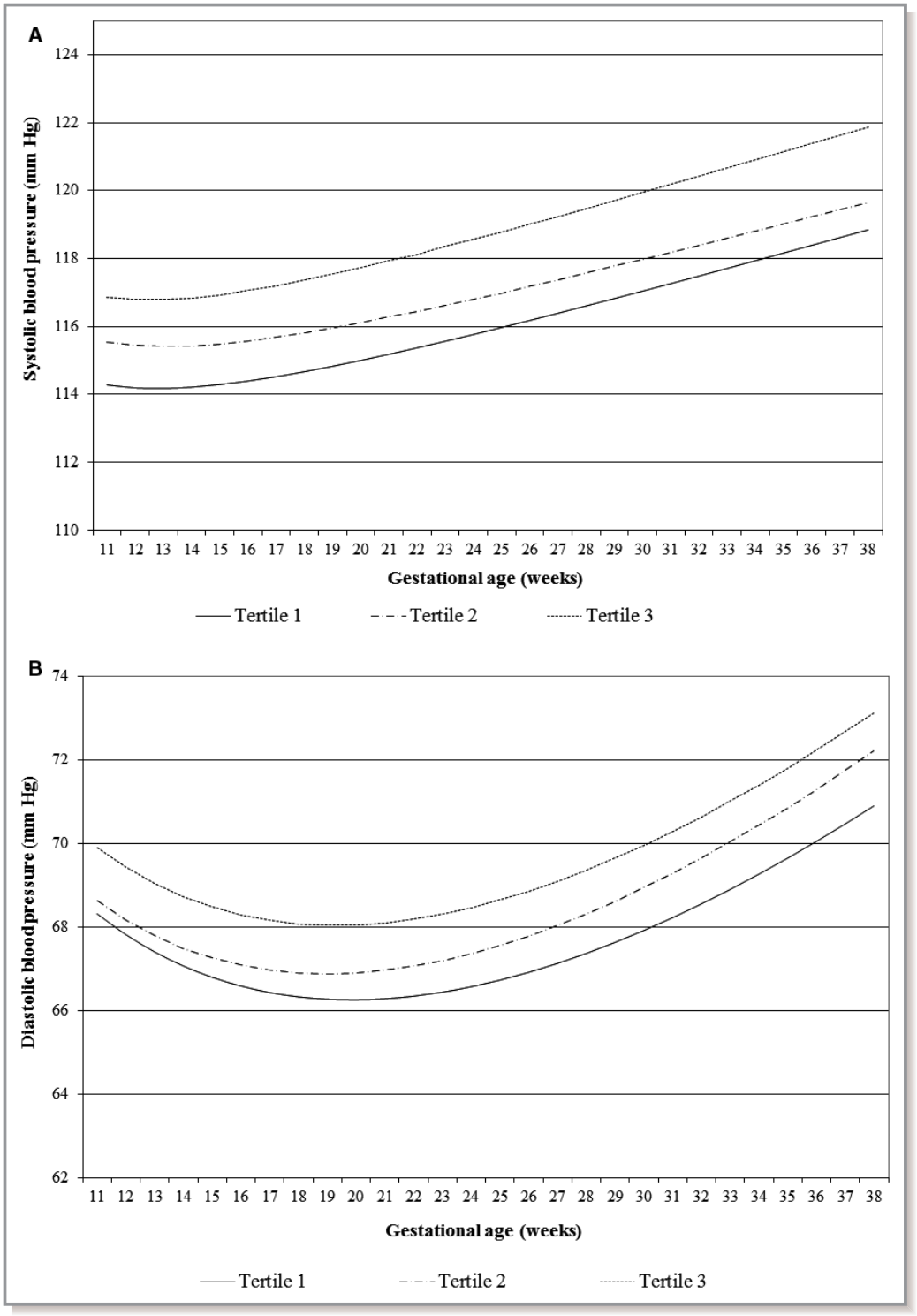

Figure 1. Maternal blood pressure patterns from children in different blood pressure tertiles (n=5310). Maternal blood pressure pattern per childhood blood pressure tertile. A, Systolic blood pressure. Difference in maternal systolic blood pressure (mm Hg) between childhood systolic blood pressure tertiles based on mixed-effects regression models. Model: Maternal systolic blood pressure=$\beta_0+\beta_1\times$child systolic blood pressure tertile$+\beta_2\times$gestational age$+\beta_3\times$gestational age$^{-2}+\beta_4\times$child systolic blood pressure tertile$\times$gestational age. B, Diastolic blood pressure. Difference in maternal diastolic blood pressure (mm Hg) for childhood diastolic blood pressure tertiles based on mixed effects regression analysis. Model: Maternal diastolic blood pressure=$\beta_0+\beta_1\times$child diastolic blood pressure tertile$+\beta_2\times$gestational age$+\beta_3\times$gestational age$^{0.5}+\beta_4\times-$child diastolic blood pressure tertile$\times$gestational age. Effect estimates (95% CIs) are given in Table S3.

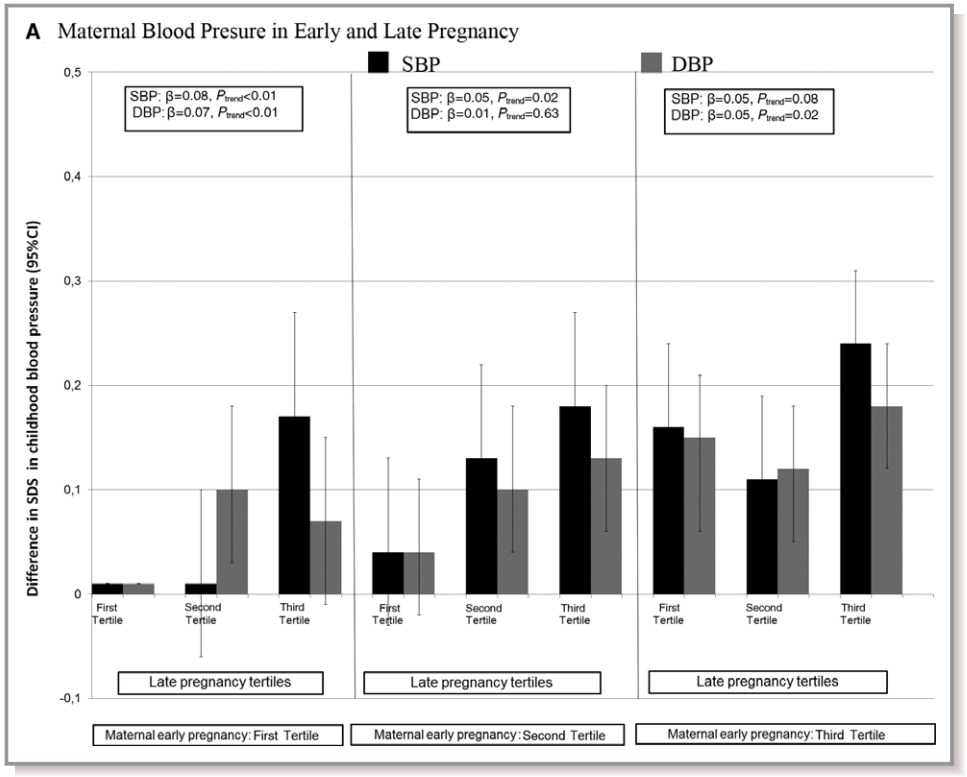

Figure 2. Combined associations of maternal and paternal blood pressure with childhood blood pressure (n=5310). A, Maternal blood pressure in early and late pregnancy. B, Maternal and paternal blood pressure. Values are regression coefficients (95% CI) from multiple linear regression models. Estimates are based on multiple imputed data. Models are adjusted for maternal age, gestational age at measurement, prepregnancy BMI, parity, ethnicity, educational level, smoking and alcohol consumption during pregnancy, folic acid supplement intake, and childhood BMI. Estimates regarding childhood SBP are assessed by combining parental SBP tertiles. Estimates regarding childhood DBP are assessed by combining parental DBP tertiles. The interaction term of maternal late and early pregnancy blood pressure and for the interaction term of maternal and paternal blood pressure were not statistically significant. BMI indicates body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; SDS, standard deviation score.

CI 0.17–0.37) and 0.19 (95% CI 0.11–0.28), respectively. Results from the confounder and birth models for these stratified analyses are given in Figure S2A through S2D. None of the statistical interaction terms were significant.

Maternal and Paternal Blood Pressure and Childhood Hypertension

Figure 3A shows the results of the combined associations of maternal blood pressure during early and late pregnancy with the risk of childhood hypertension. Children of mothers with SBP and DBP in the highest tertiles during both early and late pregnancy had a higher risk of hypertension (odds ratio 2.66 [95% CI 1.71–4.13] and 1.63 [95% CI 1.09–2.46], respectively) compared with children from mothers with SBP and DBP in the lowest tertiles during both early and late pregnancy.

Figure 3B shows the combined associations of maternal early pregnancy and paternal blood pressure. Children of mothers and fathers with blood pressure in the highest tertiles had a higher risk of having hypertension (odds ratio 2.18 [95% CI 1.25–3.79] and 2.20 [95% CI 1.25–3.93], respectively, for SBP and DBP) compared with children from mothers and fathers with SBP and DBP in the lowest tertiles.

Critical Periods of Maternal Blood Pressure for Childhood Blood Pressure and Hypertension

Figure 4A shows that maternal blood pressure in early, mid-, and late pregnancy were all independently associated with childhood blood pressure (all $P<0.05$). The strongest effect estimates were observed for early pregnancy maternal blood pressure (differences in childhood SBP and DBP by SDS 0.08 [95% CI 0.05–0.10] and 0.05 [95% CI 0.03–0.07], respectively, per standardized residual increase in maternal SBP and DBP, respectively).

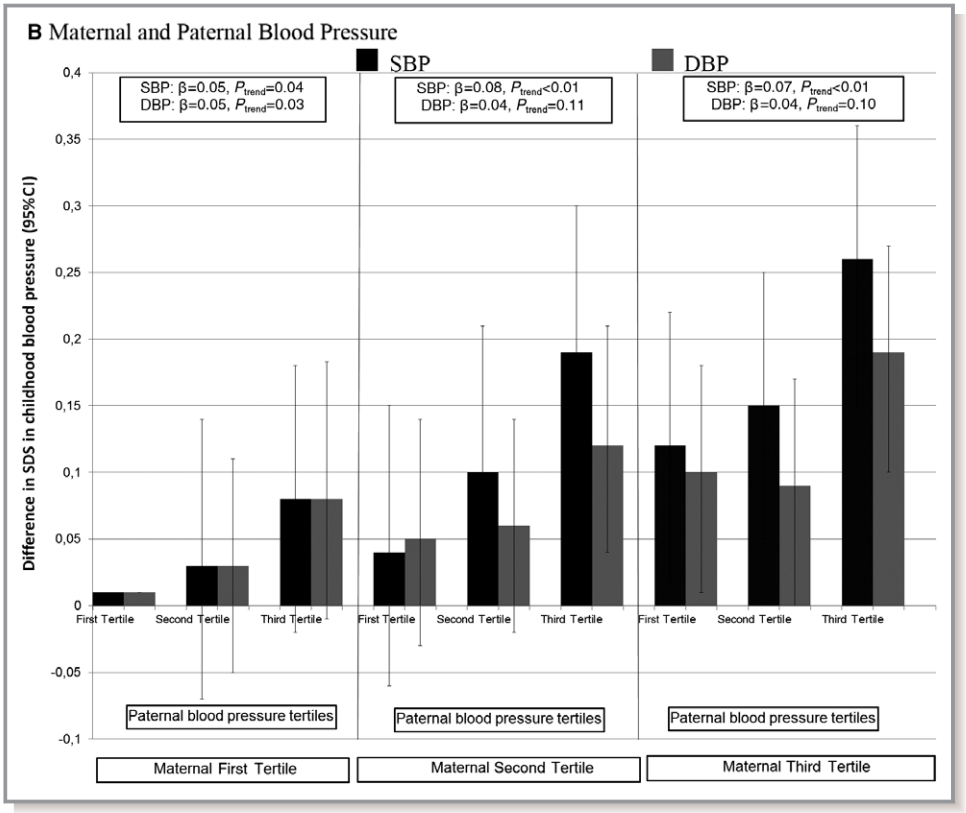

Figure 2. Continued

Figure 4B shows that maternal SBP, but not DBP, in early, mid-, and late pregnancy was independently associated with the risk of childhood hypertension (all $P<0.05$). The strongest effect estimates were observed for early pregnancy maternal blood pressure (odds ratio for childhood risk of hypertension 1.25 [95% CI 1.11–1.42] per standardized residual increase in maternal SBP).

Hypertensive Disorders in Pregnancy and Childhood Blood Pressure

Table 2 shows that children of mothers with hypertensive disorders in pregnancy had higher DBP, but not SBP, than children of mothers without hypertensive disorders in pregnancy. These associations were driven mainly by gestational hypertension (difference in DBP of SDS 0.13 [95% CI 0.05–0.21] between children from mothers with and without gestational hypertension). Preeclampsia was not associated with childhood blood pressure.

Discussion

In this population-based prospective cohort study, we observed that both higher maternal blood pressure throughout pregnancy and paternal blood pressure were associated with higher childhood blood pressure. Early, mid-, and late-pregnancy maternal blood pressure levels were all independently associated with childhood blood pressure, with the strongest effect estimates for early pregnancy. Gestational hypertension was associated with higher childhood DBP. The observed associations were largely independent of fetal and childhood growth measures.

Methodological Considerations

A major strength of our study is the prospective design from early pregnancy onward within a large population-based cohort. Furthermore, we measured maternal blood pressure in different pregnancy periods. Not all mothers had blood pressure measurements in each trimester of pregnancy. Restricting our analyses to mothers who had blood pressure measurements in all 3 trimesters (n=3842) revealed results similar to those of the full group. In addition, 65% of all children of mothers with information about blood pressure and pregnancy complications participated in the follow-up measurements at age 6 years and had blood pressure information available. Compared with children with blood pressure follow-up measurements, those without follow-up measurements had mothers with lower SBP throughout pregnancy and had lower weight and younger gestational age

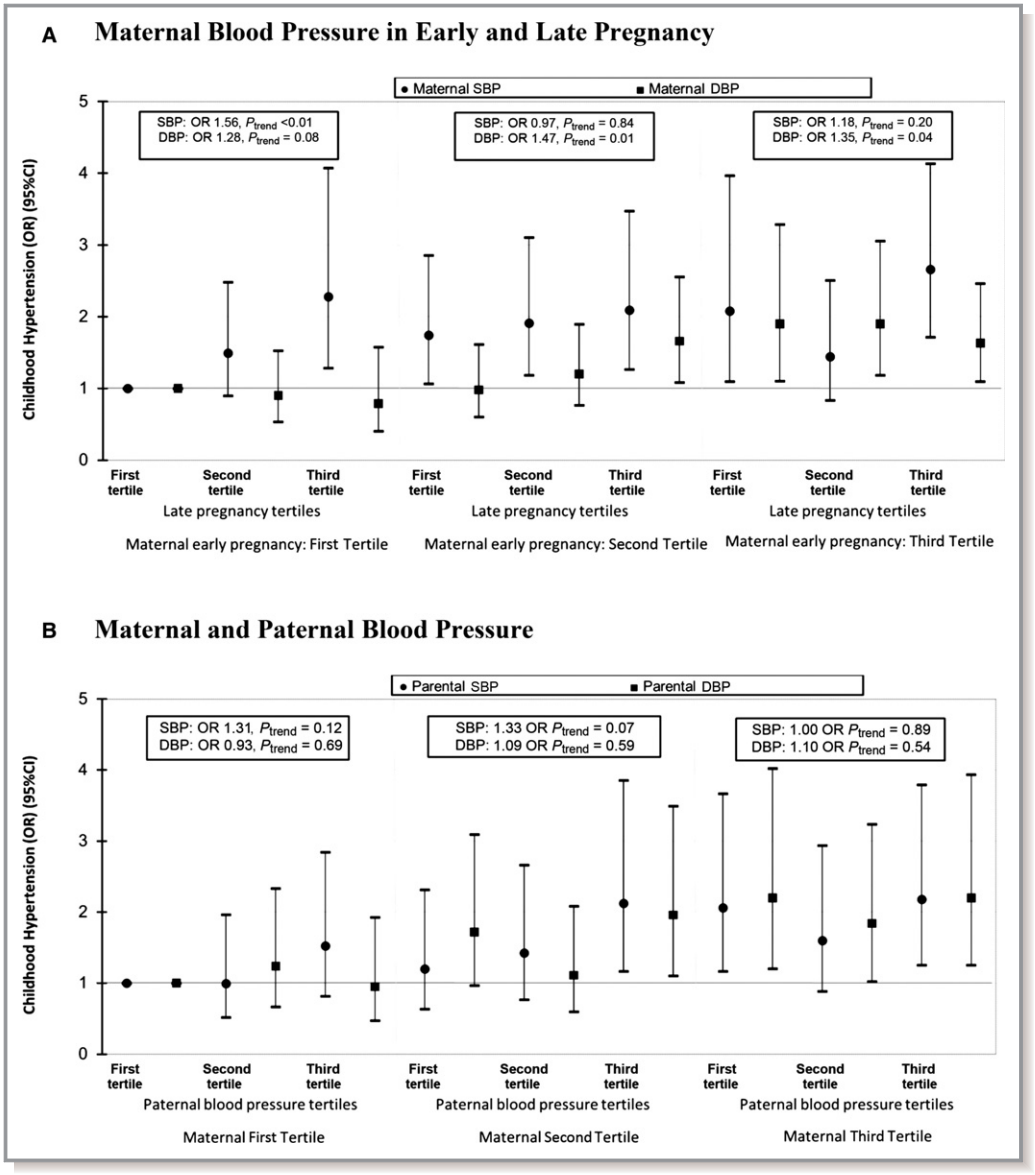

Figure 3. Combined associations of maternal and paternal blood pressure with childhood hypertension (n=5310). A, Maternal blood pressure in early and late pregnancy. B, Maternal and paternal blood pressure. Values are regression coefficients (95% CI) from logistic regression models. Estimates are based on multiple imputed data. Models are adjusted for maternal age, gestational age at measurement, prepregnancy BMI, parity, ethnicity, educational level, smoking and alcohol consumption during pregnancy, folic acid supplement intake, and childhood BMI. Estimates regarding childhood hypertension are assessed by combining parental SBP and DBP tertiles, respectively. BMI indicates body mass index; DBP, diastolic blood pressure; OR, odds ratio; SBP, systolic blood pressure; SDS, standard deviation score.

at birth. A selective loss to follow-up may have reduced variation in blood pressure development and thus reduced the power to detect differences. Moreover, loss to follow-up would lead to selection bias if the associations of maternal blood pressure with childhood blood pressure were different between those included and not included in the final analyses. Although we do not expect that this was likely, selection bias cannot be excluded. Blood pressure has large within-participant variation and is liable to measurement error. This measurement error may have led to underestimation of the observed effect estimates.[17] Furthermore, the number of participants with hypertensive disorders in pregnancy was relatively small, and this might have led to lack of power for the associations of hypertensive disorders in pregnancy with childhood blood pressure. Family history of hypertension may also influence childhood blood pressure. Unfortunately, information about family history of hypertension was available for only a small subset of our cohort.

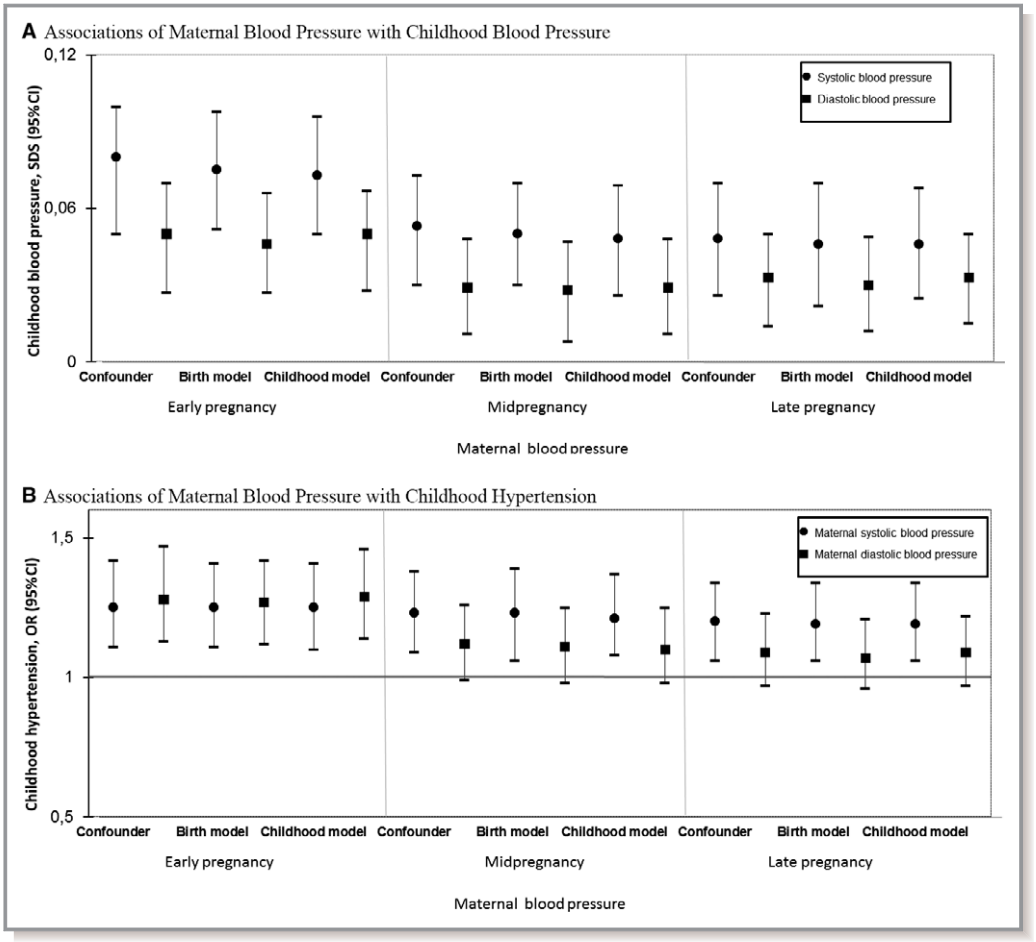

Figure 4. Associations of maternal blood pressure with childhood blood pressure and hypertension from conditional regression models (n=5310). A, Associations of maternal blood pressure with childhood blood pressure. B, Associations of maternal blood pressure with childhood hypertension. Values are linear (A) and logistic (B) regression coefficients (95% CI) that reflect the difference in childhood systolic and diastolic blood pressure per standardized residual for maternal blood pressure during each trimester of pregnancy independent of previous-trimester blood pressure measurements. Confounder models are adjusted for maternal age, prepregnancy BMI, ethnicity, parity, educational level, smoking during pregnancy, alcohol consumption, and folic acid supplement intake. Birth models are confounder models additionally adjusted for birth weight and gestational age. Childhood models are confounder models additionally adjusted for child current BMI. BMI indicates body mass index; OR, odds ratio; SDS, standard deviation score.

Finally, although we performed adjustment for a large number of potential maternal and paternal confounders, residual confounding by other socioeconomic or lifestyle-related factors might still be present, as in any observational study.

Interpretation of Main Findings

We hypothesized that higher maternal blood pressure within the normal range during pregnancy and hypertensive disorders in pregnancy influence blood pressure development in childhood. This hypothesis is based on previous studies suggesting that hypertensive disorders in pregnancy are associated with higher offspring blood pressure.[2,8,9,28] A study among 6343 mother–child pairs in the United Kingdom showed that gestational hypertension, but not preeclampsia, was associated with higher blood pressure in children aged 9 years.[8] A systemic review and meta-analysis with data from 18 studies showed that children of mothers with preeclampsia had higher blood pressure in childhood and early adulthood.[28] A recent study from the United Kingdom suggested that children of mothers with hypertensive disorders in pregnancy had higher blood pressure at the ages of 7 to 18 years.[12] In line with the results of these previous studies, we observed that higher maternal blood pressure during pregnancy was associated with higher blood pressure in children aged 6 years. Children from mothers with hypertensive disorders in pregnancy had higher DBP

Table 2. Associations of Hypertensive Disorders in Pregnancy With Childhood Blood Pressure (n=5310)

Childhood Blood Pressure (SDS)	Confounder Model	Birth Model	Childhood Model
None (n=4888)	Reference	Reference	Reference
Any complications (n=308)			
Childhood SBP	0.07 (−0.02 to 0.15)	0.03 (−0.05 to 0.12)	0.06 (−0.02 to 0.14)
Childhood DBP	0.10 (0.02 to 0.17)*	0.08 (0.01 to 0.15)†	0.10 (0.02 to 0.17)*
Gestational hypertension (n=215)			
Childhood SBP	0.06 (−0.04 to 0.15)	0.04 (−0.06 to 0.13)	0.06 (−0.04 to 0.15)
Childhood DBP	0.13 (0.05 to 0.21)*	0.11 (0.03 to 0.19)*	0.13 (0.05 to 0.21)*
Preeclampsia (n=93)			
Childhood SBP	0.14 (−0.01 to 0.28)	0.06 (−0.08 to 0.21)	0.14 (−0.01 to 0.28)
Childhood DBP	0.03 (−0.09 to 0.15)	−0.01 (−0.13 to 0.11)	0.03 (−0.09 to 0.15)

Values are regression coefficients (95% CI) based on multiple linear regression models. Estimates are based on multiple imputed data. Pregnancies without gestational hypertension or preeclampsia were taken as the reference category. Confounder models were adjusted for maternal age, prepregnancy body mass index, ethnicity, parity, educational level, smoking during pregnancy, alcohol consumption, and folic acid supplement intake. Birth models are confounder models additionally adjusted for gestational age at birth and birth weight. Childhood models are confounders models additionally adjusted for childhood current body mass index. DBP indicates diastolic blood pressure; SBP, systolic blood pressure; SDS, standard deviation score.

*$P<0.01$.

†$P<0.05$.

compared with children of mothers without hypertensive disorders in pregnancy. These associations were driven mainly by gestational hypertension and were not present for preeclampsia. Consequently, results from both previous studies and from our study suggest that maternal blood pressure during pregnancy affects childhood blood pressure. Nevertheless, not much is known about the specific maternal and paternal effects, critical periods, and role of fetal and childhood growth in the associations.

In the current study, we observed that both maternal and paternal blood pressure was associated with childhood blood pressure and risk of hypertension. In addition, within each tertile of maternal blood pressure, higher paternal blood pressure was associated with childhood blood pressure. Only a few previous studies have explored the effect of maternal and paternal blood pressure on childhood blood pressure and risk of hypertension.[29–31] These studies suggest that both higher maternal and paternal blood pressure levels are associated with an increased risk of higher childhood blood pressure in offspring.[29,31] The presence of hypertension in both parents has an additive effect on childhood blood pressure levels.[29,32] A recent study suggested that children of hypertensive parents had a higher risk of hypertension.[32] Similar associations for maternal and paternal blood pressure suggest that genetic or shared family-based factors, rather than direct intrauterine programming, may explain the associations of maternal blood pressure with childhood blood pressure.[13] Our results suggest that both maternal and paternal blood pressure levels are important, at similar magnitude, for childhood blood pressure.

We aimed to identify critical periods during pregnancy that affected childhood blood pressure. Our results suggest that early, mid-, and late pregnancy are all independently associated with childhood blood pressure. Differences between early, mid-, and late pregnancy were small, but slightly stronger effect estimates were observed for early pregnancy. A recent study from a prospective cohort in the United Kingdom also showed that early pregnancy appeared to be the period during pregnancy with the most influence on childhood blood pressure.[12] Some mechanisms have been hypothesized to underlie the association of maternal blood pressure levels during early pregnancy with blood pressure levels in offspring.[7] Higher maternal blood pressure in early pregnancy may be a marker of maternal and placental vascular maladaptations,[33] leading to fetal growth restriction and abnormal fetal vascular development[34] that may subsequently affect childhood blood pressure.[35] In addition, higher maternal blood pressure levels in early pregnancy may be predictors of hypertensive disorders in pregnancy that, in turn, may be predictors of maternal and offspring cardiovascular diseases later in life. Consequently, although maternal blood pressure in each period of pregnancy seems to be independently associated with childhood blood pressure, early pregnancy in particular may be critical for childhood blood pressure.

Consistent evidence suggests that preterm birth and low birth weight are associated with childhood blood pressure, although the effects seem to be small.[36,37] Moreover, BMI is one of the strongest predictors of blood pressure in childhood.[26] Consequently, associations of maternal blood

pressure with childhood blood pressure may be partly explained by preterm birth, low birth weight, and high BMI. We observed, however, that the effect estimates of parental blood pressure or hypertensive disorders in pregnancy with childhood blood pressure did not materially change after additional adjustment for birth outcomes or childhood BMI. We also explored whether including size at birth for gestational age, instead of birth weight, would affect the results, but this was not the case. These findings are in line with the large study from the United Kingdom showing that the effects of hypertensive disorders in pregnancy on childhood blood pressure were largely independent of maternal and childhood obesity.[2] Current results suggest that the associations of parental blood pressure and hypertensive disorders in pregnancy with childhood blood pressure are not explained by fetal and childhood growth measures.

The prevalence of hypertension in children and adolescents in Western countries has been reported at 1% to 5%.[38] In addition to the already known childhood risk factors (eg, BMI) for developing primary hypertension, other parental factors should be considered in screening guidelines.[38] Young offspring of mothers who had high blood pressure in early pregnancy or gestational hypertension may compose specific groups at risk for having high blood pressure from childhood onward. Whether these findings can be translated to primary prevention strategies for primary hypertension in children and adolescents should be studied further.

Conclusions

In summary, our results suggest that both higher maternal blood pressure throughout pregnancy and paternal blood pressure influence childhood blood pressure. Early, mid-, and late-pregnancy maternal blood pressure levels were all independently associated with childhood blood pressure, with the strongest effect estimates for early pregnancy. The observed associations were largely independent of fetal and childhood growth measures. Further follow-up studies are needed to investigate whether parental blood pressure and hypertensive disorders in pregnancy affect cardiovascular risk at older ages.

Author Contributions

Drs Miliku, Bergen, Bakker and Jaddoe conceptualized and designed the study. Drs Miliku and Gaillard carried out the analyses. Drs Miliku and Jaddoe, drafted the initial manuscript, and approved the final manuscript as submitted. Drs Hofman and Steegers critically reviewed and revised the manuscript, and approved the final manuscript as submitted. Drs Miliku and Jaddoe, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Data S1. Statistical analyses

Mixed effects regression models. We used unbalanced repeated measurement regression models to examine maternal longitudinal blood pressure patterns in tertiles of childhood blood pressure. These models take the correlation between repeated measurements within the same subject into account by modelling the correlated errors of these measurements.[1] Both gestational age-independent (difference constant over time) and gestational age-dependent (difference not-constant over time) effects were assessed. We constructed best-fitting models for maternal blood pressure patterns. We started with a linear model and examined whether adding second-degree fractional polynomial of gestational age improved the models by comparing the deviances and goodness of fit. Since adding fractional polynomials of gestational age to the model improved the model fit, we included these fractional polynomials in the final models. We used a compound symmetry covariance structure. Childhood blood pressure in tertiles were included in these models as intercept and as an interaction term with gestational age. The final models can be written as:

Maternal systolic blood pressure. Difference in maternal systolic blood pressure (mmHg) between childhood systolic blood pressure tertiles based on repeated measurement regression analysis = $\beta_0 + \beta_1$* child systolic blood pressure tertile + β_2 * gestational age + β_3 * gestational age^{-2} + β_4 * child systolic blood pressure tertile* gestational age.

Maternal diastolic blood pressure. Difference in maternal diastolic blood pressure (mmHg) for childhood diastolic blood pressure tertiles based on repeated measurement analysis = $\beta_0 + \beta_1$* child diastolic blood pressure tertile + β_2 * gestational age + β_3 * gestational age$^{0.5}$ + β_4 * child diastolic blood pressure tertile * gestational age.

Conditional regression analyses. We performed conditional regression analyses to identify the independent associations of first, second and third trimester maternal blood pressure, taking into account their correlations, with childhood blood pressure.[2] We constructed blood pressure values for each trimester, which are statistically independent from blood pressure values for other trimesters, by using standardized residuals obtained from regression of blood pressure values at a specific time point (dependent variable) on blood pressure values obtained at a previous time point.[2-4] These standardized residuals, which are assumed to be independent of the estimated regression line (and thus from the previous blood pressure), were taken forward to the regression models as independent variable with childhood blood pressure (dependent variable). As conditional blood pressure measurements are statistically independent of each other, this approach allows inclusion of blood pressure values from different trimesters simultaneously in one linear regression model when continuous childhood blood pressure was the outcome, or in one logistic regression model when childhood hypertension was the outcome. For the conditional analyses, we imputed maternal blood pressure measures. Results from these datasets were pooled and presented in the conditional results.

Table S1. Subject Characteristics in the Original and Imputed Dataset (N = 5310)

	Observed	Imputed
Maternal characteristics		
Age, y	30.9 (19.7, 39.3)	30.9 (19.7, 39.3)
Height, cm	167.5 (7.4)	167.5 (7.5)
Missing, n (%)	19 (3.6)	
Weight, kg	69.3 (12.8)	69.3 (12.7)
Missing, n (%)	18 (3.4)	
Body mass index, kg/m^2	24.7 (4.3)	24.7 (4.3)
Missing, n (%)	36 (6.8)	
Parity, n (%)		
0	2,990 (56.3)	3,008 (56.6)
≥1	2,280 (42.9)	2,302 (43.4)
Missing	40 (0.8)	
Educational level mother, n (%)		
Primary or secondary	2,673 (50.3)	2,854 (53.7)
Higher	2,295 (43.2)	2,456 (46.3)
Missing	342 (6.5)	
Ethnicity, n (%)		
European	3,135 (59.0)	3,167 (59.6)
Non-European	2,059 (38.8)	2,143 (40.4)
Missing	116 (2.2)	
Smoking during pregnancy, n (%)		
No	3,476 (65.4)	3,792 (71.4)
Yes	1,224 (23.1)	1,518 (28.6)
Missing	610 (11.5)	
Alcohol using during pregnancy, n (%)		
No	2,138 (40.3)	2,478 (46.7)
Yes	2,512 (47.3)	2.832 (53.3)
Missing	660 (12.4)	
Folic acid supplements during pregnancy, n (%)		
No	1,017 (19.2)	1,695 (31.9)
Yes	3,023 (56.9)	3,615 (68.1)
Missing	1,270 (23.9)	
Blood pressure		
Early pregnancy		

Gestational age, weeks	13.2 (9.8, 17.4)	13.4 (9.8, 17.5)
Systolic blood pressure, mmHg	115.5 (12.0)	115.5 (12.0)
Diastolic blood pressure, mmHg	68.1 (9.3)	68.1 (9.3)
Mid- pregnancy		
Gestational age, weeks	20.5 (18.5, 23.5)	20.5 (18.5, 23.5)
Systolic blood pressure, mmHg	116.8 (11.9)	116.8 (11.9)
Diastolic blood pressure, mmHg	67.2 (9.3)	67.2 (9.3)
Late pregnancy		
Gestational age, weeks	30.2 (28.5, 32.9)	30.2 (28.5, 32.9)
Systolic blood pressure, mmHg	118.4 (11.9)	118.4 (11.9)
Diastolic blood pressure, mmHg	69.1 (9.2)	69.1 (9.2)
Hypertensive disorders in pregnancy, n (%)		
Any	308 (5.8)	308 (5.8)
Gestational hypertension	215 (4.0)	215 (4.0)
Preeclampsia	93 (1.8)	93 (1.8)
Paternal characteristics		
Age, years	33.0 (22.3, 45.8)	33.0 (21.7, 45.2)
Missing, n (%)	1,284 (24.2)	
Height, cm	182.1 (7.9)	181.9 (7.7)
Missing, n (%)	1,289 (24.3)	
Weight, kg	83.9 (13.0)	83.7 (11.6)
Missing, n (%)	1,286 (24.2)	
Body Mass Index, m/kg^2	25.3 (3.4)	25.3 (3.2)
Missing, n (%)	1,293 (24.4)	
Ethnicity, n (%)		
European	2,736 (51.5)	3,274 (61.7)
Non-European	1,155 (21.8)	2,036 (38.3)
Missing	1,419 (26.7)	
Educational level father, n (%)		
Primary or secondary	1,661 (31.3)	2,896 (54.5)
Higher	1,841 (34.7)	2,414 (45.5)
Missing	1,808 (34.0)	
Systolic blood pressure, mmHg	130.2 (13.5)	130.2 (13.5)
Diastolic blood pressure, mmHg	73.4 (10.6)	73.4 (10.6)
Birth characteristics		
Female, n (%)	2,656 (50.0)	2,656 (50.0)
Gestational age, weeks	40.1 (35.9, 42.3)	40.1 (35.9, 42.3)

Birth weight, g	3,431 (548)	3,430 (548)
Missing, n (%)	8 (0.1)	
Small size for gestational age, n (%)	267 (5.0)	267 (5.0)
Appropriate size for gestational age, n (%)	4,777 (89.9)	4,777 (89.9)
Childhood characteristics		
Age, y	6.0 (5.7, 8.0)	6.0 (5.7, 8.0)
Height, cm	119.5 (6.0)	119.5 (6.1)
Missing, n (%)	7 (0.1)	
Weight, kg	23.3 (4.3)	23.3 (4.3)
Missing, n (%)	7 (0.1)	
Body mass index, kg/m^2	16.2 (1.9)	16.2 (1.9)
Missing, n (%)	7 (0.1)	
Systolic blood pressure, mmHg	102.7 (8.2)	102.7 (8.2)
Diastolic blood pressure, mmHg	60.7 (6.9)	60.7 (6.9)
*Z score Systolic blood pressure	0.53 (0.7)	0.53 (0.7)
*Z score Diastolic blood pressure	0.34 (0.6)	0.34 (0.6)
[#] Blood pressure ≥ 95th percentile, n (%)	410 (7.7)	410 (7.7)

* Values are percentages for categorical variables, means (SD) for continuous variables with a normal distribution, or medians (95% range) for continuous variables with a skewed distribution.

*Z scores of systolic and diastolic blood pressure are calculated using normative values from the "Fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents" from the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.

#Blood pressure ≥ 95th percentile (systolic and/or diastolic blood pressure ≥ 95th percentile) for age, height and sex on repeated measurement.

Table S2. Subject Characteristics in Children with and without Follow-up Blood Pressure Measurements (N = 8452)

	N = 5310	N = 3142	p-value
Maternal characteristics			
Age, y	30.9 (19.7, 39.3)	28.9 (18.5, 39.0)	< **0.01**
Height, cm	167.5 (7.4)	166.4 (7.4)	< **0.01**
Weight, kg	69.3 (12.8)	69.1 (13.6)	0.55
Body mass index, kg/m^2	23.5 (4.1)	23.6 (4.5)	0.55
Parity (%)			
0	2,990 (56.3)	1,663 (54)	**0.02**
≥1	2,280 (42.9)	1,414 (46)	
Educational level mother, n (%)			< **0.01**
Primary or secondary	2,673 (50.3)	1,781 (56.7)	
Higher	2,295 (43.2)	936 (39.8)	
Ethnicity, n (%)			< **0.01**
European	3,135 (59.0)	1,407 (44.8)	
Non-European	2,059 (38.8)	1,386 (44.1)	
Smoking during pregnancy, n (%)			< **0.01**
No	3,476 (65.4)	1,887 (60.1)	
Yes	1,224 (23.1)	783 (24.9)	
Alcohol using during pregnancy, n (%)			< **0.01**
No	2,138 (40.3)	1,471 (46.8)	
Yes	2,512 (47.3)	1,152 (36.7)	
Folic acid supplements during pregnancy, n (%)			< **0.01**
No	1,017 (19.2)	823 (26.2)	
Yes	3,023 (56.9)	1,393 (44.3)	
Blood pressure			
Early pregnancy			
Gestational age, weeks	13.2 (9.8, 17.4)	13.4 (9.5, 17.6)	< **0.01**
Systolic blood pressure, mmHg	115.5 (12.0)	114.7 (12.1)	< **0.01**
Diastolic blood pressure, mmHg	68.1 (9.3)	67.7 (9.3)	0.08
Mid- pregnancy			
Gestational age, weeks	20.5 (18.5, 23.5)	20.4 (18.5, 23.9)	0.07
Systolic blood pressure, mmHg	116.8 (11.9)	115.8 (11.8)	< **0.01**
Diastolic blood pressure, mmHg	67.2 (9.3)	66.6 (9.0)	**0.01**
Late pregnancy			

Gestational age, weeks	30.2 (28.5, 32.9)	30.3 (28.4, 32.9)	**0.02**
Systolic blood pressure, mmHg	118.4 (11.9)	117.4 (12.0)	< **0.01**
Diastolic blood pressure, mmHg	69.1 (9.2)	68.5 (9.2)	< **0.01**
Hypertensive disorders in pregnancy, n (%)			
Any	305 (5.8)	160 (5.1)	0.58
Gestational hypertension	215 (4.0)	95 (3.0)	**0.03**
Preeclampsia	93 (1.8)	65 (2.1)	**0.02**
Paternal characteristics			
Age, years	33.0 (22.3, 45.8)	31.8 (21.0, 44.5)	< **0.01**
Height, cm	182.1 (7.9)	181.8 (7.7)	< **0.01**
Weight, kg	83.9 (13.0)	83.6 (11.6)	< **0.01**
Body Mass Index, m/kg^2	25.3 (3.4)	25.3 (3.6)	0.59
Ethnicity, n (%)			< **0.01**
European	2,736 (51.5)	1,150 (36.6)	
Non-European	1,155 (21.8)	697 (22.2)	
Educational level father, n (%)			< **0.01**
Primary or secondary	1,661 (31.3)	818 (26.0)	
Higher	1,841 (34.7)	722 (23.0)	
Systolic blood pressure, mmHg	130.2 (13.5)	129.8 (13.6)	0.25
Diastolic blood pressure, mmHg	73.4 (10.6)	72.9 (10.9)	0.12
Birth characteristics			
Female, n (%)	2,656 (50.0)	1,534 (48.9)	0.30
Gestational age, weeks	40.1 (35.9, 42.3)	40.0 (35.0, 42.4)	< **0.01**
Birth weight, g	3,431 (548)	3,387 (576)	< **0.01**

* Values are percentages for categorical variables, means (SD) for continuous variables with a normal distribution, or medians (95% range) for continuous variables with a skewed distribution. Differences in subject characteristics comparing the groups with and without blood pressure measurements were evaluated using T-tests for continuous normally distributed variables, Mann Whitney for non-normally distributed variables, and Chi-squared tests for categorical variables.

Table S3. Effect Estimates from the Longitudinally Measured Maternal Blood Pressure and Childhood Blood Pressure

		Difference in systolic blood pressure		
Childhood blood pressure	**Intercept** (mmHg)	**P-value[b]**	**Slope** (mmHg/week of gestation)	**P-value[b]**
Tertile 1	109.6	P < 0.001	-0.02	P=0.51
Tertile 2	111.1	P = 0.15	-0.03	P=0.17
Tertile 3	112.0	P < 0.001	*Reference*	
		Difference in diastolic blood pressure		
	Intercept (mmHg)	**P-value[b]**	**Slope** (mmHg/week of gestation)	**P-value[b]**
Tertile 1	97.7	P < 0.001	-0.02	P=0.22
Tertile 2	97.8	P < 0.001	0.01	P=0.48
Tertile 3	99.1	P < 0.001	*Reference*	

[a]Values are based on repeated non-linear regression models and reflect the change in maternal blood pressure during pregnancy in mmHg per tertile of childhood blood pressure compared to the reference group of children in the highest tertile.
[b]P–value reflects the significance level of the estimate.

Table S4. Associations of Maternal and Paternal Blood Pressure During Pregnancy with Childhood Blood Pressure (N = 5310)

	Childhood blood pressure (SDS)		
	Confounder Model	***Birth Model***	***Childhood Model***
Maternal blood pressure (SDS)			
Early pregnancy (N = 4098)			
Systolic blood pressure	0.07 (0.05, 0.09)**	0.07 (0.05, 0.09)**	0.07 (0.04, 0.09)**
Diastolic blood pressure	0.04 (0.02, 0.06)**	0.04 (0.02, 0.06)**	0.04 (0.02, 0.06)**
Mid- pregnancy (N = 5006)			
Systolic blood pressure	0.08 (0.06, 0.10)**	0.08 (0.06, 0.10)**	0.07 (0.05, 0.09)**
Diastolic blood pressure	0.05 (0.04, 0.07)**	0.05 (0.03, 0.07)**	0.05 (0.04, 0.07)**
Late pregnancy (N = 5104)			
Systolic blood pressure	0.08 (0.06, 0.10)**	0.08 (0.06, 0.10)**	0.08 (0.06, 0.10)**
Diastolic blood pressure	0.06 (0.04, 0.08)**	0.06 (0.04, 0.08)**	0.06 (0.04, 0.08)**
Paternal blood pressure ***(N = 3805)***			
Systolic blood pressure	0.05 (0.03, 0.08)**	0.05 (0.03, 0.08)**	0.06 (0.04, 0.08)**
Diastolic blood pressure	0.06 (0.04, 0.08)**	0.05 (0.03, 0.07)**	0.06 (0.04, 0.08)**

Values are regression coefficients (95% confidence interval) based from multiple linear regression models. Estimates are based on multiple imputed data.
Confounder model is focused on maternal blood pressure are adjusted for maternal age, gestational age at measurement, pre-pregnancy body mass index, parity, ethnicity, educational level, smoking and alcohol consumption during pregnancy, and folic acid intake; Models focused on paternal blood pressure are adjusted for paternal age, body mass index, ethnicity and educational level;
Birth models are confounder models additionally adjusted for gestational age at birth and birth weight.
Childhood models are confounders models additionally adjusted for childhood current body mass index. *P<0.05 **P<0.01

Figure S1. Flow Chart of the Study Participants

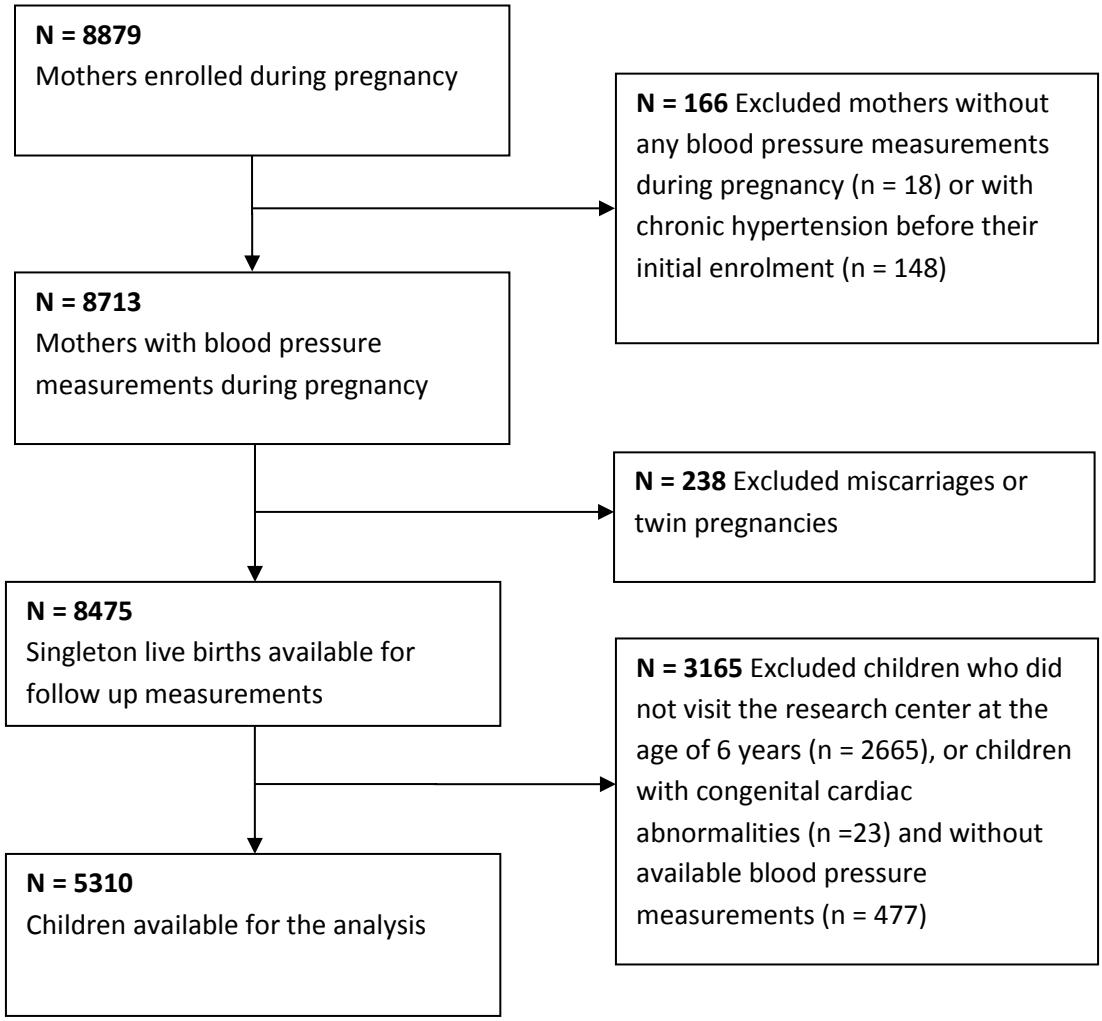
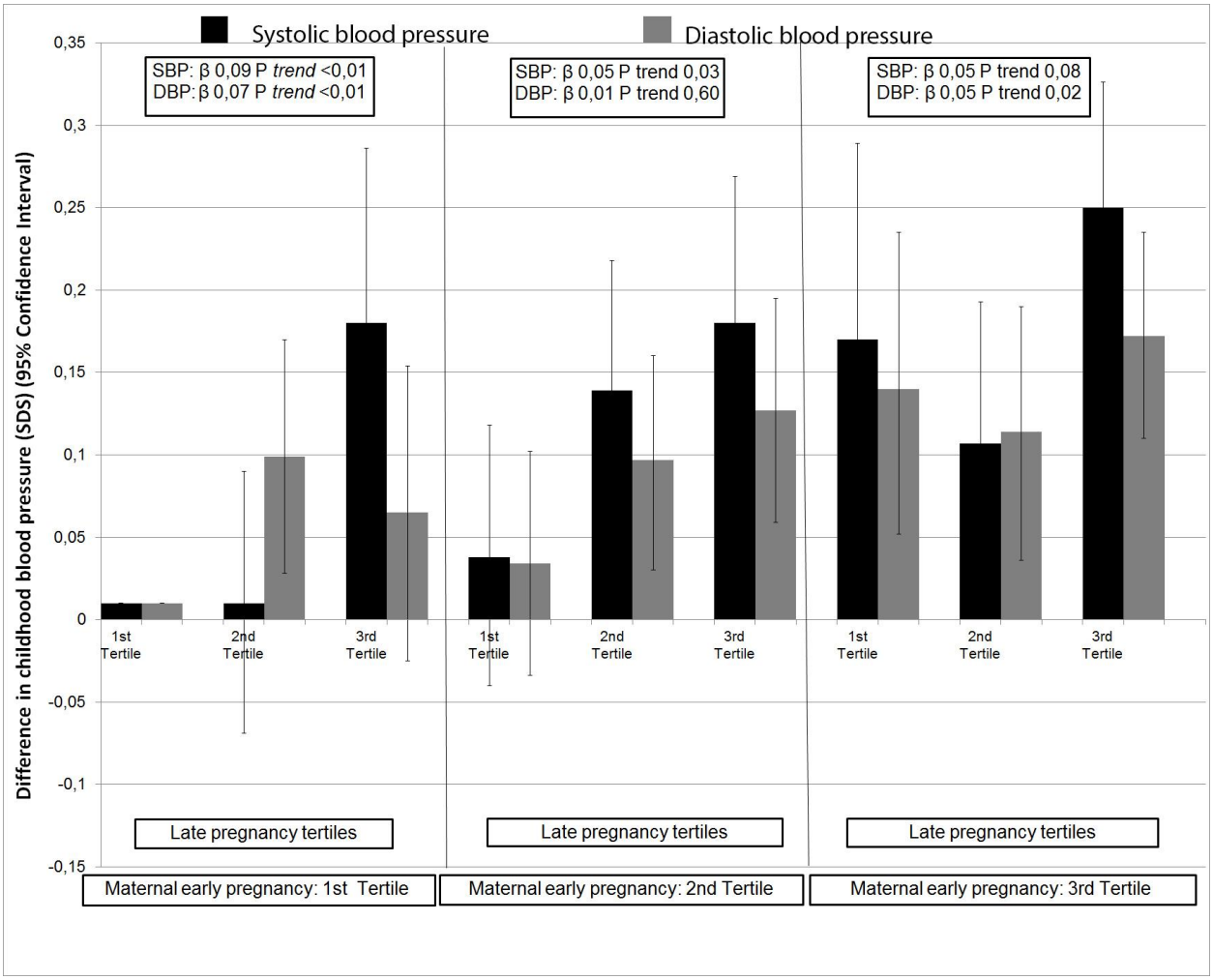


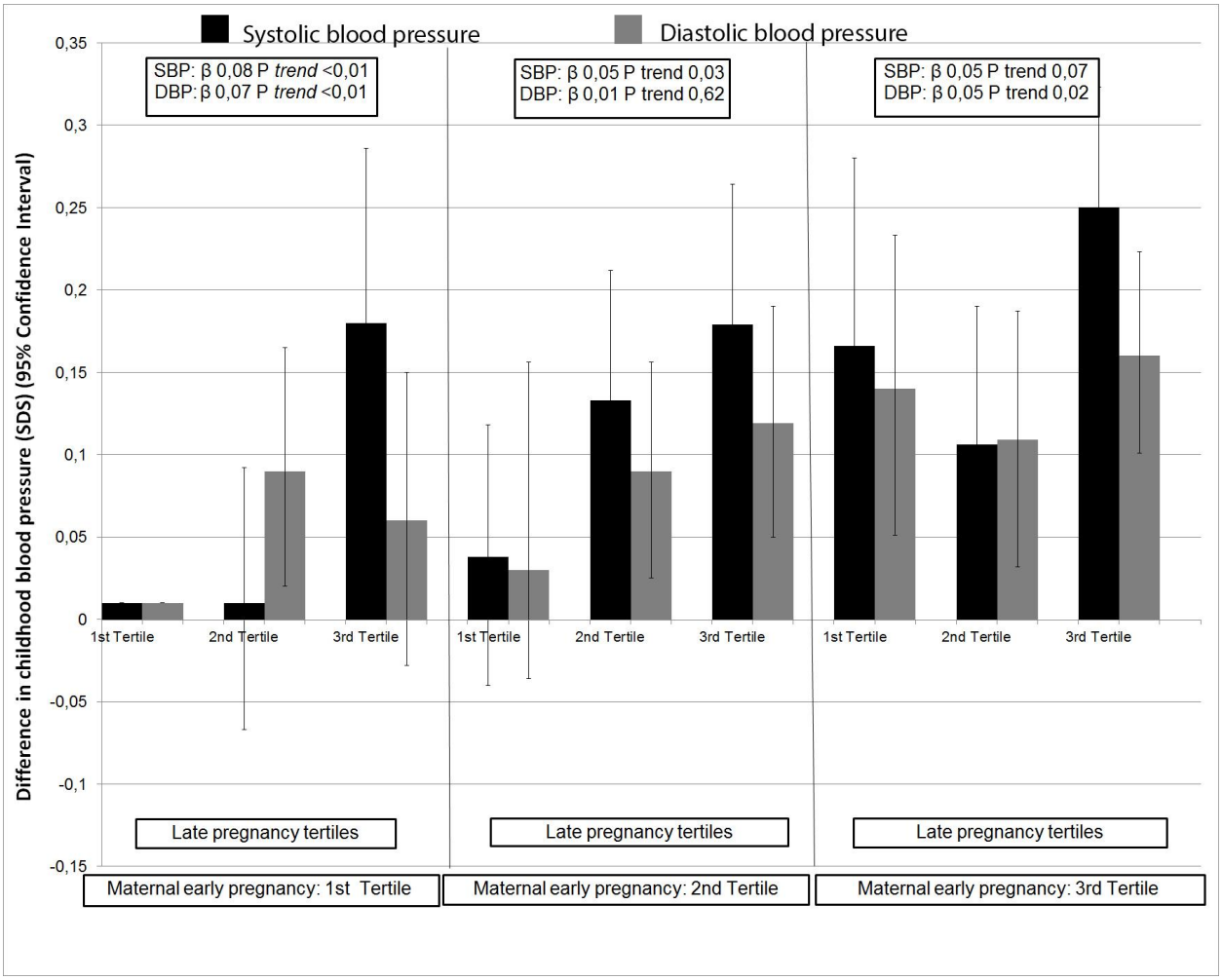
Figure S2. Combined Associations of Maternal and Paternal Blood Pressure with Childhood Blood Pressure, Confounder and Birth Models (N = 5310)

A. Maternal Blood Pressure in Early and Late Pregnancy, Confounder Model



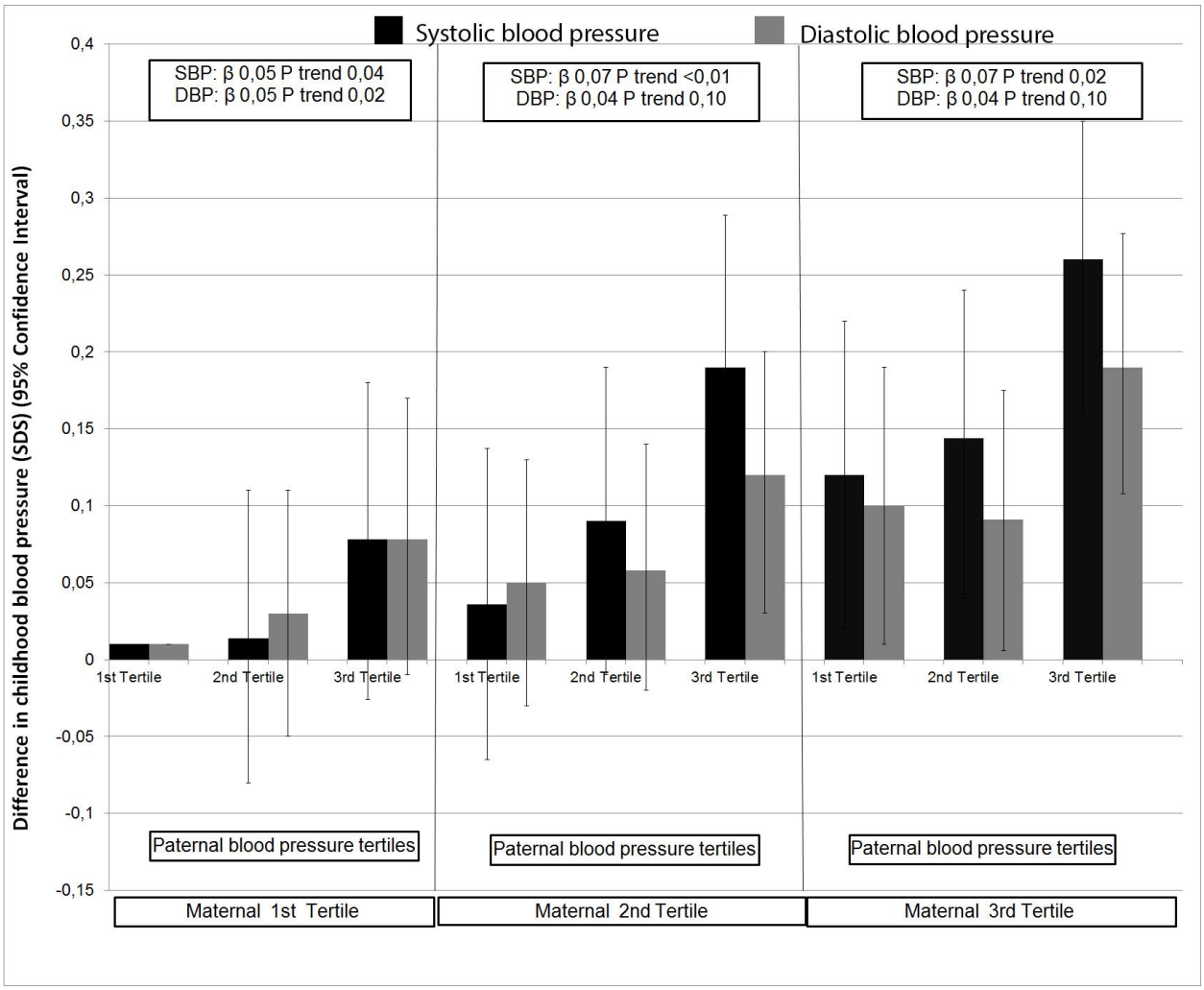
Values are regression coefficients (95% confidence interval) from multiple linear regression models. Estimates are based on multiple imputed data. Models are adjusted for maternal age, gestational age at measurement, pre-pregnancy body mass index, parity, ethnicity, educational level, smoking and alcohol consumption during pregnancy, folic acid supplement intake. Estimates regarding childhood systolic blood pressure are assessed by combining maternal early pregnancy with late pregnancy systolic blood pressure tertiles. Estimates regarding childhood diastolic blood pressure are assessed by combining maternal early with late pregnancy diastolic blood pressure tertiles.

B. Maternal Blood Pressure in Early and Late Pregnancy, Birth Model



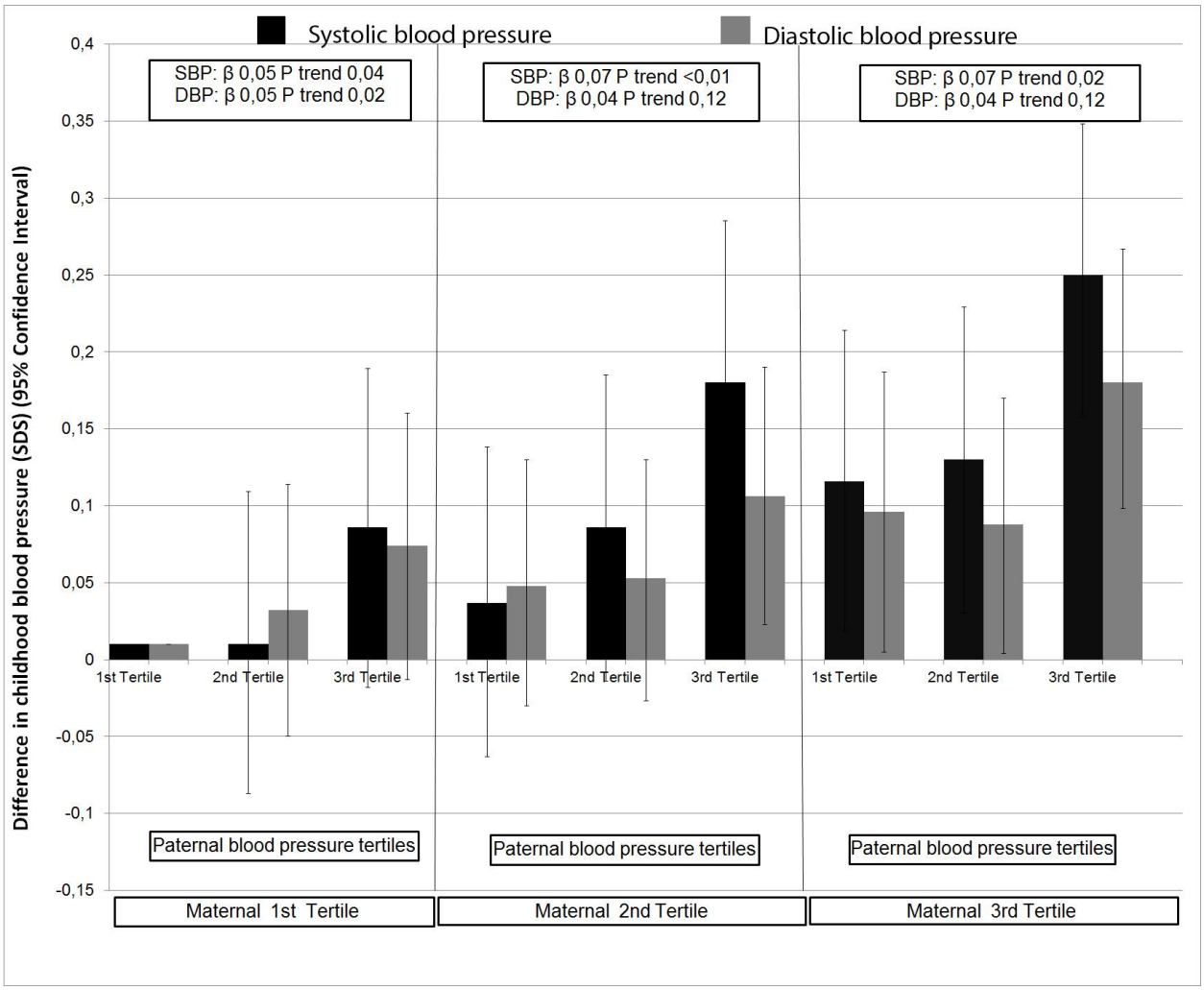
Values are regression coefficients (95% confidence interval) from multiple linear regression models. Estimates are based on multiple imputed data. Models are adjusted for maternal age, gestational age at measurement, pre-pregnancy body mass index, parity, ethnicity, educational level, smoking and alcohol consumption during pregnancy, folic acid supplement intake, birthweight and gestational age at birth. Estimates regarding childhood systolic blood pressure are assessed by combining maternal early pregnancy with late pregnancy systolic blood pressure tertiles. Estimates regarding childhood diastolic blood pressure are assessed by combining maternal early with late pregnancy diastolic blood pressure tertiles.

C. Maternal and Paternal Blood Pressure, Confounder Model



Values are regression coefficients (95% confidence interval) based from multiple linear regression models. Estimates are based on multiple imputed data. Models focused on maternal blood pressure are adjusted for maternal and paternal age, ethnicity, educational level and (pre-pregnancy) body mass index; gestational age at measurement, maternal smoking and alcohol consumption during pregnancy, folic acid supplement intake. Estimates regarding childhood systolic blood pressure are assessed by combining maternal early pregnancy systolic blood pressure tertiles with paternal systolic blood pressure tertiles. Estimates regarding childhood diastolic blood pressure are assessed by combining maternal early pregnancy diastolic blood pressure tertiles with paternal diastolic blood pressure tertiles.

D. Maternal and Paternal Blood Pressure, Birth Model



Values are regression coefficients (95% confidence interval) based from multiple linear regression models. Estimates are based on multiple imputed data. Models focused on maternal blood pressure are adjusted for maternal and paternal age, ethnicity, educational level and (pre-pregnancy) body mass index; gestational age at measurement, maternal smoking and alcohol consumption during pregnancy, folic acid supplement intake, birthweight and gestational age at birth. Estimates regarding childhood systolic blood pressure are assessed by combining maternal early pregnancy systolic blood pressure tertiles with paternal systolic blood pressure tertiles. Estimates regarding childhood diastolic blood pressure are assessed by combining maternal early pregnancy diastolic blood pressure tertiles with paternal diastolic blood pressure tertiles.

Supplemental References

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Associations of Maternal and Paternal Blood Pressure Patterns and Hypertensive Disorders during Pregnancy with Childhood Blood Pressure

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