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Maternal Pregnancy-Related Hypertension and Risk for Hypertension in Offspring Later in Life

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Abstract

OBJECTIVE—To estimate the association between maternal pregnancy-related hypertension and offspring hypertension later in life in a birth cohort from New England.

METHODS—Covariate and exposure data were collected between 1959 and 1966 through the Collaborative Perinatal Project. Follow-up information was obtained through the New England Family Study between 2001 and 2004, when study participants were between 34 and 44 years old. The study population consisted of 1,556 individuals. Participants who reported having hypertension diagnosed at least once were considered to have hypertension. Logistic regression was used to estimate the association between maternal pregnancy-related hypertension and offspring hypertension later in life. Results were adjusted for sex, maternal race, maternal body mass index, maternal socioeconomic status, maternal diabetes, and twin pregnancy.

RESULTS—Maternal pregnancy-related hypertension was associated with an increased risk of being prescribed antihypertensives compared with never having hypertension diagnosed (from 8.8% to 17.4%; adjusted odds ratio 1.88, 95% confidence interval 1.00–3.55). The association was not attenuated after adjustment for birth weight or preterm delivery. After excluding offspring of women who reported hypertension during pregnancy only, this association increased to an adjusted odds ratio of 1.97 (95% confidence interval 1.04–3.72).

CONCLUSION—In a birth cohort from New England, maternal pregnancy-related hypertension was associated with hypertension in offspring later in life.

LEVEL OF EVIDENCE: II

Besides causing maternal and neonatal morbidity in the perinatal period,¹ epidemiologic studies have demonstrated that pregnancy-related hypertension predisposes women to greater risk for cardiovascular disease later in life.^{2–6} A number of studies have suggested an association between maternal preeclampsia and elevated blood pressure among offspring during childhood and adolescence.^{7–11} Kajantie et al¹² reported an association between maternal preeclampsia and antihypertensive use by offspring later in life. Maternal race, body mass index (BMI), socioeconomic status, hypertension, and diabetes are risk factors for preeclampsia^{1,13–15} and may predict hypertension in offspring; however, none of the studies adequately controlled for this set of potential confounders.

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Endothelial dysfunction is a hallmark of preeclampsia¹⁶ and is believed to promote atherosclerosis and contribute to cardiovascular disease.^{17,18} Chambers et al¹⁹ reported that women with previous preeclampsia had impaired endothelial function compared with women with uncomplicated pregnancies; the results were independent of risk factors for endothelial dysfunction. If it is possible that preeclampsia affects maternal endothelial function, could it also adversely affect fetal endothelial function, thereby predisposing offspring to hypertension?

Our study estimated the association between maternal pregnancy-related hypertension and hypertension in offspring later in life in a birth cohort. Unlike previous studies, we control for several maternal confounders, consider nongestational hypertension as an outcome, and explore effect modification by sex. We hypothesize that individuals who were born from pregnancies complicated by hypertension would be more likely to have hypertension diagnosed during adulthood, independent of confounders, preterm birth, and birth weight.

MATERIALS AND METHODS

This prenatal cohort consisted of offspring from the Collaborative Perinatal Project (CPP) who, as adults, participated in the New England Family Study (NEFS). All baseline data were collected through the original CPP, and outcome data were obtained through the NEFS. The CPP and NEFS studies have been described elsewhere.^{20,21} Briefly, the CPP was a community-based prospective study of pregnant women, their pregnancy outcomes, and their offspring through the first 7 years of life in 12 cities across the United States.²⁰ The original objective of the CPP was to investigate the effect of pregnancy and delivery complications on disorders of childhood. Demographic, social, and medical history information was collected from participants by interview at the time of study enrollment. Information from laboratory tests and physical examinations was recorded at each prenatal study visit. Mothers of cohort members in the present study participated in the Boston, Massachusetts, and Providence, Rhode Island, sites of the CPP between 1959 and 1966. The NEFS was initiated to identify familial and early life influences on tobacco dependence and related disorders, including cardiovascular disease.²¹ Between 2001 and 2004, a multistage sampling procedure was used to identify potential participants for the NEFS. The procedure oversampled families with more than one sibling who belonged to the CPP cohort; correlations between siblings were accounted for in the analysis. NEFS screening questionnaires were mailed to a sample (n=4,579) of the 15,721 Boston and Providence CPP offspring who survived until age 7 years. Of this sample, 3,121 (68.2%) returned questionnaires, 2,271 were eligible for participation based on the inclusion criteria for three unique studies, and 1,625 individuals were successfully enrolled in the NEFS. Outcome data were collected by in-person interview when participants were 34 to 44 years old. This study was approved by the Institutional Review Boards at Brown University and Harvard School of Public Health.

The exposure of interest was termed “maternal pregnancy-related hypertension,” which is a hypertensive disorder of pregnancy excluding preexisting maternal chronic hypertension during the offspring’s gestation. After the original CPP protocol, pregnancy-related hypertension was characterized by the presence of a recorded systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg at any study visit during the index pregnancy and the development of at least one of the following after 24 weeks of gestation as determined by clinician observation and medical record review: systolic blood pressure 140 mmHg or higher or an increase of 30 mmHg or more above the usual level on at least two occasions at least 6 hours apart, diastolic blood pressure 90 mmHg or higher or an increase of 15 mmHg or more above the usual level on at least two occasions at least 6 hours apart, proteinuria of “significant degree” (+1 or more on a urine dipstick test, more

than “trace,” or more than 30 mg) on two or more successive days in the absence of a urinary tract infection, or persistent edema of the hands and face. The data did not allow us to disaggregate these symptoms into separate variables for disease subclassification. The study population was restricted to participants with mothers who had no underlying chronic hypertension at the time of pregnancy as determined by clinician observation, patient history, and medical record review.

Outcomes were self-reported. In the primary analysis, the outcome was offspring hypertension, manifested as nongestational hypertension in offspring men and women at any point during their lives or as hypertension during pregnancy in offspring women. Those who reported having hypertension diagnosed at least once by a health professional were considered to have hypertension. A secondary analysis for nongestational hypertension was performed to estimate the association between maternal pregnancy-related hypertension and offspring hypertension at a time other than during pregnancy. Offspring women who reported hypertension diagnosed only during pregnancy at the time of outcome assessment were excluded from this analysis. Participants lacking data on the exposure or outcome were excluded from all analyses.

A number of covariates that had the potential to predict the outcome or confound the relation between the exposure and the outcome were considered in this analysis. Covariate information was collected at the time of the index pregnancy or birth. Categorical covariates included sex, CPP study site (Boston, MA, or Providence, RI), maternal race (white, African American, or other), maternal parity before the pregnancy of interest (parous or not parous), maternal diabetes (ever or never), and twin gestation (yes or no). Maternal prepregnancy BMI was defined as weight divided by height squared. The maternal socioeconomic status variable was a composite index adapted from the U.S. Bureau of the Census based on yearly family income as well as educational level and occupation of the head of household.²² Linearity of the continuous variables was assessed by dividing each variable into bins of equal width, performing a logistic regression model that predicted the study outcome with indicator variables for each bin, and inspecting the step sizes of the bin variable beta coefficients. Linearity was not found for any of the continuous covariates; therefore, categorical variables were created for maternal age (younger than 20, 20–35, or 36 years or older), maternal BMI (lower than 23.0, 23.0–24.9, 25.0–29.9, or 30 or higher kg/m²), maternal history of smoking at the time of CPP study enrollment (ever smoked or never smoked), number of cigarettes smoked per day during the pregnancy (fewer than one, one to five, or six or more cigarettes/day; cut points were selected based on the associations reported from a study of smoking and preeclampsia that used CPP data²³), and maternal socioeconomic status (quartiles).

Logistic regression was used to estimate the association between maternal pregnancy-related hypertension and offspring hypertension later in life, with adjustment for potential confounders. Hypertensive offspring who reported having been prescribed anti-hypertensives and offspring with hypertension diagnosed but who were not prescribed antihypertensives were separately compared with offspring who reported never having hypertension diagnosed. Offspring with hypertension who reported having hypertension diagnosed at least twice and offspring who reported hypertension diagnosed only once were separately compared with offspring who reported never having hypertension diagnosed. Covariates that were predictive of offspring hypertension later in life (sex, maternal race, maternal BMI, maternal socioeconomic status, and twin gestation) were included in the final model, and maternal diabetes was included to reduce potential confounding by genetic predisposition to hypertension. Terms for birth weight (less than 2,500 g, 2,500–4,000 g, or more than 4,000 g) and preterm birth (less than 37 weeks or 37 weeks or more) were included in the multivariable model to determine if these factors would attenuate the

association between maternal pregnancy-related hypertension and offspring hypertension later in life. To achieve model convergence, maternal diabetes was removed from the multivariable models that assessed hypertension without antihypertensive prescription and hypertension diagnosed only once, and twin pregnancy was also removed from the models that assessed nongestational hypertension without antihypertensive prescription and nongestational hypertension diagnosed only once. The potential for effect measure modification between maternal pregnancy-related hypertension and offspring hypertension later in life by sex was evaluated with an interaction term. The analyses were performed with SAS.9.1 for Windows. All results from logistic regression models were adjusted for correlations arising within sibling sets by the GENMOD procedure in SAS with an exchangeable correlation structure.²⁴

RESULTS

Of the 1,625 NEFS cohort members, 33 (2.0%) were excluded because of missing exposure information. Another 36 (2.2%) individuals were excluded because their mothers had chronic hypertension before the index pregnancy. Our study population comprised 1,556 cohort members, including 268 sibling pairs, 39 sibling trios, and four sibling quartets. The median age of participants was 39 years at the time of outcome assessment.

In this birth cohort, 98 (6.3%) offspring were born from pregnancies complicated by hypertension. The characteristics of the study population and their mothers at the time of pregnancy or delivery are summarized in Table 1. Individuals with mothers younger than 20 or older than 35 years at the time of the index birth were more likely to be born from pregnancies complicated by hypertension than those individuals with mothers aged 20 to 35 years. Pregnancy-related hypertension occurred less frequently when maternal prepregnancy BMI was less than 23. Maternal race, maternal diabetes status, and twin gestation were not significantly associated with pregnancy-related hypertension. Individuals born from pregnancies complicated by hypertension were more likely to weigh less than 2,500 g or more than 4,000 g at birth and were more likely to be born preterm than those born from pregnancies not complicated by hypertension; however, these associations were not significant.

There were 264 offspring (17.0%) who reported that hypertension was ever diagnosed by a health professional. The age at first diagnosis of hypertension ranged from 10 to 43 years, with a median age of 34 years. The risk of being prescribed antihypertensives was 8.8% among unexposed individuals, whereas it was 17.4% among exposed individuals. Compared with unexposed individuals, the odds of being prescribed antihypertensives compared with never having hypertension diagnosed were 2.16-times higher among offspring born from pregnancies complicated by hypertension (Table 2; 95% confidence interval [CI] 1.20–3.90). After adjustment for sex, maternal race, maternal BMI, maternal socioeconomic status, maternal diabetes, and twin pregnancy, the estimate was attenuated slightly (odds ratio [OR] 1.88, 95% CI 1.00–3.55). The interaction term for sex and maternal pregnancy-related hypertension was not significant (two-sided $P=.21$). When birth weight categories were included in the multivariable model, the relation between maternal pregnancy-related hypertension and being prescribed antihypertensives fluctuated only slightly (OR 1.86, 95% CI 0.98–3.54). When preterm birth was added to the multivariable model, the estimates remained essentially unchanged (Table 2). Compared with unexposed individuals, the odds of having hypertension diagnosed without antihypertensives prescribed were 1.55-times higher among those born from pregnancies complicated by hypertension, after adjustment for sex, maternal race, maternal BMI, maternal socioeconomic status, and twin pregnancy; this estimate was not significant (95% CI 0.81–2.97).

Maternal pregnancy-related hypertension was associated with offspring hypertension diagnosed at least twice compared with never after adjustment for potential confounders (OR 1.87, 95% CI 1.06–3.29). No association was found between the exposure and hypertension diagnosed once (Table 2). Individuals who were born from pregnancies complicated by hypertension were more likely to have any hypertension (OR 1.73, 95% CI 1.06–2.83). Again, the interaction term for sex and the exposure were not significant (two-sided $P=.09$).

In the secondary analysis of nongestational hypertension, the sample size was reduced to 1,515 individuals because the 40 offspring women with hypertension diagnosed only during pregnancy and one who was missing this information were excluded. There were 223 participants (14.7%) who reported that a health professional had ever diagnosed hypertension at a time other than during pregnancy but who may have had hypertension diagnosed during pregnancy as well. Maternal pregnancy-related hypertension was significantly associated with offspring nongestational hypertension with antihypertensive prescriptions, even after adjustment for potential confounders (Table 3; adjusted OR 1.97, 95% CI 1.04–3.72). Maternal pregnancy-related hypertension was inversely associated with offspring nongestational hypertension without antihypertensive prescriptions; however, precision was low (Table 3).

The odds of nongestational hypertension diagnosed at least twice were 1.75-times higher among offspring born from pregnancies complicated by hypertension compared with those who were not (Table 3; 95% CI 0.98–3.13). After adjustment for potential confounders, the odds for any offspring nongestational hypertension were not significantly different for those born from pregnancies complicated by hypertension and those who were not (OR 1.49, 95% CI 0.86–2.57).

DISCUSSION

Adults who were born from pregnancies complicated by hypertension were more likely to report that they had ever been prescribed antihypertensives than those who were not, even after adjustment for maternal covariates. There was no evidence of effect modification by sex because the interaction terms were not significant.

Recently, Kajantie et al¹² reported that the risk of having hypertension later in life among individuals born from pregnancies complicated by severe pre-eclampsia was 1.5-times higher than that of those born after normotensive pregnancies. Unlike those of our analyses, these results did not account for several potentially important confounders such as maternal BMI, maternal socioeconomic status, maternal diabetes, and maternal hypertension.

Preterm birth and low and high birth weight occur more often in offspring born to women with hypertensive disorders of pregnancy.^{25–27} Low birth weight is associated with increased blood pressure during adulthood²⁸ and is a moderately well-established risk factor for hypertension²⁹ and cardiovascular disease later in life.³⁰ Furthermore, gestational age has been reported to be inversely associated with blood pressure in adulthood.^{31,32} Nevertheless, the association between the prenatal exposure and hypertension later in life was not attenuated by birth weight and preterm birth. Low birth weight and preterm delivery do not appear to be mechanistic explanations for the observed association. To speculate on a potential mechanism, oxidative stress associated with pre-eclampsia may cause epigenetic changes that result in a hypertensive phenotype later in life, or oxidative stress may alter the developing fetal vasculature. Future studies should compare brachial artery flow-mediated dilation and circulating markers of endothelial function in offspring born from pregnancies complicated by preeclampsia with that of offspring born after normotensive pregnancies. If

endothelial dysfunction is present in offspring born from pregnancies complicated by preeclampsia, it could serve as a potential mechanistic link between in utero exposure to hypertensive disorders of pregnancy and hypertension in offspring.

Of course, the association between maternal pregnancy-related hypertension and hypertension later in life could be explained by genetics. Family history of cardiovascular disease and hypertension are risk factors for gestational hypertension and preeclampsia.^{33,34} Furthermore, family history of preeclampsia is a risk factor for preeclampsia in the next generation.³⁵ The results of the analysis that considered offspring hypertension with antihypertensive prescription did not differ greatly from the results in the context of nongestational hypertension. Because offspring women who had hypertension both during pregnancy and at a time other than during pregnancy could not be excluded from these analyses, genetic predisposition for gestational hypertension as an explanation for our results could not be ruled out.

A major limitation of our study is that pregnancy-related hypertension could not be disaggregated into gestational hypertension, preeclampsia, and eclampsia. These disorders have unique pathophysiology and confer differing levels of neonatal risk¹ and maternal coronary heart disease later in life.⁴ An additional limitation of this study was that random exposure misclassification may have biased the results toward the null.

Another important limitation is that outcomes were self-reported and were not verified by medical record; therefore, outcome misclassification was probable. It is possible that participants who were born from pregnancies complicated by hypertension were more likely to know their true hypertensive status because they were more likely to have had a family history of hypertension. If present, we would anticipate that differential misclassification would have been minor. Martin et al³⁶ investigated the validity of self-reported diagnosis of hypertension with medical records among adults and found that self-reported health professional diagnosis of hypertension (ever compared with never) had a sensitivity of 83.3 and a specificity of 88.8.

The power to detect effect modification was limited in our study; therefore, future studies should still consider an interaction between sex and maternal pregnancy-related hypertension. Also, future studies should investigate modification of the association between maternal pregnancy-related hypertension and cardiovascular disease in offspring by preeclampsia among offspring women.

A major strength of this study is that documentation of maternal pregnancy-related hypertension and maternal factors was collected at baseline, on average more than 39 years before outcome assessment. This study design preempted recall bias and provided us with an opportunity to reduce confounding by several maternal factors.

The observed association between maternal pregnancy-related hypertension and offspring hypertension later in life could reflect residual confounding, a genetic predisposition to hypertensive disorders, an in utero programming effect, or a combination of these possibilities. Although shared genetics may explain the association, future studies should investigate the possibility of a causal relation between intrauterine exposure to preeclampsia and hypertension later in life by controlling for family history of hypertension and cardiovascular disease through sibling pair analysis.

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References

1. Roberts JM, Pearson G, Cutler J, Lindheimer M. NHLBI Working Group on Research on Hypertension During Pregnancy. Summary of the NHLBI Working Group on Research on Hypertension During Pregnancy. *Hypertension*. 2003; 41:437–45. [PubMed: 12623940]
2. Wilson BJ, Watson MS, Prescott GJ, Sunderland S, Campbell DM, Hannaford P, et al. Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study. *BMJ*. 2003; 326:845–9. [PubMed: 12702615]
3. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. *Lancet*. 2005; 366:1797–803. [PubMed: 16298217]
4. Wikstrom AK, Haglund B, Olovsson M, Lindeberg SN. The risk of maternal ischaemic heart disease after gestational hypertensive disease. *BJOG*. 2005; 112:1486–91. [PubMed: 16225567]
5. Smith GC, Pell JP, Walsh D. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study of 129,290 births. *Lancet*. 2001; 357:2002–6. [PubMed: 11438131]
6. Bellamy L, Casas JP, Hingorani AD, Williams DJ. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ*. 2007; 335:974–7. [PubMed: 17975258]
7. Palti H, Rothschild E. Blood pressure and growth at 6 years of age among offsprings of mothers with hypertension of pregnancy. *Early Hum Dev*. 1989; 19:263–9. [PubMed: 2806155]
8. Seidman DS, Laor A, Gale R, Stevenson DK, Mashiach S, Danon YL. Pre-eclampsia and offspring's blood pressure, cognitive ability and physical development at 17-years-of-age. *Br J Obstet Gynaecol*. 1991; 98:1009–14. [PubMed: 1751432]
9. Vatten LJ, Romundstad PR, Holmen TL, Hsieh CC, Trichopoulos D, Stuver SO. Intrauterine exposure to preeclampsia and adolescent blood pressure, body size, and age at menarche in female offspring. *Obstet Gynecol*. 2003; 101:529–33. [PubMed: 12636958]
10. Tenhola S, Rahiala E, Halonen P, Vanninen E, Voutilainen R. Maternal preeclampsia predicts elevated blood pressure in 12-year-old children: evaluation by ambulatory blood pressure monitoring. *Pediatr Res*. 2006; 59:320–4. [PubMed: 16439600]
11. Oglænd B, Forman MR, Romundstad PR, Nilsen ST, Vatten LJ. Blood pressure in early adolescence in the offspring of preeclamptic and normotensive pregnancies. *J Hypertens*. 2009; 27:2051–4. [PubMed: 19609220]
12. Kajantie E, Eriksson JG, Osmond C, Thornburg K, Barker DJ. Pre-eclampsia is associated with increased risk of stroke in the adult offspring: the Helsinki birth cohort study. *Stroke*. 2009; 40:1176–80. [PubMed: 19265049]
13. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. *BMJ*. 2005; 330:565–7. [PubMed: 15743856]
14. Bodnar LM, Ness RB, Markovic N, Roberts JM. The risk of preeclampsia rises with increasing prepregnancy body mass index. *Ann Epidemiol*. 2005; 15:475–82. [PubMed: 16029839]
15. Silva LM, Coolman M, Steegers EA, Jaddoe VW, Moll HA, Hofman A, et al. Low socioeconomic status is a risk factor for preeclampsia: the Generation R Study. *J Hypertens*. 2008; 26:1200–8. [PubMed: 18475158]
16. Roberts JM, Cooper DW. Pathogenesis and genetics of pre-eclampsia. *Lancet*. 2001; 357:53–6. [PubMed: 11197372]
17. Verma S, Anderson TJ. Fundamentals of endothelial function for the clinical cardiologist. *Circulation*. 2002; 105:546–9. [PubMed: 11827916]

18. Davignon J, Ganz P. Role of endothelial dysfunction in atherosclerosis. *Circulation*. 2004; 109:III27–32. [PubMed: 15198963]
19. Chambers JC, Fusi L, Malik IS, Haskard DO, De Swiet M, Kooner JS. Association of maternal endothelial dysfunction with preeclampsia. *JAMA*. 2001; 285:1607–12. [PubMed: 11268269]
20. Niswander, K. The women and their pregnancies. Washington (DC): Government Printing Office; 1972.
21. Gilman SE, Martin LT, Abrams DB, Kawachi I, Kubzansky L, Loucks EB, et al. Educational attainment and cigarette smoking: a causal association? *Int J Epidemiol*. 2008; 37:615–24. [PubMed: 18180240]
22. Myrionthopoulos NC, French KS. An application of the U.S. Bureau of the Census socioeconomic index to a large, diversified patient population. *Soc Sci Med*. 1968; 2:283–99. [PubMed: 5760819]
23. Zhang J, Klebanoff MA, Levine RJ, Puri M, Moyer P. The puzzling association between smoking and hypertension during pregnancy. *Am J Obstet Gynecol*. 1999; 181:1407–13. [PubMed: 10601921]
24. Fitzmaurice, GM.; Laird, NM.; Ware, JM. Applied longitudinal analysis. Hoboken (NJ): John Wiley & Sons, Inc; 2004.
25. Ananth CV, Peedicayil A, Savitz DA. Effect of hypertensive diseases in pregnancy on birthweight, gestational duration, and small-for-gestational-age births. *Epidemiology*. 1995; 6:391–5. [PubMed: 7548347]
26. Rey E, Couturier A. The prognosis of pregnancy in women with chronic hypertension. *Am J Obstet Gynecol*. 1994; 171:410–6. [PubMed: 8059820]
27. Xiong X, Demianczuk NN, Buekens P, Saunders LD. Association of preeclampsia with high birth weight for age. *Am J Obstet Gynecol*. 2000; 183:148–55. [PubMed: 10920323]
28. Davies AA, Smith GD, May MT, Ben-Shlomo Y. Association between birth weight and blood pressure is robust, amplifies with age, and may be underestimated. *Hypertension*. 2006; 48:431–6. [PubMed: 16880348]
29. Bergvall N, Iliadou A, Johansson S, de Faire U, Kramer MS, Pawitan Y, et al. Genetic and shared environmental factors do not confound the association between birth weight and hypertension: a study among Swedish twins. *Circulation*. 2007; 115:2931–8. [PubMed: 17515462]
30. Barker DJ. The developmental origins of adult disease. *J Am Coll Nutr*. 2004; 23:588S–95S. [PubMed: 15640511]
31. Johansson S, Iliadou A, Bergvall N, Tuvemo T, Norman M, Cnattingius S. Risk of high blood pressure among young men increases with the degree of immaturity at birth. *Circulation*. 2005; 112:3430–6. [PubMed: 16301344]
32. Siewert-Delle A, Ljungman S. The impact of birth weight and gestational age on blood pressure in adult life: a population-based study of 49-year-old men. *Am J Hypertens*. 1998; 11(Pt 1):946–53. [PubMed: 9715787]
33. Ness RB, Markovic N, Bass D, Harger G, Roberts JM. Family history of hypertension, heart disease, and stroke among women who develop hypertension in pregnancy. *Obstet Gynecol*. 2003; 102:1366–71. [PubMed: 14662228]
34. Qiu C, Williams MA, Leisenring WM, Sorensen TK, Frederick IO, Dempsey JC, et al. Family history of hypertension and type 2 diabetes in relation to preeclampsia risk. *Hypertension*. 2003; 41:408–13. [PubMed: 12623936]
35. Skjaerven R, Vatten LJ, Wilcox AJ, Ronning T, Irgens LM, Lie RT. Recurrence of pre-eclampsia across generations: exploring fetal and maternal genetic components in a population based cohort. *BMJ*. 2005; 331:877–9. [PubMed: 16169871]
36. Martin LM, Leff M, Calonge N, Garrett C, Nelson DE. Validation of self-reported chronic conditions and health services in a managed care population. *Am J Prev Med*. 2000; 18:215–8. [PubMed: 10722987]

Table 1**Baseline Characteristics by Exposure Status**

Variable	Maternal Pregnancy-Related Hypertension	No Maternal Pregnancy-Related Hypertension
Sex		
Female	55 (56.1)	867 (59.5)
Male	43 (43.9)	591 (40.5)
Maternal race		
White	85 (86.7)	1,262 (86.6)
African American	13 (13.3)	186 (12.8)
Other	0 (0.0)	10 (0.7)
Maternal age (y)		
Younger than 20	20 (20.4)	259 (17.8)
20–35	67 (68.4)	1,114 (76.4)
36 or older	11 (11.2)	85 (5.8)
Maternal prepregnancy BMI		
Lower than 23	34 (34.7)	795 (54.5)
23.0–24.9	16 (16.3)	235 (16.1)
25.0–29.9	15 (15.3)	200 (13.7)
30 or higher	16 (16.3)	61 (4.2)
Maternal SES (percentile) *		
0–25th	31 (31.6)	386 (26.5)
26th–50th	19 (19.4)	322 (22.1)
51st–75th	19 (19.4)	311 (21.3)
76th–100th	27 (27.6)	380 (26.1)
Previous pregnancy		
Yes	72 (73.5)	1,118 (76.7)
No	26 (26.5)	340 (23.3)
Maternal diabetes *		
Ever	2 (2.0)	16 (1.1)
Never	96 (98.0)	1,436 (98.5)
Maternal smoking history *		
Ever	47 (48.0)	979 (67.2)
Never	50 (51.0)	440 (30.2)
Maternal smoking during pregnancy (cigarettes/d) *		
Fewer than 1	51 (52.0)	460 (31.6)
1–5	17 (17.4)	400 (27.4)
6 or more	29 (29.6)	559 (38.3)
Site of CPP registration		
Providence, RI	55 (56.1)	762 (52.3)
Boston, MA	43 (43.9)	696 (47.7)
Twin pregnancy		

Variable	Maternal Pregnancy-Related Hypertension	No Maternal Pregnancy-Related Hypertension
Yes	4 (4.1)	41 (2.8)
No	94 (95.9)	1,417 (97.2)
Birth weight (g)		
Less than 2,500	9 (9.2)	117 (8.0)
2,500–4,000	80 (81.6)	1,239 (85.0)
More than 4,000	9 (9.2)	102 (7.0)
Gestational age at birth (wk) *		
Less than 37	10 (10.2)	115 (7.9)
37 or more	88 (89.8)	1,338 (91.8)

BMI, body mass index; SES, socioeconomic status; CPP, Collaborative Perinatal Project.

Data are n (%).

* Percentages do not add up to 100 because of missing covariate values.

Table 2**Association Between Maternal Pregnancy-Related Hypertension and Offspring Hypertension Later in Life**

Outcome	Cases	Sample Size	Univariable	Multivariable
Hypertension with antihypertensive Rx [*]	133	1,425	2.16 (1.20–3.90)	1.88 (1.00–3.55)
Additional terms				
Birth weight	133	1,425	—	1.86 (0.98–3.54)
Preterm birth [†]	133	1,421	—	1.87 (0.99–3.53)
Hypertension without antihypertensive Rx [‡]	129	1,421	1.61 (0.85–3.06)	1.55 (0.81–2.97)
Hypertension diagnosed at least twice [*]	177	1,469	2.17 (1.27–3.70)	1.87 (1.06–3.29)
Hypertension diagnosed only once [‡]	87	1,379	1.30 (0.55–3.03)	1.17 (0.50–2.74)
Any hypertensive disorder [*]	264	1,556	1.91 (1.20–3.05)	1.73 (1.06–2.83)

Rx, prescription.

Data are n or odds ratio (95% confidence interval).

Any hypertensive disorder is defined by self-report of having hypertension diagnosed at least once.

Univariable and multivariable results are adjusted for correlation between siblings.

^{*} Multivariable odds ratio and 95% confidence interval are adjusted for sex, maternal race, maternal body mass index, maternal socioeconomic status, maternal diabetes, and twin pregnancy.

[†] Four participants were excluded from this analysis because of missing preterm birth data.

[‡] Multivariable odds ratio and 95% confidence interval are adjusted for sex, maternal race, maternal body mass index, maternal socioeconomic status, and twin pregnancy.

Table 3

Association Between Maternal Pregnancy-Related Hypertension and Offspring Nongestational Hypertension Later in Life

Outcome	Cases	Sample Size	Univariable	Multivariable
Nongestational hypertension with antihypertensive Rx [*]	127	1,419	2.29 (1.27–4.11)	1.97 (1.04–3.72)
Nongestational hypertension without antihypertensive Rx [†]	96	1,388	0.94 (0.37–2.40)	0.84 (0.32–2.20)
Nongestational hypertension diagnosed at least twice [*]	160	1,452	2.03 (1.17–3.55)	1.75 (0.98–3.13)
Nongestational hypertension diagnosed only once [†]	63	1,355	0.86 (0.26–2.81)	0.76 (0.22–2.57)
Any nongestational hypertensive disorder [*]	223	1,515	1.69 (1.01–2.83)	1.49 (0.86–2.57)

Rx, prescription.

Data are n or odds ratio (95% confidence interval).

Any hypertensive disorder is defined by self-report of having hypertension diagnosed at least once.

Univariable and multivariable results are adjusted for correlation between siblings.

^{*} Multivariable odds ratio and 95% confidence interval are adjusted for sex, maternal race, maternal body mass index, maternal socioeconomic status, maternal diabetes, and twin pregnancy.

[†] Multivariable odds ratio and 95% confidence interval are adjusted for sex, maternal race, maternal body mass index, and maternal socioeconomic status.