Published in final edited form as:

BJOG. 2017 September; 124(10): 1606–1613. doi:10.1111/1471-0528.14556.

# Moderately Elevated Blood Pressure During Pregnancy and Odds of Hypertension Later in Life: The POUCHmoms Longitudinal Study

Galit Levi Dunietz, PhD, MPH, MA<sup>†,1</sup>, Kelly L. Strutz, PhD, MPH<sup>†,2</sup>, Claudia Holzman, DVM, MPH, PhD<sup>3</sup>, Yan Tian, MS<sup>3</sup>, David Todem, MSPH, PhD<sup>3</sup>, Bertha L. Bullen, PhD<sup>3</sup>, and Janet M. Catov, PhD, MS<sup>4</sup>

<sup>1</sup>Department of Neurology and Sleep Disorders Center, University of Michigan, Ann Arbor, Michigan, USA

<sup>2</sup>Department of Public Health, Grand Valley State University, Grand Rapids, Michigan, USA

<sup>3</sup>Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan, USA

<sup>4</sup>Departments of Obstetrics, Gynecology & Reproductive Sciences and of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

# **Abstract**

**Objective**—Hypertensive disorders in pregnancy signal an increased risk of cardiovascular disease for women. However, future hypertension risk among pregnant women with moderately elevated blood pressure (BP) is unknown. We examined associations among moderately elevated BP or hypertensive disorders during pregnancy and later prehypertension or hypertension.

**Design**—Longitudinal cohort study.

**Setting**—Five communities in Michigan, USA.

**Sample**—Data are from pregnant women enrolled in the Pregnancy Outcomes and Community Health Study. We included 667 women with gestational BP measurements who participated in the POUCHmoms Study follow-up 7-15 years later.

Corresponding Author: Kelly L. Strutz, PhD, MPH, Assistant Professor, Department of Public Health, Grand Valley State University, 545 Michigan St NE, Suite 300, Grand Rapids, Michigan, 49503, USA. Phone: 616-331-5536. Fax: 616-331-5550. kelly\_strutz@gvsu.edu.

†Contributed equally as first author

**Disclosure of Interests:** All authors declare that they have no conflicts of interest.

The ICMJE disclosure forms are available as online supporting information.

**Contribution to Authorship:** GLD originated the idea for this specific project, and GLD and KLS designed this project with input from CH and JMC. CH, BLB, and JMC contributed to the design of the POUCH and POUCHmoms Studies and the acquisition of the data. DT contributed to the development of the analytic plan and interpretation of results. GLD, KLS, and YT analyzed the data. GLD and KLS drafted the article. All authors reviewed and revised the drafts and approved the final version of the manuscript.

**Details of Ethics Approval:** The original POUCH Study was approved by institutional review boards at Michigan State University, the Michigan Department of Community Health, and 9 community hospitals, while the POUCHmoms Study was approved by the institutional review boards at Michigan State University and the University of Pittsburgh.

**Methods**—Moderately elevated BP was defined as two measures of systolic BP 120 mmHg or diastolic BP 80 mmHg among women without a hypertensive disorder. Weighted multinomial logistic regression models estimated odds of prehypertension or hypertension at follow-up, adjusted for maternal confounders and time to follow-up.

**Main Outcome Measures**—Prehypertension or hypertension.

**Results**—Women meeting the moderately elevated BP criteria (64%) had significantly higher odds of hypertension at follow-up (adjusted odds ratio =2.6; 95% confidence interval: 1.2-5.5). These increased odds were observed for moderately elevated BP first identified before or after 20 weeks, and for elevated systolic BP alone or combined with elevated diastolic BP.

**Conclusions**—Moderately elevated BP in pregnancy may be a risk factor for future hypertension. Pregnancy offers an opportunity to identify women at risk for hypertension who may not have been identified otherwise.

## **Keywords**

hypertension; prehypertension; blood pressure; systolic pressure; diastolic pressure; pregnancy

# Introduction

Hypertension (HTN), defined as systolic blood pressure (BP) 140 mmHg and/or diastolic BP 90 mmHg, is prevalent among 30% of the adult population in the US and England. HTN is an established risk factor for subsequent cardiovascular and renal diseases, and contributes to more cardiovascular (CVD) events in women compared to men. He addition, prehypertension (preHTN), defined as systolic BP of 120-139 mmHg and/or diastolic BP of 80-89, is a recognized risk factor for subsequent CVD. He for the systolic BP of 80-89, is a recognized risk factor for subsequent CVD.

Normal pregnancy may be a "stress test" for the mother, bringing with it numerous physiologic changes including increased cardiac output and blood volume with BP changes. <sup>10</sup> BP remains at approximately the same level from pre-pregnancy through the end of the first trimester, after which it drops. <sup>10-12</sup> It increases again in the latter part of the second trimester and continues to increase until the birth. Pregnancy-onset hypertension and preeclampsia are characterized by BP 140 mmHg systolic or 90 mmHg diastolic on two occasions after 20 weeks of gestation, with preeclampsia also including presence of proteinuria, or severe features. <sup>13, 14</sup> Chronic hypertension is diagnosed as BP 140 mmHg systolic or 90 mmHg diastolic prior to pregnancy or before 20 weeks gestation with failure to resolve postpartum. <sup>14</sup> Prevalence of these disorders, collectively known as hypertensive disorders of pregnancy (HDP), ranges from 5-10%. <sup>15</sup> However, there are no existing criteria for prehypertension during pregnancy and the long-term maternal risks associated with moderate BP elevation are unknown.

In addition to their association with adverse birth outcomes, HDP also carry long term risks for HTN and CVD. <sup>16, 17</sup> HDP have been consistently associated with increased risk of future HTN and CVD-related mortality. <sup>18-20</sup> It is not known whether risk of later-life HTN is also increased by moderately elevated BP that does not meet the diagnostic criteria for a hypertensive disorder. Therefore, our objective was to investigate the risk of later preHTN

and HTN among women with moderately elevated BP in pregnancy in addition to those diagnosed with HDP. Further, we examined whether type (i.e., elevated systolic, diastolic, or both) and timing of moderately elevated BP were differentially associated with later HTN status.

# **Methods**

# **Study Design and Analytic Sample**

We used data from the subcohort of the Pregnancy Outcomes and Community Health (POUCH) Study<sup>21</sup>. A flowchart of study participants for the current analyses is shown in Figure 1. Designed to examine pathways leading to preterm delivery, the initial POUCH Study enrolled 3,019 pregnant women from 1998-2004 receiving prenatal care from 52 clinics in five Michigan communities. Inclusion criteria were maternal age of at least 15 years, singleton pregnancies with no known congenital anomalies, a prenatal maternal serum alpha-fetoprotein (MSAFP) measure between 15 and 22 weeks' gestation, no diabetes mellitus, and competency in English. A subcohort of 1,371 participants was created to collect more detailed information and biological samples. This subcohort included all those delivering preterm (<37 weeks' gestation) or with elevated MSAFP (>2 multiples of the median), and a random sample of those delivering at term with normal MSAFP in which African-American participants were oversampled. In all analyses sampling weights are used to account for the cohort and subcohort sampling strategy. Detailed investigations of biological samples collected at mid-pregnancy and delivery and medical record abstractions were conducted for the subcohort only, and these women were the focus of follow-up studies.

POUCHmoms, the most recent follow-up study of the subcohort, was designed to examine early evidence of CVD 7-15 years after the POUCH Study pregnancy; we hypothesized that pregnancy complications reveal underlying predispositions to CVD. The POUCHmoms follow-up included an in-person interview along with measures of blood pressure, heart rate variability, anthropometrics, carotid ultrasound scans, and collection of fasting blood samples for atherogenic biomarkers. A total of 678 participants from the original subcohort completed this protocol from 2011-2014. Our analytic sample excluded 11 POUCHmoms Study participants who were missing BP measurements during pregnancy. Study procedures were undertaken with the understanding and appropriate informed consent of each participant.

# Measures

**Hypertensive status in pregnancy**—Eight BP measurements during the POUCH Study pregnancy, along with the measurement dates, were abstracted from the medical record and used for this analysis. These were the two highest systolic blood pressures (SBP) recorded *before* 20 weeks' gestation, the two highest diastolic blood pressures (DBP) recorded *before* 20 weeks' gestation, the two highest systolic blood pressures (SBP) recorded *at or after* 20 weeks' gestation and the two highest diastolic blood pressures (DBP) recorded *at or after* 20 weeks' gestation.

We categorized a participant as having moderately elevated BP if at least two of her highest SBP readings were at or above 120 mmHg or at least two of her highest DBP readings were at or above 80 mmHg and she did not have HDP (described below). The moderately elevated BP group was further subdivided by whether the elevation was in SBP only, DBP only, or both. There were only two participants with elevated DBP and normal SBP, therefore, this group was too small to analyze separately. These women were removed from analyses subdivided by type of elevation. In addition, the moderately elevated BP group was subdivided by gestational week when moderately elevated BP was first identified, i.e. < 20 weeks', 20 weeks' gestation. Approximately 26% of the total moderately elevated BP group had one (but not two) BP measure of 140 systolic or 90 diastolic and did not meet the definition of HDP.

Hypertensive disorder information was derived from medical chart reviews. For these analyses, participants were categorized with HDP if they were explicitly diagnosed with any hypertensive disorder (preeclampsia/eclampsia, pregnancy-induced hypertension, chronic hypertension) or met the criteria for any of these disorders on two separate calendar days. Preeclampsia and pregnancy-induced hypertension were defined as BP 140 mmHg systolic or 90 mmHg diastolic on two occasions after 20 weeks of gestation, with preeclampsia requiring presence of proteinuria. Chronic hypertension was defined as BP 140 mmHg systolic or 90 mmHg diastolic prior to pregnancy or before 20 weeks' gestation on two separate occasions. Women who did not have HDP or chronic hypertension and did not meet our criteria for moderately elevated BP were classified as normotensive (referent group).

Participants with a history of hypertensive medication use were classified with chronic hypertension. All models were rerun with chronic hypertensive participants (n=26) removed from the HDP group. The results did not differ, so the chronic hypertensive participants were retained in the final sample.

Hypertensive status and blood pressure at follow-up—As recommended in the Joint National Committee (JNC7) guidelines<sup>5</sup>, three consecutive BP measurements were made, one minute apart, at the POUCHmoms Study visit. Trained research assistants, who were registered nurses or ultrasonographers with experience in BP measurement, measured BP seated with the arm extended level to the heart, using either a Panasonic EW3109W (Panasonic Corp., Newark, NJ) or an Omron Hem-907 (Omron Healthcare, Inc., Lake Forest, IL) monitor with a small, medium, or large cuff as appropriate. Both digital monitors were compared with manual readings and with each other prior to data collection to ensure that readings were comparable. We averaged the second and third of these blood pressure recordings for our measure. We categorized hypertensive status at the POUCHmoms Study follow-up according to the JNC criteria. Thus, participants with SBP below 120 mmHg and DBP below 80 mmHg were classified as normotensive, those with SBP between 120-139 mmHg or with DBP between 80-89 mmHg were classified with preHTN, and those with SBP 140 mmHg or DBP 90 mmHg or using antihypertensive medications were classified with HTN.

**Covariates**—Potential confounders were variables known to be associated with HTN during and/or after pregnancy. These included race/ethnicity (dichotomized as African-

American vs. white or other), pre-pregnancy body mass index (BMI; defined as weight in kilograms divided by the square of height in meters and modeled as continuous), age (continuous) and parity (categorized as 0, 1, or 2+) at the time of the POUCH Study pregnancy, Medicaid insurance coverage at the time of the POUCH Study pregnancy as an indicator of socioeconomic status (dichotomized as yes or no), and the time between the POUCH Study pregnancy and follow-up (continuous, in years). Race/ethnicity, pre-pregnancy BMI, and Medicaid status also were tested as potential effect modifiers. BMI at follow-up (continuous) was evaluated as a potential intermediary variable or effect modifier.

## **Statistical Analyses**

We used univariate and bivariate descriptive statistics to examine variable distributions overall and across categories of hypertensive status during pregnancy and follow-up. Differences by hypertensive status were assessed with Chi-square tests; p<0.05 was considered statistically significant. Multinomial logistic regression models produced crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for preHTN and HTN at follow-up for each prenatal BP category, with normotensive as the referent category at both time points. Differences among the prenatal BP categories were tested with contrast statements. These models were run with and without BMI at follow-up, and were repeated by type and timing of moderately elevated BP. Effect modification was tested with interaction terms; none was significant and therefore they were excluded from the final models.

All analyses were run with the survey procedures in SAS v9.3 (SAS Institute Inc., Cary, NC) to incorporate the original POUCH Study sampling design and weighting. These weights accounted for the oversampling of participants delivering preterm, with elevated MSAFP and of African-American race. For example, in the POUCHmoms Study follow-up analyses, each woman remained in her POUCH Study stratum (e.g. white non-Hispanic, normal MSAFP, preterm) for the purpose of calculating sampling weights, thereby maintaining the appropriate proportionality (from the original population) of each stratum to the total follow-up sample (denominator of 667 for these analyses). The weights were not altered to account for loss-to-follow-up in the POUCHmoms Study. However, a sensitivity analysis was conducted with the unweighted data to determine whether conclusions would differ between weighted and unweighted analyses.

# Results

Characteristics of the analytic sample are compared to those of the remaining POUCH Study subcohort participants in Supplemental Table S1. The follow-up sample was more highly educated, less likely to have received Medicaid insurance at pregnancy, more likely to be of white or other race/ethnicity, and more likely to have come from the Lansing community. However, pre-pregnancy BMI, preterm delivery, delivery of a small for gestational age infant, and prenatal BP categories did not differ between women in the follow-up study and those not followed.

Maternal and pregnancy characteristics by HTN status at follow-up are displayed in Table 1. White/other women were more likely to be classified as normotensive at follow-up

compared to African-American women (60% compared to 44%). Mean BMI, both prepregnancy and at follow-up, and mean maternal age at both enrollment and follow-up displayed positive linear associations with HTN status at follow up, although age at enrollment was only borderline significant. Parity and Medicaid enrollment in pregnancy did not vary across HTN groups. Similarly, for all study groups the observed mean number of years from the POUCH Study birth to re-enrollment into the POUCHmoms Study, approximately 11 years, was not associated with HTN. Finally, HTN status at follow-up differed by HTN status in pregnancy: of the normotensive in pregnancy group, 64% were normotensive at follow-up, 28% had preHTN and only 9% met HTN criteria; among the group with moderately elevated BP in pregnancy, 59% were normotensive at follow-up, while 22% and 13% had preHTN and HTN, respectively; in the HDP group, 24% were normotensive later in life, 32% had preHTN and 43% had HTN. The maternal and pregnancy characteristics by HTN status in pregnancy can be seen in Supplemental Table S2.

Multinomial logistic regression results are shown in Table 2. Women with moderately elevated BP in pregnancy had significantly increased odds of HTN at follow-up in the crude model (Section A, Model 1: OR=2.4, 95% CI: 1.3, 4.6) and the model adjusted for pregnancy confounders (Model 2: OR=2.6, 95% CI: 1.2, 5.5) (Table 2). Adding BMI at follow-up to the adjusted model attenuated the OR slightly (Model 3: OR=2.3, 95% CI: 1.0, 5.1). Moderately elevated BP in pregnancy was not associated with follow-up preHTN in any models. As expected, HDP were positively associated with later preHTN and HTN; again BMI at follow-up modestly attenuated the effect estimates (Model 3: preHTN OR=2.5, 95% CI: 0.9, 6.6; HTN OR=13.7, 95% CI: 4.4, 42.9).

Results with moderately elevated BP in pregnancy divided by type and timing are shown in Table 2, Sections B and C, respectively. Moderately elevated SBP in pregnancy, alone and in combination with elevated DBP, significantly increased the odds of HTN at follow-up in most models (Section B). Early moderately elevated BP (<20 weeks' gestation) significantly increased the odds of HTN 3-4 fold at follow-up in all models (Section C). Late moderately elevated BP ( 20 weeks' gestation) was not statistically significantly associated with HTN at follow-up after controlling for BMI at follow-up, although it led to approximately double the odds of HTN in all models. The odds ratios for HTN at follow-up for early moderately elevated BP were significantly higher than those for later moderately elevated BP (p<0.05). The sensitivity analysis repeating all models with unweighted data produced similar results (Table S3).

# **Discussion**

# **Main Findings**

This prospective study followed pregnant women to examine their health status 7-15 years later. We found that moderately elevated BP in pregnancy is significantly associated with approximately 2 times the odds of future HTN. This is true whether SBP is elevated alone or in conjunction with elevated DBP. The observed association between moderately elevated BP and future HTN is larger when BP is elevated before 20 weeks' gestation, the gestational

cutpoint used for distinguishing chronic, pre-existing HTN from pregnancy-induced HTN, <sup>13, 14</sup> but is also seen when BP is elevated later.

# Strengths and Limitations

One limitation of this work is the differences in some characteristics between the POUCH Study subcohort participants followed versus not followed that could potentially lead to selection bias. However, it was reassuring that these differences did not occur based on pregnancy outcome (term vs preterm, small for gestational age) or on BP. In addition, the potential follow-up biases present (e.g. maternal education, Medicaid) applied equally to each of the sampling strata; therefore, our approach to using the original POUCH Study strata for calculating sampling weights did not appear to introduce additional follow-up bias. Instead, our weighting by race/ethnicity-specific strata helped to account for some of the differential in follow-up by race/ethnicity.

Additional limitations include that we were able to assess moderately elevated BP only in the POUCH Study pregnancies, without knowledge of whether it occurred in previous or later pregnancies as well. It is plausible that recurring moderately elevated BP is more indicative of later HTN risk; research in other cohorts will be necessary to test this hypothesis. We did not have measurements of pre-pregnancy BP to establish whether any participants had preHTN prior to pregnancy. However, it is worth noting that many women of reproductive age do not know this information themselves prior to entering prenatal care. Furthermore, our BP measurements in pregnancy were part of the participants' clinical care rather than standardized by a study protocol, and not all BP measurements were abstracted for the POUCH Study. Our follow-up BP categories were based on BP measured at one study visit; repeated BP measures over time might remove some intra-individual variability and provide more precise confidence limits.

Finally, given the age range of the participants at follow-up, our study was limited to examining early development of HTN and could not assess CVD-related events. However, the associations seen here between moderately elevated BP during pregnancy and HTN in young and middle-aged adults confirm the potential for identifying at-risk women earlier in their lives. Our follow-up period of 7-15 years is comparable to those of studies showing progression of preHTN to CVD outcomes in the general population. <sup>6-9</sup>

Despite these limitations, our study has several strengths. First, to our knowledge, it is the first to apply the preHTN criteria to a pregnant population to assess odds of later HTN. Second, the population represents a socioeconomically diverse community-based sample followed longitudinally. Third, both the POUCH Study and its POUCHmoms follow-up contain rich measures, including objective BP measurements that allow for deeper investigation of the mechanisms underlying the phenomena reported here.

### Interpretation

While our results confirm previous reports outside of pregnancy that elevated BP is associated with later life HTN,<sup>22-31</sup> our study is novel, as it applies the preHTN criteria used in the general population to pregnancy. Our findings extend studies of preHTN in the general population that demonstrate the importance of elevated SBP in progressing to HTN.<sup>23, 24</sup> It

had previously been assumed that only moderate to severe HDP presented a concern for maternal and infant health.<sup>29</sup> However, emerging evidence suggests that elevated BP among pregnant women without HDP is associated with increased risk of poor offspring health outcomes including fetal growth restriction and preterm delivery.<sup>32-35</sup> Our study extends these findings to an adverse maternal health outcome in later life.

Our data showing a stronger association between later HTN and moderately elevated BP before 20 weeks' gestation points to the first half of pregnancy as particularly revealing because it detects women with previously undiagnosed preHTN, and/or women who do not show the typical lowering of blood pressure in response to pregnancy-related physiological changes arising during these gestational weeks. Women in our sample with moderately elevated BP only after 20 weeks' gestation also had higher odds of HTN at follow-up, although the effect size was smaller. Women with later moderately elevated BP onset offer further evidence that pregnancy may unmask an increased risk of HTN in affected women who enter pregnancy with normotensive BP. Future research will be needed to shed greater light on these critical windows.

Given the physiological changes of pregnancy, it is not surprising that moderately elevated BP is highly prevalent in pregnancy when moderately elevated BP is defined by prehypertensive cutoffs used for non-pregnant populations. Our finding that 64% of women had moderately elevated BP in pregnancy suggests that our definition, parallel to the JNC7 definition of preHTN<sup>5</sup>, has high sensitivity but low specificity for predicting later HTN. It is surprising that there is no association between moderately elevated BP in pregnancy and later preHTN, given that preHTN is often on the pathway to hypertension. This null finding may reflect that moderately elevated BP is not a constant state, and repeated measures are needed to better identify women who truly belong in this category.

# Conclusion

In conclusion, we identified a significant association between moderately elevated BP in pregnancy and later HTN. This approach parallels that of the increasing recognition that pregnancy factors such as gestational weight gain have immediate consequences for perinatal outcomes as well as long-term impacts on maternal metabolic and cardiovascular health<sup>36</sup>. In future work, we will focus on further improving the prediction of later life HTN by considering gestational BP measurements alongside other biomarkers measured in pregnancy. Given that pregnancy represents a time of frequent contact between women and the health care system, our findings for moderately elevated BP suggest that prenatal care may be an effective time to identify women at risk of later HTN beyond identifying women with hypertensive disorders of pregnancy. Closer monitoring of women with gestational moderately elevated BP coupled with timely intervention may help curtail incidence of CVD among at risk women.

# **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

# **Acknowledgments**

None.

**Funding:** The POUCH Study was supported by the Perinatal Epidemiological Research Initiative Program Grant from the March of Dimes Foundation (20FY01-38 and 20FY04-37), the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development and the National Institute of Nursing Research (R01-HD34543), the Thrasher Research Foundation (02816-7), and the Centers for Disease Control and Prevention (U01-DP000143-01). The POUCHmoms Study was supported by the National Heart, Lung, and Blood Institute (R01-HL103825). Drs. Levi Dunietz and Strutz were funded by the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development (T32-HD046377).

# References

- Joffres M, Falaschetti E, Gillespie C, Robitaille C, Loustalot F, Poulter N, et al. Hypertension prevalence, awareness, treatment and control in national surveys from England, the USA and Canada, and correlation with stroke and ischaemic heart disease mortality: A cross-sectional study. BMJ Open. 2013; 3:e003423.
- 2. Santulli G. Epidemiology of cardiovascular disease in the 21st century: Updated numbers and updated facts. JCvD. 2013; 1:1–2.
- Cohen JD. Hypertension epidemiology and economic burden: Refining risk assessment to lower costs. Managed Care. 2009; 18:51–58.
- Cheng S, Claggett B, Correia AW, Shah AM, Gupta D, Skali H, et al. Temporal trends in the population attributable risk for cardiovascular disease: The atherosclerosis risk in communities study. Circulation. 2014:113.008506.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The seventh report
  of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood
  Pressure: The JNC 7 report. JAMA. 2003; 289:2560–2572. [PubMed: 12748199]
- Hsia J, Margolis KL, Eaton CB, Wenger NK, Allison M, Wu L, et al. Prehypertension and cardiovascular disease risk in the Women's Health Initiative. Circulation. 2007; 115:855–860.
   [PubMed: 17309936]
- Vasan RS, Larson MG, Leip EP, Evans JC, O'Donnell CJ, Kannel WB, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. N Engl J Med. 2001; 345:1291–1297.
   [PubMed: 11794147]
- 8. Guo X, Zhang X, Guo L, Li Z, Zheng L, Yu S, et al. Association between pre-hypertension and cardiovascular outcomes: A systematic review and meta-analysis of prospective studies. Curr Hypertens Rep. 2013; 15:703–716. [PubMed: 24234576]
- 9. Huang Y, Wang S, Cai X, Mai W, Hu Y, Tang H, et al. Prehypertension and incidence of cardiovascular disease: A meta-analysis. BMC Med. 2013; 11:177. [PubMed: 23915102]
- 10. Brown CM, Garovic VD. Mechanisms and management of hypertension in pregnant women. Curr Hypertens Rep. 2011; 13:338–346. [PubMed: 21656283]
- Macdonald-Wallis C, Lawlor DA, Fraser A, May M, Nelson SM, Tilling K. Blood pressure change in normotensive, gestational hypertensive, preeclamptic, and essential hypertensive pregnancies. Hypertension. 2012; 59:1241–1248. [PubMed: 22526257]
- 12. MacGillivray I, Rose GA, Rowe B. Blood pressure survey in pregnancy. Clin Sci. 1969; 37:395–407. [PubMed: 5358998]
- American College of Obstetricians and Gynecologists. ACOG practice bulletin: Diagnosis and management of preeclampsia and eclampsia. Int J Gynaecol Obstet. 2002; 77:67–75. [PubMed: 12094777]
- 14. Roberts JM, A P, Bakris G, Barton JR, Bernstein IM, Druzin M, Gaiser RR, Granger JP, Jeyabalan A, Johnson DD, Karumanchi S, Lindheimer M, Owens MY, Saade GR, Sibai BM, Spong CY, Tsigas E, Joseph GF, O'Reilly N, Politzer A, Son S, Ngaiza K. Hypertension in pregnancy: Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol. 2013; 122:1122–1131. [PubMed: 24150027]

15. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol. 2000; 183:S1–s22.

- 16. Garovic VD, Hayman SR. Hypertension in pregnancy: An emerging risk factor for cardiovascular disease. Nat Clin Pract Nephrol. 2007; 3:613–622. [PubMed: 17957198]
- Lykke JA, Langhoff-Roos J, Sibai BM, Funai EF, Triche EW, Paidas MJ. Hypertensive pregnancy disorders and subsequent cardiovascular morbidity and type 2 diabetes mellitus in the mother. Hypertension. 2009; 53:944–951. [PubMed: 19433776]
- 18. Rich-Edwards JW, Fraser A, Lawlor DA, Catov JM. Pregnancy characteristics and women's future cardiovascular health: An underused opportunity to improve women's health? Epidemiol Rev. 2014; 36:57–70. [PubMed: 24025350]
- Fraser A, Nelson SM, Macdonald-Wallis C, Cherry L, Butler E, Sattar N, et al. Associations of pregnancy complications with calculated cardiovascular disease risk and cardiovascular risk factors in middle age: The Avon Longitudinal Study of Parents and Children. Circulation. 2012; 125:1367–1380. [PubMed: 22344039]
- 20. Garovic VD, Bailey KR, Boerwinkle E, Hunt SC, Weder AB, Curb D, et al. Hypertension in pregnancy as a risk factor for cardiovascular disease later in life. Journal of Hypertension. 2010; 28:826. [PubMed: 20087214]
- 21. Holzman C, Bullen B, Fisher R, Paneth N, Reuss L. Pregnancy Outcomes and Community Health: The POUCH Study of Preterm Delivery. Paediatr Perinat Epidemiol. 2001; 15(Suppl 2):136–158. [PubMed: 11520406]
- 22. Egan BM, Lackland DT, Jones DW. Prehypertension: An opportunity for a new public health paradigm. Cardiol Clin. 2010; 28:561–569. [PubMed: 20937441]
- 23. Kurioka S, Horie S, Inoue A, Mafune K, Tsuda Y, Otsuji Y. Risk of progression to hypertension in nonhypertensive Japanese workers aged 20-64 years. J Hypertens. 2014; 32:236–244. [PubMed: 24419213]
- 24. Leitschuh M, Cupples LA, Kannel W, Gagnon D, Chobanian A. High-normal blood pressure progression to hypertension in the Framingham Heart Study. Hypertension. 1991; 17:22–27. [PubMed: 1986979]
- Redwine KM, Acosta AA, Poffenbarger T, Portman RJ, Samuels J. Development of hypertension in adolescents with pre-hypertension. J Pediatr. 2012; 160:98–103. [PubMed: 21868037]
- 26. Selassie A, Wagner CS, Laken ML, Ferguson ML, Ferdinand KC, Egan BM. Progression is accelerated from prehypertension to hypertension in blacks. Hypertension. 2011; 58:579–587. [PubMed: 21911708]
- Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: A cohort study. Lancet. 2001; 358:1682–1686. [PubMed: 11728544]
- 28. Winegarden CR. From "prehypertension" to hypertension? Additional evidence. Ann Epidemiol. 2005; 15:720–725. [PubMed: 15921930]
- Zhang H, Thijs L, Kuznetsova T, Fagard RH, Li X, Staessen JA. Progression to hypertension in the non-hypertensive participants in the Flemish Study on Environment, Genes and Health Outcomes. J Hypertens. 2006; 24:1719–1727. [PubMed: 16915020]
- 30. Allen NB, Siddique J, Wilkins JT, Shay C, Lewis CE, Goff DC, et al. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. JAMA. 2014; 311:490–497. [PubMed: 24496536]
- 31. Pletcher MJ, Bibbins-Domingo K, Lewis CE, Wei GS, Sidney S, Carr JJ, et al. Prehypertension during young adulthood and coronary calcium later in life. Ann Intern Med. 2008; 149:91–99. [PubMed: 18626048]
- 32. Fukushima K, Morokuma S, Tsukimori K, Murata M, Wake N. Blood pressure measurements within the JNC7 pre-hypertensive range after 32 weeks of gestation are a risk factor for decreased fetal growth. Hypertens Res. 2012; 35:128–130. [PubMed: 21918524]
- 33. Macdonald-Wallis C, Tilling K, Fraser A, Nelson SM, Lawlor DA. Associations of blood pressure change in pregnancy with fetal growth and gestational age at delivery: Findings from a prospective cohort. Hypertension. 2014; 64:36–44. [PubMed: 24821945]

34. Steer PJ, Little MP, Kold-Jensen T, Chapple J, Elliott P. Maternal blood pressure in pregnancy, birth weight, and perinatal mortality in first births: Prospective study. BMJ. 2004; 329:1312. [PubMed: 15561733]

- 35. Zhang J, Villar J, Sun W, Merialdi M, Abdel-Aleem H, Mathai M, et al. Blood pressure dynamics during pregnancy and spontaneous preterm birth. Am J Obstet Gynecol. 2007; 197:162.e161–166. [PubMed: 17689635]
- 36. Walter JR, Perng W, Kleinman KP, Rifas-Shiman SL, Rich-Edwards JW, Oken E. Associations of trimester-specific gestational weight gain with maternal adiposity and systolic blood pressure at 3 and 7 years postpartum. Am J Obstet Gynecol. 2015; 212:499.e491–412. [PubMed: 25446696]

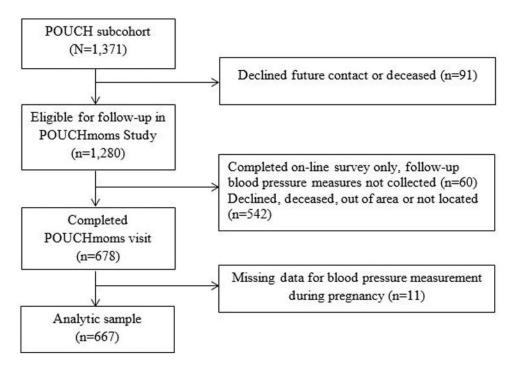


Figure 1. Flow Chart of Participants in the Pregnancy Outcomes and Community Health (POUCH) Study Followed in the POUCHmoms Study, 2011-2014

Dunietz et al.

Page 13

Table 1

Maternal Characteristics During Pregnancy and 7-15 Years Later by Hypertensive Status at Follow-up.

Characteristic Total N=667	Normotensive at Follow-Up n=366 (56%)	Prehypertensive at Follow-Up n=162 (24%)	Hypertensive at Follow-Up n=139 (19%)	P value
Race/ethnicity, n (%)				
White or other	256 (60)	98 (24)	70 (16)	
African-American	110 (44)	64 (27)	69 (29)	< 0.01
Parity at POUCH pregnancy, n (%)				
0	168 (59)	71 (25)	52 (16)	
1	124 (60)	49 (22)	44 (18)	
2+	74 (46)	42 (27)	43 (26)	0.11
Pre-pregnancy BMI, mean (range)	25.4 (16.2-50.4)	27.6 (16.3-52.1)	31.8 (17.3-60.4)	< 0.01
BMI at follow-up, mean (range)	28.6 (17.0-61.0)	32.8 (20.0-65.0)	37.3 (19.0-64.0)	< 0.01
Age at POUCH enrollment, mean (range)	26.2 (15.5-39.9)	26.5 (15.8-47.3)	27.9 (16.3-39.6)	0.05
Age at follow-up, mean (range)	37.4 (25.7-51.3)	38.0 (26.1-58.4)	39.3 (26.7-52.3)	0.02
Medicaid status in pregnancy, n (%)				
Yes	172 (51)	89 (26)	80 (23)	
No	194 (61)	73 (23)	59 (16)	0.07
Interval between birth and follow-up, mean (range), years	10.9 (7.7-14.7)	11.2 (7.7-15.1)	11.1 (8.0-14.7)	0.12
Blood pressure in pregnancy				
Normotensive	122 (64)	49 (28)	19 (9)	
Moderately-elevated BP	223 (59)	89 (22)	87 (13)	
Hypertensive disorder (HDP)	21 (24)	24 (32)	33 (43)	< 0.01

Note: all percentages and means are based on weighted data.

Abbreviations: %, weighted percent; BMI, body mass index; BP, blood pressure; HDP, hypertensive disorder of pregnancy; POUCH, Pregnancy Outcomes and Community Health.

**Author Manuscript** 

Table 2

The Relation between Blood Pressure in Pregnancy and Hypertensive Status at 7-15 Years Follow-up.

	Prehyp	Prehypertensive at Follow-Up (n=162)	(n=162)	Hyp	Hypertensive at Follow-Up (n=139)	n=139)
	Model 1: Unadjusted OR (95% CI)	Model 2: Adjusted OR <sup>ab</sup> (95% CI)	Model 3: Model 2 + BMI Adjusted OR <sup>a,c</sup> (95% CI)	Model 1: Unadjusted OR (95% CI)	Model 2: Adjusted OR <sup>a,b</sup> (95% CI)	Model 3: Model 2 + BMI Adjusted OR <sup>a,c</sup> (95% CI)
Section A: Blood pressure in pregnancy						
Normotensive (n=190)	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]
Moderately-elevated BP (n=399)	0.8 (0.5, 1.4)	0.8 (0.5, 1.4)	0.7 (0.4, 1.3)	2.4 (1.3, 4.6)	2.6 (1.2, 5.5)	2.3 (1.0, 5.1)
Hypertensive disorder (HDP; n=78)	3.0 (1.3, 7.1)	3.0 (1.2, 7.7)	2.5 (0.9, 6.6)	13.2 (5.3, 32.8)	16.3 (5.5, 49.0)	13.7 (4.4, 42.9)
Section B: Blood pressure in pregnancy by type of elevation $\boldsymbol{d}$						
Normotensive (n=190)	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]
Moderately-elevated, systolic only (n=156)	0.8 (0.4, 1.5)	0.8 (0.4, 1.5)	0.7 (0.4, 1.3)	2.1 (1.0, 4.6)	2.5 (1.1, 6.0)	2.3 (0.9, 5.7)
Moderately-elevated, both systolic and diastolic (n=241)	0.9 (0.5, 1.5)	0.8 (0.5, 1.5)	0.7 (0.4, 1.4)	2.7 (1.3, 5.3)	2.7 (1.2, 6.0)	2.4 (1.0, 5.5)
HDP (n=78)	3.0 (1.3, 7.1)	3.0 (1.2, 7.6)	2.5 (0.9, 6.6)	13.2 (5.3, 32.8)	16.4 (5.5, 49.3)	13.7 (4.4, 43.2)
Section C: Blood pressure in pregnancy by timing of elevation						
Normotensive (n=190)	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]	1 [Referent]
Moderately-elevated, early (<20 wk gestation; n=97)	0.9 (0.4, 1.9)	0.8 (0.3, 1.9)	0.7 (0.3, 1.7)	4.0 (1.8, 9.0)	3.4 (1.3, 9.0)	3.2 (1.2, 8.6)
Moderately-elevated, late ( 20 wk gestation; n=302)	0.8 (0.5, 1.4)	0.8 (0.5, 1.4)	0.7 (0.4, 1.3)	2.0 (1.0, 4.0)	2.4 (1.1, 5.3)	2.1 (0.9, 4.9)
HDP (n=78)	3.0 (1.3, 7.1)	3.0 (1.1, 7.7)	2.5 (0.9, 6.7)	13.2 (5.3, 32.8)	16.9 (5.6, 50.9)	14.2 (4.5, 44.8)

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; HDP, hypertensive disorder of pregnancy; OR, odds ratio; POUCH, Pregnancy Outcomes and Community Health.

 $<sup>^{\</sup>it a}$ Coefficients are based on weighted data.

 $<sup>^{</sup>b}$  Adjusted for race/ethnicity; pre-pregnancy BMI; age, parity, and Medicaid at pregnancy; and interval between birth and follow-up.

 $<sup>^{\</sup>mathcal{C}}$  Adjusted for all covariates listed above plus BMI at follow-up.

 $d_{\rm N}=665$  for these models, which exclude those with moderately-elevated diastolic BP only (n=2).