Published in final edited form as:

Menopause. ; 28(3): 255–262. doi:10.1097/GME.0000000000001739.

Impact of prior preterm or term small for gestational age birth on maternal blood pressure during the menopause transition in the Study of Women's Health Across the Nation

Yamnia I. Cortés, PhD, MPH, FNP¹, Maria Brooks, PhD², Emma Barinas-Mitchell, PhD², Karen A. Matthews, PhD^{2,3}, Rebecca C. Thurston, PhD^{2,3}, Janet M. Catov, PhD⁴

¹School of Nursing, The University of North Carolina at Chapel Hill, Chapel Hill, NC.

²Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA

³Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA.

⁴Departments of Obstetrics, Gynecology, and Reproductive Sciences and Epidemiology, University of Pittsburgh School of Medicine, Pittsburgh, PA; Department of Magee-Women's Research Institute, Pittsburgh, PA.

Abstract

Objective: To examine whether blood pressure (BP) accelerates more rapidly during the menopause transition for women with a history of preterm or term small for gestational age (SGA) delivery compared to women with all term and appropriate for gestational age (AGA) births.

Methods: A longitudinal analysis was conducted with 1008 parous women who had BP data at 2 study visits. We used generalized linear modelling to examine BP at before the final menstrual period, at the final menstrual period, and up to 10 years after the final menstrual period, according to pregnancy group. We assessed maternal changes in BP over time in relation to years near the final menstrual period using a piece-wise linear model, consistent with menopause-induced changes. Models were adjusted for socio-demographics, body mass index, smoking, physical activity, medications, parity, age at first birth, gestational diabetes, and gestational hypertension/preeclampsia.

Results: At baseline, women were on average 46 years old, 101 (10%) reported a prior preterm birth, and 102 (10.1%) reported a term SGA birth. Compared to women with all term AGA births, women with a term SGA birth had higher BP before the final menstrual period, at the final menstrual period, and up to 10 years after the final menstrual period; women with a preterm birth

---

Corresponding Author: Yamnia I. Cortés, PhD, MPH, FNP-BC, Assistant Professor, School of Nursing, The University of North Carolina at Chapel Hill, Campus Box 7460, Chapel Hill, NC 27599-7460, USA, 919-966-5299, yicortes@email.unc.edu.

Conflicts of Interest/Disclosures: None

Publisher's Disclaimer: *Disclaimer:* The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORHW or NIH.

*Preliminary data associated with this manuscript was presented at the 2018 North American Menopause Society Annual Meeting and published in *Menopause*.

had higher BP in the postmenopausal years. Annual rate of change in BP during the menopause transition did not differ between pregnancy groups.

Conclusions: Women with a history preterm and term SGA delivery have higher BP than women with all term AGA births during the menopause transition, but rate of change in BP does not differ in these group relative to final menstrual period.

Keywords

blood pressure; final menstrual period; menopause; pregnancy; preterm

Introduction

Hypertension is the leading risk factor for cardiovascular disease (CVD) among women, the elimination of which could reduce CVD mortality by 38%.^{1,2} Prior data suggest high blood pressure (BP) after childbirth is an important factor mediating the association between pregnancy complications and CVD in later life.^{3–6} While associations between hypertensive disorders of pregnancy and maternal CVD risk factors are well established,^{7,8} accumulating evidence suggests non-preeclamptic preterm birth (PTB; <37 weeks gestation) and term small for gestational age (SGA; 10th percentile for birth weight at 37 weeks gestation) deliveries, which affect an estimated 12% of births in the U.S annually,^{9,10} are related to maternal CVD risk.¹¹ However, most studies relating pregnancy history to future BP have been limited by samples of relatively young women (<50 years), or have been cross-sectional in design. Whether associations between preterm or SGA birth and BP persist in midlife, as women transition through menopause, has been understudied.

The menopause transition has been associated with an increased risk of CVD.¹² A recent study found that midlife women with a prior preterm or term SGA birth have a higher prevalence of hypertension than women with all term births;⁶ notably, premenopausal women with a preterm or term SGA birth have a greater odds of hypertension than their postmenopausal counterparts. However, this analysis did not consider several menopause-related factors such as time relative to the final menstrual period, use of hormone therapy, and whether menopause occurred spontaneously or by surgical intervention. In an effort to address this gap in the literature, we previously reported that women with a prior preterm or term SGA birth had higher BP and arterial stiffness, respectively, in late midlife (mean age 60 years) independent of traditional CVD risk factors compared to women without a history of hypertension during pregnancy.¹³

The current analysis builds on our earlier work in the Study of Women's Health Across the Nations (SWAN)¹³ by exploring the relationship of PTB and term SGA birth to maternal changes in BP over the menopause transition. We hypothesized that BP would increase more rapidly across years around the final menstrual period in women with a prior PTB or term SGA birth as compared to women with all term and appropriate for gestational age births (AGA). Understanding if BP accelerates more rapidly during the menopause transition for women with a preterm or term SGA delivery may guide clinical recommendations, including, whether BP should be treated more aggressively during the menopause transition

among women with a prior PTB or term SGA birth compared to women with all term AGA births.

Methods

Study Participants

SWAN is a multi-center, longitudinal, observational study of the biological and psychosocial changes that occur during the menopause transition.¹⁴ Participants were recruited from seven research sites: Detroit, MI; Boston, MA; Chicago, IL; Oakland, CA; Los Angeles, CA; Newark, NJ; and Pittsburgh, PA. Each site recruited non-Hispanic White women and women from one of four other predetermined racial/ethnic groups (African-American women in Detroit, MI, Boston, MA, Chicago, IL, and Pittsburgh, PA; Japanese women in Los Angeles, CA; Chinese women in Oakland, CA; and Hispanic women in Newark, NJ). From 1996–1997, a total of 3,302 premenopausal or perimenopausal women age 42–52 years were enrolled and provided written informed consent. Women were eligible for SWAN if they had an intact uterus and at least one ovary, had menstrual bleeding within the prior three months, were not currently pregnant or breastfeeding, and had not used reproductive hormones within the prior three months. Participants were assessed through a standardized protocol at baseline, and at 13 follow up visits approximately annually through 2013.

Of the 3,302 women enrolled in SWAN, we included women who completed a reproductive history questionnaire at the 13th follow-up visit, and those with BP measures at baseline and at least one follow-up visit (n=2148). Women were excluded if they were nulliparous (n=395), had a birth that was both preterm and SGA (n=9), or had a multiple gestation birth (i.e., twins, triplets; n=27). Omitted from the analysis were 709 women with missing final menstrual period date (n=603) or an indeterminant date of final menstrual period due to bilateral oophorectomy (n=16) or hormone therapy use (n=90). The remaining 1008 women, comprised the analytic sample. Women included in the analysis were more likely to identify as Black and reported greater financial strain than women excluded from the analysis; there were no differences in blood pressure between our sample and women excluded from the analysis. The institutional review boards at each study site approved SWAN protocols.

Pregnancy History, Preterm Birth, and Small-for-Gestational Age Status

Pregnancy history was assessed at SWAN visit 13 using an interviewer-administered reproductive history questionnaire. Women reported the gestational age at delivery (weeks) and birth weight for each live birth. PTB was defined as a delivery at <37 weeks gestation. Term SGA was determined using the World Health Organization weight percentile calculator,¹⁵ and defined as an infant with birthweight <10th percentile for delivery at 37 weeks gestation. Prior validation studies have shown that maternal recall of preterm or SGA birth is good (sensitivity >0.90).^{16,17} Women in the current analysis were categorized into 3 exposure groups: those who ever experienced a PTB, those with a prior term SGA birth, and those with all term and AGA births.

Other pregnancy-related history collected included parity (number of births), age at first and last birth, and whether each pregnancy was complicated by gestational diabetes mellitus

or hypertensive disorders of pregnancy. We adjusted for these pregnancy features in our multivariable models (see “Statistical Analysis”). Analyses have found that self-report of gestational diabetes history is excellent (100% sensitivity and 92% specificity).¹⁸ The positive predictive value of self-report of hypertensive disorders of pregnancy is 42%, but the negative predictive value is 90%,¹⁹ suggesting that although our study cannot definitively identify women with hypertensive disorders of pregnancy, we are moderately confident that women reporting a negative history of gestational hypertension/preeclampsia had a normotensive pregnancy.

Blood Pressure

BP was measured at baseline and each follow-up visit using a standardized protocol. Readings were taken on the right arm, with the participant seated and feet flat on the floor for at least 5 minutes before measurement. Respondents had not smoked or consumed any caffeinated beverage within 30 minutes of BP measurement. Appropriate cuff size was determined on arm circumference. A standard mercury sphygmomanometer was used to record systolic and diastolic pressures at the first and fifth phase Korotkoff sounds. Two sequential BP values were completed, with a minimum two-minute rest period between measures. The mean of the two readings was used in this analysis. Observed BP values were used in our descriptive analyses and generalized linear models (Table 1 and Figure 1).

Since nearly 40% of women were on anti-hypertensive medication by the 13th follow-up visit, it would be difficult to assess the natural history of BP (underlying BP if left untreated) during the study period. The Atherosclerosis Risk in Communities Study has previously shown that adding a constant of 10 mmHg to treated systolic BP, and 5 mmHg for treated diastolic BP, is a valid method for estimating underlying BP with lowest relative bias (5.3% for intercept at age 50) and average deviation from expected (0.04 to −1.79).²⁰ Therefore, in our longitudinal analyses we added 10 mmHg to systolic BP and 5 mmHg to diastolic BP for any visit on anti-hypertensive treatment. We performed additional analyses (Supplemental Digital Content 1 & 2) using the observed BP values and adjusting for BP medication use.

Other Variables

Information on demographic characteristics was collected at the baseline SWAN visit and included age, race/ethnicity, education (<high school, high school/some college, college degree/post college), study site, and financial strain (paying for basics not hard at all, somewhat/very hard to pay for basics). Age and financial strain were also assessed at each visit. Information on medical history was obtained by self-report at baseline and each subsequent visit, and included smoking status (current/past, never), physical activity, body mass index (kg/m²), and medication use (i.e., antihypertensive, antidiabetics, lipid-lowering). Physical activity was assessed using a modified Baecke Scores of Habitual Physical Activity, with higher scores indicating more physical activity.²¹ Fasting blood samples were drawn into EDTA-containing tubes between at each visit. Samples were stored at 4 °C before processing, then centrifuged; the separated plasma was frozen at −80 °C and shipped on dry ice to Medical Research Laboratories (Highland Heights, KY) for analysis. We measured glucose with a hexokinase-coupled reaction (Boehringer Mannheim

Diagnostics). Diabetes was defined as fasting glucose ≥ 126 mg/dL on 50% of at least three visits or at two consecutive visits, or any reported use of insulin/anti-diabetic agents.

Menopause status was determined based on reports about frequency and regularity of menstrual bleeding and use of hormone therapy at each visit, as previously described.²² Perimenopause was defined as bleeding in the last 3 months with some change in cycle regularity, or bleeding in past 3–12 months. Postmenopause was defined as no menses for ≥ 12 consecutive months with no other reason for the amenorrhea. The final menstrual period was the last reported menstrual period prior to being considered postmenopausal (12 months of amenorrhea); the participant's age at final menstrual period was also determined using this date. Women were excluded from the analyses if they were missing data on the final menstrual period, or had an indeterminant final menstrual period due to surgery (hysterectomy and/or bilateral oophorectomy) or hormone therapy use.

Statistical Analysis

All analyses were conducted using SAS 9.4 (SAS Institute, Cary, North Carolina, USA). Descriptive statistics were used to summarize variables. Maternal characteristics and CVD risk factors at baseline and at visit 13 were compared in women according to pregnancy group (PTB, term SGA, term AGA) using ANOVA or Mann-Whitney U Test for continuous and Chi-square or Fisher's Exact for categorical. We assessed cross-sectional BP levels according to pregnancy group using three separate generalized linear models: at baseline (up to 6 years before the final menstrual period), at the final menstrual period, and up to 10 years after the final menstrual period (visit 13). Adjusted models included current age, study site, race/ethnicity, financial strain, reproductive factors (parity, age at first birth gestational hypertension/preeclampsia, menopause status), and CVD risk factors (smoking, physical activity, body mass index, anti-hypertensives, anti-diabetic and lipid-lowering medications). Women with all term AGA births were the referent for all analyses.

Next, we evaluated the annual rate of change in BP across the menopause transition (baseline thru visit 13) by dividing the menopause transition into segments related to the final menstrual period. Two segments were identified based on the timing of the final menstrual period using the Loess method: 1) before the final menstrual period; and 2) after the final menstrual period. We tested the impact of PTB and term SGA delivery on the maternal annual rate of changes in BP in relation to the final menstrual period using piece-wise linear mixed models, which allow the slope to differ across the two segments. A BP annual rate of change (slope) that is similar across both segments is consistent with chronological aging effects, while differences in these slopes across the two segments is consistent with reproductive aging effects that are independent of chronological aging.

Piecewise linear mixed models were used to estimate and compare annual rate of change in BP in each time segment (before/after final menstrual period). All variables that were assessed at baseline and at each SWAN follow-up visit were included in the models as time-varying covariates. The autoregressive covariance structure was used in each model. Base models included years since final menstrual period (before or after), pregnancy group, and the interaction between years since final menstrual period and pregnancy group. Next, we adjusted for age at baseline, study site, race/ethnicity, and financial strain. Full-adjusted

models included reproductive factors (parity, age at first birth, and menopause status) and CVD risk factors with established associations with PTB or term SGA birth and BP (smoking, physical activity, body mass index, anti-diabetic and lipid-lowering medications). We additionally adjusted for history of gestational hypertension/preeclampsia gestational diabetes. All models censored observations in which women reported hormone therapy use after final menstrual period. We also tested interactions between race/ethnicity and pregnancy group to determine whether the effect of PTB and SGA on BP varied by race/ethnicity. Residual analyses were conducted to verify model assumptions and examine for multicollinearity. Though estimates were similar in models with and without history of gestational hypertension/preeclampsia gestational diabetes, the model fit was better including these variables. Thus, our final models adjusted for age at baseline, study site, race/ethnicity, and financial strain, parity, age at first birth, history of gestational hypertension/preeclampsia gestational diabetes, and menopause status.

Results

Among 1008 women at baseline, 101 (10.0%) had a prior PTB and 102 (10.1%) had a prior term SGA birth. A greater proportion of African-American/Black women had a prior term SGA birth and Hispanic women were more likely to report ever delivering a preterm infant (Table 1). Women with a preterm or term SGA birth were more likely to report financial strain, younger age at first birth, and more likely to have a history of gestational diabetes or hypertensive disorder of pregnancy.

Figure 1 presents mean BP before the final menstrual period (baseline), at the final menstrual period, and up to 10 years after the final menstrual period (visit 13) according to pregnancy group. After adjusting for socio-demographic factors, reproductive history, and CVD risk factors, we found that compared to women with all term AGA births, women with a prior term SGA birth had higher mean systolic BP (mmHg) before the final menstrual period (baseline: 116 ± 17 vs 121 ± 19 , $p=0.006$); at the final menstrual period (118 ± 17 vs 122 ± 19 , $p=0.04$); and up to 10 years after the final menstrual period (Visit 13: 125 ± 17 vs 135 ± 19 , $p=0.02$). Mean systolic BP was higher for women with a prior PTB up to 10 years after the final menstrual period compared to women with all term AGA births (Visit 13: 127 ± 19 vs 123 ± 17 mmHg; $p<0.001$).

Table 2 presents the results of the annual change in systolic BP before/after the final menstrual period according to pregnancy group. Increases in systolic BP before the final menstrual period were significant for women with a prior SGA birth after adjusting for socio-demographic factors (Model 2: estimate [SE]: 0.3 [0.1], $p=0.006$), but not when adjusting for CVD risk factors (Model 3: estimate [SE]: 0.2 [0.1], $p=0.12$). When comparing the annual rate of change in BP between the term SGA group and the term AGA group, we found no significant difference (SGA-Term AGA, Model 3: estimate [SE]: 0.2 [0.3], $p=0.58$). There were no significant increases in systolic BP before and after the final menstrual period for women with a prior PTB. In addition, the annual rate of change in systolic BP during the menopause transition did not differ between women with a prior PTB or those with all term AGA births.

Results for the annual change in diastolic BP before/after the final menstrual period according to pregnancy group are presented in Table 3. In full-adjusted models (Model 3), the annual rate of change in diastolic BP was not significant before or after the final menstrual period for any group and did not differ between groups. All results were similar across ethnic groups. Findings were similar when modelling for observed BP values and adjusting for anti-hypertensive medications (Supplemental Digital Content 1 & 2).

Discussion

We found that compared to women with all term AGA births, women with a prior term SGA birth had higher BP before the final menstrual period (baseline), at the final menstrual period, and up to 10 years after the final menstrual period (visit 13); women with a prior PTB had a higher systolic BP up to 10 years after the final menstrual period (visit 13). We also found significant increases in annual systolic BP among women with a history of a term SGA birth. However, the magnitude of change in BP during the menopause transition did not differ between the term SGA group and women with all term AGA births. These findings suggest that compared to women with all term AGA births: 1) women with a prior term SGA birth have higher SBP and DBP in the premenopausal years, at the final menstrual period, and in the postmenopausal years; 2) women with a prior PTB have higher SBP in the postmenopausal years relative to women with all term AGA births; and 3) annual changes in BP do not differ for women with prior preterm or SGA birth.

Our results corroborate earlier studies that have shown that women who experience a PTB or SGA delivery have modestly higher BP up to 20 years postpartum.^{3,4} In a previous cross-sectional investigation, we found that history of a PTB and multiple adverse pregnancy outcomes (including term SGA births) is associated with higher BP in late midlife women.¹³ The current analysis extends this work by examining BP at multiple time points over the menopause transition. When examining BP in separate generalized linear models before the final menstrual period, at the final menstrual period, and after the final menstrual period, we found that women with a term SGA delivery have consistently higher BP during the menopause transition than women with all term AGA births. There was a difference of approximately 4–7 mmHg in systolic BP at each time point even after adjusting for socio-demographic factors and CVD risk factors. These data are clinically significant given that a 10mmHg increment in systolic BP among adults 18–45 years is associated with a 5% increased risk of cardiovascular events, and a 5 mmHg increment in systolic BP is associated with a 10% increased risk in adults aged 65 and older.²³

When assessing the annual change in BP over the menopause transition (up to 6 years before and 10 years after the final menstrual period), we found that the rate of change in BP does not differ significantly between women with a prior preterm or term SGA birth and women with all term AGA births. In contrast, the Coronary Artery Risk Development in Young Adults study found that, from early adulthood to midlife (approximately age 25 to 45 years), changes in BP levels increased more rapidly among women with a PTB compared to women with all term births.³ Our results indicate that BP may increase proportionally across pregnancy groups during the menopause transition; women with a prior preterm or term SGA birth have a higher BP before the final menstrual period and BP remains

higher, on average, after the final menstrual period. Thus, earlier interventions prior to menopause may be necessary among women with a preterm or term SGA delivery to reduce increases in BP over midlife. The menopause transition is a time of pronounced changes in body composition and cardiometabolic health,^{12,24} and is a period in the lifespan directly preceding a heightened risk of CVD.²⁵ It is also possible that increases in other CVD risk factors during the menopause transition may attenuate the impact of PTB or SGA deliveries on BP. However, additional studies focusing on years since final menstrual period are necessary to more fully assess the potential role of menopause-associated alterations in BP among women with preterm or term SGA deliveries.

This is the first study to examine whether BP accelerates more rapidly during the menopause transition for women with a PTB or term SGA delivery. Our findings should be considered in light of important limitations. First, pregnancy data were self-reported. Although recall of preterm and SGA delivery is good (sensitivity >0.90),²⁶ our findings may have been mitigated by misclassification. Self-report of hypertension during pregnancy may have been a limitation given the low sensitivity of maternal recall of hypertensive disorders of pregnancy.^{27,28} Further, we could not account for pre-pregnancy CVD risk factors, which limits our ability to determine whether differences in BP were present before pregnancy. Although we adjusted for hypertensive disorders of pregnancy and gestational diabetes mellitus, we were unable to differentiate between spontaneous and medically indicated preterm delivery, which may have varying effects on maternal CVD risk. Strengths of our study include the relatively large sample of racially diverse midlife women. In addition, BP was assessed approximately annually over 15 years. Finally, we were able to examine the impact of a prior preterm and term SGA delivery on BP measures according to years since final menstrual in a multicenter longitudinal study of the menopause transition.

Conclusions

This study suggests that the women with a history of preterm and term SGA delivery have higher BP than women with all term AGA births during the menopause transition, but that rate of change in BP does not differ in these groups relative to final menstrual period. These findings are important as elevations in BP in these groups of women may be linked to future CVD. Our results suggest that earlier interventions and more frequent BP screening prior to menopause are necessary among women with a preterm or term SGA delivery to prevent elevated BP in midlife and future CVD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH. At the time of this analysis, Yamnia I. Cortés was supported as a

Postdoctoral Fellow in the Cardiovascular Epidemiology Training Program (T32 HL083825, PI: Orchard) at the University of Pittsburgh Graduate School of Public Health.

Clinical Centers: *University of Michigan, Ann Arbor – Siobán Harlow, PI 2011 – present, MaryFran Sowers, PI 1994–2011; Massachusetts General Hospital, Boston, MA – Joel Finkelstein, PI 1999 – present; Robert Neer, PI 1994 – 1999; Rush University, Rush University Medical Center, Chicago, IL – Howard Kravitz, PI 2009 – present; Lynda Powell, PI 1994 – 2009; University of California, Davis/Kaiser – Ellen Gold, PI, University of California, Los Angeles – Gail Greendale, PI, Albert Einstein College of Medicine, Bronx, NY – Carol Derby, PI 2011 – present, Rachel Wildman, PI 2010 – 2011; Nanette Santoro, PI 2004 – 2010; University of Medicine and Dentistry – New Jersey Medical School, Newark – Gerson Weiss, PI 1994 – 2004; and the University of Pittsburgh, Pittsburgh, PA – Karen Matthews, PI.*

NIH Program Office: *National Institute on Aging, Bethesda, MD – Chhanda Dutta 2016- present; Winifred Rossi 2012–2016; Sherry Sherman 1994 – 2012; Marcia Ory 1994 – 2001; National Institute of Nursing Research, Bethesda, MD – Program Officers.*

Central Laboratory: *University of Michigan, Ann Arbor – Daniel McConnell (Central Ligand Assay Satellite Services).*

Coordinating Center: *University of Pittsburgh, Pittsburgh, PA – Maria Mori Brooks, PI 2012 - present; Kim Sutton-Tyrrell, PI 2001 – 2012; New England Research Institutes, Watertown, MA - Sonja McKinlay, PI 1995 – 2001.*

Steering Committee: Susan Johnson, Current Chair

Chris Gallagher, Former Chair

We thank the study staff at each site and all the women who participated in SWAN.

Source of Funding:

SWAN has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). At the time of this analysis, Yammia I. Cortés was supported as a Postdoctoral Fellow in the Cardiovascular Epidemiology Training Program (T32HL083825) at the University of Pittsburgh Graduate School of Public Health.

References

1. Patel SA, Winkel M, Ali MK, Narayan KM, Mehta NK. Cardiovascular mortality associated with 5 leading risk factors: National and state preventable fractions estimated from survey data. *Ann Intern Med.* 2015;163(4):245–253. [PubMed: 26121190]
2. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation.* 2017;135(10):e146–e603. [PubMed: 28122885]
3. Catov JM, Lewis CE, Lee M, Wellons MF, Gunderson EP. Preterm birth and future maternal blood pressure, inflammation, and intimal-medial thickness: the CARDIA study. *Hypertension.* 2013;61(3):641–646. [PubMed: 23319540]
4. Fraser A, Nelson SM, Macdonald-Wallis C, 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(11):1367–1380. [PubMed: 22344039]
5. Parikh NI, Norberg M, Ingelsson E, et al. Association of Pregnancy Complications and Characteristics With Future Risk of Elevated Blood Pressure: The Vasterbotten Intervention Program. *Hypertension.* 2017;69(3):475–483. [PubMed: 28137991]
6. Xu J, Barinas-Mitchell E, Kuller LH, Youk AO, Catov JM. Maternal hypertension after a low-birth-weight delivery differs by race/ethnicity: evidence from the National Health and Nutrition Examination Survey (NHANES) 1999–2006. *PLoS One.* 2014;9(8):e104149. [PubMed: 25093324]

7. Bushnell C, McCullough LD, Awad IA, et al. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45(5):1545–1588. [PubMed: 24503673]
8. Wu P, Haththotuwa R, Kwok CS, et al. Preeclampsia and Future Cardiovascular Health: A Systematic Review and Meta-Analysis. *J Circ Cardiovasc Qual Outcomes*. 2017;10(2).
9. Ewing AC, Ellington SR, Shapiro-Mendoza CK, Barfield WD, Kourtis AP. Full-Term Small-for-Gestational-Age Newborns in the U.S.: Characteristics, Trends, and Morbidity. *Matern Child Health J*. 2017;21(4):786–796. [PubMed: 27502090]
10. Martin JA, Hamilton BE, Osterman MJK. Births in the United States, 2018. *NCHS Data Brief*. 2019(346):1–8.
11. Catov JM, Dodge R, Yamal JM, Roberts JM, Piller LB, Ness RB. Prior preterm or small-for-gestational-age birth related to maternal metabolic syndrome. *J Obstet Gynecol*. 2011;117(2 Pt 1):225–232.
12. Matthews KA, Kuller LH, Sutton-Tyrrell K, Chang YF. Changes in cardiovascular risk factors during the perimenopause and postmenopause and carotid artery atherosclerosis in healthy women. *Stroke*. 2001;32(5):1104–1111. [PubMed: 11340217]
13. Cortés YI, Catov JM, Brooks M, et al. History of Adverse Pregnancy Outcomes, Blood Pressure, and Subclinical Vascular Measures in Late Midlife: SWAN (Study of Women's Health Across the Nation). *J Am Heart Assoc*. 2017;7(1).
14. Sowers MF, Crawford SL, Sternfeld B, et al. SWAN: A Multicenter, Multiethnic, Community-based Cohort Study of Women and the Menopausal Transition. San Diego, CA: Academic Press; 2000.
15. World Health Organization. Weight Percentiles Calculator. www.who.int/reproductivehealth/.../weight_percentiles_calculator.xls. Accessed October 9, 2015.
16. Poulsen G, Kurinczuk JJ, Wolke D, et al. Accurate reporting of expected delivery date by mothers 9 months after birth. *Journal of clinical epidemiology*. 2011;64(12):1444–1450. [PubMed: 21684117]
17. Tomeo CA, Rich-Edwards JW, Michels KB, et al. Reproducibility and validity of maternal recall of pregnancy-related events. *Epidemiology*. 1999;10(6):774–777. [PubMed: 10535796]
18. Gunderson EP, Lewis CE, Tsai AL, et al. A 20-year prospective study of childbearing and incidence of diabetes in young women, controlling for glycemia before conception: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Diabetes*. 2007;56(12):2990–2996. [PubMed: 17898128]
19. Gunderson EP, Chiang V, Lewis CE, et al. Long-term blood pressure changes measured from before to after pregnancy relative to nonparous women. *J Obstet Gynecol*. 2008;112(6):1294–1302.
20. Balakrishnan P, Beaty T, Young JH, Colantuoni E, Matsushita K. Methods to estimate underlying blood pressure: The Atherosclerosis Risk in Communities (ARIC) Study. *PLoS One*. 2017;12(7):e0179234. [PubMed: 28700596]
21. Sternfeld B, Ainsworth B, Quesenberry C. Physical activity patterns in a diverse population of women. *J Preventive Medicine*. 1999;28:313–323.
22. Paramsothy P, Harlow SD, Greendale GA, et al. Bleeding patterns during the menopausal transition in the multi-ethnic Study of Women's Health Across the Nation (SWAN): a prospective cohort study. *BJOG*. 2014;121(12):1564–1573. [PubMed: 24735184]
23. Luo D, Cheng Y, Zhang H, et al. Association between high blood pressure and long term cardiovascular events in young adults: systematic review and meta-analysis. *BMJ*. 2020;370:m3222. [PubMed: 32907799]
24. Sowers M, Zheng H, Tomey K, et al. Changes in body composition in women over six years at midlife: ovarian and chronological aging. *J Clin Endocrinol Metab*. 2007;92(3):895–901. [PubMed: 17192296]
25. Atsma F, Bartelink ML, Grobbee DE, van der Schouw YT. Postmenopausal status and early menopause as independent risk factors for cardiovascular disease: a meta-analysis. *Menopause*. 2006;13(2):265–279. [PubMed: 16645540]
26. Tomeo CA, Rich-Edwards JW, Michels KB, et al. Reproducibility and validity of maternal recall of pregnancy-related events. *J Epidemiology*. 1999;10(6):774–777.

27. Carter EB, Stuart JJ, Farland LV, et al. Pregnancy Complications as Markers for Subsequent Maternal Cardiovascular Disease: Validation of a Maternal Recall Questionnaire. *J Womens Health*. 2015;24(9):702–712.
28. Stuart JJ, Bairey Merz CN, Berga SL, et al. Maternal recall of hypertensive disorders in pregnancy: a systematic review. *J Womens Health*. 2013;22(1):37–47.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.

Systolic blood pressure (unadjusted, A; adjusted, B) and diastolic blood pressure (unadjusted, C; adjusted, D) at baseline, at the final menstrual period, and at Visit 13, according to pregnancy group (n=1008) assessed separately using generalized linear models. Adjusted models controlled for age, study site, race/ethnicity, financial strain, ever smoker, physical activity, menopause status, BMI, anti-hypertensives, anti-diabetic medication, lipid-lowering medications, parity, age at first birth, history of gestational hypertension/preeclampsia and gestational diabetes. AGA=appropriate for gestational age, FMP=final menstrual period, SGA=small for gestational age.

Table 1.

Maternal characteristics at baseline and Visit 13 by pregnancy status

	Baseline (n=1008)				Visit 13 (n=940)			
Maternal Characteristics mean $\pm$ SD, median [IQR], n (%)	All Term AGA (n= 805)	PTB (n= 101)	Term-SGA (n=102)	P	All Term AGA (n=751)	PTB (n= 95)	Term-SGA (n=94)	P
Age, Mean $\pm$ SD	46.5 $\pm$ 2.7	45.8 $\pm$ 2.8 ^a	46.9 $\pm$ 2.7	0.01	61.9 $\pm$ 2.8	61.3 $\pm$ 2.8	62.2 $\pm$ 2.8	0.06
Race/Ethnicity				<0.0001				<0.0001
White	342 (42.6)	42 (41.6)	22 (21.6)		314 (41.9)	40 (42.1)	21 (22.3)	
Black	218 (27.2)	27 (26.7)	55 (53.4)		202 (27.0)	24 (25.3)	49 (52.1)	
Hispanic	54 (6.7)	13 (12.9)	8 (7.8)		51 (6.8)	13 (13.7)	7 (7.5)	
Chinese	189 (23.5)	19 (18.8)	17 (16.7)		182 (24.3)	18 (19.0)	17 (18.1)	
Education				0.21				0.27
<High school	58 (7.3)	11 (10.9)	11 (10.8)		54 (7.3)	11 (11.6)	10 (10.6)	
High school/Some college	393 (49.6)	57 (56.4)	51 (50.0)		365 (49.3)	51 (53.7)	49 (52.1)	
College degree/Post college	342 (43.1)	33 (32.7)	40 (39.2)		321 (43.4)	33 (34.7)	35 (37.2)	
How hard to pay for basics				0.0001				0.0007
Not hard at all	561 (73.9)	60 (63.2)	51 (54.8)		529 (73.5)	58 (63.7)	49 (55.7)	
Somewhat /Very hard	198 (26.1)	35 (36.8)	42 (45.2)		191 (26.5)	33 (36.3)	39 (44.3)	
Age at first birth, Mean $\pm$ SD	26.1 $\pm$ 5.9	25.0 $\pm$ 6.2	23.9 $\pm$ 5.9 ^b	0.001	26.1 $\pm$ 6.0	25.2 $\pm$ 6.2	24.1 $\pm$ 6.0 ^b	0.005
Age at last birth, Mean $\pm$ SD	31.4 $\pm$ 5.9	31.7 $\pm$ 5.6	30.8 $\pm$ 5.3	0.35	31.3 $\pm$ 5.8	31.3 $\pm$ 5.7	30.4 $\pm$ 5.8	0.52
Parity				0.0002				0.0004
1	184 (22.9)	15 (14.9)	9 (8.8)		170 (22.7)	15 (15.8)	9 (9.6)	
2	342 (42.6)	33 (32.7)	43 (42.2)		322 (43.0)	29 (30.5)	41 (43.6)	
3	174 (21.7)	29 (28.7)	27 (26.5)		162 (21.6)	28 (29.5)	24 (25.5)	
4	103 (12.8)	24 (23.8)	23 (22.6)		95 (12.7)	23 (24.2)	20 (21.3)	
Ever breastfed	556 (69.1)	63 (62.4)	58 (56.9)	0.03	521 (69.4)	60 (63.2)	54 (57.5)	0.04

	Baseline (n=1008)					Visit 13 (n=940)				
Maternal Characteristics mean $\pm$ SD, median [IQR], n (%)	All Term AGA (n=805)	PTB (n=101)	Term-SGA (n=102)	P	All Term AGA (n=751)	PTB (n=95)	Term-SGA (n=94)	P		
Gestational diabetes	43 (5.4)	7 (7.1)	13 (12.8)	0.01	42 (5.6)	7 (7.6)	12 (12.8)	0.03		
Gestational hypertension/Preeclampsia	61 (7.6)	21 (21.7)	16 (15.8)	<0.0001	55 (7.3)	20 (22.0)	15 (16.1)	<0.0001		
Menopause status				0.36				0.006		
Premenopausal	458 (57.7)	61 (60.4)	51 (51.0)		N/A	N/A	N/A			
Perimenopausal	336 (42.3)	40 (39.6)	49 (49.0)		4 (0.5)	3 (3.2)	1 (1.1)			
Postmenopausal	N/A	N/A	N/A		746 (99.5)	92 (96.8)	93 (98.9)			
Current smoker	114 (14.3)	18 (17.8)	18 (17.6)	0.46	105 (14.2)	15 (15.9)	17 (18.1)	0.66		
Physical activity	7.7 $\pm$ 1.8	7.5 $\pm$ 1.7	7.5 $\pm$ 1.6	0.24	7.7 $\pm$ 1.7	7.6 $\pm$ 1.7	7.4 $\pm$ 1.7	0.85		
BMI (kg/m ²)	28.0 $\pm$ 7.2	27.9 $\pm$ 7.3	28.5 $\pm$ 7.4	0.81	29.3 $\pm$ 7.4	29.6 $\pm$ 7.5	30.1 $\pm$ 7.3	0.64		
Diabetes	34 (2.4)	17 (8.6)	12 (7.3)	0.0006	92 (7.3)	20 (12.1)	22 (14.9)	0.005		
Medications										
Anti-diabetic treatment	15 (1.9)	6 (5.9)	5 (4.9)	0.02	79 (10.18)	15 (16.3)	17 (17.9)	0.06		
Lipid-lowering treatment	6 (0.8)	1 (1.0)	2 (2.0)	0.27	72 (10.7)	12 (16.2)	12 (14.5)	0.20		
Antihypertensive treatment	66 (8.2)	11 (10.9)	12 (11.8)	0.36	276 (37.7)	34 (37.0)	38 (40.0)	0.89		
Years since FMP	-5.9 $\pm$ 3.3	-6.2 $\pm$ 3.9	-5.1 $\pm$ 3.4	0.06	9.5 $\pm$ 3.4	9.2 $\pm$ 3.9	10.1 $\pm$ 3.6	0.17		
Systolic BP (mm/Hg)	116.4 $\pm$ 16.7	118.7 $\pm$ 17.3	122.4 $\pm$ 16.1 ^b	0.002	122.8 $\pm$ 17.0	127.6 $\pm$ 19.2 ^a	129.4 $\pm$ 19.2 ^c	0.0003		
Diastolic BP (mm/Hg)	74.7 $\pm$ 10.6	75.1 $\pm$ 11.1	78.1 $\pm$ 9.4 ^b	0.009	74.5 $\pm$ 9.9	75.9 $\pm$ 10.8	78.5 $\pm$ 10.5 ^b	0.001		

Note. BP, blood pressure; HDL, high-density lipoprotein; HOMA, homeostatic model assessment; LDL, low-density lipoprotein; PTB, preterm birth; SD, standard deviation; SGA, small-for-gestational age. Preterm birth = delivery <37 weeks; Term-SGA = birth weight <10th percentile at 37–40 weeks gestation. BP values reported are crude (not adding 10 mmHg to treated systolic BP, and 5 mmHg for treated diastolic BP).

^aDiffers from no adverse pregnancy group (p<0.05).

^bDiffers from no adverse pregnancy group (p<0.01).

^cDiffers from no adverse pregnancy group (p<0.001).

Table 2.

Difference in systolic blood pressure at final menstrual period (FMP), and annual change before/after FMP according to pregnancy group

	Model 1 (n=1008, observations=7361)			Model 2 (n=948, observations=5216)			Model 3 (n=929, observations=3970)		
	Estimate	SE	P	Estimate	SE	P	Estimate	SE	P
SBP (mmHg) at FMP (time = 0)									
PTB (versus Term AGA)	-0.6	2.1	0.79	0.03	1.9	0.99	0.3	1.9	0.89
SGA (versus Term AGA)	3.8	2.8	0.17	0.1	2.5	0.97	-0.7	2.5	0.77
Annual Change in SBP (mmHg) Before FMP (time = 0)									
Term AGA	0.1	0.3	0.72	-0.1	0.3	0.77	0.03	0.3	0.92
PTB	0.2	0.4	0.56	0.3	0.3	0.33	-0.02	0.3	0.95
SGA	0.5	0.1	<0.0001	0.3	0.1	0.006	0.2	0.1	0.12
PTB - Term AGA	0.1	0.5	0.85	0.4	0.5	0.35	-0.05	0.4	0.90
SGA - Term AGA	0.4	0.4	0.24	0.4	0.3	0.20	0.2	0.3	0.58
Annual Change in SBP (mmHg) After FMP (time > 0)									
Term AGA	0.5	0.9	0.58	0.1	0.8	0.95	0.6	1.5	0.70
PTB	0.8	0.9	0.37	0.7	0.8	0.38	1.5	1.5	0.31
SGA	1.1	0.8	0.18	0.7	0.8	0.35	1.7	1.5	0.23
PTB - Term AGA	0.3	1.5	0.83	0.6	1.5	0.63	0.9	2.3	0.68
SGA - Term AGA	0.6	1.3	0.63	0.7	1.3	0.60	1.2	2.1	0.58

Note. Reported estimates is the slope based on pregnancy group*years since FMP, unless stated otherwise. Added a constant of 10 mmHg to treated systolic BP, and 5 mmHg for treated diastolic BP.

Model 1= pregnancy group, years since FMP, pregnancy group*years since FMP

Model 2 = Model 1 + age at baseline, study site, race/ethnicity, financial strain

Model 3 = Model 2 + ever smoker, physical activity (time-varying), menopause status (time-varying), BMI (time-varying), anti-diabetic medication, lipid-lowering medications, parity, age at first birth, history of gestational hypertension/preeclampsia and gestational diabetes.

Table 3.

Difference in diastolic blood pressure at final menstrual period (FMP), and annual change before/after FMP according to pregnancy group

	Model 1 (n=1008, observations=7361)			Model 2 (n=948, observations=5216)			Model 3 (n=929, observations=3970)		
	Estimate	SE	P	Estimate	SE	P	Estimate	SE	P
DBP (mmHg) at FMP (time = 0)									
PTB (versus Term AGA)	0.7	1.2	0.56	1.1	1.1	0.35	1.2	1.2	0.31
SGA (versus Term AGA)	4.5	1.6	0.004	2.3	1.5	0.13	2.0	1.5	0.18
Annual Change in DBP (mmHg) Before FMP (time = 0)									
Term AGA	-0.1	0.2	0.43	-0.2	0.2	0.22	-0.1	0.2	0.63
PTB	0.3	0.2	0.21	0.2	0.2	0.24	0.2	0.2	0.31
SGA	0.1	0.1	0.07	0.03	0.07	0.67	0.1	0.09	0.33
PTB - Term AGA	0.4	0.3	0.14	0.4	0.3	0.09	0.3	0.3	0.26
SGA - Term AGA	0.3	0.2	0.16	0.2	0.2	0.19	0.2	0.2	0.36
Annual Change in DBP (mmHg) After FMP (time > 0)									
Term AGA	-0.4	0.5	0.50	-0.5	0.5	0.35	0.4	0.9	0.68
PTB	0.5	0.6	0.40	0.5	0.5	0.34	1.5	1.0	0.14
SGA	0.3	0.5	0.52	0.3	0.5	0.54	1.3	0.9	0.17
PTB - Term AGA	0.8	0.9	0.37	1.0	0.9	0.27	1.1	1.5	0.48
SGA - Term AGA	0.7	0.8	0.40	0.8	0.8	0.32	0.9	1.4	0.51

Note. Reported estimates is the slope based on pregnancy group*years since FMP, unless stated otherwise. Added a constant of 10 mmHg to treated systolic BP, and 5 mmHg for treated diastolic BP.

Model 1= pregnancy group, years since FMP, pregnancy group*years since FMP

Model 2 = Model 1 + age at baseline, study site, race/ethnicity, financial strain.

Model 3 = Model 2 + ever smoker, physical activity (time-varying), menopause status (time-varying), BMI (time-varying), anti-diabetic medication, lipid-lowering medications, parity, age at first birth, history of gestational hypertension/preeclampsia and gestational diabetes.