

## ORIGINAL RESEARCH

---

# Pre-Pregnancy Normal Range Blood Pressure Relationship to Birth Weight in Term Pregnancy in African American Women from the CARDIA Study Center: Research Article

---

Kellyanne R. Gold, MD<sup>1</sup>, Robert A. Gold, MD<sup>2</sup> and Jeffrey Gornbein, DrPh<sup>3</sup>

<sup>1</sup>Department of Medicine, Olive-View UCLA Medical Center, 14445 Olive View Drive, Sylmar, California 91342, USA; Health Sciences Clinical Instructor, David Geffen School of Medicine at UCLA, 10833 Le Conte Ave, Los Angeles, CA 90095, USA; kellyannerosegold@gmail.com

<sup>2</sup>Clinical Professor of Medicine, Department of Medicine, David Geffen School of Medicine at UCLA, 10833 Le Conte Ave, Los Angeles, CA 90095, USA; robertgold87@yahoo.com

<sup>3</sup>Principle Statistician, Department of Medicine Statistics Core, David Geffen School of Medicine at UCLA, 10833 Le Conte Ave, Los Angeles, CA 90095, USA; gornbein@g.ucla.edu

### **Abstract**

**Purpose:** to study the relationship between pre-pregnancy normal range blood pressure and other cardiovascular disease risk factors to term singleton pregnancy birth weight in African American women.

**Design:** longitudinal, observational, prospective cohort study.

**Setting:** community setting from four geographical areas of the United States.

**Population:** African American women with term pregnancies and without preexistent diabetes mellitus, hypertension, cardiac history, renal disease history, malignancy, tobacco usage or sickle cell anemia.

**Methods:** bivariate and multivariate linear regression.

**Results:** pre-pregnancy SBP and DBP in African American women are each negatively related to birth weight. SBP and DBP estimate the same relationship with birth weight and suggest that SBP and DBP are interchangeable. Additionally, we found that gestational age and birth weight depend upon the presence of prior pregnancy and range of BMI.

**Conclusions:** in a United States based cohort of African American women with no known CVD risk factors, pre-pregnancy normal range blood pressure is related to term birth weight.

### **Introduction**

Pre-pregnancy hypertension and the hypertensive syndromes of pregnancy are known risk factors for low birth weight/small for gestational age (LBW/SGA) infants and premature delivery (<37 weeks).<sup>1,2</sup> United States (US) born African American women are three times more likely to have LBW infants (<

2500 grams) than US white women.<sup>3</sup> A preliminary study of the CARDIA database suggests that pre-pregnancy elevated systolic blood pressure within the normal range in African American women is associated with up to a four-fold increase in risk of LBW in term pregnancies.<sup>4</sup>

The presence of abnormal cardiovascular disease (CVD) risk factors pre-pregnancy has been reported for pregnancy associated hypertension (PAH) (e.g., preeclampsia, eclampsia, gestational hypertension), gestational diabetes, and prematurity.<sup>5</sup> Pre-pregnancy hypertension is associated with pre-term and term SGA.<sup>6</sup> A recent epidemiological study from China demonstrated a relationship between blood pressure as a continuous variable and premature birth.<sup>7</sup> Additionally, high end normal range blood pressure in pregnancy is associated with low birth weight, shown in a recent study by Wikstrom.<sup>8</sup> The researchers in the Wikstrom study demonstrated a negative relationship between diastolic blood pressure (DBP) at 36 weeks gestation and birth weight/SGA.<sup>8</sup> The known future consequences to both mother and LBW/SGA infant for CVD and CVD risk factors invites the study of pre-pregnancy blood pressure and other metabolic parameters.

In order to isolate the effect of pre-pregnancy CVD risk factors on fetal growth we studied term pregnancies only (preterm excluded).

The purpose of this study is to investigate the relationship between pre-pregnancy normal range blood pressure (as a continuous variable) and other CVD risk factors to term singleton pregnancy birth weight in African American women. The results of this study may assist in answering the question whether maternal predisposition to CVD is present prior to pregnancy or whether unique processes of the complicated pregnancy set in motion the metabolic and vascular changes which are characteristic of CVD.

## ***Materials and Methods***

### **CARDIA Study Cohort**

The CARDIA study has been described in detail.<sup>9-11</sup> Briefly, the CARDIA study is a longitudinal, observational, prospective cohort study started in the United States in 1985 to study the evolution of cardiac risk factors in young men and women enrolled between 18 and 30 years old by collecting data at various points in time from 1985 to 2011.<sup>9-11</sup> The participants were recruited from four geographical areas, which included the enrollment of 2787 women (52% were African American) at inception. To study the relationship between pre-pregnancy variables and outcomes we examined the first pregnancy after enrollment into the study (regardless of parity status at enrollment, in order to obviate the effect of an interval pregnancy) over the first 5 years of data collection. Data were collected at year 0 (Time A), year 2 (Time B) and year 5 (Time C). Our study is a secondary analysis of the CARDIA data. We included African American women who were both nulliparous and parous at Time A. Metabolic, blood pressure and anthropometric data were obtained from Time A and Time B. Reproductive events were evaluated at Time B and Time C. There were 381 African American women with births recorded at Time B and Time C: 167 women delivered between Time A and Time B and 214 women delivered between Time B and Time C (who had not also delivered between Time A and Time B). Women with preterm pregnancies (defined as less than 37 weeks gestational age), who were pregnant at baseline data collection times (Time A, Time B) and with preexistent diabetes mellitus (DM), hypertension, cardiac history, renal disease history, malignancy and tobacco usage were excluded (239 subjects excluded – Figures S1 and S2). No woman with sickle cell anemia was included in baseline CARDIA data. Additionally, patients with sickle cell trait (12 subjects) and a self-reported history of pregnancy associated hypertension (15 subjects) were not excluded (see limitations section). There were three births, missing gestational age: two at Time B and one at Time C. These were presumed to be full-term based on birth weights 3515, 3969, and 4110 grams. Hypertensive patients were defined by either a patient listed as hypertensive on an anti-hypertensive medication or a patient with BP > 140/90 prior to pregnancy; patients listed as hypertensive not on anti-hypertensive medication with BP <140/90 were not excluded. 15 patients were included in the study who reported a history of hypertensive disorder during pregnancy (“toxemia” or “high blood pressure without toxemia”) at Time B or Time C for respective birth at Time B or Time C. A total sample included 142 women gave birth between Time A and Time C. These women were divided into 2 cohorts for the purpose of data analysis. The first cohort included women who delivered between Time A and Time B (74 women); the second cohort included women who delivered between Time B and Time C (68 women). There were no twin deliveries in the 2 cohorts. Seven subjects had 2 births within a cohort, with only the first birth used in the study.

### **Predictors and Time Points**

Up to 13 potential predictors were explored to predict birth weight at Time B and Time C. Birth weight at Time B indicates a delivery between Time A and Time B (first cohort). Birth weight at Time C indicates a delivery between Time B and Time C (second cohort). The systolic blood pressure (SBP), diastolic blood pressure (DBP), BMI and gestational age were utilized at Time A and Time B for birth weight analyses at Time B and Time C. Additionally, change in SBP and DBP between Time A and Time B was used for analysis with birth weight at Time C. All other explanatory variables (maternal age, prior pregnancy, fasting blood glucose (FBG), total cholesterol, triglycerides, high-density lipoprotein (HDL)) were obtained at Time A and used for analysis of birth weights at both Times B and C, because these tests were not repeated at Time B in the CARDIA study.

### **Bivariate Analyses**

The association between each continuous predictor versus birth weight was first assessed by examining the X vs Y scatter plot, and calculating the non-parametric Spearman correlation calculating the slope (rate of birth weight change per unit increase in X) with standard error (SE) and p value using simple linear regression and assessing linearity. The assessment of linearity between birth weight and a potential continuous predictor was assessed using restricted cubic splines (RCS) and a likelihood ratio test comparing linear to RCS.

Bivariate assessments were performed for the birth weight at Time B with predictors at Time A (Table S1), for birth weight at Time C with predictors at Time A and Time B (Table S2), and for combined birth weights at Times B and C with predictors at Time A and Time B (Table 2).

### **Multivariable Analyses**

Multivariate linear regression was used to assess the simultaneous relationship of the up to 14 potential predictors with birth weight. The simultaneously significant variables were chosen from the candidates such to minimize the Akaike Information criterion (AIC) (minimum AIC search). The AIC becomes smaller as the model fit to the data improves. In addition to the AIC, the R square ( $R^2$ ) statistic is reported. The  $R^2$  is the percentage of the total variation in birth weight that is explained by the variables in the regression model. The higher the value of  $R^2$  the better the model. The residual error standard deviation (SD) is also reported as another measure of accuracy. This is the SD of the errors where error = observed birth weight – model predicted birth weight. The residual errors follow a normal distribution with mean zero and the residual SD reported. For example, a residual SD of 400 grams means that about 2/3 of the predicted values are within 400 grams or less of the observed value. A perfect model has a residual SD of zero.

All two-way interaction among variables identified by the AIC search were also evaluated in the combined dataset of  $n=143$  as the larger sample size made feasible.

Residual errors were examined to confirm that these errors follow a normal (Gaussian) distribution, demonstrating that the parametric linear regression models were appropriate.

Multivariate analyses were performed for combined birth weights at Times B and C with predictors (Tables 3-4).

## Results

### Baseline Characteristics

Table 1 summarizes the distribution of maternal age (years), SBP (mmHg), DBP (mmHg), FBG, total cholesterol, triglycerides, HDL, BMI ( $\text{kg}/\text{m}^2$ ), gestational age (weeks), birth weight (grams), and prior pregnancy for 142 African American women in the CARDIA study at Times A, B, C, depending on the variable. At inception (Time A), the mean age of the women was 23.6 years old (SD 3.67, minimum 18, maximum 30). The mean SBP at Time A was 105.5 mmHg (SD 7.83) and at Time B was 104.18 mmHg (SD 9.98). The mean DBP at Time A was 65.1 mmHg (SD 7.3) and at Time B was 66.56 mmHg (SD 9.47). The mean BMI at Time A was  $25.6 \text{ kg}/\text{m}^2$  (SD 5.46) and at Time B was  $25.95 \text{ kg}/\text{m}^2$  (SD 5.6). The mean gestational age at Time B was 40.3 weeks (SD 1.74) and at Time C was 39.6 weeks (SD 1.43). The mean birth weight at Time B was 3400.4 grams (SD 497.5), at Time C was 3316.9 grams (SD 483.3), and combined Times B and C was 3360.4 grams (SD 490.8). The number of women included in the study with prior pregnancy was 100 out of 142 (70.4%).

### Linearity

The likelihood ratio results showed that the relations of the continuous predictors with birth weight were approximately linear.

### Prediction of Birth Weight Using Pre-Pregnancy Risk Factors

SBP was negatively related to birth weight (Table 3) in a non-additive model for combined birth weights at Time B and Time C with six predictors: prior pregnancy, SBP, BMI, maternal age, gestational age and total cholesterol. This model also includes interactions of prior pregnancy and BMI with gestational age. The model indicates that for every decrease in SBP by 1 mmHg, birth weight increases by an average of 10 grams, holding all else constant ( $p=0.024$ ). This interactive model posits the effect of gestational age on birth weight in term pregnancy depends on parity. History of a prior pregnancy is associated with increased birth weight at 37 weeks versus no history of prior pregnancy. The difference narrows as gestational age increases ( $p = 0.002$ ). The mean difference in birth weight at 37 weeks gestational age for prior pregnancy versus no prior pregnancy is 645 grams. The mean difference is 166 grams in birth weight at 40 weeks gestational age, prior

pregnancy versus no prior pregnancy. The model also shows the effect of gestational age on birth weight depends on the range of BMI. Increasing gestational age is associated with an increased birth weight, but the effect of gestational age is blunted by higher pre-pregnancy BMI ( $p = 0.002$ ). Mean birth weight increases by 110 grams per week of gestational age (starting at term week 37) if pre-pregnancy BMI is held constant at  $22 \text{ kg}/\text{m}^2$ . Mean birth weight increases by 49 grams per week if pre-pregnancy BMI is held constant at its mean value of  $25.8 \text{ kg}/\text{m}^2$ . Mean birth weight increases by 5 grams per week (ie, is roughly constant) if pre-pregnancy BMI is held constant at  $28.5 \text{ kg}/\text{m}^2$ . This model accounts for about one quarter of the variation in birth weight ( $R^2=25.6\%$ )

Another model (Table 4) substitutes SBP with DBP, but keeps other predictors the same. This DBP is also negatively related to birth weight. For every decrease in DBP by 1 mmHg, birth weight increases on average by 9.2 grams ( $p=0.044$ ). This model also accounts for about 25% of the variation in birth weight ( $R^2=25.1\%$ ).

## Discussion

### Main Findings

The principal finding of our study is that pre-pregnancy SBP and DBP in African American women are each negatively related to birth weight. SBP and DBP estimate the same relationship with birth weight and suggest that SBP and DBP are interchangeable. Additionally, we found that gestational age and birth weight depend upon the presence of prior pregnancy and range of BMI.

### Interpretation

A history of maternal delivery of a LBW infant or personal history of being a LBW infant impact future cardiovascular risk factors and risk of future cardiovascular disease. Pregnancy complications, including delivery of a LBW/SGA infant and hypertensive disorders, are established risk markers and independent risk factors for future maternal CVD, hypertension, dyslipidemia and diabetes.<sup>5,12-14</sup> The literature reports a variety of established CVD risk factors which not only follow complicated pregnancies but also may precede such pregnancies.<sup>5,15</sup> Pre-pregnancy CVD risk factors are associated with the hypertensive disorders of pregnancy.<sup>16</sup> SGA/LBW infants have a higher risk of neonatal morbidity and mortality, future educational and social issues and future CVD risk factors.<sup>3,17</sup> Of note, the majority of SGA births are term births.<sup>18</sup> A review of the risk factors for LBW/SGA births include many maternal risk factors (maternal age, parity, body mass index (BMI), tobacco exposure, substance abuse), maternal history of prior SGA/PAH/stillbirths, maternal medical health issues (diabetes mellitus, chronic hypertension, renal impairment, antiphospholipid syndrome) and psychosocial issues.<sup>19</sup> Risk factors for SGA overlap with those for preterm birth. The availability of pre-pregnancy CVD risk factors in the CARDIA study allows study of the effects of CVD risk factors on prematurity.<sup>20</sup> Study

of term pregnancies eliminates the confounding potential independent or overlapping risk factors with preterm delivery.

The present study adds another piece of evidence to the growing literature that subtle pre-pregnancy CVD risk factors are related to birth outcomes including low birth weight in term pregnancy in African American women.

Our study is consistent with results found by Harville in the Cardiovascular Risk in Young Finns Study which included 1142 women.<sup>21</sup> The study found a strong relationship between pre-pregnancy SBP and preterm birth and SGA/LBW in primiparous women. However, the Harville study included women with both preterm deliveries and term deliveries. Our study did not reveal a relationship between pre-pregnancy lipid fractions or fasting blood glucose and birth weight, which are suggested in the Harville study. A large Chinese cohort study did not demonstrate a relationship between preconception blood pressure and LBW/SGA.<sup>22</sup> The Chinese study, however, included Chinese women who delivered both preterm and full-term babies (between 28 to 45 weeks). A recent population-based study of Korean women did show a relationship between higher range pre-pregnancy, non-hypertensive SBP (<140/90) with higher incidence of low birth weight.<sup>23</sup>

US-born black women have been noted to have lower birth weight infants than both African-born black women (living in the US) and US-born white women.<sup>3</sup> US born black women on average have higher SBP and DBP than both African-born black women and US born white women (mean SBP/DBP 129.1/76.3, 121.0/71.9, 118.3/72.2, respectively).<sup>24</sup> Long term exposure to environmental factors may play a role in the observed higher blood pressure and lower birth weights in US-born African American women.<sup>3</sup>

This study's findings of relationship of pre-pregnancy CVD risk factors to birth weight suggest that future studies to

evaluate interventions to reduce blood pressure pre-pregnancy to improve birth outcomes may be warranted.

### Limitations

The limitations of this study include the following: Because of a small sample size, results were not validated on a validation dataset. Other factors included in our data set may account for the low amount of birth weight variation explained in our models (small  $R^2$  values). The factors may include, psychosocial stress, poverty, diet, exercise, alcohol use and family history. Some of these factors were included in the CARDIA study database, however, were difficult to qualify and quantify and thus were not included in our analysis. Women with sickle cell trait were not excluded based on demonstration of similar birth weight pregnancies in women with sickle cell trait versus non-sickle cell trait.<sup>25</sup> Women with a self-reported history of hypertension during pregnancy were not excluded from our study because of potential unreliability of maternal recall.<sup>26</sup> Furthermore, studies have demonstrated that late term pre-eclampsia may not be associated with a reduction in birth weight compared to normotensive pregnancies.<sup>27</sup> In our study, 15 women reported pregnancies with "toxemia" or "high blood pressure without toxemia," however the average birth weight for these pregnancies was 3430 grams compared to the average birth weight for the remaining 127 pregnancies which was 3352 grams.

### **Conclusion**

We found that in a United States based cohort of African American women with no known CVD risk factors, pre-pregnancy normal range blood pressure was related to term birth weight.

Figures/Tables

Figure S1: Exclusions for deliveries between Years 0 and 2

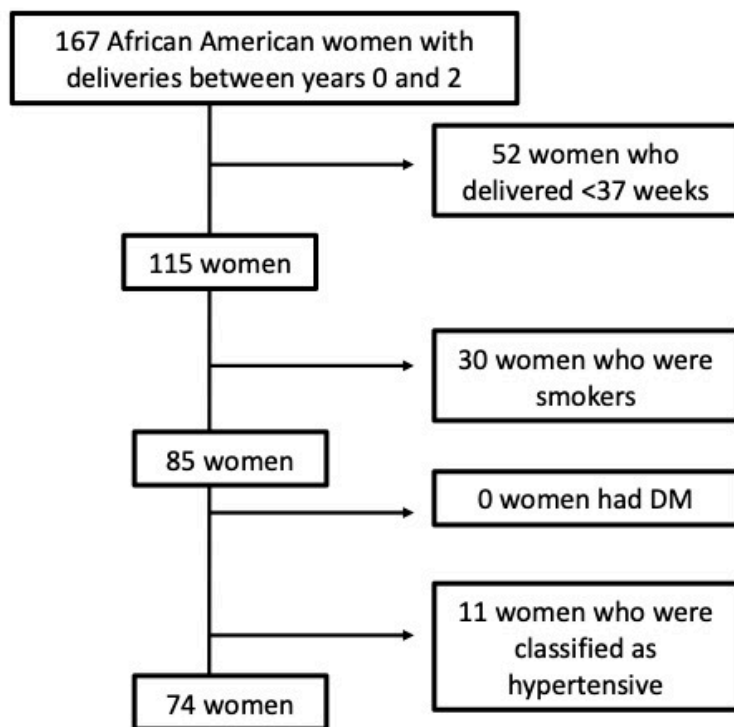


Figure S2: Exclusions for deliveries between Years 2 and 5

Footnote: women were considered smokers if listed as smoker at time B or time A if no data was listed on smoking at time B

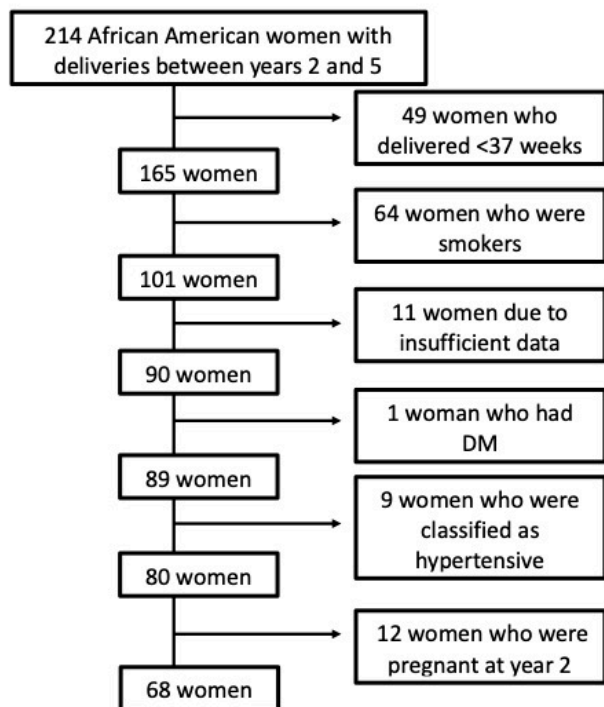


Table 1 - Descriptive statistics

Predictor		n	Min	1st Quartile	Median	Mean	3rd Quartile	Max	SD
Maternal age	Time A	142	18.0	20.0	24.0	23.6	27.0	30.0	3.67
FBG	Time A	142	62.0	74.0	78.0	78.6	83.0	99.0	7.18
Total cholesterol	Time A	142	112.0	158.0	175.0	178.5	194.8	282.0	30.98
Triglycerides	Time A	142	18.0	42.0	53.0	60.7	73.8	142.0	25.53
HDL	Time A	142	34.0	47.0	55.0	56.4	63.8	88.0	11.88
<hr/>									
SBP	Time A	74	88.0	101.0	105.5	105.5	110.8	127.0	7.83
	Time B	68	78.00	96.00	104.00	104.18	110.50	136.00	9.98
DBP	Time A	74	48.0	61.3	65.0	65.1	69.0	86.0	7.30
	Time B	68	40.00	60.00	67.00	66.56	72.00	88.00	9.47
BMI	Time A	74	17.0	21.7	24.3	25.6	28.0	41.0	5.46
	Time B	68	17.29	22.28	24.02	25.95	29.18	46.24	5.60
Gestational age	Time B	72*	37.0	39.8	40.0	40.3	42.0	47.0	1.74
	Time C	67*	37.00	38.75	40.00	39.60	40.00	43.00	1.43
Birth weight (gm)	Time B	74	2268.0	3061.7	3430.3	3400.4	3699.6	4422.5	497.5
	Time C	68	1757.7	2969.6	3274.4	3316.9	3692.5	4195.7	483.3
	Time B or C	142	1757.7	3005.0	3401.9	3360.4	3706.7	4422.5	490.8

		n	Proportion
Prior pregnancy	Time B+C	100	0.704

Time A = year 0, Time B = year 2, Time C = year 5

Footnote: maternal age is in years, gestational age is in weeks, birthweight is in grams

\*there were 2 births at time B and one birth at time C that did not report gestational age which is why n value is different

Table 2 Bivariate association with birth weight in grams at Time B or C in grams, n=142

Predictor (X)	Correlation	Rate(g/X)	SE	p-value	LR test for linear relationship	
					LR test stat	LR p-value
Maternal age - Time A	0.127	14.33	11.25	0.2047	0.240	0.9708
SBP (mm Hg) *	-0.201	-11.30	4.55	<b>0.0142</b>	3.334	0.3429
DBP (mm Hg) *	-0.212	-13.23	4.80	<b>0.0067</b>	3.379	0.3368
FBG - Time A	0.118	6.92	5.75	0.2306	4.103	0.2505
Total cholesterol - Time A	0.136	1.99	1.33	0.1355	4.459	0.2160
Triglycerides - Time A	-0.003	-0.03	1.62	0.9844	2.281	0.5161
HDL - Time A	0.026	1.62	3.49	0.6426	2.662	0.4467
BMI (kg/m2) *	0.121	8.96	7.75	0.2497	4.706	0.1947
Gestational age (weeks) *	0.171	54.88	25.25	<b>0.0314</b>	2.484	0.4782

\*most recent Time B or Time C: Time A for birthweight at B; Time B for birthweight at C

**Categorical Predictors** Q1=first quartile birth weight, Q3=third quartile birth weight

Prior Pregnancy	n	Mean	SD	p-value
No	42	3221.7	571.7	
Yes	100	3422.9	442.8	

**0.0254**

Footnote: maternal age is in years, gestational age is in weeks, birthweight is in grams

Table 3 Model 1 for birth weight in grams at Time B+C, n = 142; using SBP

Model 1: using SBP				
Predictor (X)	coefficient	SE	p-value	Rate (gm/X)**
Intercept	-19586.6	5390.0	0.0004	
Prior pregnancy (y/n)	6549.1	1977.2	<b>0.0012</b>	166.4**
Maternal age	7.9	10.7	0.4651	7.9
SBP*	-10.0	4.4	<b>0.0235</b>	-10.0
Total cholesterol – Time A	1.69	1.22	0.1667	1.69
BMI*	655.4	203.8	<b>0.0016</b>	8.20**
Gestational age (weeks) *	578.9	133.5	<b>0.0000</b>	49.2**
Prior preg x gest age	-159.6	49.4	<b>0.0016</b>	
BMI x gest age	-16.2	5.1	<b>0.0020</b>	

n	142
R square	25.7%
SD error (gm)	435.6
AIC	2139.47

\*most recent Time B or Time C: Time A for birthweight at B; Time B for birthweight at C

\*\* rates for prior pregnancy, BMI and gestational age are part of an interaction. Therefore the rate given is that holding the other variables constant at its mean

Model 1A- Birth weight in grams -Prior pregnancy x gestational age interaction

gest age	no prior preg	prior preg	mean difference= prior - no prior
37.0	2740	3385	645.1
38.0	2901	3387	485.6
39.0	3063	3389	326.0
40.0	3224	3391	166.4
41.0	3386	3393	6.9
rate/wk	161.5	1.92	

Model 1B –Birth weight in grams - BMI x gestational age interaction

gest age	BMI=22.0	BMI=25.8	BMI=28.5
37.0	2978	3194	3347
38.0	3089	3243	3353
39.0	3200	3292	3358
40.0	3310	3341	3364
41.0	3421	3391	3369
rate/wk	110.6	49.2	5.5

Table 4 Model 2 for birth weight in grams at Time B+C, n = 142; Substituting DBP for SBP

Model 2: Substituting DBP for SBP				
Predictor (X)	coefficient	SE	p-value	Rate (gm/X)**
Intercept	-19700.6	5423.3	0.0004	
Prior pregnancy (y/n)	6370.4	1988.0	<b>0.0017</b>	168.0**
Maternal age	12.2	10.6	0.2523	12.2
DBP*	-9.2	4.5	<b>0.0444</b>	-9.2
Total cholesterol – Time A	1.74	1.22	0.1572	1.74
BMI*	656.8	204.7	<b>0.0017</b>	5.54**
Gestational age (weeks) *	569.7	134.8	<b>0.0000</b>	40.4**
Prior preg x gest age	-155.1	49.6	<b>0.0022</b>	
BMI x gest age	-16.3	5.2	<b>0.0020</b>	

n	142
R square	25.1%
SD error (gm)	437.4
AIC	2140.64

\*most recent Time B or Time C: Time A for birthweight at B; Time B for birthweight at C

\*\* rates for prior pregnancy, BMI and gestational age are part of an interaction. Therefore the rate given is that holding the other variable constant at its mean

Model 2A – Birth weight in grams - prior pregnancy x gestational age interaction

gest age	no prior preg	prior preg	mean difference= prior - no prior
37.0	2774	3407	633.2
38.0	2923	3402	478.2
39.0	3073	3396	323.1
40.0	3223	3391	168.0
41.0	3372	3385	13.0
rate/wk	149.6	-5.5	

Model 2B – BMI x gestational age interaction

gest age	BMI=22.0	BMI=25.8	BMI=28.5
37.0	3013	3220	3366
38.0	3115	3260	3363
39.0	3218	3300	3359
40.0	3320	3341	3356
41.0	3422	3381	3352
rate/wk	102.3	40.4	-3.5

Table S1 Bivariate association with Time B birth weight in grams, n=74

Predictor (X)	Spearman correlation	Rate (g/X)	SE	p-value	Test for Linear relationship	
					LR chi square	p-value
Maternal age - Time A	0.068	7.95	15.83	0.6170	1.07	0.7832
SBP - Time A	-0.161	-5.74	7.46	0.4441	3.62	0.3050
DBP - Time A	-0.113	-6.97	7.98	0.3856	3.91	0.2713
FBG - Time A	0.178	9.57	8.34	0.2552	3.75	0.2901
Total cholesterol - Time A	0.147	3.13	2.26	0.1697	2.01	0.5703
Triglycerides - Time A	0.123	1.22	2.48	0.6257	0.24	0.9712
HDL - Time A	-0.029	0.44	4.92	0.9290	2.30	0.5128
BMI - Time A	0.086	6.90	10.70	0.5210	1.52	0.6784
Gest age (weeks) - Time B	0.048	14.80	34.28	0.6673	1.67	0.6444

Prior Pregnancy	n	Birth Weight (g)		
		mean	SD	p-value
No	21	3271.0	507.2	
Yes	53	3451.7	455.9	
0.164				

Footnote: maternal age is in years, gestational age is in weeks, birthweight is in grams

Table S2 Bivariate association with Time C birth weight in grams, n=68

Predictor (X)	Spearman correlation	Rate (g/X)	SE	p-value	Test for Linear relationship	
					LR chi square	p-value
Maternal age - Time A	0.212	22.37	16.05	0.1680	0.208	0.9763
SBP - Time A	-0.130	-7.95	6.29	0.2105	2.425	0.4890
DBP - Time A	-0.114	-5.27	7.50	0.4849	1.783	0.6186
FBG - Time A	0.086	5.89	8.05	0.4667	1.321	0.7242
Total cholesterol - Time A	0.162	1.60	1.65	0.3364	3.822	0.2813
Triglycerides - Time A	-0.093	-0.57	2.20	0.7978	4.269	0.2339
HDL - Time A	0.092	2.72	4.98	0.5874	1.465	0.6904
BMI - Time A	0.170	10.34	11.40	0.3680	7.147	0.0674
Gest age (weeks) - Time C	0.238	109.89	39.49	<b>0.0070</b>	4.085	0.2525
SBP - Time B	-0.295	-15.72	5.64	<b>0.0069</b>	2.082	0.5556
DBP - Time B	-0.317	-16.74	5.94	<b>0.0063</b>	1.292	0.7311
BMI - Time B	0.133	7.94	10.59	0.4559	5.758	0.1240
SBP diff: Time B – Time A	-0.156	-9.95	6.24	0.1154	6.663	0.0834
DBP diff: Time B – Time A	-0.255	-13.61	6.19	<b>0.0314</b>	0.959	0.8113
BMI diff: Time B – Time A	-0.057	-11.51	37.31	0.7587	4.122	0.2486

Prior Pregnancy	n	Birth Weight (g)		
		mean	SD	p-value
No	21	3172.4	638.5	
Yes	47	3402.00	386.3	
0.0998				

Footnote: maternal age is in years, gestational age is in weeks, birthweight is in grams; diff: Time B – Time A is difference between times B and A

**Financial Support:** statistics paid for by UCLA and personal funds.

**Conflict of Interest Statement:** Robert Gold and Kellyanne Gold are both affiliated with UCLA teaching facilities. Jeffrey Gornbein is employed by UCLA. No other interests to disclose.

**Corresponding Author:** Kellyanne R. Gold, MD, Olive View-UCLA Medical Center, Department of Medicine, 14445 Olive View Dr., Sylmar, CA 91342, USA; 1-818-292-2225; kellyannerosegold@gmail.com

### Contribution to Authorship:

Kellyanne Gold: worked on preliminary statistical analysis, drafted the paper sections, coordinated the other team members for meetings to discuss findings, provided analysis of findings, researched background information.

Robert Gold: developed the concept of the study, researched background information, worked on preliminary statistical analysis, provided analysis of findings.

Jeffrey Gornbein: performed all statistical analyses described in the methods section and drafted the methods section.



## Details of Ethics Approval

- The Olive View-UCLA IRB committee approved an IRB exemption on 11/2/2022. Reference number: IRBNet ID 1957640-1.

## REFERENCES

1. **Bramham K, Parnell B, Nelson-Piercy C, Seed PT, Poston L, Chappell LC.** Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. *BMJ.* 2014 Apr 15;348:g2301. doi: 10.1136/bmj.g2301. PMID: 24735917; PMCID: PMC3988319.
2. **Habli M, Levine RJ, Qian C, Sibai B.** Neonatal outcomes in pregnancies with preeclampsia or gestational hypertension and in normotensive pregnancies that delivered at 35, 36, or 37 weeks of gestation. *Am J Obstet Gynecol.* 2007 Oct;197(4):406.e1-7. doi: 10.1016/j.ajog.2007.06.059. PMID: 17904980.
3. **David RJ, Collins JW Jr.** Differing birth weight among infants of U.S.-born blacks, African-born blacks, and U.S.-born whites. *N Engl J Med.* 1997 Oct 23;337(17):1209-14. doi: 10.1056/NEJM199710233371706. PMID: 9337381.
4. **Gold KR, Gold RA, Schilling M, McGrady C.** Preconception cardiac risk factors in African American women with low birth rate term deliveries [22P]. *Obstet Gynecol.* 2018;131:179S.
5. **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(1):57-70. doi: 10.1093/epirev/mxt006. Epub 2013 Sep 11. PMID: 24025350; PMCID: PMC3873841.
6. **Catov JM, Nohr EA, Olsen J, Ness RB.** Chronic hypertension related to risk for preterm and term small for gestational age births. *Obstet Gynecol.* 2008 Aug;112(2 Pt 1):290-6. doi: 10.1097/AOG.0b013e31817f589b. PMID: 18669725; PMCID: PMC2596352.
7. **Li N, Li Z, Ye R, Zhu Y, Li S, Yang N, Zhang L, Li H, Liu J, Ren A.** Preconception blood pressure and risk of preterm birth: a large cohort study in China. *J Hypertens.* 2016 Nov;34(11):2243-7. doi: 10.1097/HJH.0000000000001069. PMID: 27512966.
8. **Wikström AK, Gunnarsdottir J, Nelander M, Simic M, Stephansson O, Cnattingius S.** Prehypertension in Pregnancy and Risks of Small for Gestational Age Infant and Stillbirth. *Hypertension.* 2016 Mar;67(3):640-6. doi: 10.1161/HYPERTENSIONAHA.115.06752. Epub 2016 Feb 1. PMID: 26831196.
9. **Cutter GR, Burke GL, Dyer AR, Friedman GD, Hilner JE, Hughes GH, Hulley SB, Jacobs DR Jr, Liu K, Manolio TA, et al.** Cardiovascular risk factors in young adults. The CARDIA baseline monograph. *Control Clin Trials.* 1991 Feb;12(1 Suppl):1S-77S. doi: 10.1016/0197-2456(91)90002-4. PMID: 1851696.
10. **Friedman GD, Cutter GR, Donahue RP, Hughes GH, Hulley SB, Jacobs DR Jr, Liu K, Savage PJ.** CARDIA: study design, recruitment, and some characteristics of the examined subjects. *J Clin Epidemiol.* 1988;41(11):1105-16. doi: 10.1016/0895-4356(88)90080-7. PMID: 3204420.
11. **Hughes GH, Cutter G, Donahue R, Friedman GD, Hulley S, Hunkeler E, Jacobs DR Jr, Liu K, Orden S, Pirie P, et al.** Recruitment in the Coronary Artery Disease Risk Development in Young Adults (Cardia) Study. *Control Clin Trials.* 1987 Dec;8(4 Suppl):68S-73S. doi: 10.1016/0197-2456(87)90008-0. PMID: 3440391.
12. **Park K, Minissian MB, Wei J, Saade GR, Smith GN.** Contemporary clinical updates on the prevention of future cardiovascular disease in women who experience adverse pregnancy outcomes. *Clin Cardiol.* 2020 Jun;43(6):553-559. doi: 10.1002/clc.23374. Epub 2020 Apr 17. PMID: 32304143; PMCID: PMC7298992.
13. **Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B.** 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2019 Sep 10;140(11):e563-e595. doi: 10.1161/CIR.0000000000000677. Epub 2019 Mar 17. Erratum in: *Circulation.* 2019 Sep 10;140(11):e647-e648. Erratum in: *Circulation.* 2020 Jan 28;141(4):e59. Erratum in: *Circulation.* 2020 Apr 21;141(16):e773. PMID: 30879339; PMCID: PMC8351755.
14. **Catov JM, Newman AB, Roberts JM, Sutton-Tyrrell KC, Kelsey SF, Harris T, Jackson R, Colbert LH, Satterfield S, Ayonayon HN, Ness RB.** Association between infant birth weight and maternal cardiovascular risk factors in the health, aging, and body composition study. *Ann Epidemiol.* 2007 Jan;17(1):36-43. doi: 10.1016/j.annepidem.2006.02.007. Epub 2006 Jul 12. PMID: 16843009.
15. **Rich-Edwards JW.** Reproductive health as a sentinel of chronic disease in women. *Womens Health (Lond).* 2009 Mar;5(2):101-5. doi: 10.2217/17455057.5.2.101. PMID: 19245346.
16. **Magnussen EB, Vatten LJ, Lund-Nilsen TI, Salvesen KA, Davey Smith G, Romundstad PR.** Prepregnancy cardiovascular risk factors as predictors of pre-eclampsia: population based cohort study. *BMJ.* 2007 Nov 10;335(7627):978. doi: 10.1136/bmj.39366.416817.BE. Epub 2007 Nov 1. PMID: 17975256; PMCID: PMC2072028.
17. **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 Sep;48(3):431-6. doi: 10.1161/01.HYP.0000236551.00191.61. Epub 2006 Jul 31. PMID: 16880348.
18. **Kozuki N, Katz J, Christian P, Lee AC, Liu L, Silveira MF, Barros F, Tielsch JM, Schmiegelow C, Sania A, Roberfroid D, Ndyomugenyi R, Mullany LC, Mongkolkeha A, Huybrechts L, Humphrey J, Fawzi W,**

- Baqui AH, Adair L, Oddo VM, Black RE; Child Health Epidemiology Reference Group Preterm Birth-SGA Working Group.** Comparison of US Birth Weight References and the International Fetal and Newborn Growth Consortium for the 21st Century Standard. *JAMA Pediatr.* 2015 Jul;169(7):e151438. doi: 10.1001/jamapediatrics.2015.1438. Epub 2015 Jul 6. PMID: 26147059.
19. Royal College of Obstetricians & Gynaecologists. Small-for-gestational-age fetus, investigation and management. (Green-top guideline no. 31). Available at: <https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/small-for-gestational-age-fetus-investigation-and-management-green-top-guideline-no-31/>.
20. **Catov JM, Ness RB, Wellons MF, Jacobs DR, Roberts JM, Gunderson EP.** Prepregnancy lipids related to preterm birth risk: the coronary artery risk development in young adults study. *J Clin Endocrinol Metab.* 2010 Aug;95(8):3711-8. doi: 10.1210/jc.2009-2028. Epub 2010 May 25. PMID: 20501685; PMCID: PMC2913035.
21. **Harville EW, Viikari JS, Raitakari OT.** Preconception cardiovascular risk factors and pregnancy outcome. *Epidemiology.* 2011 Sep;22(5):724-30. doi: 10.1097/EDE.0b013e318225c960. PMID: 21709559; PMCID: PMC3157236.
22. **Li N, Li Z, Ye R, Zhang L, Li H, Zhu Y, Li S, Yang N, Liu J, Ren A.** Preconception Blood Pressure and Risk of Low Birth Weight and Small for Gestational Age: A Large Cohort Study in China. *Hypertension.* 2016 Oct;68(4):873-9. doi: 10.1161/HYPERTENSIONAHA.116.07838. Epub 2016 Aug 1. PMID: 27480834.
23. **Jung YM, Oh GC, Noh E, Lee HY, Oh MJ, Park JS, Jun JK, Lee SM, Cho GJ.** Pre-pregnancy blood pressure and pregnancy outcomes: a nationwide population-based study. *BMC Pregnancy Childbirth.* 2022 Mar 19;22(1):226. doi: 10.1186/s12884-022-04573-7. PMID: 35305601; PMCID: PMC8934452.
24. **Cooper RS, Wolf-Maier K, Luke A, Adeyemo A, Banegas JR, Forrester T, Giampaoli S, Joffres M, Kastarinen M, Primatesta P, Stegmayr B, Thamm M.** An international comparative study of blood pressure in populations of European vs. African descent. *BMC Med.* 2005 Jan 5;3:2. doi: 10.1186/1741-7015-3-2. PMID: 15629061; PMCID: PMC545060.
25. **Tan TL, Seed P, Oteng-Ntim E.** Birthweights in sickle cell trait pregnancies. *BJOG.* 2008 Aug;115(9):1116-21. doi: 10.1111/j.1471-0528.2008.01776.x. Epub 2008 May 30. PMID: 18518873.
26. **Stuart JJ.** Identifying Women With a History of a Hypertensive Disorder of Pregnancy: Values, Challenges, and Opportunities. *Mayo Clin Proc.* 2018 Dec;93(12):1695-1697. doi: 10.1016/j.mayocp.2018.10.009. PMID: 30522587.
27. **Xiong X, Demianczuk NN, Saunders LD, Wang FL, Fraser WD.** Impact of preeclampsia and gestational hypertension on birth weight by gestational age. *Am J*