Published in final edited form as:

Paediatr Perinat Epidemiol. 2013 November ; 27(6): 587–597. doi:10.1111/ppe.12091.

Preconception Biomarkers of Allostatic Load and Racial Disparities in Adverse Birth Outcomes: the Bogalusa Heart Study

Maeve Wallace^a, Emily Harville^a, Katherine Theall^b, Larry Webber^c, Wei Chen^a, and Gerald Berenson^a

^aDepartment of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA

^bDepartment of Global Community Health and Behavioral Sciences, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA

^cDepartment of Biostatistics and Bioinformatics, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA

Abstract

Background—Large disparities in adverse birth outcomes persist between African American and white women in the US despite decades of research, policy, and public health intervention. Allostatic load is an index of dysregulation across multiple physiologic systems that results from chronic exposure to stress in the physical and socio-cultural environment which may lead to earlier health deterioration among racially or socio-economically disadvantaged groups. The purpose of this investigation was to examine relationships between maternal biomarkers of allostatic load prior to conception and the occurrence of preterm birth and small for gestational age infants among a cohort of white and African American women participants in the Bogalusa Heart Study.

Methods—Data from women participants were linked to the birth record of their first-born infant. Principal components analysis was used to construct an index of allostatic load as a summary of the weighted contribution of nine biomarkers representing three physiologic domains: cardiovascular, metabolic, and immune systems. A series of Poisson regression models based on samples ranging from 1467 to 375 women were used to examine race, individual biomarkers of allostatic load, and quartiles of the allostatic load index as predictors of preterm birth ($n = 150$, 10.2%) and small for gestational age ($n = 135$, 9.2%).

© 2013 John Wiley & Sons Ltd

Correspondence: Maeve Wallace, Department of Epidemiology, Tulane, University School of Public Health and Tropical Medicine, 1440, Canal St. Suite 1820, New Orleans, LA 70112, USA., mwallace@tulane.edu.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Descriptive Statistics of biological indicators measured at age 13 or the closest age to 13 within the range 11–14 among women with complete allostatic load biomarker data and all other women who participated in a BHS examination within the same age range.

Results—There was no evidence of a relationship between maternal preconception allostatic load and either adverse birth outcome in this sample. Further, there was no evidence of effect modification of by race or education.

Conclusions—More work is needed in understanding the biological mechanisms linking social inequities to racial disparities in adverse birth outcomes.

Keywords

race; allostatic load; stress; birth outcomes

African American women continue to experience disproportionately high rates of adverse reproductive health outcomes relative to women of other racial and ethnic groups in the US. These disparities persist despite decades of research and targeted intervention, and are not explained by differences in maternal education;¹ socio-economic status;² health behaviours such as smoking, alcohol, and drug use;³ and access to prenatal care.⁴ Allostatic load is an increasingly hypothesised biological mechanism through which the differential exposure to adversity in the social and physical environment place African American women at higher risk for preterm delivery and low birthweight infants relative to white women.

The theoretical construct of allostatic load refers to the cumulative dysregulation of the body's physiologic systems involved in stress response and adaptation: neuroendocrine, cardiovascular and respiratory, metabolic, and immune.⁵ It represents an indicator of physiologic 'wear and tear' that results from chronic exposure to stress in the physical and socio-cultural environment and has been studied as an antecedent to the onset of clinical disease.⁶ Repeated or prolonged activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to a loss of effectiveness and efficiency in stress hormone feedback mechanisms.⁷ As a result, exposure to chronically elevated levels of cortisol, epinephrine, norepinephrine, and dehydroepiandrosterone leads to increasingly poor regulation of the cardiovascular, inflammatory, and metabolic systems.⁸ Unsustainable over time, this cumulative physiologic burden can begin to manifest pathologically, leading to allostatic load, which has been associated with declines in physical and cognitive function and increased risk for cardiovascular diseases, cancers, autoimmune disorders, and other chronic diseases.⁹

While studies vary considerably in their operationalisation of allostatic load – including the constituent biomarkers used to measure it – results consistently implicate its role as a biologically mediated pathway between adversity and negative health outcomes.^{10,11} Allostatic load has been shown to be higher among individuals of socio-economic disadvantage,¹² those living in impoverished or deprived neighbourhoods,^{13,14} and non-white women.^{15,16}

As a model of biological risk patterned by the accumulation of exposure to adversity over the life course, it follows that allostatic load leading up to the time of pregnancy would be associated with negative birth outcomes.¹⁷ Yet, despite the theoretical plausibility of multi-systemic dysregulation as a precursor to clinical pathologies (including those that affect reproductive health), to our knowledge only one previous study has empirically measured allostatic load in pregnant women and analysed its impact on adverse pregnancy

outcomes.¹⁸ The purpose of this analysis is to examine the relationship between allostatic load prior to conception and the occurrence of preterm birth (PTB) and small for gestational age (SGA) infants, and to identify any differences in effect size by race or socioeconomic position.

Methods

Identification of study population

The women included in these analyses are participants of the Bogalusa Heart Study (BHS), a longitudinal investigation of cardiovascular disease risk began in 1973 by researchers now at Tulane University.¹⁹ Bogalusa, Louisiana, is a semi-rural town of approximately 45 000 residents. Surveys of the town's school children were repeated approximately every two years through 1994, enrolling new children as well as re-examining those previously enrolled. As children participants aged, they were eligible for re-examination in up to four of the 10 surveys conducted among adults age 18–50 occurring between the years of 1997 and 2009.

Birth records available for the proposed analysis were those issued by the State of Louisiana between the years 1990 and 2009, inclusive. This includes a total of 1 354 951 births. A three-stage data linkage procedure was used to link women from the BHS to birth record of their firstborn child using LinkPro v3.0 (InfoSoft, Inc., Winnipeg, MB) (Figure 1). Stage I consisted of a deterministic linkage based on maternal social security number, available in a subset of BHS participants and missing in only 5% of birth records. An exact match of social security number was sought for each woman with a non-missing SSN. All SSN matches (1:1, women to one birth and 1:N, women to multiple births) were considered definite matches.

Stage II was a probabilistic linkage among women who were previously unmatched by SSN and those who were missing SSN in the BHS data. Linkage was based on maternal date of birth (day, month, year), first name, last name, and Soundex codes for first and last names. Records with exact matches on all seven variables were classified as true matches. Those that matched on five or six of the seven variables were reviewed manually and classified as either true matches or non-matches.

Finally, Stage III of the linkage repeated Stage II, using the child's last name (and Soundex code) from the birth record and maternal last name from the BHS data set to identify any remaining possible matches. The same rules for minimum number of matching variables and manual review for classification of non-matches and true matches were applied.

Combining true matches from all three stages resulted in a single data set of 2773 women matched to 5227 infants. Limiting the data set to singleton first births resulted in 2743 mother–infant pairs. Of these, 1497 (54.6%) had BHS data available from an examination that occurred prior to the date of conception, 1467 (98.0%) had data from that examination on at least one of the nine allostatic load biomarkers, and 379 had complete data on all nine biomarkers. This large reduction in sample size is attributable to the panel study design of BHS and the fact that particular biomarkers were only collected during sub-studies such that

the measures are only available for participants who were present for that year's examination. While blood pressure, lipid profiles, and anthropometric measures are consistently collected at every BHS examination, collection of inflammation markers varies across exam years. Of the 1497 women who were successfully matched to the birth record of their singleton first-born child, 379 had not yet conceived when they attended either the 1987 or 1998 examinations when fibrinogen and white blood cells were measured and therefore had complete preconception allostatic load biomarker data.

Biomarker measurement

Nine biomarkers were available for use in the measurement of preconception allostatic load: systolic and diastolic blood pressure (SBP and DBP), total cholesterol, triglycerides, glucose, insulin, body mass index (BMI), fibrinogen, and white blood cells (WBC). These biomarkers were chosen as indicators of functioning across the primary domains of physiologic regulation: cardiovascular, metabolic, and immune systems, respectively.

Detailed descriptions of the BHS risk screening examinations have been published in greater detail elsewhere.¹⁹ Briefly, the physical examination involved duplicate height and weight measurements, which were used in the calculation of BMI (weight in kg/height m²). Right arm blood pressure was measured in triplicate with mercury sphygmomanometers by each of two trained observers on subjects in a relaxed, seated position; means of six replicate blood pressure readings were used for both SBP and DBP. All subjects were instructed to fast for 12 h prior to the examination and blood draw. Plasma glucose level was measured as part of a multiple chemistry profile (SMA20) with the multichannel Olympus Au-5000 analyzer (Olympus, Lake Success, NY). A radioimmunoassay kit was used to measure plasma insulin (Phadebas insulin kit, Pharmacia Diagnostics, Piscataway, NJ). Serum cholesterol and triglycerides levels were assayed enzymatically on the Hitachi 902 Automatic Analyzer (Roche Diagnostics, Indianapolis, IN). Fibrinogen data were determined using a Technicon H6000 (Technicon Instrument Corp. Tarrytown, NY). WBC count of whole blood was determined at the local Bogalusa Charity Hospital clinical laboratory using a Coulter counter method. All laboratories responsible for processing BHS samples are rigorously monitored for quality control, precision, and accuracy by independent institutions.

Allostatic load index construction

For women with complete allostatic load biomarker data, an allostatic load index was constructed using principal components analysis (PCA) in order to produce an empirical summary of the total multi-systemic variance explained by the constituent biomarkers. Previous research has similarly utilised PCA for the purposes of data reduction and development of a single linear index derived from a larger number of variables.^{20,21} Initially, each biomarker was standardised with a mean of 0 and variance 1. Item loadings on the first principal component – that which explains the largest possible amount of variation in the data²⁰ – were used to weight the contribution of each biomarker to the total allostatic load summary score. The linear allostatic load index was divided into quartiles to facilitate interpretation and comparison across levels of dysregulation.

Birth outcomes

Birthweight and gestational age data were extracted from the birth records and used to classify infants with regard to two adverse birth outcomes of interest: preterm birth (<37 weeks gestation), and small-for-gestational age (SGA; <10th percentile birthweight for gestational age based on this sample distribution). For all birth records, gestational age estimation is based on the date of the last menstrual period. When such data is missing, gestational age is based on a clinical estimate (as estimated by attendant) for birth records from 1990–2002 and later replaced by an obstetric estimate (as estimated by attendant based on all perinatal factors including ultrasound) for records after 2003.²²

Statistical analysis

Racial differences in individual allostatic load biomarkers, total allostatic load index, maternal age, education, smoking status during pregnancy, and birth outcomes were assessed in bivariate analyses. Additionally, date of conception was estimated by subtracting the number of days of gestation from the child's date of birth. For women who completed multiple BHS examinations, the one closest and prior to the date of conception was used in computing allostatic load.

A series of Poisson regression models with robust error variance were used to examine race, individual biomarkers of allostatic load, and quartiles of the allostatic load index as predictors of the two birth outcomes of interest. Allostatic load biomarkers that deviated from univariate normality were log transformed. Biomarkers were sequentially added to the models by physiologic domain. The final two models for both outcomes include the summary allostatic load index quartiles with and without the individual biomarker variables, respectively. All models were controlled for maternal education, age, length of time between allostatic load measurement and date of conception, and smoking during pregnancy. Given the broad range of years in which the woman's last preconception BHS examination may have occurred, we also controlled for date of examination. Women missing data on one or more of these control variables were not included in the regression models despite the availability of biomarker data. Therefore total *N*s in the model building tables begin slightly lower than those shown in Figure 1.

A priori tests for two and three-way interactions were considered for allostatic load, race, and maternal education at the time of birth. As a marker of socioeconomic position, we expected that a higher education level may buffer the effects of allostatic load on adverse birth outcomes among African American women.

To evaluate the robustness of our results, we conducted a sensitivity analysis by limiting the data to women with less than 5 years between the time of the allostatic load measurement and the date of conception. Given the inherently cumulative nature of physiologic dysregulation, allostatic load would be expected to increase with time as an individual ages.⁹ Therefore, we expected to find that among women with a narrower window between allostatic load measurement and pregnancy – such that a greater accumulation of physiologic burden may be apparent – the effect size on birth outcomes would be greater.

The Poisson modelling described above was repeated on the limited subset for both birth outcomes.

Results

Mean age at the time of BHS exam from which the allostatic load index was derived was approximately 12 years for both African American and white participants (Table 1). All of the participants gave birth to their first child at a relatively young age, although African American women had a slightly younger mean (20.1 years) compared to white women (21.2 years). Mean values for four of the nine biomarkers used in the operationalisation of allostatic load differed significantly between African American and white women when examined alone. Systolic blood pressure and insulin levels were higher among African American women, while white women had a higher mean level of triglycerides and white blood cells (all $P < 0.05$). Despite these differences, the distribution of women by quartile of allostatic load index did not differ by race.

Further, there was no racial disparity in the rates of PTB or SGA among the group of women with complete biomarker data.

Table 2 contains the model building for associations with preterm birth. Compared to white women, African American women were at an increased risk for preterm birth in the first three models. In the final three models, which included the addition of inflammation markers (WBC and fibrinogen) and the allostatic load index quartiles, race was not associated with an increased risk. Among the constituent allostatic load biomarkers, DBP and WBC demonstrated a consistent positive association with preterm birth (all $P < 0.05$). There was no evidence of a relationship between quartiles of allostatic load and preterm birth in both the model that contained the constituent biomarkers and the model that included only the summary index.

As with preterm birth, the racial disparity in SGA was apparent in the first three models but was no longer significant with the addition of inflammation biomarkers (Table 3). However, there was no consistent pattern in associations between individual allostatic load biomarkers and SGA. As above, there was no relationship between quartiles of allostatic load and SGA ($P = 0.23$). Finally, there was no significant effect modification by race or maternal education level on the relationships between allostatic load and PTB or SGA.

The results of the sensitivity analyses were consistent with the initial analyses. Among the women with 5 or fewer years between the time of allostatic load measurement and conception of their first child, the effect of allostatic load did not predict PTB or SGA.

Discussion

In the analyses presented here, we attempted to provide some empirical evidence of the deleterious effect that an accumulation of physiologic dysregulation leading up to the time of pregnancy can have on a woman's birth outcome. However, in the current analyses we did not find an association between allostatic load and PTB or SGA, nor was allostatic load related to continuous measures of gestational age or birthweight.

In reproductive health literature, allostatic load is a frequently proposed hypothesis to explain the disproportionate occurrence of adverse outcomes experienced by African American women.^{17,23,24} However, to our knowledge no study has investigated the relationship between pre-pregnancy allostatic load and length of gestation and birthweight or racial differences in these outcomes. Our previous work in this area includes a small prospective study of allostatic load in pregnant women (measured at 26–28 weeks gestation) and its impact on number of pregnancy outcomes.¹⁸ We found that higher allostatic load during pregnancy was associated with a shorter length of gestation, but the effect did not differ by race. Data available for the current study allowed us to measure women's allostatic load prior to her pregnancy. We believe that quantifying the relationship between a pre-pregnancy measure of allostatic load and adverse birth outcomes is important both for re-enforcing a life-course perspective and for minimising any bias due to the inherently altered physiological state of pregnancy that occurs independent of allostatic load. Despite the repeated measures design of the BHS, we had an insufficient sample of women with more than one preconception measure of multiple physiologic biomarkers and were unable to examine the longitudinal development of allostatic load leading up to pregnancy.

Much of the literature on the health effects of stress on reproduction has relied on subjective measures of stress and questionnaires that, while validated, may not capture the complex and multi-layered nature of stress from a physiological or biobehavioral perspective.²⁵ For example, Lu and Chen²⁶ found no association between stressful life events and racial disparities in preterm birth, but they acknowledge the inadequacy of their stress assessment which may have failed to capture the chronic stressors and unique contextual factors experienced by women of colour on a daily basis. To this extent, allostatic load may be a more appropriate measurement of the broader accumulation of stress over the life course.²⁵ While it is clear that individually the biological systems responsible for maintaining allostasis have direct impacts on fetal health,^{27,28} less is known about the effect of their collective dysregulation. The theoretical construct of allostatic load acknowledges their interconnected nature and emphasises a multi-systems view of reproductive health risks and differentials.

The characteristics of our unique study population may be one reason behind our null findings. The relatively young age at first birth in this population (mean = 21) and our requirement that allostatic load measurement occur prior to pregnancy implies an inherently shorter amount of time during which women in this sample may have experienced stress and accumulated physiologic wear and tear (mean age at allostatic load measurement = 13). In an analysis of a nationally representative sample of white and African American women, Geronimus *et al.*¹⁵ reported little difference in allostatic load scores among women younger than age 35 but significant and increasing racial gaps thereafter up to age 64. Second, the women included in our study represent an understudied population, given their unique location in the rural South. In a previous cross-sectional examination of allostatic load in this population, we found higher allostatic load levels among white women compared to African Americans, a peculiar and unexplained finding that suggests additional factors (poverty, lack of access to resources) may be at play. Additional studies should investigate how women in

a rural context experience and internalise chronic stressors and the extent to which it impacts their physical health.

There are limitations to the current study. First, as a secondary data analysis, this project is limited to the data available in the two linked data sets. While the BHS provides data on an extensive number of physiological biomarkers, there are no measures of stress hormones in women (cortisol, catecholamines, or their antagonists). The absence of stress hormones in a summary measure of allostatic load is arguably inadequate, as it is their over- or underproduction that mediate the pathological consequences of chronic stress. However, despite the unavailability of the primary mediators, the measures of allostatic load used in these analyses included a variety of secondary effect indicators from the metabolic, cardiovascular, and immune systems. Similarly, to date at least 12 publications based on the National Health and Nutrition Examination Survey have utilised measures of allostatic load that include only secondary effect indicators from these physiologic domains, as the survey data do not include stress hormones.²⁹ A recent publication on associations between neighbourhood poverty and allostatic load utilised only waist circumference, systolic and diastolic blood pressure, glucose, total cholesterol, triglycerides, and low- and high-density lipoproteins in their operationalisation of allostatic load.¹⁴ The measure of allostatic load used in the current study improved upon this by including fibrinogen and white blood cells in addition to these metabolic and cardiovascular indicators in order to capture immune system function. A previous study that sought to develop a meta-factor model of allostatic load demonstrated that the core domains of an allostatic load meta-factor were metabolism and inflammation, as these latent factors had the highest loadings.³⁰ Moreover, the inclusion of inflammatory biomarkers is an important distinction between allostatic load and metabolic syndrome. McCaffery³¹ *et al.* used confirmatory factor analysis to distinguish allostatic load from metabolic syndrome by including an inflammation factor (as measured by C-reactive protein and Interleukin 6) and vagal tone variables. Finally, Juster *et al.*¹⁰ suggest that the pathways leading to metabolic syndrome differ from allostatic load and that more work on the temporal sequencing of neuroendocrine dysregulation will further illuminate its effects on both of these subclinical conditions. To our knowledge, no previous study has estimated the effect of a preconception allostatic load measure –with or without stress hormones – on birth outcomes. Future studies should examine alternative biomarkers of allostatic load, including stress hormones, in order to capture a more complete measure of physiologic burden leading up to the time of pregnancy.

Second, despite the sound reliability of record linkage methodology for identifying mother–infant pairs,³² quantifying the validity and reliability of probabilistic record linkage is problematic if not impossible in many cases – as in the current study –where there is no gold standard of information to compare matches against. Incorrect linkage of mother–infant pairs is a small but unavoidable likelihood. However, stringent criteria for classifying true links, as well as verification with pregnancy-related variables available in the BHS data should have minimised this bias.

Third, only birth records issued by the state of Louisiana from 1990–2009 were available for the data linkage; therefore, the study population was limited to only those BHS participants who remained in (and gave birth in) the state of Louisiana. Moreover, since we limited the

data to first births, any BHS participant who gave birth prior to 1990 was excluded. In order to investigate the possibility of selection bias given these conditions, we did a crude comparison of race and age of women whom we successfully matched to a birth record and those who we did not (which includes women who never gave birth, those who gave birth before 1990, and those who gave birth out of state). A greater proportion of women included in our analysis were African American (40.1% compared to 34.7% of those unmatched, $P < 0.001$), and matched women were on average younger (35 compared to 42 years, $P < 0.001$). With regard to age, it is likely that the older women had given birth to their first child prior to 1990 and were therefore unmatched because of unavailability of birth records prior to 1990. Additionally, it may be that lower risk women who moved out of the state for career or educational pursuits were underrepresented. On the other hand, it may be that higher risk women who were not in contact with prenatal care and gave birth outside of the health care system were underrepresented. Given all of these possible scenarios, it is difficult to predict the direction of bias our sample selection through data linkage had on the estimates of effects. A future study based on data from a single source, such as a longitudinal cohort following women for both allostatic load and pregnancy data may yield less biased results.

Selection bias may also have occurred as a result of the panel study design of BHS, and the requirement that women included in the allostatic load analysis were those that had attended either of the 2 years' exams at which inflammation biomarkers were measured. In order to investigate how the women who attended these exams may have differed from all other women who ever attended a BHS exam, Supplemental Table S1 compares biologic characteristics measured at age 13 (or at the closest age within the range 11–14) between these two groups. Women included in the analysis had significantly higher levels of cholesterol and BMI. Blood pressure and triglyceride levels did not differ, and there was no difference in the racial distribution between the two groups. Both the BHS participants who were included in this analysis and those who were not attended at average approximately four exams to date (mean=3.9 vs. 3.6, respectively, $P < 0.01$). There is no clear distinction in the risk pro-files of those selected for analyses compared to those who were not included that would allow for prediction of the effect this bias may have had on the measures of association between allostatic load and birth outcomes.

Finally, as the primary outcome variables are based on values from the birth certificate (gestational age and birthweight), it is likely that some subjects may be misclassified with regard to preterm birth, low birthweight, and small for gestational age. In general, birthweight has shown to be a highly reliable variable from the birth record, whereas gestational age has only moderate reliability.³³ As the time frame of outcome measurement includes a span of 20 years' worth of birth records, it is likely that the quality of data changed over the course of the study years with improvements in fetal dating technology, which should reduce misclassification bias in infants born most recently. Ideally, future studies of preconception allostatic load with prospective data collection of infant weight and gestational age would overcome this limitation.

Despite its limitations, this work contributes to the literature by providing an empirical test of a frequently proposed hypothesis. Our lack of significant findings compels further investigation of the biological mechanisms linking social inequities to racial disparities in

adverse birth outcomes. These results underscore the need for further refinement of measures that capture holistically the way in which stressful conditions and experiences encountered across the life course shape the functioning and health of our bodies over time. This requires that future studies that include prospective collection of a range of biologic indicators measured in women longitudinally across critical periods of development. Concurrently, measures of the social and physical environment in which women are born, live, and work should be used to examine the stress biology in context. Finally, exploration of emerging theories of stress effects on development – such as those that focus on stress responsivity and adaptive calibration of stress mediators³⁴ – may provide superior explanations for how harmful exposures in the physical and social environment are internalised and can manifest in adverse pregnancy outcomes. Furthering our understanding of the longitudinal and contextual determinants of reproductive health – including the physical impact of societal disadvantage – can help shape policy and interventions that promote health equity among all women and their infants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was supported by grants ES-021724 from National Institute of Environmental Health Science, and AG-16592 from the National Institute on Aging and the Eunice Kennedy Shriver National Institute of Child Health And Human Development (T32HD057780 to MEW).

The content is solely the responsibility of the authors and does not necessarily represent the official views of the Eunice Kennedy Shriver National Institute of Child Health & Human Development or the National Institutes of Health.

References

1. Schoendorf KC, Hogue CJ, Kleinman JC, Rowley D. Mortality among infants of black as compared with white college-educated parents. *The New England Journal of Medicine*. 1992; 326:1522–1526. [PubMed: 1579135]
2. Berg CJ, Wilcox LS, d'Almada PJ. The prevalence of socioeconomic and behavioral characteristics and their impact on very low birth weight in black and white infants in Georgia. *Maternal and Child Health Journal*. 2001; 5:75–84. [PubMed: 11573842]
3. Goldenberg RL, Cliver SP, Mulvihill FX, Hickey CA, Hoffman HJ, Kelrman LV, et al. Medical, psychosocial, and behavioral risk factors do not explain the increased risk for low birth weight among black women. *American Journal of Obstetrics and Gynecology*. 1996; 175:1317–1324. [PubMed: 8942508]
4. Collins JW Jr, Wall SN, David RJ. Adequacy of prenatal care utilization, maternal ethnicity, and infant birthweight in Chicago. *Journal of the National Medical Association*. 1997; 89:198–203. [PubMed: 9094845]
5. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. *Annals of the New York Academy of Sciences*. 1998; 840:33–44. [PubMed: 9629234]
6. McEwen BS, Stellar E. Stress and the individual. Mechanisms leading to disease. *Archives of Internal Medicine*. 1993; 153:2093–2101. [PubMed: 8379800]
7. McEwen BS. Sex, stress and the hippocampus: Allostasis, allostatic load and the aging process. *Neurobiology of Aging*. 2002; 23:921–939. [PubMed: 12392796]

8. McEwen BS, Seeman T. Protective and damaging effects of mediators of stress. elaborating and testing the concepts of allostasis and allostatic load. *Annals of the New York Academy of Sciences*. 1999; 896:30–47. [PubMed: 10681886]
9. Seeman TE, Singer BH, Rowe JW, Horwitz RI, McEwen BS. Price of adaptation – allostatic load and its health consequences. *MacArthur studies of successful aging. Archives of Internal Medicine*. 1997; 157:2259–2268. [PubMed: 9343003]
10. Juster R, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience and Biobehavioral Reviews*. 2010; 35:2–16. [PubMed: 19822172]
11. Carlson ED, Chamberlain RM. Allostatic load and health disparities: a theoretical orientation. *Research in Nursing and Health*. 2005; 28:306–315. [PubMed: 16028266]
12. Crimmins EM, Kim JK, Seeman TE. Poverty and biological risk: the earlier ‘aging’ of the poor. *The Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2009; 64:286–292.
13. Bird CE, Seeman T, Escarce JJ, Basurto-Davila R, Finch BK, Dubowitz T, et al. Neighbourhood socioeconomic status and biological ‘wear and tear’ in a nationally representative sample of US adults. *Journal of Epidemiology and Community Health*. 2010; 64:860–865. [PubMed: 19759056]
14. Schulz AJ, Mentz G, Lachance L, Johnson J, Gaines C, Israel BA. Associations between socioeconomic status and allostatic load: effects of neighborhood poverty and tests of mediating pathways. *American Journal of Public Health*. 2012; 102:1706–1714. [PubMed: 22873478]
15. Geronimus AT, Hicken M, Keene D, Bound J. ‘Weathering’ and age patterns of allostatic load scores among blacks and whites in the United States. *American Journal of Public Health*. 2006; 96:826–833. [PubMed: 16380565]
16. Chyu L, Upchurch DM. Racial and ethnic patterns of allostatic load among adult women in the United States: findings from the National Health and Nutrition Examination survey 1999–2004. *Journal of Women’s Health*. 2011; 20:575–583.
17. Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: a life-course perspective. *Maternal and Child Health Journal*. 2003; 7:13–30. [PubMed: 12710797]
18. Wallace ME, Harville EW. Allostatic load and birth outcomes among white and black women in New Orleans. *Maternal and Child Health Journal*. 2012; 17:1025–1029. [PubMed: 22833335]
19. Berenson, GS.; McMahan, CA.; Voors, AW.; Webber, LS.; Srinivasan, SR.; Frank, GC. *Cardiovascular Risk Factors in Children: The Early Natural History of Atherosclerosis and Essential Hypertension*. New York: Oxford University Press; 1980.
20. Vyas S, Kumaranayake L, Vyas S, Kumaranayake L. Constructing socio-economic status indices: how to use principal components analysis. *Health Policy and Planning*. 2006; 21:459–468. [PubMed: 17030551]
21. Messer LC, Vinikoor LC, Laraia BA, Kaufman JS, Eyster J, Holzman C. Socioeconomic domains and associations with preterm birth. *Social Science and Medicine*. 2008; 67:1247–1257. [PubMed: 18640759]
22. Wier ML, Pearl M, Kharrazi M. Gestational age estimation on United States livebirth certificates: a historical overview. *Paediatric and Perinatal Epidemiology*. 2007; 21 (Suppl 2):4–12. [PubMed: 17803613]
23. Shannon M, King TL, Kennedy HP. Allostasis: a theoretical framework for understanding and evaluating perinatal health outcomes. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*. 2007; 36:125–134.
24. Latendresse G. The interaction between chronic stress and pregnancy: preterm birth from a biobehavioral perspective. *Journal of Midwifery and Women’s Health*. 2009; 54:8–17.
25. Hobel CJ, Goldstein A, Barrett ES. Psychosocial stress and pregnancy outcome. *Clinical Obstetrics and Gynecology*. 2008; 51:333–348. [PubMed: 18463464]
26. Lu MC, Chen B. Racial and ethnic disparities in preterm birth: the role of stressful life events. *American Journal of Obstetrics and Gynecology*. 2004; 191:691–699. [PubMed: 15467527]
27. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008; 371:75–84. [PubMed: 18177778]

28. Chappell LC, Enye S, Seed P, Briley AL, Poston L, Shennan AH. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: a prospective study. *Hypertension*. 2008; 51:1002–1009. [PubMed: 18259010]
29. Beckie TM. A systematic review of allostatic load, health, and health disparities. *Biological Research for Nursing*. 2012; 14:311–346. [PubMed: 23007870]
30. Seeman T, Gruenewald T, Karlamangla A, Sidney S, Lui K, McEwen B. Modeling multisystem biological risk in young adults: the coronary artery risk development in young adults study. *American Journal of Human Biology*. 2010; 22:463–472. [PubMed: 20039257]
31. McCaffery JM, Marsland AL, Strohacker K, Muldoon MF, Manuck SB. Factor structure underlying components of allostatic load. *PLoS ONE*. 2012; 7:e47246. [PubMed: 23112812]
32. Nitsch D, Morton S, DeStavola BL, Clark H, Leon DA. How good is probabilistic record linkage to reconstruct reproductive histories? Results from the Aberdeen children of the 1950s study. *BMC Medical Research Methodology*. 2006; 6:15. [PubMed: 16553951]
33. Vinikoor LC, Messer LC, Laraia BA, Kaufman JS. Reliability of variables on the North Carolina birth certificate: a comparison with directly queried values from a cohort study. *Paediatric and Perinatal Epidemiology*. 2010; 24:102–112. [PubMed: 20078836]
34. Del Giudice M, Ellis BJ, Shirtcliff EA. The adaptive calibration model of stress responsivity. *Neuroscience and Biobehavioral Reviews*. 2011; 35:1562–1592. [PubMed: 21145350]

Figure 1.
Linkage process flowchart and identification of study population.

Table 1

Descriptive statistics of sample demographics, biological indicators, and birth outcomes among women with complete preconception allostatic load biomarker data (N = 379)

	<u>African American (n = 151)</u>		<u>White (n = 228)</u>	
	Mean	SD	Mean	SD
Age at time of exam ^a	12.6	3.1	11.8	3.3
Age at first birth ^a	20.1	4.3	21.2	3.9
Allostatic load components				
SBP (mmHg) ^a	103.9	10.3	101.6	9.2
DBP (mmHg)	63.7	10.2	62.3	9.0
Body mass index (kg/m ²)	20.4	4.3	20.7	4.7
Total cholesterol (mg/dL)	175.5	31.1	170.1	28.6
Triglycerides (mg/dL) ^b	60.8	30.1	76.9	37.6
Glucose (mg/dL)	82.5	9.4	84.2	9.9
Insulin (uU/mL) ^a	17.2	21.7	13.0	10.1
White blood cells (1,000/ μ L) ^b	5.9	1.8	6.7	1.9
Fibrinogen (mg/dL)	267.1	85.2	260.6	82.7
	N	%	N	%
Education (at time of first birth)				
More than high school	47	31.1	71	31.1
High school	50	33.1	78	34.2
Less than high school	54	35.8	79	34.7
Allostatic load				
1st quartile (lowest)	35	23.2	60	26.3
2nd quartile	42	27.8	52	22.8
3rd quartile	35	23.2	60	26.3
4th quartile (highest)	39	25.8	56	24.6
Preterm birth	18	12.0	22	9.7
Small for gestational age	19	12.6	18	7.9

^a $P < 0.05$.

^b $P < 0.01$.

Table 2

Risk ratios (RR) and 95% confidence intervals (CI) for preterm birth associated with maternal race, education level, individual allostatic load biomarkers, and quartile of allostatic load index score^a

	<u>Model 1: n = 1,456</u>		<u>Model 2: n = 1,411</u>		<u>Model 3: n = 1,263</u>		<u>Model 4: n = 375</u>		<u>Model 5: n = 375</u>		<u>Model 6: n = 375</u>	
	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]
Race												
White	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]
African American	1.5	1.1, 2.0	1.6	1.1, 2.3	1.5	1.1, 2.3	1.5	0.8, 2.9	1.5	0.7, 2.9	1.4	0.7, 2.6
Education												
More than HS	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]
HS	0.8	0.6, 1.3	0.9	0.6, 1.3	1.4	0.8, 2.5	1.2	0.4, 3.5	1.1	0.5, 2.7	1.0	0.4, 2.5
Less than HS	1.4	0.8, 2.2	1.4	0.8, 2.3	1.0	0.7, 1.6	1.1	0.5, 2.7	1.3	0.4, 3.7	1.4	0.5, 3.5
Allostatic load biomarkers												
SBP (per 10 unit increase)	0.9	0.7, 1.1	1.0	0.8, 1.3	1.0	0.8, 1.2	0.7	0.5, 1.2	0.8	0.5, 1.4		
DBP (per 10 unit increase)	1.3	1.1, 1.6	1.3	1.0, 1.6	1.4	1.1, 1.7	1.6	1.1, 2.5	1.8	1.1, 2.8*		
BMI			1.0	0.95, 1.02	0.99	0.95, 1.0	1.0	0.9, 1.1	1.0	0.9, 1.1		
Total Cholesterol (per 10 unit increase)			1.0	0.95, 1.1	1.0	0.9, 1.1	1.1	1.0, 1.3	1.2	1.0, 1.3		
Triglycerides ^b			1.3	0.9, 1.9	1.2	0.8, 1.9	1.3	0.7, 2.5	1.5	0.8, 2.8		
Glucose ^b					0.7	0.1, 4.9	0.1	0.01, 0.8	0.1	0.01, 1.2		
Insulin ^b					1.0	0.7, 1.5	1.4	0.9, 2.3	1.4	0.9, 2.4		
White blood cells ^b							4.2	1.3, 13.4	3.9	1.2, 12.6		
Fibrinogen ^b							0.8	0.4, 1.4	0.8	0.4, 1.6		
Allostatic load index												
Quartile 1 (lowest)	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]
Quartile 2									0.8	0.4, 2.4	0.9	0.4, 2.2
Quartile 3									0.3	0.1, 1.1	0.4	0.1, 1.4
Quartile 4 (highest)									0.5	0.1, 2.6	1.2	0.5, 2.8

^a All models adjusted for maternal age at first birth, smoking during pregnancy, date of BHS examination, and years between allostatic load measurement and conception.

^b Biomarkers that deviated from normality were log (base_e) transformed before entered in the model.

BMI, body mass index; BHS, Bogalusa Heart Study; DBP, diastolic blood pressure; HS, high school; RR, risk ratio; SBP, systolic blood pressure.

Table 3

Risk ratios (RR) and 95% confidence intervals (CI) for small for gestational age associated with maternal race, education level, individual allostatic load biomarkers and quartile of allostatic load index score^a

	<u>Model 1: n = 1,456</u>		<u>Model 2: n = 1,411</u>		<u>Model 3: n = 1,263</u>		<u>Model 4: n = 375</u>		<u>Model 5: n = 375</u>		<u>Model 6: n = 375</u>	
	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]	RR	[95% CI]
Race												
White	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]
African American	1.8	1.3, 2.5	1.9	1.3, 2.7	1.9	1.3, 2.8	1.3	0.7, 2.5	1.3	0.6, 2.5	1.7	0.9, 3.1
Education												
More than HS	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]
HS	1.9	1.2, 3.2	1.9	1.1, 3.1	2.0	1.1, 3.5	1.4	0.5, 4.2	1.3	0.5, 3.3	1.5	0.6, 3.6
Less than HS	2.3	1.3, 4.2	2.3	1.3, 4.3	2.4	1.2, 4.7	2.5	0.8, 8.4	2.5	0.8, 7.3	2.3	0.7, 7.4
Allostatic load components												
SBP (scaled per 10 unit increase)	1.1	0.8, 1.4	1.2	0.9, 1.5	1.2	1.0, 1.5	1.5	1.0, 2.4	2.0	1.2, 3.3		
DBP (scaled per 10 unit increase)	0.9	0.7, 1.1	1.0	0.8, 1.2	1.0	0.8, 1.2	0.8	0.6, 1.2	1.1	0.7, 1.8		
BMI			0.9	0.9, 1.0	0.9	0.9, 1.0	0.9	0.8, 1.1	1.0	0.9, 1.1		
Total cholesterol (scaled per 10 unit increase)			1.0	1.0, 1.1	1.0	1.0, 1.1	1.0	0.9, 1.2	1.0	0.9, 1.2		
Triglycerides ^b			1.3	0.9, 1.9	1.3	0.8, 1.9	0.8	0.4, 1.6	1.0	0.5, 2.2		
Glucose ^b					0.9	0.3, 3.1	0.2	0.0, 6.0	0.4	0.02, 10.0		
Insulin ^b					1.0	0.7, 1.4	1.2	0.6, 2.4	1.3	0.7, 2.4		
White blood cells ^b							0.5	0.1, 1.7	0.5	0.1, 1.7		
Fibrinogen ^b							1.0	0.5, 2.1	1.2	0.5, 2.6		
Allostatic load index												
Quartile 1	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]	1.0	[Reference]
Quartile 2									0.4	0.1, 1.2	0.7	0.3, 2.0
Quartile 3									0.2	0.04, 0.8	0.5	0.2, 1.7
Quartile 4									0.1	0.02, 0.8	0.6	0.2, 1.8

^a All models adjusted for maternal age at first birth, smoking during pregnancy, date of Bogalusa Heart Study (BHS) examination, and years between allostatic load measurement and conception.

^b Biomarkers that deviated from normality were log (base_e) transformed before entered in the model. HS, high school; RR, risk ratio.