



Biomarkers of pre-pregnancy allostatic load and subsequent adverse birth outcomes

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ABSTRACT

Racial disparities in birth outcomes are seemingly intractable. Using person-centered methods and drawing from the life course and Weathering Hypothesis literatures, we used data from the National Longitudinal Study of Adolescent to Adult Health to group non-Hispanic White and non-Hispanic Black women ages 24–34 into latent classes based on pre-pregnancy biomarkers of allostatic load. Stratified analyses yielded four latent classes among non-Hispanic White women, characterized by: 1) high blood pressure, 2) high body mass index and waist circumference, 3) high total cholesterol and triglycerides, and low high-density lipoprotein, and 4) low-risk, and two latent classes among non-Hispanic Black women, characterized by: 1) high body mass index and waist circumference, and moderate-risk blood pressure, hbA1c, and c-reactive protein, and 2) low-risk. Allostatic load class membership and other maternal- and infant-level covariates were then included simultaneously as predictors of three separate dichotomous outcomes: preterm birth, macrosomia, and low birth weight in multilevel logistic regression models. In a separate multilevel linear regression model, the same variables were simultaneously entered to predict continuously measured birthweight. In multilevel, multivariate models, White women in the high-risk body mass index and waist circumference class, as compared to the high-risk blood pressure class, had infants with higher birthweights. Other comparisons were not significant or not of meaningful magnitude. Prioritizing temporality so that allostatic load measurement preceded first birth likely biased the composition of the analytical sample. Additional research is needed to help medical providers and public health practitioners understand the complex biological and social mechanisms underlying inequities in birth outcomes and identify prevention strategies.

1. Introduction

1.1. Preterm birth and birth weight

Preterm birth (birth at less than 37 weeks of completed gestation) (Olson et al., 2015) and low birth weight (less than 2500 g) (Ely et al., 2018; Xu et al., 2020) are the leading causes of infant morbidity and mortality in the United States. Preterm birth and low and high (more than 4000 g; macrosomia) birth weight are also associated with increased risk of cardiovascular disease, diabetes, and obesity in adulthood (Abu-Saad & Fraser, 2010; Danielzik et al., 2004; Fanaroff et al., 2007; Harder et al., 2007; Malin et al., 2014; Mathews et al., 2013). In the U.S., Black women are much more likely to have preterm (14.4%)

and low birthweight (14.2%) births than White women (9.3% preterm; 6.9% low birthweight) (Martin et al., 2021).

1.2. Racism and the Weathering Hypothesis

A recent review paper concluded that racism, working through multiple pathways and biological mechanisms, is the major upstream contributor to the persistent Black-White disparity in preterm birth in the U.S. (Braveman et al., 2021). Racism in the U.S. makes it such that “the context for childbearing among African Americans may be qualitatively distinct from that experienced by more advantaged populations” (pg. 215) (Geronimus, 1992). Specifically, “racism explains the racial disparity in socioeconomic factors— the legacy of slavery, 100

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years of Jim Crow laws, racial residential segregation, and ongoing discrimination in housing, employment, policing, and sentencing” (pg. 12), resulting in Black women being more exposed to stressful neighborhoods, fast food outlets, environmental toxins, and worse childcare, education, and healthcare than White women (Braveman et al., 2021). This conclusion dovetails with The Weathering Hypothesis, which suggests that racism, and associated cumulative life stressors, “weather” persons of color in the United States more quickly than White individuals. This “weathering” is thought to accumulate, wear down the body’s adaptive systems, and increase an individual’s vulnerability to disease (Geronimus et al., 2006). The cumulative socioeconomic disadvantage and racism experienced by Black women is hypothesized to cause their reproductive functioning to deteriorate more rapidly than that of White women (Geronimus, 1992, 1996; Seckl, 1998).

1.3. Allostatic load

The concept of allostatic load captures the prolonged activation of biomarkers as an organism attempts to maintain allostasis (homeostasis) in the face of environmental, genetic, and individual influences (McEwen & Stellar, 1993). Allostatic load is useful in characterizing the cumulative ‘wear and tear,’ or weathering, of multiple biological systems caused by stressors (McEwen & Wingfield, 2003), and has been used in previous research to link biomarkers of maternal stress with birth outcomes (Olson et al., 2015; Wallace et al., 2013a, 2013b).

1.4. Linking individual biomarkers of stress with birth outcomes

Several studies have looked at the associations between *individual biomarkers* (such as blood pressure, cholesterol, etc.) of pre-pregnancy health and subsequent birth outcomes, with mixed results (Harville et al., 2011; Magnusson et al., 2011; Moayeri et al., 2017; Smith et al., 2018; Witt et al., 2014). We are only aware of two studies that moved beyond individual biomarkers to explore the association between a cumulative risk measure (the sum of several individual biomarker indicators) of pre-pregnancy allostatic load and subsequent birth outcomes (Wallace et al., 2013a, 2013b). Both of these studies found no association. However, both studies drew from small town samples with young ages at biomarker collection (12 and 14.6 years) and first birth (21.4 years). The lack of association between pre-pregnancy allostatic load and subsequent birth outcomes could be due to limited exposure periods and the fact that variable-centered cumulative risk models, which describe associations between variables and their relative prediction of an outcome, assign equal weight to each biomarker and treat biomarkers as interchangeable. Thus, individuals can qualify as having high allostatic loads while presenting different biomarker profiles. We hypothesize that these variable-centered models fail to capture the complexities inherent in the accumulation of stress over a lifetime (weathering). Studies focused on individual risk factors also fail to account for their interconnection; person-centered approaches that cluster individuals based on their patterns of multiple existing health conditions among U.S. adults could provide new insights (Barnett et al., 2012; Boyd & Kent, 2014; Guthrie et al., 2012; Larsen et al., 2017).

1.5. What this study adds

The present study uses data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) to examine the existence and strength of an association between women’s membership in latent classes defined by patterns of biomarkers of maternal pre-pregnancy health and subsequent infant preterm birth and birthweight. We hypothesized that women in classes characterized by higher-risk allostatic load would have worse birth outcomes (i.e., more likely to have a preterm birth or an infant that is high or low birthweight) than women in lower-risk classes. We use latent class analysis (LCA), a holistic, person-centered technique that groups women with similar patterns of (both

measured and unmeasured) allostatic load. In addition to the strength of capturing patterns and potential interactions of factors through LCA, we use biomarkers as *objective* measures of preconception allostatic load in a population-based sample. Our respondents were between 24 and 34 years old at biomarker collection, and between 33 and 43 years old at age of first birth, capturing greater exposure periods (or more potential weathering) in a more diverse and larger sample than the Wallace et al. studies. These strengths may better detect the weathering effects of racism and associations with birth outcomes.

2. Methods

2.1. Data source

Add Health, launched to comprehensively study adolescent health and development in the context of peers, school, family, and neighborhood, recruited participants in grades 7–12 through their school in 1994–1995. All students who were in a sample of middle ($n = 52$) and high ($n = 80$) schools in the United States on the administration day took the in-school questionnaire ($n = 90,000$). Add Health also oversampled siblings, twins, and several racial/ethnic groups that are typically underrepresented in surveys, resulting in a sample of 20,745 respondents selected to complete the Wave I in-home interview (Harris et al., 2013). All eligible Wave I respondents were invited to participate in each subsequent wave. The allostatic load biomarkers for the present analyses are from the Wave IV dataset, collected in 2008, when respondents were aged 24–34. Over 99% of respondents consented to anthropometric and blood pressure measurement at Wave IV, and 95% consented to blood spot collection (Harris et al., 2013). To ensure that biomarker collection preceded the birth, we included only births that occurred after the Wave IV interview, as reported at Wave V (collected in 2016–2018).

2.2. Sample

Present analyses are restricted to individuals with a valid Wave V survey weight ($n = 12,300$) and region information ($n = 12,057$), who were female ($n = 6134$) and were not missing the birth section of the questionnaire ($n = 6011$). We also restrict to women who were not pregnant or probably pregnant ($n = 5599$) or in prison ($n = 5593$) at the time of Wave IV biomarker collection and were not missing information for more than 5 biomarkers ($n = 5543$). Women in our sample had to have at least one singleton birth that is reported at Wave V ($n = 3097$) with complete data on the infants’s biological sex, and birth month and year ($n = 2085$). Hispanic, non-Hispanic Asian, and women of “other” race were removed from our sample, for a latent class analysis sample size of 1644 women.¹ We then removed women who had given birth before Wave IV, resulting in a birth sample of 797 unique women giving birth to 1260 infants.

We excluded women who were pregnant or who had previously given birth at the time of biomarker collection because pregnancy is an inherently altered physiological state independent of allostatic load (Shannon et al., 2007), and parous and nulliparous women may differ on important metrics of allostatic load (Li et al., 2019). Multiple births (twins, triplets, etc.) are excluded because they are often delivered earlier and are smaller birthweight than singleton births (Martin et al., 2021).

¹ Our goal was to include Hispanic and non-Hispanic White, Black, and Asian women. However, our latent class analysis, stratified by race, resulted in one class solution for both Hispanic and non-Hispanic Asian women, forcing us to reduce our sample to only non-Hispanic White and Black respondents ($n = 1,644$).

2.3. Biomarker measurement in Add Health

At Add Health Wave IV, after consent was obtained, trained and certified field interviewers measured height and weight, which were used to compute the body mass index (BMI) of participants. Waist circumference was taken at the top of the hip bone using a circumference tape measure. Systolic and diastolic blood pressure (SBP and DBP, respectively) and pulse rate (PR) measurements were taken using oscillometric blood pressure monitors while the participant was in a seated position.

Using standard procedures, interviewers pricked a finger and then collected blood using a 7-spot capillary whole blood collection card (Entzel et al., 2009). From these samples, glycohemoglobin (HbA1c), an integrated measure of blood glucose control over the preceding 2–3 months, triglycerides (TG), low-density lipoprotein, high-density lipoprotein (HDL), and high sensitivity C-reactive protein (CRP) levels were assayed. Additional details on the collection and measurement of biomarkers in Add Health are available here: <https://www.cpc.unc.edu/projects/addhealth/documentation/guides>.

2.4. Measuring allostatic load

We used the ten biomarkers available in Add Health to group women based on latent classes of allostatic load. Consistent with previous allostatic load work, our latent class analysis was based on biomarkers dichotomized at high-risk cutpoints at the 75th/25th percentile (Seeman et al., 1997), but we also categorized the biomarker indicator as high-risk if the respondent reported a doctor or nurse ever telling them that they had that condition or if they took a medication for that condition. Data quality prohibited the release of exact biomarker values for women for total cholesterol (TC), TG, and HDL in Add Health (Whitsel, 2016). For these biomarkers, we only have decile cutoffs. To be conservative, we set our cutpoints for these biomarkers at the 8th decile for TC and TG and the 2nd decile for HDL (low, not high, HDL is considered high-risk).

Previous diagnoses of high blood pressure, cholesterol, or diabetes were captured with questions asking whether “a doctor, nurse or other health care provider ever told you that you have or had” that condition. If a respondent answered yes to the blood pressure question, they were coded as high-risk on both systolic and diastolic blood pressure, since we are unable to differentiate which was elevated based on the question. Similarly, if a respondent answered yes to the cholesterol question, they were coded as high-risk on total cholesterol, triglycerides, and HDL cholesterol.

At Wave IV, respondents were also asked about prescription medications they had taken in the last four weeks. When possible, the interviewer asked to see the medication and typed the name of each medication into the computer. Add Health then categorized medications based on the Multum Lexicon with this protocol: https://addhealth.cpc.unc.edu/wp-content/uploads/docs/user_guides/Medication_Documentation.pdf.

Respondents were coded as high-risk on: SBP and DBP if they were taking any blood pressure medication; HbA1c if they were taking any diabetes medication; CRP if they were taking any anti-inflammatories; and/or TC, TG, and HDL if they were taking any antihyperlipidemic medication.

2.5. Measuring birth outcomes

Birthweight is a continuous outcome based on mother’s report. We created dichotomized indicators of: macrosomia (births greater than 4000 g) and low birth weight (less than 2500 g). Preterm birth was assessed based on mother’s response to the question “a preterm delivery is one that occurs before 37 weeks in pregnancy (more than 3 weeks early). Was this baby born preterm?”

2.6. Maternal-level covariates

We created the following race/ethnicity categories based on respondent’s self-reported race/ethnicity at Wave V: Black or African American, non-Hispanic, and White, non-Hispanic. Educational attainment was dichotomized as college degree or higher vs. no college degree. We created dichotomized measures of whether the respondent reported pre-pregnancy: 1) binge drinking (4 or more drinks in a row for females) monthly or more frequently in the last year, and 2) smoking cigarettes on one or more days in the last 30 days. All covariates were selected based on prior literature (Athiros et al., 2013; Bailey & Sokol, 2011; Bhattacharya et al., 2010; Goldwater et al., 2019; Patra et al., 2011; Richardson et al., 2021; Wallace et al., 2013a,b).

2.7. Infant-level covariates

All infant-level covariates were assessed at Wave V. Mother’s age and the birthdate of the infant were used to calculate mother’s age at the birth of the focal infant. Infant’s biological sex is assessed with the question: “was this baby a boy or a girl?” Female infant is the referent category. Parity is categorized for each infant as first, second, and third or higher order birth. We created dichotomized measures of: 1) cigarette smoking during pregnancy, 2) whether or not the respondent was married to the pregnancy partner, and 3) receipt of prenatal care. We had so few respondents that did not receive prenatal care that this variable was ultimately dropped from the analysis. All covariates were selected based on prior literature (Bhattacharya et al., 2010; Di Renzo et al., 2007; Kramer, 1987; Murata et al., 1992; Shah et al., 2011).

2.8. Statistical analysis

We conducted analysis on two samples: LCA on women ($n = 1644$) and regressions on births ($n = 1260$) by a sample of those women ($n = 797$). Sample sizes are not the same because non-nulliparous women were removed from the analysis after the latent classes were built. Following standard LCA model fitting practice, we fit a series of models with an increasing number of classes, and each of these models was examined using various indices (the AIC, BIC, ssBIC, and Lo-Mendell-Rubin adjusted likelihood ratio test), classification uncertainty, and model interpretability, to select the best-fitting model. We examined results to determine whether or not class solutions should be stratified by race. Women were assigned to a latent class that had the highest probability of membership.

Allostatic load class membership and other maternal- and infant-level covariates were included simultaneously as predictors of three separate dichotomous outcomes: preterm birth, macrosomia, and low birth weight in multilevel logistic regression models. In a separate multilevel linear regression model, the same variables were simultaneously entered to predict continuously measured birthweight. To determine if we needed to stratify birthweight by term and preterm, we tested for interactions of term/preterm with each of our predictor variables in the birthweight model.

In Stata 16.1, data were coded and associations between predictors and birth outcomes were assessed. Latent class analyses and appropriate fit statistics were conducted in MPlus 8.4. Add Health has a complex survey design. Therefore, weighting is done for representativeness in latent class and regression analyses. In addition, regression analyses account for clustering at two levels: births within mothers and mothers within the schools where they were originally sampled, by using multilevel modeling. This study was deemed “not human subjects research” by the Institutional Review Board at The University of North Carolina at Chapel Hill.

Table 1
Prevalence of woman-level predictors of birth outcomes by race (n = 797 unique women).

	Non-Hispanic White women (n = 666)		Non-Hispanic Black women (n = 131)		Comparing White vs. Black values Weighted χ^2 p-value
	n	Weighted mean or % (95% CI)	n	Weighted mean or % (95% CI)	
White allostatic load class					
Class 1: high-risk TC, TG, & HDL	69	9.46% (6.59, 12.33)	–	–	–
Class 2: high-risk SBP & DBP	110	18.71% (13.74, 23.67)	–	–	–
Class 3: high-risk BMI & WC	107	17.47% (13.33, 21.62)	–	–	–
Class 4: low-risk	380	54.36% (47.47, 61.24)	–	–	–
Black allostatic load class					
Class 1: low-risk	–	–	82	50.49% (39.80, 61.18)	–
Class 2: high-risk BMI & WC	–	–	49	49.51% (38.82, 60.20)	–
4-year degree or higher		65.07% (58.88, 71.27)		62.53% (49.09, 75.97)	0.719
Smoker (pre-pregnancy)		36.21% (31.56, 40.86)		17.68% (7.46, 27.89)	0.001
Binge drinking monthly or more frequently (pre-pregnancy)		45.87% (41.38, 50.36)		16.06% (7.29, 24.83)	0.000

All variables in this table are from wave IV. Sample sizes (ns) are not weighted.

Table abbreviations: SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. WC: Waist circumference. TC: Total cholesterol. TG: Triglycerides. HDL: High-density lipoprotein.

3. Results

3.1. Descriptive statistics

The range, high-risk cutpoint, and weighted: mean, standard deviation, and prevalences of women categorized as high-risk for each biomarker, stratified by race, are displayed in [Appendix Table 1](#). Averaged over the full sample, most of the biomarkers are fairly close to ideal. However, the mean BMI is in the “overweight” category. Non-Hispanic Whites and Blacks statistically significantly differed on the percentages categorized as high-risk on seven biomarkers. Black women were more likely to be high-risk on SBP, hbA1c, BMI, and WC, while White women were more likely to be high-risk on CRP, TC, and TG. This suggests that the health profiles of young adult women in our sample vary by race.

3.2. Enumeration of latent classes

In stratified analyses we found different class solutions by race. In each of our race-stratified solutions, our log likelihood, AIC, BIC, and ABIC all decreased as the number of classes increased, suggesting that a greater number of classes fit the data progressively better. Among non-Hispanic Whites, the decreases in AIC, BIC, and ABIC began to level off after the 4-class solution, and the Lo-Mendell-Rubin Adjusted Likelihood Ratio Test also favors a 4-class solution ([Appendix Table 2](#)). Among non-Hispanic Blacks, the decreases in AIC, BIC, and ABIC began to level off after the 2-class solution, and the Lo-Mendell-Rubin Adjusted Likelihood Ratio Test also favors a 2-class solution ([Appendix Table 2](#)). Since classes were distinct (all classification probabilities were 0.91 or greater) and entropy was relatively high (0.805 for our Black 2-class solution, and 0.908 for our White 4-class solution), women were fixed in these classes for subsequent analyses ([Clark and Muthén, 2009](#)).

3.3. Latent classes by race

Among non-Hispanic Whites, class 1 (n = 104) comprised 8% of the weighted sample and was characterized by a high predicted probability (defined as >0.70) of high-risk TC (0.921), TG (1.000), and HDL (0.755), but low predicted probabilities (defined as <0.5) of being high-risk on the other biomarkers. Class 2 (n = 199) comprised 16% of the sample and was characterized by a high predicted probability of high-risk SBP (0.960) and DBP (0.820). Class 3 (n = 289) comprised 23% of the sample and was characterized by a high predicted probability of high-risk BMI (0.885) and WC (0.983). Non-Hispanic White class 4 (n = 666) comprised 53% of the sample and was characterized by low

predicted probabilities of being high-risk on all 10 biomarkers ([Appendix Table 3](#)).

Among non-Hispanic Black women, class 1 (n = 228) comprised 59% of the weighted sample and was characterized by a low predicted probability of being high-risk on all biomarkers. Class 2 (n = 158) comprised 41% of the sample and was characterized by high predicted probabilities of being high-risk on BMI (0.935) and WC (0.834), and moderately high (between 0.7 and 0.5) predicted probabilities of being high-risk on SBP (0.585), DBP (0.531), HbA1c (0.587), and CRP (0.601) ([Appendix Table 4](#)).

3.4. Woman- and birth-level descriptive statistics

White women were statistically significantly more likely than Black women to have smoked (36% vs. 18%) or binge drank (46% vs. 16%) pre-pregnancy ([Table 1](#)), and to be married to their pregnancy partner (90% vs. 51%) ([Table 2](#)). Focal births occurred between January 2008 and December 2018. White women in the sample had more children than Black women (among White women, 33% had 2 children, and 6% had 3 or more children, compared with 22% and 0% of Black women, respectively) ([Table 2](#)). White women had infants with higher mean birthweights than Black women (3396 vs. 3095 g), while Black women were three times as likely to have a low birthweight birth (15% vs 5%) and twice as likely to have a preterm birth (18% vs. 9%) ([Table 2](#)).²

3.5. Birth outcomes

3.5.1. White women

Preterm birth outcome. We present bivariate ([Table 3](#) and [Appendix Table 5](#)) and multivariate ([Table 3](#) and [Appendix Table 6](#)) results where preterm birth is the outcome in a binomial, multilevel logistic regression. In multivariate models, when the low-risk class is the reference category, no comparisons with other classes were statistically significant predictors of preterm birth ([Table 3](#)). However, when we look at comparisons with other classes, we see that being in the high-risk BMI and WC class (as compared to the high-risk SBP and DBP class) (OR = 6.63; 95% CI 1.59, 27.65) was associated with increased odds of preterm birth in bivariate ([Appendix Table 5](#)), but not multivariate ([Appendix Table 6](#)) models.

Birth weight outcome. We present bivariate and then multivariate

² Low birthweight and macrosomia were not associated with our allostatic load classes for White or Black women, so they are not included as outcomes in subsequent results or tables.

Table 2
Prevalence of infant-level predictors of birth outcomes by race (n = 1260 infants)

	Infants of White women (n = 1,083)	Infants of Black women (n = 177)	Comparing White vs. Black values
	Weighted mean or % (95% CI)	Weighted mean or % (95% CI)	Weighted χ^2 p-value
Birthweight (grams)	3395.67 (3348.71, 3442.64)	3095.11 (2888.21, 3302.00)	0.005
Macrosomia	10.35% (7.72, 12.98)	4.94% (0.00, 10.08)	0.061
Low birth weight	4.76% (3.14, 6.38)	15.47% (8.01, 22.94)	0.006
Preterm^a	9.07% (6.76, 11.38)	17.83% (10.12, 25.55)	0.037
Mother age at birth (years)	32.46 (32.14, 32.77)	32.76 (32.02, 33.49)	0.445
Infant biological sex- male	48.72% (45.88, 51.55)	46.17% (36.75, 55.60)	0.604
Parity			
First	61.45% (59.15, 63.76)	78.22% (71.93, 84.52)	0.000
Second	32.97% (30.90, 35.04)	21.54% (15.34, 27.73)	0.000
Third or higher order	5.57% (3.94, 7.21)	0.24% (0.00, 0.53)	0.000
Mother smoked during pregnancy	7.02% (4.24, 9.81)	4.47% (0.12, 8.83)	0.281
Mother married to pregnancy partner	89.52% (86.83, 92.21)	51.26% (39.47, 63.06)	0.000

All variables in this table are from wave V

^a A preterm birth is a birth that occurred at less than 37 weeks of completed gestation.

results of a variety of predictors where birth weight is the outcome in a multilevel linear regression. In multivariate models with allostatic load class, preterm birth, and all of our other predictors simultaneously, being in the high-risk BMI and WC class, when compared to the high-risk SBP and DBP class, was associated with higher birthweight in the multivariate model (179.73 g; 95% CI 17.04, 342.41) (Appendix Table 6).

3.5.2. Black women

In Table 4, we present the findings of multilevel logistic regression on preterm birth, and linear regression on infant birth weight, among Black women. Allostatic load class was not associated with any of these birth outcomes in bivariate or multivariate models.

4. Discussion

This study used a population-based U.S. sample to explore whether there were associations between allostatic load class membership and birth outcomes, specifically birthweight and whether or not the infant was preterm or high or low birthweight. In multivariate models, the allostatic load class characterized by White women with high-risk BMI and WC had infants with higher birthweights than women in the high-risk SBP and DBP class. Overall, however, the allostatic load classes were not associated with birth outcomes, especially when higher risk classes were compared with the low-risk class.

Our findings that the allostatic load class characterized by White women with high-risk BMI and WC was associated with higher infant birthweight (than infants from mothers in the high-risk SBP and DBP class) is consistent with previous findings. Previous studies have found that heavier women have heavier babies (Lutsiv et al., 2015; Vinturache et al., 2017), and that chronic maternal hypertension is associated with an increased likelihood of having a low birthweight infant (Bramham et al., 2014). However, membership in our high-risk BMI and WC class was not predictive of increased odds of macrosomia, which suggests that birthweights of infants born to heavier moms remain in the “normal” range, and therefore are not a cause for concern.

We hypothesized that a person-centered approach would allow us to identify more nuanced patterns of allostatic load, which in turn would allow for a more thorough examination of linkages between allostatic load and birth outcomes. We anticipated that women in the high-risk allostatic load classes, compared to the low-risk class, would have worse birth outcomes. Our results do not support this hypothesis. Previous literature indicates that many factors interact to influence birth weight (Wilcox, 2010) and preterm birth. As with other work, our

classes fail to capture all the factors and interactions that are relevant to predict birth outcomes. Despite preterm birth being “one of the greatest unmet medical challenges” (pg. 29856) (Olson et al., 2015), our current collective understanding can likely only explain about 50% of the variation in the cause of preterm birth (Kramer et al., 2013). Thus, additional work is needed, perhaps capturing chronic structural features, to better understand how maternal stressors over the life course get under the skin to influence biomarkers of health and subsequent birth outcomes.

We did not directly test Black/White differences in coefficients from our bi- and multivariate models. However, we found different class structures for White and Black women. It is unclear whether the two class solution for Black women reflects a reliable pattern or is a function of a smaller sample size and less power. We hypothesize that with a larger sample of Black women, we would have seen classes that are similar to those seen for White women.

4.1. Limitations

A limitation of this study is that we did not have the sample size to tease out classes of Black women characterized exclusively by high-risk BMI and WC and high-risk SBP and DBP as we did with the White women. In other work using a larger sample of Black women from the Add Health sample (i.e., not restricted to the temporality of births in relation to the allostatic load measurement), we found class solutions that were almost identical for Black and White women (Barry et al., 2022). This suggests that the two class solution for Black women presented in this paper was primarily a result of sample size, and is not a substantive finding.

All measures, other than our biomarkers and medication usage, are based on self-report, and may be recalled inaccurately or reflect social desirability. Results are mixed on whether mothers can accurately report preterm births (Adegboye & Heitmann, 2008; Casey et al., 1992; Dietz et al., 2014; Hakim et al., 1992; Keenan et al., 2017; McCormick & Brooks-Gunn, 1999; Sou et al., 2006; Yawn et al., 1998), but a review article of 14 studies puts the correlation between maternal recall of gestational age and medical records at around 0.9 (Sou et al., 2006). A study asking a categorical question similar to the one in Add Health found that mothers were able to reliably report that their infants were on time, late, or early, even though they were unable to accurately report exact gestational age (Yawn et al., 1998).

Birth weight is the result of both gestational age and intrauterine growth restriction, and we were unable to distinguish between these two predictors because we do not have direct measures of them. A potential

Table 3
White women-bivariate and multivariate results with preterm birth and birth weight outcomes (n = 1083 births to 666 women)

	Preterm birth (less than 37 weeks)		Birth weight (continuous grams)		
	Odds Ratio (95% CI)		Coefficient (95% CI)		
	Bivariate model	Multivariate model	Bivariate model	classes + PTB	Multivariate model
Maternal-level covariates					
Allostatic load class					
Class 1: high-risk TC, TG, & HDL	0.59 (0.17,2.08)	0.62 (0.18, 2.12)	-16.58 (-133.96, 100.80)	-45.42 (-162.17, 71.33)	-42.73 (-173.65, 88.19)
Class 2: high-risk SBP & DBP	0.38 (0.12, 1.24)	0.45 (0.14, 1.43)	-21.90 (-137.14, 93.35)	-58.70 (-167.64, 50.23)	-61.61 (-171.33, 48.12)
Class 3: high-risk BMI & WC	2.52 (0.87, 7.31)	1.87 (0.64, 5.48)	10.91 (-184.08, 205.89)	61.59 (-124.69, 247.88)	118.12 (-64.89, 301.13)
Class 4: low-risk	-	-	-	-	-
4-year degree or higher	0.41* (0.17, 0.97)	0.52 (0.22, 1.22)	-8.94 (-121.59, 103.72)	-	-61.01 (-166.25, 44.24)
Smoker (pre-pregnancy)	1.43 (0.54, 3.77)	1.37 (0.55, 3.44)	-69.52 (-192.57, 53.53)	-	-35.00 (-134.89, 64.88)
Binge drinking monthly or more frequently (pre-pregnancy)	0.41 (0.17, 1.02)	0.43* (0.21, 0.90)	122.15* (23.07, 221.23)	-	121.68** (32.18, 211.18)
Birth-level covariates					
Mother age at birth	0.94 (0.79, 1.12)	0.96 (0.84, 1.09)	14.63* (0.91, 28.34)	-	-4.66 (-20.55, 11.23)
Infant biological sex- male	0.69 (0.35, 1.36)	0.79 (0.41, 1.51)	152.80*** (90.23, 215.38)	-	141.30*** (83.18, 199.43)
Parity					
First	-	-	-	-	-
Second	0.61 (0.30, 1.26)	0.66 (0.32, 1.34)	120.40*** (67.42, 173.38)	-	114.16*** (49.81, 178.51)
Third or higher order	1.06 (0.15, 7.35)	1.22 (0.22, 6.70)	72.00 (-57.32, 201.32)	-	106.41 (-26.93, 239.75)
Mother smoked during pregnancy	2.24 (0.41, 12.10)	1.55 (0.30, 7.95)	-260.80** (-422.94, -98.67)	-	-256.30** (-417.22, -95.39)
Married to pregnancy partner	1.17 (0.43, 3.18)	2.34 (0.67, 8.13)	-7.51 (-186.22, 171.20)	-	-70.07 (-247.33, 107.19)
Preterm birth	-	-	-773.96*** (-951.32, -596.59)	-786.01*** (-963.37, -608.66)	-751.31*** (-922.19, -580.43)

In bivariate models each predictor is run individually with each outcome.

Table abbreviations: PTB: Preterm birth. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. WC: Waist circumference. TC: Total cholesterol. TG: Triglycerides. HDL: High-density lipoprotein.

*p < 0.05, **p < 0.01, ***p < 0.001.

Table 4
Black women-bivariate and multivariate results with preterm birth and birth weight outcomes (n = 177 births to 131 women)

	Preterm birth (less than 37 weeks)		Birth weight (continuous grams)		
	Odds Ratio (95% CI)		Coefficient (95% CI)		
	Bivariate model	Multivariate model	Bivariate model	classes + PTB	Multivariate model
Maternal-level covariates					
Allostatic load class					
Class 1: high-risk BMI & WC	1.40 (0.38, 5.14)	1.29 (0.30, 5.46)	47.26 (−315.25, 409.77)	91.19 (−188.31, 370.68)	96.24 (−158.99, 351.47)
Class 2: low-risk	–	–	–	–	–
4-year degree or higher	0.96 (0.23, 3.94)	1.47 (0.27, 7.99)	189.08 (−174.26, 552.43)		201.98 (−160.37, 564.33)
Smoker (pre-pregnancy)	1.61 (0.49, 5.30)	1.86 (0.35, 9.92)	−188.38 (−642.36, 265.60)		−153.76 (−496.30, 188.78)
Binge drinking monthly or more frequently (pre-pregnancy)	1.01 (0.22, 4.67)	0.94 (0.11, 7.89)	210.13 (−122.80, 543.05)		287.25* (37.77, 536.72)
Birth-level covariates					
Mother age at birth	0.86 (0.66, 1.11)	0.83 (0.61, 1.12)	33.95 (−20.56, 88.46)		−7.71 (−37.09, 21.67)
Infant biological sex- male	2.60 (0.68, 9.94)	2.71 (0.52, 14.02)	169.94 (−86.47, 426.35)		304.17*** (145.00, 463.34)
Parity					
First	–	–	–		–
Second	a	a	436.54** (175.13, 697.94)		253.03* (7.23, 498.83)
Third or higher order	a	a	35.54 (−156.25, 227.33)		−266.40* (−477.58, −55.22)
Mother smoked during pregnancy	a	a	−42.02 (−668.83, 584.79)		−59.09 (−694.84, 576.65)
Married to pregnancy partner	0.88 (0.28, 2.72)	1.16 (0.34, 4.02)	167.92 (−158.01, 493.86)		75.63 (−148.31, 299.57)
Preterm birth	–	–	−999.81*** (−1463.32, −536.30)	1005.38*** (−1476.86, −533.89)	−996.15*** (−1395.30, −597.00)

In bivariate models each predictor is run individually with each outcome.

Table abbreviations: PTB: Preterm birth. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. WC: Waist circumference. TC: Total cholesterol. TG: Triglycerides. HDL: High-density lipoprotein.

*p < 0.05, **p < 0.01, ***p < 0.001.

^a This variable has been dropped from the model due to inadequate cell size.

issue of collider stratification bias with gestational age as a collider and birthweight as the outcome could exist (Whitcomb et al., 2009). To assess the need to stratify our birthweight outcome by term and preterm, we tested for interactions by term and preterm for each of our predictor variables with birthweight as the outcome; only pre-pregnancy monthly binge drinking was significant. Given this outcome, collider stratification bias does not appear to be a meaningful issue. Another limitation is our inability to distinguish between spontaneous and medically indicated preterm birth.

For several reasons, our results may not be generalizable to all U.S. women and their births. Since biomarkers were drawn at Wave IV, and biomarker collection needed to precede birth, we were only able to examine births that occurred after the Wave IV interview, at the average age of birth at 32 years in our sample, resulting in a higher age at first birth than the U.S. average (the mean age of first birth for: Black women was 22.8 in 2008 and 25.1 in 2018; White women was 25.3 in 2008 and 27.7 in 2018) (Martin et al., 2021). A comparison of Add Health mothers who were included vs. excluded from our sample found selection bias. Black and White women who were in our sample were more socioeconomically advantaged than women who were not in our sample. This means that we are missing many of the most disadvantaged or “weathered” women, who likely would have already had children before Wave IV. Consistent with the two studies that are most similar ours (but used variable centered approaches) (Wallace et al., 2013a, 2013b), this study prioritized clear temporal order, with allostatic load measurement taken prior to any birth. This was an important strength of this study because we needed to ensure that allostatic load preceded, and was not the result of, or triggered by, poor birth outcomes. However, the tradeoff in prioritizing this temporal order was selection bias resulting from women who did vs. did not “delay” childbearing. Ultimately, in- and out-of-sample women are very different for both races, likely biasing our results towards the null. Thus, our null results could be due to significant selection bias rather than a lack of association between pre-pregnancy allostatic load and subsequent birth outcomes.

Results are not generalizable to women in racial/ethnic groups with sample sizes too small for inclusion (non-Hispanic Asian, Hispanics, and women of other or mixed races). Two other findings suggest that our sample might not be fully generalizable to all U.S. women. The percentage of births that are preterm for non-Hispanic Black women in our sample (17.83%) is identical to the percentage of births born to non-Hispanic Black women aged 30–34 nationally in 2008 (17.8%) (Martin et al., 2010), but is elevated compared to the percent in 2018 (14.4%) (Martin et al., 2021). The elevated percentage of preterm births to Black women in the later years our sample (vs. Black women of a similar age in the U.S.) may reflect the fact that Black women in Add Health (as a whole and in our sample of women who delayed childbearing, in particular) are of higher socioeconomic status than the average Black woman in the U.S., and that Black women of higher (vs. lower) socioeconomic status have worse birth outcomes (Collins & Hammond, 1996; Kramer et al., 2010; Messer et al., 2010). Additionally, White women in our sample were slightly more likely to report smoking during pregnancy than the national average (Drake et al., 2018).

Since biomarkers and other woman-level covariates were only drawn at one time point, and not preceding each birth, we may be missing important inter-pregnancy changes in biomarkers (such as changes in BMI, WC, blood pressure, etc.).

4.2. Strengths

Despite these limitations, this study contains a number of strengths. To our knowledge, it is the first to use a population-based sample of U.S. women to build classes based on pre-pregnancy biomarkers and investigate whether membership in those classes is associated with birth

outcomes. This improves upon previous literature that looked at self-reported stressors or data-verified events prior to or during pregnancy that were assumed to be stressors. Of the previous studies that looked at the correlations between pre-pregnancy allostatic load and subsequent birth outcomes (Wallace et al., 2013a, 2013b), our sample is older, with more time for allostatic load challenges to accumulate, and draws from a population-based sample.

4.3. Suggestions for future work

Future research looking at the association between pre-pregnancy allostatic load and subsequent birth outcomes would benefit from larger sample sizes of persons of color, especially Black women, who have worse birth outcomes than White women in the U.S. It would be helpful to have maternal biomarkers at multiple time points, ideally before/between each birth, in order to explore how biomarkers of health change after pregnancy and birth, and go on to affect a subsequent birth. It would also be helpful for future researchers to investigate how the relationship between pre-pregnancy health and birth outcomes are mediated by pregnancy-related factors such as perinatal infections, pregnancy complications, and gestational weight gain.

5. Conclusion

In multivariate models, the allostatic load class characterized by White women with high-risk body mass index and waist circumference, compared to the class with high-risk systolic and diastolic blood pressure, was associated with higher birthweight infants. Overall, however, the allostatic load classes among White and Black women were not associated with birth outcomes (continuous birthweight, and dichotomous measures of low birth weight, macrosomia, and preterm birth), especially when high risk classes were compared with the low-risk class. Despite the study’s holistic approach and design strengths, we did not identify consistent patterns that could be used as key markers for prevention purposes. Additional work is needed to expand on the context and lived experiences that affect women’s health and birth outcomes.

Data source

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Credit author statement

Megan C. Barry: Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Project administration, Visualization, Formal analysis, Data curation; Catherine Zimmer: Methodology, Writing – review & editing, Supervision; Carolyn T. Halpern: Conceptualization, Writing – original draft, Writing – review & editing, Supervision.

Declaration of competing interest

The authors have no conflicts of interest or financial disclosures.

APPENDIX TABLES

Table 1
Descriptive statistics and high-risk cutpoint of each biomarker, prevalence of high-risk biomarkers by race

	Full sample (n = 1,644)			By race		
	Range	Mean (SD)	High-risk cutpoint	White (n = 1,258)	Black (n = 386)	χ^2 p-value White vs. Black
				% high-risk (95% CI)	% high-risk (95% CI)	
Systolic blood pressure	77-193	120 (14)	126.5	29.5 (25.3, 34.1)	38.6 (31.3, 46.4)	0.0294
Diastolic blood pressure	31-126	77 (11)	82	27.7 (24.1, 31.7)	34.9 (28.2, 42.3)	0.1483
Pulse rate	44-118	75 (12)	81.5	23.4 (20.2, 27.0)	26.5 (20.4, 33.7)	0.4147
HbA1c	5-15	5 (0.66)	5.8	12.0 (0.97, 14.8)	39.1 (30.7, 48.3)	<0.001
Body mass index	15-79	28 (8)	31.37	22.6 (19.7, 25.8)	45.6 (38.7, 52.8)	<0.001
C-reactive protein	0.08-185	6 (12)	6.85	47.4 (43.6, 51.3)	44.1 (37.9, 50.4)	0.0312
Waist circumference	56-189	94 (19)	103.5	25.0 (21.8, 28.3)	39.2 (32.0, 46.9)	0.0001
Total cholesterol	1-10	—	decile 8	31.7 (28.9, 34.6)	21.1 (16.2, 26.9)	0.0032
Triglycerides	1-10	—	decile 8	24.0 (21.2, 26.9)	15.2 (10.9, 20.8)	0.0323
HDL cholesterol	1-10	—	decile 2	19.4 (16.9, 22.3)	16.4 (11.4, 23.0)	0.9408

The mean, standard deviation, and all percentages in this table are weighted to account for the complex sampling design of Add Health.

Both White and Black race are non-Hispanic.

For SBP, DBP, PR, hba1c, BMI, CRP, and WC, the high-risk cutpoint is at the 75th percentile.

Table 2
Latent class fit statistics (weighted), Non-Hispanic White and Black women

Non-Hispanic White women (n = 1,258)							
Number of classes	Free Parameters	Log likelihood	AIC	BIC	ABIC	Entropy	LMR adj. LRT (p-value)
1	10	-7000.624	14021.25	14072.62	14040.86	NA	NA
2	21	-6402.03	12846.07	12953.95	12887.24	0.913	0.0000
3	32	-6207.46	12478.92	12643.32	12541.67	0.913	0.0036
4	43	-6072.20	12230.40	12451.30	12314.71	0.908	0.0357
5	54	-6022.77	12153.53	12430.95	12259.42	0.883	0.6560
Non-Hispanic Black women (n = 386)							
Number of classes	Free Parameters	Log likelihood	AIC	BIC	ABIC	Entropy	LMR adj. LRT (p-value)
1	10	-2313.64	4647.27	4686.83	4655.10	NA	NA
2	21	-2163.73	4369.47	4452.54	4385.91	0.805	0.0578
3	32	-2098.47	4260.95	4387.53	4286.00	0.898	0.3003
4	43	-2059.61	4205.22	4375.32	4238.89	0.888	0.7435
5	54	-2031.50	4171.00	4384.61	4213.28	0.895	0.5464

Note: LMR adj. LRT is the Lo-Mendell-Rubin adjusted likelihood ratio test.

Appendix Table 3
Latent class probabilities, Non-Hispanic White women (n = 1,258)

		%	n	High-risk cutpoint at the 75 th %						80 th %		20 th %
				SBP	DBP	PR	HbA1c	BMI	CRP	WC	TC	TG
2-Class												
1	25%	318	0.507	0.450	0.400	0.301	0.856	0.635	0.906	0.374	0.466	0.289
2	75%	940	0.222	0.218	0.178	0.059	0.011	0.419	0.025	0.297	0.162	0.162
3-Class												
1	13%	159	1.000	0.925	0.245	0.036	0.030	0.619	0.062	0.310	0.105	0.118
2	24%	301	0.494	0.436	0.403	0.310	0.887	0.634	0.928	0.382	0.481	0.294
3	63%	798	0.066	0.076	0.167	0.066	0.015	0.382	0.029	0.293	0.176	0.173
4-Class												
1	8%	104	0.206	0.228	0.279	0.156	0.093	0.356	0.000	0.921	1.000	0.755
2	16%	199	0.960	0.820	0.261	0.055	0.051	0.622	0.058	0.265	0.045	0.086
3	23%	289	0.495	0.440	0.402	0.299	0.885	0.638	0.983	0.375	0.479	0.283
4	53%	666	0.032	0.060	0.149	0.058	0.017	0.380	0.030	0.217	0.081	0.105

Notes for Appendix Tables 3 and 4.

SBP, DBP, PR, hba1c, BMI, CRP, and WC were dichotomized based on high-risk cutpoint at the 75th percentile. In the Add Health data, data quality prohibited the release of exact biomarker values for individuals for TC, TG, and HDL. For these biomarkers, we only have decile cutoffs. To be conservative, we set our cutpoints for these biomarkers at the 8th/2nd decile.

All data are weighted to account for the complex sampling design of Add Health.

Table abbreviations: n: number of people in that row. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. PR: Pulse rate. HbA1c: hemoglobin. BMI: Body mass index. CRP: C-reactive protein. WC: Waist circumference. TC: Total cholesterol. TG: Triglycerides. HDL: High-density lipoprotein.

Table 4
Latent class probabilities, Non-Hispanic Black women (n = 386)

		%	n	High-risk cutpoint at the 75 th %						80th %		20th %	
				SBP	DBP	PR	HbA1c	BMI	CRP	WC	TC	TG	HDL
2-Class													
1		59%	228	0.243	0.218	0.239	0.252	0.114	0.326	0.076	0.194	0.108	0.139
2		41%	158	0.585	0.531	0.302	0.587	0.935	0.601	0.834	0.234	0.213	0.200
3-Class													
1		32%	125	0.617	0.536	0.339	0.582	0.944	0.656	1.000	0.253	0.232	0.199
2		22%	85	0.797	0.751	0.222	0.502	0.239	0.383	0.000	0.188	0.156	0.132
3		46%	176	0.000	0.000	0.234	0.194	0.213	0.313	0.152	0.192	0.091	0.155
4-Class													
1		22%	86	0.799	0.752	0.224	0.500	0.241	0.383	0.010	0.187	0.154	0.132
2		42%	164	0.000	0.000	0.243	0.198	0.181	0.317	0.121	0.200	0.097	0.161
3		8%	33	0.734	0.729	0.277	0.848	0.860	0.807	1.000	0.697	0.723	0.514
4		27%	104	0.533	0.430	0.340	0.455	0.990	0.576	1.000	0.074	0.035	0.071

Table 5
Comparisons of allostatic load class coefficients in bivariate models among White women

		Preterm birth (less than 37 weeks) vs. not		Birth weight (continuous grams)	
		Odds Ratio (95% CI)		Coefficient (95% CI)	
Class 1: high-risk TC, TG, & HDL vs.	Class 2: high-risk SBP & DBP	0.64	(0.14, 2.87)	-5.32	(-166.03, 155.39)
	Class 3: high-risk BMI & WC	4.27	(0.97, 18.79)	27.48	(-209.65, 264.61)
	Class 4: low-risk	1.70	(0.48, 5.99)	16.58	(-100.80, 133.96)
Class 2: high-risk SBP & DBP vs.	Class 3: high-risk BMI & WC	6.63**	(1.59, 27.65)	32.80	(-139.22, 204.82)
	Class 4: low-risk	2.63	(0.81, 8.61)	21.90	(-93.35, 137.14)
Class 3: high-risk BMI & WC vs.	Class 4: low-risk	0.40	(0.14, 1.16)	-10.91	(-205.89, 184.08)

*p < 0.05, **p < 0.01, ***p < 0.001.

Table abbreviations: SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. WC: Waist circumference. TC: Total cholesterol. TG: Tri-glycerides. HDL: High-density lipoprotein.

Table 6
Comparisons of allostatic load class coefficients in multivariate models among White women

		Preterm birth (less than 37 weeks) vs. not		Birth weight (continuous grams)	
		Odds Ratio (95% CI)		Coefficient (95% CI)	
Class 1: high-risk TC, TG, & HDL vs.	Class 2: high-risk SBP & DBP	0.73	(0.16, 3.35)	-18.87	(-194.43, 156.68)
	Class 3: high-risk BMI & WC	3.02	(0.70, 13.10)	160.85	(-71.08, 392.79)
	Class 4: low-risk	1.62	(0.47, 5.55)	42.73	(-88.19, 173.65)
Class 2: high-risk SBP & DBP vs.	Class 3: high-risk BMI & WC	4.11	(0.98, 17.33)	179.73*	(17.04, 342.41)
	Class 4: low-risk	2.20	(0.70, 6.95)	61.61	(-48.12, 171.33)
Class 3: high-risk BMI & WC vs.	Class 4: low-risk	0.54	(0.18, 1.57)	-118.12	(-301.13, 64.89)

Multivariate model controlling for maternal-level covariates: maternal education; pre-pregnancy smoking; pre-pregnancy binge drinking; and infant/birth-level covariates: mother age at birth, infant biological sex, parity, mother smoked during pregnancy, and mother married to pregnancy partner. The birth weight model also controls for preterm birth.

*p < 0.05, **p < 0.01, ***p < 0.001.

Table abbreviations: SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. WC: Waist circumference. TC: Total cholesterol. TG: Tri-glycerides. HDL: High-density lipoprotein.

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