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Maternal Allostatic Load During Pregnancy: Predicting Length of Gestation

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MATERNAL ALLOSTATIC LOAD DURING PREGNANCY:
PREDICTING LENGTH OF GESTATION

DISSERTATION

A dissertation submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in the
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ABSTRACT OF DISSERTATION

MATERNAL ALLOSTATIC LOAD DURING PREGNANCY:
PREDICTING LENGTH OF GESTATION

Allostatic load, or the "wear and tear" on the body due to stress, is thought to have a negative impact on length of pregnancy and contribute to health disparities in preterm birth. However, the magnitude of the effect on birth outcomes is unknown, in part due to questions of timing of measurement of allostatic load during pregnancy. This study used linear regression analysis of data from 156 pregnant women to test whether allostatic load is a predictor of length of gestation in the study sample, finding that third trimester allostatic load predicted length of gestation among women with full-term births. The study also compared allostatic load in each trimester to determine an optimal time of measurement for prediction of preterm birth. Findings were inconclusive because regardless of trimester of measurement, allostatic load was not a significant predictor of gestational length in the sample. Finally, the study compared allostatic load with scores on the Everyday Stressors Index, a psychosocial measure, to understand the relative benefits of allostatic load measurement during pregnancy. Neither was found to be a statistically significant predictor of preterm birth, so direct comparisons were not possible. Implications and suggestions for future research are discussed.

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Chapter 1: Introduction

Maternal and child health research has linked prenatal development to physical, cognitive, and emotional wellbeing across the life course. When a child is born premature (< 37 weeks' gestation), the child is more likely to experience a variety of health complications, including increased risk of mortality within the first year of life (Behrman & Butler, 2007). In the United States, preterm birth is a leading cause of infant mortality. At birth, preterm infants are more likely to have problems with the respiratory, gastrointestinal, immune, cardiovascular, and the central nervous systems, as well as skin, blood, hearing, and vision. "Depending on how early the delivery is and the presence of any complications at birth, infants born preterm have more pediatric visits for illness, suffer higher rates of cognitive and learning difficulties, and show poorer growth and development" (Dunkel Schetter & Glynn, 2011, p. 322). Preterm babies are more susceptible to infections, which can have long-term negative consequences for neurodevelopment, cognitive abilities, and hearing ability, among other outcomes (Behrman & Butler, 2007). Even children born at near full-term ("late-preterm births") are at higher risk of health complications than full-term babies.

Prevalence of Types of Preterm Birth

The three types of preterm birth are spontaneous preterm labor, preterm premature rupture of membranes (PPROM), and indicated deliveries. About 50% of preterm births occur as spontaneous preterm labor, which is "natural onset of labor defined as premature contractions before 37 weeks' gestation" (Dunkel Schetter & Glynn, 2011, p. 323). Another type of preterm birth is preceded by PPROM, after

which labor begins naturally or is induced. Around 30% of preterm births occur

due to PPROM. The remaining 20% of preterm births are indicated deliveries; that

is, a maternity care provider initiates labor or performs a cesarean section to

protect the fetus or mother from complications. Maternal stress has been

implicated in the former two types of preterm birth—spontaneous preterm labor

and PPROM, via the mechanisms of overproduction of cytokines, presence of

placental corticotropin-releasing hormone (pCRH), decline in progesterone, among

others (Dunkel Schetter & Glynn, 2011; Goldenberg, Culhane, Iams, & Romero,

2008). Maternal stress contributes to high blood pressure and preeclampsia, which

are causes of indicated deliveries, but maternal stress is not usually a direct cause of

these preterm births.

Maternal Stress

There is a well-established relationship between maternal stress and

preterm birth (Hobel, Goldstein, & Barrett, 2008; Ramey, Schafer, DeClerque, Lanzi,

Hobel, Shalowitz, et al., 2014; Wadhwa, Entringer, Buss, & Lu, 2011). Studies of

stress during pregnancy include a variety of conceptualizations of stress (Dunkel

Schetter & Glynn, 2011). Some studies utilize stressors (major life events[1], trauma,

everyday stressors, neighborhood crime), others measure appraisals or perceptions

of stressors (individuals' ratings of neighborhood safety, economic insecurity), and

still others use responses to stress (biomarkers, behaviors, mental health status). In

one literature review, studies were categorized by conceptualizations of stress into

five groups: "episodic forms of stress," including life events and catastrophic

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[1] Major life events could include death of a close relative, divorce, diagnosis of a
potentially fatal illness, or other life-altering event.

events[2]; "chronic strain," which included perceived stress, racism, and neighborhood attributes like crime and violence; "emotional states," such as anxiety, depression, general emotional distress, and—the most reliable predictor of preterm birth among emotional states—pregnancy-specific anxiety or stress. Dunkel Schetter and Glynn (2011) recommend "the use of multiple stress measures in future research" for the comparison of factors and construction of indices (p. 330), an approach rarely found in the current literature.

Most women exhibit a pattern of reduced physiological and psychological reactivity to stress as pregnancy progresses (Glynn, Dunkel Schetter, Hobel, & Sandman, 2008). Glynn et al. suggest that, as indicated by studies with animals, reduced psychological reactivity reflects underlying physiological responses to stress that are progressively dampened during pregnancy in order to protect the fetus. This indicates the need for measurement of stress at multiple time points during pregnancy, because increasing (instead of decreasing) stress responses during pregnancy is associated with higher rates of preterm birth (Cole-Lewis, Kershaw, Earnshaw, Yonkers, Lin, & Ickovics, 2014; Glynn, Dunkel Schetter, Hobel, & Sandman, 2008).

Allostatic Load

Researchers have used the concept of allostatic load to characterize the effects of extreme and chronic stress, as well as inadequate coping with stress, on health. While it is operationalized differently in various studies, allostatic load can

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[2] The difference between these two groups is life events are those to which individuals are exposed (divorce, death of a close relative), while populations are exposed to catastrophic events (natural disasters, terrorist attacks, wars).

be conceptualized as the "wear and tear" on the body endured by continuous responses to external and internal stressors that exceed the individual's coping ability (McEwen, 1998, 2001; McEwen & Gianaros, 2010). Allostatic load can result from one or a combination of four factors: chronic stress, lack of habituation to repeated stressors, biological stress responses that do not "shut off" when no longer helpful, and inadequate biological responses to stress which cause increased activation of other stress responses in the body (McEwen, 2001). Allostatic load is the cumulative physiological toll of stress, so systems in the body that are known to be affected by stress response processes can be included in an allostatic load index. Allostatic load measurement typically includes indicators from the cardiovascular, metabolic, immune, and endocrine systems and is inferred by combining indicators from various body systems—unhealthy extremes (usually elevated levels) of biomarkers.

Though stress is also associated with the nervous system—rates of neuroplasticity and related mental health problems (Bremner, 2006; Deppermann, Storchak, Fallgatter, & Ehlis, 2014)—direct relationships between allostatic load and specific mental health disorders are not yet well understood. The relationship is further complicated by mental health diagnoses that rely upon criteria that are more often blunt than precise, resulting in many conditions being lumped under one umbrella diagnosis (Horwitz, 2015; Wakefield & Schmitz, 2013). Given these complexities, investigating relationships between mental illnesses, allostatic load, and physical health is likely to be most fruitful in populations that do not have the added variable of pregnancy. For this analysis, then, variables from mental health

diagnostic tools (Edinburgh Postnatal Depression Scale & state anxiety inventory of State-Trait Anxiety Inventory) are used as control variables, not as study variables.

As a construct, allostatic load has been implicated in a wide range of health problems and disparities, due to the body's responses to chronic, overwhelming stress in the cardiovascular, metabolic, and immune systems (Sapolsky, 2004). Allostatic load has been used in studies of aging (Geronimus, Hicken, Keene, & Bound, 2006; Seeman, Singer, Rowe, Horwitz, & McEwen, 1997; Wikby, Ferguson, Forsey, Thompson, Strindhall, Löfgren, et al., 2005), mental health disorders (Glover, Stuber, & Poland, 2006; Kapczinski, Vieta, Andreazza, Frey, Gomes, Tramontina, et al., 2008), the effects of adverse events and conditions on children (Evans, Kim, Ting, Tesher, & Shannis, 2007), and the effects of work conditions (Schnorpfeil, Noll, Schulze, Ehlert, Frey, & Fischer, 2003).

Allostatic load has also been used in the study of maternal stress effects on birth outcomes. Some researchers have used allostatic load conceptually to interpret findings (e.g., Hilmert, Dunkel Schetter, Dominguez, Abdou, Hobel, Glynn, & Sandman, 2008; Scharber, 2014), while others have used allostatic load as an independent variable (e.g., Hux, Catov, & Roberts, 2014). Since prenatal exposure to stress is a possible origin point for allostatic load in children, Misra, Straughen, and Slaughter-Acey (2013) suggested that research in pregnancy stress and birth outcomes is uniquely suited for allostatic load research, including its operationalization and timing of measurement.

Theoretical Perspectives

Some researchers in maternal stress conceptualize preterm birth and the developmental effects of prenatal exposure as adaptive responses. Wadhwa, Entringer, Buss, and Lu (2011) posited that preterm birth may be advantageous to the mother if it allows her to redirect energy away from the fetus and towards her own survival in a challenging environment. Further, preterm birth may be adaptive for a fetus to escape an intrauterine environment that is less than optimal. Another evolutionary perspective is that prenatal exposure to maternal stress prepares offspring for survival in high-stress environments (Del Giudice, 2014). Glynn et al. (2008) draw on a related perspective, the adaptive reproductive failure model, to interpret findings on decreased reactivity to stress as pregnancy progresses. They suggested that increased stress responses in early pregnancy might increase reproductive failure in inhospitable environments. Diminished stress reactivity in later pregnancy may guard the fetus from the environment in order to protect the mother's prior and continued investment in the fetus's development. While few, if any, studies with humans have attempted to directly test these theories, evolutionary models and concepts are frequently used to interpret findings on maternal stress and birth outcomes.

Conceptual Models

Dunkel Schetter and Glynn (2011) presented a model of the relationship among stressors, mediators, and outcomes. Mediators in the model include biomarkers (e.g., cortisol, cytokines, blood pressure) and stress-affected behaviors (smoking, diet, exercise). Birth outcomes in the model were gestational age,

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preterm birth, and birth weight. In their review, the authors found few studies that tested a model including stressors, mediators, and outcomes. The authors hypothesized that much of the literature on maternal stress and preterm birth is conducted by researchers who are knowledgeable about one part of the chain but not another, specializing in either psychosocial conceptualizations of stress or biomarkers of stress responses, for example. Dunkel Schetter and Glynn (2011) recommended greater collaboration for interdisciplinary testing of more complex conceptual models.

The National Institutes of Health (NIH) Community Child Health Network (Ramey, Schafer, DeClerque, Lanzi, Hobel, Shalowitz, et al., 2014) developed the Preconception Stress and Resiliency Pathways model, a complex depiction of contributors to parental allostatic load, which in turn affects children's development by way of each child's allostatic load. This model suggests that to improve child outcomes, causal factors to address include maternal and paternal stress, resilience, social support, and resulting parental health and parenting styles.

Study Overview

Given the links between maternal stress and preterm birth, intervention with families experiencing stress is warranted. It is unclear, however, what indicators of stress have stronger associations with birth outcomes, which complicates identification of those at greatest risk. Studies of pregnant women that have used allostatic load as an independent variable have found mixed results, ranging from prediction of both preterm birth and being small for gestational age (SGA) (Hux, Catov, & Roberts, 2014) to prediction of gestational length but not of preterm birth

or other tested birth outcomes (Wallace & Harville, 2013). Both of these studies

identified timing of allostatic load measurement during pregnancy as a key research

question. Since the biomarkers that indicate allostatic load change due to

pregnancy-related physiological changes, several researchers have recommended

that for diagnostic purposes during pregnancy, allostatic load be measured

preconception or in the first trimester (Hux, Catov, & Roberts, 2014; Morrison,

Shenassa, Mendola, Wu, & Schoendorf, 2013; Wadhwa, Entringer, Buss, & Lu, 2011).

Prospective studies are needed to test whether measurement of allostatic load early

in pregnancy is a predictor of gestational length.

It is also unknown whether allostatic load is a stronger predictor of preterm

birth than more traditional psychosocial measures. In 2008, Hobel, Goldstein, and

Barrett reviewed several psychosocial instruments used for measuring stress during

pregnancy, including life events, depression, anxiety, and perceived stress

instruments. Hobel et al. lauded the development of new applications of allostatic

load measurement to pregnancy for assessment of risk for adverse birth outcomes,

although more research is needed to refine allostatic load measurement during

pregnancy. Few studies, if any, have compared allostatic load measures to

psychosocial measures of stress for prediction of pregnancy outcomes.

This study addressed these gaps in research by analyzing data on a sample (n

= 156) of pregnant women that was collected prospectively during each trimester.

The analysis tested whether allostatic load was a predictor of gestational length and

compared allostatic load among trimesters to determine when it was the strongest

predictor of preterm birth. The Everyday Stressors Index from each trimester was

then tested as a predictor of preterm birth to allow for comparisons with allostatic load. Using linear and logistic regression analyses, the study examined whether allostatic load or the ESI is a better predictor of preterm birth, which is necessary for accurate identification and effective intervention with pregnant women to improve birth outcomes.

Chapter 2: Literature Review

A substantial body of literature indicates an association between maternal stress, sometimes using the concept of allostatic load, and birth outcomes. This review of theoretical and empirical scholarship describes the findings in the field to this point and illuminates areas in need of further research.

Theoretical Perspectives

Persistent racial and socioeconomic health disparities are present in the United States as well as internationally, including disparities in life expectancy (Cincinnati Health Department, n. d.), infant mortality (MacDorman & Mathews, 2011), and rates of premature death due to cardiovascular health problems (Centers for Disease Control and Prevention [CDC], 2013). Marmot and Sapolsky (Marmot, 2004; Marmot & Sapolsky, 2014) discussed these health disparities as a social gradient in health, as lower social status is strongly correlated with higher rates of disease and mortality. Marmot and Sapolsky identified stress as a key mechanism by which low social rank affects health, including adverse birth outcomes. This occurs via maladaptive physical responses to chronic stress related to low subjective social status. This perspective suggests that allostatic load—a measurement of the physiological effects of stress—will be higher among those with lower social status, thus offering one explanation of stress-related disparities in birth outcomes.

From an evolutionary perspective, preterm birth may be advantageous to the mother as a means of redirecting energy away from the child's development in utero so that the mother can deal with a challenging environment, or advantageous to the

fetus when the environment in the womb is less than favorable (Wadhwa, Entringer, Buss, & Lu, 2011). The cumulative effect of allostatic load across the life course is a candidate factor that contributes to both the maternal and fetal environments, and is therefore worthy of research attention. Indeed, from a life course perspective,

> "preterm birth may result from not only maternal stress but also stress of the grandmother during her pregnancy, which may program the mother's endocrine and immune stress responses in utero; programmed stress hyperreactivity could put the mother at greater risk for preterm delivery when she herself becomes pregnant." (p. 369)

Generational transmission of maternal stress could occur via placental corticotropin-releasing hormone (CRH). Since CRH is sensitive to maternal stress and is involved in instigating birth, it may also be a key mechanism by which maternal stress affects preterm birth. CRH is also sensitive to a variety of behaviors and events, such as, "variations in the nutritional milieu, physical activity, infection/inflammation, hypoxia, sleep, chronobiological state, and, in the case of pregnancy, by the stage of gestation" (p. 364). These processes may interact with or moderate the relationship between psychosocial stress and preterm birth, or there may be threshold levels that are conditional for stress to have effects.

Del Giudice (2014) presented another evolutionary perspective on maternal allostatic load, stating that the concept is flawed in that long-term benefits of early stress exposure, such as responsivity to high-stress environments, are neglected. Instead, Del Giudice advocated an adaptive model of relationships among early stress experiences and reactivity to various types of stress. The Adaptive Calibration Model predicted differing experiences of maternal stress as conditioning offspring for fitness in various environments.

The National Institutes of Health (NIH) Community Child Health Network (CCHN) incorporated allostatic load into a broad model of influences on maternal, paternal, and child health (Ramey, et al., 2014). Using a community-based participatory research process in five cities, the CCHN developed a Preconception Stress and Resiliency Pathways model in which parents' resilience, social support, and stress contribute to or ameliorate allostatic load, as well as affect the parents' relationship and the home environment of the child. Each parent's allostatic load affects the parent's health, well-being, and parenting, which in turn influence prenatal development of the child and birth outcomes. Parental wellness and parenting, prenatal development, and birth outcomes are directly related to child health, behavior, and cognitive development. Causal mechanisms in the model are "the combination of interpersonal, environment, and biomedical factors over time" (¶ 14). While the model is complex, it reflects the multifaceted influences of preconception, prenatal, and parental wellbeing on child life course.

Premji (2014), in work with the Maternal Infant Global Health Team (MiGHT), has developed a model of perinatal distress (including maternal stress, anxiety, and depression) predicting preterm birth. Premji describes allostatic load as initiating biological responses from the hypothalamic-pituitary-adrenal (HPA) axis and metabolic, immune, and cardiovascular systems. These chemical changes, such as disrupted cortisol rhythms, are associated with preterm birth. Premji also includes allostatic load as a contributing factor to infant health. During pregnancy, the chemical changes related to allostatic load also affect the fetus in that "the fetus or newborn mimics the biochemical profile of the mother," which can result in

altered brain structure and function (p. 2399). Maternal depression, stress, and

anxiety can also affect maternal health behaviors (e.g., substance use), and

interaction and attachment patterns between mother and infant, which can

negatively affect the child's health and development.

Studies Measuring Allostatic Load During Pregnancy

Misra, Straughen, and Slaughter-Acey (2013) wrote a commentary on

measurement of allostatic load in perinatal epidemiology. They observed that there

is no validated standard of how to measure allostatic load across the life course, and

this is especially true in pregnancy. Some studies use an index in which one point is

given for being in the top quartile of a biomarker. Problems with this approach for

pregnancy research include timing of measurement (preconception, in a certain

trimester, post-delivery), which biomarkers to use, and whether cross-sectional

measurement of allostatic load is sufficient or longitudinal measurement is

necessary.

Hux, Catov, and Roberts (2014) examined allostatic load among women with

a history of preterm birth or low birth weight infants. Using data from the National

Health and Nutrition Examination Survey (NHANES), they combined high-risk

scores on nine biomarkers of allostatic load (e.g., BMI, C-reactive protein [CRP],

systolic and diastolic blood pressure) into an index, and tested scores as a predictor

of reports of babies born preterm and with low birth weight (PTB), as well as a

predictor of reports of low birth weight babies who were not born preterm (small

for gestational age, or SGA). Covariates included in the PTB model were African-

American race, age, and BMI. In the analysis of SGA births, African-American race

and age were included covariates. Using these two models, allostatic load was found to be a predictor of both PTB and SGA. Interestingly, the relationship between allostatic load and PTB was only apparent after including BMI as a covariate, a finding which researchers suggested was "related to higher [allostatic load] scores among normal-weight women (BMI <25 kg/m^2) with preterm vs. normal-weight births" (p. 1041).

Earlier work by Morrison, Shenassa, Mendola, Wu, and Schoendorf (2013) explored whether allostatic load among pregnant women can be measured with biomarkers due to physiological changes that occur during pregnancy. They found that allostatic load, measured using an index similar to Hux et al. (2014), differed significantly among pregnant and non-pregnant women in the NHANES dataset. Among pregnant women, well-established relationships between allostatic load and demographic variables were not present, such as higher allostatic load among those with lower income or educational attainment, or among black women when compared to white women (Morrison et al., 2013). Similarly, Wallace and Harville (2013) used data collected during the second trimester to create an allostatic load index. Of five birth outcomes tested, allostatic load was only a significant predictor of gestational age (not birth weight, birth weight ratio, birth length, or head circumference). Given these findings, Hux et al. (2014) suggest that further research should explore measurement of allostatic load among pregnant women when they are physiologically most like non-pregnant women, which is early in pregnancy.

Both Morrison et al. (2013) and Hux et al. (2014) suggest that biomarker measurement of allostatic load among pregnant women should be studied before

the physiological effects of pregnancy mask allostatic load, either early in pregnancy or before pregnancy occurs, when possible. Wadhwa, Entringer, Buss, and Lu (2011) concur, noting "greater biologic stress response in earlier compared with later gestation" (p. 358). There may be a point that is too long before conception to measure allostatic load, however. Wallace, Harville, Theall, Webber, Chen, and Berenson (2013b) utilized biomarkers measured before pregnancy in the Bogalusa Heart Study, a longitudinal study of health in the small town of Bogalusa, Louisiana, and found no association between preconception allostatic load and preterm birth, small for gestational age (SGA) status, gestational age, or birth weight. Another publication from the same study (Wallace et al., 2013a) reported the finding that allostatic load was not associated with preterm birth or low birth weight when measures of neighborhood poverty were included in the model. Researchers acknowledge that due to data collection methods and the relatively young age at which women in the study gave birth to their first child (mean age, African Americans = 20.9 [SD = 4.8]; mean age, White = 23.3 [SD = 5.1]), for many women the biomarker data used was collected during adolescence or before (mean age = 13, Wallace et al., 2013b). Theoretically, allostatic load is a cumulative concept and increases with age, so young age at measurement is likely to have contributed to the null findings.

Marmot and Sapolsky's (2014) work offers another explanation of Wallace et al.'s (2013a) findings. The social gradient in health suggests that allostatic load is a physiological response to stress, including the stress of low social rank which would likely be experienced by women living in areas of greater neighborhood poverty,

possibly resulting in the African American preterm birth rate of the study sample

that is comparable to the preterm birth rate to teen mothers (Child Trends

Databank, 2015). Thus, allostatic load and neighborhood poverty are measuring

closely related phenomena. It is understandable, then, that controlling for one

(neighborhood poverty) would reduce the association of the other (allostatic load)

with preterm birth, SGA, and birth weight. Marmot and Sapolsky's (2014) work

suggests that neighborhood poverty should be modeled as a predictor of allostatic

load instead of an alternative measure.

Other Relationships Between Psychosocial Conditions and Biomarkers

Shelton, Schminkey, and Groer (2014) examined relationships among stress,

depression, cortisol levels, and cytokines in pregnant women during the second

trimester. Stress was measured by the Perceived Stress Scale (Cohen, Kamarck, &

Mermelstein, 1983) and depression symptoms were collected using the Profile of

Mood States Depression-Dejection scale (McNair, Lorr, & Droppleman, 1992). Stress

was significantly correlated with depressive symptoms but not with any of the

biomarkers (Shelton, Schminkey, & Groer, 2014). Depression, however, was

negatively related to the proinflammatory cytokines interleukin (IL) 1β and tumor

necrosis factor alpha (TNF-α).

These findings are similar to those of Christian, Franco, Glaser, and Iams

(2009), who found depressive symptoms (but not stress) to be associated with

levels of IL-6 and TNF-α. Since the sample was of lower SES than earlier studies

(Coussons-Read et al., 2005, 2007) in which associations between stress and

cytokines were found to be significant, Christian et al. suggested that there may be a

threshold level of maternal stress over which depression is a better indicator than stress of inflammation during pregnancy. Blackmore, Groth, Chen, Gilchrist, O'Connor, and Moynihan (2014) tested the relationship in the opposite direction—pro-inflammatory cytokines as predictors of postpartum depression—but did not find evidence of association between elevated IL-6 or TNF-α and depression in the sample of pregnant women. Further research is needed to clarify relationships among stress, depression, and cytokines during pregnancy.

Similarly, Corwin, Guo, Pajer, Lowe, McCarthy, Schmiege, et al. (2013) measured levels of cortisol and cytokines in pregnant women (32-36 weeks' gestation), comparing groups by minority/non-minority race and income (operationalized as WIC participation). A key finding was a negative relationship between cortisol and ratios of pro-inflammatory to anti-inflammatory cytokines (IFNγ/IL-10, IL-6/IL-10, TNFα/IL-10, and IL-1β/IL-10) in the low risk group—white women not on WIC. This relationship was not observed in women of minority race and/or receiving WIC benefits, which researchers believe indicates disruption of the cytokine-glucocorticoid feedback loop. In another study of cortisol, Young and Breslau (2004) found a statistically significant difference in evening cortisol levels between adults who had experienced both PTSD and depression and adults who had never had either diagnosis. Taken together, these studies support the relationship between elevated cortisol and risk for physical and mental health problems, as well as the social gradient in health, in that pregnant women who are receiving WIC and/or are of minority race may be at higher risk for PTSD,

depression, and less optimal ratios of pro-inflammatory to anti-inflammatory cytokines, due to physiological responses to stress.

One study has examined correlations between stress measured by psychosocial instruments and stress biomarkers during pregnancy. Harville, Savitz, Dole, Herring, and Thorp (2009) compared participants' self-reported perceived stress, anxiety, social support, and coping style with serum cortisol and corticotrophin-releasing hormone (CRH) collected in the early second and early third trimesters. Psychosocial conditions and the biomarkers measured were not correlated, for the most part. One weak but statistically significant correlation was found between participants' score on the Perceived Stress Scale and serum CRH, both collected at 24-29 weeks gestation (r = -.063, p < .05). Research following this study has questioned the reliability of stress and allostatic load measurement during the second trimester, but this study raises yet unanswered questions about relationships between psychosocial indicators and biomarkers of those psychosocial conditions during pregnancy.

In a study of the effects of maternal deprivation on cortisol, Thayer and Kuzawa (2014) found that greater maternal socioeconomic deprivation predicted higher maternal evening cortisol at 34-36 weeks of pregnancy (β = .22, SE = .09, t = 2.51, p = .02), as well as in the infant at age 6 weeks, following vaccination (β = 4.39, SE = 1.42, t = 3.08, p = .009). Maternal morning cortisol and infant cortisol pre-vaccination did not vary by maternal material deprivation. The cortisol patterns related to higher deprivation in the sample mirror those who experience chronic stress, which supports Marmot (2004) and Sapolsky's (Marmot & Sapolsky, 2014)

theory that low social rank (of which socioeconomic deprivation is an indicator) predicts poor health via physiological responses to stress. Additionally, the study's findings suggest that cortisol reactivity to stress is transferred from mother to infant.

Measuring Stress with Psychosocial Indicators

In a review of literature, Wadhwa, Entringer, Buss, and Lu (2011) found that the stress of major negative life and community events (e.g., divorce, terrorist acts, and natural disasters) confers greater risk of preterm birth than chronic stress. Also, measures of pregnancy-specific psychosocial factors (e.g., pregnancy-related social support) have shown stronger relationships with preterm birth risk than general psychosocial states (e.g., general social support). However, the authors encourage consideration of stress fluctuation, that is,

> the number and magnitude of psychological 'ups' and 'downs' experienced by the individual over the given period of interest will produce an impact on the likelihood of stress-related health outcomes that is either independent of, or interacts with, the overall mean level of stress over that particular period. (p. 355)

Scharber (2014) applied the concept of allostatic load to interpret findings of a comparison in birth outcomes by maternal employment status as indicated on Texas birth records. She found that on average, babies born when the mother was unemployed weighed 32 grams less at birth than siblings born when the mother was employed. Also, unemployment accounted for a one percent increase in low birth weight (LBW) and 0.55 percent rise in infant mortality. Unemployment affected fetuses in difficult pregnancies most; "the average effect of unemployment among women without [pregnancy complications] appears insignificant" (p. 280).

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Citing earlier research that found stress-related mechanisms were more influential on adverse birth outcomes than other factors associated with unemployment, such as lack of access to prenatal care or frustration-related behaviors like substance use, Scharber suggests that birth outcome differences attributable to unemployment are best explained by allostatic load.

Absence of allostatic load has been found to have a positive effect on birth outcomes. Voellmin, Entringer, Moog, Wadhwa, and Buss (2013) found maternal positive affect to predict longer length of gestation and reduced risk of preterm birth. Researchers controlled for maternal stress, suggesting that positive affect and possibly other psychosocial factors tell more about risk of adverse birth outcomes when considered together than maternal stress alone.

Hilmert, Dunkel Schetter, Dominguez, Abdou, Hobel, Glynn, and Sandman (2008) studied birth weight as an outcome of stress and blood pressure and found that the interaction of high stress and high diastolic blood pressure (DBP) predicted low birth weight but not shorter gestational length. Comparisons between white and black mothers showed no significant difference in stress level and the same interaction effect of stress and DBP on birth weight, when controlling for SES, BMI, and stressful life events. Because of lack of difference between racial groups, researchers interpreted this finding as nonsupport for allostatic load as an explanatory mechanism of low birth weight. It is possible, however, that higher reactivity to stress in the form of higher blood pressure is an indicator of higher allostatic load, even if expected racial differences were not found in the sample.

Individual stressful experiences during pregnancy may contribute to allostatic load and have effects on birth outcomes and child development. King and LaPlante (2005) assessed children at age 2 for cognitive and emotional development (n = 61) and found that those who had experienced an ice storm (with power outages, travel difficulties, and other related hardships) during the second trimester in utero were developmentally different than other children. Prenatal experience of the ice storm during the second trimester predicted more than 50% of the variance in developmental play, suggesting a sensitive period to the effects of stress on later development.

Effects of Parental Allostatic Load Across the Life Course

Parental allostatic load is likely to affect early childhood development. Slopen, Loucks, Appleton, Kawachi, Kubzansky, Non, et al. (2015) examined the role of prenatal and childhood social adversity on adult levels of CRP, an indicator of inflammation. Participants' mothers were part of the sample for the Collaborative Perinatal Project (1959-1966), for which the women gave psychosocial information. From this data, researchers created prenatal and childhood adversity indices. Independently, both indices were associated with elevated CRP in participants (adult offspring). When combined into one model, only prenatal social adversity was significantly associated with CRP. These findings suggest long-term consequences for adversity experienced prenatally.

Entringer et al. (2009, 2009) studied young adults whose mothers experienced stress due to a traumatic event during participants' prenatal development. In one report (Entringer, Buss, Kumsta, Hellhammer, Wadhwa, &

Wüst, 2009), researchers describe findings that women exposed to stress prenatally did not perform as well on a working memory challenge following administration of cortisol as women in the comparison group, who were not exposed to prenatal stress. In another article (Entringer, Kumsta, Hellhammer, Wadhwa, & Wüst, 2009), researchers reported higher pituitary response to the Trier Social Stress Test in the prenatal stress group versus the comparison group. This suggests an increased reactivity to stress in the HPA axis among young adults exposed to stress prenatally. Interestingly, the prenatal stress and comparison groups did not differ in birth outcomes (birth weight, gestational age, growth percentile at birth), but putative effects of prenatal stress were evident in young adulthood nonetheless. Because of this, Entringer et al. (2009) described birth weight as a "very crude marker of prenatal conditions" (p. 297), which is not always affected by factors that may alter later development or functioning.

Along with traumatic stress, maternal stress due to bereavement has been shown to affect prenatal and postnatal development. Class, Abel, Khashan, Rickert, Dalman, Larsson, et al. (2014) found that when women in Sweden experienced the death of a family member, this increased the risk to their offspring of specific mental health diagnoses. Researchers used Swedish population registry data (e.g., Multi-Generation Registry, Causes of Death Registry, National Patient Register) to identify women with bereavement stress exposure immediately before, during, or within two years of pregnancy. When the death occurred during the prenatal period, risk to offspring of autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD) increased. When the death occurred between birth and age 2, the

offspring were at increased risk of ASD diagnosis, as well as suicide attempt and completion. No associations were found between preconception experience of death and the mental health diagnoses of interest nor between maternal bereavement stress and adult-onset mental health diagnoses of schizophrenia and bipolar disorder.

McNicholas, Healy, White, Sherdian-Pereira, O'Connor, Coakley, et al. (2014) examined the well-being of Irish early adolescents born at very low birth weight (VLBW) (< 1500 grams) compared to a control group born with normal birth weight, matched for gender. At ages 10-14, the VLBW group reported significantly lower average height and weight, and significantly higher rates of long-term illnesses, hospital outpatient services usage, and average number of school absences. Children in the VLBW group also had significantly poorer performance in several school subjects, per teacher report. This is likely a reflection of school absences due to more prevalent health concerns, as well as differences in IQ. The IQ "of these Irish VLBW survivors were approximately 1 SD below those of NBW peers, with 20% more than 2 SD below" (p. 528-529). Although SES explained 24% of the variance in IQ, birth weight explained an additional 11% ($\Delta R^2 = 0.11$, $\Delta F = 15.5$, p < .001). Further, significant differences were found between VLBW and the control group's performance on reading and math achievement tests, with a greater difference in math scores than reading.

Gaps in Research

Based on this literature review, a primary research gap in the study of allostatic load and adverse birth outcomes is to clarify the impact of allostatic load

on pregnancy by measuring it at different points in time. This study addressed this gap by comparing maternal allostatic load in each trimester to length of gestation. While several authors have hypothesized that measurement in the first trimester will provide the best indicator of allostatic load, it remains to be shown if this is the case.

Wadhwa, Entringer, Buss, and Lu (2011) made several recommendations for the advancement of research in this area. They advocated use of prospective research designs, to address selection bias; gestational length (a continuous measure) rather than the categorical measure of preterm birth; and they recommend distinguishing among type of births (preceded by spontaneous or induced labor, by the bag of waters breaking, or by cesarean section). The latter is hypothesized to show a stronger relationship between maternal stress and "near-term spontaneous births," in contrast to an expected moderating function of maternal stress in "earlier (moderate to severe) preterm births" (p. 354).

> Thus, the use of well-designed prospective studies in representative populations with serial, longitudinal assessments to determine the nature and strength of the association of naturally occurring variation in stress with subsequent birth outcomes after measuring and statistically adjusting for effects of other established sociodemographic, behavioral, and environmental risk factors can go a long way to provide the best possible evidence that either supports or refutes an underlying causal model. (p. 354)

Further, future research and theoretical models should incorporate individual variation in biological responses to stress, because

> a progressive attenuation occurs of not only maternal biological but also psychological responses to stress over the course of gestation, and that after accounting for the effects of other established risk factors, individual differences in the degree (trajectory) of this attenuation is a significant predictor of shortened length of gestation and risk of earlier delivery. (p. 357)

Additionally, the authors hypothesize an interaction relationship between maternal nutrition and maternal stress on preterm birth, but note that no known studies have tested this conceptual model.

Conclusion

This review of literature indicates that allostatic load during pregnancy—both its measurement and its clinical significance—is a developing research area. While some exploratory analyses and theoretical modeling have been completed, explanatory research is needed using longitudinal data on allostatic load in women who are pregnant, including data from the first trimester. Also, connections have yet to be made between the body of literature on allostatic load during pregnancy and social work literature. Translational research is needed in this area so that social workers can intervene effectively to improve birth outcomes among women with high levels of allostatic load.

Chapter 3: Methods

This study addressed the identified gap in literature on measurement of allostatic load during pregnancy and considered whether allostatic load predicts length of gestation. The general hypothesis for this study was that pregnant women experiencing higher allostatic load were more likely to experience earlier delivery than women with lower allostatic load. Allostatic load, measured in each trimester, was tested for prediction of gestational length via secondary data analysis of a larger multicenter trial (n = 399) that examined the impact of prenatal tobacco usage on immune response and preterm birth.

Hypotheses

The study tested three hypotheses.

H_1: Higher scores on an index of allostatic load predict shorter gestational length (measured in days of gestation).

In the literature, there is no consensus on the biomarkers used to measure allostatic load. A systematic review examining allostatic load in studies of health outcomes reported use of neuroendocrine, metabolic, immune, and cardiovascular indicators (Juster, McEwen, & Lupien, 2010). In studies examining allostatic load and birth outcomes, prenatal and postnatal biomarkers, including cardiovascular, immune system, and metabolic indicators were used to measure maternal allostatic load (Hux, Catov, & Roberts, 2014; Wallace & Harville, 2013; Wallace, Harville, Theall, Webber, Chen, & Berenson, 2013a, 2013b). These studies have found mixed results regarding the relationships between allostatic load and adverse birth outcomes. For instance, Hux, Catov, and Roberts (2014) found associations between

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allostatic load and both preterm birth and small for gestational age (SGA) births, while Wallace and Harville (2013) found allostatic load to be a significant predictor of only gestational age and not other birth outcomes. Therefore, the first aim of the proposed study was to test whether higher allostatic load predicts shorter gestational length.

H_2: High scores on an allostatic load index in the first trimester of pregnancy are more likely to predict shorter gestational length than high allostatic load index scores in the second or third trimesters.

Several of the biomarkers used to measure allostatic load are altered during pregnancy due to normal physiological processes (cytokines, for example). Morrison, Shenassa, Mendola, Wu, and Schoendorf (2013) reported allostatic load differed significantly among pregnant and non-pregnant women in the National Health and Nutrition Examination Survey (NHANES) dataset. Among pregnant women, well-established relationships between allostatic load and demographic variables were not present, such as higher allostatic load among those with lower income or educational attainment, or among black women when compared to white women. These findings suggest that measurement of allostatic load during pregnancy is a more complex phenomenon when compared to measurement of allostatic load among non-pregnant populations. Further, optimal timing of allostatic load measurement during pregnancy has not been established. Of the limited data that exists pertaining to prenatal allostatic load measurement, it has been suggested that measurement in the first trimester may be most accurate. Early

prenatal physiology when compared to late prenatal physiology most resembles the non-pregnant state (Hux, Catov, & Roberts, 2014; Morrison, Shenassa, Mendola, Wu, & Schoendorf, 2013; Wadhwa, Entringer, Buss, & Lu, 2011). The second aim of this study was to compare the ability of allostatic load in the first, second, and third trimesters to predict gestational length. Improving the timing of allostatic load measurement among pregnant women will allow better prediction of birth outcomes.

H_3: Allostatic load in the first trimester is a stronger predictor of gestational length than the Everyday Stressors Index (ESI).

The relationship between maternal stress and increased risk of adverse birth outcomes has been widely established (Wadhwa, Entringer, Buss, & Lu, 2011). Allostatic load is a measure of the physiological effects of stress, so it is likely that it is a predictor of gestational length. Since allostatic load is a cumulative measure and the biomarkers that comprise it are less affected by idiosyncratic variations (e.g., a participant's memory of stressful events, subtle influence of the person collecting data on participants' responses), it may be a stronger and more reliable predictor of gestational length than psychosocial measures, including the ESI. The third aim of the study is to test whether the ESI or the allostatic load index is a better predictor of gestational length.

Data Collection

A team of medical researchers led by Kristin Ashford, PhD, previously collected the data to be used between January 2008 and June 2013 (K. Ashford,

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personal communication, January 15, 2015). The original study was approved by

the Institutional Review Boards (IRBs) of the University of Kentucky and the

University of Virginia, and the current study was added to the original IRB approval

as a modification. Women ages 16 and older with singleton pregnancies were

recruited by research nurses or nurse practitioners into the study during the first

trimester of pregnancy at a prenatal care visit to university-affiliated prenatal clinics

in Kentucky and Virginia. Exclusion criteria were history of diabetes or heart

disease, indication of drug abuse during the second or third trimesters, second

trimester diagnosis of sexually transmitted disease, multifetal pregnancy, and for

multigravid women, history of pregnancies with complications or preterm births.

Participants were informed of possible risks and their right to leave the study at any

time without penalty, and 399 women agreed to participate. Upon completion of

each appointment at which data was collected, participants were given a $20 gift

card. If participants completed all four appointments, they were given an additional

$20 gift card, for a total of $100.00 in possible compensation for study participation.

At regular prenatal care appointments (one each trimester[3]) and the

postpartum appointment, participants completed psychosocial assessments,

including the Everyday Stressors Index, Edinburgh Postnatal Depression Scale, and

State-Trait Anxiety Inventory. The study questionnaire also included the Pittsburgh

Sleep Quality Index, medications taken, and questions about smoking and nutrition.

The first trimester questionnaire also collected dental variables, due to associations

between poor dental health and adverse birth outcomes (Albert, Begg, Andrews,

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[3] Trimesters were defined as 5-13 weeks' gestation, 14-26 weeks' gestation, and 27-36
weeks' gestation. The postpartum appointment was at six weeks after delivery.

Williams, Ward, Conicella, et al., 2011), as well as demographic variables. At the

postpartum visit, data on delivery was collected, such as complications during

delivery, birth weight and length, and gestational age.

Research nurses or nurse practitioners also collected biomarker data at one

prenatal appointment in each trimester and at the postpartum appointment.[4]

Blood, saliva, and cervico-vaginal fluid (CVF) samples were collected and analyzed

for levels of pro-inflammatory cytokines (IL-1α, IL-1β, IL-6, IL-8, TNF-α), the anti-

inflammatory cytokine IL-10, and CRP. Urine samples were also analyzed for

cotinine levels, as indication of smoking.

For consistency with literature on allostatic load during pregnancy, an

indicator of cardiovascular health was needed in the dataset. Though not collected

for the study, the consent form signed by participants stated that participants' blood

pressure might be collected (K. Ashford, personal communication, January 15,

2015). Since blood pressure was taken routinely at each prenatal appointment,

participants' blood pressures at appointments at which study data was collected

were gathered via electronic chart review and added to the dataset.[5, 6]

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[4] If a participant was getting additional prenatal serum labs collected by the clinic
phlebotomist, the phlebotomist would collect an additional serum sample for the
research nurse (K. Ashford, personal communication, April 11, 2016).
[5] When two blood pressure readings were taken at the study visit, the second blood
pressure was used in the allostatic load index to reduce the influence of the "white-
coat effect," when a patient's blood pressure increases when measured in a medical
office (Ishikuro, Obara, Metoki, Ohkubo, Iwama, Katagiri, et al., 2015).
[6] If a blood pressure reading was not recorded on a study appointment date, the
next blood pressure reading taken after the study appointment date was
substituted, as long as the date of collection was before the study appointment date
in the following trimester.

Study Variables

Predictor Variables

Two predictors of gestational length were tested: an index of allostatic load
and the Everyday Stressors Index (ESI). The variables that composed the allostatic
load index were systolic and diastolic blood pressure (measured in mmHg) and
body mass index (BMI), calculated from participants' first trimester weight (in
kilograms) divided by height (in meters), squared. Other variables in the index
were levels of cytokines (IL-1β, IL-6, IL-10) and C-reactive protein in serum
samples, measured in picograms per milliliter (pc/ml). Serum samples of
biomarkers (instead of saliva or cervicovaginal fluid) were used because more data
from serum was available in the dataset than from the other media. The pro-
inflammatory cytokines were selected based on previous analysis of the data that
found significant differences of serum levels of IL-1β and IL-6 between participants
who delivered preterm and those who did not (K. Ashford, personal communication,
September 29, 2015). Interleukin 10 (IL-10) was included because it was the only
anti-inflammatory cytokine on which data was collected.

To construct the allostatic load index, scores in the highest tertile of each
biomarker indicator were counted as one point, and these points were summed to
form the allostatic load index.[7] This method is consistent with previous research on
allostatic load during pregnancy (Hux, Catov, & Roberts, 2014; Morrison, Shenassa,
Mendola, Wu, & Schoendorf, 2013; Wallace & Harville, 2013; Wallace, Harville,

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[7] Items on which lower scores are indication of worse health, such as anti-inflammatory
cytokines, were reverse-coded.

Theall, Webber, Chen, & Berenson, 2013a, 2013b). The allostatic load index was calculated for each trimester.

The allostatic load index was compared to the ESI (Hall, Williams, & Greenburg, 1985), a psychosocial measure of stress, to determine relative strength of associations with length of gestation. The ESI has been found to have high internal reliability and construct validity (Knight, Smith, Martin, & the LONGSCAN Investigators, 2011). Two items in the ESI scale were mistakenly omitted from the survey instrument at the beginning of the study[8] and were added partway through data collection, so earlier participants have an 18-item scale and later participants have the full 20-item scale. The 18-item scale was used for all participants in this analysis because of availability of data for a majority of participants, and previous analysis of the data has demonstrated reliability and validity of the shortened scale (K. Ashford, personal communication, March 23, 2016).

Dependent Variable

The dependent variable of interest was length of gestation, computed from separate weeks of gestation and days of gestation variables. For logistic regression analysis, the dependent variable was preterm birth, a categorical measure of births before 37 weeks' gestation and births at 37 weeks' gestation or later.

Control Variables

Twelve control variables were considered for inclusion in the analysis, based on associations with either allostatic load or birth outcomes. These included age

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[8] The two items omitted from early data collection were "Concerns about how your child(ren) is(are) doing in school (day care)" and "Problems with friends and neighbors" (A. Wiggins, personal communication, January 15, 2016).

(measured during the first trimester, in years), race (initially measured in categories

of White, African American, Hispanic or Latina, Asian, or other; dichotomized as

White and non-White), and education (measured as highest education level

completed, ranging from none to graduate work beyond a college degree). Other

control variables assessed for inclusion were marital status (measured in categories

of single, dating/not living together, living with partner, married, divorced, and

separated), household annual income (measured in categories from under $5000 to

more than $50,000), and gravidity (measured as number of pregnancies).

Behavioral control variables included smoking behavior (average number of

cigarettes smoked per day in last 30 days, measured in intervals of five cigarettes);

smoking exposure (hours per day exposed to others' tobacco smoke indoors at

home); and nutrition, measured as the number of fruit and vegetable servings per

day plus type of fat used (animal fat [1], vegetable fat [2], olive oil [3]). A dental

health variable was also included, measured as no gum disease, gum disease with

bleeding gums, gum disease with loose teeth, or gum disease with both bleeding

gums and loose teeth.

The psychosocial control variables were anxiety and depression. Anxiety is

measured by the 20-item state anxiety scale from the State-Trait Anxiety Inventory

(STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), which has been

reliable when used with a variety of populations (Barnes, Harp, & Jung, 2002) and

has been shown to have content validity when used with pregnant women

(Gunning, Denison, Stockley, Ho, Sandhu, & Reynolds, 2010). Depression was

measured by the Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden, &

Sagovsky, 1987), which has 10 items. It has been used with pregnant women with reported validity for assessment of depression during pregnancy (Jomeen & Martin, 2007).

Sample

Out of a sizable sample (n = 399), systolic and diastolic blood pressure data was only available for a subset of participants (any trimester, n = 156; first trimester, n = 133; second trimester, n = 109; third trimester, n = 135). Additionally, a substantial amount of data was missing on biomarker levels in serum samples. Since larger percentages of missing data were found when using the total sample, the analysis was limited to the smaller sample of participants with available blood pressure data in any trimester (n = 156).[9]

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[9] Hereafter, the smaller sample is referred to as "the sample."

Table 1

Control Variables, Allostatic Load Index Variables, and Psychosocial Stress Variable

Control Variables	Allostatic Load Index	Psychosocial Stress Measure
Age	Systolic blood pressure (SBP)	Everyday Stressors Index (ESI)
Race	Diastolic blood pressure (DBP)	
Education	Body mass index (BMI)	
Marital status	C-reactive protein (CRP)	
Income	IL-1β	
Gravidity	IL-6	
Smoking exposure	IL-10	
Smoking behavior		
Nutrition		
Dental health		
Edinburgh Postnatal		
Depression Scale		
State-Trait Anxiety		
Inventory (STAI)		

Demographic characteristics of the sample are shown in Table 2. Over 80% of participants were white, and the median annual household income range in the sample was $40,000-$49,999. Most women (62.8%) were married, and over 50% of women had completed at least some college or vocational/trade school. Participants ranged in age from 16 to 42 years, and the average age of the sample was 27.14 years (sd = 5.47).

Table 2

Demographic Characteristics of the Sample

	Frequency	Percentage
Race		
White	126	80.8%
African American	20	12.8%
Hispanic/Latina	5	3.2%
Other	5	3.2%
Household Income[1]		
Under $5000	16	10.3%
$5000-$9999	6	3.8%
$10,000-$14,999	8	5.1%
$15,000-$19,999	7	4.5%
$20,000-$24,999	8	5.1%
$25,000-$29,999	12	7.7%
$30,000-$39,999	8	5.1%
$40,000-$49,999	18	11.5%
$50,000 or more	70	44.9%
Marital Status		
Married	98	62.8%
Living with Partner, Not Married	29	18.6%
Dating, Not Living Together	13	8.3%
Separated	2	1.3%
Single	14	9.0%
Divorced	0	0%
Highest Education Completed		
Grade 8 or Below	2	1.3%
Grades 9-11	17	10.9%
High School Graduate/GED	12	7.7%
Some College/Vocational/Trade School	36	23.1%
College Graduate	59	37.8%
Beyond College	30	19.2%

	Mean	SD
Age	27.14 years[2]	5.47

[1]Missing = 3; [2]Missing = 1

Table 3 shows descriptive statistics of the sample. The average length of gestation in the sample was 38.88 weeks, with only 16 births occurring preterm. Average scores on the allostatic load index were highest in the second trimester (2.18). Average ESI scores by trimester decreased from the first trimester (7.91) to the third trimester (6.98). The range of observed scores increased from first trimester to third trimester for both allostatic load (0-5 to 0-6) and the ESI (0-31 to 0-35).

Table 3

Descriptive Statistics of the Sample

	Mean	Range	Missing Cases
Length of Gestation (in weeks) (Preterm births = 16)	38.88	25.29-41.57	8
Allostatic Load Index			
1st Trimester	2.05	0-5	63
2nd Trimester	2.18	0-6	71
3rd Trimester	2.13	0-6	68
Everyday Stressors Index (ESI)			
1st Trimester	7.91	0-31	--
2nd Trimester	7.65	0-34	12
3rd Trimester	6.98	0-35	25
Smoking Exposure (hours/day)			
1st Trimester	1.27	0-24	2
2nd Trimester	1.09	0-24	14
3rd Trimester	1.14	0-24	11
Dental Health Scale	.08	0-2	--
Nutrition Scale	9.33	2-17	9
Gravidity	1.87	1-8	7

	Frequency	Percentage	Missing Cases
Smoking Behavior			
Smoker, 1st Tri.	33	21.2%	--
Smoker, 2nd Tri.	24	16.5%	10
Smoker, 3rd Tri.	23	15.7%	10

Data Analysis

Data analysis began with data cleaning, to ensure suitability of variables for correlation tests and multiple regression. It was found that six variables[10] contained between 5% and 15% missing data, and another five variables[11] had over 15% of data missing. For variables with 5% to 15% of data missing, missing data were replaced with the mean value (Mertler & Vannatta, 2010). A variety of methods were used to address missing data over 15%. Self-reported smoking behavior was replaced with the measurement of cotinine taken in each trimester ("nic alert"), which is an indicator of smoking and contained less missing data (no missing data in nic alert, first trimester; 6% missing in second and third trimesters, which was replaced with the mean value). The ESI, third trimester, variable had 16% of data missing. Since this was very close (a difference of one case) to the 15% missing data cut-off point and due to the variable's centrality to the hypotheses tested, missing data were replaced with the mean value.

The highest levels of missing data were found in the allostatic load indices for each trimester (missing data of 40%, 46%, and 44%, respectively). Since the sample was already limited to those with a blood pressure reading in *any* trimester, some of the missing allostatic load index scores were due to blood pressure readings missing

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[10] Edinburgh Postnatal Depression Scale [depression], second trimester; depression, third trimester; Everyday Stressors Index [ESI], second trimester; State portion of State-Trait Anxiety Inventory [anxiety], second trimester; anxiety, third trimester; nutrition scale

[11] Smoking behavior (25% missing); ESI, third trimester (16% missing); allostatic load index [AL], first trimester (40% missing); AL, second trimester (46% missing); AL, third trimester (44% missing)

from an individual trimester.[12] Of the variables in the allostatic load indices, a larger proportion of missing data was found in the biomarker variables. If either blood pressure readings or biomarkers were excluded from the allostatic load indices, the other set of variables retained (blood pressure or biomarkers) would still have a problematic amount of missing data, so both types of data were retained.

The second problem found during data screening was failure to meet test assumptions for linear regression. Examination of scatterplots indicated lack of linearity and normality in the combination of allostatic load indices and length of gestation, making them unsuitable for linear regression analysis. The one area on the scatterplot matrix with an elliptical shape, indicating a linear, normal relationship between variables, was between allostatic load, third trimester, and length of gestation, when limited to full-term births (length of gestation ≥ 259 days). Linear regression analysis was limited to these cases (n = 71). To maintain a ratio of at least 10 cases for each variable, the five control variables with highest correlation coefficients were retained in the linear regression analysis (gravidity; education; smoking behavior, third trimester; smoking exposure, third trimester; and depression, third trimester). Correlation coefficients (Spearman's rho) are shown in Tables 4, 5, and 6.

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[12] Only 55% (n = 86) of cases had blood pressure data for all three trimesters.

Table 4

Bivariate Relationships (Spearman's Rho or Eta) Between Demographic and Biological Control Variables and Predictor and

Dependent Variables

	Age (ρ)	Race (η)	Education (ρ)	Marital Status (η)	Income (ρ)	Gravid. (ρ)	Smok. Exp. 1st Tri. (ρ)	Smok. Exp. 2nd Tri. (ρ)	Smok. Exp. 3rd Tri. (ρ)	Smok. Beh. 1st Tri. (ρ)	Smok. Beh. 2nd Tri. (ρ)	Smok. Beh. 3rd Tri. (ρ)	Nutri. Scale (ρ)	Dent. Scale (ρ)
Length of Gest.	-.014	.067	.267**	.111	.199*	-.369**	-.213**	-.178*	-.201*	-.237**	-.169*	-.252**	.072	-.018
AL Index 1st Tri.	-.155	.040	-.069	.289	-.226*	-.051	.130	.121	.113	.088	.065	.166	-.056	-.316**
AL Index 2nd Tri.	-.030	.107	.019	.177	.030	-.168	-.078	.095	.164	.034	-.005	.052	-.071	-.161
AL Index 3rd Tri.	.023	.047	.056	.186	-.136	-.097	-.039	-.015	.091	.097	.138	.049	.085	.058

$**p \leq .01$, $*p \leq .05$

Table 5

Spearman's Rho Correlation Coefficients for Psychosocial Control Variables and Predictor and Dependent Variables

	State Anxiety 1st Tri.	State Anxiety 2nd Tri.	State Anxiety 3rd Tri.	Depression 1st Tri.	Depression 2nd Tri.	Depression 3rd Tri.
Length of Gestation	-.005	.131	-.053	-.029	.035	-.201*
AL Index 1st Tri.	.047	.141	.059	-.101	-.076	-.066
AL Index 2nd Tri.	.143	.133	.268*	.079	.052	.321**
AL Index 3rd Tri.	.174	.076	.154	-.009	.066	.051

$**p \leq .01, *p \leq .05$

Table 6

Spearman's Rho Correlation Coefficients for Predictor Variables and Dependent Variable

	Length of Gestation	AL Index 1st Tri.	AL Index 2nd Tri.	AL Index 3rd Tri.	Everyday Stressors Index 1st Tri.	Everyday Stressors Index 2nd Tri.	Everyday Stressors Index 3rd Tri.
Length of Gestation	1.00						
AL Index 1st Tri.	-.102	1.00					
AL Index 2nd Tri.	-.209	.596**	1.00				
AL Index 3rd Tri.	-.093	.462**	.685**	1.00			
Everyday Stressors Index 1st Tri.	-.223**	.058	.151	.143	1.00		
Everyday Stressors Index 2nd Tri.	-.161	.105	.109	.033	.702**	1.00	
Everyday Stressors Index 3rd Tri.	-.135	.184	.245*	.051	.512**	.672**	1.00

$**p \leq .01, *p \leq .05$

Though problems with linearity and normality in the distribution of the allostatic load indices did not meet test assumptions for linear regression, the data could be analyzed using logistic regression, due to the lack of assumptions about distribution of predictor variables (Mertler & Vannatta, 2010). Continuous study variables with statistically significant correlation coefficients were dichotomized[13] or converted to tertiles[14] in order to address outliers without losing cases. Examination of crosstabs between control and predictor variables with the dichotomized dependent variable of preterm birth (birth before 37 weeks' gestation/birth at 37 weeks' gestation or after) indicated a high number of cells with expected frequencies of fewer than five cases, so household income was recoded into tertiles ($0-24,999/$25,000-49,999/$50,000 and over). Second trimester allostatic load was dichotomized to address an empty cell.[15] Crosstabs between independent variables and preterm birth showed expected frequencies of fewer than five cases in 24% of cells—sufficient distribution of data to conduct logistic regression.

These methods allowed investigation of third trimester allostatic load as a predictor of length of gestation among non-preterm births, as well as the ability of allostatic load in each trimester to predict whether birth occurred before or after 37 weeks' gestation. Further, allostatic load was compared to the ESI for prediction of preterm birth. Results are discussed in the next chapter.

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[13] Smoking exposure, all trimesters (none/one hour or more per day); smoking behavior, all trimesters (cotinine levels of 0-2/3-6)
[14] Allostatic load indices, all trimesters (0-1/2/3-7); Everyday Stressors Index, all trimesters (0-4/5-8.9/9-35); Depression, third trimester (0-2/3-5/5.5-18)
[15] There were no preterm births to women in the lowest tertile of second trimester allostatic load.

Chapter 4: Results

Two analyses were used to test a model of prediction of length of gestation.

First, linear regression of length of gestation on allostatic load, third trimester, was

conducted, and second, logistic regression of preterm birth on allostatic load and

scores on the Everyday Stressors Index (ESI) in each trimester was run. Results

indicate marginal advantages to including allostatic load in models predicting length

of gestation among full-term births.

Allostatic Load as a Predictor of Gestational Length

Ordinary least squares (OLS) linear regression was used to test the first

hypothesis: higher allostatic load predicts shorter length of gestation. Because of

failure to meet test assumptions of linearity and normality in other data, the

analysis was limited to third trimester allostatic load among women with full-term

births (birth at 37 weeks' gestation or after). Of these cases, 71 had complete data

for all variables in the analysis. OLS linear regression analysis was performed to

test the strength of third trimester allostatic load as a predictor of length of

gestation. Five control variables (gravidity; education; smoking behavior, third

trimester; smoking exposure, third trimester; and depression, third trimester) were

entered in step one. Before inclusion of third trimester allostatic load, the model

significantly predicted length of gestation, though only one variable, gravidity, was a

statistically significant contributor to the model (R^2 = .159, R^2_{adj} = .094, $F(5, 65)$ =

2.46, $p \leq .05$). Third trimester allostatic load was entered in the second step, which

slightly improved the model and significantly predicted length of gestation (R^2 =

.193, R^2_{adj} = .118, $F(1, 64)$ = 2.55, $p \leq .05$).

A final model was then tested using only gravidity as a control variable[16], which was found to significantly predict length of gestation (R^2 = .121, R^2_{adj} = .096, F(1, 71) = 4.88, $p \leq$ .01). Third trimester allostatic load was a statistically significant predictor (B = -1.38, β = -.25, t = -2.21, $p \leq$ .05), indicating that an increase of one on the allostatic load index resulted in reduced length of gestation by more than one day. The final model predicted 9.6% of the variance in length of gestation, and showed that both gravidity and third trimester allostatic load have a negative relationship with gestational length: higher gravidity and higher allostatic load predicted shortened length of gestation. Standardized coefficients indicated that gravidity (β = -.27) and allostatic load (β = -.25) were comparable predictors in terms of strength. The regression coefficients are shown in Table 7 (initial model) and Table 8 (final model).

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[16] In the final model tested by linear regression, fewer variables in the model resulted in fewer cases with missing data and an increase in the number of cases included (n = 74).

Table 7

Coefficients Table for Initial Model, OLS Linear Regression of Length of Gestation on Third Trimester Allostatic Load (n = 71)

	Model 1			Model 2		
	B	SE	β	B	SE	β
(Constant)	277.43***	3.36		278.79***	3.42	
Gravidity	-4.03*	1.87	-.25	-4.29*	1.85	-.27
Education	.80	.96	.12	1.08	.96	.16
Smoking Behavior, 3rd Tri.	.42	.66	.60	.40	.65	.09
Smoking Exposure, 3rd Tri.	-.24	.25	-.14	-.17	.26	-.09
Depression, 3rd Tri.	-.28	.24	-.16	-.25	.24	-.15
Allostatic Load, 3rd Tri.				-1.03	.63	-.19
R^2_{adj}		.094			.118	
F		2.46*			2.55*	
ΔR^2					.03	

*** $p \leq .001$, **$p \leq .01$, *$p \leq .05$

Table 8

Coefficients Table for Final Model, OLS Linear Regression of Length of Gestation on Third Trimester Allostatic Load (n = 74)

	Model 1			Model 2		
	B	SE	β	B	SE	B
(Constant)	277.96***	1.16		281.05***	1.80	
Gravidity	-3.99*	1.85	-.25	-4.36*	1.81	-.27
Allostatic Load, 3rd Tri.				-1.38*	.61	-.25
R^2_{adj}		.047			.096	
F		4.64*			4.88**	
ΔR^2					.06*	

*** $p \leq .001$, **$p \leq .01$, *$p \leq .05$

Table 9

Logistic Regression Coefficients for Model Variables, Preterm Birth on Allostatic Load in Each Trimester

		B	Wald	Df	p	Odds Ratio
AL Index, 1st Tri.						
Final model (n = 90)						
-2 Log Likelihood = 54.81, χ^2 = 7.98, $p \leq .05$						
	Gravidity	2.06	6.24	1	.01	7.87
	AL Index	.03	.004	1	.95	1.03
AL Index, 2nd Tri.						
Final model (n = 78)						
-2 Log Likelihood = 35.71, χ^2 = 1.43, $p = .23$						
	AL Index	1.12	1.40	1	.24	3.06
AL Index, 3rd Tri.						
Final model (n = 84)						
-2 Log Likelihood = 57.18, χ^2 = 8.04, $p \leq .05$						
	Gravidity	1.91	5.39	1	.02	6.72
	AL Index	-.38	.85	1	.36	.68

Table 10

Logistic Regression Coefficients for Model Variables, Preterm Birth on ESI in Each Trimester

		B	Wald	Df	p	Odds Ratio
ESI, 1st Tri.						
Final model (n = 143)						
-2 Log Likelihood = 91.03, χ^2 = 9.20, $p \leq .01$						
	Gravidity	1.60	6.80	1	.01	4.97
	ESI	.21	.36	1	.55	1.24
ESI, 2nd Tri.						
Final model (n = 143)						
-2 Log Likelihood = 90.43, χ^2 = 9.79, $p \leq .01$						
	Gravidity	1.61	6.95	1	.01	4.99
	ESI	.34	.94	1	.33	1.40
ESI, 3rd Tri.						
Final model (n = 143)						
-2 Log Likelihood = 90.49, χ^2 = 9.74, $p \leq .01$						
	Gravidity	1.57	6.48	1	.01	4.78
	ESI	.35	.90	1	.34	1.41

Comparison of First, Second, and Third Trimester Allostatic Load

Logistic regression was conducted to test the second hypothesis: first trimester allostatic load is a better predictor of preterm birth in the sample than second or third trimester allostatic load. Model statistics, regression coefficients and Wald statistics are shown in Table 9. In the analysis of first trimester allostatic load, control variables of gravidity; education; smoking behavior, first trimester; smoking exposure, first trimester; and household income were entered into the model. Only gravidity was statistically significant in block one (B = 2.03, *Wald* = 5.43, $p \leq .05$). When first trimester allostatic load was included in block two, the model was no longer statistically significant (-2 Log Likelihood = 49.33, χ^2 = 7.94, p = .24). Further, first trimester allostatic load was not a statistically significant predictor of preterm birth. A trimmed, final model was then tested, using only gravidity as a control variable. The model significantly predicted preterm birth (-2 Log Likelihood = 54.81, χ^2 = 7.98, $p \leq .05$) and accounted for 16.9% of the variance in preterm birth in the sample (Nagelkerke pseudo R^2 = .169). Again, first trimester allostatic load was not a statistically significant predictor of preterm birth (B = .03, *Wald* = .00, p = .95).

Logistic regression was attempted for allostatic load, second trimester, but the lack of preterm births (n = 5) among women with complete data for the second trimester allostatic load index (n = 78) caused questionable reliability. None of the control variables entered (gravidity; education; smoking behavior, second trimester; smoking exposure, second trimester; and household income) were statistically significant predictors. Logistic regression without control variables and

second trimester allostatic load as the only dependent variable found that the model

did not significantly predict preterm birth in the sample (-2 Log Likelihood = 35.71,

χ^2 = 1.43, p = .23).

Logistic regression for allostatic load, third trimester, was also conducted. In

the initial model, gravidity was the only control variable from block one that was

statistically significant (B = 1.78, $Wald$ = 4.21, $p \le$ .05), out of education; smoking

behavior, third trimester; smoking exposure, third trimester; and depression, third

trimester. A final model was tested, using gravidity as the only control variable,

which significantly predicted preterm birth (-2 Log Likelihood = 57.18, χ^2 = 8.04, $p \le$

.05). However, third trimester allostatic load was not a significant predictor of

preterm birth.

Comparison of Allostatic Load and the Everyday Stressors Index

Logistic regression was also conducted with ESI scores in each trimester to

test the third hypothesis: allostatic load is a stronger predictor of preterm birth

than the ESI. (See Table 10.) The same control variables were entered for ESI

analyses as for the corresponding trimester's allostatic load analysis. An initial

logistic regression of ESI, first trimester, found that gravidity was the only

statistically significant control variable (B = 1.52, $Wald$ = 5.81, $p \le$ .05). A final

model with gravidity as the only control variable significantly predicted preterm

birth (-2 Log Likelihood = 91.03, χ^2 = 9.20, $p \le$ .01), but ESI, first trimester, was not a

significant predictor of preterm birth (B = .21, $Wald$ = .36, p = .55).

Similarly, for ESI, second trimester, logistic regression indicated that

gravidity was the only statistically significant control variable (B = 1.64, $Wald$ =

5.31, $p \le .05$). A trimmed model of second trimester ESI as a predictor of preterm

birth with gravidity as the only control variable was statistically significant (-2 Log

Likelihood = 90.43, χ^2 = 9.79, $p \le .01$). Again, however, ESI was not a significant

predictor in the model (B = .34, *Wald* = .94, p = .33).

Logistic regression analysis of ESI, third trimester, also indicated that

gravidity was the only significant control variable (B = 1.47, *Wald* = 4.15, $p \le .05$). A

final model with only gravidity and third trimester ESI was statistically significant in

predicting preterm birth in the sample (-2 Log Likelihood = 90.49, χ^2 = 9.74, $p \le .01$)

but again, ESI scores were not statistically significant predictors of preterm birth (B

= .35, *Wald* = .90, p = .34).

As with allostatic load, the ESI was not a significant predictor of preterm

birth in any trimester. Interpretation and implications of these results are discussed

in the following chapter.

Chapter 5: Discussion

The study tested three hypotheses concerning measurement of stress during pregnancy and prediction of preterm birth. Limited support was found for the first hypothesis: higher allostatic load is associated with shorter length of gestation. Due to missing data and failure to meet test assumptions of normality and linearity, the only relationship that could be directly tested was third trimester allostatic load as a predictor of length of gestation for births at 37 weeks' gestation or after. In this analysis, support was found for the hypothesis: when controlling for gravidity, education, third trimester smoking behavior, third trimester smoking exposure, and third trimester depression, third trimester allostatic load significantly predicted length of gestation. With gravidity, third trimester allostatic load predicted 9.6% of the variance in length of gestation, and an increase of one on the allostatic load index accounted for shorter length of gestation by over one day.

This finding is clinically significant. Beyond concerns about preterm births, there are also efforts by public health agencies to promote longer gestation, until at least 39 weeks. The Centers for Disease Control and Prevention (CDC) (2015) recommends against scheduling deliveries for nonmedical reasons before 39 weeks' gestation, citing continued development of the fetus until at least that point in pregnancy. The March of Dimes (2012b) also warns against elective scheduled births before 39 weeks' gestation to allow for additional brain, lung, and liver development, as well as weight gain, before birth. In 2011, the March of Dimes launched a public education campaign on the issue, called Healthy Babies Are Worth the Wait, which was expanded in 2012 into Strong Start, a broader campaign by the

U.S. Department of Health and Human Services (March of Dimes, 2012a). The

attention of these public health agencies to prolonging gestation beyond the 37

weeks full-term benchmark gives the finding of higher third trimester allostatic load

as a predictor of earlier birth greater importance. Third trimester allostatic load

could be used as an indicator of risk and indicate a need for medical and

psychosocial intervention, including services from social workers.

The literature contains some support for the finding that higher third

trimester allostatic load predicts shorter length of gestation. Typically, women have

greater physiological and psychological reactivity to stress earlier in pregnancy

rather than later, when the body's responses to stress become more muted (Cole-

Lewis, Kershaw, Earnshaw, Yonkers, Lin, & Ickovics, 2014; Glynn, Dunkel Schetter,

Hobel, & Sandman, 2008). Glynn et al. (2008) found that increased perceived stress

from second to third trimester was associated with preterm birth. Cole-Lewis et al.

(2014) found that third trimester pregnancy-specific stress was associated with

preterm birth (but not length of gestation), though change in pregnancy-specific

stress from the second to third trimester was associated with both preterm birth

and length of gestation. Taken together, these studies suggest that the finding of

allostatic load as a predictor of length of gestation among full-term births is part of a

general pattern: when psychological and physiological responses to stress do not

become more muted during pregnancy, earlier birth is more likely. Elevated third

trimester allostatic load, then, can be interpreted as residual or persistent stress—

stress that did not get masked by normal physiological processes during pregnancy.

Third trimester allostatic load, then, may be a better indicator of preterm birth and need for intervention than allostatic load in other trimesters.

In the study sample, mean allostatic load levels increased from the first trimester (2.05, sd = 1.39) to third trimester (2.12, sd = 1.45), which does not follow the normal pattern of stress during pregnancy and would suggest a higher preterm birth rate (Glynn, Dunkel Schetter, Hobel, & Sandman, 2008). However, the sample had a similar preterm birth rate to the general population: 16 preterm births out of 156 in the sample, or just over 10%, which is comparable to 12.6%, the Kentucky preterm birth rate in 2013 (March of Dimes, 2016). One explanation for this is that the sample is different from the general population of pregnant women. The sample could simply be unique, given its moderate median household income ($40,000-49,999) and location in Kentucky and Virginia. These factors may have resulted in a sample with many shared stressors and increasing reactivity to stress during pregnancy, but with enough supportive factors (such as quality prenatal care or high levels of social support, perhaps) to prevent higher incidence of preterm births.

It is also possible that allostatic load—the biological *effects* of stress—has a different pattern during pregnancy than stress itself. This is more likely to be true for the index used for allostatic load in this study compared to previous measurement of allostatic load during pregnancy. Systolic and diastolic blood pressure comprised two factors out of seven in this index. In past studies, systolic and diastolic blood pressure have been included as two out of nine or ten factors in allostatic load. It is common for blood pressure to rise throughout pregnancy,

irrespective of stress, so its elevated influence may account for some or all of the findings on third trimester allostatic load.

While the linear regression analysis of full-term births showed allostatic load to be an indicator of length of gestation, logistic regression analysis of allostatic load in each trimester indicated that allostatic load was not a predictor of preterm birth (birth at < 37 weeks' gestation). Models that included first and third trimester allostatic load significantly predicted preterm birth, but for both of those models, gravidity was the only significant predictor within the model. These findings show that allostatic load is not an indicator of risk of preterm birth within this sample and the hypothesis is not supported by the data.

The second hypothesis tested was that allostatic load in the first trimester is a better predictor of length of gestation than allostatic load in the second or third trimesters. This could not be directly tested because of failure of the data to meet test assumptions for linear regression. Instead, logistic regression analysis tested whether allostatic load in each trimester predicted preterm birth. Wald statistics showed that allostatic load was not a predictor of preterm birth in the sample in any trimester, so support was not found for the second hypothesis.

Though past studies of allostatic load during pregnancy have recommended first trimester (or preconception) allostatic load as a likely predictor of birth outcomes including length of gestation (Hux, Catov, & Roberts, 2014; Morrison, Shenassa, Mendola, Wu, and Schoendorf , 2013), this study did not find the hypothesized relationship. Possibly, shared stressors and resiliency factors in the sample reduced the effect of allostatic load, which may be found in other

populations. Another possible explanation is that data was collected too late in the first trimester. First trimester data could have been collected as late as 13 weeks' gestation, which may have been too late for expected first trimester allostatic load effects to be evident. This study's finding that higher third trimester allostatic load predicts earlier delivery among full-term births, however, suggests that allostatic load later in pregnancy has more of an effect than elevated allostatic load earlier in pregnancy and may make a better target for future research.

Beyond questions of timing of measurement of allostatic load, the finding that allostatic load did not predict preterm birth in any trimester calls into question whether allostatic load is a good measure for hypothesis testing of predictors of gestational length. Though Wallace and Harville (2013) found an association between second trimester allostatic load and length of gestation, their finding was not replicated by this analysis. The components of the allostatic load index in this study were not the same as Wallace and Harville's study, so it is not clear whether the two studies can be compared. Without accepted standards of how to measure allostatic load, it remains a broad construct that is difficult to operationalize.

The third hypothesis tested was that allostatic load is a better predictor of length of gestation than the Everyday Stressors Index (ESI). As discussed, this was not directly tested because of problems with the data. Logistic regression analysis was used to instead test whether allostatic load was a better predictor of preterm birth than the ESI. Neither allostatic load nor the ESI, in any trimester, were significant predictors of preterm birth in the sample. Models that included each

measure significantly predicted preterm birth, but only gravidity was a statistically significant predictor. These findings do not support the hypothesis.

It is interesting that first trimester ESI, not allostatic load (in any trimester), was significantly correlated with length of gestation (Spearman's rho = -.223, $p \leq$ .01), indicating a small effect of higher stress levels in the first trimester on reduced length of gestation in the sample. First trimester psychosocial stress may be a predictor of gestational length in other samples. As this is one of the first studies to include both allostatic load and a psychosocial stress measure during pregnancy for prediction of gestational length, further research is needed to adequately test the relative benefits of each type of indicator.

In sum, analysis of data found support for the first hypothesis, that higher third trimester allostatic load predicts shorter length of gestation among women in the sample who gave birth at 37 weeks' gestation or after. Allostatic load was not a significant predictor of preterm birth in any trimester, which fails to support the second hypothesis that first trimester allostatic load is the best predictor of length of gestation. Support was not found for the third hypothesis that allostatic load is a better predictor of length of gestation than the ESI, as neither allostatic load nor the ESI were significant predictors of preterm birth in the sample.

Implications for Social Work

The finding that higher third trimester allostatic load predicts earlier deliveries among full-term births has several implications for social workers. First, social workers in health care or community settings can educate pregnant clients and their support networks about the effects of stress throughout pregnancy,

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including the increased risk of earlier delivery associated with stress. Social workers can use case management strategies to assist clients in stress reduction, as well as provide education on relaxation techniques for stress management. As social workers assist clients who are pregnant with various social problems, they can explicitly or implicitly acknowledge stress reduction as an important clinical outcome.

Secondly, social workers can advocate for policies and programs that reduce stress for pregnant women. Preterm birth is a societal problem because its negative effects for children are experienced not only by immediate family, but also by society through increased need for medical, occupational, and educational services. Public policies, then, can benefit society as a whole by reducing stress for women who are pregnant through increased access to quality prenatal care; adequate affordable housing; safe neighborhoods; availability of Women, Infants, and Children (WIC) benefits; and social support. Social workers can advocate on behalf of women who are or may become pregnant, or organize with women beneficiaries themselves, for community supports for women who are pregnant.

Finally, social workers can utilize findings on allostatic load and length of gestation as support for funding requests for pregnancy intervention programs. Social workers in hospitals, clinics, and community programs can include findings on third trimester allostatic load as a predictor of shortened gestational length to describe why intervention services are necessary. This study found that support is specifically needed for women with moderate household income who receive

prenatal care at university clinics. Funding requests should include this finding in

descriptions of community needs.

Limitations

The study had several limitations. First, the sample for the study was not

random and is therefore not representative of a larger population. The findings are

limited to the women who participated and are likely influenced by the factors that

are unique to the sample, such as moderate median household income, residence in

Kentucky or Virginia, and receipt of prenatal services from university clinics.

Relationships found may not be present in other groups of pregnant women.

Further, the sample was limited by several exclusion criteria, including

history of heart disease and present indication of diabetes, substance use, and

sexually transmitted infections (STIs). Though these exclusions were important for

experimentally controlling for factors that affect preterm birth, it is likely that the

criteria also had the effect of excluding women with higher allostatic load. The

"wear and tear" on the body caused by stress and measured by allostatic load

includes negative effects on metabolic and cardiovascular systems that can result in

diabetes or heart disease (Sapolsky, 2004). Also, substance abuse (Panebianco,

Gallupe, Carrington, & Colozzi, 2016; Rommel, Rohleder, Wagenpfeil, Haertel-Petri,

& Kesting, 2015) and STIs (Harling, Subramanian, Bärnighausen, & Kawachi, 2014)

are known to be more prevalent among those with lower SES, which suggests

theoretical associations with higher allostatic load. Thus, excluding women from

the study who have heart disease, diabetes, substance use problems, or STIs may

have resulted in a sample with lower allostatic load. This may have affected the

analyses conducted by excluding cases for whom relationships between allostatic load and preterm birth would have been most apparent.

The sample also contained missing data on several key variables. The combination of availability of blood pressure data on a limited number of cases with data missing on the biomarkers in the allostatic load index resulted in fewer than 100 cases with complete allostatic load indices. The addition of control variables with low or moderate levels of missing data further reduced the number of cases, which produced analyses with less than 10% statistical power. Fewer cases also affected statistical analyses, especially in the logistic regression analysis of second trimester allostatic load. Low expected frequencies in cells due to a small number of preterm births (n = 5) to women with complete second trimester allostatic load indices made the analysis unreliable. It is possible that analysis of data from the same sample with less of it missing would have found different results.

More cases would have addressed some of the problems with the distribution of the data that made it incompatible with linear regression analyses. However, length of gestation is not normally distributed in the population. Though Wadhwa, Entringer, Buss, and Lu (2011) recommended prospective studies and use of the continuous measure of gestational length (as opposed to categorical measures of preterm birth) to advance research on maternal stress and birth outcomes, usable data may be difficult to achieve. While retrospective studies could address normality of the distribution of gestational length through experimental design, prospective studies would need enough cases to use a detailed ordinal measure for a

strong linear regression analysis or alternative statistical tools to test the original hypotheses of this study.

Future Research

The limitations and findings of the study suggest several avenues for future research. Replication of the study with more cases would increase the statistical power of the analyses and could validate current findings. To increase consistency with other allostatic load literature, a 10-factor allostatic load index should be used with additional metabolic and cardiovascular indicators. With a broader allostatic load index, larger sample size, and ordinal measurement of gestational length, data analysis may be able to more definitively explore relationships between allostatic load in each trimester and gestational length.

An area for potential exploration is the statistically significant correlations between second trimester allostatic load and third trimester anxiety (Spearman's rho = .268, p = .05) and depression (Spearman's rho = .321, p = .01). It is possible that allostatic load is an indicator of developing psychosocial concerns and could be used as an identifier of risk. Further research is needed to understand if this association is present in other samples and if it has clinical significance.

Additionally, it is interesting that for all three trimesters, smoking exposure and smoking behavior had statistically significant correlations with length of gestation. However, smoking variables did not significantly contribute to the regression models tested. Relationships among smoking, allostatic load, gravidity, and gestational length require further exploration to understand the relative effects of predictors on birth outcomes.

Conclusion

This study explored allostatic load as a measurement of maternal stress during pregnancy and its ability to predict length of gestation or preterm birth. Third trimester allostatic load was found to predict a small amount of variance in gestational length among women with full-term births. Allostatic load did not significantly predict preterm birth in any trimester. The ESI was also not a significant predictor of preterm birth, so cannot be conclusively compared with allostatic load. Replication of the study and extension of it to other populations will continue to improve outcomes for women and babies and reduce preterm births.

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PUBLICATIONS

Books

Clark, J. J., & Sayre, M. M. (2015). *Social work ethics: Decision making and accountability* (2nd ed.)*.* Brockton, MA: Western Schools.

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AWARDS

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